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I never realised that I don't breathe correctly': Understanding Experiences of Postural Tachycardia Syndrome and the Challenges of Altered Breathing for Intervention Development

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PhD

2022

‘I never realised that I don’t breathe correctly’: Understanding Experiences of Postural Tachycardia Syndrome and the Challenges of Altered Breathing for Intervention Development

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A thesis submitted in partial fulfilment of the requirements of the University of Northumbria at Newcastle for the degree of Doctor of Philosophy

Research undertaken in the Faculty of Health and Life Sciences

September 2022

Abstract

Background: I aimed to develop an Ocean Breathing intervention for Postural Tachycardia Syndrome [PoTS], a debilitating condition characterised by an increase in standing heart rate (>30bpm). Few interventions exist for supporting patients with their day-to-day symptom management.

Methods: A mixed-methods intervention development process. A scoping review of the PoTS literature was undertaken to examine the breadth of published works dedicated to diagnosis, symptomology and treatment. Narrative analysis of 20 online video diagnostic stories from people with PoTS was then undertaken to examine their diagnostic and symptom experiences. Finally, interviews across three key stakeholder groups– people with PoTS (n=15), healthcare professionals experienced in PoTS treatment (n=7), and yoga instructors (n=3)– were held to collate feedback on the Ocean Breathing intervention, as analysed through NPT.

Findings: Review findings demonstrated that a paucity of qualitative literature within this research field had led to limited exploration of people with PoTS' day-to-day challenges with PoTS symptoms. The YouTube work identified that storytellers communicated their understandings of their PoTS to others by drawing upon socio-medical ontologies- surrounding the autonomic nervous system- to legitimise the nature of their symptom experiences. Stakeholder feedback showed how alterations in patients' regular breathing patterns presented difficulties for identifying an agreed, 'right' intervention format. Notably, understandings of how to make sense of the potential therapeutic effects of Ocean Breathing on PoTS symptoms varied within and across the stakeholders, as they drew on alternate, differing ontological frameworks.

Conclusion: This thesis provides critical insights into people living with PoTS' communication and sense-making. It highlights how the PoTS symptom discussion between individuals with PoTS and medical practitioners- through a shared autonomic framework- can enable patients' illness experiences to be validated across healthcare contexts. Through the intervention development work, the perceived complexity of the Ocean Breath was a barrier to the diverse, patterns of breathing exhibited by people with PoTS. The further the efforts to untangle others' Ocean Breath perceptions, the more questions were left about my own understandings of the intervention I was developing. To accommodate these issues and the multiple ways breath-work could impact people with PoTS, a 'toolkit-like' strategy with a range of breath-related practices should be explored.

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Acknowledgements

This thesis is a product of the endless amounts of support, kindness and admiration that I have been fortunate enough to receive from others throughout my studies.

First and foremost, I would like to say thank you to my incredible supervision team- **Professor Tim Rapley, Professor Vincent Deary** and **Professor Julia Newton**- for all their guidance, patience, and encouragements. **Tim**, it is incredibly difficult for me to get across in words just how truly grateful I am to you for all you have done for me throughout the past four years. Thank you for always having my back, the passion and dedication you have shown to my studies, and for developing me into the person and researcher I am today. **Vincent**, thank you for believing in me since the moment I first walked through your office door at the time of my MRes degree, encouraging me to pursue PhD study and the many wonderful conversations we have had over the years. **Julia**, thank you for the clear, insightful feedback you have given to me, and for being the person who provided me with the confidence to say that I had developed a clear grasp and understanding of the PoTS medical literature.

In addition to this, I would like to say thank you to two fellow early career researchers and close friends of mine, **Jemma McCready** and **Scott Houghton**, for sharing this PhD journey with me. **Jemma**, thank you for your endless amounts of support, through not just your contributions to my thesis as a second reviewer for my scoping review, but also for the many brilliant discussions we have had at Coach Lane since starting our studies together. **Scott**, who I have known since my first day of starting university, thank you for all of the laughter, friendship, and wisdom (just not in your choice of supported football team) that you have shown to me over the years. You are both two of the most incredible and talented researchers I know, who I have learned - and continue to learn - so much from.

Thank you to the **PoTS UK** charity for kindly helping to promote my thesis research through their online social media platforms. Without your support, I would have struggled to overcome the challenges to my planned participant recruitment strategy in the face of the COVID-19 pandemic.

On a final note, in addition to **my family** for their continued support of my academic studies, I would like to close my acknowledgements with a personal thank you to three of my dear friends - **Declan James Smith, Rosie Ellen Carr** and **Sandra Gawel**. I remain truly grateful for all of the kindness, compassion and emotional support you have given to me throughout the tough times that I have encountered.

Declaration

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas and contributions from the work of others.

Any ethical clearance for the research presented in this commentary has been approved. Approval has been sought and granted through the Researcher's submission to Northumbria University's Ethics Online System on the 3rd of May, 2019.

I declare that the Word Count of this Thesis is 77,976 words.

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Date: 26th of September, 2022

Within chapter one, I present a summary of background literature which leads to the identification of the thesis rationale, to develop a novel form of intervention to assist people diagnosed with Postural Tachycardia Syndrome. I then present an overview of the thesis structure, which included the three phases of research I have undertaken through scoping review, narrative analysis and intervention development work. The chapter closes with a summary of the thesis aims and objectives.

1. Introduction

Postural Tachycardia Syndrome [PoTS] is a condition that is clinically characterised by a drastic increase in heart rate of ≥ 30 bpm in adults (or ≥ 40 bpm for adolescents) when an individual moves from a supine to an upright position (Low, Sandroni, Joyner, & Shen, 2009). Patients diagnosed with PoTS regularly experience a wide range of adverse physiological symptoms, including dizziness, fatigue and chest pains, which have a severe impact on an individual's quality of life and daily functioning (Benarroch, 2012). Although accurate prevalence rates for the condition require further research, it was previously estimated that PoTS is thought to affect half a million people in the United States of America alone (Bogle, Goodman, & Bars, 2017). The condition is five times more prevalent in females in comparison to males (Raj, 2006). Evidence has also shown that PoTS may develop following recovery from a viral infection or the occurrence of a traumatic event (Dahan, Tomljenovic, & Shoenfeld, 2016). Four distinct endophenotypes of PoTS have traditionally been identified in relation to this autonomic condition (Benarroch, 2012). These subtypes have associated PoTS with small fibre neuropathy [Neuropathic], heightened adrenaline levels [Hyperadrenergic], low blood volume [Hypovolemic] and PoTS with Deconditioning (Goodman, 2018). Nevertheless, the Canadian Cardiovascular Society has recently recommended against the labelling of patients with specific variants of PoTS during the early stages of diagnosis (Raj et al., 2020); due to differences in the accepted definitions and understandings of each PoTS subtype from one clinician to another (Arnold, Ng & Raj, 2018).

At present, only a small handful of non-pharmacological treatments exist for assisting people with PoTS with the management of their debilitating symptoms (Wells et al., 2018). Current types of interventions for PoTS have a weak evidence base (Raj et al., 2020). Pharmacological agents, which are restrictedly administered for only the most severe PoTS cases, are used 'off-label' for this condition and are limited by their aversive side-effects (Sheldon et al., 2015). Given these reflections and the need for additional PoTS interventions to be devised (Eftekhari et al., 2021), within this thesis I detail how I identified and attempted to design a novel type of

non-medicinal intervention strategy - in the form of a breathing intervention, called Ocean Breathing - that people with PoTS could employ to help manage their persistent physical complaints and other PoTS-associated symptoms.

This thesis shows that the perceptions of breath-related interventions by people with PoTS are shaped by their own specific breathing capabilities (resultant from their illness), and the ways in which they make sense of their bodily experiences of breathlessness symptoms. My intervention development work shows that people with PoTS perceived the suggested Ocean Breathing practice to be overly complex for them to undertake. Some felt that the core action of this technique, involving the slight movement of their throats, would be a difficult and physically demanding action for a person with PoTS to perform. I argue that further, 'basic science' work is needed to explore the range of alternate breathing interventions which could be utilised within this patient group. Future intervention development work should focus on the development of breathing toolkit-like interventions with an adapted form (or forms) of the Ocean Breath.

2. Understanding PoTS as a Chronic Illness

PoTS mostly affects people between the ages of young-to-late adulthood, defined as approximately 20-50 years of age and is much less likely to present in the elderly (Benrud-Larson et al., 2002). Although cases can be commonly observed in adolescent samples, research has found that these individuals are more likely to 'recover' (prior to the start of young adulthood) from PoTS (Singer et al., 2012) – in comparison to the much more sustained and persistent, or in some cases life-long, experiences of those who develop the condition during adulthood. PoTS is therefore a type of chronic illness, a term used to refer to the onset of long-term bodily health complaints which persist for over one year, or a condition that remains present until the occurrence of mortality (Petrie & Jones, 2019). Within the United States of America [USA] alone, approximately 45% of the population are estimated to suffer from a long-term condition (Raghupathi & Raghupathi, 2018). In addition to the pressures this poses upon the country's healthcare systems, chronic illness also places great economic challenges upon the USA – with the costing of direct healthcare treatments for these conditions totalling over \$1 trillion in 2016 alone (Waters & Graf, 2018). Within the United Kingdom [UK], as a nation where citizens have access to free healthcare, approximately one quarter of adults are thought to be living with a minimum of at least two different chronic diagnoses (NIHR, 2021). As the average life expectancy of the UK population continues to rise, there has also been an associated increase in the percentages of individuals diagnosed with a long-term health problem (Walker, 2018). This poses significant financial challenges and healthcare

implications upon UK health bodies. Empirical research undertaken within the last decade by the King's Fund – as presented within a commissioned report by the House of Commons Health Committee (2014) - estimated that the cost of a single chronic illness diagnosis increases annual NHS expenditure by £1000 per patient, with greater costs associated for individuals living with two (£3000) or three (£8000) comorbid health conditions.

In a similar vein to other types of chronic illnesses, patients with PoTS are required to undertake a long-term approach to (self)management, in order to effectively manage the nature of their condition(s) throughout their remaining lifespan (Rothman & Wagner, 2003). Given the lack of 'curative' treatment for PoTS, this 'symptom-control' strategy aims to facilitate the individuals' increased day-to-day functioning and (continued) integration into modern societal activities in the face of their morbidity. This is done through the allocation of interventions such as prescribed pharmacological agents and lifestyle changes. It is worth noting however that despite attempts to manage bodily complaints through these interventions - the existence of a chronic illness places serious burdens upon the wellbeing of patients. In comparison to non-chronically ill individuals, people living with long-term physical health illness are more likely to report reduced quality of life (Whittemore & Dixon, 2008), possess greater susceptibility to anxiety and depression due to the burdens of living with chronic health impairments (Kagee, 2008) and heightened levels of suicide ideation (Rogers, Joiner & Shahar, 2021). Researchers have therefore aimed to identify psychological and social factors which may contribute to the worsening of quality of life in people with chronic illness, in addition to the development of treatment paradigms which attempt to mitigate and manage the health complaints of affected populations (Chen & Li, 2009; Megari, 2013; Sansom-Daly et al., 2011).

The need to identify both socio-cultural and psychological factors which can contribute to exacerbation of chronic illness experiences is a core consideration of bio-psycho-social approaches to long-term patient management (Turk & Monarch, 2002). The study of these influences has implications upon patients' wellbeing. Evidence has identified the existence of a strong correlation between increased probability of suicide risk within chronically ill individuals and those who possess lower levels of social economic status (Gürhan, Beşer, Polat, & Koç, 2019). Within younger samples, data from meta-analyses studies has identified that children and adolescents with a chronic diagnosis are at a greater susceptibility to depression symptomology, in comparison to age-matched healthy controls (Pinquart & Shen, 2011). The additional findings of medium-to-large effect sizes ($d = .59 - .94$) have highlighted children living with fatigue-related conditions as a particularly at-risk diagnostic group who are prone to experiencing the onset of psychiatric comorbidity (due to the impact of living with their chronic diagnosis) – similar empirical findings have also been replicated within fatigued adult samples (Johnson, Cotler, Terman, & Jason, 2020). More research is therefore needed to

establish a greater evidence base for treatments aiming to improve the quality of life for those living with chronic health diagnoses who are at greater risk of heightened distress – this is especially true in PoTS (Anderson et al., 2014; Benrud-Larson et al., 2002).

2.1. Exploring the Invisible Nature of PoTS Symptoms

Many patients with chronic diagnoses face distressing and debilitating numbers of both ‘visible’ and ‘invisible’ symptoms associated with their condition. Within the UK alone, over ten million people are estimated to experience non-visible symptoms due to their chronic health condition – this estimate constitutes approximately four in five people who have a long-term disability (NHS Devon Partnership Trust, 2021). Many of these conditions however are both commonly recognised and well-established diagnoses within the medical community, that can be identified by clinicians through their ‘blended’ presentations of both visible and invisible symptoms. Nevertheless, several more salient conditions such as PoTS, are less likely to be understood or recognised by medical professionals due to their more ‘hidden’ nature (Deale & Wessely, 2001). This commonly includes those conditions which feature fatigue as a prevalent symptom, a term used to describe patients who exhibit with persistently high levels of debilitation and tiredness (Chevin, 2000). The lack of both recognition and understanding of these conditions by medical professionals has important implications upon these patients’ suffering (Wilson, 2011). Research has shown that general lack of awareness of invisible illness conditions amongst general practitioners remains a contributing factor towards delayed average diagnosis time for patients seeking primary medical assistance for their persistent physical symptoms (Pilkington et al., 2020). This barrier to an individual receiving an accurate diagnosis, in turn, produces resultant delays to the administration of treatments which are needed by patients to assist with the long-term management of their associated health complaints and underlying pathologies. Over time, these diagnostic delays can ultimately lead to worsening to the severities of the patients’ invisible illnesses – as evidenced in conditions such as chronic fatigue syndrome (Saffron & Pheby, 2009).

It has been widely reported within the PoTS literature that people experiencing PoTS commonly encounter significant delays in their time to receive diagnosis from their first initial healthcare visit – with a current estimate of 4 years (PoTS UK, 2021). To address this, more evidence is needed from patients themselves to assess what barriers they face during the PoTS diagnostic process, in addition to the need for greater understandings towards patients’ interactions with their medical communities as a whole. The current exploration of PoTS had been hindered by a lack of qualitative exploration surrounding this condition (Eftekhari et al., 2021), with only one published study adopting this approach at the time of writing (Waterman,

Opie, Waterman, & Langdon, 2021). When considering other fatigue-related health conditions, a large body of qualitative work has identified that patients with such invisible illnesses commonly attribute encountered delays in receiving their diagnosis with personal anecdotes of having the legitimacy of their symptoms frequently challenged, questioned and contested by medical practitioners (Nunes, Ventura, Encarnação, Pinto, & Santos, 2013). Work, such as the research undertaken by Nettleton (2005), has demonstrated that in the absence of visible symptoms, patients feel physicians and non-medical individuals do not grant them with the 'permission' for them to be accepted as having an illness. Due to this, patients report that their chronic illness experiences and their attempts to explain the nature of their chronic condition(s) to others are often discredited, through others' expectations that patients provide 'proof' towards the legitimacy of their condition (Murray & Lusher, 2018). Further qualitative works have highlighted that these individuals also described feelings of being allocated blame for their symptoms, through the use of psychogenic (mis)labelling of their bodily ailments (Bulow, 2003). Within the qualitative exploration of fatigue, this is evident through patients' categorisations of themselves as victims of medical gaslighting experiences - often through their reciting of their clinicians using phrases such as, "it is all in your head" - to dismiss of the authenticity of their health complaints (Sanchez, 2019).

Over time, these common, negative experiences of chronically ill individuals have in turn shaped the medical language and discourse used by both clinicians and patients to describe their PoTS, fatigue and/or other invisible conditions. Phrases such as 'medically unexplained symptoms' are now viewed as outdated terms by these patient groups – as they are perceived to be derogatory in nature, due to their association with the dismissal of an invisible condition by the medical community as lacking a biomedical basis (Picariello, Ali, Moss-Morris, & Chalder, 2015). Alternative terminology, such as the more generally accepted use of 'persistent physical symptoms', are instead advocated for– due to their removing the phrasing of symptoms as 'unexplainable', and the rendering of such bodily ailments being rooted in a physiological ('physical') basis or model, as opposed to one of psychological origins (Rebman et al., 2015).

2.2. Reflecting on Patient Narratives of Invisible Illness & Fatigue

There is also a greater need to identify how individuals with PoTS portray, and make sense of, the challenges and day-to-day experiences of living with their condition (Waterman et al., 2021). Prior qualitative literature has focused on the consideration of how the use of patient storytelling allows individuals to break down, and re-construct, the core events which constitute the progression of their chronic illness (Polkinghorne, 1995). These explorations of

patients' own personal narratives are thought to provide an opportunity for sense-making to occur (Bury, 1982), whereby the individual reciting the story is able to re-structure their experiences of becoming chronically ill in order to 'fit' these distressing events within the settings of their own, personalised frameworks and understandings (Williams, 1984; Whitehead, 2005). This re-organization of collective diagnostic events and illness progression permits patients with an opportunity to establish meaning and value to their suffering through the positioning of their 'narrative self' (Frank, 1995).

Whilst there remains a limited qualitative exploration of PoTS experiences in sufferers (Eftekhari et al., 2021), a number of cross-applications can be drawn from other fatigue-related work undertaken. Whitehead (2005) applied the three core narrative frameworks for the sharing of illness stories proposed by Frank (2005) to the study of 17 UK adults diagnosed with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis [CFS/ME]. These patients were found to use storytelling as a sense-making tool to their fatigue-syndromes, through the description of shifting between perceptions of their illness as an acute, recoverable condition (restitution narrative) to feelings of hopelessness, pessimism and despair (chaos narrative) that resulted from their inability to recover, retain concentration and their lack of treatment options available to provide a form of control over their symptoms. Finally, towards the end of their chronic illness stories, many patients were observed to adopt a quest narrative, whereby some participants expressed acceptance towards the onset of their illness and the personal developments and life changes they had gained from their experiences. Thus, qualitative exploration of the personal narratives offered by people with invisible, fatigue-related illnesses has enabled researchers to explore the ways in which patients both learn from, and communicate their own personal understandings, of their chronic health experiences to others (Polkinghorne, 1995). Therefore, further qualitative research into PoTS needs to be undertaken in order to further understand how patients make sense of their PoTS symptoms and the ways in which these experiences are communicated to others.

Whilst theoretical frameworks to explore patients' understanding of their illness have not been developed in PoTS itself, specific ontologies and models devised by both patients and clinicians are known to exist for other conditions which assist the individual in the 'making sense' of their illness and how their treatments work (Deary, Metcalfe & Wilson, 2014). Through a systematic qualitative review into patients' explanations of their medically unexplained symptoms/persistent physical symptoms, Ravenzwaaij et al. (2010) identified nine socio-medical frameworks which were commonly cited across different patient groups. These ontologies included depictions of endocrine abnormality, compromised immune systems and deficits in bodily proprioceptors. A particular model outlined within Ravenzwaaij et al. (2010) work – one which has prominent implications for fatigue-related conditions

(Cauwenbergh, Nijs, Kos, Weijen, Struyf & Meeus, 2014) - was the framework relating to the autonomic nervous system. The autonomic nervous system refers an unconscious agent in the body that is responsible for regulation and monitoring of essential living processes (McCorry, 2007). This upkeeping of bodily systems is performed by the two components of the autonomic nervous system - the 'fight-or-flight' (sympathetic nervous system) and the 'rest-and-digest' (parasympathetic nervous system) – which work in tandem with one another (Low, 2011). In relation to patients' ontologies surrounding the relevance of the autonomic nervous system to illness, prominent frameworks such as Polyvagal Theory (Porges, 2003) have outlined that pathologies may occur as the activity of these two branches being 'out of synch' with one another, whereby one autonomic sub-branch has a more prolonged, sustained and dominant activation over the other. Whilst polyvagal theory has not previously been explicitly acknowledged within PoTS literature prior to this thesis, evidence from physiological examination has supported its application through findings that people with PoTS present with heightened levels of sympathetic activity and reduced parasympathetic (vagal tone) activation (Jacob et al., 2019).

2.3. Understanding the Current State of PoTS Treatment

The understanding and development of chronic illness through theoretical frameworks and socio-medical ontologies has supported researchers and clinicians with the development of treatment approaches. Whilst there is currently a lack of understanding behind the underlying causes of PoTS itself (Goodman, 2018), a number of treatments are advised by clinicians to assist patients with the management of their symptoms. The majority of patients with PoTS are provided with only first line treatments, in the form of non-pharmacological interventions such as recommended lifestyle changes and the increase of daily intake of fluids & salt, as their sole method of managing their PoTS (Raj et al., 2020). As I will outline in more detail in this thesis, there remains however only a limited number of non-pharmacological treatments for PoTS. Given the high number of patients with PoTS who report significantly increased levels of suicide ideation and impaired quality of life (Pederson & Brook, 2017) there is a great need for the development of additional, new non-pharmacological PoTS-specific treatments which are capable of enhancing their symptom management.

Off-label pharmacological agents are provided to PoTS patients only in the most severe cases and include the use of medications such as beta-blockers and fludrocortisone (Miller & Raj, 2018). Although there has been early evidence from meta-analyses to support the use of these agents to assist patients with the management of their symptoms (Wells et al., 2018) – these lines of robust evidence remain in their infancy, as there remains both a shortage of research

synthesis within the PoTS research area relating to these medications (Eftekhari et al., 2021), in addition to a lack of large-scale randomised control trials to thoroughly evaluate their effectiveness (Raj & Robertson, 2018). Drug treatments for PoTS are also associated with aversive side-effects for patients (Miller & Raj, 2018) and most individuals will need to first undergo a 'trial-and-error' process in order to establish which medications are most effective for mitigating their symptoms. In addition to these barriers to treatment, people with PoTS also incur financial costs for purchasing their medications in nations such as the USA. Whilst psychological therapies such as cognitive behavioural therapy are also recommended as a treatment for PoTS (Opie, Raj & Arnold, 2021), to date there are no current studies which have attempted to evaluate their use within this patient group. Given that most PoTS patients are provided only with non-pharmacological approaches to self-manage their condition (Raj et al., 2020) and continue to exhibit significant impairments in their quality of life (Pederson & Brooke, 2017)– there is a critical need to develop new, condition-specific alternative treatments which are capable of further assisting patients with the management of their PoTS. Within this thesis, I aimed to support this work through exploring the development of a new Ocean Breathing intervention - designed specifically for use in a PoTS patient group - as an additional form of non-pharmacological management strategy which sufferers could employ.

2.4. Exploring the Need for an Alternative Treatment Approach for PoTS

As outlined previously, patients living with fatigue-related diagnoses and/or other invisible chronic illnesses have been found to use a number of socio-medical frameworks to explain and comprehend the nature of their symptoms – this includes the use of ontologies surrounding the autonomic nervous system (Ravenzwaaij et al., 2010). Whilst prior research has not yet examined the ontologies and theoretical frameworks used specifically by people with PoTS to understand their condition evidence within the research area has supported the development of autonomic dysfunction as a leading, underlying cause of PoTS Symptoms (Raj, 2011). Research has supported the notion that PoTS is associated with an autonomic 'imbalance', between the body's 'fight-or-flight' (sympathetic) and 'rest-and-digest' (parasympathetic) systems – as evident from findings of a heightened sympathetic response and reduced vagal tone in this patient group (Jacob et al., 2019). These descriptions of 'dysfunctions' of the autonomic nervous system are also the same narratives which are used by leading PoTS organisations – such as PoTS UK (2022) and Dysautonomia International (2022) – as a means of supporting people who are newly diagnosed with this condition to comprehend the nature of their symptoms. Thus, in a similar vein to the development of cognitive behavioural approaches which have been informed from prominent cognitive models

– such as those relating to persistent physical symptoms (Deary, Chalder & Sharpe, 2007) - the understanding of fatigue-related conditions, through the application of autonomic frameworks, can therefore also provide practical insights to guide the development of new treatment approaches for this patient group.

A large body of evidence has assessed the application of breathing interventions in relation to their effects on underlying cardiac and nervous system activity (Zope & Zope, 2013). Whilst the majority of this work has been undertaken within psychiatric samples, evidence has begun to support the use of slow-breathing techniques as suitable interventions for the improvement of autonomic activity, through increasing of vagal tone and their ability to reduce patients' overactive sympathetic activity (Jerath, Crawford, Barnes, & Harden, 2015). This 'soothing' effect over the branches of autonomic nervous system is thought to be produced by the stimulation of a part of the body known as the vagal nerve through long inhalation; this cranial nerve improves restores bodily functioning by enhancing parasympathetic activity (Carter & Carter III, 2016). Whilst evidence for the effectiveness of breathing interventions in fatigue conditions currently remains a mostly unexplored area of research, current findings have been encouraging. For example, a randomised control trial found that a 12-week breathwork programme led to significant improvements in Fibromyalgia patients' reported levels of daily functioning, fatigue and pain scores in comparison to a waiting list control-group (Toma's-Caru's et al., 2018). The application of both cognitive and autonomic theoretical models to the study of fatigue-related conditions therefore can assist researchers by providing an overarching framework to allow for the identification and potential development of new, targeted treatment approaches. These alternative strategies to symptom-control aim to enhance quality of life in the patient group, reduce comorbid psychiatric comorbidities and the stress associated with living with a chronic illness, in order to further support individuals with the self-management of their bodily complaints. These works ultimately provided rationale and justification towards my decision of utilising a breath-based practice as the primary choice of intervention format for development within a PoTS patient group.

3. Aims & Objectives of the Thesis

From my brief overview of literature within this chapter, I have identified a rationale for the development of a novel, non-pharmacological treatment for assisting people with the management of their PoTS symptoms.

Thus, as the first stage of the Medical Research Council Framework for Complex Intervention Development (Skivington et al., 2021), the aim of this thesis was therefore to develop an

Ocean Breathing practice for people with PoTS. In order to achieve this aim and to support my intervention development process, my thesis had the following objectives:

- i. To examine the breadth and nature of existing published works and empirical research within the PoTS literature field.
- ii. To expand upon limited qualitative work into the PoTS research area by exploring both the diagnostic and symptom experiences which are shared by people with this condition, within their illness narratives.
- iii. To understand factors which would serve as facilitators or barriers to the development of an Ocean Breathing intervention with a PoTS patient group and its likelihood of achieving future successful implementation.

4. Summary of Thesis Structure

Following the presentation of the thesis background literature, aims & objectives within chapter 1, my thesis presents three core phases of research I have undertaken during this PhD study. This includes: (i) a review of the existing PoTS literature (Chapters 2-4); (ii) narrative exploration of PoTS diagnostic and symptom experiences (Chapters 4-6), in addition to; (iii) intervention development work of the Ocean Breathing practice (Chapters 8-10).

The first phase of my thesis outlines how I synthesised findings from a broad range of prior published PoTS empirical works, in order to both inform my knowledge of this condition and to support my ongoing intervention development process. Within chapter 2, I present the introduction, methodology and demographic findings for the large-scale scoping review I undertook of the PoTS literature area. In addition to examining the breadth of these PoTS works - those articles dedicated to exploring its diagnostic factors, symptomology and available treatments - through this scoping review I collate current understandings, knowledge and existing research gaps for this condition. As such, narrative syntheses of the PoTS empirical literature, presented alongside relevant clinical implications and considerations for my intervention development process, were drawn for works which concerned PoTS diagnosis, symptomology and co-morbidity (Chapter 3), in addition to a summary of the non-pharmacological and medicinal treatments (Chapter 4) that have been researched and scrutinised within this condition. My scoping review findings highlight the need for greater qualitative exploration within the PoTS literature area, in order to enhance upon limited understandings towards the symptom experiences and debilitation people with PoTS face.

Phase two of the thesis therefore contains the narrative work I have undertaken into people with PoTS to address these shortcomings. Within chapter 4, I began this phase by outlining

my methodology for carrying out the narrative analysis - through the adoption of the multi-approach method recommended by Meraz et al. (2019), as informed by the narrative works of Reissman (2012) - to explore the diagnostic journeys, illness narratives and symptom experiences which people with PoTS share within their online videos. My narrative findings, presented through the undertaking of thematic, structural (Chapter 6) and performative (Chapter 7) approaches, highlight how people with PoTS depict their symptom experiences through the additional burdens they would face when undertaking their everyday, taken-for-granted activities (Bury, 1982). PoTS storytellers construct barriers in their narrative quests to receiving a PoTS diagnosis through psychological labelling of their persistent physical symptoms and the normalisation without explanations tactics employed by their medical professionals (Dowrick, Ring, Humphries and Salmon, 2004). Narrative findings ultimately support my intervention development process (Skivington et al. 2021) through the identification of an explanatory model (Kleinman, Eisenberg & Good, 1978) which PoTS sufferers rely upon in their discourses to communicate their PoTS symptom experiences to others and their own personal understandings of their chronic illness.

Within the final phase of my thesis I present the findings of my Ocean Breathing intervention development work, which was theoretically informed through the use of Normalization Process Theory (May & Finch, 2009). I start by outlining the methodology for the iterative, multi-stakeholder group, qualitative intervention development process I undertook to develop and tailor an Ocean Breathing practice to the needs of a PoTS patient group (Chapter 8). As a further step to identify possible barriers which would hinder successful implementation of the intervention within the patient group I explore people with PoTS perceptions of their own breathing and breathlessness symptoms, in addition to their reported experiences of possessing altered breathing patterns as a result of their chronic illness (Chapter 9). After this, the findings from my intervention development process - consisting of gathered feedback from across three core stakeholder groups (people with PoTS; PoTS-experienced practitioners and healthcare professionals; yoga instructors) - are presented within chapter 10.

I then conclude my thesis (Chapter 11) with a discussion of how my findings from across all phases of my PhD phases have sought to advance elements of our current understandings within the literature area. Through my expansion of the limited qualitative works undertaken within this condition, I help to begin to identify of the diagnostic challenges which people with PoTS portray experiencing within their interactions with medical professionals and healthcare services. Additionally, this is the first qualitative study of breath and breathlessness sensations within this patient group. As such, I highlight how differences in people with PoTS own, self-held perceptions of their altered breath and breathing capabilities present challenges to the process of intervention development. Within my concluding remarks of this thesis, I argue that

further PoTS works need to be carried out to explore the breathing capabilities of patients with different types of breath-focused, pranayama interventions – through undertaking of additional, mechanistic and ‘proof-of-concept’ studies. These additional, empirical studies with PoTS samples will assist in the development of a breathing toolkit intervention – one which may incorporate a form of the Ocean Breath practice – with a variety of breath-related strategies to accommodate and cater towards the range of breathing skillsets and preferences shown throughout this clinical population.

5. Conclusion

Within this chapter, I have presented an overview for the structure of my thesis, alongside a rationale for undertaking the development of a novel type of PoTS intervention, through highlighting the poor evidence base for many current non-pharmacological interventions (Raj et al., 2020) and the restricted, ‘off-label’ only use of pharmacological agents for this condition (Sheldon et al., 2015). Within the next chapter, I outline the introduction, method and initial findings of a large-scale scoping review I have undertaken of the PoTS research area.

- Chapter 2: Investigating the Characteristics and Range of Topics Focused on by PoTS
Literature pertaining to Diagnosis, Symptomology & Treatment: A Scoping Review –

Chapter 2 presents the introduction, method and initial analyses of a scoping review that I undertook to both inform my knowledge of the PoTS literature and assist with my intervention development process. My scoping review aims to map the key characteristics and range of topics that have been focused on by a large body of published PoTS academic works dedicated to diagnosis, symptomology and treatment. Within this chapter I will demonstrate that: there has been a rapid growth in the PoTS literature area throughout the past decade (2010-2019); PoTS published works mainly originate from the USA, China and the UK, whilst further showing that; there is a dominance in quantitative PoTS empirical studies, with only one qualitative article identified within the present scoping review. I then close the chapter by providing an overview of PoTS literature by other article types- such as reviews (including a small body of systematic and meta-analyses works), clinical trial registrations and case reports.

1. Introduction

Scoping reviews aim to carry out and collate a large body of academic literature dedicated to a single research field (Arskey & O'Malley, 2005). Synthesising a broad range of works that have been undertaken to examine a phenomenon allows for detailed accounts to be drawn (Pham et al., 2014), which highlight how the understanding of a health condition has been both developed and explored by both medical & research communities over time (Mays et al., 2001). Crucially, this methodology allowed me to explore the types of articles present within this body of evidence, for the purpose of identifying key gaps in the literature that are impeding researchers' current knowledge of this autonomic condition (Arskey & O'Malley, 2005).

At the time of starting my thesis, only a small body of PoTS literature, identified during the review planning stages, had attempted to assess and examine the diverse literature in the PoTS research area through a systematic approach. This includes systematic reviews concerning the complication of pregnancy by PoTS diagnosis (Morgan, Chojenta, Tavener, Smith & Loxton, 2018), gastrointestinal symptoms within PoTS (Mehr, Barbul & Shibao, 2018) and the use of ivabradine to control symptoms (Gee, Watkins, Brown & Young, 2018). However, at the time of commencing this scoping review, previous works had not attempted to map, synthesise and provide a comprehensive overview to examine the characteristics and range of topics focused on by articles within the postural tachycardia literature area.

As the main aim of this scoping review was to examine the key concepts within the literature and explore the nature of research which has been conducted within the area (Peters et al., 2015), the research question guiding the review was: **“What are the key characteristics and range of topics focused on by Postural Tachycardia Syndrome (PoTS) literature examining diagnosis, symptomology & treatment?”**.

The review had the following objectives:

- Explore the growth of PoTS literature over time, its global origins and to map out the different aims and nature of published works in this field (*presented within this chapter, following Methods*)
- Identify relevant gaps within the literature area relating to diagnosis, symptoms & treatments which warrant further exploration, in order to further our knowledge of this condition (*presented through narrative synthesis within Chapter 3*).
- Examine empirical works which have been undertaken to assess non-pharmacological interventions and pharmacological agents within PoTS populations (*presented through narrative and tabular synthesis within Chapter 4*).

Since the time of completing my scoping review during the early stages of my PhD, an evidence map of the PoTS research area has been published by Eftekhari et al. (2021) – identified through the three-year article sample update to my review database search strategy – which has also provided some considerations towards the article demographics and range of core topics that have been focused on within this literature field. It should be noted however that scoping reviews are classified as a distinct type of evidence synthesis from evidence mapping (Miake-Lye, Hempel, Shanman & Shekelle, 2016), in that, the former methodology provides unique critical insights, clinical implications and additional understandings of the research area through its presentation of narrative syntheses (Schmucker, Motschall, Antes & Meerpohl, 2013) – such as those I have provided for PoTS diagnostic, symptomology (chapter 3) and treatment (chapter 4) literature within this thesis. Furthermore, Eftekhari et al. (2021) did not present inter-rater reliability inspection for their screened articles, which I have done in my scoping review below through the undertaking of Cohen’s K statistical analyses to establish rigour and support my screening process. Within the discussion section of the current chapter, I provide further considerations between my scoping review findings with those from the evidence map undertaken by Eftekhari et al. (2021), in order identify clear implications for the PoTS research area through these critical comparisons and distinctions.

2. Method

2.1. Review Guidelines, Protocol & Registration

This review follows the guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews [PRISMA-ScR] checklist (Tricco et al., 2018). An a-priori protocol was developed for the current project and was published on the Open Science Framework (OSF) [<https://osf.io/bwa6x/>].

2.2. Ethical and Epistemological Considerations

Ethical approval for the project was granted from the Faculty of Health and Life Sciences Ethics Committee at Northumbria University [#15762]. Within my undertaken scoping review, I adopted the assumptions associated with a subjectivist stance (Thomas et al., 2020). This epistemological position, which has been commonly employed within scoping review works (Arksey & O'Mallory, 2005), understands evidence collation and synthesis as a non-sequential - yet dynamic process - arising through the interactions between the included research works/review sample subset with the backgrounds and cultural factors of the research team (Thomas et al., 2020). Through this lens, it was important that I acknowledged and reflected upon how, through reflexive note-taking during the undertaking of the project (see Fig. 1), my own understandings and interpretations of research findings (that I had gained from the PoTS literature included within my review), had been influenced by my own, personal educational and socio-cultural experiences (Lincoln & Guba, 1985).

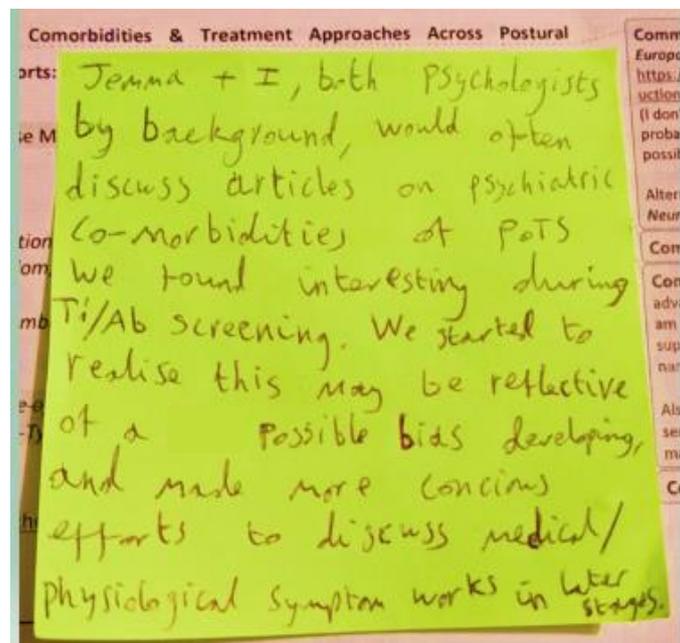


Fig. 1. Reflexive note example concerning a reflection made during the scoping review screening, whereby Jemma – the second article reviewer for the scoping review - and I considered how our shared academic backgrounds and roots within psychology may have unconsciously influenced the early stages of our article selection. Due to this, we tried to purposely set aside time within our review

discussions to discuss articles which we had found interesting which concerned the exploration of physiological symptoms/ other (non-psychiatric) co-morbidities in PoTS patients.

2.3. Eligibility Criteria

An article was considered eligible for the review if it concerned patients who were diagnosed with PoTS and I included all subtypes (e.g. *neuropathic, hyperadrenergic*). No age restriction was applied to the participants recruited by past research, thus articles which explored both adult and paediatric populations (< 18 years) were examined for their relevancy. No restrictions were placed on the publication year of the article for eligibility.

As the main aim of this scoping review was to map the key concepts across a wide body of PoTS-related literature and explore the breadth of research which has been conducted within the area (Peters et al., 2015), all study designs were considered for inclusion. For empirical studies, this included the following: quantitative, qualitative and mixed-methods studies. Non-systematic review articles, review articles which featured a systematic search strategy, meta-analyses and case reports were included. In regard to the types of grey literature which were also screened, the review considered any conference abstracts, editorial letters, consensus & clinical guidelines, dissertations/thesis and clinical trial registrations which were identified by the search strategy for inclusion.

2.4. Exclusion Criteria

The exclusion criteria of the review included non-human studies. Additionally, due to the background of the research team, only articles available in English were included within the final article subset. Articles which focussed on a range of orthostatic intolerance disorders - where it was not clear whether the authors had specifically examined patients diagnosed with PoTS within their sample (and/or where the authors had not drawn clear implications for the diagnosis, symptomology or treatment of PoTS patients in particular) - were excluded from the review. Articles which focussed upon the development of psychometric measures were also removed from the sample, as this body of literature did not reflect the aims of the review.

2.5. Information Sources & Search Strategy

Five databases were searched for the current report. This included **Pubmed (1996-), CINAHL (1961-), Cochrane Library (2005-), Web of Science (1997-) & Proquest (1938-)**. In a similar manner to previous systematic reviews within this area (Nagiub, Moskowitz & Fortunato, 2018; Morgan, Chojenta, Tavener, Smith & Loxton, 2018), databases were first searched using PoTS synonyms (“*postural tachycardia syndrome*”; “*postural orthostatic tachycardia syndrome*”). Using the Boolean operators (AND / OR), these synonyms were then combined with additional terminology relating to three broad concepts of interest to the research team:

Diagnosis, Symptomology (“psychological”, “stress”, “cognition”, “emotion”, “fatigue”, “quality of life”, “anxiety”, “depression”, “sleep”, “brain fog”, “suicide”), and Treatments (“intervention”, “treatment”, “exercise”, “non-pharmacological”). The selected search terminology for each concept was identified through the use of Medical Subject Headings [MeSH] and from the reading of PoTS literature by the research team during the project planning stages.

A qualified librarian from the University of Northumbria was consulted to develop the final search strategy (see Table 1). The finalised search strategy was then applied to the six databases on the 8th of April, 2019. Three years later, 8th of April 2022, the search strategy was reapplied a final time to the databases in order to update the captured sample articles.

Table 1. An example of the search strategy for the current scoping review. Performed on the database Web of Science on the 8th of April 2019.

Set	Search Terms	Number of Retrieved Articles
#1	“postural orthostatic tachycardia syndrome”	848
#2	“postural tachycardia syndrome”	1080
#3	#2 OR #1	1080
#4	“diagnosis”	1,443,349
#5	#4 AND #3	243
#6	“symptom”	580,607
#7	“psych*”	1,061,382
#8	“brain fog”	334
#9	“emotion”	129,005
#10	“syncope”	15,139
#11	“fatigue”	218,650
#12	“quality of life”	444,061
#13	“cognit*”	616,964
#14	#13 OR #12 OR #11 OR #10 OR #9 OR #8 OR 7 OR #6	2,744,126
#15	#14 AND #3	692
#16	“intervention”	956,629
#17	“treatment”	4,374,949
#18	“exercise”	411,078
#19	“non-pharmacological”	6,218
#20	#19 OR #18 OR #17 OR #16	5,391,096
#21	#20 AND #3	333
#22	#21 OR #15 OR #5	774

2.6. Selection of Evidence Sources (Screening)

Following the searching of the databases, all articles were downloaded to an Endnote library and duplicates were removed from the sample. The remaining articles were then uploaded to a Rayyan software database (Ouzani, Hammady, Fedowicz & Elmagarmid, 2016). This programme was employed to guide the screening process of the review, where myself and Jemma McCready – who acted as the second article screener for the review - first examined the title, abstract and index term of each article for eligibility.

Independently, we screened first screened an initial, random selection of fifty articles within the sample. Initial inspection of Inter-rater agreement analysis was promising and indicated a substantial agreement between raters, Cohen's Kappa (k) = .640 [95% CIs = .436; .844]. We met to discuss disagreements in their article decisions. From this discussion, the decision was made to adapt the inclusion criteria to provide further clarity on non-empirical papers which were deemed ineligible for the current review. We then independently screened one-eighth (12.5%) of the total sample and met on a second occasion to resolve discrepancies. Inter-rater agreement analysis again indicated substantial agreement between raters and a reduction in confidence interval span was also observed alongside this, k = .640, [95% CIs = .526; .754]. We then met on a third occasion, where substantial agreement was again found to be maintained for screening of 30% of the review sample, k = .675 [95% CIs = .589; .761]. Following this, the remaining articles within the sample were screened independently and we had an additional meeting to discuss conflicts between our decisions. Non-excluded articles then underwent full-text screening (again, carried out by myself and Jemma) to ensure they were in line with the inclusion criteria. As a further check to ensure consistency, 100 articles were independently screened during full-text stage by us. Cohen's Kappa indicated strong agreement between raters' decisions, k = .815 [95% CIs = .658; .972]. Remaining articles were screened by me.

2.7. Data Charting Process

A first draft of the data extraction form [<https://osf.io/bwa6x/>] was developed for the project and piloted across five articles by myself and one of my supervisors, Tim Rapley. Following feedback, aspects of the data extraction form were simplified to increase its usability by the myself. This was done in order to more easily accommodate to the extraction of information relating to the diverse range of study types captured by the search strategy. Furthermore, I made additional adaptations to the extraction form in regard to case reports within the sample, in an effort to synthesise additional information (such as the use of psychometric assessments) which had been used as part of the patient's evaluation by the clinical care team.

2.8. Data Items

The data extracted for each article within the final review subset varied by article type. For empirical research studies, information was collated which included the *Authors*, *Year*, *Country of Publication*, *Lead Institution(s)*, *Source of Publication (e.g. name of Journal where disseminated, etc.)*, *Aims*, *Study Design*, *Participants/ Sample*, *(Primary) Outcome Measures*, *Methods*, *Main Findings and Implications*. For Review articles, information was charted concerning *Authors*, *Year*, *Country of Publication*, *Lead Institution(s)*, *Source of Publication*

(e.g. name of Journal where disseminated, etc.), Aims of the Review, Summary of Main Discussion points & Article Implications for future research / clinical practice. Additionally, detail relating to the searching of databases was also captured for reviews which employed a systematic search strategy and/or meta-analyses. For case reports, information concerning the articles' Authors, Year, Country of Publication, Lead Institution(s), Source of Publication (e.g. name of Journal where disseminated, etc.), Patients' Diagnoses / Comorbidities, Diagnostic Tests & Treatments were recorded. Clinical trial registrations within the dataset had their employed Intervention, Dosage & Trial Arm(s), Principal Investigator, Location, Year, Participant Sample, Study Design, Primary Outcome Measure(s) and Current Trial Status recorded. From editorial articles, information extracted included Authors, Year, Country of Publication, Lead Institution(s), Source of Publication (e.g. name of Journal where disseminated, etc.), Aim(s) & PoTS-related Implications/ Future Research. Conference abstracts within the sample were recorded through information related to Authors, Location, Aims, Participants (if eligible), Methodology/ Design, Major Findings & Implications. In regards to consensus statements and clinical guidelines, I charted information relating to Authors, Type of Document, Aims / Purpose & Organisations. Finally, dissertations within the sample were recorded through Authors, Degree Classification & Department, Aims & Major Findings.

2.9. Synthesis of Results

In order to provide an overview of the PoTS research area, the final subset of articles was examined by a series of frequency-based analyses to inspect the growth of the literature area through number of publications arising over time and the number of articles per geographical location (country). The subset was then divided into the different types of article (e.g. empirical/experimental; case study; review) to assess the proportion of each within the sample. Each characteristic identified was provided with a weighting score (%) of how abundant these types of articles are within the final subset.

As the aims of this scoping review were to explore how research pertaining to the diagnosis, symptomology and treatment of PoTS, a fifteen-category thematic coding scheme was developed by myself and Jemma from the reading of articles during the screening stages of the review. Each of the fifteen categories concerned a core concept(s) within the PoTS research field which were featured as a primary aim/ interest explored within each article – a summary of which can be found within Table 2 below. This coding scheme was then applied to each article in the sample in order to assess and map the focus of literature dedicated to each concept. As various articles included cross-discipline works between two or more of the identified core research areas of PoTS, the coding categories were not mutually exclusive in nature; this purposefully allowed articles to be coded under a number of the different

categories, based on the nature of that paper/ research. A summary of coding for all final categories in the final article subset can be found within OSF [<https://osf.io/k8y75>].

A synthesis of empirical works identified from the scoping review article subset has been used to inform the generation of a narrative literature review within Chapter 3. This chapter specifically focuses on the exploration of research relating to the diagnosis, symptomology and co-morbidities of PoTS. Furthermore, within Chapter 4 of the thesis, an additional narrative commentary was produced from relevant works in the final article subset which focused on the examination of non-pharmacological and pharmacological interventions for PoTS.

Table 2. An overview of the fifteen coding categories by review concept which were applied within the thematic analysis of each article within the final article subset.

Review Concept	Thematic Coding Category	Description
Diagnosis	<i>Aetiology & Underlying Pathophysiology</i>	<ul style="list-style-type: none"> ▪ Empirical works exploring the Cardiovascular and Genetic properties of patients ▪ Articles which concern discussion of the possible underlying bodily mechanisms of the condition.
	<i>Child & Adolescent Research</i>	<ul style="list-style-type: none"> ▪ Empirical works which include the recruitment of a purposeful sample of under 18s diagnosed with PoTS, defined as those who present with an orthostatic heart rate increase of 40 bpm or higher. ▪ Papers which include specific discussion on the effects of PoTS in relation to young patients
	<i>Diagnostic Tools & Autonomic Evaluation</i>	<ul style="list-style-type: none"> ▪ Papers concerning the use of Tilt-table Testing, Standing / Schellong test for diagnosis of PoTS ▪ Discussion/ exploration of other autonomic tests used to assess dysautonomia in PoTS, such as <i>Deep Breathing, Valsalva Manoeuvre & QSART</i>.

<i>Autoimmunity & Virus Research</i>	<ul style="list-style-type: none"> ▪ Papers concerning the development of PoTS following a post-viral infection (e.g. Lyme disease). ▪ Articles examining evidence for an autoimmune basis of PoTS, and/or comorbidity with an autoimmune or rheumatology condition (<i>such as Sjögren's syndrome</i>). ▪ Research concerning the onset of PoTS following injection with the HPV vaccine. 				
<i>Endophenotypes of PoTS (Hyperadrenergic; Neuropathic)</i>	<ul style="list-style-type: none"> ▪ Articles / Works concerning attempts to categorise or subtype patients based on their pathophysiological properties. ▪ Research which has specifically examined samples of a particular endophenotypes of PoTS, including <i>Hyperadrenergic & Neuropathic</i> variants. 				
> <i>Deconditioning</i>	<ul style="list-style-type: none"> ▪ Research which categorises patients who would experience / present with deficits when partaking in physical activities. 				
> <i>Hypovolemia</i>	<ul style="list-style-type: none"> ▪ Articles which discuss / aim to explore evidence and causes for blood volume reduction in PoTS. 				
Symptomology	<table border="0" style="width: 100%;"> <tr> <td data-bbox="470 1283 566 1317"><i>Fatigue</i></td> <td data-bbox="842 1283 1380 1664"> <ul style="list-style-type: none"> ▪ Works including the inspection of loss of motivation and lack of energy in patients. ▪ Research assessing the prevalence rates of fatigue symptoms in PoTS. ▪ Papers concerning the co-morbidity of PoTS with Chronic Fatigue Syndrome other fatigue conditions, and factors which predict the presence of cases with possible co-morbidity. </td> </tr> <tr> <td data-bbox="470 1715 582 1749"><i>Syncope</i></td> <td data-bbox="842 1715 1380 1989"> <ul style="list-style-type: none"> ▪ Articles which aim to identify factors for discriminating a diagnosis of PoTS from other fainting related conditions, such as vasovagal syncope. ▪ Works which have examined the prevalence of syncope rates of PoTS patients. </td> </tr> </table>	<i>Fatigue</i>	<ul style="list-style-type: none"> ▪ Works including the inspection of loss of motivation and lack of energy in patients. ▪ Research assessing the prevalence rates of fatigue symptoms in PoTS. ▪ Papers concerning the co-morbidity of PoTS with Chronic Fatigue Syndrome other fatigue conditions, and factors which predict the presence of cases with possible co-morbidity. 	<i>Syncope</i>	<ul style="list-style-type: none"> ▪ Articles which aim to identify factors for discriminating a diagnosis of PoTS from other fainting related conditions, such as vasovagal syncope. ▪ Works which have examined the prevalence of syncope rates of PoTS patients.
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<i>Gastrointestinal, Bladder & Urination Related Symptomology</i>	<ul style="list-style-type: none"> ▪ Empirical studies which examine biomarkers which can predict syncopal responses and/or successful treatment response for this symptom. ▪ Articles which concern the digestive & urinary systems of patients. ▪ Papers concerning the impact of co-morbid gastrointestinal disorders on the PoTS.
<i>Sleep-based Symptoms/ Disturbances</i>	<ul style="list-style-type: none"> ▪ Studies exploring subjective and objective measurements of patients' reported sleep quality and duration. ▪ Research which has linked poor sleep quality in PoTS to suicide ideation.
<i>Brain Fog & Cognitive Ability</i>	<ul style="list-style-type: none"> ▪ Papers dedicated to the examination or discussion of mental cloudiness symptoms in PoTS. ▪ Factors concerning cognitive assessment of PoTS patients, including performance on IQ, Memory and Attention tests. ▪ Neuroimaging research which has linked brain fog and/or cognitive functioning in PoTS to blood-oxygen level diffusion signals in patients.
<i>Psychological Functioning</i>	<ul style="list-style-type: none"> ▪ Works concerning the psychiatric comorbidities of PoTS patients. ▪ Studies involving the assessment of anxiety, depression, attention-deficit hyperactivity, somatic vigilance and other mental health disorder symptomology. ▪ Papers which explore the quality of life and functioning status of patients with PoTS.
<i>Other Co-morbid Diagnosis and/or Health Condition</i>	<ul style="list-style-type: none"> ▪ Works concerning other comorbidities with PoTS, including Ehler-Danlos Syndrome/ Joint Hypermobility syndrome, Fibromyalgia, Mast Cell Activation Syndrome & Multiple Sclerosis.

Treatments*POTS Interventions*

- Works including - Dietary & Lifestyle changes, Salt intake, compression garments, physical exercise programmes, patient education concerning their condition, psychological therapies & occupational therapy involvement.

 - Works including – Beta-Blocker Therapy, Ivabradine, pyridostigmine, Clonidine, Methyldopa, Fludrocortisone, Erythropoietin, Octreotide, Midodrine, Modafinil, Droxidopa, Desmopressin & anti-depressants.
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3. Results

3.1. Selection of Sources of Evidence (PRISMA Flow Diagram)

The initial PRISMA flow chart for the scoping review can be found below (see Fig. 2).

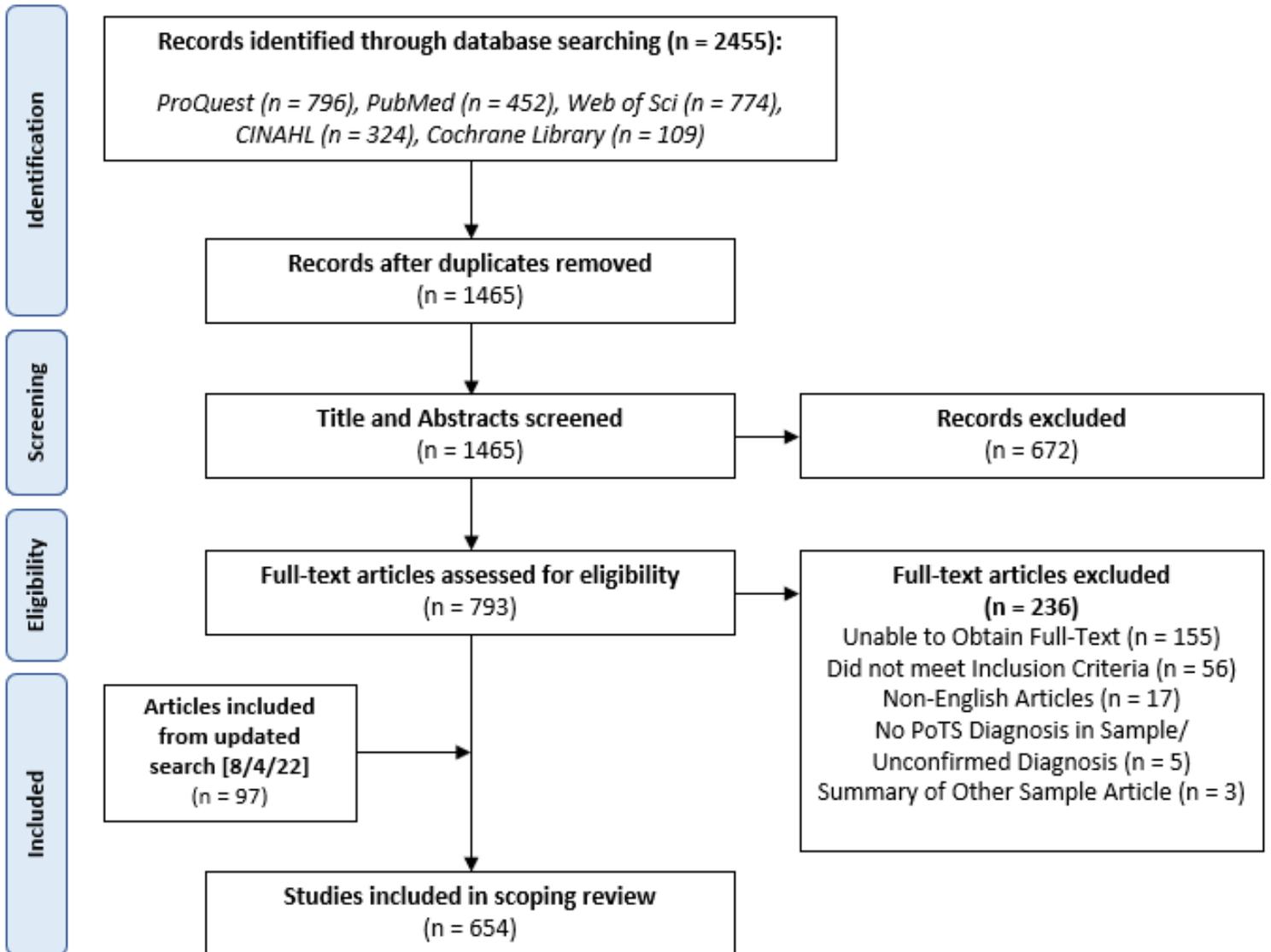


Fig. 2. PRISMA flow chart for the identification of the article sample for the current scoping review.

The first application of the review search strategy to the selected five databases returned 2455 academic texts. Following the removal of 990 duplicate papers, the remaining 1465 articles were entered into the Rayyan QCIR software programme. Jemma and I completed the title and abstract screening for the remaining articles and met after each round to reach a decision on any discrepancies within their rater decisions. 672 articles at the title and abstract stage were not found to meet the inclusion criteria and were therefore removed.

I then performed the full-text screening, with Jemma examining a subset of articles (n=100). For 155 articles, I was unable to obtain the full-text for the article which led to these being excluded. 56 articles did not meet the inclusion criteria for the study at the full-text screening stage and were omitted from the sample. A further 17 articles were deleted from the sample, due to their texts not being available in English. For 5 of the excluded empirical studies at the full-text stage – it was unclear whether their participant sample contained individuals diagnosed with PoTS or other forms of orthostatic intolerance disorders. Finally, 3 papers were found to be summary versions of other articles within the sample and were therefore removed. The remaining 557 articles were originally put forward to the final sample. Following an update to the search strategy three years later, the final review sample consisted of 654 articles.

3.2. Demographical Analysis

- *Overview of Literature Area Over Time*

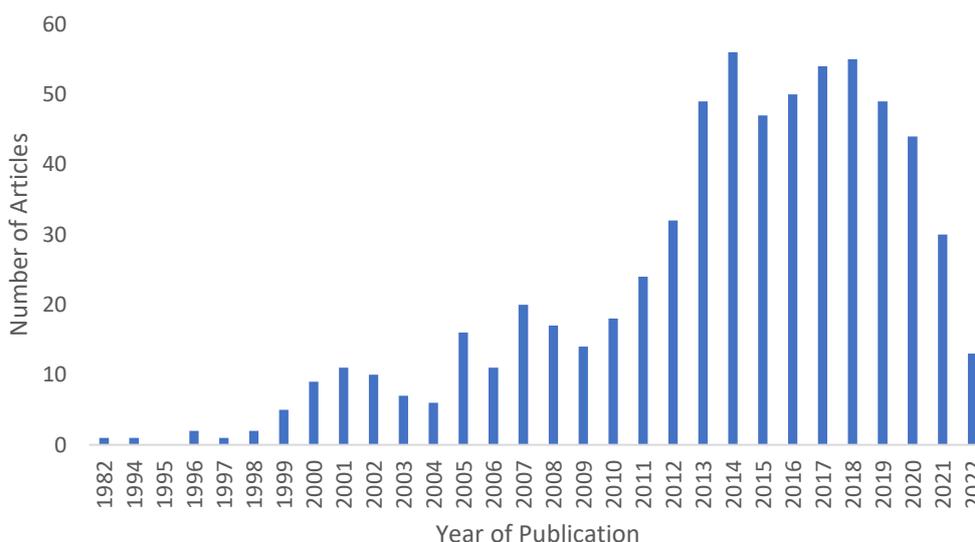


Fig. 3. Number of yearly PoTS-related articles published within the final article subset. N = 654.

A descriptive analysis was undertaken upon the final subset of articles (see Fig. 3). This frequency-based analysis revealed a left-tailed distribution, whereby a paucity of PoTS literature was identified during the first two decades of this research field (1982-1999). Within the sample, the term ‘postural tachycardia syndrome’ was first used during the early 1980s to describe the first recorded case report of a patient (Rosen & Cryer, 1982). However, research into PoTS began to emerge during the 1990s, where the earliest article within the sample labelled the condition as ‘postural orthostatic tachycardia syndrome’ (Schondorf & Low, 1993). During the next decade (2000-2009), there is a gradual yet small increase in the number of articles in the field (7–21 PoTS articles published per year). Over the course of the current

decade (2010-2020), this is followed by a more rapid growth of the literature base where the number of academic works published ranges from 18–56 articles per year.

- *Geographical Breakdown of Final Article Subset*

All articles in the final subset were examined by their geographical location (see Table 3).

Table 3. *Frequency & Percentage of PoTS articles published by each geographical location. N = 654.*

Country	Frequency	Sample Proportion (%)
USA	356	54.4
China	55	8.4
UK	53	8.1
Canada	34	5.2
Japan	23	3.5
Australia	21	3.2
Germany	16	2.4
Netherlands	14	2.1
Korea	12	1.8
Croatia	8	1.2
Sweden	7	1.1
Switzerland	6	0.9
Italy	6	0.9
Israel	5	0.8
Turkey	3	0.5
Belgium	3	0.5
Denmark	3	0.5
Portugal	3	0.5
Mexico	3	0.5
Pakistan	3	0.5
Brazil	2	0.3
New Zealand	2	0.3
Singapore	2	0.3
Chile	2	0.3
Finland	1	0.2
Argentina	1	0.2
Azerbaijan	1	0.2
Lebanon	1	0.2
Iran	1	0.2
Spain	1	0.2
Taiwan	1	0.2
Czech Republic	1	0.2
Austria	1	0.2
Poland	1	0.2
India	1	0.2
France	1	0.2

This frequency-based analysis revealed that the largest proportion of PoTS literature captured by the search strategy has emerged from researchers based within the United States of America. This body of American literature featured several publications from prominent autonomic clinics and patient centres such as the New York Medical College (Stewart, Glover, & Medow, 2015), the Vanderbilt Autonomic Dysfunction Centre in Nashville Tennessee (Plash et al., 2013) and the Mayo Clinic in Rochester, Minnesota (Low, Sandroni, Joyner & Shen, 2009). These are all sites which are well established for their works on PoTS.

The second most prominent centre for PoTS work was China (n=55; 8.4%), which features the Peking university hospital for the study PoTS and syncope (Zhang et al., 2012). The UK (n=53; 8.1%) was the third most prominent country for the study of PoTS. This features many prominent clinical centres for the study of PoTS, fatigue and syncope – this includes a multi-disciplinary team of clinicians based at a NHS CRESTA clinic in Newcastle upon Tyne in England who treat fatigue trans-diagnostically across a range of conditions (Strassheim, Welford, Ballantine & Newton, 2018).

Following this, research emerging from Canada was identified to have the second highest frequency of PoTS publications within the sample (n=34; 5.2%). This location features the clinical works of Satish Raj & colleagues, who are based at the Autonomic Investigation & Management Clinic in Calgary (Raj et al., 2020). Other prominent locations which featured in the sample were Japan (n=23; 3.5%), Australia (n=21; 3.2%), Germany (n=16; 2.4%), Netherlands (n=14; 2.1%) and Korea (n=12; 1.8%).

3.3. Proportion of PoTS Literature by Article Type

Visual inspection during the full-text screening stage was undertaken to identify the article type for each paper within the sample (see Table 4 below). Frequency-based analysis revealed that empirical research exploring PoTS was found to be the largest proportion of article type within the final subset (n=364, 55.7%), followed by review articles (n=154, 23.5%).

Table 4. Proportion of PoTS literature within the final sample by article type. N = 654.

Article Type	Frequency	Sample Proportion (%)
Empirical Research (Journal)	364	55.7
Review / Commentary Paper	154	23.5
▪ <i>Non-systematic</i>	139	21.3
▪ <i>Systematic Search performed</i>	12	1.8
▪ <i>Systematic Review & Meta-Analysis</i>	3	0.5
Case Report	77	11.8
Clinical Trial Registration	26	4.0
Editorial / Letter to Editor	14	2.1
Conference Abstract	12	1.8
Consensus Statement/ Clinical Guideline	5	0.8
Dissertation / Thesis	2	0.3

- *Empirical Research Articles*

In regard to their adopted study designed, quantitative research dominated the PoTS empirical research literature with only one qualitative study by Waterman et al. (2021) being identified during an updated search within the final review article sample. Empirical works (original research papers) were coded across fifteen categories of PoTS research areas that were identified by the research team (see Table 5). These works mainly pertained to the exploration of PoTS aetiology and underlying pathophysiology (n=110), child/adolescent PoTS samples (n=93), PoTS comorbidities (n=79), in addition to PoTS diagnosis assessments (n=77).

Table 5. Frequency of empirical research articles coded into each of the developed fifteen thematic categories. *N* = 364.

Thematic Category	Article Frequency	Sample Representation (%)
Aetiology & Underlying Pathophysiology	110	16.8
Child & Adolescent Research	93	14.2
Diagnostic Tools & Autonomic Evaluation	77	11.8
Autoimmunity & Virus Research	20	3.1
Endophenotypes of PoTS	23	3.5
Deconditioning	9	1.4
Hypovolemia	19	2.9
Fatigue	28	4.3
Syncope	46	7.0
Gastrointestinal, Bladder & Urination	28	4.3
Sleep-based Symptoms/ Disturbances	16	2.4
Brain Fog & Cognitive Ability	23	3.5
Psychological Functioning	52	8.0
Other Co-morbid Diagnosis and/or Health Condition	79	12.1
Treatments/ Interventions	80	12.2

*Articles were coded to more than one category to capture cross-disciplinary nature of some works.

Within Chapter 3 of the thesis, a synthesis of empirical works identified from the scoping review article subset has been used to inform the generation of a narrative literature review (this serves as the background reading chapter to this thesis). This chapter specifically focuses on the exploration of research relating to the diagnosis, symptomology and co-morbidities of PoTS. Furthermore, within Chapter 4 of the thesis, additional narrative commentary and analysis is provided for empirical articles which focus upon non-pharmacological and pharmacological treatments for PoTS.

- *Review Articles*

Of the review articles included within the review (n=154), 139 reviews were non-systematic in nature, 12 articles featured the use of a systematic search strategy whilst 3 articles were systematic review & meta-analyses. The aims and content of all review articles within the final sample were coded by and categorised across the fifteen areas of PoTS research identified by the research team (see *Table 6*). The majority of review articles pertained to exploration of

PoTS diagnostic assessments (n=63), treatments (n=55) and aetiology/ underlying pathophysiology (n=50).

Table 6. Frequency of review articles coded into each of the developed fifteen thematic categories. N = 154.

Thematic Category	Article Frequency	Sample Representation
Aetiology & Underlying Pathophysiology	50	32.5%
Child & Adolescent Research	16	10.4%
Diagnostic Tools & Autonomic Evaluation	63	40.9%
Autoimmunity & Virus Research	11	7.1%
Endophenotypes of PoTS	25	16.2%
Deconditioning	12	7.8%
Hypovolemia	15	9.7%
Fatigue	10	6.5%
Syncope	19	12.3%
Gastrointestinal, Bladder & Urination	6	3.9%
Sleep-based Symptoms/ Disturbances	8	5.2%
Brain Fog & Cognitive Ability	9	5.8%
Psychological Functioning	13	8.4%
Other Co-morbid Diagnosis and/or Health Condition	35	22.7%
Treatments/ Interventions	55	35.7%

*Articles were coded to more than one category to capture cross-disciplinary nature of some works.

○ *Reviews Employing a Database Search Strategy*

Within the sample of review articles, twelve of these papers which included a systematic search of at least one literature database (see Appendix_A) had been conducted. Seven reviews were systematic in nature (Gales & Gales, 2007; Gee et al., 2018; Morgan et al., 2018), four of which featured the use of meta-analyses [*further details of systematic reviews featuring meta-analyses is provided in the following sub-section*], one paper was a scoping review (Benarroch, 2012) whilst the remaining articles featured a narrative format (Brady et al., 2005; Butts et al., 2017; Eftekhari et al., 2021; Fedorowski, 2019; Roma et al., 2018; Ruzieh et al., 2017; Ruzieh & Grubb, 2018; Xu, Jin & Du, 2016).

For the twelve reviews which did not feature a meta-analysis, three reviews focussed on providing an overview of PoTS to the reader, including pathophysiology and management strategies (Benarroch, 2012; Eftekhari et al., 2021; Fedorowski, 2019)– whilst a third review assessed these topics in relation to child & adolescent populations specifically (Xu, Jin & Du, 2016). Furthermore, two additional reviews focused on exploring other possible other pathophysiological basis for PoTS– including literature concerning evidence of autoantibodies

in PoTS and orthostatic intolerance patients (Ruzieh et al., 2017), and a collection of works exploring orthostatic intolerance onset following the HPV vaccine (Butts et al., 2017). Two reviews also synthesised literature surrounding PoTS co-occurring with pregnancy (Morgan et al., 2018; Ruzieh & Grubb, 2018). Two systematic reviews examined empirical research assessing the efficacy of two pharmacological treatments for PoTS – ivabradine (Gee et al., 2018) and pyridostigmine (Gales & Gales, 2007). The final two articles reviewed literature dedicated to PoTS alongside two other health diagnoses – inappropriate sinus tachycardia (Brady et al., 2005) and joint hypermobility/ Ehler-Danlos syndromes (Roma et al., 2018).

Databases examined by the review articles included MEDLINE (n = 6), PubMed (n = 6), EMBASE (n = 6), MedScape (n = 1), Medline (N = 1), PsychInfo (n = 1), CINAHL (n = 1), International Pharmacological Abstracts (n = 1) and the Cochrane Library (n = 1). Seven of these review articles stated that the use of hand-searching was conducted on the reference lists of the articles within their final subsets to identify additional academic sources to examine. Furthermore, only one review examined sources of grey literature (Morgan et al., 2018) – this was done through searching clinicaltrials.gov and two PoTS-related charity & organisational websites (PoTS UK & Dysautonomia International). This review was also the only non-meta-analysis article to provide a quality assessment and evidence appraisal of its identified studies and case study (through the *McMasters Critical Review Form for Quantitative Studies* and *National Health and Medical Research Council (NHMRC) Evidence Grading Matrix* respectively).

- *Systematic Reviews featuring Meta-Analyses*

In addition to the aforementioned articles, a further three systematic reviews which incorporated the use of meta-analyses were identified in the article sample. These works included the examination of beta-blocker therapy (metoprolol) in child and adolescent PoTS patients (Deng et al., 2019), the comparison of heart rate and heart rate variability between PoTS and control groups (Swai et al., 2019) in addition to an evaluation of efficacy rates for conventional PoTS treatments (Wells et al., 2018). In total, the four meta-analysis assessed seven RCTs (3 of which were specified as being small-scale), twenty five case series, twenty case-control observational and four non-RCT studies. Databases searched included EMBASE (n = 3), PubMed (n = 2), Medline (n = 1), Cochrane Library (n = 1), Sinomed (n = 1), SCOPUS (n = 1), and CENTRAL (n = 1).

- *Case Reports*

The 77 case report articles identified within the final review article subset detailed a total of 98 PoTS cases. Whilst a summary of major frequency findings has been presented within the main body of this report (see *Table 7 for an overview*), full tabular and narrative synthesis of all PoTS cases has also been provided within appendices (*Appendix_B*).

Table 7. Frequency of Published PoTS cases by Gender, Age Group, Diagnostic Method, Co-Morbidities & Reported Treatments (Non-Pharmacological & Medicinal) within the analysed case report articles. Number of Case Study Articles = 77; Number of PoTS Cases = 98.

Case Variable	Frequency	Proportion of Sample (%)
Gender		
<i>Female</i>	75	76.5
<i>Male</i>	20	20.4
<i>Natal Female Identifying as Male</i>	3	3.1
Age		
<i>0-9</i>	1	1.0
<i>10-19</i>	35	35.7
<i>20-29</i>	26	26.5
<i>30-39</i>	19	19.4
<i>40-49</i>	11	11.2
<i>50-59</i>	3	3.1
<i>60-69</i>	2	2.0
<i>70+</i>	1	1.0
Primary PoTS Diagnostic Test for PoTS		
<i>Tilt-Table</i>	65	66.3
<i>Standing/Schellong Test</i>	19	19.4
<i>Other</i>	3	3.1
<i>Not Stated</i>	11	11.2
PoTS Co-Morbidities		
<i>Chronic Fatigue Syndrome</i>	6	6.1
<i>Syncope</i>	6	6.1
<i>Ehlers-Danlos Syndrome/Hypermobility</i>	6	6.1
Psychiatric Co-Morbidities		
<i>Anxiety-Related Disorders</i>	7	7.1
<i>ADHD</i>	4	4.1
<i>Depression</i>	3	3.1
<i>Bipolar Disorder</i>	3	3.1
Non-Pharmacological Interventions		
<i>Increased Fluid Intake</i>	30	30.6
<i>Increased Salt Intake/Supplements</i>	26	26.5
<i>Exercise/Physical Activity</i>	13	13.3
<i>Compression Garments</i>	9	9.2
<i>Psychological Therapies</i>	4	4.1
<i>Patient/Family Health Education</i>	2	2.0
<i>Occupational Therapy</i>	2	2.0
Pharmacological Agents		
<i>Fludrocortisone</i>	30	30.6
<i>Midodrine</i>	27	27.6
<i>Propranolol</i>	18	18.4
<i>Metoprolol</i>	13	13.3
<i>Bisoprolol</i>	7	7.1
<i>Ivabradine</i>	8	8.2
<i>Pyridostigmine</i>	8	8.2

*Several reports featured more than one PoTS patient and/or types of explored treatments.

Demographic breakdown of the 98 cases in the sample identified 75 female patients (76.5%), 20 male patients (20.2%) and three natal females who identified as male (3.0%). The dominance for female cases within the sample is representative of the higher PoTS diagnosis rates for this sex, which has been estimated at a rate of five females for every one male presenting with the condition (Low et al., 2009). Patient ages ranged from 8 to 70 years old (Mean Age = 27.3; SD = 12.8). The finding of a right-tailed distribution for case age groups is in line with evidence that PoTS is more commonly observed in younger individuals and rarely reported within patients aged 50 or over (Low & Sandroni, 2012). In regard to reports which had focused on child and adolescent cases of PoTS, 25 patients [25.5%] were below the age of 18.

Where possible, tabular analysis also examined the primary type of PoTS diagnostic method that had been undertaken to confirm the diagnosis of PoTS for each case within the sample. Use of a tilt-table/head-up tilt test - utilised for two-thirds of cases (66.7%) in the sample - was the most commonly employed method, whilst 19 cases (19.2%) within the sample were diagnosed through an active standing (Schellong) test.

In regard to PoTS treatments, only 56 cases (57.1%) referred to details of the non-medication management of patients' PoTS with the most frequent being the increase of fluids (30.6%) or salt (26.5%) in patients' diets. Alternatively, 88 case reports [89.8%] included the medication usage of the patient. The most frequent treatments administered to control PoTS symptoms were fludrocortisone (30.6%), midodrine (27.6%), and propranolol (18.4%). Further explanation of PoTS treatments and their medicinal actions on PoTS symptoms are outlined within Chapter 4.

- *Clinical Trial Registrations*

The final review subset contained the registrations of 26 clinical trials for PoTS research (See Appendix_C). Twenty of the trial registrations originated from the USA, three were registered from research teams based in Canada, whilst single trials were also recorded Germany, South Korea and the Philippines respectively. Nineteen of the projects reported that they would employ the use of a randomised crossover design, with one study opting for the use of a non-randomised crossover design. Furthermore, three registrations reported they would employ the use of a randomised parallel-assignment, and three studies had a randomised single-group assignment.

Seventeen projects aimed to investigate the effects of pharmacological agents upon PoTS symptomology. Of these studies, medications which were examined by the clinical trials

included: Pyridostigmine (n=4), Propranolol (n=5), Ivabradine (n=3), Bisoprolol (n=2), Losartan (n=1), Ascorbic acid (n=1), Atenolol (n=1), Droxidopa (n=1), Moxodine (n=1), Modafinil (n=1) and Northera (n=1). Planned sample-sizes for studies which examined pharmacological agents in PoTS ranged from 8 participants to a maximum of 150 (Mean Sample Size=48.4). Four of these trials sought to investigate the effects of intravenous (IV) infusions. These subsets of trials included the examined the effects of: salt water (saline) infusions on oxygen consumption capacity; iron sucrose infusions on autonomic (COMPASS-31) and orthostatic (orthostatic symptom scale) symptomology; immunoglobulin infusions, in addition to; Albumin infusions in relation to orthostatic symptoms, head-up tilt table test and maximal exercise capacity in adolescent PoTS patients. Samples ranged from 17–40 (Mean Sample Size=29.0).

The remaining nine trials sought to examine non-pharmacological interventions and their effects on PoTS symptomology. Two studies sought to examine the effects of altering posture in PoTS patients to examine the subsequent effects on cognitive functioning in a Stroop task, the Cogstate identification task and in relation to hypermobile Ehler-Danlos syndrome diagnostic criteria. Additionally, three clinical trial registrations aimed to assess the use of compression garments in relation to orthostatic symptoms and cardiovascular examination during a tilt-table test. Finally, the sample also included two trials on the effects of transdermal vagal nerve stimulation, and single projects which sought to investigate the effects of a sodium diet and an inspiratory-threshold device. Sample sizes for non-pharmacological intervention trials ranged from 8–100 participants (Mean Sample Size=47.7).

- *Other Article Types*

A summary of PoTS literature through Editorial Letters, Conference Abstracts, Consensus Statement & Clinical Guidelines & Dissertations has been provided within appendices (Appendix_D).

4. Discussion of Demographic Findings

4.1. Summary of Evidence

The current scoping review aimed to map the key characteristics and range of topics focused on by diagnostic, symptomology and treatment literature within the PoTS research field. Demographic analysis highlighted a slow but gradual increase in the number of PoTS-related articles which have been published over time (1982-2009), followed by a more rapid growth

of the area over the course of the previous decade (2010-2020). Assessment of geographical location revealed that the USA, China, the UK and Canada possessed the highest number of PoTS-related publications within the sample. Furthermore, frequency-based analysis demonstrated that the types of PoTS literature in the final sample was dominated by the prevalence of empirical research papers (of which, only one study featured a qualitative design), followed by review articles and case reports.

The review identified a marked increase in the publication of PoTS literature over the past decade, as also identified by Eftekhari et al. (2021). This particular growth could be attributed to an increased awareness of the condition over time. This is evident from the incorporation of PoTS into both the clinical guidelines published by the Japanese Society of Psychosomatic Pediatrics (Tanaka et al., 2009), and the updated orthostatic hypotension consensus statement released by the American Autonomic Society, European Federation of Autonomic Societies, Autonomic Research Group of the World Federation & the Autonomic Disorders section of the American Academy of Neurology (Freeman et al., 2011) at the start of the 2010s period. Over recent years (2017-2020), there has been a further increase in the numbers of clinical guidelines and society statements featuring information for the diagnosis and clinical management of PoTS (Wang et al., 2018; Kim et al., 2019; Raj et al., 2020). These documents may be vital not only in assisting healthcare practitioners who actively attend to the treatment of this condition within their care facilities, but also in promoting a general awareness of PoTS throughout the medical community. This growth in awareness over time is supported by evidence from a large online survey of 4835 patients with PoTS, which found that patients' delay to obtaining a diagnosis of PoTS after the year 2009 was on average 11.6 months shorter than individuals who had been diagnosed within the prior decade [2000-2009] (Shaw et al., 2019).

Whilst the research area is still relatively within its infancy, the findings of the thematic coding strategy within this scoping review revealed that empirical works have placed a strong emphasis on discovering the possible cardiovascular mechanisms involved in both the aetiology, symptom presentation and onset of PoTS. Similar findings were achieved by Eftekhari et al. (2021), who identified the study of aetiology as one of seven guiding topics for PoTS evidence within their findings from the employment of mapping analysis. Unlike Eftekhari et al. (2021), who labelled this under a singular homogenous coding group, within the current scoping review I provided greater crucial insights by categorising literature across a more detailed thematic coding strategy – comprising of fifteen PoTS-specific categories. Through the use of a more rich thematic coding scheme, I have advanced the findings of Eftekhari et al. (2021) by highlighting further insights into the study of PoTS. For example, I have drawn more detailed implications for articles that have explored the investigation of PoTS

aetiology, through also identifying the proportion of empirical literature that has been dedicated to the study of specific PoTS subtypes – such as neuropathic and hyperadrenergic (n = 23, 3.5%), hypovolemic (n = 9, 1.4%) and PoTS with deconditioning (n = 19, 2.9%).

It is worth noting however that PoTS still continues to be an elusive and poorly understood condition by both public and medical communities alike (Raj & Sheldon, 2016). As a result of this, a core challenge of treating PoTS in clinical settings is the barrier of symptomatic patients not receiving the appropriate referrals to specialised autonomic or cardiac facilities by their first-line healthcare practitioners. This prevents individuals from undergoing the necessary autonomic screening tests which are needed to confirm the correct diagnosis of PoTS, and can result in medical therapy for an alternate, misdiagnosed condition (commonly anxiety) being pursued (Kavi, Gammage, Grubb & Karabin, 2012). As such, further action is needed to develop interventions which aim to improve, train and expand on the knowledge of dysautonomia-related conditions by first-line healthcare practitioners to help combat these issues (Raj & Robertson, 2018).

Within the final article subset of the current project, approximately one in five articles in the sample were review papers. This included reviews which stated that the authors had performed a systematic search strategy of at least one academic database in preparation of their manuscripts. Nevertheless, several of these examined reviews did not make clear the full details of their article screening processes, eligibility or article exclusion criteria. Furthermore, my findings identified from article extraction indicated that only a handful of these works opted to undertake quality appraisal of the article subsets. In light of this, further future works within the PoTS literature area should adopt a more systematic approach to the collation of evidence. Where possible, these reviews should be carried out in accordance with PRISMA guidelines, to ensure that the quality of the works meets the standards imposed by professional bodies such as those by the Cochrane organisation.

Furthermore, when gathering these works I also identified only a small body of systematic reviews and meta-analyses that have been undertaken to synthesise and critically assess the available evidence for existing treatments of PoTS. This restricted evidence base consisted of works dedicated to pyridostigmine (Gales & Gales, 2007), ivabradine (Gee et al., 2018), metoprolol use in child-adolescent PoTS patients (Deng et al., 2018) and conventional PoTS therapies for volume expansion and heart rate reduction (Wells et al., 2018). Taken together, these limited number of works reflect a bias towards the examination of literature dedicated to medication-based therapies for PoTS in particular. This highlights that there is a current lack of research synthesis existing for the assessment of individual non-pharmacological PoTS interventions. In a similar way, examination of twenty-six clinical trial protocols also indicated

that there was a preference towards the examination of medicinal PoTS agents (n = 17) over non-pharmacological treatments (n = 9). Case reports also featured pharmacological agents (n = 88, 89.8%) more commonly than non-pharmacological interventions (n = 56, 57.1%). This is an important point for consideration, given that pharmacological interventions are traditionally reserved only for use in patients who appear non-responsive to first line non-drug treatment for PoTS (Raj et al., 2020). Therefore, one implication of my scoping review is the need for further, more comprehensive accounts of PoTS treatments to be carried out and synthesised in order to fully assess the scale of the evidence base which exists for methods which treat this autonomic condition. I explore this more in Chapter 4, where I consider empirical works in the final review subset which have explored PoTS treatments.

The data charting and inspection of 101 PoTS case reports identified through the employed search strategy – an article type not synthesised by Eftekhari et al. (2021) in their evidence map - revealed that over two-thirds of patients examined within the report sample had been diagnosed with PoTS following the conduct of a table test. Whilst it was not possible in the current review to analyse the type of healthcare practitioners who had made this diagnosis for each individual case, it is worth considering in future how this finding relates to prior research which has estimated that 41% and 15% of patients' PoTS diagnoses are made by specialist cardiologists and cardiac electrophysiologists (respectively). These two types of specialists are known to be responsible for the conduct of head-up tilt table examinations (Shaw et al., 2019). Within the scoping review, the findings also revealed that instruments for assessing anxiety and depression symptomology were amongst the most commonly utilised psychometric tools within case reports, whilst several cases had presented with psychiatric co-morbidity. Empirical works examining the association between PoTS and psychological co-morbidity have indicated that patients may exhibit with mild levels of depression and elevated ADHD symptomology (Raj et al., 2009). Despite this however, only four of the examined case reports within the sample had noted that the patient(s) had received cognitive/psychological therapies to assist the individual with their mental health condition, and/or their adjustment to living with the new diagnosis of a chronic and invisible illness. Although the recommendation for the treatment of PoTS by the Canadian Cardiovascular Society (Raj et al., 2020) is that healthcare practitioners and specialists should adopt a multi-disciplinary approach to treating their patients, only a small number of cases in the sample referred to the inclusion of allied health professionals, like occupational therapies and strategies like the family education of PoTS to support the patient. Either past case reports failed to report on such practice, or such types of interventions are rarely made available to support each patient.

4.2. *Limitations*

Limitations of the current study must be acknowledged. First, the current scoping review did not perform the search strategy within a database of grey literature. A prior PoTS review conducted by Morgan et al. (2018), which aimed to examine literature pertaining to PoTS diagnosis and pregnancy, performed a grey literature search upon the websites www.dysautonomiainternational.com and www.potsuk.org. Due to the sheer size and diverse nature of PoTS published literature the decision was made not to perform a similar search to that of Morgan et al. (2018), due to the time restraints applied to the current project. It should be noted however that whilst I did not perform a specific search for grey literature, the current review purposefully included a broad inclusion criterion which deemed multiple diverse types of articles eligible for examination, including those which are traditionally associated as being commonly identified through the conduction of grey literature strategies (notably, clinical trial registrations, conference abstracts, consensus statements, clinical guidelines, dissertations). This broad eligibility criteria was a purposeful decision, as the project wished to synthesis and map a large body of diverse works dedicated to the study of this topic. Furthermore, whilst the use of quality assessment is an optional step in a scoping review (Askey & O'Malley, 2005), this decision was not carried out within the current project. In light of this, I acknowledge that the conclusions drawn regarding the interpretations of the findings may have been biased due to this lack of inclusion. Given that the current scoping review identified only a limited number of review articles which had undertaken this approach, future, more focused reviews within the PoTS literature area should adopt the use of quality assessments within their works in an effort to promote a greater and more critical approach to the examination of evidence within this field.

Despite this, I also highlight strengths in my undertaken method through the development of a more rich and detailed thematic coding strategy, in comparison to the seven coding categories identified within the Eftekhari et al. (2021). Furthermore, in comparison to other PoTS review articles which have utilised systematic database search strategies, I have employed the use of Cohen's K statistical analyses to support my screening processes - through the inspection of agreement between raters' final article decision. I therefore highlight the importance of incorporating statistical analyses to examine inter-rater reliability within future PoTS evidence synthesis works.

4.3. *Conclusion*

To conclude, chapter 2 presented the introduction, methods and demographic findings of the scoping review, as the first step of PoTS research literature synthesis to support my

intervention development work. Within the next chapter, I build upon the current findings through the presentation of a narrative synthesis of PoTS empirical works dedicated to the exploration of PoTS diagnosis, symptomology and co-morbidity.

- Chapter 3: Narrative Synthesis of PoTS Literature on Diagnosis, Symptomology & Co-Morbidities -

This chapter uses the scoping review data (see Chapter 2, for methodology), to offer an overview of research in this field on the diagnosis, symptomology and comorbidities for this autonomic condition. This chapter initially shows that: clinicians need to remain cautious when identifying specific PoTS subtypes in their patients; PoTS is difficult to distinguish in clinical practice from chronic fatigue syndrome- or syncope-only diagnoses, and that; people with PoTS are at a heightened risk of suicide ideation and reduced quality of life. From this synthesis, relevant clinical implications are drawn to inform practitioners with key additional knowledge for assisting with both the diagnostic process and management of patients who present with PoTS symptoms. The chapter concludes by highlighting the greater need for additional, qualitative works to be undertaken in the PoTS research field, in order to further explore the symptom experiences and debilitations of people with PoTS. Finally, I argue for the need to identify and develop further non-pharmacological interventions in PoTS, which are capable of improving aspects like sleep-related deficits in PoTS patients.

1. Defining and Diagnosing PoTS

1.1. How is PoTS Characterised? Subtypes & Aetiology

A number of works within the final article sample consisted of discussions concerning the presentation of PoTS patients. As noted in the introduction, PoTS is a heterogeneous syndrome, whereby the condition's presenting symptomology, symptom frequency and intensity often varies from patient to patient (Benarroch, 2012). To date, four distinct subtypes have been outlined in the literature. Each of these is associated with putative underlying pathophysiological processes (Raj, 2006). The four types identified are: Neuropathic PoTS, Hyperadrenergic PoTS, Hypovolemic PoTS and PoTS with Deconditioning.

- *Neuropathic PoTS*

It has been estimated that half of the PoTS patient population can be diagnosed with a neuropathic subtype of the condition associated with disruption to the sympathetic nerves (Low, Sandroni, Joyner, & Shren, 2009). Sympathetic nerves are responsible for controlling blood vessel constriction (Bonyhay & Freeman, 2004). In neuropathic PoTS patients, peripheral sympathetic denervation occurs which damages the small fibre nerves that regulate vasoconstriction (Low, Vernino, & Suarez, 2003). This length-dependent impairment leads to blood pooling in the lower limbs, reduced foot perspiration, and a blunted norepinephrine response within the legs when patients adopt an upright posture (Benarroch, 2012). On

autonomic diagnostic tests, neuropathic PoTS patients may exhibit mild decreases in blood pressure (Low, Sandroni, Joyner & Shren, 2009).

- *Hyperadrenergic PoTS*

Hyperadrenergic PoTS is characterised by abnormally high norepinephrine levels in the bloodstream whilst standing [exceeding 600pg/ml] (Ross, Ocon, Medow, & Stewart, 2015). These high concentrations of norepinephrine are resultant from heightened sympathetic activity (Low & Sandroni, 2012), and may be due to a mutation within norepinephrine transporter genes that hinders reuptake of these neurotransmitters from the synaptic cleft (Raj, 2006). Prior work has explored the clinical features which distinguish this hyperadrenergic PoTS condition from other subtypes. When undertaking supine postures, hyperadrenergic PoTS patients demonstrate higher resting heart rates, lower vagal tone and a greater dominance of the sympathetic autonomic nervous system [ANS] branch than other PoTS subtype patients. Hyperadrenergic patients also present with syncope episodes more rapidly in response to orthostatic challenge (Crnošija et al., 2016). Hyperadrenergic patients are more prone to experiencing anxiety, cold perspiration in the extremities, increased urination following long periods of staying upright and frequent bodily shaking (Kanjwal, Saeed, Karabin, Kanjwal, & Grubb, 2011). Whilst limited research has examined the presentation of hyperadrenergic PoTS within paediatric samples, evidence from a retrospective analysis by Zhan, Chen, Li & Du (2014) has implied that adolescent patients with this subtype experienced episodes of headaches, shaking and dizzy spells more frequently than non-hyperadrenergic PoTS adolescents; they also possessed a greater increase in heart rate and blood pressure (systolic) in response to tilt table testing.

There appears to be some uncertainty in regards to the prevalence rates for the hyperadrenergic subtype of PoTS across the literature. Whilst some researchers have concluded that this hyperadrenergic PoTS constitutes approximately 30%-60% of the patient population (Thieben et al., 2007; Crnošija et al., 2016); other works have claimed that the true representation of this subtype may be as low as 10% (Raj, 2006; Kanjwal et al., 2011). Further works are vital for establishing the true diagnostic rates of this condition (and its subtypes) across global populations (Raj & Robertson, 2018).

- *PoTS § Hypovolemia*

Up to 30% of patients with PoTS experience co-existing hypovolemia in the thorax, a condition which is characterised by a decreased volume of blood (Thieben et al. 2013). Hypovolemic PoTS patients develop tachycardia due a reduced volume of deoxygenated blood being returned to the heart, in compensation, heart rate rises to ensure that oxygenated blood can be circulated across the body at a much faster rate to maintain metabolism (Raj & Robertson,

2007). Previous empirical studies have shown that hypovolemic PoTS individuals possess significantly lowered concentrations of renin and aldosterone than healthy controls (Stewart, Glover, & Medow, 2015). Both of these substances play pivotal roles in blood volume regulation, and this has provided evidence for a possible pathogenesis for this PoTS subtype (Raj et al, 2005). In addition to hypovolemia, reports of a reduced red blood cell count (anaemia) alongside PoTS are not uncommon within both adult (Hoeldtke, Horvath, & Bryner, 1995) and adolescent (Jarjour, Hernandez & Jarjour, 2013) populations.

- *PoTS § Deconditioning*

Deconditioning, a condition where muscles atrophy occurs due to a lack of regular exercise, can affect patients with PoTS (Joyner & Masuki, 2008). Deconditioned PoTS patients are known to be affected by reduced stroke volume (Masuki et al., 2007), cardiac atrophy and hypovolemia (Joyner, 2012). Autonomic clinicians have previously tried to assess the prevalence and effects of deconditioning within the PoTS patient population. Within a prior retrospective review of 84 PoTS and 100 orthostatic intolerance patients who attended the Mayo Clinic over a five-year period, Parsaik et al. (2012) found that deconditioning - defined by the authors as an individual exhibiting less than 85% oxygen consumption [VO₂ Max] during an exercise test – was apparent within 90% of patients in both groups. Whilst these findings indicate that a large majority of the PoTS patient population are deconditioned, it is important to note that deconditioning is not a direct cause of the PoTS itself (Blitshteyn & Fries, 2016). Prior evidence has indicated that in addition to displaying low VO₂ Max during exercise, PoTS patients also demonstrate lower ventricular pressures during physical activity which may underlie this impairment (Oldham, Lewis, Opatowsky, Waxman, & System, 2016).

- *Critical Perspectives with PoTS Subtypes*

It is important to note that PoTS endophenotypes are not mutually exclusive from one another, and that a single patient may present with two or more co-occurring PoTS variants during diagnostic assessment (Zhao & Tran, 2019). This can prove to be a challenging obstacle for clinicians to overcome during the development of a treatment plan for the patient, and as such an integrated approach of combining different treatments is advised to manage the varying symptoms which are recognised within this heterogeneous condition (Wells et al., 2018). Furthermore, researchers from the Vanderbilt Autonomic Dysfunction Center in Tennessee have recently expressed concerns that clinicians may differ in terms of their accepted definitions and understandings of each PoTS subtype, and that this may lead to unnecessary confusion between practitioners during the patients' treatment (Vanderbilt Autonomic Dysfunction Center, 2020). In an effort to overcome this issue with "labelling" an individual,

the center advocates a more open approach by asking practitioners to simply “characterise” a patients’ PoTS presentation holistically during diagnostic assessments.

1.2. *How is PoTS Diagnosed? Autonomic Functioning Tests*

Several papers focused on the methods and explicit tests used to identify the presence of PoTS. When an individual is referred to a specialised centre for suspected PoTS, they will undergo a number of different functioning assessments to determine their diagnosis.

- *Head-Upright Tilt Table Testing*

The head-upright tilt [HUT] table test is the most well-known assessment used to investigate orthostatic intolerance symptoms and syncope episodes (Kerry, O’Shea, & Parry, 2000). During this test, a patient lies across a table and is slowly tilted (60°–80°) to an upright position to purposefully simulate the pressures of orthostatic challenge (Sutton & Bloomfield, 1999). Straps and a metal foot plate are used to support the individual’s weight during the procedure (Parry et al., 2009). Through a finometer, cardiovascular activity is continually monitored throughout the assessment. Changes in heart rate and blood pressure are used as clinical indices to determine the appropriate diagnosis of a cardiac, autonomic and/ or syncope condition (Tan, Duncan, & Parry, 2009). If an adult patient displays a heart rate increase of 30 bpm within a ten minute period following tilt (or an increase of 40 bpm for children/adolescents) this indicates the presence of PoTS (Sutton & Bloomfield, 1999). When patients develop syncope (prefaced by a sharp drop in blood pressure), the table is lowered back to a supine posture and clinical observation continues for a further twenty-minute period (Parry et al., 2009). Patients who do not experience PoTS symptoms or syncope during the 45 minutes of the test may receive glyceryl nitrate, isoproterenol or a minor pain stimulus to provoke orthostatic intolerance (Adamec et al., 2013; Kurbaan et al., 1999).

Prior research has also shown that an individual’s hemodynamic response during HUT testing during diagnostic assessment can provide clinicians with guidance towards the particular PoTS subtype(s) each patient presents with. Patients with hyperadrenergic PoTS are known to exhibit elevated blood pressures (above 10mm hg) in reaction to tilt (Thieben et al., 2007), whilst mild decreases in blood pressure or pulse-pressure may be observed in neuropathic and deconditioned PoTS patients respectively (Low, Sandroni, Joyner, & Shen, 2009). In addition to an increased heart rate during HUT, PoTS patients also demonstrate significantly higher respiration rate, increased respiration depth and decreased end-tidal carbon dioxide volume in comparison to healthy controls (Novak et al., 1998). Decreased end-tidal carbon dioxide - the concentration of carbon dioxide that is expelled during the exhalation - has been

linked to hyperventilation onset during tilt, which is observed in approximately one fourth of PoTS patients (Stewart et al., 2018; Shin et al., 2016).

- *Limitations of the Tilt-Table Test*

Prior researchers have critically evaluated both the accuracy of tilt table test, the differences in assessment duration by different research facilities and the use of an arbitrary cut-off point (a criterion of >30 bpm increase in heart rate within ten minutes following tilt) to support a diagnosis of PoTS from patient observation. During a retrospective study by Plash et al. (2013) of 15 PoTS patients and 15 healthy controls, tilt table testing was found to achieve high rates of sensitivity during both ten-minute (sensitivity= 93%) and thirty-minute (sensitivity= 100%) assessments. Nevertheless, Plash et al. (2013) also found evidence to suggest that the thirty-minute tilt-table test condition would require an optimal increase in heart rate of 47bpm in order to accurately distinguish PoTS patients from controls. Furthermore, the use of the orthostatic heart change criterion of >30 bpm in the ten-minute assessment led to an abnormally high false positive rate [60%] of 'PoTS' cases within the healthy control group (poor specificity). A number of researchers have therefore argued that current PoTS diagnostic guidelines may not be compatible with specific tilt-table test assessment durations (Kirbiš, Grad, Meglič & Bajrović, 2013; Plash et al., 2013). Whilst other institutions are known to utilise slight variations in the angles (60°–80°) they employ during the HUT; evidence suggests this may not lead to substantial differences within paediatric PoTS patients' hemodynamic responses (Lin et al., 2015). The use of a metal plate to support the patients' bodily weight within the HUT tilt table test has also been criticised for not accurately mimicking a supine-to-upright posture change, as this aspect of the procedure does not fully reproduce the body's reaction to orthostatic challenge (Plash et al., 2013). Namely, this prevents a number of somatic responses which would occur in the patient's body to mitigate blood pooling within the legs and feet during active standing (Garland, Celedonio, & Raj, 2015).

Due to these limitations, clinicians may employ the use of a Schellong (active standing) test as an alternative assessment to HUT. This screening assessment simply requires the patient to stand for a short period of time following two-minutes of supine rest, alongside minute-by-minute recordings of heart rate, blood and pulse pressure changes (Roma, Marden, & Rowe, 2018). Whilst a handful of researchers have supported use of the Schellong test to provide a quick indication of whether the patient possesses an orthostatic intolerance disorder (Fanciulli, Campese, & Wenning, 2019), several studies have questioned the effectiveness of the test in comparison to HUT. Winker, Prager, Haider, Salameh & Rüdiger (2005) undertook a prospective study to compare the use of an active standing test and tilt table testing in 35 military personnel with symptoms of orthostatic intolerance and 32 military individuals without presenting symptoms. Whilst the researchers found a good level of specificity (100%) for both

the tilt table test and the Schellong test to reject a PoTS diagnosis in healthy controls, the Schellong test demonstrated a poorer rate of sensitivity in comparison to the HUT table assessment (Schellong Test= 61%; Tilt Table= 97%). Therefore, whilst the Schellong test may serve as a quicker and more cost-effective method for clinicians to examine patients' responses to orthostatic challenge, suspected cases of PoTS are recommended to be followed-up by table tilt examination to confirm that diagnosis is appropriate (Jungblut, Frickmann, Römer & Glifrich, 2006).

- *Valsalva Maneuver*

The Valsalva maneuver refers to a four-phase cardio-vagal response to the forced exertion of air through the patient's ears (Goldstein & Chesire, 2019). This effect can be produced by asking the patient to attempt to breathe out whilst keeping the mouth and nostrils closed, and also serves as a method of controlling episodes of tachycardia (Smith, Morgans & Boyle, 2009). Within PoTS diagnosis, Valsalva maneuver are used to assess the sympathetic and parasympathetic branch influences on the regulation of heart rate (Palamarchuk, Baker, & Kimpinski, 2015). The Valsalva maneuver can also examine the effects of hyperadrenergic PoTS as an underlying cause of patients' tachycardia, as the excessive level of norepinephrine associated with this PoTS subtype is associated with an over-activity of the sympathetic system (Shinbao et al., 2005). During phase four of the Valsalva technique when blood is returned back to the heart, approximately 50% of PoTS patients are known to demonstrate a characteristic overshoot in blood pressure (Low, Sandroni, Joyner & Shen, 2008). Patients also show an overly-decreased blood pressure response during phase two, where enhanced thorax pressure serves as a barrier to the blood entering the heart (Sandroni et al., 2000). Abnormal responses to the Valsalva Maneuver have been linked to reports of headache symptoms (Low, Sandroni, Joyner, Shen, 2008).

- *Other Diagnostic Assessments (Catecholamine Inspection; Quantitative Sudomotor Axon Reflex & Urine Sodium Levels)*

To assess whether the patient is showing a hyperadrenergic state, blood plasma samples (taken from both supine and upright positions) are analysed to see if norepinephrine levels exceed 600pg/ml during standing (Low et al., 2008). To assess for impairments in small fibre neurons (neuropathic PoTS), Quantitative Sudomotor Axon Reflex Testing [QSART] is utilised (Ashangari & Shuleman, 2015). The QSART consists of passing a small electrical current through the patient's sweat glands of the upper arm and lower leg to stimulate perspiration, with neuropathic patients presenting with reduced sweating in the lower limbs (Low et al.,

2008). Furthermore, clinicians may request that patients provide a urine sample to assess for evidence of co-occurring hypervolemia through checking the levels of sodium excreted (Zhang, Liao, Tang, Du, & Jin, 2012). Deconditioning is assessed through the patients' maximum oxygen consumption during short aerobic exercises (Joyner & Masuki, 2008).

2. PoTS Symptomology & Associated Conditions

PoTS is a multifaceted condition which features a wide range of differing and debilitating symptoms which vary from patient-to-patient (Raj, 2006). Alongside tachycardia, PoTS patients may present with episodes of fatigue, syncope, migraines, brain fog, sleep-related deficits, bodily pain, gastrointestinal symptoms and psychiatric symptoms (Mathias et al., 2012).

2.1 Fatigue in PoTS

An estimated 91% of PoTS patients who struggle with episodes of daily fatigue (Kavi et al., 2016). Fatigue can be described as a reduction in mental energy and lowered motivational state that is experienced by an individual for a sustained period of time (Shen, Babera, & Shapiro, 2006). Healthcare practitioners face a challenging task with helping their patients to manage this prevalent PoTS symptom (Strassheim, Welford, Ballatine, & Newton, 2018).

- *PoTS § Chronic Fatigue Syndrome (CFS)*

Several empirical works within the review subset concerned the exploration of PoTS patients who present with co-occurring Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis [CFS/ME]. CFS is characterised by UK NICE guidelines as the presence of persistent medically unexplained fatigue lasting a period of three months or more (Collin et al., 2018). The prevalence of CFS/ME has been approximated to a rate of 0.2% of individuals within the UK population (Nacul et al., 2011).

Patients with CFS/ME report a wide range of symptoms including difficulty with maintaining concentration/experiencing brain fog, muscle pain, regular migraines and reoccurring episodes of insomnia (Collin, Heron, Nikolau, Knoop & Crawley, 2018). There is a number of common elements between the presentation of CFS and PoTS. In a similar manner to PoTS, CFS onset has been linked to the post-recovery stage following a recent viral infection (Skufca, Ollgren, Ruokokoski, Lyytikäinen, & Nohynek, 2017). Additionally, CFS is also more commonly diagnosed within females (Jason, Porter, Hunnell, Rademaker, & Richman, 2011) and is associated with high levels of functional disability (Hadlandsmayth & Vywles, 2009). Orthostatic intolerance remains a common challenge for CFS patients, and in several cases it

is thought that these symptoms of autonomic dysfunction may be explained by the presence of an underlying PoTS diagnosis (Gardener & Baraniuk, 2019).

Past empirical works that have examined co-morbid PoTS-CFS diagnosis have attempted to distinguish the clinical presentation of patients with both of these conditions from those with PoTS or CFS/ME alone. Within a prospective study to explore the haemodynamic profile of both conditions, Okamoto et al. (2012) had 47 PoTS patients complete two questionnaire measures relating to fatigue and health-related quality of life before undergoing a thirty-minute standing test. Thirty participants (63%) met co-morbid CFS diagnostic criteria (PoTS-CFS group) whilst seventeen did not (PoTS-only). During the standing test, the co-morbid group demonstrated increased low-frequency blood pressure variations and greater concentrations of the enzyme renin in comparison to the PoTS-only patients. The PoTS-CFS patients also demonstrated a more abnormal response on the early-late phases of the Valsalva maneuver. These findings suggest that PoTS-CFS patients may possess increased levels of sympathetic nervous system activity in comparison to singular forms of each condition. Furthermore, whilst high levels of fatigue were prevalent amongst the PoTS patients who did not meet the criteria for CFS, it is also important to note that the researchers found scores on the physical functioning component of the Rand-36 Health Survey to be comparable amongst the two groups. This evidence has supported the notion that the co-morbidity of chronic fatigue symptoms may feature as part of a 'continuum' of PoTS symptoms presentation (Bennarroch et al., 2012). Therefore, PoTS-CFS should not be considered as a distinct clinical entity by itself, unlike hyper-adrenergic or neuropathic subtypes.

Further research has aimed to explore the association between CFS and PoTS, in addition to the clinical markers which are capable of differentiating patients who present with this co-morbidity. Lewis, Pairman, Spickett and Newton (2013) examined 179 CFS patients who were recruited primarily from specialised UK fatigue centres. During a standing test, 13% of the CFS patients were found to exhibit the characteristic orthostatic increase in heart rate of over 29 beats per minute that signified the presence of underlying PoTS co-morbidity. Additional comparative analysis between the CFS-PoTS patients and CFS-only individuals revealed that the co-morbid group were significantly younger, had lowered fatigue scores on the Chalder Fatigue Scale, and decreased depression component scores on psychometric measures. Whilst there were no significant differences between the two groups between their reported pain, cognitive impairment or functional domain scores on the SF-36; the CFS-PoTS group possessed greater daytime sleepiness and orthostatic intolerance symptom severities than the CFS-only group.

Crucially, Lewis et al. (2013) also found that the combination of Epworth Sleepiness Scale (a score of 9 or below) and the Orthostatic Grading Scale (a score of 9 or higher) were capable of uniquely identifying all patients within the CFS-PoTS group. This therefore suggests that

whilst the crossover between PoTS and CFS should not be treated as a unique clinical entity within itself; the early identification of this co-morbidity from simple psychometric assessments could encourage the more rapid diagnosis of both conditions. In light of recent evidence which has shown that the tilt-table test demonstrates a low sensitivity for identifying a PoTS diagnosis in CFS patients (Van Campen, Rowe, & Visser, 2018), the use of psychometric measures may therefore be a more effective and easily administered diagnostic tool.

Similar co-morbidity rates to those of Lewis et al. (2013) were identified by Reynolds, Lewis, Richardson and Lidbury (2014). Within a cohort study, Reynolds et al. (2014) had 306 patients referred to a specialised chronic fatigue clinic in Australia undergo a twenty-minute standing test, of which 35 patients (11%) were identified with PoTS. Whilst the finding that co-morbid patients are significantly younger than their CFS-only counterparts was replicated from Lewis et al. (2013), Reynolds et al. (2014) demonstrated that CFS-PoTS individuals also exhibit significantly lowered diastolic blood pressure during the first two minutes of the standing test and had a shorter CFS illness duration. During further logistical regression analyses of all 306 participants, both absolute average heart rate change, and heart rate change during the first two minutes of standing, were found to be significant predictors of determining which patients could complete the standing test. Variation in participant's perceived difficulty of the standing task could also be predicted by both absolute change in heart rate and female gender. As absolute heart rate change was used as a proxy measure of heart rate variability, these findings may indicate that autonomic dysfunction could serve as an underlying cause of patient's fatigue complaints in both CFS-PoTS and CFS-only patient groups (Reynolds et al., 2014). Nevertheless, further research which employs the use of more standardised measures of heart rate (such as an electrocardiogram) is needed to investigate this possibility further.

2.2. *Syncope*

PoTS patients may present with syncope (fainting) or pre-syncope (dizziness/black-out) during periods of orthostatic challenge (Deb, Morgenshtern, Culbertson, Wang & Hohler, 2015). Neuro-cardiogenic syncope refers to the short-term loss of consciousness that occurs following momentary decreases in blood pressure (Chen-Scarabelli & Scarabelli, 2004); whilst pre-syncope is defined as an experience of dizziness, light-headedness and/or blackout which is accompanied by a drop in blood pressure without a loss of consciousness (Mathias, Deguchi, & Schatz, 2001). In several cases, neuro-cardiogenic syncope can result from issues surrounding blood vessel constriction and dilation processes (Hainsworth, 2003). During an episode of syncope, the activity of the parasympathetic branch (vagal tone) is heightened whilst the influence of sympathetic activity over bodily functions is damped by the brainstem (Zaqqqa & Massumi, 2000).

- *Does Syncope in PoTS Differ to Orthostatic Intolerance?*

Although syncope is a common occurrence within disorders of orthostatic intolerance, there is evidence to suggest that PoTS patients may be at higher risk of experiencing fainting in comparison to other related conditions (Ohja et al., 2010). This is thought to be due to differences relating to the pressure of the baroreceptor system between the two conditions, which is responsible for regulating the maintenance of blood flow and pressure throughout the body (Ohja et al., 2010; Abed, Ball & Wang, 2012). Not all patients who are diagnosed with PoTS experience syncope, and for those individuals who are prone to fainting, the frequency and degree of debilitation of this symptom varies from person-to-person. Whilst further large PoTS cohort studies are needed, it has been estimated that up to 30-38% of patients have regular episodes of syncope (Raj, 2006; Ohja et al., 2010), with an estimated 32% syncope prevalence for children diagnosed with the condition (Ohja, Chelimsky, & Chelimsky, 2011). Evidence from a retrospective chart review of 18 PoTS individuals with presenting syncope found that patients exhibited an undetectable trace of the heart rate (asystole) during syncope which persisted between 10-32 seconds (Kanjwal, Sheik, Karabin, Kanjwal, & Grubb, 2011).

- *Examining the Hemodynamic Response to Syncope in PoTS*

Early research from a prospective study by Sandroni, Opfer-Gehrking, Bennarroch, Shen and Low (1996) has explored the underlying cardiovascular mechanisms which differentiated PoTS patients who fainted and patients who did not during HUT. Sandroni et al. (1996) found that individuals who passed out during tilt demonstrated reductions in total peripheral resistance, pulse pressure, systolic and diastolic arterial blood pressure. A further prospective-design study by Diehl, Linden, Chalkiadaki, and Diehl (1999) expanded on the findings of Sandroni et al. (1996) by comparing seven syncope-presenting PoTS against non-PoTS syncope-presenting individuals. During the start of tilt, PoTS patients demonstrated both continuous reductions in cerebral blood flow volume and developed syncope at a significantly quicker mean rate than the syncope-only group (10.6-minutes vs. 16.6-minutes); these episodes were accompanied by sudden decreases in heart rate, arterial blood pressure and further drops in cerebral blood flow volume. Diehl et al. (1999) concluded that syncope in PoTS is linked with a gradual rise in the resistance to the blood flow within the brain during orthostatic challenge. Furthermore, this increased cerebrovascular resistance may result from an abnormal activity of the muscle-sympathetic nerves within PoTS patients – these neurons are known for their involvement in the constriction of blood vessels (Muentner Swift, Chakoudian, Dotson, Suarez, & Low, 2005).

- *Comparing Syncope in PoTS to Vasovagal Syncope*

Several prior studies have aimed to examine the diagnostic and symptomatic discrepancies between PoTS-related syncope and vasovagal syncope (Lambert & Lambert, 2014). Vasovagal syncope is a type of neuro-cardiogenic syncope where fainting occurs due to an overwhelming emotional response, prolonged standing or upon the sight of disgust-provoking stimuli (Owens, Low, Critchley, & Mathias, 2017). Differentiating between PoTS and vasovagal syncope can prove to be a diagnostic challenge for physicians, yet this remains crucial for ensuring that patients are provided with the most suitable treatment plan (Raj & Sheldon, 2016). Due to this, clinicians need to carefully examine the patient's clinical history before performing a HUT tilt test and should also consider conducting further physiological assessments in order to discriminate between the two diagnoses (Anderson & Willis, 2017). Prior works have focussed on aiding this process by examining the unique underlying cardiovascular properties and symptomology associated with each condition. This includes findings that PoTS patients demonstrate a 32% greater reduction in systolic blood flow than vasovagal-only individual prior to syncope occurrence (Hermosillo et al., 2006). Furthermore, PoTS patients have also been shown to possess higher levels of norepinephrine release than vasovagal-only patients (Goldstein et al., 2002) and increased psychiatric co-morbidity (Owens et al., 2017). In relation to adolescent patients, individuals with PoTS have recently been shown to possess greater levels of blood plasma hydrogen sulphide (Zhang et al., 2012) and unique heart-rate variabilities [daytime ultra-low frequency] (Wang, Zhang, Chen, Jin, & Du, 2019) in comparison to vasovagal syncope children, suggesting these findings could be used to differentiate the type of syncope. Nevertheless, further work is needed to expand on current diagnostic methods and to develop non-invasive techniques for correctly determining the presence of PoTS or vasovagal syncope in younger patients (Wang, Du, & Jin, 2019).

2.3. *Brain Fog & Impaired Cognitive Functioning*

Mental cloudiness (brain fog) is also a common symptom of PoTS which refers to a reduced state of general 'awareness' and difficulty with concentration (Ocon, 2013). Brain fog symptoms are exacerbated in patients by tiredness, poor sleep and dehydration (Ross, Medow, Rowe, & Stewart, 2013). Experiences of mental cloudiness have been linked to the possession of inattention traits associated with ADHD measures, which PoTS patients are known to score highly on (Raj et al., 2009). Neuro-cognitive assessments have been employed in PoTS research to examine the neural explanations behind brain fog and the impact of these symptoms on an individual's cognitive ability during orthostatic challenge [for a tabular summary, see Appendix_E].

A number of prior studies have assessed patients' cognitive functioning through the use of working memory assessments. During five angles of incremental tilt, Stewart et al. (2012) compared the performance of 25 patients diagnosed with co-morbid PoTS & chronic fatigue syndrome against 20 healthy controls on a four-stage n-back task. During this working memory test participants are presented with a changing set of integers, and are asked to recall whether or not the number or letter presented to them on each trial matched the digit which they had been shown four sequences ago (Mackworth, 1959). Whilst the performance and response time between the two groups was not found to significantly differ within the supine condition; PoTS patients demonstrated significantly longer reaction times and reduced correct responses for each level of the n-back task within each of the tilted conditions. Changes in patients' cerebral blood flow volume were however found to be unrelated to their task performance during tilt. As a result, Stewart et al. (2012) were unable to establish the neurological mechanisms which account for cognitive deficits in PoTS and mental cloudiness. Nevertheless, the methodology of Stewart et al. (2012) was criticised by Ocon et al. (2012) for failing to control for other factors which are known to influence changes in cerebral blood flow, such as age, gender and end tidal carbon dioxide. In response to this, Stewart et al. (2015) conducted a further study to assess changes in cerebral blood flow volume during a cognitive task. During this, the authors also examined neurological coupling - a term which refers to specific changes in the blood flow to active tissues (hyperaemia) - in order to ensure sufficient neurological resources for completing cognitively demanding tasks (Wells et al., 2019). In comparison to healthy age and gender matched controls, PoTS patients displayed decreased n-back task accuracy on non-supine testing angles and were also found to display decreased functional hyperaemia during the n-back task. This evidence suggests that brain fog may be underpinned by the interplay of changes in cerebral blood flow during orthostatic challenge and reduced hyperaemia. Nevertheless, the authors outline that further neurological works remain crucial for establishing causal links between these mechanisms and brain fog.

Further research has explored the performance of patients on other cognitive domains and how their functioning relates to psychiatric symptomology. Anderson et al. (2014) had patients undertake a battery of neuro-cognitive tests (during tilt) to assess their performance on verbal IQ, non-verbal IQ, full scale IQ and a digit span task, in addition to a quality-of-life measure and a structured clinical interview to assess depression and anxiety co-morbidity. PoTS patients were found to perform significantly worse than a control group on all examined cognitive and affective domains. Furthermore, post-hoc regression analyses indicated that participants' performance on each of the cognitive tasks could be predicted by their scores on the depression and anxiety measures, in addition to the number of years they had spent in education. From their findings, Anderson et al. (2014) argue that treatment plans for the

management of PoTS would benefit from the addition of psychosocial interventions (a topic further explored in sub-section 2.5).

2.4. Sleep in POTS

Several empirical research studies have explored the effects of a PoTS diagnosis in relation to sleep-related parameters (see Appendix_F for a tabular summary). Findings have shown that in comparison to healthy controls, people with PoTS exhibit significantly worse sleep latency scores on psychometric measures and report greater morning tiredness (Bagai et al., 2013). Prior researchers have argued that specific PoTS interventions, those which can subdue the increased flight-or-flight response in PoTS, may also be capable of reducing the frequency of insomnia episodes in this patient group (Bagai et al., 2013; Bagai et al., 2016; Pederson & Brook, 2017).

The need to identify a treatment for sleep quality remains highly important in PoTS patients. Recently, Pederson & Brook (2017) recruited 705 adult PoTS patients through an online survey method where participants were required to complete the Pittsburgh Sleep Quality Index (PSQI) and the revised Suicidal Behaviours questionnaire. Notably, PoTS patients were found to possess significantly higher suicidal ideation scores than healthy controls ($n = 170$). The conduct of further regression analysis indicated that patients' suicide ideation scores could be predicted by poorer sleep scores on the (PSQI), age and illness due to PoTS. In light of these findings, Pederson & Brook (2017) state that health care providers should prioritise the treatment of sleep quality issues within PoTS patients in an effort to decrease suicide risk.

2.5. Functional Disability & Psychiatry Co-Morbidity

Notably, one in four PoTS patients are registered as disabled and are unable to work or attend schooling (Grubb, 2008). Functional disability in PoTS is also associated with sensations of bodily pain, which can arise from co-morbid physiological conditions such as fibromyalgia (Staud, 2008). Whilst prior research into PoTS has primarily examined patients' physical and mental functioning components on health-related quality of life measures (Anderson et al., 2014) these studies have also aimed to identify the factors which determine PoTS-related functional disability in order to identify treatment targets for intervention development.

Within a between-subjects design, Benrud-Larson et al. (2002) recruited 113 patients diagnosed with PoTS. Participants were required to complete the SF-36 questionnaire and the autonomic symptom severity scale. In comparison to a healthy control group, PoTS patients were found to show significant levels of impairment across all six domains of the health-related quality of life measure. Within the PoTS group, patients' autonomic symptom

severity and level of disability were found to significantly contribute to their physical functioning scores; no significant variables were identified for the prediction of mental functioning component scores within the group however. A path analysis within a follow-up study, found that participants' experiences of catastrophic cognitions, in addition to their scores on somatic vigilance, anxiety sensitivity and neuroticism measures, were all identified as correlates of functional disability within the PoTS adult sample (Benrud-Larson et al., 2013). These findings have supported the notion that psychological symptoms are key predictors for determining both the capabilities of those experiencing PoTS, and that these factors are key targets for treatment of functional disability within this condition (Junghans-Rutelonis et al., 2018).

Further studies have explored the predictors of functional disability within children diagnosed with PoTS. Within a retrospective analysis of 99 adolescents with various orthostatic intolerance disorders (including PoTS), patients' functional disability was found to be predicted only by their depression symptomology and pain severity (Kritzberger et al., 2011). Interestingly, neither participants' orthostatic heart rate change on the HUT, nor their orthostatic symptom severity, were found to significantly correlate with their functioning status. Nevertheless, further research has demonstrated that positive relationships do exist between PoTS adolescent patients' orthostatic symptom burden and both their levels of depression severity and poor quality of life scores (Moon et al., 2016). In light of these findings, this evidence therefore hints towards the existence of an indirect relationship between PoTS symptom burden and functional disability, whereby patients' levels of functioning are mediated by their underlying psychiatric co-morbidity (McTate & Weiss, 2015). To further examine this possibility, further research, which employs the use of mediation analysis and larger patient samples, are needed to fully assess this conclusion. Research is also needed to examine whether PoTS symptoms within adult populations directly correlates with their functional disability scores.

3. PoTS Co-Morbidities

PoTS commonly presents in patients with other diagnosed illnesses and chronic conditions (Benarroch, 2012). For example, gastrointestinal symptoms associated with PoTS such as bloating, constipation and diarrhoea may be due to a co-morbid irritable bowel syndrome (Wang, Culbertson, Deb, Morganshtern, Huang & Hohler, 2015). PoTS is often reported in patients with Mast Cell Activation Syndrome [MCAS], a disorder associated with abdominal pain, nausea and vomiting (Bonamichi-Santos, Yoshima-Kanamori, Giavina-Bianchi, & Aun, 2018). Individuals with MCAS are known to possess an abnormally high levels of mast cells within their bodies – these immune cells are involved in the allergic response and are known to produce the chemical histamine for vasodilation processes (Valent et al., 2001). MCAS has been suggested as a possible explanation to account for episodes of skin flushing which

occurs in a number of PoTS patients, particularly those who possess high levels of noradrenaline (Shibao et al., 2005).

- *PoTS § Ehler-Danlos Syndrome*

PoTS also has a high association with the heritable disorder Ehler-Danlos Syndrome [EDS] (Wallman, Weinberg, & Hohler, 2014). Patients with EDS possess a genetic mutation within their bodies' connective tissue(s) such as collagen. This mutation results in pathological changes to the individual's muscle joints, skin tissue and blood vessels linings (Nuytinck et al., 2000). There are thirteen known distinct subtypes of EDS, and each form of the condition is thought to be dependent upon the type(s) of genetic mutation that has occurred in the individual (Kohn & Chang, 2020). Whilst each subtype presents with a similar range of symptoms across the patient's skin and muscle joints, the severity and daily impact of the condition varies by the specific EDS form (Voermans, Knoop, Bleijenberg, & van Engelen, 2010).

In relation to co-morbid PoTS, research has focused on one common form of EDS, hypermobile-EDS [hEDS], as a cause of the dysautonomia and orthostatic symptoms that are experienced in this condition (Celletti et al., 2017). The hEDS-POTS subtype is characterised by muscle joint hypermobility, frequent dislocation and pain, fatigue, skin bruising, gastrointestinal symptoms and fatigue (Castori, Sperduti, Celletti, Camerota, & Grammatico, 2011). Within a prospective study of eighty hEDS patients, de Wandele et al. (2016) identified PoTS within 41% of individuals during a tilt-table test. Findings also indicated that hEDS-PoTS daily fatigue severity could be predicted by their patients' response to the tilt-table test, in addition to their reported orthostatic symptomology. This therefore suggests that sensations of low motivational states and a lack of energy reported in hEDS patients may be associated with their PoTS co-morbidity.

Miglis, Schultz, & Muppidi (2017) compared twenty hEDS patients, diagnosed with co-morbid PoTS, against a control group of twenty PoTS-only individuals on various autonomic tests (including HUT and QSART). The authors also examined each group's use of the healthcare services alongside other information obtained from the patients' medical records. Whilst the hEDS-PoTS patients demonstrated similar results on the autonomic assessments to the PoTS-only group; trends in the data suggested that the co-morbid group may have possessed lower heart rate variability and decreased blood pressure on the HUT test. hEDS-PoTS patients were also more likely to be prescribed with a greater number of pharmacological agents to manage their condition(s), and to visit their healthcare professionals more frequently to discuss their sensations of pain. This is in line with prior grounded theory research that has been conducted in relation to EDS, where patients related their experience of daily pain as a

cause of them living with a “restrictive” lifestyle (Berglund, Nordstrom, & Lutzen, 2000). Within this qualitative study, EDS participants felt that even after they had attended multiple GP visits healthcare practitioners were unlikely to understand the extent of their pain, and the patients felt that their clinicians were quick to dismiss their complaints as being ‘psychogenic’ in nature.

4. Discussion

4.1. Clinical Implications for PoTS Drawn from Narrative Synthesis

In light of the review of PoTS diagnostic and symptomology literature within this chapter, it remains clear that the identification and management of PoTS in clinical practice remains a challenging task for clinicians to undertake (see Table 1).

Table 1. Identified clinical implications drawn from the narrative synthesis of collated PoTS diagnostic and symptomology literature within the undertaken scoping review.

Identified Clinical Implications
<ul style="list-style-type: none"> ▪ Healthcare Practitioners who treat patients should primarily consider all underlying complaints which are worsening each patient’s PoTS– avoid attempts to “categorise” the individuals with a singular, specific PoTS subtype. ▪ Primary care clinicians can use the Schellong active standing test as a simplistic, “quick” method of assessing patients who present with symptoms common in PoTS. ▪ Patients who fail or show difficulty with completing an active stand should be referred to a specialised cardiology or autonomic medical centre for follow-up tilt-table testing, to confirm their diagnosis. ▪ PoTS-CFS should not be considered as a distinct clinical entity, unlike hyperadrenergic or neuropathic subtypes of the condition. ▪ Clinicians should not rely on the use of tilt-table testing alone to identify the presence of PoTS in CFS patients- due to its low sensitivity in the latter population for identifying PoTS. ▪ Diagnosis of co-morbid PoTS & CFS in a patient should be supported by the use of psychometric measures– such as the combination of Epworth Sleepiness Scale (a score of 9 or below) and the Orthostatic Grading Scale (a score of 9 or higher). ▪ In order to differentiate PoTS from vasovagal syncope, clinicians need to carefully examine the family history of the patient prior to them undergoing a tilt-table test. ▪ Co-morbid psychiatric diagnoses and greater levels of norepinephrine release can be used to help support a diagnosis of PoTS over vasovagal syncope. ▪ Clinicians should consider assessing adolescent patients’ hydrogen sulphide blood plasma levels & daytime ultra-low frequency heart-rate variabilities to distinguish between a diagnosis of PoTS or vasovagal syncope for those present with recurring fainting.

In order to accurately identify and manage PoTS within clinical practice, it is recommended that healthcare professionals try to view the patients’ condition holistically and consider all pressing underlying issues which may be exacerbating the patients’ symptoms (Raj et al., 2020). Furthermore, whilst an active standing test can be used by a primary care physician to

support the working suspicion of PoTS or an orthostatic intolerance condition- patients who struggle with this assessment need to be referred to a specialised cardiology or autonomic medical centre for tilt-table test examination, before a PoTS diagnosis can be formally made for the individual (Jungblut et al., 2006). Whilst the use of tilt-table testing alone can serve as an effective method of identifying the presence of PoTS, healthcare professionals need to consider using this diagnostic method in conjunction with other tools to accurately distinguish PoTS from other related-conditions. This includes the use of certain psychometric measures to assess for co-morbidity with CFS (Pairman et al., 2013), and the examination of norepinephrine release (Goldstein et al., 2002), family history and psychiatric diagnoses (Anderson & Wallis, 2017) in the individual to support the differentiation of a PoTS diagnosis from that of vasovagal syncope. It may also prove fruitful to distinguish PoTS and vasovagal syncope in adolescents by examining patients' levels of hydrogen sulphide in the blood plasma and their unique heart-rate variabilities during testing (Zhang et al., 2012; Wang et al., 2019).

4.2. Advancing Knowledge of PoTS Symptoms - Identified Literature Gaps in the Research Field

Within the review, I highlighted that people with PoTS experience a wealth of highly debilitating symptoms, such as burdensome fatigue, rapid syncope onset and cognitive impairments during orthostatic challenge (Raj, 2009). Further to this, my review identified that prior empirical works which have examined PoTS symptomology have mainly focused on both identifying the prevalence of individual PoTS symptoms across the patient cohort (Kavi et al., 2016), and the study of orthostatic-induced symptom worsening, through comparative analysis of patients' capabilities on psychometric assessments within supine and upright postures (Anderson et al., 2014). These highly debilitating symptoms are known to contribute towards the poor psycho-social outcomes in PoTS patients that have been widely reported within the literature including poor functional abilities (Mathias et al., 2014), reduced quality of life (Benrud-Larson et al., 2013) and heightened risk of experiencing suicide ideation (Pederson & Brook, 2017).

Nevertheless, whilst a link exists between these poor outcomes and PoTS symptomology; currently, there is a lack of knowledge within the PoTS research area which has explored what experiences and understandings people with PoTS draw from their own illness experiences. Within other related conditions, such as EDS (Berglund et al., 2000), these lines of studies benefit researcher and practitioners' understandings through the comprehension of how the daily experience of persistent physical symptoms are responsible for resultant impacts on patients' psychological wellbeing and everyday struggles of managing their bodily complaints.

As I identified within chapter 2, the absence of symptoms experience studies in PoTS, currently only explored by Waterman et al. (2021), is likely due to a lack of qualitative research methodology adoption throughout the PoTS research field. This finding is also supported within the evidence map undertaken by Eftekhari et al. (2020), where only quantitative empirical studies were identified during screening. Due to this finding and the need to further examine these critical areas of importance in PoTS research, within chapters 5 and 6 of this thesis I outline how I undertook a narrative analysis of online video stories (recorded by people with PoTS) to examine the diagnostic and symptoms experiences described by those living with this debilitation condition.

4.3. Implications of Narrative Synthesis for PoTS Intervention Development Work

In addition to further qualitative research that is necessary for exploring people with PoTS experiences of their symptoms, these recommendations also highlight the importance of identifying appropriate interventions that are needed to address and improve the poor psychosocial outcomes commonly reported within this patient group. In addition to reduced quality of life and heightened suicidal ideation scores (Pederson & Brook, 2017), the review also highlighted that people with PoTS report issues sleep-related deficits and struggles with insomnia (Bagai et al., 2013; Miglis, Schultz, & Muppidi, 2017; Xu et al., 2016). Despite this, as I will further outline within chapter 4, non-pharmacological interventions remain limited in scope for PoTS with many currently existing non-medicine symptom management strategies lacking robust RCT studies and a strong evidence-base to support their use (Eftekhari et al., 2020; Raj et al., 2020).

Additionally, it is worth noting that evidence exists to demonstrate that commonly used PoTS medications in the literature may also be insufficient for managing these complaints, with some having been associated with a negative impact on sleep-related outcomes in this patient group. Xu et al. (2016) found that PoTS patients who were taking fludrocortisone were more likely to encounter difficulty with falling asleep, whilst pyridostigmine users reported significantly greater dissatisfaction with their sleep than non-pyridostigmine prescribed patients. This finding therefore demonstrates the importance of identifying and carefully select novel, non-pharmacological interventions for management of the range of issues people with PoTS face. As recommended by PoTS sleep researchers, these techniques should be capable of improving sleep symptoms through the subduing of patients' increased sympathetic responses (Bagai et al., 2013; Bagai et al., 2016; Pederson & Brook, 2017).

Within chapter 1, I previously outlined the use of pranayama breathing techniques as the primary format for PoTS intervention development, due to these practices' perceived

capabilities for soothing autonomic activity within their literature base (Jerath et al., 2015). Whilst I discuss this further within my intervention development work (see chapter 8, for rationale and methodology), these types of interventions have previously been found to have beneficial actions on sleep-related outcomes and quality of life (Chaudari, Chaudari, Rankhambe, Kochupillai & Tiwari, 2021; Yüce, & Taşçı, 2020). Thus, the findings of my narrative synthesis of PoTS symptomology literature therefore lends further accreditation to the applications and development of a breathing techniques for a PoTS patient group.

4.4. *Conclusion*

In conclusion of chapter 3, the synthesis of diagnostic, symptomology and comorbidity literature enabled identification of clinical implications to be drawn which could assist practitioners with the difficulties they may encounter with diagnosing and managing of PoTS in clinical practice. Within the next chapter of the thesis, I conclude my scoping review work of the PoTS literature through the presentation of findings gathered from the tabular and narrative collation of empirical works on PoTS treatment studies, for both non-pharmacological and pharmacological intervention types.

- Chapter 4: Synthesis of Empirical Literature of Existing PoTS Treatments -

This chapter continues the exploration of the PoTS literature, identified through the scoping review sample (see Chapter 2, for methodology), and provides a narrative synthesis of empirical research on the exploration of the treatments for the management of patients' symptomology. This chapter first provides an overview of the commonly used non-pharmacological methods, such as those which work through adapting the patient's lifestyle or improving their understanding of living with this chronic condition. My findings highlight that there is currently only a limited number of these existing intervention types available for PoTS, with a mixed evidence base to support their use. Following this, empirical studies of a wide variety of medication-based treatments – which primarily focus on controlling PoTS Symptoms through reducing tachycardia episodes, raising blood volume and the contracting of blood vessels - are reviewed. These studies show that whilst propranolol and midodrine use in PoTS has been widely supported by empirical literature within PoTS; other types of 'off-label' PoTS medications currently lack a strong evidence base and require higher-quality studies & evidence synthesis to support their applications. The chapter closes by outlining the need for additional, new PoTS-interventions to be developed in order to further support people with PoTS self-management of their condition.

1. Exploration of Empirical Works on PoTS Treatments

PoTS remains a challenging condition for the clinician to address due to the condition's varying and diverse presentation (Raj & Miller, 2018). Through tabular examination undertaken within my scoping review, I identified 80 empirical research articles in the final review subset which had examined interventions with PoTS patients (see *Table 1*).

Table 1. Tabular Extraction of Empirical Studies identified within final Scoping Review Article Subset which include examination of a Non-Pharmacological and/or Pharmacological PoTS intervention. N = 80.

Author(s)	Intervention	Study Design	Sample Type	Number of Recruited PoTS Patients	Physiological Measures	Non-Physiological Measures
Sandroni et al. (1999)	Salt Supplementation, Beta-Blockers	Cross-Sectional	Adult	40	-	Orthostatic Symptom Measure, Functional Ability, Employment Status
Freitas et al. (2000)	Bisoprolol, Fludrocortisone	Case-Control	Adult	11	Heart Rate, Blood Pressure	-
Gordon et al. (2000)	Clonidine, Propranolol, Phenobarbital, Midodrine, Saline	Non-Randomised Control Trial	Adult	21	Heart Rate, Blood Pressure	PoTS Symptoms Measure
Shen et al. (2001)	Sinus Node Modification	Non-Randomised Control Trial	Adult	7	Heart Rate	Autonomic Symptom Measure
Stewart, Munoz & Weldon (2002)	Phenylephrine, Esmolol	Non-Randomised Control Trial	Child/Adolescent	14	Heart Rate & Blood Pressure Variability, Peripheral Blood Flow, Arterial Resistance	-
Raj et al. (2005)	Pyridostigmine	Randomised Control Trial (Crossover)	Adult	17	Heart Rate, Blood Pressure	PoTS Symptoms Measure
Hoeldtke et al. (2006)	Octreotide, Midodrine	Non-Randomised Control Trial	Adult	9	Heart Rate	Standing Time
Hoeldtke et al. (2007)	Octreotide	Non-Randomised Control Trial	Adult	7	Heart Rate; Blood Pressure	Fatigue, Dizziness Symptoms

Masuki et al. (2007a)	Exercise (Graded Cycling)	Non-Randomised Control Trial	Adult	13	Heart Rate, Arterial Pressure	-
Masuki et al. (2007b)	Exercise (Graded Cycling)	Non-Randomised Control Trial	Adult	13	Heart Rate, Arterial Pressure, Stroke Volume	-
Mayuga, Butters & Fouad-Tarazi (2008)	Angiotensin-Receptor Blocker	Retrospective Chart Review	Adult	190	Heart Rate, Blood Volume	-
Stewart et al. (2008)	Losartan	Randomised Control Trial	Adult	12	Blood Flow (in Calf)	-
Raj et al. (2009)	Propranolol	Randomised Control Trial (Crossover)	Adult	54	Heart Rate, Blood Pressure	PoTS Symptoms Measure
Safder et al. (2009)	Fludrocortisone	Retrospective Chart Review	Child/Adolescent	59	-	Orthostatic Intolerance Symptom Measure
Z'Graggen et al. (2010)	Fluid Intake	Randomised Control Trial (Crossover)	Adult	7	Heart Rate	-
Chen et al. (2011)	Midodrine, Metoprolol	Randomised Control Trial	Child/Adolescent	53	-	PoTS Symptoms Measure
Galbreath et al. (2011)	Exercise Programme (3-Months)	Non-Randomised Control Trial	Adult	17	Heart Rate Variability; Blood Pressure Variability	-
Kanjwal et al. (2011a)	Pyridostigmine	Retrospective Chart Review	Adult	203	Heart Rate; Blood Pressure	Orthostatic Intolerance Symptoms, Frequency of Tachycardia, Fatigue Episodes
McDonald, Frith & Newton (2011)	Ivabradine	Retrospective Chart Review	Adult	20	-	Orthostatic Intolerance
Sukul, Chelimsky & Chemlimsky (2011)	Beta-Blockers	Retrospective Chart Review	Child/Adolescent	100	-	Orthostatic Intolerance

						Symptom Measure
Fu et al. (2011)	Propranolol, Exercise Training	Randomised Control Trial	Adult	19	Heart Rate, Stroke Volume, Aldosterone: Renin Ratio	Health-Related Quality of Life
Zhang et al (2012a)	Midodrine	Randomised Control Trial	Child/Adolescent	57	Pro-Adrenomedullin (within Blood Plasma)	-
Zhang et al. (2012b)	Salt-Supplementation	Randomised Control Trial	Child/Adolescent	30	24 Hour Sodium Secretion	POTS Symptom Measure
Coffin et al. (2012)	Desmopressin	Randomised Control Trial	Adult	30	Heart Rate, Blood Pressure	Vanderbilt Orthostatic Symptom Score
Kanjwal et al. (2012a)	Methylphenidate	Retrospective Chart Review	Adult	24	-	Frequency of Syncope, Fatigue, Presyncope
Kanjwal et al. (2012b)	Octreotide	Retrospective Chart Review	Adult	5	Blood Pressure	Syncope, Fatigue, Palpitations Episodes
Kanjwal et al. (2012c)	Erythropoietin	Retrospective Chart Review	Adult	39	-	Orthostatic Intolerance Symptoms
Shibata et al. (2012)	Exercise Training	Randomised Control Trial	Adult	19	Stroke Volume, Exercise Capacity (VO2 Max), Heart Rate	-

Mustafa et al. (2012)	Angiotensin Infusion	Non-Randomised Control Trial	Adult	15	Aldosterone: Renin Ratio; Urine Sodium Excretion; Arterial Pressure; Renal Plasma Flow; Baroreflex Sensitivity	-
Yang et al. (2013)	Midodrine	Randomised Control Trial	Child/Adolescent	28	Erythrocytic H2S Levels	-
Liao et al. (2013)	Midodrine	Randomised Control Trial	Child/Adolescent	108	Heart Rate, Flow-Mediated Vasodilation	PoTS Symptoms Measure
Arnold et al. (2013)	Propranolol, Metoprolol	Randomised Control Trial	Adult	11	Heart Rate, Stroke Volume, Exercise Capacity (VO2 Max)	-
Zhang, Chen, Li & Du (2014)	Metoprolol	Non-Randomised Control Trial	Child/Adolescent	27	Norepinephrine Levels (within Blood Plasma)	-
Zhao et al. (2014a)	Metoprolol	Randomised Control Trial	Child/Adolescent	49	Copeptin (within Blood Plasma)	-
Zhao et al. (2014b)	Midodrine	Non-Randomised Control Trial	Child/Adolescent	33	Copeptin (within Blood Plasma)	-
Deng et al. (2014)	Midodrine	Retrospective Chart Review	Child/Adolescent	104	Blood Pressure	-
Green et al. (2014)	Melatonin	Randomised Control Trial	Adult	78	Heart Rate, Blood Pressure	PoTS Symptoms Measure
Kpaeyeh et al. (2014)	Modafinil	Randomised Control Trial (Crossover)	Adult	45	Blood Pressure	PoTS Symptoms Measure
Mar et al. (2014)	SSRI (Sertraline Hydrochloride)	Randomised Control Trial (Crossover)	Child/Adolescent	39	Heart Rate, Blood Pressure	-

McDonald et al. (2014)	Beta-Blockers, Ivabradine, Diltiazem, Verapamil, Fludrocortisone, Midodrine, Octreotide, Clonazepam, Antidepressant, Salt Only	Cross-Sectional	Adult	136	-	Fatigue Severity, Daytime Sleepiness, Cognitive Functioning, Autonomic Symptom Burden, Functional Impairment, Anxiety & Depression Scores (HADS)
Nwazue et al. (2014a)	Propranolol, Atropine	Non-Randomised Control Trial	Adult	48	Heart Rate	-
Nwazue et al. (2014b)	"Placebo"-only	Randomised Control Trial (Crossover)	Adult	21	Heart Rate, Blood Pressure	-
Ross et al. (2014)	Midodrine	Randomised Control Trial (Crossover)	Adolescent & Young Adult	20	Heart Rate, Calf Blood Flow, Mean Arterial Pressure, Calf Vascular Resistance	-
Figueroa et al. (2014)	Salt Supplementation	Non-Randomised Control Trial	Adult	19	Exercise Capacity (V02 Peak), Stroke Volume, Cardiac Output	-
Barzilai & Jacobs (2015)	Ivabradine	Non-Randomised Control Trial	Adult	8	Heart Rate Variability; Blood Pressure Variability	-
Lin et al. (2015)	Metoprolol	Non-Randomised Control Trial	Child/Adolescent	34	Plasma C-Type Natriuretic Peptide	-

Sheehy et al. (2015)	Ketamine	Longitudinal Observational Cohort	Child/Adolescent	6	-	Pain Scores (Numeric Rating Scale)
Gamboa et al. (2015)	Impedance Threshold Device	Randomised Control Trial (Crossover)	Adult	26	Heart Rate, Stroke Volume	-
Fortunato et al. (2016)	HIRREM Neurotechnology Device	Non-Randomised Control Trial	Child/Adolescent	7	Heart Rate Variability, Temporal Lobe Electrical Activity	-
Li et al. (2016a)	Salt Supplementation (Intravenous Saline), Patient Education	Non-Randomised Control Trial	Child/Adolescent	45	Baroreflex Sensitivity, Heart Rate	-
Li et al. (2016b)	Oral Rehydration Solution (Fluid Intake)	Randomised Control Trial	Child/Adolescent	54	-	Body Mass Index, PoTS Symptom Measure
Lu et al. (2016)	Physical Therapy - Including Orthostatic Training, Skin Rubbing, and Belly Movements	Randomised Control Trial	Child/Adolescent	40	QT Interval	PoTS Symptom Measure
McTate & Weiss (2016)	Intensive Pain Rehabilitation Programme	Non-Randomised Control Trial	Adolescent & Yong Adult	79	-	Functional Ability, Depression Scores, Pain Scores, Perfectionism Scores, Anxiety Scores
Moak et al. (2016)	Intravenous Hydration	Retrospective Chart Review	Adolescent & Yong Adult	24	-	Quality of Life, Frequency of Side Effects
Bruce et al. (2016)	Interdisciplinary Therapy (including Cognitive Behavioural Therapy,	Non-Randomised Control Trial	Child/Adolescent	33	-	Functional Impairment, Depression Scores, Anxiety

	Occupational Therapy, Physical Therapy, Relaxation Techniques)					Scores, Pain Scores
Ruzieh et al. (2017a)	Droxidopa	Retrospective Chart Review	Adult	37	-	Orthostatic Intolerance Symptom Measure, Frequency of Side Effects
Ruzieh et al. (2017b)	Ivabradine	Retrospective Chart Review	Adult	49	Heart Rate, Blood Pressure	-
Ruzieh et al. (2017c)	Intravenous Hydration, Intravenous Saline	Non-Randomised Control Trial	Adult	57	-	Orthostatic Symptom Measure, Health-Related Quality of Life
Freedenberg et al. (2017)	Mindfulness-Based Stress Reduction	Randomised Control Trial	Child/Adolescent	22	-	Anxiety, Depression, Stress Scores
Kluck et al. (2017)	Intensive Pain Rehabilitation Programme	Non-Randomised Control Trial	Child/Adolescent	83	-	Pain Scores, Functional Disability Inventory
Lin et al. (2017)	Sleep-Promoting Programme	Non-Randomised Control Trial	Child/Adolescent	40	Salivary Cortisol Concentrations	Sleep Quality
Lu et al (2017)	Oral Rehydration Salts	Non-Randomised Control Trial	Child/Adolescent	35	Heart Rate, Mean Corpuscular Haemoglobin Concentration	-
Roerink et al. (2017)	Cognitive Behavioural Therapy	Longitudinal Observational Cohort	Adult	80	-	Fatigue Symptom Score

Boris & Bernadzikowski (2018a)	Fludrocortisone, Midodrine, Desmopressin, Metoprolol, Pyridostigmine, Erythromycin, Duloxetine, Clonidine	Retrospective Chart Review	Child/Adolescent	708	-	Frequency of Light-Headedness, Headache, Nausea, Dysmotility, Insomnia, Pain Scores
Donne et al. (2018)	Ivabradine	Retrospective Chart Review	Child/Adolescent	22	Heart Rate	PoTS Symptoms Measure
Moon et al. (2018)	Propranolol, Bisoprolol, Pyridostigmine	Randomised Control Trial	Adult	103	-	Orthostatic Intolerance Symptoms, Beck Depression Inventory-II, Health-Related QoL (SF-36)
Boris & Bernadzikowski (2018b)	Methylphenidate, Amphetamine Salts, Dexamethylphenidate, Lisdexamfetamine, Atomoxetine, Modafinil, Armodafinil	Retrospective Chart Review	Adult	517	-	Brain Fog, Cognitive Functioning
Junghans-Rutelonis et al. (2018)	Intensive Pain Rehabilitation Programme	Retrospective Chart Review	Adult	118	-	Functional Ability, Depression Scores, Pain Scores
Wang et al. (2019)	Metoprolol	Non-Randomised Control Trial	Child/Adolescent	45	Heart-Rate Variability	-
Schofield & Chemali (2019)	Intravenous Immunoglobulin	Retrospective Chart Review	Adult	38	-	Functional Ability Score

Rodriguez et al. (2019)	Fluid Intake	Randomised Control Trial	Adult	8	-	Working Memory, PoTS Symptom Measure, Health-Related Quality of Life, Depression Scores
Tsai Owens et al. (2019)	Intensive Pain Rehabilitation Programme	Retrospective Chart Review	Adolescent & Yong Adult	96	-	Cognitive Functioning - Attention, Working Memory
Li et al (2019)	Oral Rehydration Salts, Patient Education	Randomised Control Trial	Child/Adolescent	32	Heart Rate	-
Nardone et al. (2020)	Neck Compression Collar	Randomised Control Trial (Crossover)	Adult	10	Heart Rate, Respiratory Rate	Orthostatic Symptom Measure (Vanderbilt)
Reilly et al. (2020)	Breathlessness Physiotherapy Intervention	Retrospective Cohort	Adult	100	Respiratory Rate, Breath Hold Time	Nijmegen Score
Towheed et al. (2020)	Ivabradine	Retrospective Chart Review	Child/Adolescent	27	Heart Rate, Blood Pressure	Syncope Frequency, Light-headedness Frequency, Fatigue Episode Frequency.
Wang et al. (2020)	Metoprolol	Retrospective Cohort	Child/Adolescent	53	Heart Rate	PoTS Symptom Measure
Yozgat et al. (2020)	Oral Rehydration Salt, Propranolol	Randomised Control Trial	Child/Adolescent	72	-	Syncope Frequency, PoTS Symptom Measure

Taub et al. (2021)	Ivabradine	Randomised Control Trial	Adult	22	Heart Rate, Norepinephrine Levels (within Blood Plasma)	Quality of Life
Bourne et al. (2021)	Compression Garments	Randomised Control Trial (Crossover)	Adult	30	Heart Rate, Blood Pressure (Beat-to-Beat)	Orthostatic Symptom Measure (Vanderbilt Orthostatic Symptom Score)

2. Non-Pharmacological Interventions

PoTS remains a challenging condition for the clinician to address due to the condition's varying and diverse presentation (Miller & Raj, 2018). The Canadian Cardiovascular Society (2023) advise that first-line treatment for PoTS should aim to manage the symptoms of the condition through:

- the implementation of lifestyle & dietary changes
- the promotion of physical activity
- clinical support to the patient and their family.

2.1. *Implementation of Dietary & Lifestyle Changes*

Conventional primary PoTS treatments include the increase of salt and water intake in the patient's diet as a means to combat the issue of hypovolemia, in addition to patient education to manage their health condition (Mathias & Young, 2004). In examination of this, fourteen studies in the final sample (total sample= 435), including six Randomised Control Trials [RCT] (Li et al., 2016b; Li et al., 2019; Rodriguez et al., 2019; Yozgat et al., 2020; Z'Graggen et al., 2010; Zhang et al., 2021b), five Non-Randomised Control Trials [N-RCT] (Figuroa et al., 2014; Gordon et al., 2000; Li et al., 2016a; Lu et al., 2017; Ruzieh et al., 2017c), two cross-sectional designs (McDonald et al., 2014; Sandroni et al., 1999) and one retrospective chart review (Moak et al., 2016), had explored the effects of salt supplementation, saline and fluid intakes within PoTS samples (Adult= 8; Child/Adolescent= 5; Adolescent/Young Adult= 1). Despite strong recommendations by the Canadian Cardiovascular Society Statement on PoTS that patient treatment should include increased water intake (three litres) and salt consumption (10 grams) per day; only low-quality evidence was recognised in support of these claims (Raj et al., 2020).

It is worth noting the low number of studies identified within my scoping review that have examined patient education. Only two empirical articles have assessed these interventions, albeit alongside other conventional, first-response PoTS management strategies (Li et al., 2016a; Li et al., 2019). Given this lack of evidence, further works are needed to identify the effectiveness of patient education strategies alone in PoTS and the most effective ways of communicating understandings and the importance of condition management to patients.

Finally, compression interventions, such as those for abdominal compression and stockings for the lower-extremities, are thought to be effective methods to partially compensate for the excessive dilation of blood vessels that is resultant from the neuropathic PoTS subtype (Heyer, 2014). Despite these claims, only limited evidence was identified within the current scoping

review subset to have examined this intervention. Two crossover-design RCT studies [total sample = 30] within the final sample had explored the use of compression interventions in adult PoTS patients - this includes the study of garments (Bourne et al., 2021) and a neck device (Nardone et al., 2020). Whilst this evidence is currently limited, findings by Bourne et al. (2021) within 30 adult PoTS patients indicated that the wearing of compression clothing may be capable of subduing orthostatic changes in heart rate and PoTS symptom severity.

2.2. Promoting Physical Activity

Regular aerobic exercise is reported to play an important role for the patient in their recovery from PoTS, which aims to develop tolerance in people with PoTS towards orthostatic pressures over time (Mathias et al., 2014). Whilst many patients with PoTS are deconditioned or present with an intolerance towards the performance of physical activities, it is suggested that treatment exercises can first be provided to the individual at lower intensities (Johnson et al., 2010). As the patient becomes adapted towards this, the difficulty and duration of the physical activity are gradually increased over time to improve their reconditioning. Within the current scoping review, only a small body of evidence was identified to explore these types of interventions. Exercise programmes (total sample = 121) - including three RCTs (Fu et al., 2011; Lu et al., 2016; Shibata et al., 2012) and three N-RCTs (Galbreath et al., 2011; Masuki et al., 2007a; Masuki et al., 2007b) - and physical therapies - one RCT (Lu et al., 2016) and one N-RCT (Bruce et al., 2016) - were found to have been examined by only seven studies with PoTS samples (Adult= 4; Child/Adolescent= 3) within the final review subset. A meta-analysis undertaken by Wells et al. (2018), who also identified only a limited number of empirical works which had examined this intervention, supported the use of exercise interventions through findings of a moderate efficacy rate on symptom severity. Wells et al. (2018) however cautioned that additional, larger-scale RCT studies are needed to further examine possible observations of large participant drop-out rates and poor tolerance towards these interventions.

2.3. Clinical Support

In addition to the promotion of lifestyle adjustments and exercise recommendations that are advised, healthcare practitioners are also advised to provide a range of multi-disciplinary and integrative approaches to support the individual throughout the initial diagnosis and treatment course (Benrud-Larsen et al., 2002). This includes the use of CBT to help people with PoTS manage their distressing their cognitions and to adjust to live with having a chronic illness (Raj,

Opie & Arnold, 2018). Nevertheless, these integrated therapy approaches were found to be a weak recommendation by the Canadian Cardiovascular Society, who criticised the lack of research in adult PoTS patient samples which had been employed to examine the use of multiple therapies (Raj et al., 2020). The notion of clinician-led therapies having a limited-evidence base is also further echoed by the findings of my scoping review synthesis - which identified no RCT studies for these types of interventions. Instead of this, only eight studies (total sample = 629) within the final review subset had examined the use of clinician-led therapies on PoTS patients (Adult= 2; Child/Adolescent= 4; Adolescent/Young Adult= 2). This included: two N-RCTs (Bruce et al., 2016; Lin et al., 2017) and one longitudinal cohort study (Roerink et al., 2017) which included psychological interventions/CBT; two N-RCTs (Kluck et al., 2017; McTate & Weiss) and two retrospective chart reviews (Junghans-Rutelonis et al., 2018; Tsai Owens et al., 2019) for pain management programmes, in addition to; a retrospective chart review of a respiratory-physiotherapy intervention (Reilly et al., 2020). Thus, in addition to the need for larger research to be carried out examining the effects of such interventions together, further high-quality evidence studies (large-scale RCTs with use of adequate placebo and/or control arms) are specifically needed to support the use of such interdisciplinary therapies within PoTS samples.

3. Pharmacological Agents

If conventional non-medication treatment proves to be insufficient for managing the patients' symptoms, clinician are also advised to prescribe pharmacological agents to alleviate the burden of the individual's PoTS as a last resort (Raj, 2013). However, at the time of writing, there are currently no drug treatments which have been formally sanctioned by the Food and Drug Administration specifically for the treatment of PoTS (Connor, Sheikh, & Grubb, 2012) or the National Institute for Health and Care Excellence. Previous researchers have argued that this is resultant from the lack of randomized control trials which have been conducted in relation to this condition (Miller & Raj, 2018). Despite this however, clinicians within dysautonomia medical centres across the world instead employ a "symptom control" approach to PoTS by "off-label" prescribing of medications to address the most burdensome issues faced by each individual (Raj, 2006). Medication-use in PoTS primarily aims to reduce the characteristic tachycardia associated with the condition (*Beta-Blockers; Ivabradine; Pyridostigmine*), increase blood volume (*Fludrocortisone; Erythropoietin*) and promote the constriction of blood vessels (*Octreotide; Midodrine*). I will now review the evidence for these and show that whilst propranolol and midodrine have strong evidential backing; other types of

'off-label' PoTS medications, particularly those for enabling vasoconstriction, require additional RCT studies due to their low-quality evidence bases (Raj et al., 2020).

3.1. *Medications which Combat Tachycardia*

Many medications are prescribed within PoTS in order to reduce the characteristic, rapid heart rate increase patients experience in response to orthostatic challenge.

- *Beta-Blocker Therapies*

A subset of articles within the final sample concerned the use of beta-blocker medications [Appendix_G]. This category of pharmacological agents lower heart rate by binding to the cell-surface receptors which adrenaline would normally act upon; this subsequently blocks the effects of this neurotransmitter (Khan, 2006). Beta-blockers are therefore highly important in the treatment of patients with the hyperadrenergic form of the condition, as their PoTS symptoms occur from the abundance of norepinephrine that is released into the synaptic cleft due to sympathetic over-excitation (Raj, 2013). Known side-effects of beta-blockers include fatigue, reduced temperature within the extremities, weight gain, depression and sleeping difficulties (MckAinsh & Cruickshank, 1990). There is also concern that beta-blocker treatment leads to adverse effects in hypovolemic PoTS patients, due to the action of these drugs interfering with the patients' renin and aldosterone ratios which are pivotal for their regulating blood volume (Jacob et al., 1997).

Within the current scoping review, a large amount of evidence examination was collated in regards to beta-blocker therapies. This included 19 studies (total sample= 1,598) including seven RCTs (Arnold et al., 2013; Chen et al., 2011; Fu et al., 2011; Moon et al., 2018; Raj et al., 2009; Yozgat et al., 2020; Zhao et al., 2014a), 7 N-RCTs (Gordon et al., 2000; Zhang, Chen, Li & Du, 2014; Lin et al., 2015; Nwazue et al., 2014a; Stewart, Munoz & Weldon, 2002; Wang et al., 2019; Wang et al., 2020), two retrospective chart reviews (Boris & Bernadzikowski, 2018a; Sukul, Chelimsky & Chemlimsky, 2011) and one case-control (Freitas et al., 2000) that had explored beta-blocker therapies in PoTS samples (Adults= 9; Child/Adolescent= 10). Collated beta-blocker therapies (McDonald et al., 2014; Sandroni et al., 1999; Sukul, Chelimsky & Chemlimsky, 2011) examined included: propranolol (n= 7: Arnold et al., 2013; Fu et al., 2011; Gordon et al., 2000; Moon et al., 2018; Nwazue et al., 2014a; Raj et al., 2009; Yozgat et al., 2020); metoprolol (n = 8: Chen et al., 2011, Arnold et al., 2013; Boris & Bernadzikowski 2018a; Lin et al., 2015; Wang et al., 2019; Wang et al.,

2020; Zhang, Chen, Li & Du, 2014; Zhao et al., 2014a), bisoprolol (n=2; Freitas et al., 2000; Moon et al., 2018), and; esmolol (Stewart, Munoz & Weldon, 2002).

Nevertheless, evidence presented by the Canadian Cardiovascular Society Statement for PoTS has recommended that propranolol should be considered as the first line of treatment for treating tachycardia sensations in adult PoTS patients, due to their findings of a moderate evidence base for only this specific beta-blocker drug (Raj et al., 2020). Other examined beta-blockers such as metoprolol were found to have low-quality evidence by the Society (Raj et al. 2020). It must be noted that empirical studies which have examined the efficacy of propranolol in PoTS samples have also been criticised through a recent systematic review and meta-analysis for possible publication bias due to their common poor recording of participant drop-out rates and adverse events (Wells et al. 2018). Thus, although findings for this treatment have been supportive of its capabilities for reducing PoTS symptom burden, it is possible that the efficacy rates of propranolol may be inflated due to these concerns. In addition to this, despite the findings by Raj et al. (2020) that metoprolol has a poor PoTS evidence-base, a systematic review and meta-analysis of eight studies has highlighted this drug as a more effective treatment in comparison to conventional, non-pharmacological treatments (salt and fluid intakes) for children (Deng et al., 2019).

- *Ivabradine*

Ivabradine, a medication which reduces heart rate by blocking f-channels in the sinoatrial node without affecting blood pressure, is also commonly prescribed off-label to POTS patients. Seven studies (total sample= 284) in the final sample included examination of Ivabradine within PoTS samples (adults= 5; child/adolescent= 2). This included one RCT (Taub et al., 2021), one N-RCT (Barzilai & Jacobs, 2015), one cross-sectional study (McDonald et al., 2014), and four retrospective chart reviews (Donne et al., 2018; McDonald, Frith & Newton, 2011; Ruzieh et al., 2017b; Towheed et al., 2020). Evidence from the examination of 22 patients by McDonald, Frith & Newton (2011) has also supported the use of ivabradine in PoTS populations by finding that 11 of the patients who had persisted with this therapy reported reduced episodes of palpitation and tachycardia; of which, 44% of this group who had exclusively reported improved tachycardia also experienced lowered fatigue. A recent systematic review of the use of ivabradine in 13 studies with a total of 132 PoTS concluded cautiously favourable results to support the use of this drug within clinical practice, but highly recommended that further placebo-controlled randomized clinical trials are necessary to assess the drug's true efficacy rates (Gee et al., 2018). Findings of a low-quality evidence

base for ivabradine in PoTS have also been raised by the Cardiovascular Society (Raj et al. 2020).

- *Other Medications to Reduce Tachycardia*

One medication which can be used to control heart rate is the acetylcholinesterase inhibitor pyridostigmine, which has been shown to be capable of alleviating tachycardia and symptom burden in PoTS over a short four-hour time-frame (Raj, Black, Biaggioni, Harris & Robertson, 2005). Four studies (total sample= 703), two RCTs (Moon et al., 2018; Raj et al., 2005) and two retrospective chart reviews (Boris & Bernadzikowski, 2018a; Kanjwal et al., 2011a), included examination of pyridostigmine (adult= 3; child/adolescent=1). Evidence from a retrospective study of 203 PoTS patients found that pyridostigmine use led to reduced orthostatic intolerance symptoms in 43% of the sample, in addition to improvements in palpitations (60%), fatigue (55%) and syncope (48%) symptoms (Gales & Gales, 2007). Other researchers have cast doubts on the ability of this drug to continue treating orthostatic complaints over time (Abed, Ball, & Wang, 2012). Clonidine and methyldopa may also be prescribed to patients to reduce their tachycardia by ‘subduing’ the effects of the sympathetic nervous system (Zadourian, Doherty, Swiatkiewicz, & Taub, 2018). However, there is a lack of empirical research which has reviewed their effectiveness in relation to PoTS populations specifically.

- *Summary of Sub-Section 3.1. Findings*

In review of the evidence identified from PoTS literature for the management of tachycardia episodes, propranolol (Raj et al., 2020) was identified as having the greatest support in adult PoTS patients. Alternative medications, such as ivabradine, need further RCT studies to scrutinise their efficacy rates (Gee et al., 2018). Metoprolol application has support for its use within child samples with PoTS (Deng et al. 2019).

3.2. Increasing Blood Volume

Medication use in PoTS may also aim to enhance the reduced volume of blood which is present in a number of patients with the hypovolemic subtype of this condition. Fludrocortisone is a corticosteroid which works by reducing the amount of sodium that is lost in urinary output – this increases the concentration of these ions in the body and ultimately bolsters blood volume (Miller & Raj, 2018). Fludrocortisone is also used in the treatment of postural

hypotension due to its ability to raise blood pressure (Veazie et al., 2017). Only a small amount of supporting articles, four studies (total sample= 904) in the review subset - two retrospective chart reviews (Boris & Bernadzikowski; Safder et al., 2009), one cross-sectional (McDonald et al., 2014) and a case-control design (Freitas et al., 2000) - included examination of fludrocortisone (adult= 2; child= 2). The retrospective chart review by Safder et al. (2009) on 59 PoTS paediatric patients highlighted the potential benefits of this medication for relieving patients' orthostatic complaints. Nevertheless, it must be acknowledged that fludrocortisone has been criticised in the treatment of PoTS for its limited-quality evidence base (Raj et al. 2020), and also worsening migraine symptoms and for depleting levels of renin (Abed, Ball, & Wang, 2012; Jacobs et al., 1997).

An alternative pharmacological agent is the hormone erythropoietin, which enhances blood volume by stimulating an increased production of red blood cells following injection (Grubb, Kanjwal, & Kosinski, 2005). Erythropoietin may serve as a more effective form of treatment for patients with refractory PoTS. Only one empirical study was identified for this treatment within the current scoping review. In a retrospective study of 39 individuals whose PoTS was resistant to commonly-used pharmacological agents including fludrocortisone, a six-month erythropoietin therapy (10,000-20,000 international units per week) lead to improvement in subjective orthostatic symptoms for 71% of patients at the post-treatment stage; there was also evidence of decreased syncope occurrence and a reduced diastolic blood pressure when seated (Kanjwal et al., 2012). Nevertheless, erythropoietin therapy can be costly, and patients who undergo this type of treatment need to undertake regular complete blood counts in order to ensure the proportion of their red-blood cells does not become too high [haematocrit] (Abed, Ball & Wang, 2012). Erythropoietin has also been linked with a heightened risk of cardiovascular mortality (Miller & Raj, 2018).

- *Summary of Sub-Section 3.2. Findings.*

The scoping review findings therefore indicated that there is overall a weak evidence base for the pharmacological medications that focus on increasing blood flow in people with PoTS.

3.3. Facilitating Vasoconstriction: Octreotide and Midodrine

PoTS patients often present with inadequate and impaired constriction of their blood vessels (Benarroch, 2012). Patients who are diagnosed with the neuropathic subtype of PoTS are known to present with blood pooling in the lower limbs due to this (Jacob et al., 2000). Whilst other PoTS pharmacological treatments such as fludrocortisone (Raj, 2006) and erythropoietin

(Garland, Celedino, & Raj, 2015) are known to possess vasopressor qualities, one particular pharmacological agent used to narrow blood vessels in PoTS is octreotide (French et al., 2011). Octreotide - a drug administered to patients through either a series of short-lasting [administered 2-6 times per day] injections or long-duration [administered once every four weeks] injections - facilitates abdominal vasoconstriction by stimulating receptor cells for growth hormone-inhibiting hormones in the patient (Zidek, 2015).

There have been a few small studies of this drug's use in PoTS. Only four studies (total sample= 157) in the review subset - two N-RCT (Hoeldtke et al., 2006; 2007) one retrospective chart review (Kanjwal et al., 2012b) and one cross-sectional (McDonald et al., 2014) - included examination of octreotide in adult PoTS patients. One study explored the efficacy of a long-acting octreotide therapy [*10 mg dosage initially - gradually increased to 30 mg*] in a three-month pilot trial of seven individuals with PoTS and orthostatic intolerance patients. By the end participants demonstrated improved standing time, a reduced upright heart rate and alleviated fatigue symptoms at the post-treatment stage (Hoeldtke, Bryner, Hoeldtke, & Hobbs, 2007). Nevertheless, octreotide therapy is limited by its invasive method of administration and its debilitating side-effects for the individual. These include the risk of developing excessive blood pressure (Hoeldtke et al., 2007). Due to the associated high costs with this medication, octreotide use in PoTS is usually reserved only as a last resort method for patients who are unresponsive to other forms of treatment (Zidek, 2015), although evidence from a retrospective chart analysis of twelve patients has implied that this drug was an effective agent for this specific sample (Kanjwal, Saeed, Karabin, Kanjwal, & Grubb, 2010).

An additional vasopressor medication is the alpha-1 adrenergic agonist midodrine. Midodrine, a pharmacological agent which possesses a short half-life [3-4 hours], increases blood vessel constriction and blood pressure by binding to noradrenaline receptor sites and mimicking the action of this neurotransmitter within the body (Raj & Miller, 2018). Eleven studies (total sample= 1,277) in the final review subset - including four RCTs (Liao et al., 2013; Ross et al., 2014; Yang et al., 2013; Zhang et al 2012a), five N-RCTs (Chen et al., 2011; Gordon et al., 2000; Hoeldtke et al., 2006; Zhao et al., 2014b), two retrospective chart reviews (Boris & Bernadzikowski, 2018a; Deng et al., 2014) and one cross-sectional design (McDonald et al., 2014) - examined midodrine in PoTS samples (adult= 3; child/adolescent= 6; adolescent/young adult= 1). Midodrine has strong evidential backing in the literature, as identified through meta-analysis of an identified efficacy rate of 66% in paediatric samples (Wells et al., 2018), in addition to strong recommendations for its use in adults by the Cardiovascular Society through having a moderate quality evidence base (Raj et al., 2020).

Whilst specific NICE guidance for PoTS does not currently exist, midodrine is currently recommended by the NHS for orthostatic hypotension – a similar diagnosis to PoTS - at a dosage of 2.5mg three times per day . Findings from a prior small randomized double-blind placebo-controlled crossover study of twenty PoTS patients (aged 12-20) has supported arguments that the use of midodrine may lead to more pronounced effects in patients who possess the neuropathic PoTS subtype (Ross, Ocon, Medow & Stewart, 2014). In comparison to other medications which elicit vasoconstriction, midodrine and octreotide have been shown to possess comparable effects on patients' orthostatic heart rate change and standing time duration (Hoeldtke, Bryner, Hoeldtke, & Hobbs, 2006). Nevertheless, it is noted that not all patients will respond positively to midodrine therapy. In a similar manner to octreotide use, one side-effect of midodrine is that it produces excessive supine blood pressure (Ross et al., 2014). Although, some researchers have suggested that it may be possible to alter the administered dosage of midodrine hydrochloride to ensure that it remains an effective agent on eliciting vasoconstriction in PoTS patients, without resulting in a concerning level of hypertension (Chen et al. 2011). As only small amounts of midodrine may pass through the blood-brain barrier, this drug is not associated with severe side effects on the central nervous system (Singer et al., 2014).

Prior works have compared the efficacy of midodrine treatment against beta-blocker use. Chen et al. (2011) compared the effects of a midodrine hydrochloride [2.5 mg] against the sole beta-blocker metoprolol [0.5 mg/kg, administered twice daily] and a drug-naïve group in a sample of 53 PoTS patients over a short-term (three-six month) period. Non-pharmacological conventional PoTS therapies were provided to patients in each arm. The number of individuals who were curative in response (defined as patients who scored zero on a follow-up orthostatic symptom measure) to treatment was found to be significantly higher for the midodrine (68.4%) prescribed patients, in comparison to the metoprolol (42.1%) or medication-naïve (20.0%) groups. This efficacy for midodrine was also found for the number of patients who reported a 50% or greater symptom improvement following the short-term intervention use. Over a longer-term follow-up (5-24 months) period, the proportion of patients who reported a recurrence of PoTS symptomology was significantly lower in the midodrine group. Nevertheless, not all evidence has supported the effectiveness of midodrine therapy over beta-blocker use. Lai et al. (2008) conducted a retrospective chart review analysis of 121 children patients who had been admitted to the Mayo Clinic with suspected PoTS over a three year period. In comparison to beta-blocker use, a significantly lower proportion of midodrine-users believed their medication use was accountable for reductions in their PoTS symptomology. Within a follow-up survey, midodrine-users reported a significantly lower improvement in their scores on the Walker Functional Disability Inventory than the beta-

blocker group; the midodrine patient group was also unable to outperform a pharmacologically-naïve treatment group on this measure.

- *Summary of Sub-Section 3.3. Findings*

My scoping review findings indicate that octreotide has weak evidence to support its use in a PoTS sample for the management of vasoconstriction. Whilst midodrine use has a stronger level of empirical support and backing in the literature (Raj et al. 2020); it is unclear whether the medication can impact on improving paediatric patients' daily functioning abilities due to mixed findings (Lai et al. 2008; Wells et al. 2018).

3.4. Other Medication Use

PoTS patients report high levels of mental cloudiness symptoms which cause interference to their mundane, day-to-day tasks (Anderson et al., 2014). A drug called modafinil has been suggested as an effective agent for treating brain fog symptoms and feelings of sleepiness in patients (Kpaeyeh et al., 2014). Nevertheless, the advantages of modafinil may be offset somewhat by its possible side-effect to heighten episodes of tachycardia (Sheldon et al., 2015). This problem is also thought to occur during droxidopa therapy – a medication which is recommended in neuropathic PoTS to elicit vasoconstriction by increasing the levels of norepinephrine in the body (Raj & Miller, 2018). Desmopressin, a medication which aims to reduce urination in an effort to enhance sodium retention levels in patients, can also be prescribed to PoTS patients and is associated with improved symptom burden and reduced upright heart rate (Coffin et al., 2012). Within a retrospective design of 54 PoTS patients who were prescribed droxidopa, Ruzieh, Dasa, Pacenti, Karabin and Grubb (2017a) found that whilst this medication led to reduced syncope and fatigue at the post-treatment stage, 40.5% of these individuals choose to suspend their treatment prior to the end of their course. This suggests that whilst droxidopa may be a suitable drug for mitigating orthostatic-related conditions within PoTS- further research is needed to explore the factors surrounding its tolerability and whether or not the drug may be effective at lower dosages. Within the current scoping review, limited forms of evidence were identified to support these alternative treatment and further high-quality (RCT) studies remain needed.

4. Discussion

4.1. Summary & Further Implications of Treatment Review Findings

Through the tabular and narrative synthesis of empirical literature concerning PoTS treatments within this scoping review, I identified that only two interventions - propranolol and midodrine, both pharmacological in nature - currently present with having strong levels of evidence for symptom management in this condition (Raj et al., 2020; Wells et al., 2018). Although the review identified mixed evidence towards its general effectiveness, metoprolol-use was also supported by meta-analysis data to have a 66% efficacy rate in PoTS rate in paediatric samples (Deng et al., 2019). Despite this, the highlighted findings of my review are consistent with prior criticisms of PoTS management strategies, whereby most other treatment strategies for PoTS, both other medication and non-medication based alike, are perceived to possess low-quality evidence, through their lacking of sufficient large-scale, placebo-controlled RCT studies and evidence synthesis (Eftekhari et al., 2021; Raj et al., 2020; Raj & Robertson, 2018). These conclusions are particularly true for non-medication strategies, with only a small handful of RCT studies having been undertaken to examine salt-based treatments and exercise programmes for PoTS exclusively.

Within chapter 3, I highlighted the need for a greater understanding towards the co-morbid psycho-social impacts associated with a PoTS diagnosis. Within the current evidence review of PoTS treatment empirical literature, little research was identified generally to have assessed the efficacy of psychological therapies, such as CBT, within this patient population (Raj, Opie, & Arnold, 2018). This remains a key issue of concern, given the high levels of poor quality of life scores which are commonly reported by PoTS patients (Anderson et al., 2014). This is also an issue within the empirical research studies which had examined pharmacological PoTS agents within the final review article subset, were only a small handful of studies have considered the effects of medication use in PoTS as a form of co-morbid psychiatric symptom management as an outcome variable. One study demonstrated that beta-blocker therapy may serve as a possible effective treatment in its own right for the alleviation of depressive symptoms in PoTS patients (Moon et al., 2018). These findings are however restricted by the need for the patient to be provided access to medication-use for their PoTS (only provided in severe cases), and are also hindered the adverse side-effects these drugs can have on patients (Jacob et al., 1997). A number of researchers have also suggested modafinil as a medication which may be capable of treating cognitive and sleep-related symptoms associated with the condition, although there remains a lack of evidence which has assessed the utility of this (Kpaeyeh et al., 2014). Further high-quality research through the conduct of large-scale RCT studies are therefore required, in order to examine the effects of other (both medication and non-medication) interventions on the psychopathological symptoms which people with PoTS may encounter for the improvement of patients' wellbeing and life quality.

4.2. Justification for the Development of Additional, Novel PoTS Treatment Strategies

Due to the restricted use of 'off-label' medication use to only the most severe presentation of PoTS cases (Benarroch, 2012); non-pharmacological treatments for PoTS remain the primary, first-line form of treatment for assisting people living with the condition (Raj, 2012). It is also worth noting that some non-pharmacological interventions, such as those involving exercise programmes or access to psychological therapies, both identified to have a poor evidence base within this scoping review, may be inaccessible or unfeasible to a substantial proportion of people with PoTS, due to their reliance on healthcare professionals for delivery or long waiting periods associated with accessing psychological therapies within the UK. Thus, the importance of developing an evidence base for accessible, non-medicated interventions remain crucial for those people with limited access to healthcare facilities or clinician support; in that, for many people with PoTS, these specific strategies may serve as the only form of symptom management these individuals may receive.

Despite this, my scoping review findings however indicated that only a select number of available strategies for people with PoTS to use, centred around dietary changes and compression garments (Lu et al., 2017; Bourne et al., 2021) had mixed evidence to support the use of these strategies. Whilst further high-quality evidence is needed to further examine these treatments, more research is currently needed to identify, develop and specifically tailor further types of non-pharmacological interventions for PoTS patient groups, in order to support peoples' self-management of their chronic illness. These findings therefore further support my decision to develop a new, novel and unexplored breathing-related intervention for PoTS as a primary choice of intervention format.

4.3. Conclusion

The findings of this chapter showed the limited range of (evidence-based) treatments available to people with PoTS. Within the next chapter, I introduce the next phase of my research - the narrative exploration of people with PoTS' online stories - to expand upon PoTS symptom exploration in the research area, through supporting the undertaking of a qualitative approach within this patient group.

As identified by the narrative findings of the scoping review (chapter 3), chapter 5 outlines the rationale and methods for the qualitative exploration of PoTS diagnostic and symptom experience. A secondary, purposeful sample of 20 vlogs of people with PoTS sharing their diagnostic journeys videos (obtained from iterative searches from the online platform YouTube) were analysed through the employment of narrative analysis. Findings identified from the narrative strategy, through structural and performative analytic approaches, are presented within thesis chapters 6 and 7 respectively.

1. Introduction

As part of the scoping review of PoTS literature (see Chapter 3, I examined the nature of previous published works dedicated to exploring PoTS diagnostic literature. The findings of that review highlighted that published works within in the research field have focused on examining how common underlying physiological issues in the patient group may relate to the possible existence of PoTS endophenotypes (Raj, 2006), the identification of factors which can improve the accuracy of tilt-table assessments to improve diagnostic rates (Plash et al., 2013) and the differentiation of its clinical presentation from other autonomic- and syncope-related pathologies (Lambert & Lambert, 2014). Whilst these prominent works have assisted clinicians working in autonomic fields with the quicker identification of PoTS and the signposting towards the correct management strategies for each patient – prior research has not yet attempted to understand how the patients themselves actually perceive, or try to make sense of, their own interactions with the different types of medical professionals and healthcare systems they engage with during the diagnostic processes they undergo. Given that PoTS remains a largely misunderstood – and at times, contested - condition within the medical community (Bennarroch, 2012), and that this uncertainty surrounding the condition often leads to patients receiving misdiagnosis (Kavi et al., 2015) - it is crucial that further exploration of patients' diagnostic experiences are undertaken in order to 'un-ravel' how misconceptions of PoTS symptoms are produced.

Given the widespread nature of PoTS presentation and the invisibility of its associated bodily complaints, patients with PoTS are commonly referred between numerous healthcare practitioners and medical consultants as part of the medical inspection of their persistent physical symptoms (Gill, 2018). Due to this, people with PoTS are likely to engage with a variety of healthcare practitioners across differing specialisms and backgrounds. Following the conduct of a cross-sectional online survey undertaken by Shaw et al. (2019) of 4835 patients, participants with PoTS reported engaging with an average of seven different

physicians before receiving their diagnosis. Furthermore, approximately one in five (21%) of these patients reported consulting with a total of ten or more medical professionals prior to the identification of their PoTS. In a similar vein to other invisible chronic health conditions that are known to be often misunderstood and poorly recognised by medical communities, prior PoTS literature has acknowledged patients' common anecdotes and reports of their persistent physical symptoms being frequently discredited, mislabelled or dismissed as psychogenic in origin by clinicians (Kavi et al., 2015). This remains a particularly concerning issue to address in PoTS, with an estimated three in four individuals in the patient group reporting having received a misdiagnosis (Shaw et al., 2019). Despite this however, at present no prior study of PoTS has yet attempted to explore patients' own personal experiences of both symptom onset and the challenges they face during the medical journeys they embark upon to acquire a PoTS diagnosis.

The lack of research exploring diagnostic experiences in PoTS is reflective of a broader issue within the research area. As identified within the scoping review findings (see Chapter 2) and from a recent evidence map undertaken by Eftekhari et al. (2021), there is currently a paucity of qualitative literature within the PoTS field. Due to this, whilst empirical works have demonstrated patients with PoTS to consistently report significantly reduced levels of quality of life and heightened levels of suicide ideation (Pederson & Brook, 2017) - there is currently a lack of understanding towards how PoTS symptoms are experienced by these individuals, and in turn, how these experiences relate to these undesirable outcomes. To my knowledge, only one recently published article has utilised a qualitative approach within the study of PoTS. Waterman, Opie, Waterman and Langdon (2021) conducted a study of self-recorded home-made videos by eight patients with PoTS over a seventeen-day period discussing their experiences of living with the condition. Participants expressed that they felt that several of their healthcare practitioners had previously neglected the importance of their quality of life as a core part of PoTS treatment. Participants also disclosed how they would commonly encounter difficulties with explaining the burdens of their symptoms to others, which in turn would amplify patients' own internal feelings of distress (Waterman et al., 2021). Further works are therefore needed not only to understand experiences of PoTS symptom onset and diagnostic experiences of the patient group, but also to comprehend the ways in which patients with PoTS attempt to explain, share and **communicate** both experiences of their symptoms and their own understandings of their condition with others.

Whilst there is currently a paucity of literature regarding patients' communication of PoTS symptoms and diagnostic stories specifically, some limited comparisons can be drawn from prior research conducted within other invisible illnesses. Research undertaken from Ravenzwaaij et al. (2010), which aimed to synthesise qualitative literature on a broad range

of medically misunderstood and persistent physical symptom related conditions, has identified that patients often explain their chronic health diagnoses and symptoms through the employment of unique socio-medical frameworks or 'ontologies' that ground the physiological origins of their bodily complaints. Furthermore, experiences of invisible chronic illnesses have also been explored through the use of narrative analyses (Nettleton, 2007; McMahon, Murray & Simpson, 2012). Narrative analysis aims to examine the ways in which patients portray and construct their encounters with medical communities in order to comprehend the ways in which individuals present their struggles with illness (Williams, 1984; Whitehead, 2005). Prior researchers have argued that patients' sense-making and own personal understandings of their chronic illness arise from the reciting and (re)framing of the core life events which constitute the diagnostic journeys they have embarked upon (Polkinghorne, 1995). Narrative approaches therefore represent a powerful tool for enabling a researcher to 'unpick' how a storyteller positions their 'narrative self' (Frank, 1995) within their anecdotes - in order to understand how patients generate meaning and value from their own personal suffering.

The current study therefore aimed to employ the use of a narrative approach to better examine how individuals with PoTS share experiences of their condition and their personal stories of engaging with medical communities to receive an appropriate diagnosis. The research was guided by two research questions:

- (i) How are diagnostic and symptom experiences constructed by people with PoTS within the core narrative events of their shared diagnostic stories (see Chapter 6)?
- (ii) How do people with PoTS communicate understandings of their chronic illness to their virtual audiences through their online vlog stories (Chapter 7)?

2. Method

2.1. Approach

The current study utilised narrative analysis to understand how people with PoTS share their diagnostic stories, through the inspection of a secondary dataset comprising of 20 online recorded vlogs sourced from the video platform YouTube.

Narrative approaches seek to understand the ways in which individuals generate meanings and assign significance to prominent life events, through the transforming and sharing of their personal experiences into retold stories for others (Polkinghorne, 1995). Prominent guides to undertaking narrative works, such as those proposed by Reissman (1993), encourage the analysis of story structure through the close inspection of the person's organisation of the tale (Nasheeda, Abdullah, Kauss & Ahmed, 2019), consideration of key moments where the narrative is chosen to be 'progressed' by the storyteller through turning points (Lillrank, 2003; Reissman, 2002), and how start and end points are clearly designated within each narrative. Whilst some narrative approaches can explore the examination of a tale within its entirety (holistic), alternative analyses can be undertaken to focus upon the key, specified timepoints (categoric) or core events which are re-constructed and emphasised by the individual within their discourse (Beal, 2013; Lieblich, Tuval-Mashiach & Zilber, 1998). In this sense, due to the complexity associated with analysing an individual's narrative as a complex social phenomenon (Andrews, Squire & Tamboukou, 2016), methods of studying chronic illness narratives serve as an 'umbrella' cluster or 'toolkit' of qualitative analyses which encapsulate a variety of different approaches, that ultimately lack a rigid or universal structure for their application (Reissman, 2008). Given this, the concept of rigour is devised in narrative analysis through the intentional combination of multiple approaches by a research team, whereby each separate analytical phase aims to explore a different aspect or characteristic of an explored story (Meraz, Osteen & McGee, 2019).

Within the current study, the conduct of narrative analysis to explore diagnostic stories in PoTS was guided through the three-phased approach proposed by Meraz et al. (2019), as derived from the works of Reissman (2008). This began with the identification of what core events and experiences people with PoTS commonly chose to present within their expressed narratives (thematic approach). The next phase of the narrative analysis further developed upon the initial thematic approach by examining how people with PoTS portrayed, constructed and organised the structure of these core events and experiences into a complete, holistic story (structural analysis – see chapter 6). Given that storytellers continually re-construct and share their narratives across changing groups of intended listeners and different social contexts (Esin, Fathi & Squire, 2013), the final phase of the narrative approach sought to consider the

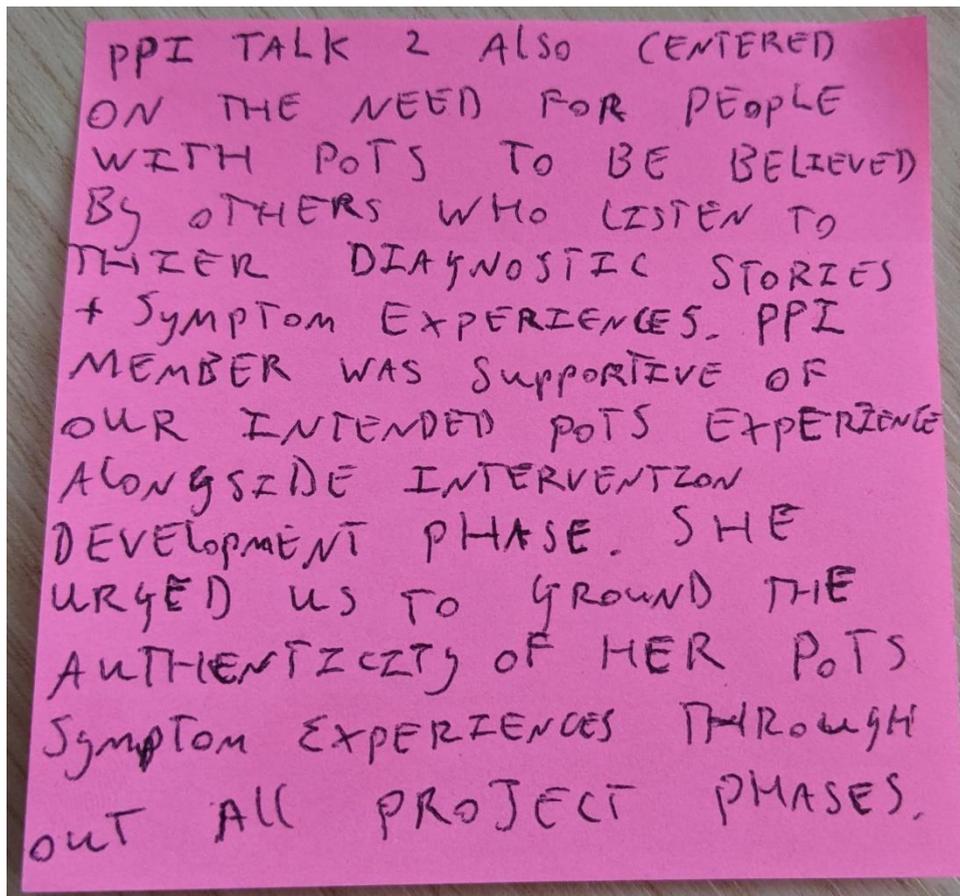
purpose of story vlog dissemination by PoTS storytellers. This performative approach (see chapter 7) of the narrative analysis was undertaken to understand the ways in which people with PoTS attempted to communicate understandings and awareness of their chronic illness, through orientation towards their intended virtual audiences. Further details of the analysis strategy are outlined within sub-section 2.7.

2.2. Reflections on Methodological and Epistemological Assumptions

During project conception, my supervisors and I reflected on the underlying assumptions which would guide the conduct of narrative analysis and data interpretation. These types of analyses acknowledge narratives to be a form of social phenomenon in itself (Polkinghorne, 1995), which are continually restructured and repurposed by people with chronic illness to derive new meanings and the generate human knowledge from their experiences. Furthermore, it is important to note that the narratives shared by people with chronic illness are shaped not just from their own personal beliefs, cultural values and social backgrounds; the expression of these stories is also influenced by the intended listener(s) and social contexts in which narratives are purposefully shared (Stephens & Breheny, 2013). Narrative analyses ultimately lack a universal structure or singular criteria for a researcher to undertake when employing these methods (Reisman, 2008); they serve as an amalgamation of various techniques and methods for exploring different aspects of datasets. Researchers who undertake narrative analyses are actively encouraged to engage with multiple qualitative approaches within the exploration of their data, such as the combination of analyses related to thematic and constructionist underpinnings (Esin et al., 2014), as a means of demonstrating rigour in their utilised methods (Meraz et al., 2019).

When considering the application of this method to the study of PoTS understanding, symptom and diagnostic experiences, the supervisors and I reflected on how aspects of the narrative analysis – specifically the structural approach which aims to comprehend how storytellers portrayed, organised and re-expressed their personal experiences as a cohesive story to others (Reissman, 2012) - shared parallels to stances of social constructionism. In this manner, I aimed to understand the meanings which people portray from living with PoTS, through comprehending the ways in which speakers use their discourse to **shape, construct and reformulate** their symptom experiences through stories. Constructionist perspectives draw on the concept of narrative being its own social phenomena, in that each story told by a teller constitutes its own subjective reality. In this sense, these stances assume that narratives are shared by people with PoTS in order to perform the social actions of constructing the states, emotions and meanings of the self through their **retold** (symptom and diagnostic)

experiences to others, within a confined medium or setting (Andrews et al., 2016). Thus, given that each retelling of a narrative to different listeners or social contexts is assumed to comprise of its own unique reality (Esin et al., 2014), constructionist elements of narrative analysis emphasise the importance of understanding the portrayal of diagnostic experiences in PoTS as a constantly evolving multi-reality phenomena; as opposed to examining or valuing the 'objective reality' experiences of the speakers directly (Esin et al., 2014).



PPI TALK 2 ALSO CENTERED ON THE NEED FOR PEOPLE WITH PoTS TO BE BELIEVED BY OTHERS WHO LISTEN TO THEIR DIAGNOSTIC STORIES + SYMPTOM EXPERIENCES. PPI MEMBER WAS SUPPORTIVE OF OUR INTENDED PoTS EXPERIENCE ALONGSIDE INTERVENTION DEVELOPMENT PHASE. SHE URGED US TO GROUND THE AUTHENTICITY OF HER PoTS SYMPTOM EXPERIENCES THROUGHOUT ALL PROJECT PHASES.

Fig. 1. Reflexive note generated when considering patient public involvement (PPI) activities for the intervention development and PoTS symptom experience work for the project. During the project planning stages, the supervisors and I reflected on how the examinations of participants' meanings and understandings, through re-told stories related to their experiences of having their PoTS diagnosis contested by others, initially posed challenges to our employed methodology.

From this perspective, there was concern that these relations to a constructionist framework for guiding the narrative analysis— through its study of PoTS experience as multiple, ever-changing subjective (over objective) paradigms— may conflict with the true realities of symptoms which sufferers face, as people with PoTS commonly have the legitimacy of their chronic illness contested by others (see Fig. 1 above). It was therefore crucial to ensure that the constructionist elements of the narrative approach did not undermine the significance of these realities for people with PoTS.

As such, strategies were implemented in order to address this. First, data triangulation was employed – whereby during the conduct of interviews with people with PoTS within the intervention phase of the project, preliminary (ongoing) analysis findings from the narrative work were routinely discussed with participants during conversations concerning their symptom experiences. Discussing early understandings of the data with participants during the time of data analysis enabled me to understand if people with PoTS were able to ‘ground’ and make sense of the narrative findings within their own PoTS experiences and realities of chronic illness. Furthermore, reflexive notes were generated to critically reflect on the relationship of people with PoTS’ accounts to their need for medical recognition throughout the project (see Chapter 7, where findings include reflection on how people with PoTS attempt to legitimise their diagnosis to others). Through these actions, I ensured that the conduct of the constructionist elements associated with the narrative analysis did not invalidate the illness experience and biological validities which define people with PoTS’ chronic illness sensations, and their disclosed accounts of experiencing a recognised, legitimatised medical condition.

2.3. Ethical Considerations

The current study was reviewed and granted ethical approval by the Faculty of Health and Life Sciences Ethics Committee at Northumbria University [#23128]. To ensure the narrative analysis project respected the privacy, confidentiality and anonymity of the people with PoTS whose vlogs would be collected and analysed, my supervisors and I held numerous discussions to carefully reflect on and critically consider the ethical considerations associated with our secondary data work.

We first critically considered whether we would need to obtain participant consent for the analysis of participants’ vlogs. Prior internet-mediated researchers have argued that participant consent does not need to be obtained for analysis of YouTube content, as long as videos or comments have non-restricted access and are watchable within the public domain (Toye, Seers & Barker, 2020; Devan et al., 2021). This statement is further supported by British Psychological Society Guidelines for Conducting Internet-Based Research (Kaye et al., 2021), which outlines that the requirement of collecting participant consent can be waived for researchers collecting data obtained in public spaces where users would anticipate, or had deliberately sought after, the observation of their (online) content by strangers. Given this, and the explicit acknowledgement that YouTube is a video sharing platform situated within the public domain, consent of video creators was not sought after for the inclusion of PoTS vlogs within our project. Instead of this, to ensure that the data had been sourced entirely from

content originating within the public domain, I examined only vlogs which did not require sign-in access in order to be watched for possible inclusion within the research.

Following this, we then reflected on the privacy concerns of our planned data collection strategy in order to protect videos within the final vlog sample from being identifiable during research dissemination. Researchers undertaking secondary data projects which have employed a qualitative approach— specifically those which seek to analyse written texts collated from website comment sections, social media forums, discussion boards or online blog posts – may opt to employ the use of paraphrasing of users’ quotations (Talbot & Branley-Bell, 2021). Whilst this strategy serves as one method of minimising the probability that anonymity of users would be breached through online search engine tracing of participant written quotes back to their original sources (Roberts, 2015) - the repurposing and alteration of participants direct quotes poses considerable risk, whereby researchers’ interpretations of the data during analysis may not be reflective of participants’ true views and original meanings (Kaye et al., 2021). In addition to this, the decision to deliberately change participants’ extracts restricts researchers from utilising in-depth forms of qualitative analyses- such as those wishing to examine the discursive properties of the participants’ spoken words and how personal symptom experiences are (re)constructed through their verbal and non-verbal communications. It is therefore important that the strategies undertaken to minimise risks to participant anonymity are balanced and do not ultimately compromise the scientific integrity of the research being conducted (Roberts, 2015; Kaye et al., 2021).

Given these concerns, and the need to perform a rich, detailed multi-approach analysis of people with PoTS’ narratives in order to achieve sufficient trustworthiness and rigour in our utilised methodology (Meraz et al., 2013), after careful consideration I ultimately decided to forgo this paraphrasing strategy. To minimise risks of analysed data being identified, I instead first made the decision to only utilise vlog-based data sources within the formal analysis stages - as quotes taken from video content are not directly traceable back through search engines (Ryan-Vig, Gavin & Rodham, 2019). All searchable information from YouTube videos, such as video titles, URLs and hashtags, were anonymised. Whilst several PoTS written blog posts were read and discussed during the project planning stages for guiding the conduct of the work (see sub-section 2.7. for further details of this), no extracts from these data sources were present within the formal analysis (only vlog extracts were used from collation of secondary data sources). As a precaution alongside the use of video quotes, I undertook an alternative strategy, whereby participants’ vlog quotes used within the generation of this thesis were entered into Google and YouTube Search Engines to ensure that their associated video did not appear within the search results for any of their presented extracts. Finally, during the transcription process for each video, all personally identifiable information concerning

participants was anonymised prior to the conduct of analysis taking place. Only generalised summaries of demographical information across the collective final vlog sample have been presented within sub-section 2.5.

2.4. Search Strategy and Vlog Eligibility Criteria

In order to identify a purposeful sample of vlogs which featured a person with PoTS sharing their diagnostic stories for the project, the video-based media platform YouTube was iteratively searched. YouTube – a platform widely utilised by social science researchers for the analysis of patients' video-stories across a multitude of chronic health conditions (Devan et al, 2021; Chou, Hunt, Folkers & Augustson, 2011) - was chosen as the primary type of data source for project analysis. The use of vlogs over text-based sources of data provided a much richer level and greater wealth of data to understanding how speakers reinforce their portrayal and emphasise of key story events and plot progression, through additional transcription of non-verbal actions. This included notable gestures by the speaker, visual imagery & storyteller's presentation, in addition to the inclusion of edited or 'montaged' footage for analysis purposes such as real-time recordings of major events that had been captured during the diagnostic process.

Searches were undertaken during April-May 2020 and featured one naming term of the condition [*'pots'*, *'postural tachycardia syndrome'*, *'postural orthostatic tachycardia syndrome'*, *'dysautonomia'*], combined with the Boolean operator 'AND' alongside *'story'*, *'journey'*, *'diagnosis'*, *'vlog'*, *'awareness'*, *'experience'*, or *'dysautonomia awareness month'* until data saturation had been achieved. Search results were ordered by 'relevance' and I screened the first four search results pages for each strategy employed. This decision was made due to reflections upon the considerations by Stellefson et al. (2014) within their content analysis of online chronic obstructive pulmonary disease educational videos, on the iProspect research conducted on users' search behaviour which indicated that only one out of ten individuals are likely to click past the initial three results pages of online search databases- similar YouTube strategies have been undertaken within past research (Ryan-Vig et al., 2019).

The undertaken search strategy (see Table 1) did not contain any restrictions on upload date or geographical location. Due to the language restrictions, only vlogs with an English speaker were considered for inclusion. Only vlogs which possessed a minimum video duration length of five minutes were considered for inclusion. This decision increased the likelihood of identifying only those videos which contained whole, composite narratives of PoTS diagnostic experiences.

Table 1. Full details of the video screening criteria employed by the research team for identifying the final purposeful sample of PoTS vlogs.

Criteria	Definition
Sample	<p>Vlogs identified for the project needed to contain an autobiographical narrative, expressed by the person with PoTS themselves, of their experiences from symptom onset to receiving their diagnosis.</p> <p>Eligible videos needed to possess a minimum duration of 5 minutes in length to ensure sufficient data was captured for analysis purposes.</p>
Demographics	No restrictions were placed on upload date or geographical location. Videos featuring only English speakers were included within the project, due to the language restrictions within the research team.
Format	<p>Videos needed to be presented in a monologue format told by a single person with PoTS retrospectively sharing their story to an intended virtual audience of YouTube users.</p> <p>Videos which had been recorded live on YouTube, with an interacting virtual chat-based audience present at the time of recording, were excluded.</p>
Editing	<p>Vlogs which included ‘snippets’ of recorded montage footage captured real-time during the diagnostic experience - <u>which had been integrated alongside the storytellers’ holistic monologue</u> – were considered eligible for possible inclusion, if they were not deemed to not detract from the retrospective re-telling of speakers’ holistic narrative.</p> <p>As videos needed to feature the retrospective re-telling of a holistic narrative by the speaker - vlogs which <u>relied too heavily on (or were solely constituted of)</u> real-time footage that had been recorded during the diagnostic experience for the sharing of the PoTS narrative - were not considered eligible for inclusion.</p>
Accessibility	Included videos must be viewable without the need for a ‘sign-in’ option, to ensure that the final vlog sample remained accessible and belonged within the public domain.
Presentation	Eligible PoTS stories needed to be contained to a single video. Narratives which had been presented by speakers across a series or multiple vlogs were excluded.

2.5. Demographical Characteristics of Final Vlog Sample

Twenty videos were ultimately retained in the final stage of the search, following further re-watching and additional reviewing of each vlog against the employed eligibility criteria. Given the nature and type of secondary data collected as part of the research, only limited types of demographic information were consistently available to be collected for each video and vlogger (see Table 2). Total duration of the analysed vlogs amounted to 273.24 minutes (Mean = 15.18 Minutes), with individual videos ranging between 8-26 minutes in length. Vloggers were mainly located within the United States of America (83%) and were primarily female in sex (94%). Two-thirds (66%) of the final sample videos had been posted between 2018-2020. Visual inspection of video view count through a histogram revealed a skewed left-tailed

distribution, demonstrating that the majority of online vlogs within the final sample had been widely viewed within the public domain (Median View Count = 2155).

Table 2. Demographic information and frequency data collated from the final sample of PoTS Vlog Stories by Video Duration, Geographical Location, Vlogger Sex and Year of Vlog Posting.

Demographical Information	Variable	Frequency
Vlog Duration (Minutes)	08.00-09.59	3
	10.00-14.59	7
	15.00-19.59	3
	20.00-24.59	4
	25.00+	1
Geographical Location	USA	15
	UK	2
	Australia	1
Vlogger Sex	Female	17
	Male	1
Year Of Vlog Posting	2012	1
	2014	1
	2015	1
	2016	1
	2017	1
	2018	5
	2019	4
	2020	3

2.6. Transcription of Final Vlog Sample

To become familiarised with the dataset, each vlog was viewed a minimum of three times. Upon first viewing, an initial verbatim transcript containing only the spoken words of each video was first produced. All personally identifiable information was anonymised during verbatim transcription. To allow for a greater level of depth to the qualitative analysis, upon second viewing video transcripts were further developed through application of the transcription protocols developed by Poland (2002). Care was taken to include each notable pause (*denoting between short and long pauses through additional periods within the parentheses*), utterance, laugh (*through parentheses*), emphasised or emotive language (*through upper case letters*), unclear words (*through the addition of question marks within square brackets*) or garbled ('xxx') speech of PoTS storytellers. Upon the final viewing of the video, in order to support the performative approach which was being undertaken and to reflect how people with PoTS orientate towards their intended virtual audiences, transcription using square brackets was employed to denote pronounced verbal actions, settings and imagery contained with

PoTS vlog. The addition of red and green coloured font to the transcription key was utilised to distinguish the presentation of edited or montaged footage from the recorded monologues of speakers' PoTS narratives.

2.7. Analysis Strategy

Narrative analysis (see *Fig. 2*), was undertaken through the three-phrase approach developed by Meraz et al. (2019), as theoretically informed by the works of Reisman (2008), comprising of thematic, performative and structural analyses. Throughout all stages of analyses, reflexive notes were generated and supervision team data sessions were held to reflect on the interpretations of the data.

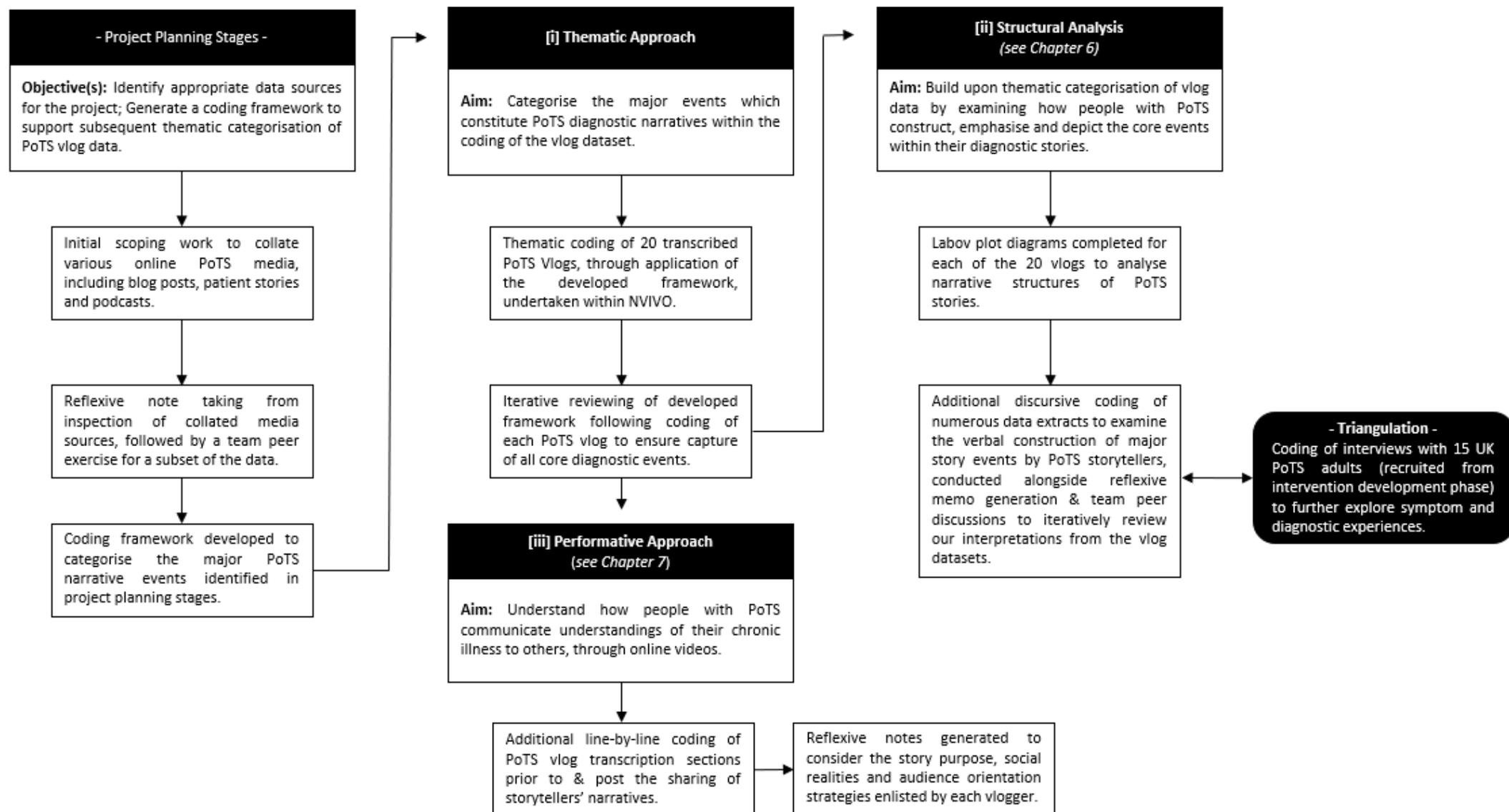


Fig. 2. Analysis strategy of PoTS vlog narratives undertaken by our research team through integration of thematic, performative & structural approaches.

- *Thematic Approach*

The thematic stage of the narrative approach aimed to identify what common diagnostic events and experiences were depicted by people with PoTS within their stories. In preparation for the coding of vlog data, I first aimed to familiarise myself with the types of narratives which people with PoTS present with. I collated various online PoTS-related blog postings, patient stories and podcast discussions. Whilst these sources were not subjected to formal analysis within the current project, reflexive comments and summary notes were created from the listening and reading of these narratives. Following discussion about a subset of this sample, an initial coding framework was developed to capture the common experiences and events from the PoTS stories.

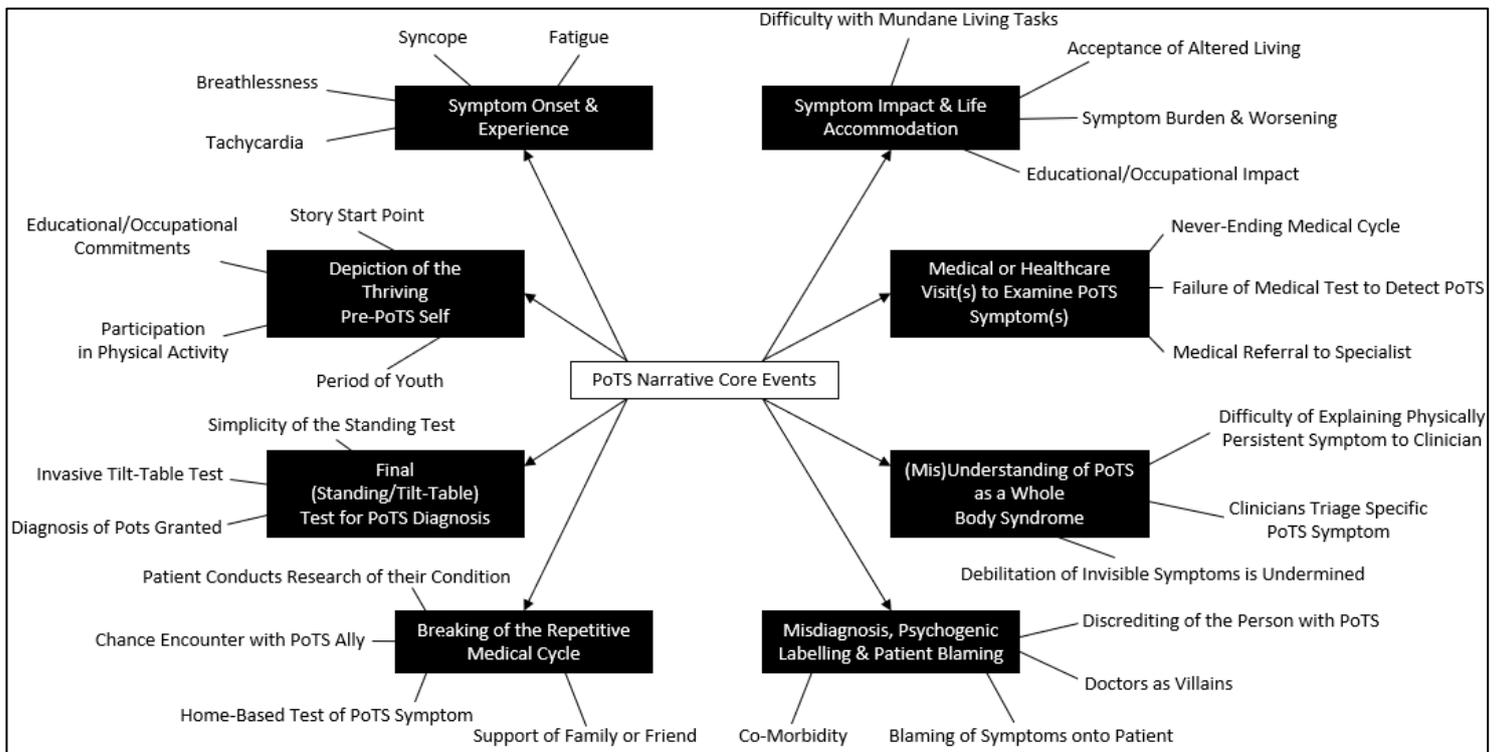


Fig. 3. Thematic map, developed from the application of the final coding framework to the final PoTS vlog sample, representing the core events in vloggers' diagnostic stories.

This thematic framework was then applied as the initial phase for the coding of PoTS vlog data through NVIVO software. During this process, the coding framework was iteratively adapted following the coding of each video to ensure that all relevant PoTS diagnostic experiences and codes were incorporated during our analysis. Following this, codes were then merged into themes which represented the core stages outlined in PoTS narratives (*a thematic map can be found within Fig. 3*).

- *Structural Analysis (see Chapter 6)*

Structural analysis, which sought to build upon the thematic approach, aimed to identify how people with PoTS constructed the core experiences which constituted their diagnostic stories through their discourse and their organisation of these narrative events into a complete, holistic narrative. Labovian plot diagrams (Labov, 1972) were completed for each PoTS vlog. Labovian plot diagrams are a common tool utilised in narrative analysis to assess the beginning (abstract), settings & characters (orientation), major plot events (complicating actions), meanings (Evaluation), story outcomes (Resolution), and closure (Coda) of each narrative.

Following this, for each significant narrative event identified within thematic analysis, open coding was undertaken. Given that elements of the structural approach aimed to comprehend how speakers had (re)constructed their experiences through their spoken words, elements of the open coding examined the discursive properties of participants' language and the devices they employed to portray the stages of their narrative. Simultaneously, memo generation and open codes, in addition to plot diagrams, were utilised to produce a flow diagram (see Fig. 4) which mapped the journey of PoTS storytellers from symptom onset to receiving diagnosis.

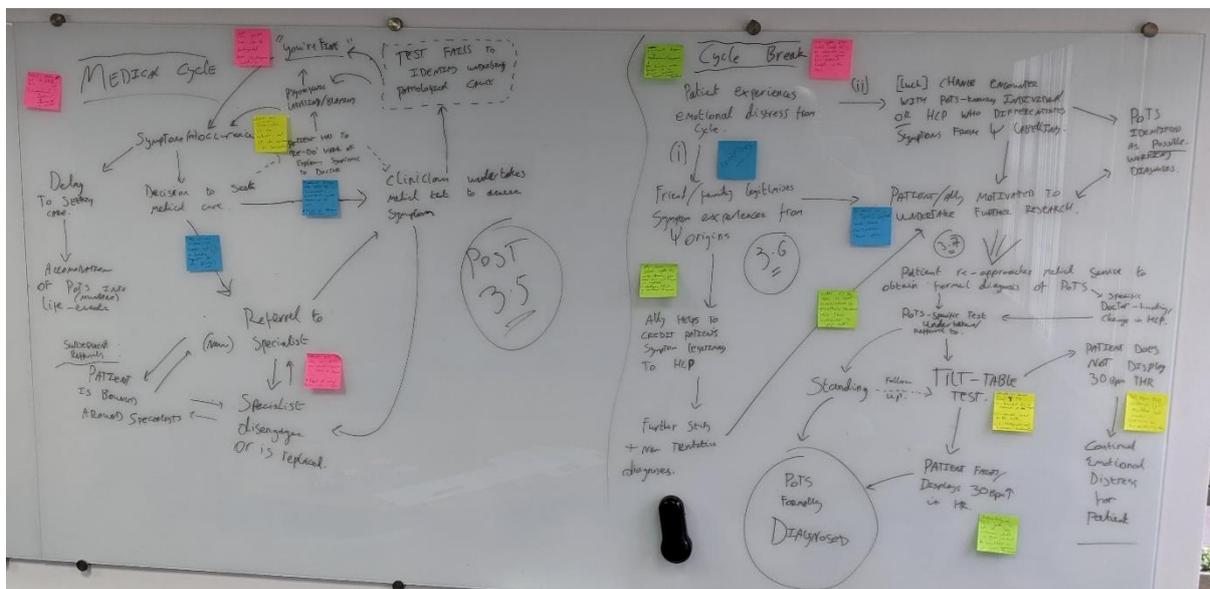


Fig. 4. Analytical work undertaken to collate thematic findings, plot diagrams, open vlog coding and reflexive memos into a model which portrayed the medical interactions which people with PoTS would depict encountering within their vlog diagnostic stories.

- *Triangulation with PoTS Interviews*

To further support structural analyses, data triangulation was implemented through the recruitment of a purposeful sample of 15 people with PoTS (Mean Age = 35.3, SD = 12.1; 14

Females, 1 Male) who underwent interviews as part of the intervention development work (see *chapter 8 for details of participant recruitment*). During discussions surrounding their symptom experience of PoTS, early findings from the narrative work were discussed with participants. This was undertaken in order to gain further insights into how these individuals were able to relate, make sense of and ground the commonly depicted experiences of PoTS which had been identified through our secondary data analyses.

Findings for each core diagnostic event from all analytical methods undertaken within structural analysis have been collated and presented back into each of their representative themes within chapter 6.

- *Performative Approach (see Chapter 7)*

Performative analyses aim to understand why storytellers choose to share their stories, in addition to exploring the purpose(s) and intended messages which they relay to their respective audiences (Meraz et al., 2019). Given that vlogs were selected for the current project if the speaker with PoTS had rationalised the sharing of their stories with the need for PoTS awareness and advocacy; the performative approach phase of the narrative analysis was undertaken to specifically examine how people with PoTS communicated understandings of their chronic illness to their virtual audience of YouTube watchers.

In order to examine this, further line-by-line open coding was undertaken upon the opening and closing segments of each vlog transcript, to explore commentaries by the speakers concerning their PoTS prior to and post-narrative. Moments where storytellers had interrupted or broke from their narrative telling were also subjective to additional coding, to provide further insights into the purpose(s) for why they would do this. Open codes generated from this analysis considered how PoTS storytellers introduced their condition, their attempts to simplify the complex nature of their chronic illness and symptoms, the description of PoTS-specific jargon and related medical ontologies to viewers, use of emotional appeals and the observation of employed orientation strategies towards both PoTS-naïve and PoTS-audiences. Findings from the performative analyses are presented within chapter 7.

2.8. *Evaluation of Narrative Phase*

Strengths and limitations of our methods and analysis strategies for our examination of PoTS narratives must be considered. First, our undertaken data collection approach employed the use of triangulation through the merging of PoTS vlog-based data alongside interviews with PoTS patients. Throughout the project, a series of reflexive notes to reflect on interpretations

of the data were generated. This included the creation of memos from reading of patient stories presented in blog and podcast formats, which were used to develop an initial coding framework for the thematic approach. Furthermore, in order to develop sufficient trustworthiness in the adopted narrative analysis, I undertook three separate analyses of the collected vlog data. This was undertaken from the recommendations by Meraz et al. (2019), who encourage the use of a multi-phase approaches for the study of narratives in order to establish rigour with this methodology.

In regard to limitations, the depiction and construction of PoTS diagnostic experience may differ across countries. Three different countries of vlogger origin were identified and examined within the current study within the final vlog sample (UK, USA & Australia). Given that narratives are shaped by a person's own social and culture experiences (Esin et al., 2013), it is possible that deviations in healthcare- such as whether the individual has access to free or paid medical care- may ultimately lead to notable alterations and common events within the construction of their PoTS stories. Furthermore, the circulation of narratives by people with PoTS may also differ in relation to the types of medical professionals they are likely to engage with, in addition to their own cultural interactions with (differing) local communities. The collation of a larger dataset is needed to thoroughly assess these possibilities.

2.9. Reflexivity

28th of November, 2019

Patient & Public Involvement Work [First Activity]

Location: Northumbria Café.

Attendees: Mitchell, one patient attendee (one patient dropped out prior to meeting; one non-respondent).

Notes from Meeting:

- When talking about her experience of PoTS symptoms (when I asked for her thoughts on us asking about this in the focus groups), attendee talked about how this may be difficult for some patients to answer, as at times she struggles to differentiate whether the day-to-day symptoms she experienced each day were due to PoTS specifically or her other condition(s).
- During the discussion, attendee talked about "energy" a lot and the importance of us understanding this for patients. The attendee discussed this as her ability or inability to perform everyday tasks, and she was keen to ask if there was any way in which the breathing intervention would be able to help with this (this was one of the improvements she would most like to see).
- Attendee wanted us to discuss with patients about how the intervention could be developed to be adaptable for people [who have PoTS] with varying levels of energy, and also to ensure it was safe for each individual to use.
- Participant discussed her frustrations at a previous life experience involving ambulance staff who did not understand her PoTS.
- Attendee wanted us to ask about the level of support (or lack of) patients receive from family & friends during/ post diagnosis. Attendee mentioned that she had experienced some problems with this in the past from relatives who did not understand her condition.

Fig. 5. A condensed series of notes produced from the first Patient and Public Involvement activity, undertaken to support the intervention development work. Parts highlighted in yellow signify notes which concern brief- yet detailed- glimpses into how this person understood, and has tried to make sense of, the sensations she experiences from her PoTS – in addition to how others around her perceive and react to her chronic illness diagnosis. Discussions such as these, which highlight the complex nature of individuals' PoTS experiences, led to the development of the narrative work I have undertaken to fully explore the nature of PoTS symptoms, diagnostic events and their impacts on the daily lives of sufferers.

My utilised methodology of focusing primarily on patient stories identified from YouTube videos for my narrative phase was - *in part* - incorporated into my thesis study for practical reasons. In that, the use of a secondary data collection strategy enabled me to rapidly collect and analyse data during the COVID-19 pandemic, at a time where I had to quickly overhaul my original interview recruitment strategy of identifying patients with PoTS from an NHS Fatigue clinic.

Despite this however, looking back now at the end of my PhD study, it has made me realise just how necessary the narrative work was to support the study of diagnostic and symptom experience work alongside my interviews with people who have PoTS. Even during the early stages of my project planning and the Public and Patient Involvement activities of my research (see Fig. 5), the interactions I would have with people with PoTS highlighted the sheer complexity and wealth of possible insights which needed to be considered alongside these people's own experiences – whether it was with family members, primary healthcare workers

or their work colleagues and line managers – as they tried to navigate life with a (contentious) chronic illness diagnosis.

Furthermore, in addition to this, in many senses the use of online patient stories as the main data source to analyse and inform my understandings of PoTS mirrors the ways in which many people with PoTS themselves will try to learn more about their own condition. Online patient groups, which have been widely associated with conditions of persistent physical symptoms in the academic literature (such as those recently formed around long-COVID), serve as a powerful source of information and ‘voice’ for individuals who often report feeling ‘ignored’ or ‘neglected’ by their healthcare practitioners. In this sense, my use of online PoTS stories as the primary source of my narrative data collection may serve as a more ‘naturalistic’ form of analysis, in order to truly understand the contexts in which their shared communities, identities (*such as being people who label themselves as “a PoTSie”*) and condition-specific jargon terminology (*e.g. ‘dysautonomia’*) emerge from.

3. Conclusion

To conclude, within chapter 5 I argued for a greater need to analyse the diagnostic and symptom experiences of people with PoTS, through the study of their online shared illness stories and narratives. I further argued that, in order to conduct a thorough and rigorous analysis of these online PoTS diagnostic stories, a multi-approach- comprising of thematic, structural and performative approaches- of narrative needed to be adopted to fully comprehend the complexity, sense-making and drawn meanings contained within their narratives (Meraz et al., 2019). Within the next chapter, through the employment of structural analyses, I further the core PoTS diagnostic events I have identified within this chapter through the described thematic approach (*see Fig. 3*) to depict how people with PoTS organise these events into a singular, cohesive story.

- Chapter 6: Journey of the Dysautonomia Hero: Structural Analysis of PoTS Diagnostic Stories through Online Patient Vlogs -

In the previous chapter, I outlined that there had been a lack of qualitative exploration within PoTS to comprehend the diagnostic and symptom experiences which these people face. These studies are sorely needed to examine how these individuals structure and portray their barriers to obtaining their diagnosis, through the analysis of the core stages they depict within their illness narratives. Within the current chapter, we build upon the identification of the common, central events which people with PoTS depict (through our employed thematic approach) with the presentation of findings interpreted from the conduct of structural analysis upon their vlog stories. From this, I demonstrate that people with PoTS present their burdens of fatigue, syncope and breathlessness through the additional work they need to perform when undertaking their routine, mundane daily tasks. I further outline that people with PoTS portray many barriers to their diagnostic quests - including clinicians' use of normalisation without explanation tactics and the psychological labelling of storytellers' persistent physical symptoms. Finally, I reflect on how people with PoTS depict themselves as empowered, 'little doctor' characters within the later stages of their narratives, who are presented as leading the investigation of their medically unexplained symptoms.

Structural analyses explored how people with PoTS had constructed their experiences of the core events of their diagnostic stories during the sharing of their narratives within YouTube vlogs. Initially, I focus on examining how people with PoTS construct themselves prior to PoTS symptom onset. I then show how storytellers depict their interactions with their healthcare services as them being stuck within a (seemingly) 'never-ending cycle', before then exploring the roles of ally and hero-like characters in the narrative who empower the storyteller to continue with their diagnostic quest.

1. Labovian Plot Diagrams

The structural approach included the production of a Labovian plot diagram (Labov, 1972) for each vlog included within the final sample (see example diagram within Table 1). Plot diagrams of individual PoTS narratives enabled me to explore how individual storytellers had organised the core events of their diagnostic experiences (as identified through the former thematic approach) into one, coherent story. Diagrams were also utilised to assist with the generation of a flow chart which mapped the medical interactions and processes people with PoTS would describe undergoing (see sub-section 2.5. within this chapter).

Table 1. Example of a Labovian Plot Diagram completed for one PoTS vlog generated during the structural analysis.

Labovian Concept	Definition	Findings [Vlog #A]
Abstract	<i>How the speaker attempts to summarise and/or introduce their narrative.</i>	Speaker discloses that their story started two years prior to publishing their video online, where they had started to experience PoTS symptoms.
Orientation	<i>Notable settings and/or characters which are introduced to provide context to the story.</i>	Protagonist is a healthy, young individual who partakes in sporting events & regular gym visits.
Complicating Actions	<i>Summary of major plot events captured within the analysis.</i>	<ul style="list-style-type: none"> - Symptom onset affects speaker's ability to compete at sporting events and partake in mundane exercises. - Syncope occurrence and debilitating fatigue facilitate the speaker to visit their doctor. - Medical tests are conducted and determine (PoTS) symptoms are due to a mono diagnosis. Speaker doubts the validity of their mono diagnosis and she decides to research the causes of her own symptoms. - A friend with PoTS suggests to the speaker that her symptoms are similar to their own. - Speaker performs a home-based poor man's tilt test and demonstrates a characteristic PoTS heart rate response.
Evaluation	<i>The purpose(s) behind the speaker disseminating their narrative to others.</i>	Sharing of the story was inspired by the Dysautonomia Awareness Month campaign.
Resolution	<i>Outcomes and end point of the expressed narrative.</i>	Speaker reapproaches GP with new information and receives a diagnosis of PoTS (along with medication) following conduct of a standing test.
Coda	<i>Consideration of how the closing of the narrative is connected to life in the present by the speaker; portrayed moral(s) of the story.</i>	<i>"I wish that I could tell you that there's one easy fix or cure but there really isn't... don't let that scare you (.) that doesn't mean that you can't live a happy life and that you can't you know maybe someday get back to the things that you love doing"</i>

2. Core Events of the PoTS Diagnostic Narrative

2.1. [Abstract]: Overview of the PoTS Narrative Through Montage

Prior to the analysis of story content, the project explored how video-based storytellers had chosen to portray the opening sections of their vlogs as the prelude stages to their stories. A number of vloggers were found to introduce their content through a short compilation of self-recorded video footage or clips, which focused primarily on introducing themselves – as the

primary protagonist of their stories - within a variety of different healthcare settings and contexts:

- Video Opening – Total Duration: 23 Seconds

[Transition to video of P being carried across the street at night on stretcher by paramedics to an ambulance]

P: oh hey (.) why is this my life?

[Transition to phone-recorded footage of P lying in an ambulance]

P: I'm in an ambulance right now! (.) I guess I passed out.

[Transition to phone-recorded footage of P in a medical treatment room]

P: I'm getting my echocardiogram here goes nothing

[Transition to phone-recorded footage of P in car, wearing a heart electronic monitor]

P: finished at the cardiologist so I will be wearing these for two weeks

[Transition to phone-recorded footage of P lying in a medical bed]

P: I just did my tilt table test

[Transition to phone-recorded footage of P lying in the same medical bed at a later point in time]

P: hey (.) so I finished my last test

[Vlog B]

Vloggers who chose this style of opening format used it to draw the watcher's attention towards the key moments within their story. Within the extract above, the storyteller has done this through the presentation of a montage of self-recorded phone-footage captured during moments where she was experiencing the events of her story. This fast and short presentation of these clips aims to rapidly progress the listener through her own medical experiences at different points of time, through her encounters with various healthcare providers and their testing procedures (*ambulance following initial syncope onset; cardiology-related assessment; follow-up tilt-table test; end of symptom assessment period*). Notice how, within less than half a minute of watching, a listener to the story has already been led through the entire synopsis of the storyteller's diagnostic journey. This is reminiscent of commentaries by De Fina (2017) on earlier works on narrative structure by Labrov (1997), which had argued that chronic illness sufferers will commonly begin the description of their diagnostic experiences with an 'abstract' that aims to summarise the main story features. The use of an abstract by the PoTS vlogger in this manner assists with the construction of their forthcoming narrative to their virtual audiences, through the carefully framing of key, core events within their story as emphasised plot progression points which constitute the chronological structure of their diagnostic journey.

Other vloggers who had adopted a similar format to their video openings through transitions of self-recorded footage opted for a blended approach, consisting of a montage of themselves within different healthcare contexts alongside clips recorded within their homes:

- Video Opening – Total Duration: 12 seconds

[Speaker (S) is presented alone on camera]

P: I started going into pre syncope like almost every time I stood up from a lying down position I started seeing like literal stars and feeling dizzy and breathless

[Video Transitions - features quick compilation of recorded footage – including images of S lying in a hospital bed, S singing outside, S playing with her cat, S with her family, S taking infusions & medicine – Total Duration: 18 seconds]

[Video Transition - Speaker (P) is presented alone on camera in real-time, to begin monologue]

P: hey guys. so today I really wanted to talk with you all about my dysautonomia and pots.

[Vlog E]

These videos featured the quick presentation of core story elements, from real-time recordings of the storyteller receiving medical assessment or treatments for their condition (e.g. *footage of vlogger receiving infusions; lying in hospital bed*), alongside the presentation of the individual in non-PoTS related settings where the vlogger is presented alongside their family, friends and/or pet(s) in the home environment. Vloggers used this blended approach within their opening video transitions as a means of representing their experiences of chronic health condition as both managed and recurrent aspects of their daily life. By combining presentation of the medical care events with footage of the storyteller's family and home life during story introduction, vloggers enlisted this strategy to demonstrate that they possessed sufficient experience of the phenomena (they are exposed to the difficulties of living with PoTS), whilst simultaneously aiming to normalise and construct themselves – and ultimately, to ground their protagonists - as relatable, everyday characters to the viewer through footage of their social interactions with loved ones.

2.2. [Orientation]: The Normalized Pre-PoTS Self

The online stories of people with PoTS within the dataset were often found to be structured in a manner akin to a 'fairy tale' like narrative (Yorke, 2014). People with PoTS described the events which led up to them receiving a diagnosis of PoTS as a journey.

I was diagnosed with pots right before (.) it took me three whole years to get diagnosed. I know some people it takes a lot longer (inhale) but I wanted to share my story with you today.

[Vlog D]

Over the whole trajectory of the narrative, they routinely positioned and framed themselves in a central protagonist role, whereby they sought to embark upon the quest and challenges associated with obtaining a diagnosis. These narratives often began with the use of scene-setting (Horton-Salway, 2001), a device whereby storytellers provide their listeners with sufficient information of the main character and their background to provide a context to their tales (Sümer, 2016). Across all of the examined stories, people with PoTS would initiate the sharing of their narratives through first constructing their life prior to the onset of their PoTS:

so I guess the first thing I want to say (.) is growing up but I was much younger (inhale) I didn't really have pots symptoms.

[Vlog E]

Centrally, they would mark a PoTS-free life, rendering it in some ways in a calm and peaceful manner to the audience. They established this peace-time presentation of their lives prior to PoTS by referring to common core elements at the start of their stories. This is akin to the narrative phase of orientation depicted by Labov (1972), in which storytellers detail the key individuals and social contexts of their tales. For people with PoTS, they constructed themselves at the start of their narratives through references to their young age and success with occupational activities at the start of young adulthood (usually within the early twenties). Centrally, throughout the openings of their stories, they portray themselves, their protagonists, as a healthy, normal and everyday member of society.

The presentation of health and good wellbeing status was further built upon within a number of stories through references to their very high level of engagement in various physical activities prior to their PoTS onset.

so prior to becoming sick I was very active (.) urm I loved exercising doing anything outside but my true passion was rock climbing (.) I would climb you know five plus days a week spend three to four hours in the gym (.) a day and I loved training and climbing and (.) it just made me happy and it made me so excited.

[Vlog A]

Notice the strong emotive language, how they 'loved' undertaking exercise alongside their 'true passion' for rock climbing. This passion here could be rendered as an obsession, given the very high level of physical exercise outlined here, climbing 'five plus days a week', as well as 'three to four hours' at a gym every day. Whether they rendered themselves as someone whom 'loved exercising' or a person who 'just working and enjoying life', speakers linked these everyday activities and roles with their experiences of positive affective states. These findings therefore demonstrate how PoTS storytellers established orientation within their story introductions through their accounts of relatable, wellbeing-associated activities as healthy living 'anchors' in their monologues to normalise themselves. These anchors aimed to orientate their audiences and establish similarities between the story protagonists and listeners who had not experienced long-term illness.

2.3. [But then...]: Disruption with Symptom Onset

Through the depiction of their lives prior to the onset of chronic illness as a normal, relatable everyday living experience, speakers then used this as a basis of producing stark contrasts which highlighted changes in their health following initial symptom presentation.

I was completing daily conditioning workouts (.) I was doing basketball and volleyball summer league and I was participating in a lot of softball camps. but in July I felt sick.
[Vlog C]

Notice how connotations of good physical health are emphasised by authors– such as the use of a triplet device above (*'workouts', 'basketball', 'volleyball'*)– alongside other key achievable activities and goals associated with good health and wellbeing, which in turn are purposely and intrinsically connected by the storyteller to the time point of PoTS onset (*'but in July I felt sick'*).

By recalling the moment of symptom onset within the narrative, this provided speakers with an opportunity to speak openly with their audiences about how their own self-held beliefs of health had been challenged through their own personal experiences.

Erhh (.) right after I turned 21 years old and I kind of started noticing my symptoms of pots (inhale) it started with I was waking up feeling tired most throughout the day and at this time I was bartending (.) maybe four days a week? and you know to with me being (.) twenty-one years old I used to go out partying and I thought (.) I was (..)
P: pretty much untouchable (.) with anything
[Vlog Q]

Within the above passage, the storyteller elicits this through the use of an overt, retrospective voice to question health misconceptions surrounding her character's young adulthood (*'twenty-one years old and I thought I was pretty much untouchable'*). This is done purposefully by the speaker to upset the notion that their young age is a perceived representation of their invulnerability to disease and illness. Within this story, the vlogger has used a retrospective reflection within the openings of their narratives as a mechanism for breaking-down the established health-statuses of their protagonists to their audiences. This is representative of how people with PoTS deliberately recalled anecdotes of experiencing initial symptom onset as an intentional, disruptive plot device within their diagnostic stories to deconstruct the established health and wellbeing statuses of their characters.

Through orientating back to these relatable living anchors during moments in the diagnostic story where the storyteller's health or wellbeing has been deconstructed, people with PoTS convey to their PoTS-naïve audiences the full extent of their illness debilitation, through these

exemplifications of the widespread impacts of symptom burdens upon their activities, goals and quality of life.

2.4. *[Making Sense of Burden]: Accommodation of PoTS Symptoms into Daily Routines*

Narrative analysis highlighted the ways in which PoTS symptom presentation, prior to diagnosis, was focused on by people with PoTS as an initial struggle to their day-to-day living activities.

I would be very fatigued (.) all the time and whenever I would walk just simply from one door to the next or a couple steps that would get very winded. and its not fun. you'd have to stop every couple of paces just so I could catch up and catch my breath.

[Vlog M]

Specifically, people with PoTS recited how their experiences of enduring with breathlessness and fatigue would require them to make changes to the ways in which they undertook their habitual routine tasks. Even actions which may appear simplistic in nature for others to perform, those that normally required little thought to be enacted- such as a 'walk just simply from one door to the next'- were described as now requiring a greater level of conscious consideration and readjustment from the person with PoTS, in order for the task to now allow for resting periods as forms of accommodating their symptom burden ('you'd have to stop every couple of paces just so I could catch up and catch my breath'). This finding is concurrent with notions by Bury (1982), who defines chronic illness experienced through the additional work which sufferers need to undertake to still meet their daily obligations and functional commitments.

Some people with PoTS discussed how they had continued to live with their bodily complaints for an extended period of time before they made the decision to pursue healthcare intervention. Crucially, these individuals discussed employing the use of symptom masking. Vloggers and interview participants focussed on sharing the consequences and challenges they faced from enduring with their symptom worsening over time across educational, social and occupational engagements.

I'd lived on the [ground level] floor but I had a like walk a flight of stairs to get to the building. a lot of the time (.) depending on how [I] got there (.) I started seeing like literal stars (inhale) and feeling dizzy and breathless when I got at the top of the stairs. and it's not like this had never happened to me before but it had never happened continuously (exhale) like every single time I'm doing it or basically every time (inhale) I also started seeing stars and feeling dizzy (.) breathless

[Vlog E]

Crucially, participants discussed how the experience of their orthostatic and syncope-related experiences had, over time, gradually become accepted as a regular aspect of their everyday rituals. An example of this is referred to in the extract above, whereby the storyteller describes a once seemingly simplistic task for her (prior to PoTS) of walking up a flight of stairs to her higher education dormitory. Specifically, this experience is described in terms of having evolved from an occasionally more difficult task in light of her breathlessness and dizziness symptoms ('seeing like literal stars (inhale) and feeling dizzy and breathless'), into the regular occurrence of a much more complex and distressing activity which occurred 'every single time'. These accounts ultimately portray how the accommodation of PoTS symptoms and practices of symptom masking by sufferers prior to medical intervention had become embedded as integrated and unavoidable aspects of their daily routines.

The regularity of these disruptive episodes of symptoms- such as the possibility of a sudden, unpredictable syncope episode occurring- led to additional burdens within their everyday duties and work. During an interview with a former nurse below, the participant described the great lengths she would go to in order to disguise and mitigate the impact of PoTS on her debilitation, in an effort to continue with the care of patients with complex medical issues within their homes:

I can remember quite clearly it was just natural for me to get up turning away from them. And then take the bowl of water back to the sink and by the time I got to the sink I was nearly hanging because I felt so faint. But I knew getting up from that positional change from being down to being up would make me feel faint.

[K10MA]

First, notice the procedural nature in which this activity has been described, whereby the enactment of this routine occupational task at hand- emptying the cleaning bowl- has been broken down into a linear series of three events faced by the participant: the adoption of upright posture and facing away from patient; placing of the bowl in the sink; resistance of fainting-like sensation. Through this segregation and isolation of the individual aspects of the task, the participant illustrates how the unnoticed, taken for granted components of a daily work objective need to be considered and re-structured. Such tasks need to be undertaken and managed in accordance with her orthostatic complaints, in order for her to still 'actualise' her work with her now reduced physiological levels of energy.

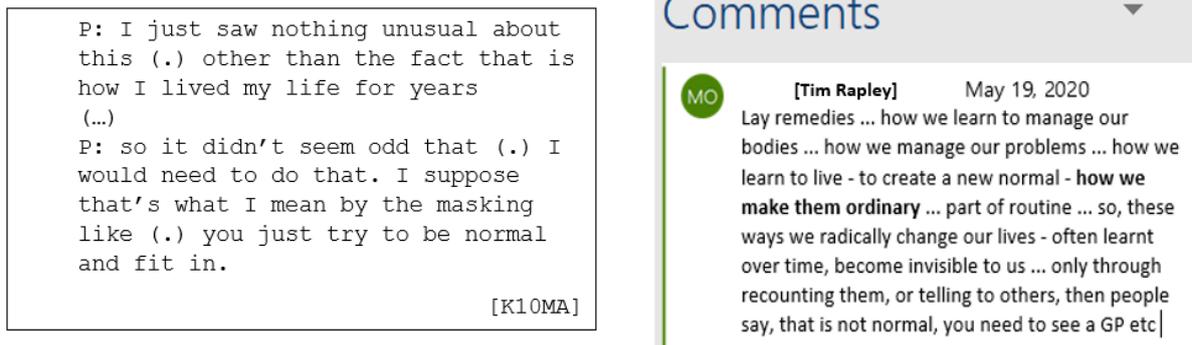


Fig. 1. Reflexive comment [TR] created during the initial project planning stages, which informed interview schedule item generation surrounding exploration of PoTS symptom experiences, was referred back to by MJH whilst undertaking line-by-line coding of transcripts [K10MA]. Incorporating questions for the intervention development phase of the project, informed by ongoing secondary data work, allowed me to expand on my initial understandings of PoTS symptom masking by directly asking participants how they related and made sense of their symptom experiences at different points throughout their stories. Ultimately, the reflection and extract above demonstrates reasoning for the decision to triangulate the analysis of vlog-based PoTS stories with further participant responses obtained from interview work, in order to capture further insights from the wider PoTS community.

Following prompt by the interviewer, the participant goes on to recall this facilitation of symptom masking to be an unconscious experience, which she 'saw nothing unusual about' performing as part of her daily work. Specifically, note how the implementation of the new adaptive procedure she needs to undertake to accomplish the work has become unnoticeably embedded into her day-to-day healthcare practices, as evidenced through her confession that this routine and habituated pattern – which she would 'need to do' and had been repeating 'for years' – 'didn't seem odd' to her. Only through a retrospective lens, where she has since been able to re-construct her experiences at a much later point time (see Fig. 1.), does she label this process as 'masking' and tries to rationalise this construction of her actions to the interviewer through her attempt to 'just try to be normal and fit in'. Through triangulation with interview work, this extract therefore builds upon narrative findings by demonstrating how people with PoTS would attempt to justify and support their descriptions of partaking in symptom masking to others.

2.5. [The Medical Realm]: Repetitive Cycle of Healthcare Services for PoTS Symptoms

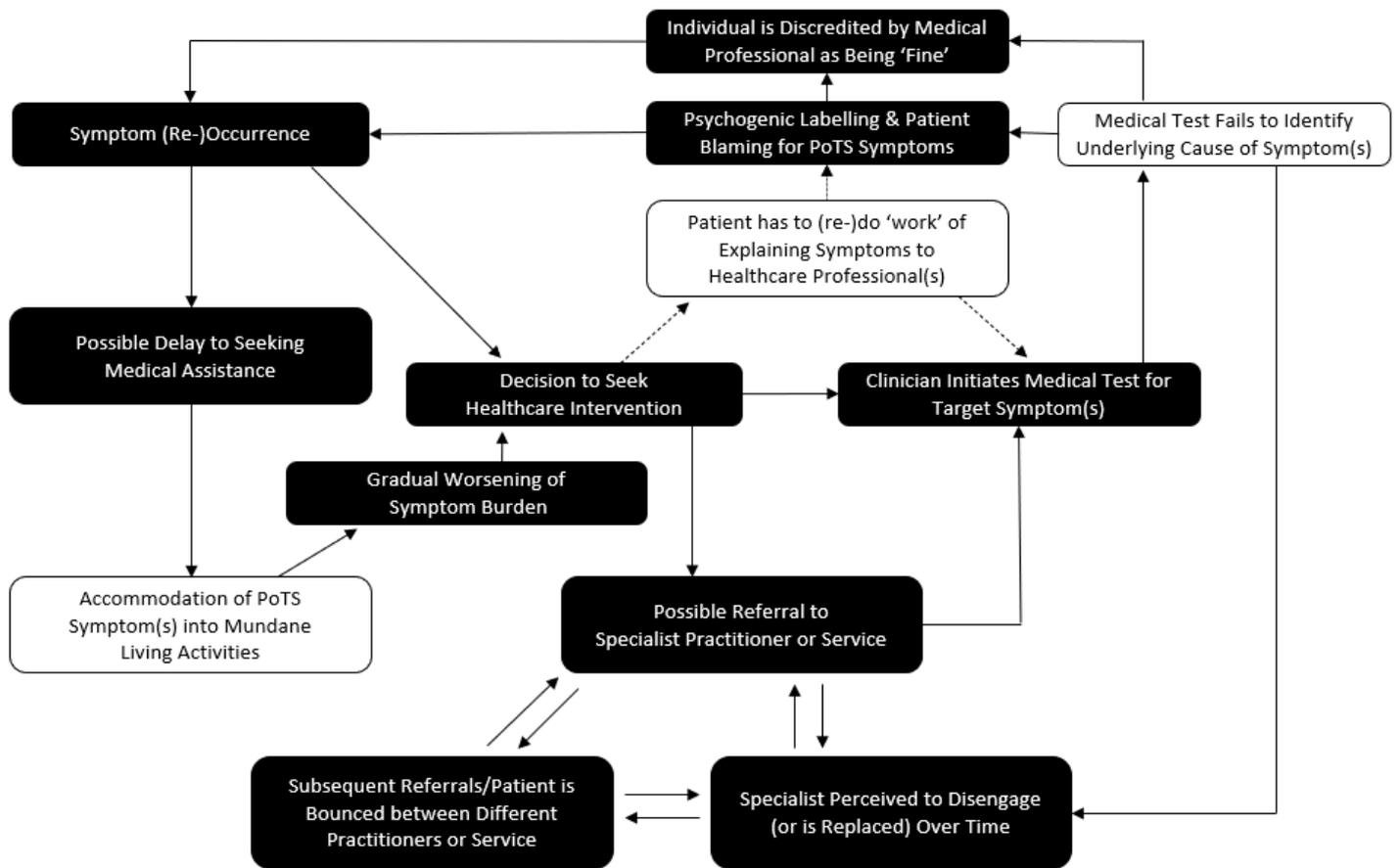


Fig. 2. Diagram of the medical cycle - produced from mapping of core vlog story events - representing people with PoTS' portrayed interactions with healthcare services and barriers to receiving diagnosis.

People with PoTS presented the medical inspection of their persistent physical symptoms by healthcare practitioners as an extensive and laborious process (see Fig. 2). This process often began with the failure of medical assessments to detect the abnormality or underlying cause(s) behind the patient's debilitation.

so I went into the hospital and they would always do the same series of tests (.) they'd do an ECG (.) twelve lead (.) they did pressure blood tests and then I'd be sent home and they would go (mimicking) "huh well everything seems okay." They'd never quite catch it.

[Vlog G]

As such, these patients portrayed their PoTS as a disguisable, undetectable entity which masked itself from common testing procedures. Speakers would comment on how this in turn made it difficult for practitioners to identify tentative working diagnoses ('They'd never quite catch it'). Several stories commented upon how the standardised testing procedures employed by practitioners to investigate their medically unexplained symptoms had, over time, become part of a habituated routine, in which storytellers would find themselves repeatedly

discharged and needing to re-approach healthcare services at later points in time, in order to manage symptom flare-ups ('they would always do the same series of tests').

I mean I was constantly getting dizzy and anytime I went to a doctor en (.) or at a hospital (.) they would just tell I'm fine (.) all my lab results look good and just send me back

[Vlog Q]

Within the extract above, one storyteller recalls how they would be subjected to similar series of medical examinations on each healthcare admission, prior to being repeatedly discharged by their healthcare teams due a lack of conclusive findings from testing ('they would just tell I'm fine'). Notice how the vlogger has chosen to portray the doctor's labelling of the their health status as 'fine' as being rationalised solely from their interpretation of the patient's examination results ('all my lab results look good'), and how this compares against the debilitating, subjective experience of 'constantly getting dizzy' described by the speaker in the story. This is representative of how some people with PoTS used contrast within their narratives to construct the act of dismissal towards the ordeal of their symptoms by key individuals in the wider healthcare community

I sat there and cried because (.) no one could figure out what was wrong with me. I had been to every kind of specialist that you could think of. I had every test done (.) I mean I got EEGs (.) CAT scans (.) MRIs and (.) nothing was to be found.

(..)

I pretty much went through this (.) six months cycle

[Vlog Q]

These contrasts would include references to the emotional tolls the individual would face as a result of not having their symptoms made sense of, or fully understand, by their doctor ('I sat there and cried because... no one could figure out what was wrong with me'). At these points of the story, these accounts were often connected to vloggers' use of extreme case formulations [ECFs] - a discursive device which functions to exacerbate the recalling of story features and events in order to impose a specific, constructed account of past events (Kiyimba, 2020) – to highlight the high number of medical tests they would routinely find themselves undergoing to explore their medically unexplained symptoms ('I had every test done').

Notably, people with PoTS used ECFs in their tales as a tool to impose their perceptions towards the ineffectiveness of these medical assessments, which is then further emphasised again through the use of a three-part list ('I got EEGs CAT scans MRIs and nothing was to be found).

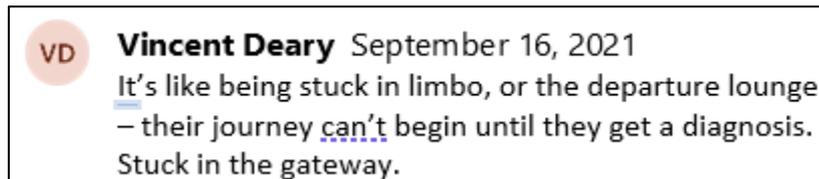


Fig. 3. Reflexive comment [VD] generated from reading the prior vlog extract during the results drafting phase. This reflection signifies the ways in which my supervisors and I tried to make sense of the slowed pace of narrative progression that we observed when vloggers with PoTS described interactions with healthcare practitioners.

In this sense, medical assessments were depicted by vloggers as thresholds to accessing care in their stories (see Fig. 3.), whereby people with PoTS described being dependent upon their results in order for them to translate the validity of their subjective symptom experiences to healthcare practitioners. The failure of these tests to detect the vlogger's PoTS would in turn act as a barrier, which trapped people with PoTS and prevented them from being able to break the 'cycle' ('I pretty much went through this six months cycle', Vlog_Q) of accessing medical care and experiencing continual discharge without the receipt of diagnosis or effective symptom management (treatment) that would be needed to progress their narratives further.

Common medical assessments of medically unexplained symptoms in PoTS were therefore presented by storytellers as a hinderance to their quest of obtaining a valid diagnosis for their condition, as negative test findings are portrayed as providing healthcare professionals with the justification of 'you're fine'. In turn, PoTS storyteller described this justification of 'you're fine' as a resource which could be enlisted by medical practitioners to facilitate the relinquishing of their suspicions towards the severity of a possible underlying patient health problem. Through this action, this final decision completes the practitioners' work during the consultation process by permitting patient discharge, whereby the responsibility for the patient's health is portrayed by the storyteller as being assigned back to the patient ('so we will leave you to it') or to an alternate medical practitioner through referral to a specialist practice ('I had been to every kind of specialist that you could think of', [Vlog_Q]).

People with PoTS ultimately described their experiences of the examination process as a gateway process to an altered patient experience, that results in them feeling trapped within their health systems over time (see Table 2).

Table 2. Three core requirements to medical treatment, derived from reflexive notes generated throughout the analysis & coding process, presented as quest barriers by PoTS Storytellers.

Requirement	Barriers Portrayed by PoTS Storytellers	Supporting Extract
Identification of PoTS as a Candidate Diagnosis	Failure of medical tests to identify physiological abnormalities or underlying causes	<i>I went to the doctor and they did some tests and everything came back like fairly normal [Vlog_A]</i>
Understanding of PoTS Symptoms are a Holistic, Whole-Body Experience	Primary medical practitioners are constructed by the PoTS community to triage and isolate specific symptoms over others through referral	<i>for many it is a years-long process... they go through so many different doctors and specialists searching for answers [Vlog_F]</i>
Recognition towards the Legitimacy of Patients' Bodily Complaints	People with PoTS describe experiences of being psychologised, blamed or discredited during medical interactions	<i>they would just tell me (mimicking) "you know you're young... you're not sure you are. you're probably just having really bad anxiety" [Vlog_S]</i>

2.6. [Mislabelled]: Practitioners Neglect the 'Entire-Body' Nature of PoTS Symptoms

As part of the repetitive cycle of engaging with the medical community, storytellers would outline incidents where their PoTS had been mislabelled or incorrectly diagnosed. Speakers would often start recalling these notable moments of their diagnostic journeys by discussing the struggles they had encountered with trying to explain the true extent of their bodily complaints with their practitioners.

I mean I'm talking to like a lot of doctors and everything from cardiologist (.) neurologist errr (.) gastroenterologist. because it was (.) as you guys know it's an (.) it's an entire body syndrome (..)

P: where do you start!? Do you start with the dizziness? Do you start with the weirdness?

[Vlog P]

This can be seen within the passage above, during a moment where the vlogger has shared an anecdote to describe their experiences of seeking assistance for her medically unexplained symptoms. From the perspective of the speaker, this difficulty was the individual with PoTS symptoms being unable to begin describing the wide multitude of symptoms ('where do you

start!?) they were experiencing to the healthcare professionals. Speakers explained how this was due to the nature of PoTS being a syndrome, in that storytellers such as this vlogger would disclose how they felt incapable of being able to identify and distinguish what were the major complaints of their health from amongst the widespread cluster of symptoms they were encountering ('Do you start with the dizziness? Do you start with the weirdness?'). Furthermore, notice too, how this issue is represented by the speaker's self-categorisation of their PoTS as 'an entire body syndrome', and how this naming of their health complaints is then justified by the speaker through a consensus with the assumed knowledge and familiar experiences of their intended, fellow virtual PoTS audiences ('as you guys know').

all of my doctors would try to focus on one little part of my symptoms (inhale) they would say (mimicking) "oh you have headaches (.) let's take you to a neurologist" and they would only look at my headaches and then they'd say "oh you have stomach aches (.) we're gonna send you to a GI doctor and only look at your GI symptoms" (.) but with PoTS (.) it just affects every part of my body

[Vlog J]

This (complex) experience of a widespread cluster of PoTS symptoms, which 'just affects every part of [the] body', was depicted by storytellers as posing significant issues for their medical teams.

Healthcare teams are portrayed as struggling to determine the appropriate medical specialists to assist with their patients' complaints. In this respect, some medical professionals were presented by speakers during their PoTS stories as characters who would try to over-simplify the complicated nature of their patient's ailments - through their attempts to prioritise or triage specific medically unexplained symptoms over others ('all of my doctors would try to focus on one little part of [their] symptoms').

they would just focus on one small thing and not see the whole picture.

[Vlog D]

These attempts by practitioners to over-simplify the nature of their patients' illness through this described triage-approach was commonly criticised by PoTS storytellers ('they would just focus on one small thing'). Speakers would then use these challenges to demonstrate their arguments and beliefs that their medical teams did not understand the 'entire body' [Vlog_P] nature of their complaints, as these individuals could 'not see the whole picture' and were not able to grasp the syndrome-like elements of PoTS.

2.7. [Doctors As Antagonists]: Psychogenic & Patient Blaming of PoTS Symptoms

Experiences of PoTS symptoms being perceived to be psychological in nature by medical practitioners were prominent throughout both vlog and interview datasets. Anxiety was reported to be the most common misdiagnosis which people with PoTS had received during their diagnostic journeys.

And (.) I went to every doctor under the sun and (.) they ended up finding some minor things (.) but nothing that really would explain how I felt. and so after going to so many doctors they were just kind of like (mimicking) “you know (sharp nasal inhale) we're gonna mark this as anxiety (.) you have anxiety.” and I was like (mimicking) “you're crazy! I'm not having anxiety!”

[Vlog K]

The extract above depicts a vlogger discussing the moment in the story where they had received a diagnosis of anxiety following numerous consultations (emphasised by the storyteller through the use of an ECF, ‘I went to every doctor under the sun’). Notice how, within the above passage, the speaker recalls the healthcare practitioner as saying “we're gonna mark this anxiety”, as opposed to this doctor stating a much more direct statement such as, “*you have anxiety*”. In this respect, the confidence of the practitioner when diagnosing anxiety is undermined by the storyteller through hedging to instil doubt. The practitioner's conclusion of anxiety is not presented to be a definitive or satisfactory answer to account for her medically unexplained symptoms (‘nothing that really would explain how I felt’), but is instead shown to be an action-orientated decision that has been undertaken by the medical team. This decision forces the progression of the speaker's medical interactions, as it provides the healthcare practitioner(s) with a rationale for discontinuing her need for further medical testing.

A similar moment in the story was discussed from an interview participant below, who had visited a consultant for assistance with her syncope episodes.

And the consultant just stared at me. It wasn't of any relevance to him (.) he didn't want to know erm he didn't understand it (.) he didn't want to know (.) and obviously to him I was just somebody with anxiety (.) who was highly strung and that was causing me to feel like I was going to collapse a lot.

[K10MA]

Negative portrayal of some healthcare practitioners was a common pattern identified across PoTS stories, whereby storytellers would justify these perceptions of their practitioner(s) through their portrayed unwillingness to understand or attempt to learn about their ailments (‘he didn't understand it (.) he didn't want to know ‘). People with PoTS explained how they believed the diagnosis of an anxiety disorder served as a form of a personal attack by the doctor upon their own characteristics (‘and obviously to him I was just somebody with anxiety who was highly strung’). Through this, storytellers highlighted how, through the allocation of

an anxiety diagnosis, they construct an experience of how their healthcare practitioner(s) had tried to discredit their complaints and instead place blame onto them. The shifting of blame was viewed as an attempt by practitioners to make their patient(s) feel culpable for the symptoms they were presenting with ('and that was causing me to feel like I was going to collapse a lot').

The psychogenic labelling of PoTS symptoms by healthcare professionals in this manner was therefore perceived by storytellers to be a heuristic strategy, employed by practitioners to quickly dismiss of patients who presented with persistent physical symptoms. Within the extract below, a vlogger disclosed how she had perceived healthcare practitioners to view her during consultations:

it's like if I don't have a particular problem or something that screams the name (.) they don't know what to do. they (.) they would think it's anxiety or depression or (.) that just because I'm a thin girl (.) that I have an eating disorder and I don't. it's just genetics you know. I mean (.) I'm thin I can't help it.

[Vlog M]

This passage provides further insight into the underpinnings of how people with PoTS have understood the events and actions which lead their healthcare practitioner to use this described heuristic technique. The storyteller first breaks-down this sequence by addressing their doctors' unfamiliarity with the condition that they are presenting with- in that, the vlogger has retrospectively assumed that PoTS was absent from the practitioner's repertoire of medical knowledge at the time of consultation ('I don't have a particular problem or something that screams the name'). The healthcare professionals therefore 'don't know what to do' with their patient and need to adopt an alternative method, in order to still successfully complete their work of diagnosing their patient during the practice. The speaker constructs this as a heuristic-like strategy were healthcare practitioners resort to the use of stereotypical assumptions made about the individual, relating to her gender and body size ('I'm a thin girl').

Storytellers presented doctors as trying to classify and fit their medically unexplained symptoms into a group of diagnoses, that was consistent with the practitioner's pre-existing medical knowledge and schemas. The severity of their complaints was then represented to be mitigated by the recalling of healthcare professionals downplaying their illness.

at that point they just thought this was anxiety and you know (mimicking) "follow up with your regular doctor (.) follow up with your psychologist and you know (.) get these panic attacks under control (.) figure out what's going on with you".

[Vlog F]

The psychiatric labelling of their medically unexplained symptoms had lead practitioners to also over-simplify the severity of their health complaints, due to them being perceived as 'a

thin girl' (Vlog_M), or being dismissed by medical professionals who 'just thought this was anxiety' (Vlog F). Practitioners were viewed as also using this label as a reasoning to off-load and allocate responsibility for the management of their symptoms back to their patients themselves, where it was seen to be the sufferer's role to get their 'attacks under control', 'work it out' and to 'figure out what's going on with you'. Because of this, people with PoTS felt that they would receive a limited or unsatisfactory level of care from their practitioners to help manage their bodily complaints.

2.8. *[Allies & Heroes]: Breaking of the Medical Cycle*

Storytellers described how their (seemingly endless) experiences with healthcare professionals and ongoing referral processes would lead their protagonists to experiencing an emotional lull, whereby they had given up on trying to find answers. Storytellers described two key methods of breaking these cycles in order to progress their own PoTS diagnostic narratives.

that afternoon when my mom started doing research while I (.) went to bed she was sure almost immediately that PoTS was indeed my diagnosis (inhale) and as usual I was a bit more sceptical (.) I wasn't quite ready to bet the farm on it. but I was also really just too tired at that point to spend the energy to even care what the answers were.

[Vlog C]

The first method involved the recruitment of a pivotal individual in the story, who could serve as a supportive ally character in the form of a close friend, significant other or family member. Once a family member or significant other had been recruited, storytellers would describe how these characters would push forward the investigation of their physical persistent symptoms, during moments where the protagonist had been incapacitated through their struggles with hopelessness and thoughts of withdraw from their quests ('I was a bit more sceptical (.) I wasn't quite ready to bet the farm on it'). These ally individuals were therefore portrayed as pivotal characters in the story, who needed to be relied upon by protagonists in order to prevent the discontinuation of their narratives through the undertaking of research on behalf of the protagonist. Family and friends were ultimately represented by PoTS storytellers as core plot devices in their narratives, which would progress their diagnostic journeys when the primary character had been 'too tired at that point to spend the energy to even care what the answers were '.

Alternatively, a second method was depicted through a chance-encounter with a notable individual(s) with looser associations to storytellers. Within some narratives, this came in the

form of specific healthcare professional(s), who unlike other portrayed medical practitioners in the story, had distinguished the storyteller's persistent physical symptoms from those of psychological causes. These healthcare professionals took the form of hero characters in the narrative, in that they were portrayed as providing empowerment to the storyteller during their time of emotional despair.

P: [Psychologist] said (mimicking) "this is your first (.) and this is gonna be your last (.) session because you don't have anxiety. you definitely have something going on with you medically and you're just not in the right hands yet. once you get in the right hands (.) you'll get an answer."

[Vlog K]

This is highlighted within the extract above, where a storyteller recalled being referred for a psychological evaluation by a healthcare professional who had challenged the contentious nature of her bodily complaints. Notice how, within this example, the psychologist is recalled to empower the protagonist through a two-fold strategy – whereby she has first provided her with reassurance towards the 'underlying cause' of her journey ('you definitely have something going on with you medically'). The healthcare professional then motivates the storyteller, through reminding her of the promised reward – the correct diagnosis – that she will receive for continuing to embark upon and successfully complete her character's quest ('once you get in the right hands... you'll get an answer'). This interaction therefore demonstrates how people with PoTS attached significance in their diagnostic stories towards individuals who had not refuted the medical basis of their condition.

So me and the (.) emergency doctor had a conversation about um when I was being discharged he pulled me aside and said (mimicking) "hey you know (.) this might be this condition called pots (.) you might want to look into it".

[Vlog V]

Note that family/friend (ally) + healthcare practitioner (Hero) roles are similar but distinct.

- Family/Friend are relied on by people with PoTS to investigate their symptoms/possible causes. (Ally).
- Healthcare practitioners (as HEROES) Empower the person with PoTS to become their own researcher.

Fig. 4. Reflexive note [MJH] generated during line-by-line coding of Vlog V, demonstrating how healthcare practitioners (presented here as 'Hero' characters) can be portrayed as empowering the PoTS storyteller to become their own researcher. This was distinguished from the presented role of 'Ally' Friends/Family by storytellers, who instead were understood to be responsible for conducting the investigation of underlying symptoms cause on behalf of the person with PoTS.

In some stories, these heroic healthcare professionals (see Fig. 4) were recalled as the first people to introduce and signpost the protagonist towards PoTS as a possible solution to their ailments ('hey you know (.) this might be this condition called pots '). Storytellers described being motivated by these encounters, in which they were spurred on to undertake their own further research into the possible causes of their symptoms ('you might want to look into it').

you know you get all like investigative (.) and you think like this little doctor err (.) thinking that you have this X Y & Z or whatever. so you talk to your doctor about it and she was like (mimicking) "actually you know that makes sense (.) let's do some labs on that".

[Vlog F]

As such, stories which featured a hero character would lead storytellers to depict themselves as a 'little doctor'. This term (coined by Vlogger F) represents how their storyteller's character would undertake a research-like role to in effort to identify tentative explanations for a diagnostic category they belonged to through deductive reasoning ('thinking that you have this X Y & Z or whatever '). Through the act of conducting their own research, some storytellers felt empowered to re-approach and work alongside their medical practitioner(s), in an effort to out-rule the possible tentative diagnoses their research has identified ('so you talk to your doctor about it').

so I went to boots which is the pharmacy (.) I bought the cheapest blood pressure monitor that they had (.) and I started measuring for the next three weeks myself lying down (.) right when I woke up in the morning (.) and then also standing up.

[Vlog E]

Storytellers would advance and certify their own portrayed status as a 'little doctor' [Vlog_F] by demonstrating that they had also - where possible - carried out their own medical investigations and home-based tests of their physiological responses. This often was commonly performed through the monitoring of heart rate and blood pressure changes, through home-based applications such as a smart device or wrist monitor. The performance of these investigations, which storytellers would perform at different times of the day and during the up-taking of various postures ('I started measuring for the next three weeks myself lying down (.) right when I woke up in the morning (.) and then also standing up'), enabled people to test the numerous working hypotheses they had developed through their research to account for their bodily ailments.

I even like did the poor man's tilt table test where you know (.) you lay down for a while and take your heart rate (.) and then sit up and stand up and (.) stand for a while (.) and you know take your heart rate.

[Vlog A]

In some stories, self-testing performed by storytellers would also extend to the conduct of a standing test in the home when PoTS was suspected. Storytellers recalled how this observation of a significant heart rate change in response to orthostatic challenge ('my heart rate was like seventy plus beats higher when I was standing up'), would in turn end the investigation process carried out by their 'little doctor' [Vlog_F] by corroborating the individual's working hypothesis that their condition could be identified through the diagnostic label of PoTS.

2.9. [Final Challenge] Torture of the Tilt-Table

After PoTS had been identified and acknowledged as a candidate diagnosis, storytellers would describe returning to visit medical care practitioners in order to pursue confirmation of this through certified medical testing. PoTS-specific tests were conducted either through standing test or tilt-table assessment. At times, standing test findings alone had been deemed sufficient to end their narrative quests by granting them the sought-after diagnosis of PoTS.

so you stand up (.) you sit (.) you lay down (.) you sit (.) you stand up. they take your heartrate (.) they take your blood pressure in those times. so basically that means that my heart rate spiked over thirty.

[Vlog T]

The performance of a standing test itself was ultimately described by these storytellers to be a non-invasive and relatively simplistic procedure ('so you stand up... you sit... you lay down... you sit... you stand up. they take your heartrate'). During the anecdotes of PoTS testing during the narrative, it was commonly noted that storytellers would highlight to their audiences how they had evidenced their diagnosis by achieving the necessary minimum heart rate change of thirty beats per minute upon standing ('so basically that means that my heart rate spiked over thirty'). The observation of this physiological change served as the final threshold storytellers would need to surpass in order to access care (see sub-section 2.5).

Storytellers also explained how healthcare professionals would refer them to undergo tilt-table testing as a (final) method to confirm the presence of PoTS.

and he said "we can do a tilt table test if you want to". so I said "yes I need to find out what's going on".

[Vlog O]

In the interaction above, notice how the storyteller – as the patient – depicts themselves as the person who ultimately makes this decision to undergo the tilt-test ('yes I need to find out what's going on'), rather than it being a decision made by the healthcare professional, who is portrayed to merely suggest this ('we can do a tilt table test if you want to'). This echoes back

to previous moments in the narrative (sub-section 2.8), whereby people with PoTS present themselves as active and empowered characters in the later stages of the narrative - who become responsible for leading the medical investigations of their own symptoms and working alongside practitioners to accomplish this goal.

the first part wasn't that bad. it was uncomfortable and I just felt like (mimicking) "oh like this sucks (.) like I want to sit down" (inhale) but the second part of the test is when it (.) was (.) horrible

[Vlog B]

Tilt-table testing was segregated by some people with PoTS as a multi-stage process. The 'first part' of which involved the setting up of the test, establishment of a resting heart rate and a small initial incline of the patient from a supine position where protagonists felt 'uncomfortable'. The 'second part of the test' - involving the subsequent raising of the table to place the patient at a more upright, standing position – was dubbed as a 'horrible' experience by storytellers, through the intense worsening of their orthostatic symptoms ('oh like this sucks (.) like I want to sit down').

People with PoTS constructed the 'unpleasant' experience of tilt-table test through descriptions of their bodies experiencing states of hyper-arousal, which would leave them feeling 'weak', 'shaky all over' [Vlog_C] and 'just out of control... of [their] body' [Vlog_J]. Speakers also spoke about how these heightened physiological sensations had been purposely elicited through the administration of chemical agents by the medical team to evoke a characteristic PoTS heart rate response.

they gave me adrenaline and my heart was racing (.) that's what adrenaline does (.) and I was breathing heavy because it felt like I was running but it's literally strapped onto a table laying down. and that's another thing is whenever I'm strapped down (.) like it freaks me out. like not having control over like (.) to leave or move. it freaks me out. so I was like trying to keep myself calm in general being like strapped to this table.

[Vlog B]

This final test was described as the need for storytellers to remain 'calm' with being 'strapped down' onto the tourniquet, and their inability to 'to leave or move', is employed alongside emotive language use as a way to construct storytellers' recalled state of vulnerability ('whenever I'm strapped down... like it freaks me out'), due to their portrayed susceptibility to the heightened bodily sensations 'I was breathing heavy because it felt like I was running). Recounting of being physical restrained during the tilt-testing procedure – where they were 'literally strapped onto a table laying down' – represented storytellers' use of torture-like analogies to describe their experiences. These representations were used by people with

PoTS in their stories to (re-)construct sensations of psychological distress during this crucial moment in the narrative.

Following successful completion of their diagnostic assessment, people with PoTS discussed their newly acquired diagnosis as a 'relief':

the results came back that i have PoTS. that's kind of when the clarity hit like (mimicking) "okay i'm not crazy" like (.) ha "told you it's not crazy i didn't make up passing out."

(..)

that day i remember the feeling of like (.) no you don't feel good that you just got diagnosed with a chronic illness (.) like no it's not a good feeling. but just that you fought so hard for it and you like (.) the stories that i tell from the past and like

(..)

P: it's so much relief

[Vlog X]

This is illustrated in the extract above, whereby the storyteller discusses the irony ('you don't feel good that you just got diagnosed with a chronic illness') of experiencing catharsis after receiving confirmation of the chronic, long-term condition which she had 'fought so hard for'. In this sense, she attempts to rationalise her feelings of 'relief' through the explanation that her diagnosis was a resource, which could be employed by her as a method of proving the legitimacy of their symptoms to others, who may label their condition as contentious or purely psychological ('okay i'm not crazy like... ha "told you" it's not crazy i didn't make up passing out').

2.10. *[The Dystopia]: Dis-congruent PoTS Narrative Endings*

that took like over a week for them to get back to me

(..)

and the report read that it was absolutely consistent with pots (.) but you know further clinical correlation needed to be made.

[Vlog F]

In a small number of stories analysed by our research team, some vloggers discussed their dissatisfaction, or unclear results from, their initial tilt-table tests. Often this was explained as a lack of further confirmation, hesitancy or follow-up being required for doctors and health-care practitioners to give their final seal of approval on confirming PoTS as the final diagnosis- despite storytellers reporting that they had been told their test results were 'absolutely consistent with pots'.

but I know a friend who also has pots and she did not pass out on her tilt table test either (.) however her heart rate did show the pots results where mine started out in

like low fifties (.) because I am kind of like an athlete (.) I exercise a lot so I've like a lower resting heart rate (.) and then they said when they tilted me up it went up to ninety

[Vlog B]

Some speakers also discussed differences in the results they had received on their diagnostic test, in comparison to what they had perceived as more typical experiences of those in the PoTS community. Storytellers did this as a way of demonstrating the wide heterogeneity of external factors which could interfere and alter the results of the tilt-table, where factors such as the athletic prowess of the person with PoTS could alter the heart rate changes their practitioners would observe. Notice as well, how storytellers would place emphasis upon the need to demonstrate a necessary, orthostatic heart change of at least thirty beats per minute as the key to evidencing their right to being granted a PoTS diagnosis ('however her heart rate did show the pots results'). In this respect, the ability of storytellers to present this specific physiological change that was consistent with PoTS on the tilt-table test was sometimes expressed as a chance-like event by people with PoTS. The failure of the test to detect this key change was attributed by storytellers to their own concerns towards the use of an arbitrary, thirty beats per minute criteria within the assessment, as being an insufficient and inaccurate method for granting legitimacy towards the confirmation of their PoTS.

P: the reason why that tilt table was so weird was because I was exactly this many beats off

(..)

P: ZOOM INTO IT

[Participant holds up one finger on screen with caption "IT'S A ONE" – 5 seconds]

P: THIS MANY

[Video effects – participant's face & finger rotate around screen momentarily – 3 seconds]

P: beats off (.) this many from being diagnosed with pots! One. Single. Beat. of my heart. that's frustrating (.) um so i'm PoTS like (.) it's something I have to process

[Vlog V]

The extract above demonstrates this further. In this vlogger's tale, the arbitrary criterion of needing to display a thirty beat per minute increase in heart rate during the assessment was blamed and criticised by the storyteller for causing their failure of the test; as they had exhibited a orthostatic change of just twenty-nine beats per minute. Notice how, even though the speaker has failed the test by such a small margin - only 'One. Single. Beat' - this denial of the diagnostic category is portrayed as having significant ramifications for the speaker, as they are now unable to claim upon category entitlement to label themselves as a person with PoTS. Instead of this, the speaker is now forced to 'process' and self-describe themselves as someone who is 'PoTS like', whereby they continue to live with the effects of this condition without certified recognition of this by others and those in the medical community. This extract

therefore demonstrates how failure to secure a PoTS response on tilt assessment had influenced and altered the terminology the speaker could use to describe their illness, and subsequently how they encountered difficulties with being able to frame and make sense of their symptoms. This draws parallels to works by Frank (1995) on their chaos narrative theory, whereby storytellers whose diagnoses remain unclear will depict themselves in their stories to be confused, and to continue to struggle with comprehending their bodies and illness.

and I'd had a tilt table test where they strapped you to this table (.) and then it's tilted up and then twenty minutes in (.) I passed out and they had some data from that (.) and they were saying (mimicking) "well you know we could give her a pacemaker" and then "no she's too young (.) there's too many risks" and then (mimicking) "we should monitor her she should have (.) this device inserted" someone else would say "no".

[Vlog G]

Insights from chaos narrative theory (Frank, 1995) can also be observed from the narrative in the extract above, whereby the failure of a tilt-table to recognise the presence of PoTS was explained by these storytellers as leading to significant digressions and conflicts in their healthcare practitioners' intended plans for treatment. The above extract, explained by the storyteller as the first time they had undergone a tilt-table test, illustrates this scenario by representing the complexity and uncertainty of her situation, through the inability of the medical team to decide upon the most suitable approach to follow-up and manage her observed abnormal cardiological activity.

3. Discussion

3.1. Summary & Literature Considerations of Structural Findings

Undertaking of structural analysis explored the ways in which people with PoTS constructed diagnostic and symptom experiences when sharing their narratives. Narrative analysis first identified that people with PoTS began their stories through attempts to normalise their pre-PoTS selves as relatable characters in their discourses, through the citing of their involvement in attainable living goals and healthy activities. PoTS storytellers then purposefully deconstructed these established health statuses, as furthered through retellings of the additional burdens they would face whilst undertaking mundane living duties. This purposeful deconstruction of health status observed in PoTS narratives is characteristic of works on biographical disruption proposed by Bury (1982), whereby sufferers adapt and reconfigure the social, material and cognitive resources at their disposal to accommodate sudden and gradual worsening of chronic illness (Williams, 2000). Our findings demonstrated that people with PoTS construct experiences of biographical disruption within their narratives, through

describing the ways they would need to break-down daily activities and mundane work into a series of small, procedural-like steps. In a similar manner to findings by Whitehead (2006) concerning narratives of chronic fatigue syndrome, people with PoTS portray procedural-like strategies within their stories to convey both the extent of their illness debilitation, and the unnoticeable, taken-for-granted work they would need to perform in order to mitigate impacts of fatigue, breathlessness and orthostatic complaints.

Biographical disruption findings were also further elaborated through triangulation with the interview work, whereby some PoTS storytellers employed the use of multi-voice within their own narrative retellings. Through this voicing (by their present selves), some participants retrospectively reflected on how, over time, they had only become consciously aware of these unnoticeable changes to their mundane rituals after the obtaining of formal diagnosis. In this respect, these findings of voicing are representative of notions by Polkinghorne (1995), who argues that narrative construction serves as a powerful social phenomenon whereby the re-telling of personal experiences is a necessary action for facilitating the generation of human knowledge and meanings behind a patient's illness sufferings. Crucially, findings are akin to those from Morden, Jinks & Ong (2017), where chronic joint pain sufferers also employed retrospective voicing during narrative construction. Their participants used voicing as a method of rationalising why they had not previously been consciously aware of the changes they would make to their working routines when minimising their physical discomfort. Through these considerations, the current study therefore expands on prior understandings of PoTS by demonstrating that people with this condition also use retrospective voicing during their narrative descriptions of biographical disruption, in efforts to justify and make sense of their participation in symptom masking behaviours.

People with PoTS were also found to present their complex interactions with medical investigations and primary healthcare assessments of their symptoms as repetitive cycles, driven by symptom flare-ups and the negative results from conducted medical tests. Healthcare experiences during these moments of the narrative can be defined as a core part of the construction of illness careers (Freidson, 1988) portrayed by people with PoTS within their stories. Illness careers, which depict the orderliness of events and social interactions which individuals encounter during their diagnostic journeys (Rossen, Buus, Stenager & Stenager, 2019), are employed by chronic illness storytellers to narratively reflect how changes to their social identities are produced over time (Goffman, 1990). In a similar vein, it is worth noting that PoTS narrative stages which included these depictions of 'endless' engagements with medical and healthcare interactions mirror literature on chaos narratives (Frank, 1995). Elements of chaos narratives were observed through people with PoTS being

unable to make sense of their own identities and health experiences at these points in their diagnostic journeys- due to them lacking knowledge of their underlying symptom cause.

Findings also showed that storytellers only began to (re)construct their identities later in their narratives once these medical cycles had been broken, through the 'turning point' (Reissman, 2002) of a PoTS ally character or healthcare practitioner debunking the psychogenic or contentious labelling of their persistent physical symptoms. This is reflective of narrative findings by Lillrank (2003) on female chronic back pain, where in order for them to restore their social identities, women needed the authenticity of their symptoms to be recognised by a clinician as non-psychological in nature. Through considerations with the similar story turning point (Reissman, 2002) observed within the current study, our research builds on this work by demonstrating that people with PoTS construct new narrative identities following these experiences- through their self-presentations of themselves empowered 'little doctors' who are responsible for researching their own medical investigations and the conduction of home-based tests. One possible explanation for why they present themselves in this manner may be to serve as a form of patient activism (Johansson, Isind, Lindroth, Angenete & Gellerstedt, 2021), whereby storytellers may seek to appeal towards and incentivise others who are experiencing PoTS-like symptoms, as a moral or 'internal coda' (Labov, 1972) to their diagnostic stories. Further works are therefore needed to explore how people with PoTS respond and interact with patient activism messages within online spaces.

Psychogenic blaming and contentious labelling are commonly reported patient experiences within both PoTS and wider communities of conditions associated with invisible symptomatology (Gill, 2018). The narrative findings further understandings of these issues in PoTS specifically, as prior research has largely neglected to explore sufferers' personal and subjective accounts of these experiences (Waterman et al., 2021). In addition to psychogenic labelling of PoTS symptoms, structural findings also revealed that storytellers constructed negative results of medical tests and understandings of their PoTS as major barriers to their narrative quests of obtaining diagnosis. The construction of negative test results by people with PoTS, as a resource which healthcare professionals could use to deter further investigation of persistent physical symptoms, is representative of the normalisation without explanations strategies which general practitioners undertake to reduce the severity of patients' unexplained symptoms (Dowrick, Ring, Humphries & Salmon, 2004).

3.2. Conclusion

Structural analyses of people with PoTS' narratives provided insights into the ways in which speakers reconstructed their illness experiences during the retellings of their diagnostic

journeys. The current study was also the first to explore people with PoTS' portrayal of their experiences of undergoing tilt-table tests; this was depicted as a highly invasive process through the heightened physiological arousal states storytellers would describe. Future research is needed to explore the factors which may help to mitigate and managing the anxieties people with PoTS present with during the time of tilt-table testing. This could be examined by first exploring the types of conversations and dialogues medical practitioners have with these individuals during the time of test conduction, to examine how reassurance is given to the patient and which forms of support serve as the most effective for easing this aversive experience.

Within the next chapter, we conclude the narrative analysis work with the presentation of findings from performative analysis. This final approach of my narrative analysis examined how people with PoTS communicated understandings of their PoTS diagnosis and symptom experiences to their online audiences.

- Chapter 7: Exploring the Language & Ontologies of PoTS through Performative Analysis -

Following the Introduction, Methods and presentation of the Thematic (chapter 5) and Structural (chapter 6) phases of the narrative work, the current chapter concludes the exploration of PoTS diagnostic and symptom experience work by portraying findings identified from the Performative analysis. This chapter emphasises the importance of recognising people with PoTS' utilised medical ontologies- those surrounding the autonomic nervous system in which they employ to communicate understandings of their chronic diagnosis to others- for comprehending their symptom experiences. Through these models, people with PoTS depict experiencing a heightened awareness of their physiological processes, due to their understandings of PoTS causing a perceived 'disruption' to their body's unconscious pathways. These frameworks are also used through metaphoric language to allocate blame towards their bodies for their chronic symptom experiences, as forms of personification devices. This focus on ontologies guided elements of the framework I have utilised for the intervention development work, through the careful framing of the perceived benefits of the Ocean Breathing intervention to people with PoTS and healthcare professionals (see chapter 8).

Performative approaches are an uncommon- yet highly insightful- form of analyses that can be employed within the study of narrative. These approaches seek to comprehend the purposes behind why a narrative is being shared by a storyteller, alongside the underlying "morals" of their story and the strategies in which speakers employ for communicating these messages to their intended, overt audiences (Meraz et al., 2019).

In this respect, research question (ii) of the project aimed to examine how people with PoTS communicate understandings of their chronic illness within their vlog stories to their virtual audiences.

1. The Language of PoTS

1.1. 'Making PoTS Accessible'

Vloggers frequently initiated their conversations around their chronic health condition to their audiences by first referring to the mnemonic-naming of PoTS - 'so pots stands for postural orthostatic tachycardia syndrome'.

so pots stands for postural orthostatic tachycardia syndrome and basically what it means is that (.) when somebody stands up from (.) you know sitting or laying down position their heart rate increases by like a crazy amount

[Vlog A]

A pattern was observed within the dataset, whereby this description of the PoTS acronym by speakers would subsequently be followed-up with immediate comments which attempted to present a lay definition of the condition - 'basically what it means is that'. Speakers did this as a way of explaining the meaning behind the 'orthostatic' aspects of their PoTS:

'when somebody stands up from (.) you know sitting or laying down position their heart rate increases by like a crazy amount'.

They would substitute the phrase 'orthostatic' with a more comprehensible, lay explanation that simple changes in their bodily posture would give rise to prominent symptoms, such as episodes of tachycardia or syncope.

Vloggers would also take their listeners through the medical terminology which constitutes its diagnostic acronym by breaking down the understanding of each key phrase in sequence:

but um so today I'm gonna be talking about postural orthostatic tachycardia syndrome. the condition is legit in its name postural meaning posture (.) sitting to standing (.) laying down (.) orthostatic. orthostatic intolerance. basically it's known as orthostatic intolerance and tachycardia means high heart rate. syndrome being it's a syndrome so it can be temporary and it can (..) it can last a long time or that it can be chronic.

[Vlog T]

In the example above, notice how the speaker does this as a way of simplifying these seemingly complex words and phrases to their PoTS-naïve audiences. This was facilitated by replacing core diagnostic terminology, which could otherwise be dismissed as scientific jargon by a listener, with a series of short, easy-to-comprehend lay definitions for each word that requires little medical knowledge from the watcher in order to be understood : 'the condition is legit in its name postural meaning posture'; 'sitting to standing (.) laying down (.) orthostatic.'; 'and tachycardia means high heart rate'. Through this strategy, the speaker demonstrates how people with PoTS would be observed as attempting to un-pack and normalise the unfamiliar, taken-for-granted medical language of PoTS, in order for them to introduce their chronic illness and make PoTS accessible for their virtual audiences.

Speakers also used categorisation at the start of introducing their conversations around PoTS by drawing listener's attention to the condition's medical classification as a 'syndrome' - 'it's a syndrome so it can be temporary and ... it can last a long time or it can be chronic'. This framing of their medical condition as a syndrome was exploited as a resource by some

speakers, to initiate conversations surrounding the high diversity of symptoms people with PoTS present with and to account for differences in illness duration from one person with PoTS to another.

although currently my symptoms are dormant (inhale) I do have pots. it's something that never goes away like once you have it or (.) I don't (.) I don't even know if you acquire it or if you're born with it or what but I have it. I just (.) I don't have any symptoms right now.

[Vlog I]

One example where a participant discusses their perceptions of the variability associated with their condition and symptoms can be viewed above. When discussing her own experiences with PoTS, the participant emphasises the chronic status of her diagnosis - 'it's something that never goes away like once you have it'- as a disclaimer, following her initial claim that 'currently my symptoms are dormant'. By distinguishing her own, current subjective experience with PoTS - 'I don't have any symptoms right now' - from her perceived experience of living with a long-term health syndrome- 'it's something that never goes away like once you have it'- the vlogger uses this differentiation to communicate the sporadic nature of her PoTS to her audiences. People with PoTS would then utilise orientation tactics to further these discussions with self-disclosures surrounding the invisible nature of their symptoms:

P: Most people have symptoms for years before they're diagnosed (.) just because of the lack of awareness with people and doctors

[P grabs t-shirt and makes the full printed text visible on the clothing – "OCTOBER DYSAUTONOMIA AWARENESS MONTH"]

P: that's why October is national dysautonomia awareness month

(...)

P: because most people with dysautonomia look healthy. So also doctors try and diagnose it with anxiety or many other different things.

[Vlog W]

One of these observed strategies is detailed above, whereby people with PoTS would deliberately make explicit references to PoTS awareness campaigns and organisations during the opening segments of their vlogs, prior to story sharing. This demonstrates how vloggers with PoTS would attempt to educate their PoTS-naïve viewers of their debilitating, unnoticeable illness experiences – (with Vlog W noting that 'most people with dysautonomia look healthy') – commonly included alongside PoTS advocacy messages ('most people have symptoms for years before they're diagnosed... just because of the lack of awareness with people and doctors' Vlog W), through addressing the uncertain and invisible nature of their PoTS symptoms as a hidden (yet recurrent) burden on their everyday life.

In addition to PoTS-naïve audiences, some people with PoTS also demonstrated specific orientation strategies towards viewers who shared their chronic diagnosis, as exemplified

below:

- Video Opening – Total Duration: 3 Seconds

[Speaker (P) is presented alone on camera lying down on WHAT]

P: can I sit like this for a video?

[Opening Titles – Video compilation of speaker with dog alongside “jolly” musical jingle – 15 seconds]

P: hi guys so today I am making my pots journey video.

[Vlog V]

On face value to a PoTS-naïve listener, the significance of the phrase ‘*can I sit like this for a video?*’ is unlikely to elicit any particular form of meaning. Conversely however, when a listener who has experienced the PoTS themselves hears this phrase, the speaker is aware that such watchers are capable of recognising the significance of this behaviour. Unlike a viewer who lacks experience of the phenomenon, a person who has lived with PoTS symptoms is more likely to notice the adoption of a supine posture by the speaker as a method undertaken to manage their PoTS-related orthostatic complaints. This therefore illustrates how storytellers can both rely and capitalise on the shared, condition-specific knowledge of these specific parts of their audiences in order to orientate their viewers through such shibboleth-like strategies. Through doing this, speakers lay the groundwork for these specific audiences to start establishing a sense of authenticity and credibility towards their depiction of PoTS-related experiences within their narratives.

1.2. *Communicating PoTS Ontologies*

Following the introduction of their condition to their audiences, vloggers would then go on to focus more on explaining the underlying causes of their invisible symptoms and how they are perceived.

it's just the disease that affects your autonomic nervous system which affects the blood flow (.) which causes all different symptoms (.) like any possible symptom you can think of is associated with pots. everybody experiences different symptoms however (inhale) my symptoms mainly were nausea (.) migraines headaches (.) dizziness and flushing.

[Vlog I]

When discussing the bodily complaints they are regularly faced with, vloggers would try to make their audiences understand how their PoTS was responsible for the high number of debilitating symptoms they would describe experiencing. To do this, speakers would draw upon the concept of their nervous systems as a biological network in the body that is being affected by PoTS. Notice how, within the extract above, the participant carefully sequences and steps their listener through a lay scientific process to explain how their symptoms are

produced – whereby, PoTS is first rendered as a ‘disease that affects your autonomic nervous system’, which means that it ‘affects the blood flow’, and therefore resultantly ‘causes all different symptoms’. The participant then draws upon this portrayed medical model to support their view that their own distinctive, commonly experienced PoTS symptoms, is part of a wider collection of symptoms - shared amongst the patient group as a whole- that can also be accounted by the disruption of this physiological pathway in the body- ‘everybody experiences different symptoms however (inhale) my symptoms mainly were nausea (.) migraines headaches (.) dizziness and flushing’. As such, this example represents how people with PoTS rely upon medical ontologies surrounding the autonomic nervous system to actualise, authenticate and ground the realism of their PoTS symptoms when communicating their experiences with others. A further occasion can be seen here:

I had an autonomic nervous system disorder also known as dysautonomia.

[Vlog S]

A vlogger has drawn upon this biological system to depict their PoTS as a ‘autonomic nervous system disorder’. This is representative of how people with PoTS were found to legitimise and relate their experiences of ill health to their PoTS-naïve virtual audiences through the citing of tangible, physiological processes in the body being disrupted through the syndrome itself. By doing this, vloggers appear to aim to provide their viewer(s) with a medico-scientific framework which both evidences and accounts for the nature of their symptoms, to allow others to make sense of their condition.

It was also observed that people with PoTS used their own distinct medical terminology – such as the phrase ‘dysautonomia’ (Vlog S, above) – to distinguish their condition from other chronic illnesses, which cannot be explained through the ontology of the dysfunctional autonomic nervous system.

[PoTS] is further classified as a dysautonomia disorder. dysautonomia is kind of like an umbrella term that classifies all of the disorders that attack your autonomic nervous system. your autonomic nervous system is responsible for all of your natural bodily functions like digesting (.) pumping blood (.) that type of thing. things that you don't think about doing (.) but your body does naturally for you. basically with dysautonomia it causes it not to work properly.

[Vlog X]

In the quote above, the vlogger first aims to generalise their PoTS to the listener by categorising their condition as part of this collective group of diagnoses, that PoTS ‘is further classified as a dysautonomia disorder’. The framing of PoTS as belonging to the ‘umbrella’ dysautonomia group is then employed by the speaker as a way of them accessing the same medico-scientific framework rhetoric that was described within earlier participant extracts - whereby PoTS is both positioned and authenticated by vloggers as a medical condition,

through their explanation that it is a 'disorder' which is affecting - 'attack' - the nervous system of the body- 'all of the disorders that attack your autonomic nervous system'. By relating the actions of the condition to the disruption of bodily processes, an understanding of PoTS is constructed and legitimised by the PoTS storyteller as a medical condition towards their virtual audiences.

People with PoTS would then further solidify their medical ontological discussions by detailing how the unconscious roles of the autonomic nervous system were of great importance in maintaining the day-to-day functioning of the human body - 'things that you don't think about doing (.) but your body does naturally for you'. Speakers would place emphasis on explaining how the actions of the nervous system are unnoticeable to a person, yet were of great importance in the regulation of essential bodily processes:

Erm (.) so the condition itself it affects the autonomic nervous system. (inhale) which is the system controlling the things your body should do automatically without you thinking. So (inhale) your heart rate your (.) blood pressure your (.) temperature regulation (.) your digestion
(..)
all of that sort of thing should just be controlled (.) without you thinking about it. with pots that system doesn't work as it should and one of the ways in which it can fail is (.) as I said (.) fainting.

[Vlog G]

The extract above exemplifies how vloggers would attempt to educate their audiences of the (unnoticeable) work of the autonomic nervous system, in maintaining day-to-day bodily living processes - such as breathing and circulation of the blood - that are essential to survival - 'the system controlling the things your body should do automatically without you thinking'. The work of this mechanism in the body was described by speakers as an automatic process, in that the upkeep of bodily processes by the nervous system should not involve any conscious action or awareness required from a person in order to be performed. As such, speakers would describe the occurrence of their PoTS as a disruption to this unseen work of the autonomic nervous system - 'with pots that system doesn't work as it should'. In turn, this ontology concerning failure of the nervous system was employed by people with PoTS to account for the symptoms they would experience - 'one of the ways in which it can fail is as I said fainting'.

Speakers within PoTS vlogs also spoke about how this presence of having a dysautonomia condition had resulted in them developing a greater conscious awareness of their bodies over time.

so from sitting to standing the blood falls out of my head and once my (.) once my nervous system fails to kick in my heart keeps it and it doubles and with that I've experienced fatigue (.) brain fog (.) like it's changed my vision completely.

[Vlog H]

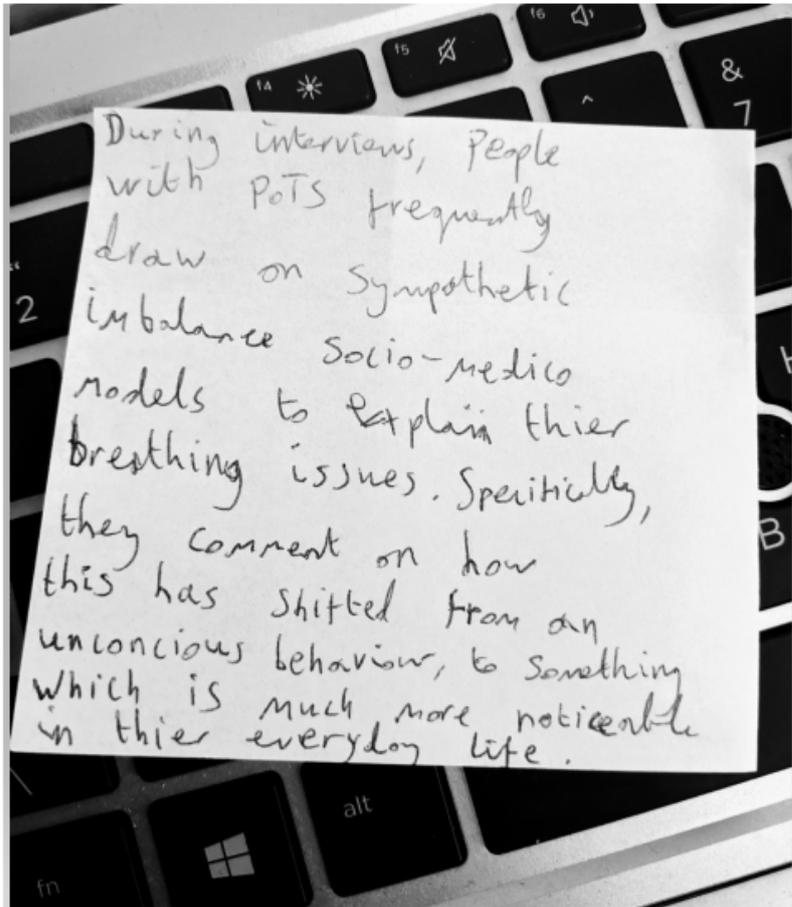
One vlogger with PoTS discussed the process that would lead her to experience this increased level of awareness of her body during times where she would encounter orthostatic symptoms from standing upright. During these moments where their 'nervous system fails to kick in', people with PoTS viewed their bodies as attempting to compensate for this by trying to shift the responsibility for this work away from its unconscious actions, and instead towards the functions of major organs such as the heart - 'my heart keeps it and it doubles'. In this respect, whilst people with PoTS are unable to 'see' the unconscious work of the (dysfunctional) autonomic nervous system that they depict in their medical ontologies, vloggers expand on these analogies (as the basis of their symptoms) by linking these accounts back to their own, internal sensation of experiencing a heightened arousal state, through their increased pulse rates.

I could literally feel like my blood vessels expand if that makes sense? I could feel like my heartbeat in my fingers and stuff like that. it was like really weird.

[Vlog S]

Over time, people with PoTS would describe becoming hypervigilant towards the beating of their hearts - 'I could feel like my heartbeat in my fingers'. The close monitoring of this beating sensation by people with PoTS was justified as acting as a signpost to the individual, which would alert the person to flare-ups of their condition – such as to the oncoming occurrence of fatigue or syncope episodes. Therefore, whilst people with PoTS are unable to directly share the experience of their invisible symptoms with others - vloggers rely on medical ontologies of the autonomic nervous system to not only justify the factual basis of their illness through biological models, but also to defend the subjective and embodied strategies which they have developed for inferring changes in their subjective health and functioning each day.

Interview participants also made frequent references to the concept of the autonomic nervous system as a central, illness framework for guiding the understanding of their PoTS symptoms, specifically in relation to breathlessness experiences (see Fig. 1).



So everything you don't usually think about (.) your heart rate (.) your breathing (.) they're all affected because PoTS comes under the umbrella of dysautonomia. I have problems with all sorts of those things. I sometimes understand it as my wiring is faulty (.) my body just didn't get the memo
[MA07TA]

Fig. 1. Reflexive comment generated [MJH] from the early stages of intervention development work with people who have PoTS. This reflection notes how, similar to PoTS vloggers, ontologies of the autonomic nervous system were also employed by interview participants as a way to “rationalise” the more conscious awareness of their bodily experiences which they would develop - specifically in relation to their regular, everyday breathing - following symptom onset. Considerations such as this helped me to understand how central the model of the autonomic nervous system was for the sense-making processes of people with PoTS, in order to comprehend their breathlessness experiences and how these concepts inform and shape their understandings of breath-related interventions.

Within the extract above [MA07TA], notice how the participant also categorises themselves in the same manner which many vlog storytellers have done, by assigning their illness with the shared identity of belonging to ‘the umbrella of dysautonomia’ conditions. Through self-categorisation with this wider illness cluster, the participant communicates to the interviewer their understandings and own sense-making for the heightened awareness of their physiological sensations – ‘heart rate’, ‘breathing’ – they experience. These bodily processes – those which ‘you don’t usually think about’ – are understood by the participant as not being regulated by their body’s nervous systems, as communicated through the metaphor of their nerves (‘wiring’) being ‘faulty’. As this salient, unconscious work of the autonomic nervous system is described by the individual to not have been undertaken properly – because their ‘body just didn’t get the memo’ – the participant depicts their increased conscious awareness of these processes as a compensatory mechanism for this dysfunction.

1.3. *The Body 'Fighting Itself'*

it's a lot of like your body is kind of in control of you.

[Vlog X]

Some people with PoTS would then go on to further their medical ontological discussions of the autonomic nervous system through the use of personification, a device in which inanimate objects and systems are provided with humanistic features by the speaker (Dorst, 2011). Through the characterisation of their bodies, vloggers would communicate the emotional difficulties they faced through their feelings that they had lost their sense of control over their bodies.

those of us with dysautonomia our bodies work against each other so (.) things that should firmly like (inhale) breathing (.) heart rate (.) temperature (inhale) it's (..) all out of whack and our bodies don't function properly.

[Vlog Q]

People with PoTS did this by describing their bodies to their audiences through a battle-like analogy, whereby the nervous system was depicted to be at conflict with itself- 'our bodies work against each other' - to highlight the physical burdens they faced with living with PoTS. In the extract above, notice how this conflict is represented through the speaker commenting upon how their core bodily processes are 'all out of whack'. People with PoTS portrayed their dysautonomia through this metaphoric language as a means of depicting their PoTS as disrupting an established balance, or a co-ordination between, key physiological processes such as the respiratory and cardiovascular systems. Referring to what others may see and think, a vlogger notes that:

at first glance they would never think that on the inside my body is pretty much fighting itself.

[Vlog Q]

Speakers drew on the rhetoric of their autonomic nervous systems not being capable of completing the unconscious work of regulating core physiological processes ('our bodies don't function properly') as a means of portraying their bodies as counter-productive entities- 'inside my body is pretty much fighting itself'.

Through the use of personification devices speakers also aimed to distance and situate their body as separate beings from their own sense of self:

i was not myself and I felt (.) just terrified 24/7 because my body all the sudden was just like (mimicking) “hey I'm not gonna work for you anymore” (inhale) and I was just so scared of the unknown.

[Vlog F]

Within the quote above, notice how the vlogger first separates the characterisation of their body, as a separate entity to their sense of self ('i was not myself'). Through this distinction, the vlogger is able to designate blame for their symptoms towards the entity of the body, as a personified character ('my body all the sudden was just like'). This othering of the body, which is portrayed, via a reported thought, as acting through its own malicious intention- “hey I'm not gonna work for you anymore”. Through doing this, the person with PoTS positions themselves to be framed as a victim of this other character's inaction- 'I was just so scared of the unknown'. This extract therefore begins to demonstrate how vloggers with PoTS use personification devices as a strategy to manage culpability for the impacts of their condition on their health and wellbeing.

I mean I am tired all of the time. I try to get some rest but my body doesn't seem to like me and (.) I can't really get any rest. I (.) I try to go to sleep and I wake up. I tired (.) my body aches

[Vlog M]

As such, people with PoTS would depict themselves as being at the mercy of their condition and its symptoms, through the characterisation of the body, at times, as an external agent or other which intended to cause harm to their being': I try to get some rest but my body doesn't seem to like me'. This portrayal of helplessness demonstrates how people with PoTS would disclose to their audiences how they had, over time, developed intrusive thoughts and cognitions towards themselves as a result of 'fighting' (Vlog_Q) with their dysautonomia.

Other vloggers choose to further build their conflict analogy into the medical ontologies which they had used to underpin their PoTS symptoms, through references to its sympathetic, 'fight-or-flight', and parasympathetic, 'rest-and-digest', sub-branches.

Erm (inhale) so basically all pots is its failure of my (.) my autonomic nervous system and you ave (.) there's two branches of your nervous system I think (.) the sympathetic is your fight-or-flight which is (.) you know your adrenaline rush your anxiety (.) whatever. And then your asympathetic is your rest and digest. So if you think about a gas [pedal] on a car as your sympathetic and a brake pedal (inhale) for your asympathetic. So basically at some point there is an imbalance in my nervous system

[Vlog H]

Notice above, that the speaker uses metaphor to compare the two sub-systems of the autonomic nervous system as the pedals of a car. By doing this, the vlogger communicates a

simple analogy to highlight to their audience how the ‘go’-like bodily function of the fight-or-flight branch (seen as the accelerator) contrasts against the ‘pause’ function of the rest-and-digest branch (‘brake pedal’).

As such, people with PoTS choose to communicate a lay understanding of their PoTS as being the result of an ‘imbalance in [the] nervous system’, through relatively simple analogies surrounding the lack of synchronisation between the actions of their body’s starting and stopping systems. This can also be seen below:

dysautonomia is a dysfunction of your autonomic nervous system. so there's two parts to it (.) we'll just call them A and B. and usually with someone who has a regular autonomic system (.) their parts work together to make the body function properly.

[Vlog Q]

In this case a different speaker has chosen to minimise the importance of the medical description of these two autonomic branches (‘so there's two parts to it (.) we'll just call them A and B’). Alternatively, as a way of demonstrating an understanding of this experience to their audience, they have focused on simplifying this medical ontology by describing only the lack of co-ordination between these two systems (‘usually with someone who has a regular autonomic system (.) their parts work together to make the body function properly ‘). Participants also described PoTS as a lack of body co-ordination more generally, in relation to specific organs.

if you don't know the vagal vessel is like the (.) like the central system to your organs and communication. So basically when I explain PoTS to people I will say my brain does not know what gravity is. so my brain and my heart don't communicate together.

[Vlog T]

Notice how, throughout several of the aforementioned extracts above, PoTS is defined medically by vloggers as causing damage and disruption to the synonymous actions of two or more organs or bodily systems, that would typically ‘work together to make the body function properly’ [Vlog_Q]. The nature of PoTS is purposefully simplified and presented by people with PoTS to their virtual audiences as being responsible for a poor co-ordination between key bodily processes, whereby they ‘don't communicate together’. PoTS is therefore presented by people with the condition as an entity which has dysregulated the body’s ‘central system’ [Vlog_T] – the pathway responsible of communicating and counter-balancing the processes of the body with one another to ensure they ‘work together’ [Vlog_Q] in tandem - by causing an ‘imbalance’ [Vlog_H]. This notion echoes back to earlier participant comments within the section, where people with PoTS would introduce the medical explanations of their PoTS

symptoms, through discussions surrounding the inability of their autonomic nervous systems to fulfil this overseeing and regulatory role in the body.

2. Discussion

2.1. Summary & Literature Considerations of Performative Findings

Performative analysis, as the final phase of the narrative exploration of PoTS diagnostic and symptom experiences, examined how vloggers with PoTS communicated understandings of their chronic illness to their online audiences.

The findings demonstrate that People with PoTS initiated their online discussions by breaking down the complex medical terminology associated with the naming of their condition. These findings are reflective of the work undertaken by Gardner, Warren, Addison & Samuel (2019), through their grounded theory analysis of 60 Parkinson's vlog stories of receiving deep brain stimulation therapy. In a similar manner to be people with PoTS, Parkinson's disease vloggers use simplified terminology (*such as the notion of their bodies "shaking" to depict tremor symptoms*) of medical phrases to communicate and describe their own personal experiences with illness to their online audiences. My findings also identified that people with PoTS would employ specific orientation strategies towards their PoTS-naïve audiences. This was done through momentary interruptions to their own narratives, through their explicit references to PoTS awareness and advocacy campaigns, in order to disclose their personal subjective experiences of facing invisible illness. This use of a 'non-direct' strategy to initiate conversations around symptom invisibility were also noted by Groenevelt (2021), who undertook a series of online examinations of eight female YouTube and Instagram users with contested illnesses over a thirteen-month period. These vloggers undertook strategies to manage their 'healthy' appearances online— such as appearing on-camera without make-up— which they then utilised as a resource (through explicit apology messages to their audiences) for the deviations in their appearances, which in turn facilitated conversations surrounding burdens of invisible symptom flare-ups.

Performative analysis also identified that people represented their struggles of enduring dysautonomia through the portrayal of their bodies as personified, antagonistic characters separated from their sense of self. These findings are characteristic of the classic works of Charmaz (1980; 1994), who argues that chronic illness sufferers commonly depict their bodies through this manner when they 'struggle against [their] illness' (p663, Charmaz, 1995). This is proposed to be undertaken as a form of identity work, whereby the concept of the self is deliberately disentangled by the individual from their physiological being, in effort to protect

against resultant impacts from their condition. Whilst the works of Charmaz (1980) remain heavily cited within the chronic illness literature, prior works have not previously acknowledged the relevance of these considerations to the study of people with PoTS. It should be noted however that parallels to these frameworks can be drawn not just from the identification of the findings in this chapter, but also those from those arising from the IPA study PoTS by Waterman et al. (2021). During their analysis of self-recorded videos by eight people with PoTS within their homes, participants expressed that they felt reduced control over their bodies as a result of their illness. Given the consistency of their finding with those from our narrative work, and also the arguments of Waterman et al. (2021) for the need for greater psychological intervention within PoTS treatment to help sufferers manage and adjust to their chronic diagnosis (Opie, Raj & Arnold, 2020), it is interesting to consider what therapeutic implications may be derived through the notion that people with PoTS disclose these self-held, described perceptions of their bodies as the result of their PoTS illness experiences. Further works are therefore needed to understand whether this 'othering' of the body (Charmaz, 1980) in people with PoTS serves as a protective or harmful cognitive response to their chronic illness experiences.

It is worth noting that the findings and conclusions drawn from the dataset are specific to the context of story sharing for an online audience of YouTube watchers. This may not be replicated across other video-based social media platforms where people with PoTS also share their experiences. Whilst YouTube was purposefully chosen within the current study to increase the chances of identifying PoTS stories which contained a holistic narrative due to the longer durations of videos; it is worth noting the increased popularisation of PoTS vlogging across other newer social media platforms. Whilst it is not possible to aggregate the total number of PoTS-specific videos that have been uploaded to TikTok, at the time of writing a search for the #potssyndrome on this social media platform reveals that PoTS videos containing that hashtag culminate to a total of over 327 million views. Furthermore, it is also worth noting that there is evidence to infer that people with chronic illness assign different goals and rationales behind the specific social media platforms they choose to disseminate their illness and diagnostic experiences, such as the use of Facebook to locate information regarding their symptom experiences, or the use of Tumblr or Instagram to fulfil emotion-specific needs (Sannon, Murnane, Bazarova & Gay, 2019). Given this and the considerations that TikTok video length are short in duration and designed for rapid communications, further research should build on the current performative findings by exploring how people with PoTS communicate rapid and quick understandings of their PoTS through formats such as this.

2.2. Implications for Breathing Intervention Development

A major finding of the performative analysis highlighted how the use of medico-socio frameworks, specifically ontologies centred around the autonomous nervous system, were relied upon and portrayed by vloggers to authenticate and legitimise their PoTS to others. The current study is the first to examine and scrutinise the ways in which these medical models are drawn on by people with PoTS specifically within discourse to express their own, personal understandings of their symptom causes. This builds upon the work of Ravenzwaaij et al. (2010), who identified autonomic ontologies as one of their recognised typologies which patients who experience persistent physical symptoms may employ to account for the nature of their chronic illness(es). From a literature perspective, extensive medical investigations of sympathetic activity and vagal tone have been widely reported within the study of PoTS (Raj, 2013), including evidence that has supported the clinical observation of parasympathetic withdrawal as a commonly presenting feature within this patient group (Jacob et al., 2019). Intriguingly, the current narrative findings demonstrate that people with PoTS themselves also utilise similar medical conventions- where metaphoric language was used by vloggers to signify their understandings of PoTS as stemming from a dysfunctional relationship between their two autonomic branches- as forms of patient-derived explanatory models (Kleinman, Eisenberg & Good, 1978), to situate their own lay medical accounts of PoTS symptoms. As I denoted earlier within a reflection upon my findings (*see Fig. 1., presented within sub-section 1.2. of the current chapter*). Whilst additional work is needed to further comprehend how explanatory models are shaped by the social and cultural experiences of people with PoTS, the identification of these frameworks accepted use in patients' discourse holds great promise for the shaping of future, tailored treatment strategies for this debilitating condition.

Unrelated – Notes from Informal Conversation with GP during Lunch Break of GCP Course [December 2019]

- GP knew of PoTS, recalled experiences with one of his patients who he had treated with the condition. Became aware of the condition from reading the patient's cardiology notes and then reading around the condition.

- During the conversation, I gave the GP a brief overview of our intervention, GP saw a benefit to this. He liked that the breathing technique was explained in the context of the vagal nerve. In practice, GP instructs one of his PoTS patients to rub neck (vagal nerve) areas to control tachycardia episodes and that he explained to her through this action "soothing" the autonomic nervous system.

- GP spoke about his priority as a practitioner was to help the PoTS patient manage their tachycardia, the use of beta-blockers to aid with this. GP wanted to see a physiological change in response to intervention change.

Fig. 2. Partial summary notes generated [MJH] from an informal conversation I had with a general practitioner who sat next to me in the James Cook Hospital cafeteria, during the lunch break of a NIHR Good Clinical Practice course I had attended prior to the commencement of my intervention work. Notice how, when discussing my research with this individual, the doctor found the concept of my breathing intervention to be feasible for PoTS, because I had described the Ocean Breath's therapeutic actions to him as being achieved through the technique's influences on the autonomic nervous systems of patients (through interactions with their vagal nerves). Looking back now, this interaction demonstrated – even within the early project stages – just how significant and important these autonomic ontologies were to the development of my PoTS intervention, as a way of enabling both people with PoTS and their healthcare practitioners to both establish trust towards the utility of the Ocean Breathing practice for this patient group.

The importance of reflecting upon the accepted explanatory models of a patient group remains a crucial factor to consider during intervention development work (see Fig. 2. above, for a reflexive passage). This is especially true for health conditions prominently associated persistent physical symptoms, where evidence suggests that these individuals may be less willing to engage with strategies that they do not perceive to be beneficial, or interventions which they struggle to comprehend its perceived mechanism(s) and effects for intended symptom relief (Menon et al., 2016). As highlighted within the discussion of scoping review findings conducted on the examination of PoTS treatments (see chapter 4), there is currently a limited number of recognised non-pharmacological strategies for assisting patients' own management of their PoTS, with only a small (yet growing) supporting evidence base behind these treatments (Eftekhari et al., 2021). The implementation of an existing, widely-utilised explanatory model by people with PoTS- through the careful framing of how a designed PoTS-specific intervention interacts with patients' underlying autonomic systems- may help to elicit greater confidence, uptake and continued compliance of a new, tailored treatment strategy within the PoTS community through these explanations of its perceived actions. This is particularly relevant for the development for our ocean breathing intervention, whereby the underlying actions associated with this technique and its effects in the body are grounded

within medical and pranayama literature of 'soothing' autonomic activity, through its action of producing vagal nerve stimulation (Carter & Carter III, 2016; Zope & Zope, 2013; Jerath et al., 2015). Given the consistency of this technique with patient-utilised autonomic ontological explanatory models to describe its perceived action on symptoms, I therefore argue that the performative findings of the narrative work further solidify the decision to pursue ocean breathing as the primary choice of intervention for development and tailoring within PoTS.

2.3. Conclusion

The reporting of the performative analysis conducted of the final vlog sample concludes the exploration of secondary data work of PoTS narratives exploration. The next chapter of this thesis contains the start of the final phase of this thesis, which concerns the intervention development work undertaken for the ocean breathing intervention. Within this chapter, I outline my methodology for the iterative, multi-stakeholder group qualitative process I undertook, in order to gather, collate and synthesise feedback on the Ocean Breathing practice.

The purpose of this chapter is to introduce the intervention development work I have undertaken for the development of an Ocean Breathing intervention for people with PoTS. I first begin this chapter with a summary of the literature, which emphasises the need for greater attention towards the experience of breathing within the PoTS literature and development of treatments. I then propose arguments which support the use of breathing interventions for the treatment of PoTS symptoms, through their complimentary explanatory models of symptom-relieving effects by their depicted interactions with vagal nerve and autonomic nervous system activity. Finally, a method section is presented for the research which details how my research was guided by both the Medical Research Council Framework for Complex Intervention Development, and the use of Normalization Process Theory (May & Finch, 2009).

1. Introduction

Within the current chapter, I outline how I aimed to design a new non-pharmacological treatment for PoTS through the development of an Ocean Breathing intervention for the management of PoTS symptoms. As discussed within chapter 1, there are no curative treatment for the chronic illness of PoTS (Raj, 2013). The focus of research within this area has therefore been to explore treatments which enable patients to adopt a symptom-control approach of their PoTS, through mitigating the impacts of flare-ups and symptom episodes on their everyday lives (Conner, Sheikh & Grubb, 2012). Pharmacological treatments for PoTS, which are administered through off-label use to patients, are only provided in the most adverse cases (Uhrich & Hartung, 2015); most agents also currently lack large-scale randomised control trials to determine their true efficacy rates (Eftekhari et al., 2021). Due to this, most individuals with PoTS remain heavily reliant upon non-pharmacological methods of management for controlling their persistent physical symptoms (Eftekhari & Bruce, 2021). Nevertheless, as identified within the scoping review of PoTS treatments (see chapter 4), at present only a limited number of non-pharmacological management interventions exist for assisting patients.

In effort to tailor the development of a specialised breathing practice for use in a PoTS patient group, factors which may hinder the future successful implementation of the intervention need to be identified throughout the intervention development process. One possible implementational barrier to consider is the experience of breathlessness symptoms, of which up to a third of people with PoTS are estimated to face (Stewart & Pinnosi, 2021). Despite this, the impacts of this condition upon individuals' breathing patterns and breathlessness experiences are rarely acknowledged within published academic literature. Numerous leading

PoTS organisations, including PoTS UK (2022) and Dysautonomia International (2022), advocate for people with PoTS to try breathing techniques, mindfulness and other breath-related meditation practices to assist with alleviating their PoTS symptoms. However, prior literature has neglected to explore the efficacy of these breathing techniques within this patient group. To date, only the empirical work undertaken by Reilly et al. (2020) - a study which was published when undertaking the intervention development work - has empirically assessed the effects of breathing in PoTS. Through a retrospective observational cohort study, Reilly et al. (2020) explored the effects of a clinical physiotherapy intervention (provided alongside a breathing educational programme) to 100 people with PoTS who had been referred to a specialist UK respiratory healthcare service. Within the post-intervention stage, participants demonstrated significant improvements in their ability to retain the breath, their respiratory rates and hyperventilation scores, with over one in five patients no longer meeting the clinical diagnostic threshold for hyperventilation syndrome following physiotherapy training.

The findings of Reilly et al. (2020) provide a promising start for demonstrating the therapeutic effects breath-based interventions in PoTS. It is important to note however that this intervention is currently restricted by the delivery methods, whereby patients with PoTS are reliant upon referrals to appropriate healthcare services and trained physiotherapists in order to receive the intervention. Findings arising from my structural analysis of PoTS patient narratives (see chapter 6) also need to be considered alongside this. People with PoTS commonly described anecdotes of encountering barriers - such as doctors' use of normalisation without explanation tactics (Dowrick et al., 2004) - which hinder their access to diagnosis and appropriate treatments for their symptoms. In turn, such experiences question the choice of healthcare services as the only appropriate format for the delivery of PoTS-specific breathing interventions, as such experiences reflect potential restrictions to receiving timely access to such treatments. It would therefore be advantageous for new, more simplistic PoTS breathing techniques to also be developed, which are designed in nature to self-administrable and disseminatable to PoTS sufferers across a range of alternate delivery formats and social contexts (such as through online resources). Furthermore, as noted by Reilly et al. (2020), additional work is also needed to develop breathing interventions which are capable of producing significant changes within the diminished psychological, social and functioning outcome variables commonly reported by empirical works in PoTS samples. This includes reduced quality of life, poor sleep quality and high suicide ideation scores (Pederson & Brook, 2017).

Although limited research has examined the therapeutic effects of breathing interventions within PoTS specifically at present, evidence exists to demonstrate their potential in other persistent physical symptom and breathlessness-related chronic conditions. Favourable

changes from slow-breathing practices, those developed from pranayama yoga practices which focus on the examination of psycho-social outcomes, have been reported within fibromyalgia (Toma's-Caru's et al., 2018), chronic obstructive pulmonary disease (Donesky-Cuenco, Nguyen, Paul & Carrieri-Kohlman, 2010) and multiple sclerosis (Shohani, Kazemi, Rahmati & Azami, 2020). In order to develop a breathing technique for the management of PoTS symptoms however, it is important to ensure that the therapeutic effects and benefits of these interventions can be clearly communicated and understood by people with PoTS. Patient groups with physical persistent symptom conditions are more likely to discontinue with interventions that do not integrate with the specific socio-medical frameworks which they employ to comprehend their illness burdens (Menon et al., 2016). It is crucial that interventions are developed to be consistent with the explanatory models utilised by PoTS sufferers. Through the performative analysis of the narratives (see chapter 7), I identified that people make sense of their PoTS experiences by depicting ontologies surrounding a disrupted autonomic 'imbalance' between their sympathetic and parasympathetic autonomic branches; this explanation of their symptoms has also been supported by medical investigations into PoTS (Jacob et al., 2019). So, specific types of breathing intervention need to be carefully selected, considered and narrated – they need to align, at least in part, with the depiction of underpinning mechanisms interacting with patients' autonomic nervous systems.

One possible way of addressing the need for autonomic-complimentary explanatory models within PoTS treatments is through the identification of breathing techniques which influence vagal nerve activity (Gadze, Kovac, Adamec, Milekic & Sulentic, 2018). The vagal nerve, informally named as the 'mind-body' connection, is a cranial nerve which exerts continuous influence over bodily autonomic activity (Groves & Brown, 2005). When stimulated, the vagal nerve helps to restore autonomic balance by increasing parasympathetic (vagal tone) activity within the body – this autonomic branch is thought to be diminished in PoTS patients, who typically present with sympathetic dominance (Jacob et al., 2019). A recent systematic review which explored use of vagal nerve stimulation in other related conditions has supported the use of this socio-medical mechanism as a guiding framework for the development of interventions to subdue PoTS symptoms (Diedrich et al., 2021). Crucially, the therapeutic actions arising from vagal nerve stimulation for soothing the autonomic nervous system can be achieved through certain types of breathing techniques, particularly those which feature prolonged exhalations (Jerath et al., 2015; Zope & Zope, 2013).

In order to achieve this within the current project, my supervisors and I identified Ocean Breathing (also known as the Ujjayi Breath) as a primary choice for PoTS intervention development. Ocean Breathing is a practice derived from pranayama yoga which instructs users to constrict their larynx muscles in the throat (Jerath et al., 2015). Due to this, the

beneficial effects from vagal nerve stimulation are achieved through the purposeful lengthening of the inhalation and exhalation processes (Carter & Carter III, 2016). In addition to its complimentary explanatory autonomic model, ocean breathing was also chosen due to its associations with enhanced sleep quality and improved quality of life (Bankar, Chaudhari & Chaudhari, 2013) - two outcomes which are frequently reported to be reduced in people with PoTS (Bagai et al., 2011; Pederson & Brook, 2017). Previously, during my postgraduate Psychology MRes studies, one of my supervisors and I had worked closely alongside a yoga practitioner to develop a basic form of this intervention for use in anxiety (Hogg, Deary & Collard, 2021)– a condition which is also associated with an over-sympathetic response in patients (Brown & Gerbarg, 2013). This technique, which was found to demonstrate improved wellbeing scores in participants, was designed to require minimal training (through a single 20-minute researcher-led introductory session) and to be self-administrable for participants to perform within their own homes. Therefore, within the current PoTS project, a form of this developed Ocean Breathing intervention was utilised as the initial basis for tailoring a breathing practice for the needs of people with PoTS.

1.1. Aims & Research Questions for Guiding Intervention Development

- *Project Aims*

As guided by the initial phase of the Medical Research Council [MRC] Framework for Complex Intervention Development (Skivington et al., 2021), the current study aimed to develop an Ocean Breathing practice for use in people with PoTS. Skillington et al. (2021) recommend the development of complex intervention through the identification of underlying programme theories (explanatory models) which demonstrate the perceived therapeutic effects of the technique, and the involvement of key stakeholders for intervention delivery in the development process. In this respect, my decision to use Ocean Breathing as a basis for intervention development in PoTS was rationalised from both medical research on PoTS autonomic dysfunction (Jacob et al., 2019) and pranayama yoga literature behind the actions of this technique (Carter & Carter III, 2016), in addition to its reliance on an explanatory model which is complimentary to the socio-medical frameworks utilised by sufferers with this condition (see chapter 7).

The current project featured an iterative, multi-stage qualitative approach. Through series of interviews, I collected intervention feedback on the Ocean Breathing practice from across three key stakeholder groups: [i] people with PoTS (including the use of member checking as the final intervention development stage), [ii] PoTS-experienced professionals and healthcare practitioners, in addition to; [iii] pranayama yoga professionals. The project was iterative in

nature, whereby feedback and suggested changes to the intervention obtained from one group would be synthesised and presented back to the next stakeholder group for scrutiny.

Given the lack of empirical work which has previously examined sensations of breathlessness symptoms in PoTS, during the current study I also examined the experiences and relations people with PoTS have to their sensations of breathing - this was undertaken in order to identify possible implementation barriers to the intervention. During the stage of intervention development of the Ocean Breathing practice and subsequent stages of feasibility and evaluation in future, it is important to identify factors which may facilitate or hinder the future likelihood of achieving successful implementation of the intervention within the patient group. In order to consider such factors during intervention development I utilised Normalization Process Theory (May & Finch, 2009) within my analysis of stakeholder feedback. The application of Normalization Process Theory to intervention development enables researchers to critically consider both the deployed contexts where the intervention could be introduced into, and the key drivers which will push forward the continued effectiveness of the practice, through careful defining of intervention parameters (Murray et al., 2010).

- *Justification for Normalisation Process Theory*

Prior to my final decision to utilise Normalization Process Theory (May & Finch, 2009) for guiding the process of designing and tailoring my Ocean Breathing intervention to the needs of people with PoTS, other supporting frameworks for intervention development were explored. Namely, this included consideration of the Person-Centred Approach (Yardley, Ainsworth, Arden-Close & Muller, 2015), a model which focuses predominately on enhancing the acceptability and feasibility of interventions through a qualitative-led development process (Yardley, Morrison, Bradbury & Muller, 2015). Nevertheless, in comparison to Normalization Process Theory (May & Finch, 2009), a model which possesses four theoretically derived core constructs that identified intervention barriers can be easily mapped on to (and thus 'made sense' of) throughout the analytical process, the Person-Centred Approach framework (Yardley, Ainsworth, Arden-Close & Muller, 2015) itself does not outline a clear strategy for allowing my team to critically examine each stakeholders groups' identified issues with the Ocean Breath, and how these factors would in turn influence its likelihood of achieving successful implementation within a PoTS patient group in future. Thus, due to these reflections, I ultimately decided upon Normalization Process Theory (May & Finch, 2009) for supporting my intervention development process, due to the greater levels of insights it would bring to understanding the various perceptions of the Ocean Breath by people with PoTS,

PoTS professionals & healthcare practitioners, in addition to a recruited group of pranayama yoga instructors.

- *Intervention Development – Guiding Research Questions*

The current investigation was guided by the following research questions:

- What experiences of (altered) breathing do individuals with PoTS encounter as a result of their chronic illness? (*Findings presented in Chapter 9*)
 - What core factors identified during the process of intervention delivery will facilitate or hinder the likelihood of achieving future implementation of an Ocean Breathing practice for People with PoTS? (*Findings presented within Chapter 10*).
-

2. Methods

2.1. Approach

Data collection and analysis for the intervention development phase of the project undertook an iterative multi-stage qualitative design (see Fig. 1.), which was theoretically guided by Normalization Process Theory (May & Finch, 2009). The research team initially intended to offer participants with the choice of partaking in up to two interviews and/or focus groups for the project through face-to-face, telephone or online formats. In order to comply with government guidelines during the UK COVID-19 lockdown however, data was only collected through the use of non-face-to-face methods. Reflexive thematic analysis (Braun & Clarke, 2019), an analytical method which is flexible with a range of different epistemological stances, was utilised by the current study to interpret participants' responses.

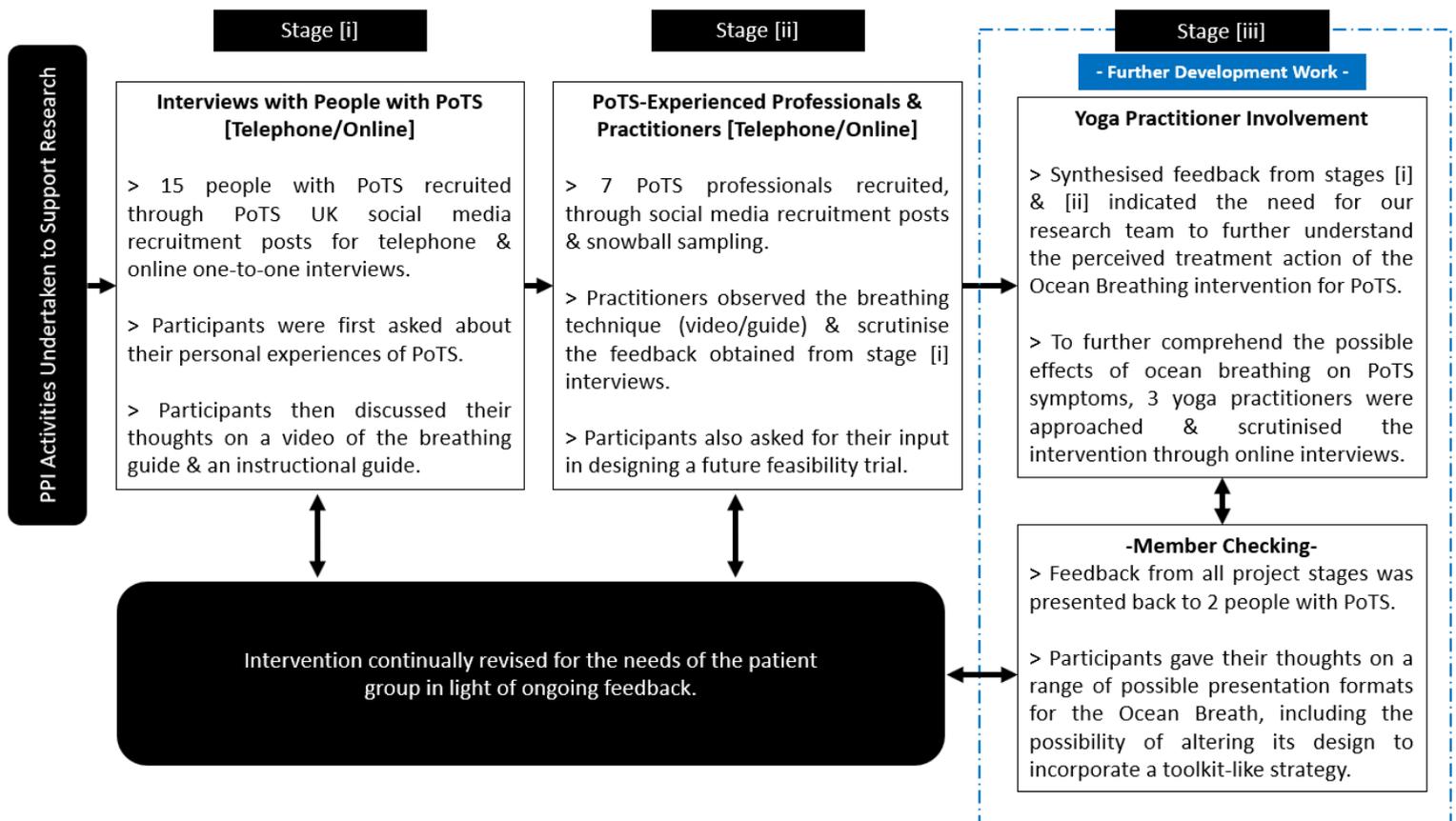


Fig. 1. An overview of the intervention development phase of the project, featuring interviews with the people with PoTS Group [Stage [i], n = 15], PoTS-Experienced & Healthcare Practitioners [Stage [ii]; n = 7], Pranayama Yoga Practitioners [n = 3] & Follow-up Interviews with People who have PoTS to finalise the intervention [Stage [iii], n = 2].

2.2. Reflections on Methodological and Epistemological Assumptions

The MRC framework advocates the importance of understanding the complexities associated with developing an intervention (Skivington et al., 2021). In order to achieve this, a thorough consideration of the relationships must be acknowledged between the social circumstances and infrastructures to which the intervention is being implemented within (contexts), in addition to the interaction of the intervention with bodily systems, cognitive and social factors (mechanisms) that are responsible for eliciting its action (Pawson, 2013). In this manner, the resultant effects (or lack of effect) arising from the intervention within a patient group (outcomes) can be understood as having been produced from the (un)successful activation of its mechanisms within specific, applied social contexts (Bonell et al, 2013).

When undertaking the intervention development phase of the project, I considered how my own use and application of methodology for guiding the development of the Ocean Breath for people with PoTS - through the MRC framework (Skivington et al., 2021) - was reflective upon the assumptions of critical realism (Bhaskar & Hartwig, 2010). A wealth of academic literature has considered the application of realist philosophies towards the evaluation phase of the complex intervention development framework (Blackwood, O'Halloran & Sorter, 2010). Nevertheless, only a limited number of works have considered its applications to other key stages of this model; this is specifically true in regard to the understandings of how insights from critical realism may contribute towards the initial steps of undertaking intervention development (Fletcher et al., 2016). The MRC framework (Skivington et al., 2021) advises that the conduct of intervention development should be led by identification of explanatory underpinning mechanisms, through socio-medical models and principles (programme theories) which account for a technique's intended therapeutic action(s) - as devised from theoretical evidence and stakeholder involvement. As noted above, in relation to the development of the Ocean Breathing intervention, my supervisors and I identified this technique through its underlying explanatory model of influencing vagal nerve activity (as the programme theory of this technique) being consistent with the dysfunctional autonomic nervous system ontologies that underlie PoTS understandings. Fletcher et al. (2016) supports the application of critical realist assumptions to the intervention development process, through their ability to progress and comprehend a programme theory by careful defining its associated core mechanisms and contexts (Bonell et al., 2012).

During interviews, people with PoTS sometimes expressed different views of the Ocean breath's perceived difficulty, based on their experiences of (changing) functional levels each ^{day} & their 'combination' of symptoms in comparison to others with PoTS. Important for our team to therefore reflect on how these illness experiences influence patients' relations to the developed intervention.

Fig. 2. Reflexive note generated [MJH] during stage [i] data collection through interviews with people who have PoTS. Within this memo, I reflected upon how participants at times reached radically different conclusions towards the perceived difficulty of specific instructional steps within the Ocean Breath, through their own consideration(s) of the unique PoTS symptom clusters they presented with (in comparison to others). This demonstrates how understandings of the intervention are influenced by them drawing upon the objective and authenticated experiences of their own exhibited PoTS symptom cluster, which lead to subjective sense-making of the Ocean Breath's employed steps and procedures for enactment.

Because of this, I reflected upon how people with PoTS would apply understandings of their chronic illness as a way of making sense the Ocean Breathing intervention and its instructional steps. Previously within chapter 5, during my work to explore PoTS diagnostic and symptom experiences, I acknowledged the importance of recognising that people with PoTS' narratives are constructed (Esin et al., 2013) from authenticated PoTS illness experiences, that are grounded within an objective reality. People with PoTS themselves substantiate understandings of their chronic illness within physical bodily systems (see chapter 7), through the citing of ontologies surrounding the autonomous nervous system to legitimise the medical basis for their symptom experiences as a form of lay explanatory model (Kleinman et al., 1978; Menon et al., 2016). Through these autonomic socio-medical frameworks, people with PoTS are also able to account for observed differences in the diverse symptom presentations

between one person with PoTS to another. Thus, whilst it is argued that there is an objective medical basis to the experience of PoTS illness debilitation, the unique combinations and diversity in symptom presentation which different individuals exhibit leads to unique sense-making opportunities and subjective interpretations being drawn from these experiences, which in turn influence the processing of social phenomena and perceptions of interventions for PoTS (see *Fig. 2*). This is in keeping with assumptions of critical realism for intervention development, whereby I acknowledge that objective underpinnings of the intervention exist within reality, and that participants perceptions and relations to its mechanisms are influenced by a range of social, subjective, and cognitive factors (Bhaskar, Collier, Lawson & Norrie, 1998).

2.3. Patient and Public Involvement [PPI] Work

In an effort to support the conduct of the intervention development phase, people with PoTS' perspectives on the design and conduct of research were collected (Boote, Baird & Beecraft, 2010). PPI activities were undertaken from December 2019 to March 2020, through one-to-one discussions with four people who had a diagnosis of PoTS (and one person's partner). PPI members were brought on in a consultancy-based capacity (Brett et al., 2012) to provide feedback on the intended recruitment strategy, interview and focus group procedure, in addition to critiquing items within the developed interview schedules.

Whilst PPI work was suspended earlier than planned due to the occurrence of the COVID-19 pandemic, sufficient feedback was obtained from these individuals to implement changes to the conduct of our research. First, in addition to offering research participants with multiple breaks during their interview or focus group to help ease the possibility of fatigue symptoms, the decision was also made to provide participants with the opportunity of dividing their interview across two or three shorter sessions. Furthermore, in support of our narrative work (see chapters 4-6), some interview schedule items were adapted by people with PoTS to include more discussion surrounding the diagnostic and symptom experiences of living with the condition – this included the exploration towards the perceptions of living with invisible symptoms.

Finally, from drawing on their personal experiences of encountering contentious labelling of their PoTS symptoms from their general practitioners, three of the four PPI respondents also requested that our team included a primary care clinician to give their perspective on the development of a PoTS-specific intervention. Given this, when seeking healthcare professional feedback on the Ocean Breathing practice from practitioners with clinical experience of treating PoTS, a general practitioner trainee with prior experience of working in

a Falls and Syncope unit as part of his training was also approached and recruited to take part in the research.

2.4. Participants

- *Stage [i] – Interviews with People with PoTS*

A purposive sample of a group of people diagnosed with PoTS was recruited for the research through social media advertisements promoted through the charity organisation PoTS UK (see Fig. 3.). The inclusion criteria for this stage of the research required participants to: (i) possess a current PoTS diagnosis that had been diagnosed by a healthcare professional, (ii) be aged 18 years or older, in addition to: (iii) currently be living within the UK at the time of recruitment. Furthermore, exclusion criteria barred entry to the study for participants with insufficient English language and reading skills which were needed to take part in an interview discussion.

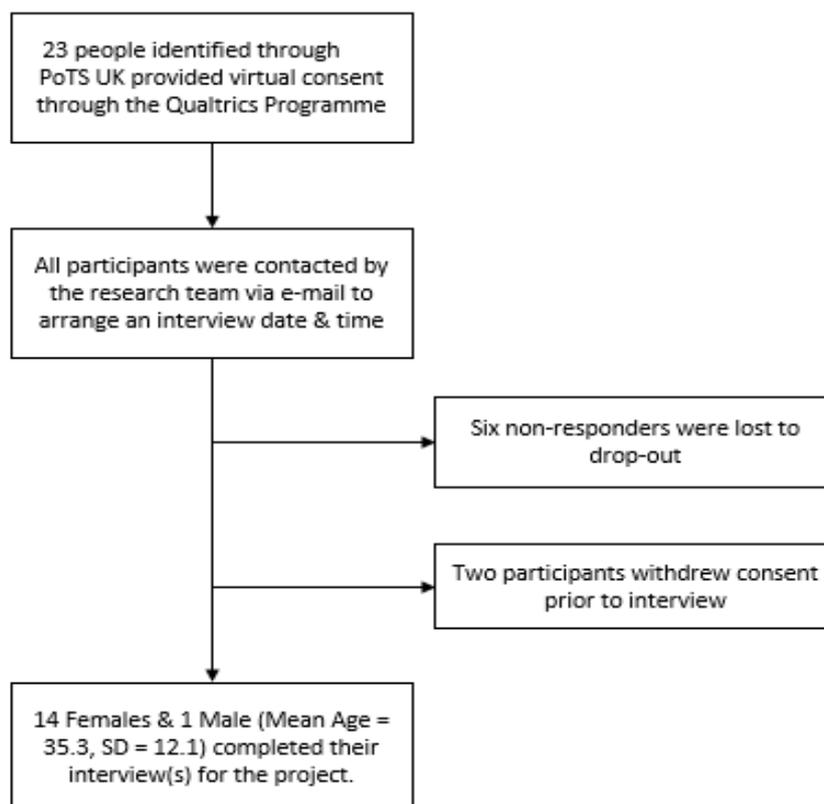


Fig. 3. Flow diagram illustrating the recruitment process for people with PoTS interview stage.

Forty-three participants responded to the social media advertisements and provided consent. The first twenty-three individuals were contacted by the research team. Four participants did not respond to the research team's e-mail, whilst a further two individuals could not be

contacted at the scheduled time of their interviews – these participants were ultimately lost to drop-out. Of the remaining participants, a further two individuals choose to withdraw their consent prior to their interview commencing. Ultimately, fifteen participants completed their interviews for the project. Participants were located across England (n = 13) and Ireland (n = 2).

- *Stage [ii]– Interviews with PoTS-Experienced Practitioners & Healthcare Professionals*

During the second stage of the research, I aimed to explore perceptions of the Ocean Intervention with a second stakeholder group of PoTS-experienced professionals and healthcare practitioners with clinical experience and knowledge of working alongside PoTS patients. A purposive sample of eight UK-based healthcare professionals, who provided virtual informed consent through the Qualtrics programme, were recruited from social media advertisements (through the platform Twitter) and e-mail invitations to participate within the research. Snowball sampling was also implemented, whereby two participants had directed their colleagues towards the online study recruitment posts. One participant who was unable to attend and re-arrange their scheduled interview time was subsequently lost to drop-out. This left a final sample of seven participants (Mean Age = 46.6, SD = 8.8) consisting of five females and two males.

Occupational backgrounds of the recruited PoTS-experienced professionals and healthcare professional participants included: advanced nurse practitioner, advanced syncope nurse, occupational therapist, physiotherapist, cognitive behavioural therapist, two Pilates instructors, and a general practitioner trainee who had worked in a syncope unit during their training. Each participant took part in a sole interview with the principal investigator, either through an online format or via telephone. All participants were located across England (n = 7)

- *Stage [iii]– Interviews with Pranayama Yoga Instructors*

During the research, it emerged that the healthcare professional groups held differing opinions upon what actions the Ocean Breathing intervention would have within the PoTS patient group. To further understand the perceived effects of the chosen intervention on PoTS symptoms within the research, three yoga practitioners were approached and invited to take part in the project through e-mail invitations.

All of the three contacted yoga practitioners gave their virtual consent and took part in a one-to-one telephone or online interview, where they discussed the use of the Ocean Breath (Ujjayi) within their own practices and their insights into how the intervention would affect people with PoTS. This participant sample (Mean Age = 47.3, SD = 12.4) consisted of two females and one individual who did not provide information of their sex. Prior to the interview, yoga practitioners were signposted by the research team towards publicly accessible online resources, developed by PoTS charity organisations, to familiarise themselves with the condition.

- *Stage [iii] – Member Checking: Final Interviews with People who have PoTS*

Following the collated feedback across the people with PoTS, PoTS-experienced professionals and healthcare practitioner, as well as pranayama yoga instructor groups– a number of people with PoTS, who had taken part in the primary stage of the research, were re-approached one year following their interview by our research team to take part in a second discussion for the project. These participants had previously expressed an interest to take part in a subsequent stage of the research at the time of providing their consent during stage [i]. These participants were contacted through e-mail invitations, containing a weblink to an online information sheet and informed consent document via Qualtrics, where they were asked to re-provide their virtual informed consent for taking part in stage [iii].

The aims of the follow-up discussions with people with PoTS were to: (i) to make them aware to the changes to the intervention made to the intervention by the research team in response to their feedback; (ii) gather their thoughts on the issues raised by the healthcare professional and yoga practitioner groups; (iii) finalise further changes to the intervention the research team would need to undertake in order to make the breathing practice suitable to the needs of the patient group.

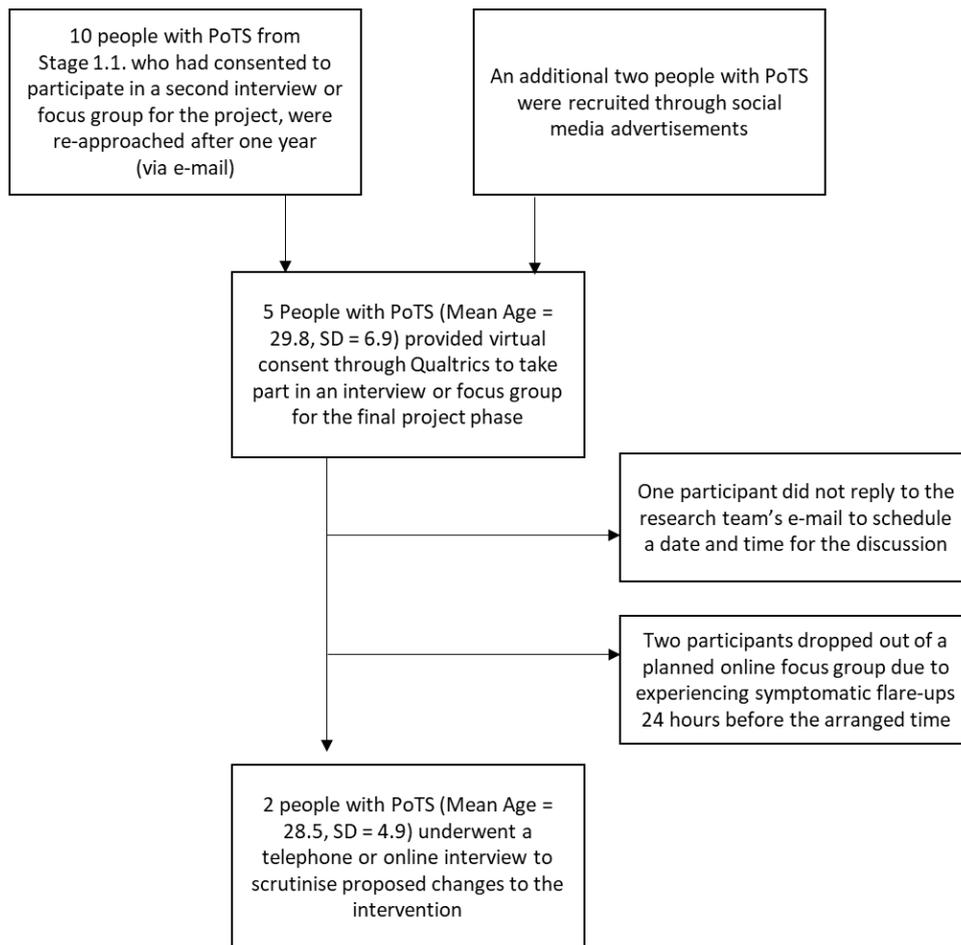


Fig. 4. Flow diagram of the recruitment process for the final interviews with people who have PoTS.

Ten participants from stage [i] were approached for the follow-up discussions. Only three of these participants responded to e-mail invitations and provided their consent (Mean Age = 30.3, SD = 9.2, all female). Two of these participants were unfortunately lost to drop-out prior to the focus group taking place. Whilst our attempts were ultimately unsuccessful, efforts were made by the research team to still collect feedback from these individuals through the offer of rescheduling one-to-one interviews with these participants at a more appropriate time.

Due to the lack of participant responses and observed drop-out rates for those who had responded (*see Fig. 4.*), an additional two participants - who had not taken part in the first stage of the research - where recruited through social media. After providing their virtual consent, one of these participants did not respond to the e-mail sent by the research team to arrange a time and date to hold the discussion with them. In total, following participant drop-outs from the five females who had provided their consent (Mean Age = 29.8, SD = 6.9) to participate in stage [iii], this left a final sample of two females with PoTS who completed one-to-one interviews with the researcher during the final stage of the intervention development project.

2.5. Materials

- *Initial Written Instructional Breathing Guide*

An initial instructional ocean breathing guide [Appendix_H], which featured nine individual steps to provide practical guidance on how to perform an ocean breathing practice, was forwarded to all participants for inspection prior to their interview. This instructional guide was created as part of a previous pranayama breathing intervention that had been developed by myself and one of my supervisors for individuals with sub-clinical levels of anxiety (Hogg, Collard & Deary, 2018). The guide also described a short belly-and-thorax breathing exercise conducted at the start of the practice which aimed to facilitate conscious awareness of how the abdomen moves during each inhale and exhale. Finally, the practice closes with a short laying down (savasana) practice to allow the person with time to reflect upon their experiences of performing the technique. As a safeguard for the research, people with PoTS were required only to read through the guide for the purposes of providing verbal feedback (they were instructed not to attempt performing the intervention).

- *Video Demonstration of the Breathing Technique*

As an objective of the project was to identify the most suitable method(s) of delivery for the intervention, written and video formats for the intervention were considered by the participants for scrutiny. Thus, in addition to the instructional breathing guide, all participants in stages [i] and [ii] received a link to a short YouTube video [Duration = 2.47 Minutes] which demonstrated the ujjayi breathing technique [www.youtube.com/watch?v=JsbpqW0Baog&t=10s]. The video featured a young, white female yoga practitioner sat in an upright position who first discussed the history and benefits of conducting the Ocean Breathing technique, before she then demonstrating the practice to the watcher.

- *Interview Schedules*

Interview and focus group schedules [Appendix_I] were devised within the early stages of the project. Items on the schedule were divided across three categories. Within stage [i], the first seven questions concerned the exploration of the participant's own experiences of receiving a PoTS diagnosis, the impact of the condition on their day-to-day life and their management of the condition. Feedback collected from PPI activities lead to revisions being made to a number of these items within stage [i]. Changes made reflected respondents' encouragement for us to pursue further discussion with participants surrounding: PoTS as an invisible (chronic)

illness, how people with PoTS' perceive their PoTS symptoms in relation to their other co-morbid health conditions, in addition to; the understanding of participants' PoTS diagnosis by family, friends and colleagues.

During stage [ii] and [iii], the initial items on the interview schedule concerned asking about the occupational background of each PoTS-experienced professional, healthcare practitioner and pranayama yoga instructor. Notably, participants were asked to describe their job title, day-to-day roles & responsibilities and their previous training or positions which has led to their current occupation and their thoughts on treatments for people with PoTS.

The second item set (stages [i], [ii] & [iii]) focussed on gathering the participants' thoughts on the Ocean Breathing intervention. Separate items were created to collect participants' feedback on the video demonstration of the intervention and the breathing guide independently. As the research team incorporated the use of Normalization Process Theory (May & Finch, 2009) throughout each stage of the intervention development process, several items were designed in light of the four constructs of this framework (see Table 1).

Table 1. Application of NPT constructs to the generation of questions during interview schedule development.

NPT Construct	Application of Construct to Ocean Breathing Intervention Development	Example Question(s) in Interview Schedule
Coherence	Understanding how participants try to make sense of, and seek to understand, the ocean breathing intervention and its steps.	> <i>Which specific steps or terminology within the instructional guide may you [or a person with PoTS] have difficulty with understanding?</i>
Cognitive Participation	Consideration of the ways in which participants perceive how other people in their day-to-day lives, PoTS treatment or healthcare professions would affect their ability to continue, and comply with, the breathing technique.	> <i>If you were to regularly undertake the breathing exercise, how might your close family and friends perceive or react to this?</i> > <i>How would you feel about approaching the subject of you trying a breathing intervention for your PoTS with a healthcare practitioner?</i>
Collective Action	Exploration of participants' thoughts concerning what work would be required of a person with PoTS to both undertake and operationalise each aspect of the ocean breathing technique.	> <i>If asked, would you be prepared to invest the time and effort into learning the technique? (why/why not)</i>
Reflexive Monitoring	Comprehension of how the intervention is appraised and scrutinised by each participant group.	> <i>What effects do you perceive the ocean breathing intervention having on your [a patient's] PoTS symptoms?</i>

The final set of items examined other factors which may influence the likelihood of patient acceptability with the intervention. This included further discussion of other possible delivery methods to support the intervention learning by the people with PoTS group - such as participants' perceptions on the potential use of mobile-phone application, social media support groups and/or the organisation of face-to-face training sessions.

As the project adopted an iterative nature, within stage [ii] and stage [iii], healthcare professional and pranayama yoga instructor participants respectively were both made aware of the feedback collated from prior participant groups and asked to scrutinise their suggested alterations to the intervention. Healthcare professionals were also asked for their thoughts on the designing of a future clinical trial which will aim to assess the breathing practice following the completion of intervention development. Specifically, feedback was sought on: (i) the identification of physiological outcome measures; (ii) identification of psychometric outcome measures; (iii) the implementation of qualitative evaluation within the trial; (iv) patient

recruitment and sample; (iv) study design and (v) intervention arms/ possible inclusion of an (active) placebo group.

- *Additional Breathing Instructional Guides*

To support the final interviews with people with PoTS during stage [iii], four different additional breathing guides to the Ocean Breathing intervention (Appendix_J) - identified from publicly available online resources - were sent to participants ahead of their interviews for further feedback purposes. Types of breathing included were: Buteyko Breathing, Diaphragmatic Breathing (NHS), Square Breathing, and the STOP Mindfulness technique. These guides were collated as examples of breathing techniques which participants from across all three project stages had described as possessing a (perceived) possible benefit to the management of PoTS symptoms. These guides were used to facilitate discussion surrounding their comparisons with the Ocean Breathing technique as well as around the layout and format of delivery materials/written guide. I was also interested in discussing their perceived compatibility with the Ocean Breath practice, due to considerations by my team of altering the design of the Ocean Breathing practice to incorporate a toolkit-like strategy, for better accommodations of the diverse symptom presentation and ranging functional abilities of PoTS patients.

2.6. Procedure

Ethical approval for the research was granted by the Faculty of Health & Life Sciences Postgraduate Ethics Committee of the University of Northumbria at Newcastle upon Tyne [#16030]. Given that prior to the COVID-19 pandemic I had originally intended to recruit people with PoTS and healthcare practitioners from an NHS CRESTA fatigue clinic for undertaking intervention development work, the project was also assessed by the Health Research Authority & Research Ethics Committee of London – Brighton & West Sussex, who granted favourable approval for the research following proportionate review [IRAS ID = 254616; REC Reference = 19/LO/1078]. The onset of the COVID-19 pandemic however caused untimely delays to the start of my research, due to the Hospitals trust no longer having capacity for non-COVID research. This forced a change to the planned recruitment strategy to the use of social media recruitment posts (*see Fig. 5 for reflexive passage*), which were promoted by the PoTS UK charitable organisation.



Mitchell James Hogg



(Reflective comment, feel free to skip) Looking back now when approaching the end, I wonder how our data / intervention development process may have differed if we had recruited through this.

I actually feel – having gone through the charity – we got a better and representative sample, as not all people with PoTS have access to support services which the CRESTA clinic can offer. Some have to "go it alone"... and as we seen through narrative work... likely have to rely much more heavily on their families, "PoTS allies", online communities, etc. Also, additional reflection – I wonder, if we had stuck to the clinic only route of recruitment – if those patients would be more inclined towards specific ontologies/ways of coherence for the ocean breath format & sense-making for its perceived effects, given the frameworks staff members would cite

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Fig. 5. Reflexive note generated [MJH] through the drafting of this chapter. Within this comment, I considered how changes to my recruited sample of people with PoTS during intervention development, through the identification of social media users instead of those receiving NHS treatment, may have influenced the shape of the research. In consideration for other qualitative studies on PoTS going forward, it is interesting to reflect on how the recruitment of people with PoTS through only healthcare or other NHS services may, in part, prevent their research teams from collecting feedback and narratives from key individuals in this patient group - who receive little or no clinical help for the control of their symptoms. From reflections such as this, I realised that these individuals with PoTS, who remain almost solely reliant on their own use of non-pharmacological management strategies, were therefore a key target sub-group which the Ocean Breathing intervention needed to aim to engage with.

Participants within the people with PoTS (Stage [i]), healthcare practitioner (Stage [ii]) and pranayama yoga professional (Stage [iii]) first accessed the study information sheet through a Qualtrics survey link posted across social media or e-mail advertisements. After having been provided with the opportunity to contact the research team (through e-mail) to ask any queries concerning the research, participants who wished to take part in the project provided their virtual consent through this system. Following this, each participant was required to create a unique study ID code – this was used to anonymise any personal data collected from each individual over the course of the project. The participant then provided both their demographical (Age & Sex) and relevant contact (Telephone Number/ Online MS Teams) information that was required of them for conducting the interview.

Participants were then individually contacted to arrange each interview and sent a copy of the breathing instructional guide, alongside a weblink to a short video demonstration of the technique. As fatigue is a prevalent symptom of PoTS (Benarroch et al., 2012), two protocols-identified from our PPI work during the project planning stages were implemented to mitigate the impact of this on participants from the patient group. Participants were first provided with the opportunity to divide their interview across two (thirty-minute) or three (twenty-minute) separate, shorter sessions with me. Furthermore, participants were offered a break at the half-way point during their interviews. Prior to the interview taking place, participants across all stages of the research had also been made aware that they were free to take a break at any point during the discussion, simply by informing me that they wished to do so. Duration of

interviews ultimately ranged between 45 – 120 minutes in total across all stages of the research.

Following the conclusion of the interview, participants were thanked again for their time. Participants in the people with PoTS group were made aware of a future opportunity to take part in a follow-up stage of the research (Stage [iii]). One year later from their first interview date, these participants who had expressed an interest in participating in this further stage of the research were contacted again by e-mail. This contained a Qualtrics weblink to an information sheet detailing the final stage of the research and virtual informed consent document. Participants who still wished to take part in this final phase of the research gave their virtual consent and were contacted to arrange an appropriate date and time for their discussion. Interviews were one-hour in length and conducted through telephone and Microsoft Teams. Interviews for the final stage of the project were designed to be unstructured in nature, in order for participants to freely discuss what they felt their thoughts and concerns with the breathing techniques.

2.7. Transcription & Analysis Strategy

Following the conclusion of each participants' discussion and re-listening to audio recordings to ensure data familiarisation, each interview was carefully transcribed verbatim by myself. During transcription, I documented each pause, vocalisation, verbal action (e.g. cough; sneeze; laughter) and overlap between the speakers' speech through the use of the transcription key produced by Poland (2002), as previously outlined within thesis chapter 5. A series of reflexive notes – recorded and captured through written memos on transcripts, post-it notes, electronic applications and audio recordings captured throughout the time of recruitment, transcription and analyses stages - were maintained throughout the project.

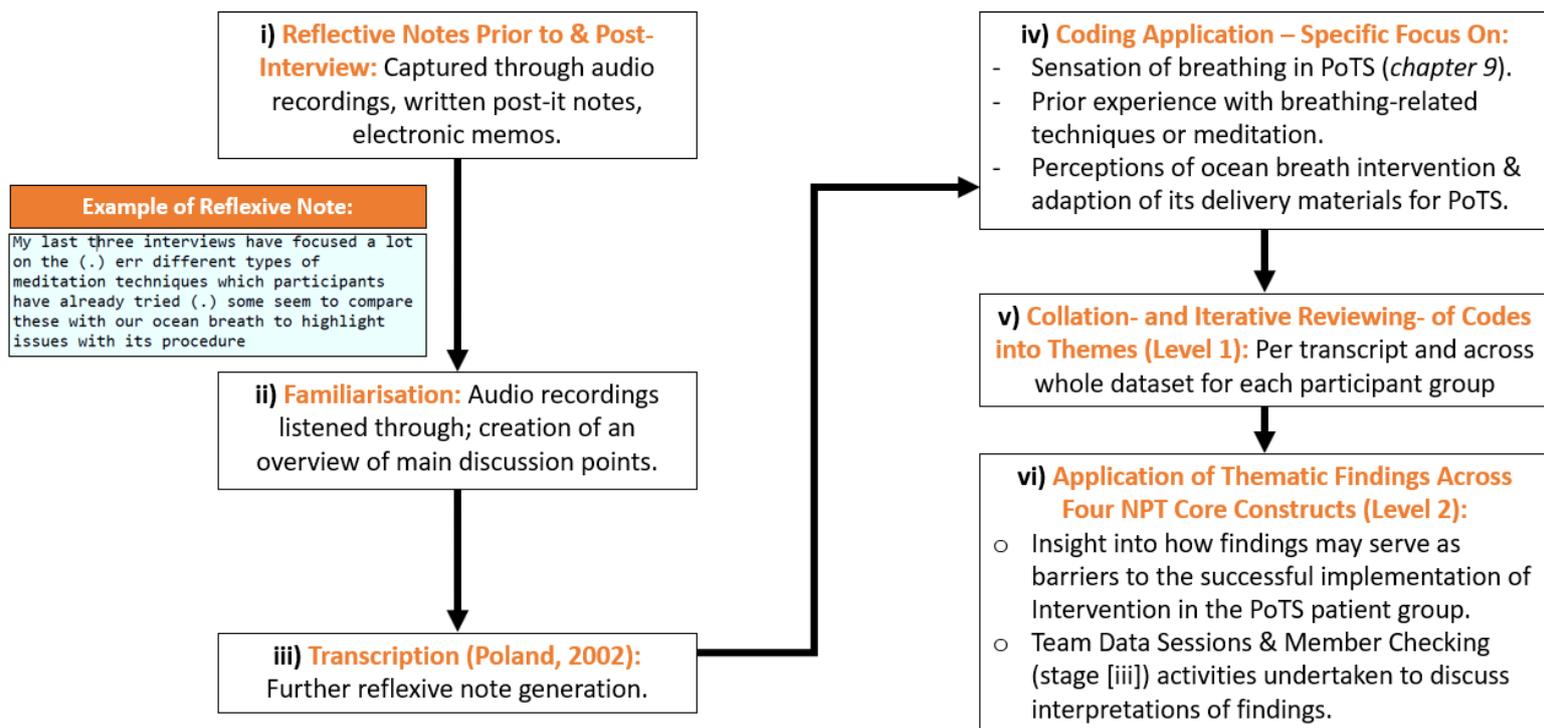


Fig. 6. Flow diagram representing the application of Reflexive Thematic Analysis (Braun & Clarke, 2019) to the development of the Ocean Breathing intervention.

Transcripts for the project were analysed (see Fig. 6) through reflexive thematic analysis (Braun & Clarke, 2019), which was theoretically informed by Normalization Process Theory (May & Finch, 2009). During the initial analysis stages, each transcript was read through on a minimum of two occasions prior to coding commencing. Line-by-line coding of printed transcripts was then undertaken, whereby I aimed to identify extracts within the data concerning the participants' thoughts and opinions towards the ocean breathing practice, in addition to their suggested intervention changes. Furthermore, during coding I also focussed on noting aspects of each data source which highlighted their experiences of their (altered) breathing and encountered breathlessness symptoms arising from PoTS (as explored in chapter 9), in addition to participants' prior and/or current experiences of performing a similar meditation (e.g. yoga; mindfulness; general meditation). This decision was made to help support the future implementation of the ocean breathing intervention within the intended patient group, by identifying which similar barriers participants could incur when attempting to engage with the current practice.

Following the completion of this for each data source, marginal comments and notes were then collated, reviewed & grouped together within each individual transcript to identify common patterns of interest and to generate initial themes which were relative to the research question (Level 1). Initial themes were then contrasted and applied across the four Normalization

Process Theory constructs (Level 2). The application of the initial themes across the four constructs was conducted to enable a better understanding of how each identified intervention change or issue would impact and determine the likelihood of successful future implementation of the ocean breathing practice within the PoTS patient group. Following this, themes identified across transcripts were reviewed continuously across the transcript sample – whereby initial themes for each participant were compared, merged and/or altered against one another - to produce major themes, which encapsulated the core aspects of feedback from all participants' responses for each stage. Tabular presentation of the results (see chapter 10) was then produced to present the final themes of the research, in light of each dominant Normalization Process Theory construct.

2.8. Study Evaluation of Intervention Development Phase

Strengths and limitations of the undertaken intervention development strategy must be considered. First and foremost, my strategy for developing the Ocean Breath for PoTS has included the use of Normalization Process Theory (May & Finch, 2009). The adoption of these principles during data analysis was beneficial to our process and future stages of the MRC framework (Skivington et al., 2021), through assisting with the early identification of core factors which will influence the probability of successful implementation of the Ocean Breathing intervention within the PoTS patient group. Furthermore, my supervisors and I have taken a number of steps to rigorously examine the interpretations, assumptions and sense-making processes we have utilised to draw conclusions from our analysis of collected data. We have done this through team discussions during supervision sessions, the generation of reflexive notes throughout the lifetime of the project phase and through undertaking member checking with people who have PoTS during the final stage of data collection.

With considerations to the limitations of the research, I acknowledge the impact of the COVID-19 pandemic on the data collection strategies. Due to this and the pressures it produced on delaying the timescales of the intended research recruitment strategy, I was unable to undertake a mixed stakeholder-group - consisting of participants from across all three stages of the research - to present back final interpretations and analysis findings from the collated intervention feedback to finalise changes to the intervention. This would have been beneficial to addressing the issues that were identified in regard to the coherence of the Ocean Breathing intervention across PoTS stakeholders (see chapter 10). However, efforts were made to address this during member checking by having people with PoTS consider alternate breathing techniques which could be combined alongside the Ocean Breathing intervention to serve as part of a toolkit strategy.

2.9. Reflexivity

It is important to reflect on the types of demographical data which I have collated from people with PoTS throughout the time of undertaking of my thesis. In efforts to minimise the amount of personally identifiable information collected throughout the project from participants, details concerning participants' ethnicities were not recorded when identifying PoTS diagnostic story vlogs, nor was it collected for the interview work that I undertook to support the development of my Ocean Breathing intervention. To date, no academic works within the PoTS research field have specifically examined whether people with PoTS' diagnostic and symptom experiences may differ due to their ethnicity. I therefore recognise this as a limitation of my research and encourage fellow PoTS researchers to examine these possibilities further within their future works.

Furthermore, it is interesting to consider the similarities and differences between the qualitative responses obtained by people with PoTS, between my employed data collection strategies (vlogs; interviews). Whilst people with PoTS in vlogs and interviews both drew upon the same concept of an autonomic nervous system ontology model within their speech; anecdotally speaking, I found these references to be more commonly drawn upon within my analyses of the discourses of PoTS vloggers. One likely candidate explanation for this may be due to PoTS interview participants not feeling as much of a need to legitimise and authenticate their illness experiences to myself, due to their assumption that I am a "PoTS-knowledgeable" researcher. Alternatively, PoTS vloggers may be more aware that they have a range of audiences which they will need to appeal the nature of their illness experiences towards (both PoTS-naïve individuals and other, fellow people with PoTS). Nevertheless, it should be noted that autonomic nervous system explanatory models were still relied upon by interview participants to understand and make sense of their PoTS symptomology - specifically in relation to breathlessness (see Chapter 9 for further reflexive comment, within Fig. 2), where they also separated their bodies from their sense of "the self" (Charmaz, 1980).

Finally, one additional observation I made between the analysis of PoTS diagnostic stories and PoTS interview participants concerned the construction of doctors within each groups' discourses. Within interviews, only a small handful of participants were critical of the healthcare practitioners they had interacted with during their medical journeys. The majority of interview participants constructed their doctors as hero characters (in a similar manner to how PoTS vloggers would at times do this), who had been pivotal in aiding them with managing their symptomology. It is interesting to therefore consider why the negative construction of medical professionals appeared to be more prominent in PoTS vloggers' story narratives. At times, I did also notice that interview participants would commonly construct other key

individuals – such as their previous employers, old friends and family members they had since lost touch with – in a negative light, through personal anecdotes where these people had not shown understanding towards the nature of their condition. It would be interesting therefore, in a future follow-up project, to re-develop the interview schedule in order to further explore these differences more thoroughly. Perhaps by utilising member-checking with people with PoTS (ideally, involving those who are also PoTS vloggers themselves by background) alongside a more comprehensive interview schedule, this will be able to shed further insights behind these observed differences between vlog and interview data sources.

3. Conclusion

To conclude, within this chapter I have outlined my methods for gathering feedback on the Ocean Breathing intervention I was developing for PoTS through interviews with three core stakeholder groups. Within Chapter 9, I present findings identified through the examination of people with PoTS' own, self-held perceptions of their (altered) breathing behaviours and their symptom experiences of encountering breathlessness within their day-to-day lives. I then consider how these findings have informed the shape, format and tailoring of the Ocean Breath for the needs of this patient group.

Within the current chapter, I present initial findings from of a reflexive thematic analysis of interviews undertaken with people diagnosed with PoTS, in order to examine their sensations of breathing and experiences of living with a breathlessness condition. I identified that people with PoTS described experiencing an altered breathing pattern as a result of their illness, which was depicted through their own portrayals of subjective experiences with air hunger symptoms. Furthermore, participants explained that, due to these altered breathing patterns, they would need to utilise conscious efforts in order for them to fully engage the movement of their lower-abdomens within the performance of a breath. Finally, people with PoTS noted that they had identified their 'dysfunctional' breathing patterns as needing to be corrected and retrained, through the use of breathing practices or clinical interventions. These findings supported my intervention development process by identifying possible factors – such as the need for breath-related interventions developed for PoTS to be 'customisable' in nature and to avoid upper-chest exercises - which would influence the likelihood of the Ocean Breath practice achieving future successful intervention implementation within the patient group.

1. Exploring the (Altered) Breath in PoTS

Breathlessness - particularly in regard to how these symptoms are experienced by individuals with a chronic illness – has remained an understudied phenomenon within the study of PoTS (Stewart & Pinnosi, 2021). Of the few published articles which have touched on this sensation within the literature, researchers have explored possible medical aetiologies which account for the presentation of these symptoms within the patient group – such as findings linking the breathlessness to reduced venous pressure within these individuals (Oldham et al., 2016).

Although none currently exist within the PoTS literature, a small body of qualitative works has explored patients' sensations, experiences and sense-makings of their breathlessness symptoms predominately within COPD (Gysels, Bausewein & Higginson, 2007). Whilst meta-synthesis of these works has shown that these articles often neglect the importance of including reflexivity within the reporting of their interpreted participant themes (Harrison et al., 2014), their findings have nonetheless highlighted the importance of understanding phobias which COPD sufferers depict as experiencing surrounding the sensation of air hunger within their day-to-day lives, in addition to explanations behind their reluctance to access medical assistance for their dyspnoea-related complaints (Gruffydd-Jones et al., 2007).

Through the presentation of findings within this chapter, I further expand upon these limited qualitative works by exploring the sensation of breathlessness within a PoTS patient group.

Following semi-structured interviews with 15 people who had PoTS, reflexive thematic analysis (Braun & Clarke, 2019) was undertaken to examine participants' experiences of breathing and their breathlessness symptoms (see Fig. 1). Thematic findings identified that people with PoTS: (i) become aware of their altered breathing through the labelling of it being 'dysfunctional' by practitioners; (ii) experience hyper-arousal towards the physiological movement of their bodies during respiration, and; (iii) express their desires to 'correct' their breathing patterns through interventions.

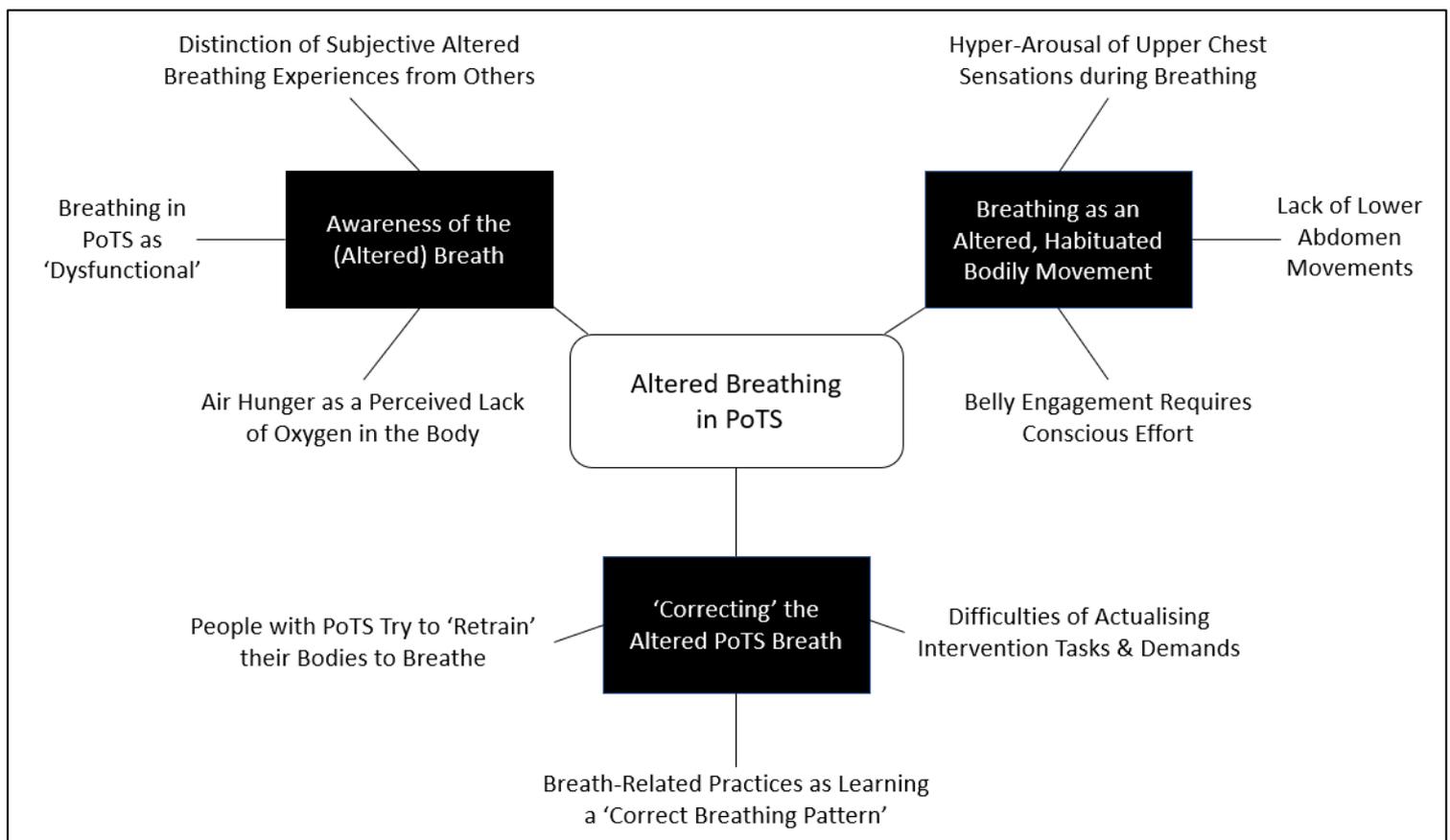


Fig. 1. Thematic Map representing the findings from the exploration of breathing experiences and breathlessness symptoms in people with PoTS, synthesised through Reflexive Thematic Analysis. *N* = 15.

1.1. Awareness of the (Altered) Breath in PoTS

People with PoTS distinguished their regular, everyday patterns of inhaling and exhaling from the breathing behaviours of those without a breathlessness condition. Participants discussed how their own awareness of possessing an altered pattern of breathing was commonly initiated by speaking with a specialist healthcare professional, who had been assigned to aid with the general diagnosis and treatment of their long-term health condition:

he basically said to me, cause hes seen a lot of PoTS patients with this problem, erm
(.) he said to me that I have (.) that I don't breathe correctly.

[EM08IP]

Within the extract above, a participant recounts the moment where a clinician had first made her aware that her habituated, day-to-day pattern of breathing differed to that of other people. In this encounter, the clinician - through drawing on their portrayed expertise of having 'seen a lot of PoTS patients' as a resource - is recalled as labelling her distinct breath response to be in some way an abnormal behaviour. In this respect, the person with PoTS begins to perceive her regular breathing pattern as a 'problem', whereby she is potentially accountable ('I') for not being able to 'breathe correctly'.

Some people with PoTS then described how they had initially struggled to comprehend how they did not 'breathe correctly', after this 'problem' had had been highlighted by their healthcare professional(s):

P: the doctor who diagnosed me with PoTS he also had me on an exercise bike and had me do a breathing test

R: oh okay

P: and from there he noticed that I had dysfunctional breathing. I don't know what is the dysfunction but something [in] my breathing is not proper

[SA09RH]

Similar to the prior extract [EM08IP], the healthcare practitioner in this interaction [SA09RH] also identifies their breathing patterns as a clinical problem. As supported from the results of a performed 'breathing test', the doctor uses these medical findings to label their patient as possessing 'dysfunctional breathing'- to denote that their habituated breathing cycles are presented as an incorrect or wrongful pattern. Nevertheless, notice as well that the participant is not provided with an explanation by the clinician behind 'what is the dysfunction' in their breathing. Due to this, many people with PoTS expressed how they were left trying to comprehend which aspects of their breathing experiences are altered and 'not proper'.

Those patients left without an explanation disclosed that they had been left to undertake a process of substantial questioning and guesswork, in order to understand how their respiratory cycles differed from those of individuals without a PoTS diagnosis. Whilst multiple hypotheses were put forth by people for PoTS to account for this, many participants explained how they

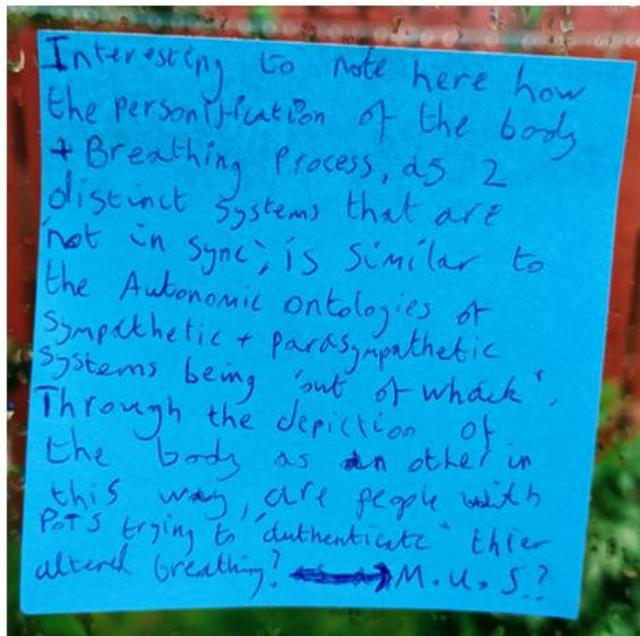
had tried to understand these differences through an inductive approach, undertook through self-reflection about their personal experiences of breathlessness symptoms within their day-to-day lives:

P: now the problem with people who have pots um (.) because it's a dysautonomia (.) we have erm... we don't breathe properly. So I actually realised that I've erm I've been holding my breath when I've been breathing. I'm not breathing like a normal person would. You get like an air hunger that makes you feel like you can't breathe

[MA07TA]

Within the extract above, the participant first renders altered breathing, as a collective experience across PoTS sufferers, as a distinct, clinical phenomenon- whereby they 'don't breathe properly'. Through the use of a pronoun shift from 'we' to 'I', notice that the participant then denotes how their own PoTS symptoms - those responsible for them not 'breath[ing] properly' - can be distinguished from that of a wider experience of altered breathing that is shared amongst other people with PoTS. Through describing their own experiences of struggling with 'air hunger' and their need for 'holding... breath', the participant therefore depicts experiencing a unique, subjective reality surrounding their own sensations of breathlessness symptoms and altered breathing. Through the description of their own, marked struggles of breathing, some people with PoTS highlight how their own experiences differ from the breathing issues encountered by both others with PoTS, as well as the experiences of a 'normal person' without diagnosis.

Other participants also elaborated on the nature of their altered breathing through carefully defining their own experienced states of 'air hunger' [MA07TA]:



It's like I am trying to say as if I have got the air there (.) but it isn't there? But it feels like I haven't got it or my body is trying to catch up to breathing. I don't know if that makes sense but it's the only way I can describe it.
[CC10NE]

Fig. 2. Reflexive note [MJH] detailing how findings from my narrative analysis of PoTS stories, specifically in relation to how people with PoTS communicated understandings of their chronic illness, were reflected upon during the analysis of interview participants' altered breathing experiences. Through these understandings I identified how the comprehension of breathlessness symptom- as a persistent physical symptom- was made sense of by people with PoTS, through the use of similar medical ontologies to those they employ for describing their dysautonomia, whereby the body is portrayed as an 'other' and 'personified' from another entity (their 'process of breathing' within the example).

Notice within the above passage, that the participant depicts their 'breathing' process and the 'body' as two separate systems (see Fig. 2). This depiction of the body and the respiration process as separate entities is utilised by the person with PoTS to explain their breathlessness sensations, by portraying these two systems as being out of sync with one another - through a personification device (Dorst, 2011) - whereby one (the body) is 'trying to catch up to' the other (breathing). As they attempt to account for their breathlessness to the interviewer, they offer some candidate descriptions which highlight their potential inability to clearly perceive the sensation of the breath entering their body- 'but it feels like I haven't got [the breath in]'. As they cannot fully perceive the breath through their own physiological sensations, the participant describes not being able to infer whether their respiratory system has successfully 'got the air there' into their body. As such, due to their breathlessness symptoms, the participant expresses their concern that the oxygen their body needs for functioning just 'isn't there', as they note and expect that they should be able to 'feel' the transfer of air movement - through their own physiological bodily sensations. Thus, the altered breathing experiences of this participant are subjectively rendered in their discourse to highlight their struggles with comprehending the movement of the breath itself within their body.

Others marked their experiences of altered breathing through their perceptions of a restricted air intake during their inhalations:

P: its like sometimes you are having to force your lungs to take in more air

R: oh okay so its like shallow breathing?

P: yes (.) and I think I've gotten use to it. But you know if you are waking up with

brain fog then you are not getting enough oxygen (.) that scares me you know the long terms of that.

[DO06OM]

Here, the altered breathing experiences of this individual's PoTS are portrayed as being made accountable to specific bodily organs - the lungs and their inability 'to take in more air'. Due to this, the participant explains how they need to engage themselves within conscious work during their breathing processes, through their own actions of 'having to force' their lungs to work efficiently to ensure that they are 'getting enough oxygen' for their body. In this sense, the act of breathing - typically a salient, taken-for-granted and autonomous activity for individuals without breathlessness symptoms - is represented by the participant as a now conscious, adapted activity for them to undertake. They had 'gotten use to' this work overtime as a result of them compensating for these organ's (perceived) inability. Note also how, at times when the individual is unable to perform this conscious work - such as when they are asleep - they depict symptoms as arising in the body ('waking up with brain fog') from this lack of additional 'oxygen'.

The importance of oxygen was further used as a resource to validate people with PoTS' subjective accounts of altered breathing, during an interview with a participant who was wearing a smart-watch device during our discussion:

P: its quite strange (.) you get quite out of breath. I don't know if it comes over across the phone but I (.) I keep having to (.) keep a breath in?

R: oh okay

P: I am not quite getting (.) you know the oxygen. Now my oxygen right now is ninety-eight (.) the saturation levels are perfectly fine (.) yet I feel like I can't get a breath properly.

[MA07TA]

This participant above highlights the 'strange', subjective experience of her breath-related symptoms through a disparity, whereby her own feelings of 'not quite getting... the oxygen' in her body are not reflected through the (digital) mechanical objectivity (Daston, 1992) of the investigation of oxygen 'saturation levels'. Although the conclusions of her digital assessment results are 'perfectly fine', she is not left with an explanation for why she is 'out of breath'. As such, she describes the need to continue with performing her own conscious work - by 'keep[ing] a breath in' - during her respiratory processes, as a way for her to ensure that she is able to 'get a breath properly'. Understandings towards the experience of having an altered

breath is therefore made sense of by people with PoTS through the conscious, additional work they need to undertake when performing their inhalations and exhalations.

1.2. PoTS Breathing as an Altered, Habituated Bodily Movement

Through people with PoTS' described conscious engagements with their altered breathing patterns, these individuals noted how they would become consciously hyper-focused - 'very aware' - of the physiological sensations of their bodies when undertaking breath work:

what I found was if I start thinking about my breathing (.) I start thinking about it too much. I become very aware of my breathing

[AD06AN]

In the extract above, notice that the process by which the participant becomes 'very aware' of their breathing is presented as being uncontrollable in nature. Through even the just simple act of 'thinking about... breathing', these cognitions would quickly initiate them into becoming heavily fixated upon their own breathing sensations ('thinking about it too much'). The participant further elaborates on how this hyper-awareness would in turn facilitate her attenuation towards the physical movements of her body:

P: and as I was saying before about meditation (.) as soon as you start doing an exercise when you're told to breathe as you usually would and you start to feel your ribs moving (.) you actually stop breathing as you would because you feel your ribs moving

R: because you feel

(..)

R: too over-conscious? (.) in a sense?

P: yes exactly

[AD06AN]

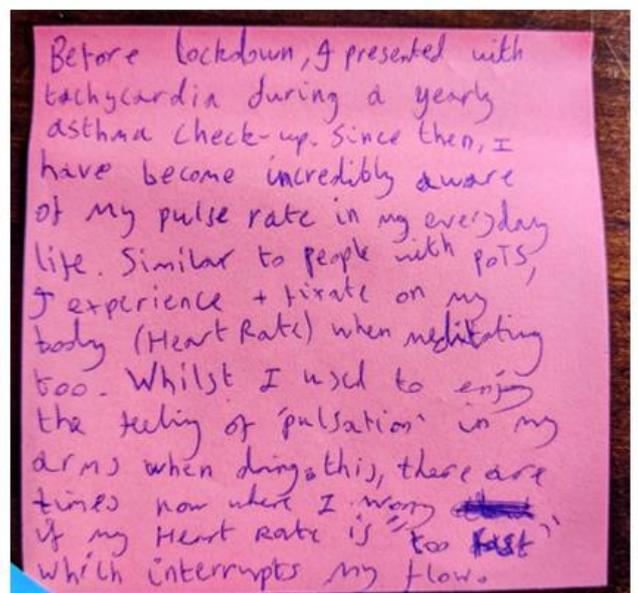


Fig. 3. Reflexive note [MJH] examining how, during my PhD studies, I have also found myself developing an increased-awareness towards one of my own bodily sensations (Heart Rate), following a time where I had presented with a fast heart rate during a routine Asthma Nurse check-up (February 2020). During the data collection and analysis phases of my research, I often found myself reflecting upon this experience and its parallels with the heightened bodily sensations which people with PoTS described experiencing. Similar to the participant's extract here, I also now find that the sensations from my body- specifically the sensation of hyper-focusing on my arm's pulse rate when slowly breathing out- to be an unavoidable, and at times overwhelming, experience when I meditate. Since my heart rate was made aware to me during my Asthma check-up, I have grown more aversive towards this sensation. Considering reflections such as this during analysis enabled me to carefully consider and break-down the ways in which people with PoTS can use their internal physiological sensations to appraise the effects of their breathing and similar interventions.

When asked to undertake her regular, routine day-to-day breathing - inhaling and exhaling as she 'usually would' - this participant described that she would become 'over-conscious' of the role and involvement of her upper chest, as a part of her habituated breathing cycle. Her heightened sensitivity to these physiological sensations during breathing (see Fig. 3), rendered by the participant as the 'feel' of her 'ribs moving', is depicted as an aversive experience - to the point where the participant would consciously try to momentarily 'stop breathing' to reduce hyper-arousal of these rib movements.

Many other participants depicted their sensations of bodily movements during their altered breathing experiences, as also originating from their chests:

I find that I breath through my top half a lot more than my bottom half.

[TH23PL]

The quote above highlights how participants would couple their increased feelings from movement of their upper chests - the 'top half' - alongside a lack of physiological sensations and involvement of their bellies - the 'bottom half' - during their regular breathing patterns. In this sense, many participants depicted their altered breathing experiences as producing a dysregulated, synonymous relationship between the work of the belly and chest areas of the abdomen during breathing:

So I've (.) I over breathe if that makes sense? my breathing pattern is not correct so its almost like a hyperventilation (.) so we get breathless and things. Like we breath (.) well personally I breath from my chest area and not my stomach

[EM08IP]

The individual above demonstrates this further by detailing how she would use the physical sensations of her body to draw her own meanings from, and to make sense of, her experiences of encountering common PoTS complaints. She does this by first addressing breathlessness - 'we get breathless' - as a shared symptom experience which exists across the PoTS patient group. Following this, she then utilises a pronoun shift - 'personally I breath' - to mark her own subjective meanings from breathlessness. This subjective experience, rendered through her sensations of the chest and belly areas as being over- and under-active respectively, is derived by the participant as a possible explanation put forward for why she 'over breathe[s]'. Thus, through the explanation that she breathes from her 'chest area and not [her] stomach', the participant is able to generate and present her own rationale to account for why her 'breathing pattern is not correct'.

Some participants expressed how they would recognise the movement of their chest during breathing as a problematic action of their body:

P: in my mind the way to make myself feel better is to breathe through the belly...
becoz I've had PoTS for years ave been figuring out (.) what's the best [way] to
breathe

(...)

P: do the breathing. And I know its definitely not the chest stuff. So that's my own
little alarm signal in my head when I'm not feeling it, "oh where's my chest going?
Why's it doing that?"

[CH03HU]

The awareness that they exhibited an over-involvement of chest movements during their routine breathing patterns - depicted here to act as their 'own little alarm signal' by one participant - was presented by people with PoTS to lead them to critically considering the impact of their condition on their breathing. Through these reflections and thoughts, some participants would express how they had tried to make attempts at 'figuring out' what bodily movements they should (and should not) be experiencing for the undertaking of a non-altered breath - 'I know its definitely not the chest stuff'. Some participants recognised the action of them trying to 'breathe through the belly' as having a medicinal-like action for their PoTS, whereby they intended to use this exercise as a way of making themselves 'feel better'.

Whilst breathing from the belly was depicted as a beneficial exercise by people with PoTS, this action was not seen by many to be an easy task for them to enact.

Coz I noticed that doing mindfulness they tell you to breathe in and (.) try to breathe the air into your belly and not in the top part of the chest and I don't do that. Usually. I mean I do if I focus on it. But I don't do that.

[SA09RH]

The extract above concerns a participant describing her attempts to undertake belly breathing as part of a mindfulness class she regularly attended. Notice how, in contrast to the action of her naturally breathing into the 'top part of the chest' as an effortless activity; the participant describes needing to consciously 'focus' upon her new task - to 'breathe the air into [the] belly' instead - in order for her to engage with and achieve this more demanding activity. In this respect, breathing through the 'bottom half' [TH23PL] of her abdomen is not presented by the participant to be part of her habituated, regular cycle breathing that she routinely performs in her daily life. She does not experience the engagement of belly movements alongside her in-taking of breath to be a normal aspect of her breathing patterns.

This understanding of people with PoTS needing to maintain mental and cognitive efforts to engage the lower abdomen when trying to breathe was supported by many other participants. One participant describes the difficulties she would encounter during the practice of yoga:

when I am at yoga (.) I get bits where my breathing goes weird and I have to consciously think about how I am going to keep breathing through my belly (.) or slow it down.

[CH03HU]

For this individual, the moments where she has to 'consciously think about' how she is able to 'keep breathing through [the] belly' are depicted as fluctuating in nature, and occur in response to her perceiving that her regular breathing pattern is experiencing a (deliberately induced) change- 'bits where my breathing goes weird' - that is resultant from performing elements of yoga. These findings therefore demonstrate how purposeful attempts to change the altered breathing patterns of people with PoTS can lead to further induction of a hyper-arousal state in these individuals, centred towards their physiological sensations of upper-chest involvement within their breath work.

1.3. Attempts by People with PoTS to "Correct" their Altered Breath

At times during interviews, people with PoTS expressed their desires for trying to manage, adapt and change their problematic altered breathing patterns they had become aware of:

err yeah it is helpful actually I never realised that I don't breathe correctly. And its so strange because I've obviously got to try and retrain myself (.) to breathe correctly.

[EM08IP]

The extract above echoes back to prior findings identified within the first theme (see subsection 1.1.), whereby the participant has the 'strange' experience a healthcare professional informing them that they 'don't breathe correctly'. Notice here though, how the participant then goes on to portray themselves as being held accountable, in that they perceive it was their responsibility for needing to address this clinical issue they have presented with ('I've obviously got to try'). Through the description that they need to 'retrain' their bodies 'to breathe correctly', the participant portrays their altered breathing as an adapted behaviour their body has learned to undertake following PoTS onset. This learnt routine, a dysregulated pattern, now needs to be un-learnt in order for a non-altered breathing pattern to be restored.

As one possible method to 'retrain' their dysfunctional patterns, some people with PoTS described how they would undertake breathing, respiratory and meditation practices in efforts

to address their issues. One participant, who shared her own experiences of regularly performing a breathing cycles intervention within her home to help with the management of her fatigue symptoms, discusses this:

You know with PoTS (.) doing the breathing cycles (.) it will get me into that correct breathing cycle (.) you know it should.

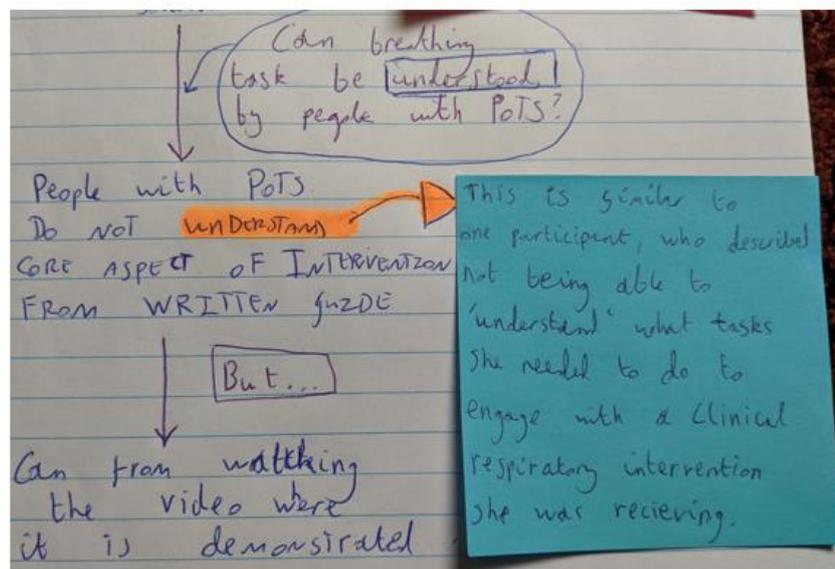
[MA07TA]

She explains that she continues to persist with her intervention, as she perceives the benefits of her breath-related practice to have this described action of re-training her body, through helping to restore it back to a 'correct breathing cycle'. Some people with PoTS will attempt and be motivated to try self-initiated practices of breathing-related practices, through their wishes to remedy and 'correct' their altered breathing.

In rare instances within interviews, a small number of participants also described receiving clinical intervention from a healthcare professional to assist with the management of their altered breath. One participant, who had recently received respiratory therapy for her PoTS, discussed how she had initially encountered difficulty with comprehending the tasks she needed to undertake for performing her practitioner's instructions:

in my first session when she was erm (.) err asking me to do things I couldn't do it. and I was like (mimicking) 'I don't understand what you are asking me to do'.
[EM08IP]

Fig. 4. Reflexive note [MJH] taken from a project notepad used for informal note-taking and reflections upon people with PoTS's Ocean Breath intervention feedback. The image demonstrates how I had tried to apply the experiences and barriers that people with PoTS would mention that they had encountered with trying other forms of breath-related interventions in their pasts, in order to try and make sense of why (and crucially – how) they were perceiving issues with comprehending the instructional steps of the Ocean Breath practice.



Within the extract above, the participant recounts how she had struggled during her initial treatment sessions to actualise the clinical respiratory intervention that was being provided to her. Notice here, how this is not a refusal to undertake the task itself, but rather an issue with its perceived comprehension. In that, she did not know how to perform the actual steps - how to enact, facilitate and actualise - the specifics of this respiratory intervention, because of the restricted movements she has her normal, everyday altered breath. Given her altered

breathing experiences, the participant 'couldn't do it', as she did not 'understand' what actions her body would need to perform for engaging with this method of treatment (see Fig. 4).

The participant also described how this situation had created disparity between herself and her mother, who had not previously experienced an altered breathing pattern. When observing her daughter's struggles to engage the belly within the respiratory intervention, this family member was unable to recognise the difficulties her daughter had encountered for performing what is a (seemingly easy) 'normal' activity for the mother to enact:

my mum was in the session with me and she was like (mimicking) 'I don't understand like how do you not understand how to do this? Its just normal' And the lady was saying (mimicking) 'she wont coz her breathing pattern has completely changed and she wont like be able to do it and she'll have to like train her body to do it again'. [EM08IP]

This short exchange highlights how the distinctive nature of disordered breathing can lead to the development of separate, conflictory and unique perceptions towards the experiences of breathing between PoTS sufferers and PoTS-naïve individuals. By first recalling their mother's use of the phrase 'its just normal', this is employed by the participant to highlight how their own personal, subjective experiences from possessing an altered, everyday pattern of breathing, remains invisible, undetectable and hidden from others around them. From the mother's own experiences of possessing a non-altered breath, she struggles to comprehend why the use of the lower diaphragmatic areas are not an unconscious and automatic action for her daughter to enact during breathing – as the mother argues that her own body requires little effort or conscious will in order for her to perform this task ('how do you not understand how to do this?'). The mother overestimates her daughter's ability to carry out the respiratory intervention, as she is unable to recognise that the patient's altered habit of breathing - which has 'completely changed' in the wake of PoTS onset - has not (re-)learned to involve this unconscious movement of the belly during breathing. Through recalling the intervening of the healthcare professional, the participant demonstrates how her mother's own understanding of 'normal' breathing needs to be mediated in the interaction, in order for her to start understanding how this differs from that of an altered 'normal' breathing experience. Because of this, the participant explains how she needs to continue working with the respiratory service, in order to correct her (mal)adaptive breathing patterns and to 'train her body to do it again', over time.

Another participant had also recalled how her healthcare practitioner had introduced her to a clinical intervention for her breathlessness symptoms. Within this example, the participant is forewarned that she would likely encounter orthostatic intolerance symptoms when trying to engage herself in the deep breathing activity:

she said that (.) (mimicking) 'if you keep doing it your body will get used to it and you should kind of get used to it as well (.) and that should hopefully stop the dizziness'

[CC10NE]

Within this instance, notice how the healthcare practitioner is depicted as trying to motivate the participant to persist with the technique, through reassuring her that their encountered symptom flare-ups during deep breathing would begin to dissipate over time. Within the extract, this dissipation is described as "your body will get used to it" by the healthcare practitioner. This highlights how the action of people with PoTS trying to 'retrain' [EM08IP] their bodies to learn a new, deep pattern of breathing - one which is distinct from that of their altered PoTS cycles by including movements of the belly - needs to become embedded once again within the unconscious, routine and automatic behaviour of the body.

2. Discussion

Thematic findings identified from interviews with people who have PoTS aimed to explore experiences of their (altered) breathing behaviours and breathlessness symptoms.

2.1. Summary of Altered Breathing Findings & Literature Considerations

Participants commonly reported that they had become aware of their altered breathing through the labelling of their breathing patterns as a non-correct, 'dysfunction' by their healthcare practitioners. As noted within chapter 8, dysfunctional breathing - known clinically as dyspnoea - is a common presentation in PoTS, that is estimated to affect up to one in three patients (Stewart & Pinnosi, 2021). My findings showed that people with PoTS depicted their struggles with dyspnoea through describing subtle deviations in their own personal experiences of encountering air hunger and breathlessness symptoms; crucially, these sensations were distinguished from that of a shared symptom experience amongst the wider patient group. This notion, whereby people with PoTS claimed to have developed their own unique perceptions and internal sensations towards their altered breathing and breathlessness experiences, is akin to phenomenological work on the study of breath as a social phenomenon (Williams & Carel, 2018). In this respect, despite the existence of common breath shortness, air hunger and shallow inhalations issues across the patient group, subjective realities are presented by patients, to mark perceived differences between the altered breathing patterns of each individual sufferer (Williams & Carel, 2018).

People with PoTS were found to explain how they had made sense of their own regular, altered breathing patterns through detailing of the **conscious**, routine 'work' they would need to undertake when breathing. One such example of this was the participant's who described the work of trying to hold their breath when breathing, through their perceptions of their body struggling to retain air. Links to these findings can be drawn from a qualitative study by Tieck, Mackenzie and Lovell (2019), who examined perceptions of refractory breathlessness within six patients recruited from a UK specialist clinic. Through thematic analysis, their participants were also found to present their breathlessness experiences by portraying the act of inhaling to be a highly conscious process for them to undertake. Similar to the disclosures by people with PoTS, these refractory breathing patients stated that they also experienced increased awareness and cognitive engagements during respiration; as explained through their perceptions that their bodies did not 'breathe deep enough'. These commonalities in my findings with those of Tieck et al. (2019), whereby participants' altered breathing experiences are understood through the additional, conscious tasks which patients need to perform within their routine everyday breaths, is further supported by Kauppi, Axelsson, Herlitz, Jiménez-Herrera and Palmér (2022). Their phenomenological findings of 14 participants highlighted how these breathlessness patients would try to 'handle' their air hunger symptoms through their deliberate conscious actions - such as purposefully trying to breathe more deeply - within their day-to-day breaths. In respect to these comparisons with the works of Tieck et al. (2019) and Kauppi et al. (2022), the current findings indicate that people with PoTS depict their increased awareness of undertaking conscious work during breathing as forms of self-initiated strategies that they utilise for managing their altered breathing experiences.

Participants were also found to describe how they had developed a hyper-awareness towards the physiological movements of their bodies when undertaking their everyday breaths. Specifically, people with PoTS reported that they had become averse towards the excessive movements of their upper chests - and wary of a lack of their belly-area movement - within their regular, habituated breathing cycles. This depicted dominance of chest-focused movements during breathing by people with PoTS is a commonly observed feature of a dysfunctional breathing pattern (Barker & Everard, 2015). Due to this described dysfunctional pattern, patients with diagnoses of other breathlessness conditions such as COPD (Cahalin, Braga, Matsuo & Hernandez, 2002) and asthma (Leonés-Macías et al., 2018) have been found to present with reduced diaphragmatic muscle movements during their routine breathing behaviours. This is an important consideration to note, given that evidence arising from empirical studies have highlighted numerous positive health outcomes to be associated with interventions serving to increase diaphragmatic breathing within these conditions, such as quality of life (Prem, Sahoo & Adhikari, 2013) and exercise capacity (Yang et al., 2022).

Whilst further works are sorely needed to further comprehend the effects of diaphragmatic breathing in a PoTS patient group, it is worth highlighting that the physiotherapy intervention for PoTS developed by Reilly et al. (2020) has a similar explanatory mechanism, whereby PoTS patients are taught to reduce their excessive upper-abdomen movements. Within the current study, some people with PoTS expressed that they had recognised that their breathing patterns needed to be 'corrected', with some trying to make conscious efforts to increase the engagement of their lower abdomen areas when undertaking their breathing activities. Whilst findings in the current study have begun to explore participants' experiences of receiving interventions for their breathlessness, additional qualitative works are needed to fully explore how people with PoTS make sense of these 're-training' processes and the embedding of a new, corrected breathing cycle into their routine inhalations and exhalations.

2.2. Implications for Ocean Breath Intervention Development

Through undertaking of this analysis, I aimed to identify possible factors which would influence the likelihood of the Ocean Breath achieving successful future intervention implementation within the patient group. Within the current chapter, my findings identified people with PoTS to have subtle, yet noteworthy, differences in the perceptions of their own altered breaths and breathing capabilities from one another. Given this, my current findings indicated a need for my team to gather feedback upon the ways in which we could make elements of the Ocean Breath to be 'customisable' and adaptable in nature for people with PoTS during its development. This was an important factor to consider, in order to ensure the intervention could be designed in nature to be able to account for these perceived differences and variations in the abilities of PoTS patient-to-patient (*see chapter 10 for further details of these considerations during our development work*).

The current findings also enabled me to understand why people with PoTS were perceiving issues with the preparation stage of the Ocean Breath within my early stage [i] interviews. Within the initial version of the Ocean Breath practice written instructions, a preparation exercise had been originally included. This activity involved people with PoTS undertaking an activity where they would need to breathe through their upper and lower abdomens regions separately, before they would go on to perform a form of Ujjayi breath. This preparation exercise was implemented into the Ocean Breath during my earlier Masters-level project (Hogg, Collard & Deary, 2017), following a yoga instructor's suggestions that this activity would help intervention users to become more familiar and aware of how their bodies naturally move in response to their breathing. Nevertheless, the findings of this analysis indicated that this preparation step would likely prove to be an unfeasible practice for some members in the

PoTS patient group to perform - due to them already experiencing an aversive, hyper-awareness of their rib movements during breathing. As such, these findings enabled our team to make sense of early collated feedback from people with PoTS, where participants had stated that the intervention would likely need to be adapted to remove the chest exercise within this activity, in addition to their recommendations for changing its preparation step from a mandatory to an optional activity.

2.3. *Conclusion*

The current chapter highlighted that people with PoTS distinguished their altered breathing patterns from others through describing a greater, conscious awareness of bodies during the respiratory process. Furthermore, people with PoTS expressed how they had found the heightened sensations of their chest movements to be an aversive experience during breathing, which needed to be 'corrected' through conscious efforts to engage their belly-areas within the routine breath. Within the next chapter of the thesis, I present the final thesis findings of the intervention development process I undertook for the Ocean Breathing practiced, as synthesised through the feedback obtained from interviews with three key stakeholder groups: people with PoTS; healthcare professionals; pranayama yoga professionals.

The penultimate chapter of the thesis features the iterative, multi-phase intervention development process I undertook for designing and tailoring an Ocean Breathing practice for the needs of people with PoTS. Feedback on the intervention obtained by people with PoTS indicated that they struggled to understand the 'overly-complex' nature of the Ocean Breath. These individuals also expressed their need to reconfigure the intervention, in order to enact the central element(s) of the Ocean Breath which underpin its intended therapeutic effects on PoTS symptoms. Feedback obtained from the healthcare professional group supported suggestions by people with PoTS for implementing an online format of intervention delivery into the Ocean Breath, which should feature a PoTS patient as a deliverer of the technique. Healthcare professionals however perceived differing effects of the Ocean Breathing intervention arising within the PoTS group. Further feedback from a third stakeholder group, consisting of three pranayama yoga practitioners, indicated that different (perceived) effects of the Ocean Breath may arise due to participants' differences in the rates and ratios of their breath during its performance. Member checking activities with people who have PoTS supported the possibility of improving future implementation of the Ocean Breath by adapting its format to a 'toolkit-like' strategy. Further mechanistic work is however first needed to clarify the range of potential, breath-related interventions that could be employed, and their demonstrable actions within, a PoTS patient group.

1. Development of the Ocean Breathing Intervention

The involvement of core stakeholders for obtaining feedback on an intended intervention is an important step within the development process. These steps are undertaken in efforts to identify foreseen issues which may hinder the likelihood of the intervention being successfully implemented within the intended patient group in future (Skivington et al., 2021).

In efforts to develop an Ocean Breathing practice for PoTS, qualitative feedback from three key stakeholder groups– [i] people with PoTS (n = 15), [ii] PoTS-experienced professionals and healthcare practitioners (n = 7) & [iii] pranayama yoga practitioners (n = 3)- was collated and synthesised. Findings were analysed through Reflexive Thematic Analysis (Braun & Clarke, 2019), which was theoretically informed by Normalisation Process Theory (May & Finch, 2009).

1.1. Stage [i]- Intervention Feedback from People with PoTS

Thematic findings highlighted a range of perceptions towards the Ocean Breathing (Ujjayi) practice by the people with PoTS (see Table 1). Centrally, core feedback captured from people with PoTS where related to both the perceived complexity of performing the Ocean Breath, and the importance of carefully framing the core aspects of the intervention through its possible delivery formats.

Table 1. Ocean Breath intervention feedback obtained by People with PoTS in light of NPT constructs. N = 15.

NPT Construct	Stage [i] - Feedback & Perceptions of Intervention
<p>Coherence: <i>Can patients comprehend and make sense of the breathing practice (& its mechanism of action)</i></p>	<ul style="list-style-type: none"> ▪ The Ocean Breath is differentiated from other similar interventions due to its perceived complexity. ▪ Most participants were able to understand the autonomic explanatory ontology of the intervention – but struggle to understand how the actual instructional steps of enacting the breathing practice translate into practical, real-world symptomatic improvements.
<p>Cognitive Participation: <i>Would patients be willing to engage with the instructional steps of the technique, and if so, what factors would determine their persistence with this?</i></p>	<ul style="list-style-type: none"> ▪ Participants perceive benefits of a general breathing intervention to their PoTS – however, mixed views on the application of the Ocean Breath technique specifically. ▪ Posture change during exercise seen to be a barrier – possible trigger of orthostatic symptom flare-up prompts unwillingness to attempt the intervention. ▪ Intervention not always seen to be appropriate to varying levels of functioning across PoTS patient group – participants may need to “organise” themselves each day depending on level of their debilitation.
<p>Collective Action: <i>Are patients able to perform the various steps of the intervention, and if so, what support is required for enacting this?</i></p>	<ul style="list-style-type: none"> ▪ Video demonstrator seen to deliver the intervention in a clear manner; most people with PoTS would prefer someone with PoTS to be involved in performing the technique however to demonstrate it is feasible for the clinical group. ▪ Preference for an online-based, video format as a primary format of intervention delivery to ensure treatment is accessible to bed-ridden PoTS patients. ▪ Social Media Support Groups to allow patients to interact and share their experiences of the intervention will likely promote continued intervention compliance.
<p>Reflexive Monitoring: <i>How do people appraise the application of the breathing intervention for the treatment of their PoTS symptoms?</i></p>	<ul style="list-style-type: none"> ▪ Participants discuss their desire to adapt the source of their breathing during the practice to mouth or nostrils only – mixed feedback; Patients want to simplify the instructions needed for the core “HAAAAH” aspect of ujjayi. ▪ From their own experiences with dysfunctional breathing, participants see benefit of belly breathing exercise within the preparation stage – chest breathing may induce dizziness. ▪ Participants have specific needs/outcomes (e.g. pain management; anxiety reduction around syncope episodes; sleep; energy reclaiming etc.) they want the intervention to achieve; some argue the need for a toolkit approach.

- *'Complexity of the Intervention is a Barrier to Understanding the Patient's Work'*

From discussions surrounding their prior experiences of meditation and yoga practices, participants were found to hold pre-conceptions towards the shape and format of which the Ocean Breathing intervention should conform towards. These pre-conceptions were guided, in part, by the importance of the patients' ability to both quickly comprehend and 'make sense' of the work which the meditation exercise requires of them. One participant had developed a 'heuristic'-like strategy to their current practice:

P: yeah this is it! square breathing (.) you breathe in for three you hold for three you breathe out for three-

R: (overlap) ah!

P: you hold for three (.) which is why it's a box

[ME09MA]

The basic naming and description of the activity alone – 'square breathing ... box' - had enabled her to quickly memorise and break down the technique into a series of simple, accomplishable tasks for them to perform. The contrast of the ocean breath against other breathing-related exercises was used by people to highlight their concerns that the nature of the intervention is overly-complex. They were unable to 'decipher' the actions the practice requires of them to perform in order to achieve engagement:

I just think some people might find it ... moved on a wee bit too quick to follow. Ya know a second ago I was breathing (.) it was coming out of my mouth but then I go to just breathing in and out without opening my mouth?

[DO06OM]

Many participants struggled to see the underlying logic behind instructions within the breathing guide, where they felt the changes to the ways they took breaths in during the practice occurred 'too quick to follow'. As such, the rationale behind altering the source of their inhaling and exhaling actions during the flow of the Ocean Breathing was questioned.

The instructed actions of Ocean Breathing were seen as unnecessary bodily changes by people with PoTS to enact. In some cases, this was viewed as an overly demanding physical task for someone with the condition to accomplish. Participants further explained their concerns towards the various steps and flow of their bodily actions presented within the technique:

especially if you're doing it to try and make [yourself] feel better you're trying to (.) you know its (mimicking) "in through the nose out through the mouth hold it for this

long breathe out for this long” (.) and if you’re doing it to try and make yourself feel better you’re already probably a bit stressed and anxious

[PR03EL]

Such questioning of the intervention’s methods led to perceptions from participants that others with PoTS could develop feelings of being ‘stressed and anxious’ if they were to attempt the practice. This concern that the intervention could have an emotionally detrimental impact on people with PoTS prevented participants from being able to understand how the specified actions of the practice could be translated into beneficial, therapeutic impacts upon their PoTS symptoms:

R: So the actual mechanism of sort of (.) getting people to sort of use the mouth and then the nose?

P: yeah I could (.) I couldn’t (.) ah I like to understand the benefit of the things I’m doing and I couldn’t see what that would be doing to be helpful

R: yeah

P: why not just deeply breathe?

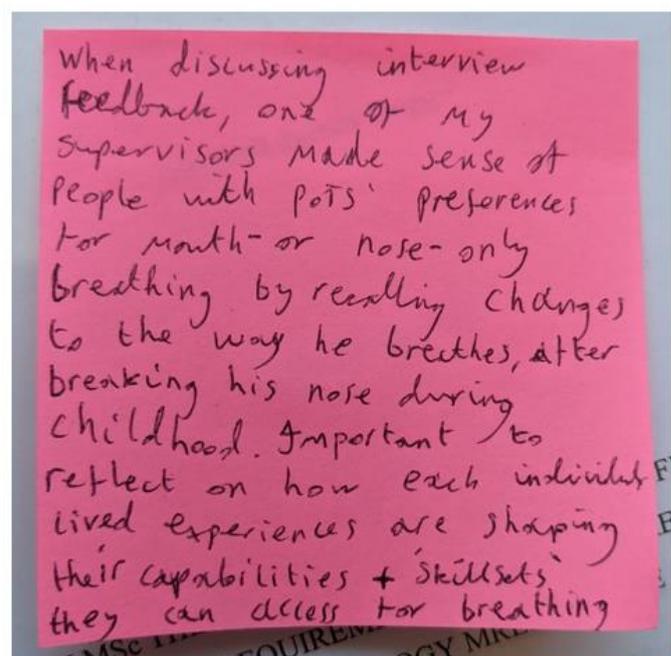
[ME09MA]

This participant notes that – due to this need to (unnecessarily) shift from the ‘use the mouth and then the nose’ - she is unable to ‘understand the benefit’ of the Ocean Breathing intervention, nor how performing its actions would be ‘helpful’ for alleviating her persistent physical symptoms. She then questions the logic of this intervention and tries to simplify the intervention down to only one, core step – ‘why not just deeply breathe’ – which she does perceive to have a practical, therapeutic effect on her PoTS symptoms.

With PoTS my nose is always blocked. So I do try the breathing exercises but there are times where I struggle to breath properly as well.

[D0060M]

Fig. 1. Reflexive note generated [MJH] when reflecting on team supervision discussions concerning the interview findings. This note demonstrates how my supervisors and I would make try to make sense of people with PoTS’s preferences for mouth or nose breathing, through our own personal experiences of breathing. Conversations such as this convinced our team of the importance of taking these discussions forward to the healthcare practitioner and yoga professional groups for their thoughts on how to adapt the intervention towards people’s unique breathing capabilities and skillsets.



Differing preferences for either maintaining the performance of the breathing exercises through either **solely** the mouth or nostrils - throughout the entirety of the practices - were expressed amongst participants as solutions to these possible barriers (see *Fig 1*). These decisions were justified by patients as a practical action they would need to take in order to enhance the workability of the technique for their own needs. For one participant, she expanded on this and rationalised her choice between these two sources:

once you've got your mouth open I just think (mimicking) 'argh it just requires so much more energy' um but with the mouth closed I think (mimicking) 'that's just easier' um so yeah. I liked that.

[EM08IP]

For this individual, inhaling with the mouth closed was rendered as a more energy consuming and demanding process for someone with PoTS to perform. Tailoring in such a way would mitigate the challenges she felt her experiences with fatigue symptoms would impose upon her ability to tolerate the intervention. Patients therefore began to consider the ways in which they themselves could reconfigure aspects of the Ocean Breathing intervention, in order to ease the burden(s) which the practice placed upon them.

Everyone with PoTS (.) everyone who I have spoken to are affected slightly differently from it. So for some people the breathing bits might be absolutely fine for them (.) for another it might just trigger them right off into a flare. So you know its just (.) I think everyone just has to be mindful you know (.) this is what you've been told to do but its about them making it adaptable (.) for themselves.

[CA09PL]

The motivations behind participants' desires to change were focused on generating their own set of manageable, workable tasks for partaking within the intervention. These adaptations – which participants rationalised through the differences in the PoTS symptom presentations and functional abilities across the patient group ('everyone with PoTS... are affected slightly differently from it') - aimed to establish a more realistic initial point of entry to the technique. Through the action of making the Ocean Breathing intervention to be 'adaptable... for themselves', the individual with PoTS could start to effectively engage with the breathing practice.

Some participants also put forward one additional barrier which saw to hinder people with PoTS from being willing to attempt the Ocean Breath:

Can I just mention just as well (.) the video? One of the first things she said (.) which sort of rung alarm bells for me was the first thing she said (.) which was that it creates heat in the body. I was thinking “OOOOH. I don’t want any extra heat in my body”

[AD06AN]

These participants associated the Ocean Breathing practice as having an up-regulation effect on their bodies, in that the performance of this intervention would lead to PoTS flare-ups occurring from the raising of core body temperature.

The fact that she was breathing from her neck (.) or breathing from her throat I mean you know (.) and that she’s explaining that it heats up the body. I think that’s really interesting (.) I find that fascinating

[DO06OM]

Nevertheless, for another individual with PoTS, the possibility of the Ocean Breath to have a bodily heating effect actually acted as an intervention facilitator which made him want to engage with the intervention.

- *‘Delivery Method Establishes Perceptions of Coherence for Core Intervention Aspects’*

In addition to participants’ suggestions of altering the shifting of mouth to nostril breathing within the practice, they also disclosed that they had encountered difficulty with comprehending the written instructions which had been provided to explain the core element of the ocean breath.

I thought it was a nice idea I just couldn’t quite (.) without trying it it seemed a bit complicated. And then it said um (.) (whisper) where was it (quoting guide) “constrain the slight of your throat on your inhalations”. I didn’t know how I would do that

[ME09MA]

In particular, participants were unable to make sense of the actions they would need to physically undertake in order to create the central ‘haaaah’, *wave-like* sound of the Ocean Breath technique. This inability to effectively visualise the required actions – through people with PoTS perceiving themselves as being unable to effectively embody its required actions - was blamed upon the incomprehensibility of the language used within specific steps of the written instructional guide.

P: the other thing in [step] two (.) it says (reading guide) “either imagine your breath is fogging up a window (.) or blowing out the candles on a cake”. Well I sort of put my mouth in both positions (.) and they weren’t the same.

R: right (.) there was a mismatch?

P: I wouldn’t say those were comparable (.) unless I was blowing candles out strangely.

[AD06AN]

Whilst changes were made to improve the clarity of the written instruction for performing this core Ocean Breath element of the practice after the initial five interviews of stage [i], further feedback from participants indicated that this step was still unclear to them.

Further emphasis was placed upon the inadequacy of these written instructional steps by participants, through the direct comparison of the guide document with the alternate video delivery format.

I think the video was fine. It is very clear on what to do erm you know it was (.) you know I am visual I love something that I can watch and follow along to. When I read the [written] document I was kinda like (mimicking) “okay (.) I think I’ve kinda got my head around it?” But just having the video alongside it makes it SO much clearer. In terms of what the breathing was [participant mimicks the ujjayi sound] HAAAAAH (.) what it was going to look like... it just made it much more clear in my head about what it was going to look like.

[CA09PL]

The video-based approach of introducing people to the ocean breathing technique provided participants with a greater sense that these particular requirements of the intervention would be feasible for someone with PoTS to undertake. By observing how the wave sound is produced by the presenter in the video, a sense of competence with the intervention arose from participants being able to break down and see how the tangible actions associated with this exercise could be accomplished.

Participants also often suggested that the written instructional should be revised to incorporate a diagram-based strategy, which more clearly demonstrates the technique. The possible addition of images into the instructional guide document was viewed to serve as a more effective method of demystifying the ambiguities arising from the issues caused by the phrasing issues of the instructional guide steps.

I think you could have it together (.) becoz you just take stills from that don’t you and just put it into the: (.) paper guide so it all matches

[PR03EL]

This image-based solution was seen to be a better way of enabling participants to understand how to re-enact the core element of the ocean breath. Some patients - who favoured a blended approach consisting of both written and video methods for intervention delivery - also referred to the use of imagery as a means of merging the two formats into one, singular approach to produce a more coherent and 'holistic' package to the intervention.

A number of other advantages were put forward by interviewees to support the use of a video format for delivering the intervention to people with PoTS. A crucial benefit seen by the participants to the use of a video format was that it would allow for participants to be able to enrol themselves onto the breathing regime through the internet. The possibility of an online delivery was perceived by participants as an effective method of bolstering the accessibility of the intervention - as patients with a range of different functioning levels of PoTS would be able to access and try the intervention.

P: (overlap) yeah I think (.) well for me and other people more so I imagine thinking
(.) travelling to the thing and back

R: yeah

P: that would be a whole week's energy you know it would be a real big commitment
(inhale)

[ME09MA]

Participants' had concerns that the travel requirements associated with in-person training may provoke fatigue symptoms in patients. The need to attend a face-to-face training session would also make the intervention inaccessible to patients who are home-bound by their PoTS. Whilst participants in the PoTS group unanimously agreed that they saw the implementation of an online delivery format as advantageous to the Ocean Breathing intervention, they presented with mixed views on the presenter in the video.

yeah coz theres nothing worse (.) theres nothing worse than seeing someone sitting
up and thinking (mimicking) 'is this for PoTS?' (laughter) why is the person not lying
down?

[ME09MA]

Several participants expanded upon this by commenting on how they felt that the presentation of a high-functioning, healthy female in the video in particular would serve as a barrier to the enrolment for patients into the intervention - particularly for individuals who are highly debilitated by their PoTS. Due to these challenges posed by the speaker, this generated an

issue of perceived trust in the Ocean Breath - whereby these people with PoTS were unable to interpret the appropriateness of the intervention for their condition.

This issue trust was also linked by many other participants to the adoption of an upright posture by the presenter during the video demonstration. This led to anxieties being expressed from participants that the intervention may appear unfeasible for the majority of PoTS patients, who would be unable to complete the exercise due to the triggering of their orthostatic symptoms. Participants therefore felt that they were unable to buy into the intervention, as they were unable to perceive how the technique had been identified as suitable for use with their PoTS:

P: I think it would be easier at least for me if I was doing it all in the same position (.) without changing the position

R: okay so just keep it all lying down?

P: yeah (.) or lying down or sitting. You could give people the choice because people will be at different fitness levels... like today it's a really bad day so I might want to do it laying down (.) whilst if it's a good day then I'm still doing it but I am sitting.

[SA09RH]

Whilst feedback from people with PoTS indicated for the posture change to be removed from the intervention, many expressed that wanted to see the implementation of different intervention formats, whereby they could perform the intervention 'lying down or sitting', in order to accommodate daily changes fluctuations in their functional ability.

As an additional method of tackling the foreseen issue of a lack of patient buy-in with the Ocean Breath, participants mentioned that the presenter of the video could be altered to make the appropriateness of the intervention more apparent for PoTS. Many participants were keen to suggest that the speaker could be an individual who is also living with the condition:

you know you don't get to see like videos about (.) or things about a lot. So I just think if there was a video with somebody talking about things about PoTS or even somebody with PoTS on there you know (.) its gunna get other people with the same condition interested I would think

[EM08IP]

When discussing the possible use of a fellow person with PoTS within the delivery of the intervention, participants felt that this opportunity would help the video to convey more realistic expectations of performing the practice to others – as the speakers could disclose her

experiences with trying the techniques with her PoTS, and the ways in which she had adapted the practice to overcome issues from when she was first learning the technique. Overall, altering the video demonstrator in this manner was seen as an effective method of combating the trust issues identified, as it allowed patients to more readily understand how the technique specifically relates to their own experiences of the condition:

1.2. Stage [ii]- Intervention Feedback from PoTS-experienced professionals & healthcare professionals

Additional feedback was obtained following a series of interview with seven PoTS-experienced professionals and healthcare professionals (see Table 2). Findings from this stage of intervention development focused on the scrutiny of the Ocean Breath feedback obtained from people with PoTS, in addition to the exploration of professionals' differing understandings towards the (perceived) effects of the intervention within the target patient group.

Table 2. Ocean Breath intervention feedback obtained by the PoTS-experienced professionals and healthcare professionals stakeholder group in light of NPT constructs. N = 7.

NPT Construct	Stage [ii] - Feedback & Perceptions of Intervention
<p>Coherence: <i>Can practitioners comprehend and make sense of the breathing practice (& its mechanism of action)</i></p>	<ul style="list-style-type: none"> ▪ Practitioners agreed that they saw benefits to general breathing practices for the PoTS patient group. Some participants had gained this confidence through their own clinical experiences; whilst others had gained knowledge of the benefits of breathing from well-known experts (e.g. Wim Hoff; Buteyko Leaders) or other clinicians they had worked alongside. ▪ Practitioners however were found to hold different and distinct ontologies and beliefs towards the intended actions of the Ocean Breath for PoTS. ▪ Some practitioners saw the technique as upregulating, whilst others saw the technique as producing a purely down-regulating action in patients.
<p>Cognitive Participation: <i>Would practitioners be willing for PoTS patients to engage with the instructional steps of the technique, and if so what factors would determine their persistence with this?</i></p>	<ul style="list-style-type: none"> ▪ Mixed views from practitioners (majority favourable) that intervention is safe for patient group to perform and attempt. ▪ Some practitioners emphasised the need for an interactional element alongside the intervention, whereby participants could get further feedback from practitioner(s) or share their experiences with other patients/ make sense of their bodies through breathwork. ▪ Two participants were concerned over the religious affiliations which could be made from this yoga-based technique; they felt that a practitioner would need to discuss this with a patient and make them aware of the 'science' underpinning the technique. ▪ Some practitioners explained how they saw the Ocean Breath as a form of resting activity itself. Some expressed that they could see patients implementing this technique alongside their regular care.

Collective Action:

Do practitioners see PoTS Patients of being able to perform the various steps of the intervention, and if so, what support do they see as being required to facilitate this?

- Practitioners saw the patient group as being able to perform breathing exercises with their suggestions of an online delivery – some linked this to their personal use of Zoom/Teams to treat patients during the 2020 UK lockdown.
- Practitioners unanimously agreed that written instructions should be complemented with diagrams – however, group was unsure of the best way to represent this (some suggested photography, cartoons)-there was confusion over how to show movement of the breath through imagery.
- Two practitioners stated that the intervention needs to be broken-down more and simplified. Both focussed on the need to focus on ‘just breathing... getting [them] use to breathing diaphragmatically’ as an initial stepping point, which they would build upon with the patient.

Reflexive Monitoring:

How do practitioners appraise the application of the breathing intervention for the treatment of PoTS symptoms of patient group?

- Majority of practitioners understood the intervention explanatory model of its autonomic/vagal nerve actions; but participants were less optimistic that intervention would be capable of leading to significant changes in physical outcome measures to reflect this.
- Issues above was however related back to the difficulty of controlling for extraneous factors known to exacerbate PoTS in research.
- Participants saw benefit to collecting qualitative data from people with PoTS during a possible follow-up feasibility trial of the intervention to explore participants’ relations to this.
- Some practitioners saw benefit to the intervention as helping the patient group through reducing general stress that may be experienced with living with PoTS, quality of life, assisting with the managing their fatigue levels and improving their functioning abilities.

- *Practitioner Scrutiny of Stage [i] Intervention Feedback*

Practitioners were universally supportive of suggestions by people with PoTS to favour the implementation of an online format for teaching the Ocean Breath to the patient group:

P: Anything can be done virtually (.) that’s what I’m learning from lockdown. In the ideal world to have erm in person or an in-person class would be the best option (.) BUT in terms of making it accessible to [someone with PoTS] online (.) a video would be great. Alongside as much instructions as possible. So you’ve got pictures (.) you’ve got videos (.) you’ve got tools

R: So it needs to be multi-modal in a sense?

P: Yeah I think so

[Pilates_#1]

Many professionals cited how their confidence in the use of internet-based resources – as the primary choice for intervention delivery - had stemmed from their own personal experiences of delivering PoTS treatments during the UK Lockdown, via Zoom or Microsoft Teams. Nevertheless, practitioners still saw a benefit to the Ocean Breath adopting a ‘multi-modal

approach', whereby online videos demonstrating the technique would be supported alongside written instructions and diagram-based tools.

Further feedback on online delivery from the practitioners centred on the video intervention deliverer. Although most practitioners found the online video to be clear and engaging for people with PoTS to be introduced to the Ocean Breath, some changes were requested concerning the pace and clarity of the video deliverer – 'just slowing down her speed of talking' [Advanced Syncope Nurse] - to make the intervention more manageable with patients' common complaints of brain fog. In addition to this, stage [i] recommendation of having a person with PoTS appear as an intervention deliverer within the online materials were also supported by the professional and practitioner group. Some practitioners argued for the need to include both a person with PoTS and a medical professional in the video, as the latter was seen to present a greater confidence to the intervention as having a medicinal and therapeutic actions for PoTS symptoms. They suggested this could be implemented through having a 'teacher and learner style' format within the online video, whereby the people with PoTS can rely on the professional expertise of the practitioner to give credibility to the intervention's use in their patient group. In addition to this, they also described how the act of patients seeing someone with PoTS be the 'learner' would allow them to perceive the Ocean Breath practice as achievable for themselves:

I understood where these people were coming from (.) that when they can't breathe it is scary because a lot of people don't understand that in fitness land (.) they don't understand what that breathlessness feels like. But because I did [from my experiences of a respiratory condition] (.) I think they could relate to it and I think that does help people when they've got a condition. it may be that if [the Ocean Breath] is delivered by somebody with pots or (.) you know that [if the video deliver does] recognise that they know where they're coming from then it's much more relatable.

[Pilates_#2]

Ultimately, practitioners stressed the importance of having an individual in the video that people with PoTS would find 'relatable' as a video deliverer. Whether that was 'somebody with pots' or a healthcare practitioner who could 'recognise that they know where they're coming from', the development of trust from the patient group in the intervention was seen by practitioners as being built up through these key individuals demonstrating that they are knowledgeable of PoTS experiences and that they 'understand what... breathlessness feels like'.

Practitioners also gave feedback on the different ways in which people with PoTS would express for adapting and individualising the intervention for their specific PoTS needs, such as performing the practice through mouth, or nostrils, only breathing:

So people who start off with just diaphragmatic breathing. Doesn't matter which way (.) in through your nose (.) out through your mouth if you can. Building up that pathway. How does that feel? Just do five breaths and have a rest because its hard work.

[Physiotherapist]

Whilst one practitioner was in favour of having people with PoTS perform the Ocean Breath through the nose only, others downplayed the importance of the dictating the sources of breathing within the intervention. Criticisms of the Ocean Breath intervention were raised by practitioners however regarding its complexity, as an explanation for why people with PoTS were stating their need to reconfigure its instructional steps. A physiotherapist in particular argued that the intervention may be seen to be 'hard work' for people with PoTS to perform, and that it should be simplified to 'just do(ing) five breaths' as a way of making it more accessible.

In a similar manner, professionals often questioned the rationale and utility behind the specific requirements of the Ocean Breathing intervention for its intended user group:

Whether just one technique is the way to go I don't know. One technique to cover everything (.) that's quite challenging... because there's so many bits to breathing (.) you know? It's like do you do it through the mouth (.) through the nose? Do you do a longer exhalation than an inhalation? You know (.) I think in your [instructional guide] it talks about having an even breath (.) you know having an inhalation the same length as an exhalation. Should it be?

[Pilates_#1]

Here a Pilates instructor break-down a series of complicated decisions and aspects underpinning the Ocean Breath – through its possible performance 'through the mouth', 'through the nose', and its timing of 'inhalation' and 'exhalation' in relation to one another. She does this to demonstrate the sheer complexity that needed to be considered within the development of breathing intervention for PoTS. As such, practitioners queried the choice of 'just one technique' of breathing as the basis for the developed PoTS intervention.

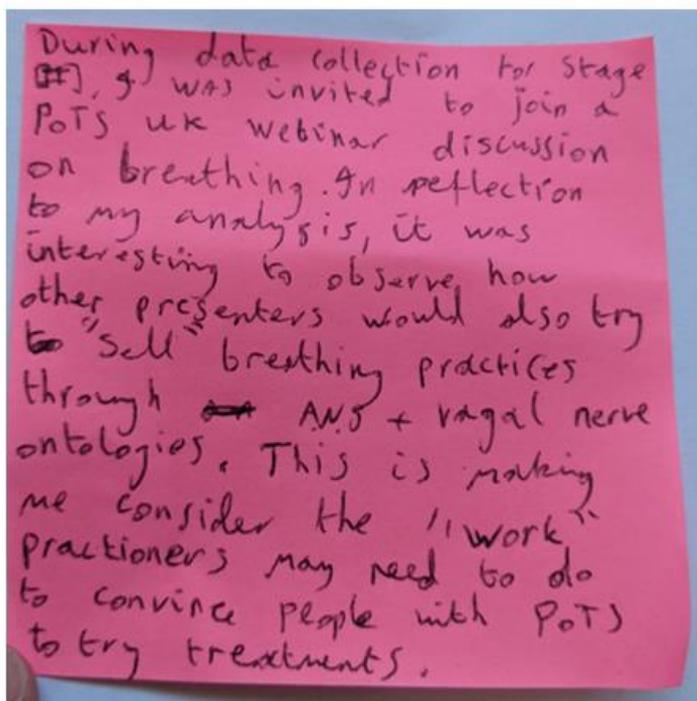
you know I see it like a toolkit? I don't see it as just one activity (.) this one tool is going to make all of the difference. I personally don't think it will erm but I guess you don't know if that's the active ingredient that's going to help facilitate all of the changes.

[Occupational Therapist]

Following these considerations, recommendations were put forward by two practitioners that the format of the Ocean Breathing intervention needed to be adapted into a 'toolkit'-like strategy, which encompassed a range of different types of breathing techniques. During the member checking activities, I explored the possibility of incorporating a toolkit-format into the Ocean Breath, through examining the perceptions of people with PoTS for a range of alternative breathing techniques (see sub-section 1.4).

- *Clinicians Perceive the Ocean Breath Producing Both Up-Regulatory and Down-Regulatory Effects in People with PoTS*

Within stage [i], unclear feedback from people in the PoTS group perceived a possible heating effect being produced in the body from the Ocean Breath, as both a barrier and facilitator for this intervention being implemented within the patient group. To further clarify the interactions of the intervention within the patient group, feedback was sought after from the PoTS-experienced professionals and healthcare professional group from what actions they expected to arise from the Ocean Breath upon PoTS symptoms.



I think the whole trying to influence the autonomic nervous system (.) I think there is something in that.

[Pilates_#1]

Fig. 2. Reflexive note [MJH] generated from my experiences of engaging with a PoTS UK webinar on breathing. During this discussion, I noticed how the use of breathing strategies in PoTS was sold by presenters as a 'sales pitch'. Similar to the Ocean Breath, they would at times also draw upon the concepts of the autonomic nervous systems and vagal nerves to try to convince people with PoTS to try breath-related and meditation interventions. These considerations made me critically consider the frameworks which other types of PoTS healthcare professionals use to try to convince their patients to engage with their employed treatment strategies, as I was undertaking further interview work & analysis.

Following my fieldwork reflections during the time of data collection (see Fig. 2), during interviews with these individuals I purposely initiated discussions around the intended autonomic explanatory model behind the devised intervention. Healthcare practitioners however frequently drew upon their own, diverse sets of other medical, psychological and social frameworks during discussions surrounding the Ocean Breath. These models were

utilised by practitioners as ways of them reaching their own conclusions towards their perceived action(s) of the intervention, and the associated safety concerns for its use, within a PoTS patient group:

P: I could see that it could work with people (.) I could see why you are doing it. I could see (.) concentrating on the outbreath is a good idea because you are getting them into their parasympathetic nervous system and that's where we want them to be more often. Erm I could see the purse lipped breathing is going to increase thoracic pressures (.) so what is that going to do to venous return?

R: ok

P: well purse lipped breathing is also going to trigger abdominal work (.) and do we want abdominal work? That can cause an impedance of the blood down to your feet.

[Physiotherapist]

In this example, a physiotherapist first focuses on one central element within the Ocean Breath – its 'concentrati[on] on the outbreath' - as the core aspect of the practice, which she perceives as beneficial for alleviating PoTS symptoms. This depiction of a therapeutic PoTS action is then supported through her citing of an autonomic nervous system explanatory model ('you are getting them into their parasympathetic nervous system and that's where we want them to be more often'). Whilst the physiotherapist presents a possible benefit to this aspect of the Ocean Breath for PoTS, notice how she then goes on criticise a second element of its instructions, 'purse lipped breathing'. She does this by drawing on additional, secondary medical ontologies - surrounding 'abdominal work', 'thoracic pressures' and 'venous return'- to question the safety of the intervention. Through these frameworks, the practitioner expresses wariness towards the intervention, by identifying that its mechanisms may lead to an **adverse, up-regulatory** effects in PoTS patients through the worsening of common blood pooling symptoms ('impedance of the blood down to your feet').

Whilst all practitioners were receptive in discussions towards the use of an autonomic nervous system and vagal nerve explanatory model for guiding intervention development for people with PoTS, there was disagreement in regard to what outcomes the Ocean Breathing intervention would be seen to have within the patient group.

P: So I quite like that and I think there is a place (.) there is a place for [breathing interventions] in people with PoTS. I'm not as convinced that it's necessarily (..)

P: it'll be interesting to see what your results show cuz (.) I don't necessarily think [the Ocean Breath] would potentially impact on autonomic nervous system because we don't know enough about the effects of PoTS on the autonomic nervous system... I'm

not convinced it'll necessarily impact on the autonomic nervous system (.) but I think it'll just help people manage what's (.) what is potentially you know (.) quite stressful condition really.

[Advanced Syncope Nurse]

An advanced syncope nurse casts doubt towards the effects of the Ocean Breath's ability to demonstrate a physiological, measurable outcome change on people with PoTS' autonomic functioning during future trialling – ('I'm not convinced it'll necessarily impact on the autonomic nervous system'). However, she argues that the Ocean Breath still has 'a place ... in people with PoTS' through her perceptions of the intervention having a down-regulatory effect in the patient group, which can assist them with the management of stresses surrounding their chronic illness experiences.

Another practitioner, an occupational therapist, also described perceiving a beneficial effect of the Ocean Breath in people with PoTS:

for people who really struggle with rest and exhaustion (.) introducing something that they have to do which can help them recover some energy can be quite helpful (.) something like a breathing activity. And the way I have sold rest is that it is something to recover energy or as something to return your physiology back to whatever it needs to be.

[Occupational Therapist]

They also depicts the Ocean Breathing having a down-regulatory action in the patient group– 'people who really struggle with rest and exhaustion'- similar to the perceptions of the advanced syncope nurse above. Notice though how, despite this similarity, the application of the intervention ('something like a breathing activity') is rationalised for use in PoTS through its perceived action on treating a different symptom cluster, fatigue, by enabling sufferers to 'recover some energy'.

And that feeds into the spoon theory and might get you a spoon back. Its an activity which is going to help energise you. And you know we talk about energising activities and draining activities. Energisers and drainers (.) and there are some which are still activities but they still are energising you in a way.

[Occupational Therapist]

Furthermore, note also how the occupational therapist goes on to describe that this beneficial, perceived 'rest' effect of the Ocean Breath needs to be 'sold' to people with PoTS. To do this, she references two patient-derived frameworks for explaining fatigue management to people with PoTS – through ontologies relating to 'spoon theory' and energy 'energisers and drainers'.

These explanatory models are suggested by the occupational therapist as a way of enabling people with PoTS to better comprehend and see the possible benefits of the intervention for their fatigue symptoms, through the practice allowing them to ‘get you a spoon back’. These findings therefore demonstrate how practitioners would try to create a stronger rationale for translating the benefits of the practice, in order to improve the probability that people with PoTS would be willing to engage with the Ocean Breath.

Given the diverse findings, depictions of multiple, differing effects of the Ocean were identified across the first stakeholder group and PoTS-experienced practitioners themselves, the findings demonstrated a lack of agreement (Intervention Coherence) across participants in both stakeholder groups. Whilst some interpreted its impacts as aversive, upregulating (heat generation; blood pooling); others saw the Ocean Breath as producing down-regulatory effects (stress-relieving; rest for initiating energy restoration) that were beneficial. To further clarify the effects of the Ocean Breath, which was derived from pranayama yoga technique of Ujjayi, further feedback on the intervention was sought from yoga practitioners (see sub-section 1.3).

1.3. Stage [iii]- Intervention Feedback from Pranayama Yoga Practitioners

During the prior stage, key differences were identified in the ways in which PoTS-experienced practitioners comprehended, appraised and made sense of the effects of the Ocean Breath and its effects in a PoTS patient group. Due to this, I decided to seek further feedback during the intervention development process through a third stakeholder group of three yoga practitioners for additional intervention scrutiny. Furthermore, I also approached the pranayama yoga professionals for their guidance on the possible ways you could simplify the intervention. The need for this was identified through stage [i] findings, where people with PoTS expressed that they would need to reconfigure the Ocean Breath intervention in order to enact its core component - the slight constriction of the throat (production of the “HAAHH” sound).

Amongst the yoga practitioners, there was variation in their perceptions of the Ujjayi technique. One yoga practitioner was highly critical of our decision to utilise this technique for the basis of our intervention:

Can you imagine Mitchell someone feeling a [PoTS] attack coming on and they have to try doing ujjayi breath? ... its not practical. That’s why I keep banging on about it (laughing) I don’t think it’s the right technique for what I think you want it to do... its too technical and not necessarily appropriate for helping people (.) as they are going into an episode.

[Yoga_#1]

This practitioner felt that the ujjayi was a too advanced, heavily 'technical' practice that was not appropriate for beginners. She furthered these arguments through stating that she did not see the Ocean Breath as having a practical, fast-acting benefit for alleviating patients' PoTS symptoms during their sudden, unexpected flare-ups:

I don't know why you have chosen ujjayi breathing... its not something we would teach to beginners as one of the first pranayama techniques. Erm it has some contraindications. So if you are saying if people coming into the study may also suffer from anxiety (.) you (.) you don't teach ujjayi to people who are already internalising.

[Yoga #1]

This practitioner also raised concerns of safety for the use of this intervention for some in the patient group, who may be 'internalising' and 'anxiety'-like. Because of this, this practitioner did not see a way in which we could adapt the 'slight constriction of the throat' step of the Ocean Breath in order to make it more suitable for people with PoTS.

Notably, the other two practitioners interviewed praised the choice of Ujjayi for the Ocean Breath as a beginner-friendly practice for PoTS treatment:

P: yeah as far as I can see the two things you can achieve with breathwork (.) that would be related to PoTS would be first the ujjayi (.) to create the vagus nerve tone

R: yeah

P: and the ratio and rate of the breath going towards... just downregulating.

[Yoga_#3]

Practitioner #3 saw practical benefits to the use of ujjayi for alleviating PoTS symptoms, through the aim of the Ocean Breath to produce 'just downregulating' effects in sufferers. They support their view through the citing of the autonomic, 'vagus nerve tone' ontology explanatory model which I had identified as complimentary to people with PoTS' understandings of their illness (see chapter 7). Notice as well however, that this 'downregulating' effect of ujjayi is explained through the 'ratio and rate of the breath', whereby the practitioner expresses that the production of a down- or up-regulatory effect can be controlled through these factors.

Practitioner #3 further build on this explanation of participants being able to consciously control the regulatory actions they experience from an Ujjayi breath by adapting 'the rate and ratio of the[ir] breath', through simplistic analogies which compare the Ocean Breath to the actions of drinking "water or whisky":

P: [Ujjayi] tends to be used as a water breathing technique (.) so neutral breath or with down-regulating (.) so like a whisky category breath... if I constrict ujjayi then we are slowing down the rate of oxygen.

P: Because whether we are upregulating (.) downregulating or coming to neutral (.) **its all just based upon the rate and ratio of the breath.** So you know if I try it now (.) this is a coffee breath with ujjayi

[P performs fast, bullet like deep nasal breath]

P: HU HA HU HA HU HA HU HA

(..)

P: this would be water

[P performs elongated, deep nasal breaths]

P: HUUUUOHH (.) HOOOOHH (.) HAA HOOOHH

(..)

P: and then whisky would be something more like

[P performs *slower* elongated, deep nasal breaths]

P: HUUUUUUHH (.) HMMMM

[Yoga #3]

Notice how the concept of performing a fast-paced Ujjayi is compared similar to the action of drinking coffee (a drink which increases bodily metabolism) to account for upregulation. In a similar sense, a slowed Ujjayi practice is compared to drinking whisky (whereby alcohol slows the body's responses) to explain the possibility of the Ocean Breath exhibiting a down-regulating effect, and as water (associated by the practitioner with bodily rehydration, restoration) as a 'neutral' activity for some people. This use of metaphoric language by the practitioner, regarding changes which are produced by just altering 'the rate and ratio' of the Ocean Breath, can therefore illustrate how the intervention itself has been seen by different PoTS stakeholders to produce differing regulatory effects in the PoTS patient group. In a similar vein, practitioner #2 also described how people with PoTS could adapt the Ocean Breath practice through practical means in order to minimise the possibility of adverse, 'energetic' up-regulatory effects from occurring:

P: One of the things you could say about an ujjayi based practice is that it doesn't have to be energetic. I mean you could do an ujjayi breath where you are making lots of noise

(.)

P: HHUUUUUUHHHHH [participant demonstrates noisy ujjayi]

(.)

P: Or you can just breathe slowly but only slightly constricting the throat. So you still get the ujjayi breath (.) but its not necessarily an energetic breath (.) or a more energetic breath than you might usually use.

[Yoga_#2]

She recommended that this is avoided through the softening of inhalations and exhalations during the Ocean Breath, by having people with PoTS 'just breath[ing] slowly but only slightly constricting the throat'. In relation to how our team could practically adapt these understandings into the Ocean Breath for use in people with PoTS, practitioner #2 further described a different method that our intervention could implement in order to safeguard the patient group during the performance of an Ujjayi:

P: So I looked at the ways you introduce it and you use the "HAAHHHHH" method (.) with the open mouth? Like teaching people the fogging mirror version?
R: yeah
P: so I really like the video that you've sent with the "haaaaaah" [participant demonstrates gentle ujjayi breath]. I have had in classes people who have had asthma.
R: yeah (.) I have too actually!
P: ah well they find the open mouth breathing really challenging and even anxiety producing. So I erm (.) use to teach it with an open mouth (.) but you can use the ASCH-ARRHH
R: The ash-arr?
P: Yep (.) so ASCH breathing in [demonstrating inhale] "Ascchh" (.) ARRHH breathing out [demonstrating exhale] "ARRHH" ... so for people who frightened of (.) [like] asthma (.) may be uncomfortable with doing [ujjayi] with an open mouth (.) I tell them to close the lips and they can still do the asch-arrh (.) but imagining it more as if you are saying it more inside your mouth
(...)
[P demonstrating] ASH-HA-HA-HARR (.) ASSHHH-HM-HARR.

[Yoga_#2]

'Trying the technique this way (.) as an asthmatic myself (.) does seem to be easier. Like err (.) in the sense that I feel I am doing the technique correctly now.

'I don't have any issues with the fogging of the mirror technique itself um... the ASCH-ARR method just feels more natural (.) to me.'

'I think offering this as an alternate (.) adapted way of within the PoTS intervention will be something they really like.. Also its really fun to try these different style (.) it actually makes me want to do meditations more often again' – MJH Reflexive Commentaries [Audio Recordings]

Fig. 3. Reflexive note [MJH] obtained from phone, recorded a week after the second yoga practitioner interview, after I had attempted their suggested alternate Ujjayi method. Being able to draw on my own experiences of having a breathlessness condition helped me to understand the importance of making the Ocean Breath accessible for people with PoTS by allowing for 'customisation' of its practice. Because I had, up until this point, only performed Ujjayi in the way I had been originally taught back in 2017, I had not been open to (or aware) that a change to my own practice would lead a positive, personal change upon my experiences of enacting this technique. In this sense, I myself began to develop Intervention Coherence in the prospect of being able to adapt the Ocean Breath to make it more suitable for others.

Through their experiences of adapting the ujjayi technique for use in another breathlessness condition (asthma – see Fig. 3), the practitioner recommended that changes to the sound of the Ocean Breath– from a "HAAHHHHH" sound to the performance of an 'ASCH-ARRHH'- could be implemented during its delivery to a PoTS group to improve its perceived safety. Notice as well, how this 'ASCH-ARRHH' method described by the practitioner is a compatible format of the Ocean breath for people who were aversive to mouth breathing, in relation to several people with PoTS who exhibited preferences for nostril breathing during stage [i].

Finally, in regard to concerns from people with PoTS that the Ocean Breath could produce a heating effect in the body, two practitioners advised our team that we could introduce the use of 'cooling breaths' into the intervention in order to counteract this.

But when I have been to workshops where we have talked about it then we would give them cooling breaths (.) to try and cool the body down. But you're getting into to (..) P: its complicating it. Its complicating it for beginners who are going to be learning it through a short video over a screen.

[Yoga #1]

Nevertheless, professional #1 was wary that introducing the use of a cooling breath alongside the Ocean Breath would cause further 'complicating' of the already, overly-complex nature of the intervention.

1.4. Stage [iii]- Member Checking with People with PoTS ($n = 2$)

Findings from stage [ii] of the intervention development process indicated that healthcare practitioners did not perceive the Ocean Breathing intervention to be a sufficient technique on its own for producing a therapeutic action on PoTS symptoms. Because of this, during member checking activities with two participants from the people with PoTS group (see Table 3), four alternative breathing techniques - that had been suggested to our research team throughout our development process from stakeholders across all three groups - were presented alongside the Ocean Breath for scrutiny. Participants were supportive of the adaption of the intervention to a toolkit strategy and saw Square Breathing as the most compatible technique for incorporating alongside this. Given its easy to comprehend naming, and the simplicity of a four-sided box representing two equal-length inhalations and exhalations, participants felt that the lengths of these exercises could easily be decreased or increased to alter its difficulty to perform. By easily altering the difficulty of the technique, participants expressed that this would help people with PoTS accommodate frequent, daily changes in their functioning and fatigue levels. Finally, when discussing findings from our research that the Ocean Breath is perceived to be overly-complex by PoTS stakeholders, one participant suggested the format of the intervention could be simplified through an acronym-like strategy. Through the possible (re)adaption of its instructions into a 4-step ('W-A-V-E') or 5-step ('O-C-E-A-N') procedure, this participant felt people with PoTS would be more likely to perceive the work of performing the intervention as simplified and easy-to-enact.

Table 3. Notes sent to our team by one of the participants [SA09RH] which she had produced in preparation for the member checking discussion, detailing her thoughts behind each alternate breathing technique and the Ocean Breathing intervention. Red font signifies changes made by the research team (for clarity).

Technique	Interesting, safe for pots?	Like	Dislike	Graphic [Presentation]
Square breathing	Yes I think	Easy to do and to remember, can be done anywhere, flexible ie longer or shorter	I don't like holding my breath as I feel my heart beating (possibly faster)	Great, simple, everyone can follow it, easy to remember
Stop [Mindfulness]	Not really	[Participant left this box blank]	Really strong dislike about it. Has too many expectations which are bound to fail and frustrate the person, driving them away from the practice. Impossible to follow without an instructor, thoughts cannot be stopped it's the way the brain works (and its not friendly for people that have anxiety or are neurodiverse). Some people might struggle to notice or go into their feelings. Other grounding exercises might be more effective than this	Really dislike it, [the person with a] quote [on the page], who is she? Saying mindfulness is easy can make people feel like they're failing, there is no mindful self compassion and self love in this. The proceed part is explained poorly
Buteyko	Yes	The drawings of the nose. It's judgement free, explained in a neutral way	What is a normal breath? I would guess many people with pots also have dysfunctional breathing so I feel it should be more precise than "as you normally would" as our normal might be too fast or too shallow be we would not know. Also poor proprioception is common so maybe give people a way to check how they're breathing (ie a book or hands on chest and belly to see what is moving). I would struggle to hold the breath - maybe suggest alternative options/what to do? Clarify if it can be done in other positions/walking etc	Like it and I enjoy the science bits, might give me more hope on the effectiveness and that it's not someone saying it's all in our mind, go do this and don't bother me. Not sure the different fonts are easy to read for dyslexic [individuals]
Diaphragmatic breathing	Yes	Really easy to follow	The assumption that everyone will feel their diaphragm - I've tried many times and I just can't feel it due to poor proprioception. 40 mins a day of practice might be too much for some, maybe suggest that any practice is good?	Bit too grey, looks old? Name not catchy/easy to remember (people might not know what diaphragm means)
Ocean breathing	Yes definitely	Easy to do, can be done almost anywhere, flexible,	Maybe put some pictures for visual learners?	Really well explained!

2. Discussion

2.1. *Summary of Intervention Development Findings & Literature Considerations*

The final phase of this thesis aimed to develop an Ocean Breathing intervention for use in a PoTS patient group, undertaken as the first stage of the MRC framework for Complex Intervention Development (Skivington et al., 2020).

Whilst participants across all three key stakeholder groups agreed that they saw benefits for the application of breathing techniques to PoTS symptoms, their feedback indicated mixed perceptions towards the utility of the Ocean Breath in this patient group. Findings obtained from the analysis of interviews with people with PoTS, through their integration into NPT constructs (May & Finch, 2009) during analysis, revealed that the Ocean Breath was perceived to be overly-complicated in nature by its intended user group. Due to this, people with PoTS expressed a need to reconfigure and adapt the instructional steps of the intervention, in order to individualise the actions of the practice around their specific breathing capabilities and restricted skillsets from PoTS symptom impact. These findings are similar to those of Arden-Close, Tardley, Kirby, Thomas and Burton (2017), who explored implementation facilitators and barriers of 16 people with asthma who participated in a video-delivered breathing retraining programme. Concurrent with the Ocean Breath findings, people with asthma also needed to adapt the technical elements of the respiratory exercises, as a way of simplifying the tasks they would need to complete for undertaking the intervention. Through this comparison with the feedback obtained from people with PoTS, our findings emphasise the importance of designing breathing interventions in a manner which are very 'flexible' whilst working alongside patient groups who experience breathlessness symptoms. By allowing each patient to personalise and adapt the elements of their practices around the individual, specific breathing issues they present with, these more 'workable' interventions can be developed to counteract foreseen future implementational barriers – whether tied to coherence, cognitive participation and collective action (May & Finch, 2009) - during future evaluation and trialling stages.

During the intervention development process, mixed views of the Ocean Breath were also acquired from PoTS-experienced professionals and healthcare practitioners. Understandings of this stakeholder groups' collective feedback in relation to NPT (May & Finch, 2009) - identified from practitioners' confusions that the intervention would demonstrate different, up- and down-regulatory effects across PoTS patients- were reflective of poor intervention coherence. Similar findings have been presented by Slocum-Gori, Howard, Balneaves and Kazanjian (2012) within their feasibility trial of a yoga therapy programme for breast cancer

survivors. Their obtained qualitative feedback from key healthcare practitioners also raised concerns that other professionals would not be able to effectively comprehend the yoga therapy and its use in patients. They further argued that the yoga therapy needed to be delicately framed to this stakeholder group, in order for healthcare practitioners to establish a sense of acceptance and engagement with the intervention during implementation. In regard to the current study, given that PoTS clinicians demonstrated poor coherence towards the Ocean Breath practice, the future delivery of the Ocean Breath through clinical practice would likely lead to several barriers arising that would hinder the probability of its successful implementation. This lends further credibility to recommendations that the Ocean Breath practice should instead be delivered through an online, internet-based delivery format - as supported from findings of both people with PoTS and healthcare practitioner groups – as the primary format of intervention dissemination. Feasibility trials for intervention-based delivery of breathing interventions have previously been examined within COPD (Mark, Ikehara, Matsuura, Hara & Li, 2013) and asthma (Ainsworth et al., 2019) patient groups, demonstrating promising findings to support the use of these online formats.

Furthermore, it is also worth noting that, to my knowledge, the current study is the first in the PoTS literature area to have undertaken qualitative exploration with a group of healthcare professionals identified through their clinical expertise of treating PoTS. Whilst the application of qualitative methods in PoTS remains a relatively unexplored area with only one published study of data obtained from patients to date (Waterman et al., 2021); further examination of how PoTS practitioners communicate understandings of their treatment methods to patients holds great implications for improving delivery of PoTS therapies. Within the current study, practitioners demonstrated how they would 'graft' the use of their own psychological, sociological and medical explanatory models (Kleinman et al., 1978) alongside the use of autonomic nervous system ontologies, to demonstrate to their patients how their treatments would interact with their understandings of PoTS symptoms. Further works, those seeking to explore healthcare professionals' experiences of delivering psycho-social interventions to people with PoTS, may assist with improving the delivery of these treatment methods through the identification of further factors which communicate clear understandings of treatments' therapeutic effects and underpinning explanatory models to patients.

2.2. Reflections on Ocean Breath Intervention Development and Further Stages

During interviews, healthcare practitioners also gave their input towards the design of a future clinical feasibility trial that my supervisors and I had originally planned to undertake for

assessing intervention compliance within the PoTS patient group. Despite this however, the central issues relating to cognitive participation, collective action (people with PoTS) and poor intervention coherence (all stakeholder groups) were identified, challenged the basis that the intervention (within its present form) would be capable of achieving future successful implementation. Thus, in keeping with its informally dubbed title as a ‘trial killer’ (p3, Murray et al., 2010), findings interpreted from the application of NPT within our intervention development process did not support the decision to progress the Ocean Breath to the feasibility assessment stage of the MRC framework (Skivington et al., 2020). Crucially, the issue of coherence – which was apparent across all three stakeholder groups – was seen as a central issue for rationalising my decision to prevent further progression of the intervention at present, due to the lack of agreement between stakeholder groups towards the anticipated effects of the Ocean Breath within a PoTS patient group. Given that further intervention development work is needed, member-checking activities with people with PoTS supported the possibility of (partially) addressing these implementation issues, through alteration of Ocean Breath format into a toolkit-like strategy comprising of several, multi-faceted breathing techniques.

The possible adaption of the Ocean Breath to incorporate other, additional types of breathing strategies is akin to how researchers have previously examined Ujjayi practices within the empirical literature. Ujjayi techniques have typically been delivered to patient groups as just one component of larger, multi-breath technique programmes, such as Sudarshan Kriya Yoga (Brown & Gerbarg, 2005); the sole effects of Ocean Breath interventions within general chronic illness groups have rarely been studied in isolation (Epe, Stark & Ott, 2021; Gerbarg & Brown, 2015). Adaption of the current Ocean Breathing practice into a multi-component intervention may therefore sound appealing for enabling people with PoTS to tailor their practices around their specific breathing capabilities and needs, such as those which people with PoTS describe experiencing from their altered breathing experiences (see chapter 9). However, it must be noted that multi-technique pranayama programmes have been criticised for their common observations of high drop-out rates during feasibility assessment and randomised-control trialling (Cramer, Haller, Dobos, Lauche, 2016). Thus, in an effort to prevent this, it is critical that any further development of the Ocean Breath intervention must place emphasis upon its need for a ‘toolkit-like’ nature as opposed to a regimented, set programme or schedule of breath-related activities that must be followed. Participants need to be able to retain their ‘flexibility’ by freely choosing which of its comprised techniques they decide to engage with and attempt.

To support this line of work, more mechanistic studies of breathing within PoTS samples need to be undertaken. The aim of these studies would be to comprehend which specific elements

of breathing activities, both those of pranayama origin and other-related disciplines outside of yoga, are most suitable. Through these works, studies can be undertaken to compare techniques- such as those which utilise only mouth or nostril breathing methods – led to distinguished, demonstrable effects in people with PoTS. In this vein, these empirical studies in people with PoTS will generate a greater evidence base for strengthening toolkit development, through justifying the inclusion of only those breathing strategies which are found to be most appropriate, potentially beneficial and adaptable for people with PoTS to engage with. Furthermore, undertaking of mechanistic studies will also allow people to explore suggestions proposed by the yoga practitioner group (*such as the use of “ASSCHH-ARRHH” or alterations to the rate-and-ratio of the breath*), for testing the ways in which we can adapt the Ocean Breath (Ujjayi) technique itself to accommodate PoTS symptoms.

2.3. Conclusion

In conclusion of the intervention development phase of the thesis, designing of the Ocean Breath was challenged through its perceptions as an overly complex technique by people with PoTS. Whilst people with PoTS and healthcare practitioners saw practical benefits to the application of breath-related interventions for use in PoTS and agreed that the use of an online platform would serve as an suitable form of intervention delivery; confusion arose surrounding the perceived effects of the Ocean Breath in a PoTS patient group. Feedback obtained from yoga practitioners and member-checking with two people with PoTS indicated that these implementation barriers could (partially) be tackled, through: (i) the adaption of the performance of the Ujjayi practice itself to simplify its requirements, in addition to: (ii) the format of the Ocean Breath into a toolkit strategy. Nevertheless, further mechanistic studies with PoTS samples are first needed to support further intervention development. The next chapter, which serves as the overall discussion and conclusion of the thesis, reflects on how my undertaken research from across all three phases of the PhD (Scoping Review; Narrative Work; Intervention Development) has furthered knowledge into the study of PoTS.

- Chapter 11: Concluding Remarks -

This chapter, which serves as the final chapter of my thesis, first reflects upon the aims and objectives which have guided my PhD study. Following this, I reflect upon how the contributions identified from across my undertaken scoping review work, narrative analyses of PoTS diagnostic stories and Ocean Breath intervention development process, have advanced knowledge within the academic PoTS research field. Throughout this chapter I acknowledge the strengths and limitations of my work, core implications for PoTS researchers and outline clear directions for further research to be undertaken for the future investigation of PoTS. This includes the need for more proof-of-concept studies to be undertaken to fully support the development of additional, breath-related intervention within this patient group.

1. Reminder of Thesis Aims & Objectives

My PhD thesis research served as the first stage of the Medical Research Council Framework (Skivington et al., 2021), for the development of a complex intervention for a PoTS patient group. Within the presented background literature summary within chapter 1, I outlined that there was a lack of existing treatments, specifically those of a non-pharmacological nature, to assist people with PoTS with the day-to-day management of their PoTS symptoms (Kichloo, Aljadah, Grubb & Kanwal, 2021). This notion was further built upon from the findings of my narrative synthesis of empirical works that examined existing PoTS treatments within chapter 4. Within that chapter, I highlighted that the current non-pharmacological interventions have been identified as having a weak evidence base for their applications to PoTS patient groups (Raj et al., 2021) with many of these symptom-control strategies lacking high-quality RCT studies to thoroughly assess their efficacy rates (Raj & Robertson, 2018; Wells et al., 2018).

The aim of this thesis was to begin to develop a potential new non-pharmacological intervention, an Ocean Breathing practice, for people with PoTS. In order to support my intervention development process throughout my PhD study, my thesis had the following objectives:

- i. To examine the breadth and nature of existing published works and empirical research literature within the PoTS literature field.
- ii. To expand upon limited qualitative work into the PoTS research area by exploring both the diagnostic and symptom experiences which are shared by people with this condition, within their illness narratives.

- iii. To understand factors which would serve as facilitators or barriers to the development of an Ocean Breathing intervention within a PoTS patient group and its likelihood of achieving future successful implementation.

2. Considerations of Implications for Core Thesis Research Findings

2.1. Implications for PoTS Researchers

Throughout the research I have undertaken, my findings have highlighted key implications and recommendations to inform PoTS researchers and the core future directions for their empirical works going forward. In order to examine the breadth of the existing PoTS research area and current clinical understandings for this autonomic condition, I undertook a large-scale scoping review (see chapters 2-4) to explore literature that had been dedicated to the study of its diagnosis, symptomology and treatments. Within the final article review subset, only a small, yet growing, body of review articles into PoTS featured the use of high-quality evidence synthesis, which included a limited number of identified systematic reviews (Gales & Gales, 2007; Gee et al., 2018; Morgan et al., 2018) and/or meta-analyses (Deng et al., 2019; Swai et al., 2019; Wells et al., 2018). These findings of my scoping review are consistent with notions from other PoTS researchers (Wells et al., 2018) that have emphasised the importance for further systematic works to be undertaken within the PoTS research base, particularly in regard to non-pharmacological treatments (Eftekhari et al., 2021). Despite this, my findings from data extraction also revealed that several of these existing works had poor reporting standards - such as those lacking clear descriptions of their review inclusion and exclusion criteria (Brady et al., 2005; Benarroch, 2012; Fredorowski, 2019; Ruzieh et al., 2017; Ruzieh & Grubb, 2018), or reviews which had neglected the reporting of key details for their utilised key words and employed database searching strategies (Ku et al., 2016; Ruzieh et al., 2017; Ruzieh & Grubb, 2018). Thus, whilst prior works have recommended the pressing need for a greater expansion of evidence synthesis and collation in the PoTS research area (Eftekhari et al., 2021; Wells et al., 2018), my scoping review findings place a strong emphasis on PoTS researchers to establish a greater quality of reporting standard within their evidence reviews. Future researchers should establish rigour when undertaking their evidence synthesis of PoTS literature, through compliance with standardised reporting review guidelines within their works - such as the conventions imposed by PRISMA and Cochrane.

In addition to this, further findings from my scoping review demonstrated that research into PoTS has been dominated by research with a medical or clinical focus, with substantial proportions of the literature base dedicated to exploring the aetiology, endophenotypes and

medical pathologies underlying this condition. This finding, supported by Eftekhari et al. (2021), reflects that the physiological origins behind PoTS symptoms are still recognised as a poorly understood medical phenomena within the literature (Raj & Sheldon, 2016). These works have enabled clinicians to identify appropriate PoTS clinical interventions and treatment targets, through common findings of patients' low blood volumes, difficulties with vasoconstriction and their needs to control orthostatic heart rate responses (Raj, 2012). Despite this, my synthesis of PoTS treatment literature within chapter 4 highlighted that many of these treatments have a limited supporting evidence base (Raj & Robertson, 2018; Raj et al., 2020; Wells et al., 2018). Thus, my scoping findings emphasise the need for PoTS researchers to aim towards undertaking greater, large-scale RCT studies going forward, in order to better determine the efficacy rates of these existing treatments within PoTS patient cohorts.

This dominant focus upon the clinical investigation of within the PoTS literature base has led to other, central issues – those identified with great importance for the patient group - to be heavily neglected by researchers. My narrative synthesis findings, within Chapter 3, identified that the paucity of PoTS qualitative studies had led to a poor understanding of PoTS symptom experience within this field. Whilst prior research has identified that people with PoTS possess reduced quality of life (Benrud-Larson et al., 2013), poor levels of functioning (Mathias et al., 2014), regular sleep disturbances (Miglis et al., 2013) and increased suicide ideation (Pederson & Brook, 2017); there is little empirical knowledge about people with PoTS' experiences and understandings of illness burdens, diagnostic journeys and subjective symptom accounts (Waterman et al., 2021). This lack of qualitative investigation is unfortunately not uncommon across diagnoses which include persistent physical symptoms, as has been previously noted within conditions associated with chronic back pain (Snelgrove & Lioffi, 2013). The application of more qualitative work - which allow the voices of the target patient group to be 'listened to' by researchers and taken forward as priority research areas for exploration (Snelgrove & Lioffi, 2013) - have great potential in PoTS, for identifying the core barriers which hinder the improvement of peoples' day-to-day quality of live, as well as assisting the future development of condition-specific interventions (Ma, 2000). Currently, researchers' lack of involvement of people with PoTS – as qualitative research subjects and in the inception, conduct and dissemination of research - has limited the process of intervention development itself for this condition. As acknowledged by the conclusions of Bourne et al. (2021), PoTS qualitative works are vital for supporting the implementation and embedding of treatments into the day-to-day lives of people with PoTS, through examining patients' own perceptions of these non-pharmacological strategies and the sense-making processes they employ towards an intervention. Through my own experiences of actively

engaging people with PoTS into my research and listening to their feedback for the development of the Ocean Breathing intervention (as discussed further within this chapter), my thesis highlights the importance for PoTS researchers to shift their research focus towards co-development work alongside individuals from this patient group.

2.2. Implications for Qualitative Studies of PoTS & Persistent Physical Symptom-related Researchers

Through the examination of PoTS storytellers' online diagnostic stories, the findings from my narrative analysis have demonstrated that people with PoTS utilise biographical disruption (Bury, 1982) as a purposeful, narrative tool to emphasise the debilitation they encounter from their PoTS symptoms. Whilst similar findings had previously been observed in Chronic Fatigue Syndrome patients (Whitehead, 2006), my findings also drew on Bury's (1982) work within a PoTS patient sample. Previous qualitative works into people with persistent physical symptom conditions (such as PoTS) have highlighted that people often express that they struggle to communicate the true extent of their illness burdens to others; these difficulties are further confounded by the complex nature of their condition(s) and the wide multitude of symptoms which they face (Maatz et al., 2016). My narrative findings therefore highlighted a possible discursive strategy which people with PoTS employ to enable them to communicate their difficulties with fatigue, breathlessness and pre-syncope more effectively to others, through the individual describing the additional burdens their symptoms place upon the completion of their (relatable) everyday, taken-for-granted living activities.

In addition to this, my findings also demonstrate the rich and insightful understandings that can be drawn from the lives of people with PoTS, through the examination of their narratives as a social phenomenon itself. Narrative analysis (Reissman, 2002), of which my research had been the first to utilise within the PoTS research field, understands patient sense-making of chronic illness through individuals' (re)construction of their symptom debilitation and diagnosis-related impacts on their life into shared stories, as ways of sufferers' deriving new meanings and knowledge from their illness experiences (Polkinghorne, 1995; Frank, 1995). Given the complexity associated with the social phenomena of narrative, my research expanded upon prior chronic illness narrative analyses works by undertaking a multi-approach of three separate analyses (thematic; structural; performative) to draw more insightful, detailed understandings of the experiences of PoTS storytellers. Although a multi-phase analysis of narratives is recommended for the establishment of rigour and trustworthiness, many prior narrative works into other chronic health conditions have commonly neglected the importance

of this through their use of singular approaches only (Menon et al., 2016). Future qualitative investigations into PoTS – and other conditions - should also utilise such rigorous methodologies, in order to thoroughly explore the core elements and understandings of patients' symptom debilitatingations.

My narrative research was the first study in the PoTS research area to explore internet-situated PoTS communities from the social media platforms accessed by people with PoTS, through examining their online video diagnostic stories. Whilst online vlogs or other types of media platforms had not previously been examined by PoTS researchers, empirical works within other chronic health diagnoses have associated several benefits to these virtual communities for individuals with persistent physical symptom conditions. This includes their usefulness for allowing sufferers to make sense of their own symptom complaints through sharing and relating to others' illness experiences within postings and comments (Sannon et al., 2019), their ability to act as an information resource by assisting members with their symptom management (Coulson, 2013), in addition to, emotional support (Lasker, Sogolow & Sharim, 2005). These are important implications to note, given that individuals who have 'contested' medical illness such as PoTS – whose symptom experiences may not be understood by their family, friends or healthcare practitioners - often remain highly dependent on these online sources for the coping and management of their chronic health condition (Lasker, et al., 2005; Sannon et al., 2019). My narrative work also highlighted the importance of understanding and analysing these online platforms as a way of identifying the use of PoTS-specific jargon (such as 'dysautonomia', 'PoTSies') and signposting strategies which people with PoTS employ - as ways to communicate understandings of their chronic illness with other PoTS-diagnosed individuals. In light of this, my narrative findings therefore represent only a small proportion of the wealth of potential insights which can be obtained from examining these existing online patient communities within PoTS. As social media platforms continue to rise over time, additional works are needed to examine how the communication of PoTS diagnostic and symptom experiences may differ across different apps or sites. This includes the future investigation of PoTS-specific TikTok vlogs, where (in comparison to YouTube video sharing) people with PoTS need to more rapidly disseminate their video messages to their online audiences due to the more digestible, shorter video durations associated with this platform.

2.3. Implications for PoTS Clinicians & Healthcare Practitioners

It is important to consider how the examination of PoTS storytellers' diagnostic narratives can inform practitioners who interact with PoTS patients within their clinical practice. Prior to my

research, previous PoTS works had neglected to explore patients' own recollections and experiences of consulting with clinicians and practitioners during the investigations of their persistent physical symptoms. Whilst prior PoTS works had identified that patients commonly face multiple delays and misdiagnoses prior to receiving their correct diagnosis (Raj, 2013), explanations behind these encountered delays had remained limited in scope. My findings expanded upon these works by demonstrating that people with PoTS construct barriers to receiving their diagnosis - as representations of their illness carers (Rossen et al., 2019) – through their portrayal that they are made to feel culpable for their symptoms, by the allocation of portrayed psychogenic labelling by their healthcare professionals. In addition to this, storytellers also constructed experiences of the severity of their symptoms being dismissed by clinicians, through their use of normalization without explanation tactics (Dowrick et al., 2004), as evidenced via the citing of negative test results from their performed medical investigations.

There are two potential implications for guiding and assisting healthcare practitioners with the clinical management of patients who present with PoTS symptoms. First and foremost, more work is needed to examine - and inform - the interactions and dialogues which clinicians have with these individuals within their medical consultations. As outlined above (*see sub-section 2.2.*), people with PoTS utilise specific jargon and strategies to demonstrate understandings of their illness experiences to others. In addition to the need to enhance the knowledge of PoTS throughout the medical community (Eftekhari et al., 2021), further work should be undertaken to examine whether these symptom communication strategies (those used by PoTS storytellers) can be embedded within the discourses which are used by clinicians during their patient interactions. In this sense, through the use of patient derived illness terminologies and socio-medico frameworks (such as those surrounding the autonomic nervous system, *see chapter 7*), it may be possible that these PoTS-specific strategies could be 'exploited' by clinicians to demonstrate greater understandings and recognition towards their patients' PoTS experiences. Through drawing upon a shared illness language and framework, this would help PoTS sufferers to see their illness experiences as having been legitimised and respected as a genuine medical (as opposed to 'psychogenic') condition, throughout their healthcare interactions. In addition to this, my research findings also highlight the potential need for a new psychological-based intervention for PoTS to be developed – ones which aim to support and enhance patients' emotional resilience and their options for seeking support. These types of interventions are needed help protect these individuals against the negative impacts which they commonly report from experiencing from the contentious labelling of their symptoms by others, within both medical consultations and their wider, everyday lives.

The final phase of my narrative analysis featured the inspection of PoTS storytellers' online narratives through a performative approach, which examined how these individuals communicated personal understandings of their chronic illness to others (Meraz et al., 2019). My results further highlighted how people with PoTS depict their struggles with PoTS symptoms through the personifications of their own bodies as antagonistic, out-of-control characters. These findings were reflective of the classic works of Charmaz (1980; 1994), who proposed that people with chronic illness may 'disentangle' their sense of 'the self' from their physiological being to protect their own personal identities. It is currently unclear whether this 'othering' of the body by people with PoTS serves as a learnt self-performed protective strategy, and/or if this behaviour is representative of a potentially harmful patient cognition surrounding their illness that could require clinical intervention. Nonetheless, further psychological exploration towards people with PoTS's own perceptions of their bodies could be undertaken, in order to support clinicians who are involved in the psychological treatment of patients with PoTS. These works could inform the development of PoTS-specific strategies - such as those featuring techniques from CBT – to assist clinicians with tackling these issues within their clinical work.

2.4. Implications for PoTS Intervention Development & Breath-Related Researchers

A core strength to the intervention development process that I have undertaken was my identification of a patient-derived intervention explanatory model. I therefore supported my decision to pursue an Ocean Breathing practice as the primary format for PoTS intervention development, through the qualitative work I had performed with people who have PoTS. Within chapter 7, I identified that people with PoTS commonly relied upon ontologies surrounding the autonomic nervous system, whereby, they depict a disruption between the balance of the body's sympathetic and parasympathetic branch activity, as an employed socio-medical framework to communicate their PoTS symptoms and illness experiences to others (Ravenzwaaij et al., 2010). Whilst prior PoTS aetiology empirical works have acknowledged this as a possible underlying pathophysiological model behind the condition's symptoms (Jacob et al., 2019), my work begins to identify and examine the use of these frameworks within the discourses of people with PoTS themselves. By undertaking further examination of patients' own experiences and understandings of PoTS symptoms through performative analyses, I therefore identified a suitable explanatory model (Klein et al. 1978) for use in a PoTS patient group, to further support the applications of the Ocean Breath to this condition. This is an uncommon (yet recommended) approach within intervention development, whereby other researchers will opt to identify an explanatory model solely from understandings within

academic literature base (Skivington et al., 2021). Nevertheless, Menon et al. (2016) have emphasised the importance of identifying a condition-specific ontology that is supported by persistent physical symptom patient groups themselves, as these individuals are unlikely to see the benefits of (and adhere to) interventions that do not have appropriate, 'explainable' mechanisms for promoting their intended symptom relief. Therefore, I argue that it is pivotal for intervention developers within the PoTS research field to utilise co-development, and/or additional qualitative strategies alongside people with PoTS, to both inform, support and establish credibility to their treatment strategy development processes.

I further engaged people with PoTS within my intervention development process for the Ocean Breathing practice by examining their self-held perceptions towards their own sensations of breathing and breathlessness symptoms (*see chapter 9*). Prior to this work commencing, dyspnoea had been a relatively neglected area of research within PoTS literature with prior works having focused on the medical investigation of its underlying pathophysiological causes (Oldham et al., 2016; Stewart & Pinnosi, 2021). As such, this was the first qualitative study to explore the sensation and perceptions of breathing within PoTS, and I found that these individuals described themselves as possessing an 'altered', adapted pattern of regular breathing as a result of their illness. Whilst the qualitative exploration of patients' perceptions of their breath in other chronic health works remain limited in scope, findings from COPD literature has demonstrated the importance of acknowledging their air hunger sensations, as a way of understanding the phobias which patients describe developing towards their breath as a result of their dyspnoea symptoms (Harrison et al., 2014).

Additionally, my research recognised PoTS habituated breathing as a highly conscious, and at times invasive, process for this patient group, through their hyper-fixations upon the movement(s) of their upper chests during their routine breathing cycles. From these conversations I have had with people with PoTS, they also taught me about how they had, at times, developed this uncomfortable 'fixation' only after a practitioner had labelled their breathing pattern as 'dysfunctional' in nature. Given this and the association of the phrase 'dysfunctional' with the aversive bodily sensations reported by some people with PoTS (as highlighted within my findings), throughout this thesis I have found myself favouring the term 'altered' breathing when describing the adapted breathing patterns of this patient group. It is also worth noting that many of these participants did not recall seeing their own regular breathing as a 'problem' prior to these liaisons with healthcare professionals. As such, researchers and clinicians may want to be cautious about using the phrase 'dysfunction' with people with PoTS, and to instead consider replacing this with usage of the term 'altered breathing' within their clinical practices. This recommendation is made in efforts to try and

mitigate against the potentially harmful physiological sensations which some people with PoTS describe beginning to fixate upon, if they believed their breathing patterns were 'wrong' or 'incorrect'. Further empirical and clinical works are needed to thoroughly examine these considerations.

My final research study (see *chapter 10*) featured the use of an iterative, multi-stakeholder group qualitative intervention development process. From this, I collated feedback upon the Ocean Breathing intervention from people with PoTS, PoTS-experienced practitioners & healthcare professionals, and pranayama yoga instructors. Whilst feedback from these stakeholder groups indicated that they saw a general benefit to the use of breathing interventions for as a PoTS treatment method and the use of an online format as feasible for its delivery; mixed views were identified regarding the Ocean Breath practice. People with PoTS perceived the performance of the core, beneficial throat-constriction element of the Ocean Breath- associated with its health benefits (Jerath et al., 2015)- to be an overly-complex aspect of the intervention. They also expressed their desires to reconfigure this element of the practice, in order to make it workable around their specific and individualistic (altered) breathing capabilities and skillsets.

There was also a lack of agreement between PoTS-experienced professionals and healthcare practitioners for the technique's perceived, beneficial actions upon PoTS symptomology. Some individuals highlighted the use of the Ocean Breath for fatigue management, whilst others confined the use of the intervention for only assisting patients with the improvement of their general well-being. Through these findings and the lack of agreement between stakeholder groups, my team and I realised how little understandings we had of the intervention we were developing. With each passing interview, informal discussion or analysed transcript, I was left with more and more questions about what the actual – seemingly ranging – effects of the Ocean Breath would be for people with PoTS. Given these considerations and its perceived poor intervention coherence across participant groups, the collection of further intervention feedback should aim to employ the use of a mixed stakeholder group - comprising of representatives from people with PoTS, PoTS-experienced healthcare practitioners and yoga instructors - to formally scrutinise feedback on, collate and adapt, an 'agreed' format of a breathing intervention together.

Through the alignment of my thematic findings (Braun & Clarke, 2019) from each stakeholder group alongside its four core constructs, the use of Normalization Process Theory (May & Finch, 2009) ultimately indicated that the Ocean Breathing practice - within its current form - was unlikely to lead to successful implementation within the PoTS patient group, if the intervention was allowed to be proceeded to the feasibility stage of the Medical Research

Council Framework (Skivington et al., 2021). These notions were due to the identification of difficulties related to cognitive participation, collective action and intervention coherence across the three PoTS stakeholder groups. I decided to suspend my planning for undertaking a future clinical feasibility trial of the Ocean Breath practice, in order to pursue further intervention development work following the conclusion of this thesis. Whilst additional steps are needed to support this further work, suggestions considered during member checking activities with people included the possibility of altering the intervention format to incorporate the use of a toolkit design, or an acronym-like approach, in an attempt to simplify its perceived complexity by people with PoTS.

Conversely however, my thesis also emphasises the importance of performing future mechanistic, 'proof-of-concept' studies of breathing capabilities in PoTS at a later stage, in order to fully support any adapted changes made to the format of the Ocean Breath. These studies are of great importance to this patient group, due to my observations during my intervention development process that a PoTS-breathing intervention would need to be designed in a manner in which it could be 'customisable' in nature for its intended target users. This is due to the specific - yet, at times differing – breathing capabilities and skillsets being described by each person with PoTS (*such as the lengths of time they can hold their breath, inhale or expire for*). These 'basic science' studies - defined as experimental paradigms which seek to demonstrate that the intended, therapeutic actions of an intervention are capable of being actualised within a target patient group (Campbell, Gilron, Doshi & Raja, 2019) - are sorely needed with PoTS patient groups. These studies should aim to explore whether minute differences in the ways which patients with this condition describe needing to personalise (and reconfigure) the performance of a breath-related intervention, around the difficulties and challenges induced by their altered breathing patterns and breathlessness symptoms (*as detailed within chapter 9*), are capable of eliciting similar or differing effects upon their PoTS symptoms.

To further exemplify the need for these lines of work, feedback identified from yoga professionals during the intervention development work had indicated that an alternative method of performing the Ujjayi breath (the "ASCH-ARRH" method) could be offered to PoTS patients who struggle with performing a nostril breathing version of the Ocean Breath. In this respect, a proof-of-concept study could first be employed within a PoTS group to examine whether the performance of mouth or nostril versions of the intervention leads to significant differences in patients' observed physiological responses. Proxy measures of their underlying autonomic activity, through the examination of heart-rate variability during these procedures, may be employed as evidence that the intervention is capable of influencing PoTS

symptomology or to evidence their proposed autonomic explanatory models. Therefore, the undertaking of proof-of-concept breathing studies in people with PoTS would enable researchers and intervention developers to identify what breath-related techniques serve as the 'active ingredient(s)' and core mechanisms for instigating autonomic symptom relief.

3. Evaluation of Employed Methods & Analysis Strategies

Core limitations of each utilised research approach have previously been outlined within the method chapters describing the three adopted research methodologies within this thesis (see chapters 2, 5 and 8). Within the scoping review work, I acknowledged that whilst I had included a large variety of article types traditionally associated with grey literature for possible inclusion in my evidence synthesis- which included clinical trial registrations, conference publications, dissertations, consensus statements and clinical guidelines- a specific search of a grey literature database was not performed. As identified from my demographic findings, this is also a common critique within other review works into PoTS were only very few published reviews papers have performed this (such as Morgan et al., 2018). Further efforts are needed to improve the reporting standards across these collective works. Furthermore, within my undertaken narrative analysis of online PoTS vlog diagnostic stories - comprising of video originating from the USA, UK and Australia - I acknowledge that cultural differences in the healthcare systems of these countries may lead to differences in the core diagnostic events people with PoTS depict and emphasise in their narratives. At the time of identifying the vlog sample for my analysis, only a limited number of these videos existed online which had matched my employed video inclusion criteria. Larger samples of PoTS vlogs – including those collated across alternate social media platforms (in addition to YouTube) - are therefore needed to thoroughly assess these conclusions. In regards to my intervention development work, I acknowledge the impact which COVID-19 has had upon undertaken development process as a restriction for my thesis study. These issues caused significant delays to my research, through the need to amend my ethical approval and planned recruitment strategies in light of the pandemic. Whilst these events were unavertable, one silver lining from this was that people with PoTS and healthcare practitioners expressed that they had developed confidence towards the utility of online platforms for the delivery of the Ocean Breathing intervention, as a direct result of their own, personal experiences with using Microsoft Teams and Zoom programmes during the UK lockdown.

Finally, I acknowledge that, due to my decision to develop a PoTS intervention for adult patients, my intervention process has neglected children and adolescents who have a PoTS

diagnosis. It is interesting to consider the ways in which the development of a breathing intervention, and the undertaken research process for exploring this, may differ to the work I had done within my thesis. In addition to the need to secure additional ethical approvals and to identify different intended recruitment strategies for accessing these groups, the involvement of children and adolescents in research may have possibly led to a more simplified (or, quite possibly, even entirely different) version of intervention ontology or explanatory model being developed – due to the (assumed) likelihood that younger individuals may possess less knowledge towards the medical frameworks behind their PoTS. It therefore would be of great interest for further qualitative research to be carried out, in order to explore how children and adolescents alike communicate and convey understandings of their own PoTS to others.

4. Conclusion

To conclude, the aim of my thesis was to develop an Ocean Breathing intervention for a PoTS patient group. Through the undertaking of a large-scale scoping review of the existing published literature, I synthesised current knowledge and key clinical implications for PoTS to inform the basis of my intervention development process. Through the employment of narrative analyses to examine the diagnostic stories of people with PoTS shared within their online vlog stories, I advanced current insights within the PoTS research field by expanding upon the previously limited understandings of people with PoTS' endured symptom experiences. Through this line of work, my demonstrated findings that people with PoTS employ the use of socio-medical ontologies surrounding the autonomic nervous system to communicate understandings of their chronic illness experiences to others, served as a suitable explanatory model for supporting the application of the Ocean Breathing intervention to this patient group. Finally, from my intervention development work, I found that perceived issues of intervention coherence, collective action and cognitive participation with the Ocean Breath practice would hinder its future implementation to a PoTS patient group within its currently presented form. Additional studies - those including the use of mixed qualitative stakeholder groups and proof-of-concepts methods - are therefore needed to support the further development of this intervention and its perceived applications to a PoTS patient group.

Appendix A - Synthesis of Review Articles featuring Database Systematic Search & Meta-Analyses

Table 1. A table to present the Authors, Aims, Searched Databases, Search Terminology, Article Nature, Presentation of Findings, Analysis & Implications/ Future Research Directions for each article which featured a systematic database search strategy within the final subset. N = 11.

Author(s)	Aim(s) of Review	Database(s) Examined	Key Search Terminology	Nature of Articles Retrieved	Method for Presentation of Findings	Main Analysis Focus	Implications / Future Research
Butts et al. (2017)	To examine evidence for a causal relationship between Human Papillomavirus Vaccine and PoTS onset.	PubMed; MedScape	“POTS HPV”; “Postural Orthostatic Tachycardia Syndrome HPV Vaccine”	- 8 Case Reports / Series - 1 Brief Report - 1 Editorial - 2 Cohort Studies - 1 Analysis (Cluster) - 1 Review - Government and Medical Advisory Committee Statements / Reports (<i>quantity not specified</i>)	Tabular; Narrative	Tabular & Narrative description of peer-reviewed literature by article type	- No conclusive evidence found to support the existence of a causal relationship between PoTS and the HPV vaccine. - Future population-based studies are required to compare prevalence of PoTS in Adolescents who have received the HPV vaccine against non-vaccinated individuals.
Fedorowski (2019)	To define the Clinical Presentation, Aetiology & Management of PoTS	PubMed (<i>Jan 1993-August 2018</i>); <i>Hand searching</i>	Orthostatic Tachycardia; Postural Tachycardia; Postural (Orthostatic) Tachycardia Syndrome	No restrictions on article type specified within review	Narrative (Primarily); Tabular	Narrative description of PoTS features concerning: - Diagnostic Criteria	- Future research is needed to further explore the pathophysiology of PoTS. - More randomised controlled trials

						<ul style="list-style-type: none"> - Clinical Presentation - Cardiovascular Symptoms - Non-Cardiovascular Symptoms - Aetiology - Management <p>Tabular analysis of PoTS features, concerning:</p> <ul style="list-style-type: none"> - Diagnostic criteria - Clinical presentation - Associated autoantibody prevalence - Diagnostic tests - Treatments (non-pharmacological & pharmacological) 	needed to determine efficacy rates for individual PoTS treatments.
Gales & Gales (2007)	To examine whether Pyridostigmine is an effective treatment for orthostatic intolerance	MEDLINE; International Pharmaceutical Abstracts (1966- Dec 2006); <i>Hand-searching</i>	Pyridostigmine; Acetylcholine Inhibitor; Orthostatic Intolerance; (Neurogenic) Orthostatic Hypotension; Postural Tachycardia Syndrome; Tachycardia; Orthostatic Tachycardia.	Clinical Trials; Case Reports	Narrative	Narrative description of clinical trials and case studies for:	- Insufficient longitudinal evidence to support the routine administration of Pyridostigmine bromide for management of

				one longitudinal survey-based study. English articles only.		- Neurogenic Orthostatic Hypotension - Postural Tachycardia Syndrome (2 clinical trials; 1 case report)	PoTS symptomology. - Authors recommend this treatment be limited only to patients who are unresponsive to other OI treatment options.
Gee et al. (2018)	To evaluate the evidence for the efficacy and safety of Ivabradine in PoTS Treatment	MEDLINE (1956 – Aug 2017); EMBASE (1957 – 2017)	Postural Orthostatic Tachycardia Syndrome; Postural Tachycardia Syndrome; Chronic Orthostatic Intolerance; Ivabradine	Following article types concerning clinical outcomes of oral Ivabradine: - 2 Prospective open-label trials - 3 Retrospective cohort studies - 8 Case reports Non-English & Animal articles were excluded.	Tabular; Narrative	Tabular presentation of clinical studies concerned: - Study design - Participant number - Ivabradine dosage - Treatment duration - Outcome - Results - Adverse reactions Tabular presentation of Case Reports concerned: - Age; Sex - Ivabradine Dosage - Treatment Duration - Outcome	- Review was in favour of the use of Ivabradine for the management of PoTS symptoms and as a method of reducing heart rate. - Authors recommend an initial daily low dosage of 2.5 mg is provided to symptomatic patients twice a day - this can then be altered based on patients' needs. - To further understand the efficacy of Ivabradine for PoTS treatments, more placebo-controlled randomized

						<ul style="list-style-type: none"> - Adverse reactions - Case Notes <p>Narrative description of each article</p>	<p>controlled trials are needed.</p> <p>-More research also needed to compare this treatment against other pharmacological agents used for symptom management in PoTS (such as propranolol).</p>
Morgan et al. (2018)	<p>(i) Evaluate the quality of evidence available surrounding pre-existing PoTS in pregnancy;</p> <p>(ii) Explore current understandings of PoTS during Pregnancy;</p> <p>(iii) Identify future research directions</p>	<p>MEDLINE; EMBASE; PsychInfo; CINAHL; Cochrane Library; <i>hand-searching</i></p> <p>www.clinicaltrials.gov;</p> <p>www.dyautonomiainternational.org;</p> <p>www.potsuk.org</p>	<p>Postural tachycardia syndrome; postural orthostatic tachycardia syndrome; orthostatic intolerance; Pregnancy</p>	<ul style="list-style-type: none"> - 8 Case Reports (each concerning 1 – 7 patients) - 1 Self-reported questionnaire; longitudinal follow-up - 2 Retrospective chart reviews (one case report also featured a retrospective chart review) 	<p>Tabular; Narrative; Quality Assessment & Evidence Appraisal</p>	<p>Quality Assessment – <i>McMasters Critical Review Form for Quantitative Studies</i></p> <p>Evidence Appraisal – <i>National Health and Medical Research Council (NHMRC) Evidence Grading Matrix</i></p>	<ul style="list-style-type: none"> - No articles reviewed explored the patients' experience. Further research is needed to explore this in an effort for identifying patient-centered priorities during antenatal and postnatal care, in addition to help establish guidelines for clinicians / patients. - Many medications used for the treatment of PoTS have not been sufficiently explored for their safety in pregnant women.

							<ul style="list-style-type: none"> - The quality of the final article subset was rated favourable with the McMasters criteria. - However, a poor NHMRC score was allocated - due the majority of articles being case reports with small patient samples.
Brady et al. (2005)	To provide a broad overview of Inappropriate Sinus Tachycardia Syndrome (IAST), PoTS and Overlapping Syndromes	MEDLINE (- 2005).	Inappropriate Sinus Tachycardia Syndrome; Postural Orthostatic Tachycardia Syndrome; chronic orthostatic fatigue syndrome	<ul style="list-style-type: none"> No restrictions on article type specified within review English-only articles included 	<ul style="list-style-type: none"> Narrative (Primarily); Tabular 	<ul style="list-style-type: none"> Narrative analysis concerned: <ul style="list-style-type: none"> - Definition and Diagnosis of IAST + POTS - Therapy and Management Tabular analysis concerned: <ul style="list-style-type: none"> - Definition, Clinical Presentation + Proposed Mechanisms of examined conditions - Autonomic Reflex Screening Techniques 	<ul style="list-style-type: none"> - Further examination of psychological status should be undertaken in patients with psychosomatic resulting from both conditions. - Other identified future research directions are IAST-specific.

Benarroch (2012)	To synthesise and provide a broad overview on what is known about PoTS.	PubMed (Jan 1990 – June 2012); <i>Handsearching</i>	POTS; Postural Tachycardia Syndrome; Orthostatic; Orthostatic; Syncope; Sympathetic; Baroreceptors; Vestibul sympathetic; Hypovolemia; Visceral Pain; Chronic Fatigue; Deconditioning; Headache; Chiari Malformation; Ehlers-Danlos; Emotion; Amygdala; Insula; Anterior Cingulate; Periaqueductal Gray; Fludrocortisone; Midodrine; Propranolol; B-Adrenergic; Pyridostigmine	No restrictions on article type specified within review	Narrative	Narrative analysis concerned: - Orthostatic intolerance symptoms in PoTS - Subtypes - Comorbidities & Pathophysiology - Evaluation & Management - Treatment Resistance / Intolerance	- Article lacks clear directions for future research; aim to synthesise what is known about PoTS and to provide an overview of this. - Authors highlight the importance of understanding the contribution of psychological factors, deconditioning and poor sleep to a dominance of sympathetic nervous system in PoTS.
Roma et al. (2018)	To review literature exploring the overlap between joint hypermobility and orthostatic intolerance.	PubMed (1988- Sept. 2017); EMBASE (1988- Sept. 2017); <i>Handsearching</i>	Ehler-Danlos syndrome; joint hypermobility; orthostatic; hypotension; tachycardia; syncope; autonomic.	Excluded abstracts, review articles and letters to editors which did not contain primary data or a single case report concerning joint-hypermobility/ EDS with pain, gastrointestinal, orthopaedic, headache, psychiatric or obstetrical disorders.	Narrative	Narrative review pertaining to: Overview of EDS; Association between Orthostatic Intolerance and circulatory dysfunction in JH/EDS; Justification of screening orthostatic intolerance for EDS/JH.	- Screening for EDS/ JH in PoTS and Orthostatic Intolerance patients can improve the management of an individual by a clinical team, detect rare forms of the condition and ensures appropriate physical therapy is prescribed during the treatment plan. - Researchers should also screen

							PoTS / Orthostatic Intolerance patients to ensure the characteristics of their participant sample are fully described, reduce biased assignment within pathophysiology studies, prevent individuals who are likely to be non-respondent to a treatment from taking part in an intervention study, and to avoid drawing non-causal conclusions from their research.
Ruzieh et al. (2017)	To review literature surrounding autoimmunity and orthostatic intolerance syndromes.	PubMed; Medline; EMBASE; <i>Handsearching</i>	Not specified	Not specified – review examined studies exploring antibodies in orthostatic intolerance syndromes.	Narrative; Tabular	Tabular analysis of empirical studies by: Author(s), Year, Patient Group(S), Receptor-Associated Autoantibodies Examined & % of Sample Groups who are positive for autoantibody. Second Tabular analysis for	- Evidence supports the notion that onset of orthostatic intolerance may occur due to cholinergic and adrenergic autoantibodies. - There is a lack of large-scale controlled studies which have been undertaken to examine an autoimmune basis

						empirical studies on cholinergic autoantibodies following the same format (with comments).	for PoTS and other OI disorders. - Further research is needed to explore whether treatment response in orthostatic intolerance disorders may tolerate with the type of autoantibodies possessed by the patient.
Ruzieh & Grubb (2018)	To synthesis literature relating to the management of PoTS during pregnancy and obstetric settings.	PubMED; Medline; Embase- (all 1970 – 2017); <i>Handsearching</i>	Not specified	Exclusion criteria not specified – authors retrieved studies on PoTS & pregnancy	Narrative	Narrative review of PoTS literature on pregnancy, recommendations by the authors for how the condition has been managed - both intrapartum & post-partum	- Clinical use of anaesthesia use should be based solely on the obstetrical/ surgical reasoning – not due to patient's PoTS. - More research is needed to explore outcomes for PoTS patients who undergo a pregnancy.
Xu, Jin & Du (2016)	Review on the pathogenesis of PoTS and the progress of individualised treatment approaches in	PubMED; Embase	Not Specified	Original research papers & Critical Reviews	Narrative	Narrative review concerning the pathogenesis (low blood volume; high catecholamine levels; abnormal vascular	- Further large-scale, multicentre research is needed to examine the underlying pathophysiology of PoTS.

Children /
Adolescents

tension;
reduced skeletal
muscle pump
activity) &
individualised
treatments (oral
rehydration
salts; beta-
blocker therapy;
alpha-
adrenoreceptor
agonists) for
PoTS in
children/
adolescents.

- Further non-
invasive and
simplistic non-
pharmacological
treatments for
PoTS need to be
identified for
children and
adolescent
samples.

Table 2. Tabular overview presenting the Authors, Aims, Searched Databases, Search Terminology, Review Article Breakdown, Examined Participant Group, Intervention(s), Outcomes, Major Findings & Implications for each **systematic review & meta-analysis** article within the final subset. N = 3.

Author(s)	Aim(s) of Review	Database(s) Examined	Key Search Terminology	Summary of Studies Examined	Participant Group(s) Examined	Intervention Examined	Outcome(s)	Major Findings / Implications
Deng et al. (2019)	To undertake a systematic review and meta-analysis of Beta-Blocker therapy (Metoprolol) in Child-Adolescent PoTS patients.	PubMed; Embase; Cochrane Library; Sinomed; <i>Hand-referencing (one article)</i> English and Chinese papers were eligible for inclusion.	“Postural tachycardia syndrome”; “postural orthostatic tachycardia syndrome”; “POTS”; “treatment”; “therapy”; “intervention”; “management”; “βblocker”; “metoprolol”; “propranolol”; “betalocatenolol”	- 4 RCT Studies - 4 Non-RCT Studies	PoTS patients diagnosed through HUT, aged younger than 20. Exclusion criteria – patients with systemic diseases, metabolic disturbances and cardiogenic diseases.	Orally-administered Beta-blockers compared against a standard/conventional treatment, assessed for at least 1 month.	- Effectiveness rate, defined as the ratio of participants with symptoms relieved following treatment. - Change in heart rate; Winker Symptom Score; Heart Rate Change on HUT; Adverse Reactions.	- Groups who received metoprolol displayed significantly better effective rates at the end of short-term follow-up than controls. - Five studies where difference in heart rate was measured showed a significantly greater heart rate reduction in metoprolol groups than controls. - Six studies which examined symptom score showed significantly greater improvement in metoprolol groups than controls. - Seven articles reporting adverse effects found no

								severe adverse effects were reported; all participants reporting adverse events completed treatment.
Swai et al. (2019)	To examined studies which have compared Heart Rate and Heart Rate Variability in PoTS vs. Controls following HUT.	Medline (PubMed Interphase) ; EMBASE; SCOPUS; <i>Handsearching</i> . English papers were only eligible for inclusion.	"Postural Orthostatic Tachycardia Syndrome"; "Heart Rate"; "Variability"	20 Case-control Observational Studies	Patients with PoTS, compared against a healthy control group.	N/A	- Heart Rate - Heart-Rate Variability [HRV], assessed through Frequency Domain Measures (FDM) & Time Domain Measures (TDM)	- From 18 studies, heart rate was significantly greater in the PoTS patient group than controls. - From three studies, mean R-R interval rate (HRV) was significantly lower in PoTS groups. - From all studies, root of the mean of squares of successive R-R interval differences (rMSSD) signified significantly lowered HRV in the PoTS patient groups. - PoTS and control groups did not significantly differ on low-frequency (n = 5) or high-frequency (n = 7) power HRV – however, trends for both outcomes suggested PoTS patient may have

								had reduced variability.
								- PoTS and control groups did not significantly differ on low-frequency power-normalized unit (n = 4), high-frequency power-normalized unit (n = 4) or low frequency power /high frequency power ratio (n = 5).
Wells et al. (2018)	To identify and evaluate the evidence base for PoTS therapies for volume expansion & heart rate reductions.	CENTRAL; PubMed; Embase	"Postural"; "Tachycardia"; "Syndrome"	- 25 Case Series - 3 Small-Scale RCTs Studies included have 4 or more participants.	PoTS patients – both child/ adolescent and adult samples.	Any PoTS intervention were the outcomes can be related to a specific treatment method, and the intervention effects has been examined longer than a 24 hour period.	Efficacy rate, defined as the proportion of responders within each study cohort.	- Intravascular volume efficacy, assessed within five articles, was found to have a 53%-93% efficacy rate. - Vasopressor therapy, assessed within three articles focussing on Midodrine, was found to have a 66% efficacy rate. - Heart rate reduction - assessed within six articles examining cardioselective beta-blockers, was found to have a 60% efficacy rate.

- Heart rate reduction
- assessed within two articles examining non-cardioselective beta-blockers, was found to have a 51% efficacy rate.

- Heart rate reduction
- assessed within two articles examining ivabradine, was found to have a 64% efficacy rate.

Appendix B: Tabular & Narrative Syntheses – All PoTS Case Reports

Table 1. Overview of PoTS patient Case Reports & Series captured by the employed search strategy (N. of Individual Cases = 99).

Authors (Year)	Age	Gender	Notable Diagnoses / Co-morbidities	Primary Test to Establish PoTS Diagnosis <i>(Tilt-Table, Standing)</i>	Additional Performed Autonomic Tests <i>(Valsalva, QSART, Deep Breathing)</i>	Psychometric Assessments Undertaken	Pharmacological Treatments Attempted by Patient	Non-Pharmacological / Surgical Treatments Attempted
Rosen and Cryer (1982)	32	Female	PoTS, Diabetes Mellitus	Standing	Non-Specified	Non-Specified	Fludrocortisone	Sodium Loading
Sumiyoshi et al. (1999)	16	Male	PoTS	Tilt-Table	Non-Specified	Non-Specified	Midodrine Propranolol	Non-Specified
Kishi et al. (2001)	28	Female	PoTS, Anorexia	Tilt-Table	Valsalva QSART Deep Breathing	Non-Specified	Saline Infusion Midodrine Hydrochloride	Non-Specified
Nogués, Delorme, Saadi, Heidel and Benarroch (2001)	45	Female	PoTS	Tilt-Table	Valsalva Deep Breathing	Non-Specified	Benzodiazepines Domperidone Chlorpromazine Atenolol Fludrocortisone	Non-Specified
O'Leary, Smith, Erickson, Eidelman and Chancellor (2002)	31	Female	PoTS, Sepsis <i>(experienced following a stillbirth)</i>	Tilt-Table	Thermoregulatory-Sweat	Non-Specified	Postoperative Treatments: Verapamil Calcium Chloride Three Years Following Operation: Oral Anticholinergic Drugs	Timed Voiding

Seeck, Blanke and Zaim (2002)	20	Female	PoTS, Right Temporal Epilepsy, Dissociative Disorder	Tilt-Table	Non-Specified	Non-Specified	Carbamazepine Metoprolol Bisoprolol	Non-Specified
Morishima et al. (2004)	26	Male	PoTS, Brugada Syndrome	Tilt-Table	Non-Specified	Non-Specified	Midodrine	Implantable Cardiovascular Defibrillator (<i>offered to patient but ultimately refused</i>)
Glatter, Tuteja, Chiamvmonvat, Hamdan and Park (2005)	26	Female	PoTS, Morbid Obesity, Pregnant	Tilt-Table (Pre-existing PoTS Diagnosis)	Non-Specified	Non-Specified	Midodrine	Early Elective Pregnancy (<i>induced through Cesarean Section</i>)
	24	Female	PoTS, Pregnant	Tilt-Table (Pre-existing PoTS Diagnosis)	Non-Specified	Non-Specified	Unmedicated (<i>prior response to Midodrine & Beta-Blocker Therapy unsuccessful</i>)	Early Elective Pregnancy (<i>induced through Cesarean Section</i>)
Prilipko, Dehadast, Zaim and Seeck (2005)	42	Female	PoTS, Chiari Type-1 Malformation	Standing	Non-Specified	Non-Specified	Non-Specified	Surgical Osteodural Decompression with Posterior Fossa Craniectomy, C1 Laminectomy, Dissection of Arachnoid Adhesion, Duroplasty

Corbett, Reiter, Schultz, Kanter and Habib (2006)	30	Female	PoTS (Hyperadrenergic), Pregnant (39 weeks), Mitral Valve Prolapse	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Non-Specified	Metoprolol	Anaesthesia (to control tachycardia during childbirth)
Balasundaram and Blake (2007)	41	Male	PoTS	Tilt-Table (GTN Provocation)	Non-Specified	Non-Specified	Beta-Blocker Therapy	Increased Salt Intake, Management of Work Shift Pattern
	21	Female	PoTS, Asthma	Tilt-Table (GTN Provocation)	Non-Specified	Non-Specified	Becotide Salbutamol	Increased Salt Intake
	43	Female	PoTS	Tilt-Table (GTN Provocation)	Non-Specified	Non-Specified	Metoprolol	Increased Salt & Fluid Intake
Ewan, Norton and Newton (2007)	15	Female	PoTS, Chronic Fatigue Syndrome, Asthma	Standing	Non-Specified	Fatigue Impact Scale, Orthostatic Grading Scale	Ivabradine	Non-Specified
Grubb and Karabin (2007)	25	Female	PoTS, Lightning-related Injury	Tilt-Table	Non-Specified	Non-Specified	Modafinil Erythropoietin	Non-Specified
	18	Female	PoTS, Lightning-related Injury	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Midodrine Fluxetine	Non-Specified
Russo, De Crecenzo, Ammendola,	36	Male	PoTS	Tilt-Table	Non-Specified	Beck Anxiety Inventory	Atenolol	Weight Loss Advised, Increased Fluid Intake

Santangelo and Calabrò (2007)								
Abdelmoneim, Moustafa and Mookadam (2008)	59	Female	PoTS, Degenerative Spine Spondylosis	Tilt-Table	Valsalva QSART Deep Breathing	Non-Specified	Beta-Blocker Therapy Imipramine (Low-Dose) Calcium Channel Blockers Sublingual Nitrates	Advised to avoid PoTS precipitating factors
Carew et al. (2008)	21	Female	PoTS, Vasovagal Syncope	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	Non-Specified
Lelonek and Goch (2008)	27	Male	PoTS, Labile Hypertension	Tilt-Table	Non-Specified	Non-Specified	Metoprolol, Anti-Anxiety Medication, Moxodine Betaxolol	Non-Specified
Graham and Ritchie (2009)	20	Female	PoTS, Diabetes Mellitus(Type I)	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone, Bisoprolol	Increased Salt & Water Intake, Advised to Drink Cold Water at Start of PoTS Episodes
Kanjwal, Karabin, Kanjwal and Grubb (2009)	37	Female	PoTS, Joint Hypermobility Syndrome	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Midodrine Methylphenidate Duloxetine Cerefolin	Non-Specified

Khan, Hamid and Rinaldi (2009)	44	Female	PoTS (pre-existing), Raynaud's Syndrome	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Non-Specified	Diltiazem Ivabradine	Non-Specified
Kanjwal, Karabin, Kanjwal and Grubb (2010)	62	Male	PoTS (following Electrical Injury)	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Midodrine Methylphenidate Duloxetine Pyridostigmine	Non-Specified
	43	Male	PoTS (following Electrical Injury)	Tilt-Table	Non-Specified	Non-Specified	Midodrine Pyridostigmine Propranolol	Non-Specified
Kernan and Tobias (2010)	17	Female	PoTS, Scoliosis	Tilt-Table	Non-Specified	Non-Specified	Midodrine Metoprolol During Surgery: Esomol + Metoprolol (to treat tachycardia) Phenylephrine (to combat hypotension)	Non-Specified
Kimpinski, Iodice and Low (2010)	26	Female	PoTS, Peripartum Cardiomyopathy	Tilt-Table	Valsalva Deep Breathing	Composite Autonomic Symptom Severity Scale	Beta-Blocker Therapy Midodrine Nadolol	Increased Fluid & Salt Intake, Increased Exercise
Pande, Tan and Lee (2011)	37	Male	PoTS, Brain Injury	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	Physical Rehabilitation, Cognitive Rehabilitation, Increased Water Intake

Johnson, Bonnicksen, Julsrud, Burkhart and Hagler (2011)	16	Female	PoTS, Convulsive Syncope, Neuro-cardiogenic Syncope	Not Specified (Pre-Existing PoTS Diagnosis)	Tilt-Table	Non-Specified	Midodrine Propranolol	Increased Salt & Water Intake, Reveal Loop Recorder
Nakatani, Mizumaki, Nishida and Inoue (2011)	42	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Ivabradine	Catheter Ablation, Atrioventricular Node Ablation, Dual Chamber Pacemaker Implantation
Fernex et al. (2012)	29	Male	PoTS, Aortic Coarctation, Upper Airway Resistance Syndrome	Tilt-Table	Non-Specified	Epworth Sleepiness Scale, Fatigue Severity Scale, Beck Depression Inventory	Venlafaxine Amlodipine Vasartan Aspirin Propranolol	Exercise Rehabilitation Programme, Increased Salt & Liquid intake
Gaw et al. (2012)	23	Female	PoTS, Mitral Valve Prolapse, Bipolar Disorder, Intermittent Chest Pain	Tilt-Table	Valsalva (Ratio)	Non-Specified	Non-Specified	Non-Specified

Škerk, Pintarić, Delić-Brkljačić, Popović (2012)	28	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	'Orthostatic Home Training', Management of Salt & Fluid Intake
Yun, Choi and Oh (2013)	51	Female	PoTS, Migraine, Fibromyalgia	Tilt-Table	Valsalva QSART Deep Breathing	ACR Criteria 2010, Widespread Pain Index, Symptom Severity Scale, Fibromyalgia Impact Questionnaire , Beck Depression Inventory	Topiramate, Antidepressants, Antiepileptic GABA Medication, Propranolol, Midodrine, Fludrocortisone	Increased Salt & Water Intake, Aerobic Exercise, Compression Garments
Giesken and Collins (2013)	46	Female	PoTS (Hyperadrenergic)	Tilt-Table	QSART	Non-Specified	Metoprolol Lamotrigine Escitalopram	Increased Salt & Water Intake, Increased Exercise
Sidhu, Obiechina, Rattu and Mitra (2013)	37	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Propranolol Sertraline Midodrine	Non-Specified
	33	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	Avoidance of Triggers (prolonged standing), Increased Fluid Intake

Su, Lee, Gunn and Jefferies (2013)	15	Male	PoTS, Diabetes Mellitus (Type I)	Standing	Non-Specified	Non-Specified	Fludrocortisone	Increased Fluid & Sodium Intake; Increased Potassium Intake; Increase Exercise
Clark and Davis (2013)	13	Female	'Pan-Autonomic Nervous System Failure' (including PoTS, Gastroparesis)	Tilt-Table	Non-Specified	Non-Specified	Intravenous Methylprednisolone, Intravenous Immunoglobulin Therapy	Non-Specified
Landero (2014)	22	Female	PoTS, ADHD, Chronic Anemia	Tilt-Table	Non-Specified	Non-Specified	Beta-Blocker Therapy, Anxiolytics, Volume Expansion Medication, Losartan Multivitamins	Non-Specified
Berganzo, Tijero, Zarranz and Gomez-Esteban (2014)	17	Female	PoTS, Joint-Hypermobility	Tilt-Table	Non-Specified	Beighton Scoring Scale	Non-Specified	Non-Specified
Blitshteyn (2014)	20	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Pyridostigmine Bupropion Modafinill	Increased Salt & Fluid Intake
	22	Female	PoTS	Tilt-Table	Valsalva QSART	Non-Specified	Midodrine Fludrocortisone	Increased Salt & Fluid Intake

	12	Female	PoTS	Standing	Non-Specified	Non-Specified	Fludrocortisone	High Salt Diet
	15	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Sertraline	Non-Specified
	14	Female	PoTS	Tilt-Table	Valsalva QSART Deep Breathing	Non-Specified	Metoprolol Amitriptyline	Non-Specified
	18	Female	PoTS	Standing	Non-Specified	Non-Specified	Duloxetine Doxepin	Non-Specified
Kinoshita et al. (2014)	13	Female	PoTS, Complex Regional Pain Syndrome	Standing	Non-Specified	Non-Specified	Gardasil NSAIDs Bisoprolol Fumarate	Non-Specified
	15	Female	PoTS, Complex Regional Pain Syndrome	Standing	Non-Specified	WAIS-III	Gardasil Limaprost Alfadex	Non-Specified
Popatia and Subramaniam (2014)	16	Female	PoTS, Tourette's Syndrome	Not Specified	Standing Test	Non-Specified	Fludrocortisone	Salt Supplementation, Compression Stockings, Supervised Exercise
Zundel, Pattyn, Chelimsky, Riess (2015)	32	Male	PoTS, Chronic Fatigue Syndrome	Tilt-Table	Standing Test (to examine arterial waveform changes)	Non-Specified	Beta-Blocker Therapy Midodrine Fludrocortisone	Regular Caffeine Intake in Diet

Abdulla and Rajeevan (2015)	70	Female	PoTS, Polymyalgia Rheumatica, Hypertension, Anxiety	Tilt-Table	Non-Specified	Non-Specified	Propranolol	Non-Specified
Bruce et al. (2015)	19	Male	PoTS, Dysphagia, Depression, Panic disorder	Tilt-Table	Non-Specified	Functional-Disability Index, Center for Epidemiologic al studies-Depression-Children-Scale, Psychiatric Evaluation	Citalopram Oxybutynin, Mylanta Lidocaine, Ondansetron Loratadine	Non-Specified
Grigoriou, Boris and Dormans (2015)	13	Male	PoTS, Ehler-Danlos Syndrome	Standing	Non-Specified	Non-Specified	Metoprolol, Fludrocortisone, Pyridostigmine	Patient & Family Education, Education of Dietary Changes, Physical Exercise Therapy, Boston Overlap LSO Brace, Occupational Therapy
	17	Female	PoTS, L1 Vertebral Hemangioma	Standing	Non-Specified	Non-Specified	Methylphenidate Meclizine Ondansetron Gabapentin Tizanidine	Patient & Family Education, Education of Dietary Changes, Physical Exercise Therapy

Khan, Ouyang, Perkins, Somauroo and Joseph (2015)	24	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Bisoprolol Paroxetine Midodrine Ivabradine Octreotide (via Insulin Pump)	Increased Salt & Fluid Intake
Khan, Ouyang, Perkins, Somauroo and Joseph (2015)	14	Female	PoTS, Depression	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Midodrine Octreotide (via Insulin Pump)	Increased Salt & Fluid Intake
Lida and Haeri (2015)	34	Female	PoTS, Pregnant	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Non-Specified	Propranolol	Non-Specified
	26	Female	PoTS, Pregnant	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Non-Specified	Fludrocortisone Propranolol	Non-Specified
Meyer et al. (2015)	19	Female	PoTS (Hyperadrenergic), Diabetes Mellitus (Type I), Post-Traumatic Stress Disorder	Tilt-Table	Deep Breathing	Non-Specified	Ivabradine	Psycho-Social Support
Noyes and Kluger (2015)	37	Female	PoTS	Standing (supported by electrophysiological data)	Non-Specified	Non-Specified	Propranolol	Increased Water Intake (9 Glasses per Day)

	17	Female	PoTS, Acne, Scoliosis	Tilt-Table	Non-Specified	Non-Specified	Midodrine	Educated about Dietary Changes (Gluten Free), Increased Water Intake (One glass every 2 hours; 10 in total), Advised to begin Exercise Routine
Adamec, Bilić, Lovrić, and Habek (2016)	18	Male	PoTS, Chronic Inflammatory Demyelinating Polyneuropathy	Tilt-Table	Valsalva Deep Breathing	Non-Specified	Intravenous immunoglobulin, Fludrocortisone	Non-Specified
Baldwin, Murray, Garcia & Bateman (2016)	34	Male	PoTS, Asthma, Chronic Fatigue Syndrome, Fibromyalgia, Irritable Bowel Syndrome	Other (<i>Orthostatic Heart Rate Increase Observed from Patient Adopting a 45° Position in Bed</i>)	Non-Specified	Beck- Depression Inventory; Beck-Anxiety Inventory	Hydrocortisone (Low- Dose), Fludrocortisone, Midodrine, Propranolol, Desmopressin, Bupropion, Escitalopram, Vortioxetine	Compression Garments, Increased Salt and Fluid Intake
Blitshteyn and Brook (2016)	18	Female	PoTS, Chronic Fatigue Syndrome	Tilt-Table	Valsalva QSART Deep Breathing	Non-Specified	Plasmapheresis (5 treatments), Prednisone	Non-Specified
Brock et al. (2016)	65	Female	PoTS, Sjorgren's Syndrome, Hypertension,	Tilt-Table	Non-Specified	Karnofsky Score	Propranolol	High Salt Diet, Increased Fluid Intake, Bilateral T2 Sympatholysis, Neurolysis

Oztunc, Atik, Dedeoglu, Alp and Gokalp (2016)	13	Female	Chronic Non-Specific Back Pain, Chronic Fatigue Syndrome, Depression PoTS, Homocystinuria	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	Increased Fluid Intake, Avoid Dehydration, Avoidance of PoTS Triggers
	17	Female	PoTS, Raynard's Syndrome	Tilt-Table	Non-Specified	Non-Specified	Metoprolol Ivabradine	Non-Specified
Pohlgeers and Stumbo (2016)	21	Female	Mononucleosis-Induced Postural Tachycardia Syndrome	Tilt-Table	Non-Specified	Non-Specified	Ondansetron, Ibuprofen, Promethazine, Intramuscular Ketorolac	Increased Salt & Fluid Intake
Ralston and Kanzler (2016)	40	Female	PoTS, ' <i>Adjustment Disorder with Anxiety</i> ', ' <i>Psychological Symptoms affecting a General Medical Condition</i> '	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Beck Anxiety Inventory, SF-36, Subjective Units of Distress Scale, Psychiatric Evaluation performed by Health	Fludrocortisone, Pseudoephedrine, Diazepam, Magnesium Supplements, Four Fluid & Electrolyte Infusions in Hospital	Non-Specified

						Psychology Clinic		
Tito and Hess (2017)	18	Female	PoTS	Not Specified (Pre-Existing PoTS Diagnosis upon Referral)	Non-Specified	WHO-QOL- Brief Questionnaire	Bystolic Fluoracortisone Nuun Tablets	Lower Limb Compression Garments, Aquatic Therapy,
Mohr (2017)	19	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Midodrine	Diet Changes, Increased Exercise, Psychiatric Treatment
Marrow (2017)	20	Female	PoTS, Chronic Migraines	Not Specified (Pre-Existing PoTS Diagnosis upon Surgery Referral)	Non-Specified	Non-Specified	Fludrocortisone, Ivabradine, Midodrine, Sertraline, Pyridostigmine, Ferrous Sulfate, Magnesium, Oral Contraceptives	Arthroscopic Anterior Cruciate Ligament (ACL) Repair of the Right Knee
Richardson, Nordon-Craft and Carrothers (2017)	34	Female	PoTS	Standing	Non-Specified	Non-Specified	Cefdinir, Prednisolone, Claritin D (OTC), Mucinex DM	Sodium Supplements, Regular Exercise, Increased Fluid Intake, Dietary/Nutrition Changes (Restriction of Alcohol & Caffeine),

								Physical Aerobic Training Therapy, Strengthening Therapy
Tomichi et al. (2018)	24	Male	PoTS, Diabetes Mellitus(Type II)	Tilt-Table	Non-Specified	Non-Specified	Propranolol	Non-Specified
Tripathi and Bernitsas (2018)	30	Female	PoTS, Radiology Isolated Syndrome	Tilt-Table	Non-Specified	Non-Specified	Metoprolol Spironolactone Glatiramer Acetate	Non-Specified
Weinstock, Brook, Myers and Goodman (2018)	43	Female	PoTS, Mast Cell Activation Syndrome, Restless Leg Syndrome	Tilt-Table	QSART	Non-Specified	Midodrine, Amphetamine, Droxidopa, Cromolyn Sodium, Monteleukast, Antihistamines, Acetylsalicylic Acid, Low-dose Naltrexone, Intravenous immunoglobulin, Rifaxin	Support Stockings
Kim, During and Miglis (2018)	18	Female	PoTS, ADHD, Anxiety, Narcolepsy Type II, Inappropriate Sinus Tachycardia, Amygdala and Thalamus Lesions	Tilt-Table	Valsalva QSART Deep Breathing	Epworth Sleepiness Scale	Sustained-Release Amphetamine-Deoxstroamphetamine, Sertraline, Prednisone, Modafinil, Sodium Oxybate, Propranolol	Non-Specified

Mayuga, Ho, Shields, Cremer and Rodriguez (2018)	36	Female	PoTS	Tilt-Table	Valsalva QSART	Non-Specified	Fludrocortisone	Cardiac Surgery (Septal Mycetomy)
Schofield and Hendrickson (2018)	11	Female	PoTS (Neuropathic), Alopecia, Raynaud's Syndrome, Neuro-cardiogenic Syncope	Tilt-Table	Valsalva	COMPASS-31	Intravenous Immunoglobulin Therapy	Conservative Therapy
Tomljenovic, Colafrancesco and Perricone (2019)	14	Female	PoTS, Raynaud's Syndrome, Vasovagal Syncope, Chronic Fatigue Syndrome	Standing	Non-Specified	Psychiatric Evaluation	Non-Specified	Non-Specified
Varriale, Greco, De Simone, Pozzessere and Stagi (2019)	8	Male	PoTS, Vasovagal Syncope	Tilt-Table	Non-Specified	Non-Specified	Midodrine Hydrochloride, Fludrocortisone, Acetate	Non-Specified
Kato et al. (2019)	53	Female	PoTS, Spontaneous Intracranial Hypotension, Tinnitus	Standing	Non-Specified	Non-Specified	Saline Infusion, Theophylline	Compression Garments, Increased Salt & Water, Epidural Blood Patch

van der Zalm et al. (2019a)	24	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Propranolol Fludrocortisone Modafinil Desmopressin	Increased Salt & Water Intake, Compression Garments, Exercise, Psychological Therapy
van der Zalm et al. (2019b)	44	Male	PoTS	Tilt-Table	Non-Specified	Non-Specified	Non-Specified	Increased Water Intake Salt Tablets
Harding, Hyndman and Burns (2019)	37	Female	PoTS, Pregnant, Pneumonia	Standing	Non-Specified	Non-Specified	Phenylephrine Infusion Metaraminol (during-birth) Intravenous Oxytocin	Non-Specified
Boris, McClain and Bernadzikowski (2019)	16 (Age at Diagnosis - 2014)	Natal Female identify -ing as Male	PoTS, Gender Dysphoria, Hypermobility Ehlers–Danlos Syndrome, Asthma (Exercise-Induced), Overweight	Standing	Non-Specified	Non-Specified	Cyclobenzaprine Ibuprofen Naproxen Cyproheptadine Fludrocortisone Pregabalin Midodrine Desmopressin Duoxetine Metoprolol Testosterone Therapy	Non-Specified
	17 (Age at Diagnosis - 2017)	Natal Female identify -ing as Male	PoTS, Gender Dysphoria, Attention Deficit Disorder with Hyperactivity, Bipolar Disorder,	Standing	Non-Specified	Non-Specified	Strattera Trazodone Albuterol Quetiapine Atomoxetine Cyproheptadine, Fludrocortisone Pyridostigmine	Physical Therapy For Education For Joint Protection and Stabilization, Exercise Therapy For Pots, Salt Capsules

			Exercise-Induced Asthma, Hypermobile Ehlers–Danlos Syndrome, Obsessive-Compulsive Disorder				Desmopressin Midodrine (Low Dose) Testosterone Therapy	
	16 (Age at Diagnosis - 2015)	Natal Female identifying as Male	PoTS Gender Dysphoria, Anxiety Disorder, Obsessive-Compulsive Disorder, Depression, Hashimoto's Thyroiditis, Bicuspid Aortic Valve with Trivial Aortic Valve Insufficiency, No Stenosis, Juvenile Idiopathic Arthritis	Standing	Non-Specified	Non-Specified	Albuterol, Azelastine, Diclofenac, Fludrocortisone, Fluoxetine, Fluticasone/Salmeterol, Folic Acid, Gabapentin, Levothyroxine, Melatonin, Methotrexate, Ranitidine, Tramadol, Zolmitriptan, Lansoprazole, Desmopressin, Methylphenidate, Midodrine Testosterone Therapy	Salt Tablets, Exercise Protocol for PoTS
Cheema, Zain, Ullah and Cheema (2019)	19	Female	PoTS	Tilt-Table	Non-Specified	Non-Specified	Fludrocortisone Ivabradine	Increased Sat & Fluid

Del Pozzi, Enechukwu and Svetlana (2019)	29	Male	PoTS	Tilt-Table	Non-Specified	Non-Specified	Beta-Blocker Therapy	Avoidance of PoTS Triggers, Increased Salt & Water Intake
Loughan, Hertz and Perna (2019)	22	Female	PoTS, Anxiety, Depression, Bipolar Disorder, Agoraphobia, Hyperthyroidism, Gastroesophageal Reflux Disease	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Judgement of Line Orientation, Boston Naming Test, California Verbal Learning Test, Delis-Kaplan Executive Functioning System, Wisconsin Card-Sorting Task, Hooper Test of Visual Organisation, Multilingual Aphasia Examination - Token Test, Personality Assessment Inventory, WAIS-IV, WMS-IV, Wechsler Test of Adult Reading, Word Memory Test,	Duloxetine, Fludrocortisone, Pyridostigmine Bromide, Esomeprazole Magnesium, Quetiapine Fumarate, Levothyroxine Sodium, Metoprolol Succinate, Bupropion	Non-Specified

					Beck Depression Inventory II, Beck Anxiety Inventory		
19	Female	PoTS, ADHD, Ehlers-Danlos Syndrome (Type III), Fibromyalgia, Hypothyroidism	Not Specified (Pre-Existing PoTS Diagnosis)	Non-Specified	Judgement of Line Orientation, Boston Naming Test, California Verbal Learning Test, Delis-Kaplan Executive Functioning System, Wisconsin Card-Sorting Task, Hooper Test of Visual Organisation, Multilingual Aphasia Examination - Token Test, Personality Assessment Inventory, WAIS-IV, WMS-IV, Weschler Test of Adult Reading,	Dextroamphetamine, Modafinil, Sumatriptan, Topiramate, Duloxetine, Levothyroxine, Promethazine, Celecoxib, Norethindrone + Ethinyl Estradiol, Ibuprofen, Gabapentin, Ciprofloxacin, Multivitamin, Hydroxyzine, Oxycodone	Non-Specified

						Word Memory Test, Beck Depression Inventory II, Beck Anxiety Inventory		
Umapathi et al. (2020)	39	Male	PoTS, COVID-19, Acute Hyperhidrosis, Diabetes Mellitus, Right Leg Ischemia	Tilt-Table & Standing	Non-Specified	Non-Specified	Remdesivir Amlodipine Insulin Metformin Fludrocortisone Pyridostigmine	Embolectomy & Endovascular Repair, Salt Tablets
Dani et al. (2020)	26	Female	Post-Viral PoTS, COVID-19	Unknown	Non-Specified	Non-Specified	Non-Specified	Non-Specified
Miglis et al. (2020)	26	Female	PoTS, COVID-19, Asthma (Exercise-Induced), OCD (Resolved)	Tilt-Table	QSART Valsalva	Unspecified Joint-Hypermobility Assessment (Negative)	IV Fluid Azithromycin (5-Day Course), Propranolol, Clonidine	Increased Fluid & Salt Intake, Compression Garments

Babra, Youn & Devendra (2021)	35	Female	PoTS, Breast Cancer	Not specified	Non-Specified	-	Beta-Blocker Therapy	-
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- *Patient Demographic Characteristics (Gender & Age)*

Demographic breakdown of the 98 cases in the sample identified 75 female patients [76.5%], 20 male patients [20.4%] and three natal females who identified as male [3.1%]. The dominance for female cases within the sample is representative of the higher PoTS diagnosis rates for this sex, which has been estimated at a rate of five females for every one male presenting with the condition (Low et al., 2009). Patient ages ranged from 8 to 70 years old (Mean Age = 27.3; SD = 12.8). Case age breakdown consisted of one person aged between 0-9 years old [1.0%]; 35 cases aged 10-19 years [35.7%]; 26 individuals within the 20-29 year bracket [26.5%]; 19 patients aged between 30-39 years [19.4%]; 11 cases within the 40-49 years old bracket [11.2%]; three cases of the ages 50-59 [3.0%]; two cases aged 60-69 [2.0%], in addition to; one patient aged 70 [1.0%]. The finding of a right-tailed distribution for case age is in line with evidence that PoTS is more commonly observed in younger individuals and rarely reported within patients aged 50 or over (Low & Sandroni, 2012). In regards to reports which had focused on child and adolescent cases of PoTS, the sample was found to consist of 25 patients [25.5%] who were below the age of 18.

- *Comorbid Diagnoses & Other Health Conditions*

Case reports featured a diverse range of comorbid health diagnoses and/ or conditions. One of the most prevalent comorbidities reported in the samples was chronic fatigue syndrome/ME, which was reported in six cases [6.1%]. Allocation of a specific syncope-related condition, which had been distinguished from the PoTS itself, was reported in six [6.1%] cases – this included labels of vasovagal syncope [n = 3, 3.0%], neuro-cardiogenic syncope [n = 2, 2.0%] and convulsive syncope [n = 1, 1.0%]. Ehler-Danlos syndrome, another frequently co-morbid condition with PoTS, was present within four cases [4.0%] whilst a further two patients [2.0%] had a diagnosis of a hypermobility-related condition. Six patients [6.1%] possessed a diagnosis of an anxiety or panic disorder – one further case also had post-traumatic stress disorder (Meyer et al., 2015). Furthermore, six cases were diabetic [6.1%] whilst six individuals had asthma [6.1%]. Four patients had a diagnosis of Reynard's syndrome [4.0%], whilst a further four cases were found for patients who had an attention-deficit/hyperactivity-related disorder. Three cases [3.0%] in the sample were each found for fibromyalgia, bipolar disorder, depression and hypertension. Three patient reports which had been published during the 2020 Coronavirus pandemic noted cases where patients had been infected with COVID-19 prior to the onset of their PoTS (Dani et al., 2020; Miglis et al., 2020; Umapathi et al., 2020). Other medical conditions (with a total of two cases or less) can be found in table 1. Eight cases within the article sample examined patients with PoTS who were also pregnant [8.1%].

- *Diagnostic Tests & Autonomic Screening*

Where possible, tabular analysis also examined the primary type of diagnostic method that had been undertaken to confirm the diagnosis of PoTS for each case within the sample. Use of a tilt-table / head-up tilt test (terminology used interchangeably between case reports) - utilised for two-thirds of cases [66.7%] in the sample - was the most commonly employed method. Alternatively, 19 cases [19.2%] within the sample were diagnosed through the performance of an active standing (Schellong) test. One case report which featured a standing assessment referred to the specific use of the ten-minute NASA lean protocol to assist with the diagnosis of a patient (Baldwin et al., 2016), whilst a further case utilised both a combination of standing and tilt-table assessments to identify the presence of PoTS (Umapathi et al., 2020). In addition to this, for one case where PoTS had been suspected from a standing test conducted by the clinical care team – the patient had been subsequently referred to a PoTS specialist and the type of test conducted to confirm this diagnosis was not stated by the authors (Popatia & Subramaniam, 2014). Furthermore, a single case referred to the diagnosis of PoTS through the examination of heart rate change when the patient was asked to adopt a 45° angle whilst in bed (Chung et al., 2020). Ten case reports of patients [10.1%] pre-diagnosed with PoTS did not contain details of the primary diagnostic method that had originally been undertaken to detect the condition, whilst for one additional case the primary diagnostic method used was unknown (Dani et al., 2020).

In addition to the primary diagnostic assessment used for each patient case, the tabular analysis also examined usage of four other commonly-used methods of assessing autonomic functioning when PoTS is suspected: Valsalva Maneuver, Deep Breathing Test, & QSART. The Valsalva was found to be the more prevalent test which researchers reported as having been performed [n = 14, 14.1%], whilst a similar number of case reports explicitly referred to the conduction of QSART [n = 11, 11.1%] and deep breathing [n = 10, 10.1%] assessments.

- *Psychometric Assessment*

Information relating to the use of psychometric assessments administered to the patient during clinical assessment was also charted for each case report. Tests were used by the clinical care team of sixteen articles (20.3%) to support their patient symptom evaluation. Measures which examined depression symptomology [n = 6; 6.1%] – including the Center for Epidemiological Studies Depression Scale for Children (Weissman et al., 1980) [n = 1] and the Beck Depression Inventory I/II (Beck, Ward, Mendelson, Mock & Erbaugh, 1961; Beck,

Steer & Brown, 1996) [n = 5; 5.0%] – and anxiety symptomology [Beck Anxiety Inventory (Steer & Beck, 1997) only, n = 6; 6.1%] were the most common psychometric tools used throughout the sample. Furthermore, three cases [3.0%] completed a measure of autonomic dysfunction, including two cases [2.0%] which undertook the Composite Autonomic Symptom Severity scale [Low, 1993] / COMPASS-31 (Sletten, Suarez, Low, Mandrekar, & Singer, 2012) and one case who was administered with the Orthostatic Grading Scale (Schrezenmaier et al., 2005).

Psychometric assessments used to screen for common co-morbidities with PoTS included: the use of fatigue measures in two cases [2.0%] [Fatigue Impact Scale (Fisk et al., 1994) & Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989)], in addition to one case which used the Epworth Sleepiness Scale (Johns, 1991); two cases [2.0%] which screened for hypermobility through Beighton Scale (Beighton & Horan, 1969), in addition to; two cases [2.0%] which assessed Fibromyalgia symptoms through the use of the Fibromyalgia Impact Questionnaire (Burckhardt, Clark, Bennett, 1991) and Widespread Pain Index (Sullivan, Bishops, & Pivik, 1995). Additional measures of symptom severity / pain, used within two cases, included the Symptom Severity scale (Levine et al., 1993) and the Subjective Units of Distress Scale (Courtney et al., 2010). With regard to measures of quality of life [QoL], two cases [2.0%] undertook measures of health-related QoL [SF-36 (Hays, Sherbourne & Mazel, 1993) & WHO-QOL-BREF Questionnaire (Whoqol Group, 1998)], whilst one case study referred to use of the Functional Disability Inventory (Walker & Greene, 1991).

- *Pharmacological Interventions*

Data was also charted in regards to the reported pharmacological treatments which had been provided to the patient by the clinical care team, or previously prescribed to the patient to control their PoTS symptoms. 88 cases [88.9%] included comment on the medication usage of the patient. The volume expander fludrocortisone [n = 29; 29.3%] was found to be the most prevalent medication given to PoTS patients (one additional case reported by Rosen & Cryer (1982) specifically referred to the medication fludrohydrocortisone being prescribed). A similarly high number of cases were also reported to have received midodrine for their PoTS symptoms [n = 27, 27.3%] (of which, two case reports specifically mentioned the use of the drug midodrine hydrochloride). In regards to beta-blocker therapy use, propranolol [n = 18, 18.2%] and metoprolol [n = 13, 13.1%] were the most frequently reported medications tried by patients, followed by bisoprolol [n = 7, 7.1%] (one of which referred to the specific use of bisoprolol fumarate). No case reports within the sample mentioned the use of labetalol for the treatment of PoTS. Whilst in eight cases the use of beta-blocker therapy [8.2%] was reported,

the specific drug(s) that had been administered to the patient was not stated. Ivabradine, another medication targeted at alleviating tachycardia episodes, was reported as having been taken by eight patients within the case reports [8.1%]. A comparable number of cases had tried pyridostigmine [n = 8; 8.1%], modafinil [n = 5, 5.1%] and desmopressin [n = 5; 5.1%]. Other pharmacological agent treatments for PoTS included octreotide [n = 2; 2.0%], erythropoietin use [n = 1; 1.0%] and the alpha-agonist clonidine [n = 1; 1.0%].

- *Non-Pharmacological Interventions*

Furthermore, data pertaining to the recommendations of non-pharmacological treatments by the clinical care team was also assessed across the sample. Only 56 cases [56.5%] referred to details of the non-medication management of patients' PoTS. The most prevalent treatment within the case reports was the recommendation of increased daily water or fluid intake in the diet, as noted within 30 case reports [30.3%]. For two cases reported by Noyes & Kluger (2015), specific amounts of water were advised by the clinicians – this included recommendations nine glasses of water per day and one glass of water be ingested every two hours by each patient respectively. For one additional case within the sample, the patient was advised to place her face in cold water whenever she would experience a flare up of her PoTS (Graham & Richie, 2009). The increase of salt (sodium) in the diet was advised within 22 cases [22.2%] within the sample. Four cases [4.0%] also reported that the patient was provided with salt or sodium supplements by their clinical care team. One early case within the sample referred to the use of 'Sodium Loading' as a treatment, however it was unclear what method the clinical team had used to administer this (Rosen & Cryer, 1982). Other case reports with dietary changes included two cases who were advised to manage their caffeine use (Zundel, Pattyn, Chelimsky, & Riess, 2015; Richardson, Nordon-Craft & Carrothers, 2017), one individual who was advised to refrain from alcohol use (Richardson, Nordon-Craft & Carrothers, 2017) and one case report where the patient was placed on a gluten-free diet (Noyes & Kluger, 2015).

Within 13 cases [13.1%] in the sample, the patient was advised to increase their levels of physical activity. This included seven cases where the patient was referred to exercise rehabilitation, training or therapy programmes; in addition to one patient who undertook a physical therapy programme specifically for their Hypermobility Ehler-Danlos syndrome (Boris, McClain & Bernadzikowski, 2019). The wearing of compression garments or support stockings was advised by the clinical team within nine case reports [9.1%]. Other notable types of non-medication treatments provided to PoTS patients were sparsely reported. Only a minority of case reports examined included reference to the use of psychological or cognitive therapies

(n = 4); education of PoTS provided to the patient's family (n = 2), and; occupational therapies and management of the patient's work pattern (n = 2).

Appendix C: Tabular Synthesis – PoTS Clinical Trial Registrations

Table 1. A tabular analysis of the Intervention, Dosage & Trial Arm(s), Principal Investigator, Location, Year, Participant Sample, Study Design, Primary Outcome Measure(s) and Trial Status (at time of data extraction) for each clinical trial registration identified within the final review subset. N = 19.

Intervention	Dosage / Arms	Principal Investigator(s)	Location	Year	Participants	Design	Primary Outcome Measures	Current Trial Status
Pyridostigmine	One 180mg Capsule for 3 days Placebo Tablet	Low, P. A.	Maryland, USA	2006	50 patients diagnosed with PoTS (aged 15-55)	Randomized, Parallel Assignment, Quadruple Masking	COMPASS-31, HR, Plasma Nor-epinephrine (NE) Levels	Recruiting
Propranolol	One 20mg Tablet 1 hour before exercise test Placebo Tablet	Biaggioni, I.	Tennessee, USA	2008	12 Patients diagnosed with Orthostatic Intolerance or PoTS (aged 18 to 65)	Randomized, Crossover, Double-Masking	Maximal Oxygen Consumption Capacity (VO ₂ max), HR	Recruitment Complete
Salt Water (IV Infusion)	Saline infused 3-6 hours prior to exercise study Placebo- Lactose Tablet	Raj, S.	Tennessee, USA	2009	40 PoTS patients (aged 18-65 years)	Non-randomised, Crossover, None-masking (open label)	VO ₂ Max, Inert Gas Breathing technique Cardiac Output (Inert Gas Breathing technique)	Active, Not Recruiting
Losartan, Ascorbic Acid	Losartan dosage increased over 3 weeks: 12.5mg, 25mg, 50mg Ascorbic Acid: 60mg/kg	Stewart, J.	New York, USA	2010	74 PoTS patients (aged 14 – 29)	Randomized, Crossover, Double-Masking	HR, BP response to Tilt-test Sympathetic nerve readings and Doppler	Recruitment Complete

	Placebo: Saline						blood flow in leg	
Ivabradine	10mg	Tel-Aviv Sourasky Medical Center	Tev Aviv, Israel	2012	20 PoTS patients (aged 18 – 55)	Randomized, Double-Blind, Single-group	HR, BP	Unknown
Sodium Diet	Low-sodium diet (10 milliequivalent/day) High-sodium diet (300 milliequivalent/day)	Biaggioni, I.	Tennessee, USA	2012	13 PoTS patients with PoTS or Syncope (aged 18-60)	Randomised, Crossover, Single-masking,	Change in OI symptoms (measure not specified), HR	Study Terminated due to funding not being secured
Atenolol, Droxidopa	Atenolol (50mg qd), droxidopa 100 mg/300mg and placebo.	Freeman, R.	Massachusetts, USA	2012	8 PoTS Patients (aged not specified)	Randomised, Crossover, Triple Masking	HR, Chalder Fatigue Questionnaire, BP, SF-36, HADS	Study Terminated (Slow recruitment, participant withdrawal)
Modafinil, Propranolol	Modafinil (200 mg), Propranolol (20 mg), Placebo	Biaggioni, I.	Tennessee, USA	2013	20 PoTS patients (aged 18-60)	Randomized, Crossover, Triple Masking	CogState test battery- Stroop, Visual and Learning Memory, Working Memory, HR	Active but no longer recruiting
Compression Garment	Abdominal and LE compression - Zoex compression garment during tilt testing (all straps) Abdominal compression only - Zoex compression garment use during	Heyer, G.	Ohio, USA	2013	20 Adolescent patients with PoTS or Syncope (aged 12-19)	Randomized, Parallel-assignment, No masking (open label)	HR, OI Symptom onset during Tilt	Study Completed

	tilt table testing (straps 4 and 5 fastened around thighs and abdomen)							
	Lower Extremities & Thigh Compression - Zoex compression garment use during tilt table testing (straps 1-4, lower extremity and thighs, fastened)							
Iron Sucrose Infusion	Intravenous Iron Sucrose (5 mg/kg) - supplied as Venofer (TM) with a maximum dose of 200mg	Jones, A. E.	Minnesota, USA	2013	30 Adolescent PoTS patients (aged 12-19)	Randomized, Controlled, Quadruple Masking	COMPASS-31, PedsQL, Orthostatic Symptom Scale, IV/Venipuncture (CBC, ferritin, iron, TIBC, percent of iron saturation, upright and supine catcholamine).	Study terminated (due to recruitment difficulty)
Transdermal Vagal Nerve Stimulation	Vagal Nerve stimulation through Transdermal low current	Diedrich, A. & Biaggoni, I.	Tennessee, USA	2014	18 PoTS patients (aged 18-75; originally aimed for 20 participants)	Randomised, crossover assignment, double- blinded	HR, Orthostatic Symptoms (via Subjective analog symptoms scale), Orthostatic Tolerance	Active, Recruitment Complete

Propranolol, Bisoprolol, Pyridostigmine	Propranolol - Propranolol started 10mg bid, and then increased dosage up to 20mg after one month if tolerable	Chu, K.	Seoul, Phillipines, South Korea	2016	150 in total. PoTs patients (estimated to achieve 120) aged 15 to 85	Randomised, single-group assignment, no masking (open label)	Subjective OI symptom survey, HR, BP, QoL	Active, Recruitment Complete
	Bisoprolol - Bisoprolol started at 2.5mg qd., then increased dosage up to 5mg qd. if tolerable							
	Propranolol + Pyridostigmine - Propranolol & pyridostigmine started 10mg bid +30mg bid, and then increased dosage up to 20mg bid+30mg bid. if tolerable.							
	Bisoprolol + Pyridostigmine - Bisoprolol + pyridostigmine started 2.5mg qd+30mg bid, and then increased dosage up to 5mg qd+30mg bid.							
Northera	Study 1: Acute - Acute Single large dose (600mg) of Northera Study 2: Chronic	Stewart, J.	New York, USA	2017	10 PoTS patients with 2 or more episodes of vasovagal syncope in the	Randomised, Crossover, Quadruple Masking	Splanchnic and lower extremity pooling QoL - Rand-36 & COMPASS- 31,	Active, Recruiting

	- Doses of Northera are titrated upwards by 100mg/dose every 48 hours, from a starting dose of 100mg three times a day to a maximum of 600mg three times a day (for two weeks)				past year (aged 18-30)		HR & BP	
Ivabradine	Ivabradine - One dose of Ivabradine twice a day for one month (dosage not specified)	Taub, P.	San Diego, USA	2017	20 PoTS patients (aged 18-65)	Randomised, Crossover, Quadruple Masking	HR, Quality of Life - SF-36	Active, Recruiting
Albumin Infusion	Albumin (Human) 5%, USP. Intravenous Solution. Plasma Substitute/Blood Derivative Placebo Normal Saline 0.9% Infusion Solution Bag	Siddiqi, Z.	Alberta, Canada	2017	17 PoTS patients (aged 18-69)	Randomised, Crossover, Single-Blind	Orthostatic Symptom Grading Scale (OSGS) scores Patient-Reported Outcomes Measurement Information System, Health Assessment Questionnaire (HAQ -20) HUT Test Improvement (10 minute) Change in maximal exercise	Active, Not Yet Recruiting

							capacity - peak oxygen consumption (VO2).	
Pyridostigmine	Pyridostigmine 60mg by mouth one day Placebo (Lactulose 50mg) by mouth on a different day	Stewart, J.	New York, USA	2017	80 participants - PoTS and healthy controls	Randomized, Crossover, Quadruple-masking	"Cognitive Ability" – includes Working Memory assessment Cardiovagal Baroreflex during orthostatic stress Cardiac output measure by inert gas breathing technique BP, HR, Systemic Vascular Resistance	Active, recruiting
Posture (Crossed Legs)	Lying Posture - Cognitive tests are performed during lying in all groups (SFN, AAN, EDS, POTS and controls) Standing Posture	Maier, A. Schaueremann, J.	Nordrhein Westfalen, Germany	2018	100 participants in total – including POTS, autoimmune autonomic neuropathy (AAN), SFN, Ehlers Danlos Syndrome (EDS)	Randomized, Parallel-assignment, No masking (open label)	Cognitive function: Stroop test, Trial Marking Test A and B in different postures	Active, Recruiting

	- Cognitive tests are performed during active Standing in all groups (SFN, AAN, EDS, POTS and controls)				patients and healthy controls		BP, HR, Cerebral blood flow velocity	
	Crossed Legs Posture - Cognitive tests are performed during leg crossing in all groups (SFN, AAN, EDS, POTS and controls) Intervention: Procedure: leg crossing							
Compression Garment	LifeWrap Compression Garment Arm 1 - fully secured with all straps Arm 2- Abdominal and Pelvic Compression Arm 3 - Lower limb compression Arm 4- No compression	Raj, S.	Calgary, Canada	2018	40 PoTS Patients (aged 18-60)	Randomized, Crossover, None-masking (Open label)	HR, Vanderbilt Orthostatic Symptom Score Symptom Rating, BP, Stroke Volume, Cardiac Output, Systemic Vascular Resistance, Cerebral Blood Flow Velocity	Active, Recruiting
Posture	Arm: Standing Participants will stand and complete cognitive tests.	Miller, A.	Pennsylvania, United States	2018	100 participants in total – PoTS patients & healthy controls (aged 13-60)	Randomized, Crossover, None-masking (Open label)	Executive Functioning - Stroop Attention –	Active, not recruiting

Arm: Supine
Participants will complete cognitive tests while supine.

Cogstate Identification Task

Hypermobile Ehlers-Danlos Syndrome evaluation-Diagnostic Criteria

Table 2. Updated Search Strategy - A tabular analysis of the Intervention, Dosage & Trial Arm(s), Principal Investigator, Location, Year, Participant Sample, Study Design, Primary Outcome Measure(s) and Current Trial Status of each clinical trial registration identified within the final review subset. N = 7.

Intervention	Dosage / Arms	Principal Investigator(s)	Location	Year	Participants	Design	Primary Outcome Measures	Current Trial Status
Ivabradine, Propranolol	Ivabradine – 5 mg Propranolol – 20 mg Placebo	Dysautonomia International / Raj, S.	Calgary, Canada	2019	20 PoTS Patients (Aged 18-60)	Double-blind Placebo-Controlled Randomized Crossover	Orthostatic Heart Rate Change, Vanderbilt Orthostatic Symptoms Score [VOSS]	Not Yet Recruiting
Propranolol, Bisoprolol, Pyridostigmine	Propranolol - 10 mg, raised to 20 mg if tolerable Bisoprolol - 2.5 mg, raised to 5 mg if tolerable	Chu, K.	Seoul, South Korea	2014	150 PoTS Patients (Aged 15-85)	Randomized, Single-Group, Open-Label	Subjective Symptom Survey Orthostatic Heart Rate & Blood Pressure change	Recruitment Completed

	Propranolol & Pyridostigmine - Propranolol: dosage same as above - Pyridostigmine:30 mg						Quality of Life, Depression Symptomology	
	Bisoprolol & Pyridostigmine - Both doses same as above							
Moxonidine	Moxonidine - 0.4 mg, single oral dose Placebo	Diedrich, A.	Tennessee, USA	2019	48 PoTS Patients (Aged 15-55)	Randomized, Double-Blind, Placebo-Controlled Crossover	VOSS, Orthostatic Symptom Burden	Suspended (Due to COVID-19 Pandemic)
Breathing Device	Inspiratory Threshold Device (Res-Q-Gard ITD) Placebo (Sham Breathing Device)	Gamboa, A.	Tennessee, USA	2009	30 PoTS Patients (Aged 18-80)	Randomized, Crossover, Single-Masking	Orthostatic Heart Rate Change	Active, Not Recruiting
Low Body Negative Pressure (During fMRI)	Lower Body Negative Pressure Placebo (Sham Pressure)	Arnold, A.	Pennsylvania, USA	2019	55 Participants – Healthy Volunteers & Patients Diagnosed with PoTS (Aged 18-60)	Randomized, Double Blind, Crossover	Cognitive Brain Region Activation (BOLD signals) Brain Oxygen Perfusion, Blood Pressure, Heart Rate	Not Yet Recruiting

							Stroop-Word-Colour Score, N-Back Task	
Intravenous Immunoglobulin (Gammunex-C / IVIG)	<p>IVIG (Gammunex-C) infusion - 0.4 gm/ kg, Administered every 7 days for 4 weeks; then every 14 days for 8 weeks.</p> <p>Placebo (Albumin Infusion) - Same protocol as for IVIG above</p>	Vernino, S.	Texas, USA	2019	20 PoTS Patients (Aged 18+)	Double-Blind Placebo-Controlled, Crossover, Pilot	COMPASS-31	Enrolling by Invitation
Parasym (TM) Transcutaneous Electrical Nerve Stimulation (TENS) Device	<p>(i) TENS Device -> Sham</p> <p>(ii) Sham -> TENS Device</p>	Kem, D. & Stavrakis, S.	Oklahoma, USA	2019	<p>30 PoTS Patients (aged 18 – 80 years)</p> <p>- Group (i): n = 20</p> <p>- Group (ii): n = 10</p>	Randomized, Crossover, Triple Masking	<p>Orthostatic Heart Rate Change</p> <p>M2 Muscarinic Autoantibody Levels</p> <p>Alpha 1-Adrenergic Autoantibody Levels</p> <p>Beta 1-Adrenergic Autoantibody Levels</p> <p>Heart Rate Variability</p>	Active, Not Recruiting

Appendix D: Additional Syntheses – PoTS Editorial Letters, Conference Abstracts, Consensus Statements/ Clinical Guidelines & Dissertations

▪ ***Letters to Editor / Editorials***

A tabular analysis was performed for letter to the editor/ editorial paper retrieved by the final article subset (see *Table 1 below*). Inspection of geographical location revealed that eight articles originated from the USA, three articles were located from Japan whilst single articles were identified from the UK and Germany. Two papers featured the use of primary data collection (Lkhagvasuren et al., 2010; Lkhagvasuren, Tanaka, Sudo, Kubo & Oka, 2014). The first study assessed PoTS co-morbidity in a sample of depressed, anxious and somatoform syndrome adolescent patients against an age-matched control group (Lkhagvasuren et al., 2010); whilst the second article explored evidence for higher rates of PoTS diagnosis in children presenting with psychogenic fever in comparison to a healthy control group (Lkhagvasuren, Tanaka, Sudo, Kubo & Oka, 2014).

Other editorial articles focussed on the following topics: deconditioning in PoTS (Blitsheyn & Fries, 2016); the interplay between autonomic nerve activity and inflammation (Chobanyan-Jürgens & Jordan, 2015); visceral sensitisation in PoTS and joint-hypermobility syndromes (Farmer, Fikree & Aziz, 2014); the use of exercise and beta-blocker medications for PoTS symptom management (Joyner, 2011); critical evaluation of evidence assessing sleep disturbances in individuals with PoTS (Kawada, 2013); underpinning cardiovascular mechanisms for PoTS orthostatic symptoms (Low, Schondorf & Rummsans, 2001); child & adolescent research on PoTS (Lkhagvasuren et al., 2010; Lkhagvasuren, Tanaka, Sudo, Kubo & Oka, 2014; Medow, 2011; Raj, 2013); the use of a radioactive chemical [I-MIBG] to assess norepinephrine uptake in PoTS patients (Mustafa & Robertson, 2010); salt supplementation and sodium excretion in adolescents with PoTS (Raj, 2013), in addition to; autonomic condition onset in elderly populations (Shams & Morley, 2018).

Table 1. Tabular overview of Letter to Editor/ Editorial articles identified within the final article subset by reference, location, journal, coded thematic category, aims & future research/ implications. N = 12.

Reference	Location	Journal	Coded Thematic Categories	Aim(s)/ Summary	Future Research / PoTS Implications
Blitsheyn & Fries (2016)	USA	Pulmonary Circulation	<i>Deconditioning; Non-Pharmacological Treatment</i>	To emphasise that deconditioning is a secondary condition to a PoTS diagnosis.	Further large-scale studies are needed to compare the performance of PoTS patient populations against healthy controls on cardiopulmonary exercise tests / programmes.
Chobanyan-Jürgens & Jordan (2015)	Germany	American Journal of Physiology - Heart and Circulatory Physiology	<i>Aetiology & Underlying Pathophysiology; Immunology</i>	To describe the interaction between autonomic nerves and inflammation (using PoTS & obesity as an example condition of increased sympathetic branch activity).	As an autonomic condition, patients with PoTS may present with Sympathetic hyper-activity and reduced parasympathetic drive. This autonomic pathophysiology of PoTS may lead to greater levels of interleukin-6 secretion in patients with co-morbid obesity (Okamoto et al, 2010).
Farmer, Fikree & Aziz (2014)	UK	Clinical Autonomic Research	<i>Aetiology & Underlying Pathophysiology</i>	To argue for a biological basis for PoTS pathophysiology & to argue for the importance of considering joint-hypermobility syndrome as a co-existing condition.	Future studies accessing visceral sensitisation in PoTS should control for co-morbid joint-hypermobility syndrome

Joyner (2011)	USA	Hypertension	<i>Deconditioning; Non-Pharmacological Treatment; Pharmacological Treatment</i>	To comment on literature examining the effects of exercise programmes and beta-blocker medications	Promotion of exercise programmes over beta-blocker use in patients with PoTS could be a further area of exploration.
Kawada (2013)	Japan	Autonomic Neuroscience: Basic & Clinical	<i>Sleep-based Symptoms/ Disturbances</i>	To critically evaluate the findings of Bagai et al. (2013), who examined objective sleep parameters in PoTS patients.	Further longitudinal research is needed to examine sleep disturbances in individuals with PoTS.
Lkhagvasuren et al. (2010)	Japan	Psychotherapy and Psychosomatics	<i>Child & Adolescent Research; Psychological Functioning; Co-morbid Diagnosis or Health Condition</i>	To examine the co-morbid rates of PoTS in individuals diagnosed with anxiety (n = 31), depression (n = 36) or somatoform disorder (n = 34)- against a control group (n = 30).	PoTS was diagnosed in 6 (16.6%) depressed patients, 1 (3.2%) anxiety patient, 2/34 (5.9%) somatoform patients and 3 of the healthy controls. Psychiatric patients reported significantly increased fatigue and light-headedness than control patients
Low, Schondorf & Rummins (2001)	USA	Clinical Autonomic Research	<i>Aetiology & Underlying Pathophysiology; Diagnosis & Autonomic Evaluation</i>	To comment on evidence which has examined the underlying pathophysiological causes of orthostatic symptoms in PoTS.	Screening possible cases of PoTS through the use of both autonomic and psychiatric assessments is recommended for clinicians
Medow (2011)	USA	The Journal of Paediatrics	<i>Child & Adolescent Research; Diagnosis & Autonomic Evaluation</i>	To collate research findings which have been conducted on child & adolescent studies of PoTS.	Further work is needed to standardised the diagnosis of PoTS across autonomic clinical centres (not just for paediatric cases)

Mustafa & Robertson (2010)	USA	Journal of Neurology, Neurosurgery and Psychiatry	<i>Diagnosis & Autonomic Evaluation</i>	To comment on the use of I-MIBG to examine the role of norepinephrine & norepinephrine transporters [NET] in PoTS.	Authors advise clinicians to perceive a diagnosis of PoTS as a "starting point" in the care of the patient, and encourage that further assessment is undertaken.
Lkhagvasuren, Tanaka, Sudo, Kubo & Oka (2014)	Japan	Psychotherapy and Psychosomatics	<i>Child & Adolescent Research; Psychological Functioning; Co-morbid Diagnosis or Health Condition</i>	To report the findings of a study examining PoTS diagnosis in 24 adolescents presenting with psychogenic fever and 24 age & gender matched controls.	Significantly higher number of the psychogenic fever group (n =9; 38%) demonstrated evidence of PoTS than the control group (n = 1; 4%). Psychogenic fever adolescents may portray an orthostatic heart rate change which is characteristic of PoTS.
Raj (2013)	USA	Autonomic Neuroscience: Basic & Clinical	<i>Child & Adolescent Research; Gastrointestinal, Bladder & Urine-related Symptomology; Non-pharmacological Treatment</i>	To comment on findings from a Beijing study which examined 24-hour sodium urine excretion in children with PoTS and healthy controls following salt supplementation.	Further prospective studies are needed to assess whether or not salt supplementation is actually a necessary treatment in patients who already incorporate moderate levels of salt intake within their diet.
Shams and Morley (2018)	USA	The Journal of Nutrition, Health and Aging	<i>Diagnosis & Autonomic Evaluation; Non-Pharmacological Treatment; Pharmacological Treatment</i>	To provide an overview of a range of autonomic conditions which elderly individuals may present with.	PoTS is rare within individuals aged over 50 may present alongside syncope and diabetes. First-line treatments for PoTS in the elder which are recommended by the authors include increased salt intake, use of compression garment, abdominal binding and beta-blocker medications.

- **Conference Abstracts**

A limited number of conference submissions were retrieved from the employed search strategy. Two studies examined the use of compression garments for PoTS (Bourne et al., 2016) – one of which examined this non-pharmacological intervention in conjunction alongside beta-blocker therapy (Okamoto et al., 2015). Four other conference publications, which featured the examination of a medicinal agent to relieve PoTS symptomology, included the evaluation of Albumin infusions (Siddiqi, Blackmore & Soloway, 2019), carbidopa use to counter excess sodium excretion in PoTS patients' urine (REF), high-dose octreotide in individuals with co-morbid PoTS and hEDS (French et al., 2011); midodrine in PoTS & neuro-cardiogenic syncope (Hamer & Roberts, 2018). Two studies examined a sample of patients with PoTS that had been resistant to treatment (French et al., 2011; Siddiqiet al., 2019). Studies which had examined the prevalence of PoTS alongside a co-morbid condition included coeliac disease (Penny et al., 2016), mast cell activation syndrome & hypermobile Ehler-Danlos syndrome (Chang & Vadas, 2019), bronchial asthma (Ishikawa et al. 2020) and pulmonary arteriovenous malformations (Santhirapala et al., 2013). The remaining two articles explored RyR2 gene mutation as a possible underlying mechanism to account for PoTS (Quing et al., 2013) and gluten sensitivity in this patient group (Penny et al., 2003).

- **Consensus Statements & Clinical Guidelines**

Five articles within the sample contained reports published by autonomic societies across the world (see *Table 2*). This contained two clinical guidelines – both of which related to the diagnosis and treatment of OI conditions & PoTS in children / adolescents populations (Tanaka et al., 2009; Wang et al., 2018). The remaining three articles where described as consensus (Freeman et al., 2011; Kim et al., 2019) and society position (Raj et al., 2020) statements which were focussed on updating the established definitions of orthostatic intolerance disorders (Freeman et al., 2011; Kim et al., 2019), and evaluating evidence concerning treatments and recommendations for PoTS (Raj et al., 2020).

Table 2. Clinical guidelines and consensus statement articles by Authors, Article Type, Aim(s)/ Purposes and Contributing Organisations. N = 5.

Authors	Article Type	Aim(s) / Purpose	Organisation(s)
Tanaka et al. (2009)	Clinical Guidelines	- Recommendations to support with the assessment, diagnosis & treatment of Orthostatic Dysregulation conditions in child / adolescent populations.	- Japanese Society of Psychosomatic Pediatrics
Freeman et al. (2011)	Consensus Statement	- Clarification and further guidance on the previously established definitions of Orthostatic Hypotension, published in 1996. - Agreed definitions for Neurally-Mediated (Reflex) Syncope and PoTS were added by the societies.	- American Autonomic Society - European Federation of Autonomic Societies - Autonomic Research Group of the World Federation - Autonomic Disorders section of the American Academy of Neurology
Wang et al. (2018)	Clinical Guidelines	- Provide guidance to clinicians for the diagnosis and treatment of vasovagal syncope, postural orthostatic tachycardia syndrome, orthostatic hypotension and orthostatic hypertension in child/ adolescent populations.	- Chinese Pediatric Cardiology Society - Chinese Medical Association/ Committee on Pediatric Syncope - Chinese Medical Doctor Association - Chinese College of Cardiovascular Physicians - Beijing Pediatric Society
Kim et al. (2019)	Consensus Statement	- Outline diagnostic criteria for the inclusion of hemodynamic orthostatic dizziness/ vertigo in the International Classification of Vestibular Disorders.	- Committee for the Classification of Vestibular Disorders of the Bárány Society.
Raj et al. (2020)	Position Statement; Systematic Review	- To update & review evidence pertaining to the evaluation and treatment of POTS, using GRADE methodology [<i>Grading of Recommendations; Assessment; Development; Evaluation</i>]. - To develop clinical recommendations from the Canadian Cardiovascular Society approach to position statements.	- Canadian Cardiovascular Society

- **Dissertations**

Two academic dissertations which focused on PoTS were identified within the sample. The first dissertation, which was submitted for the reward of PhD within the School of Medicine of Imperial College London, was authored by Iodice et al. (2013). During this thesis, Iodice et al. (2013) developed psychometric tools to assess the severity of autonomic functioning (Cardiovascular Autonomic Functioning Score) and a quality of life measure for patients with dysautonomia-related conditions (Autonomic Questionnaire and Quality of Life Scores). The thesis also explored small-fibre neuropathy in PoTS patients and the use of Octreotide to relieve autonomic complaints. The second dissertation in the sample, submitted for the fulfilment of a Master's of Science degree in Engineering at the University of Wisconsin-Milwaukee, was authored by Kadamati & Ranji (2017). This project aimed to develop the use of a cytoximeter system to measure cytochrome c oxidase [CCO] activity in patients with PoTS during near-infrared spectroscopy studies. This enzyme, located within the mitochondria, plays a role in respiration processes. By assessing CCO activity using the developed cytoximeter system, this allowed researchers to more closely monitoring oxyhaemoglobin changes in this patient group (against healthy controls) during HUT to provide further insight into the pathophysiological properties that underpin the condition (Kadamati & Ranji, 2017).

Appendix E: Tabular Synthesis – PoTS-Related Brain Fog & Cognition Empirical Research Studies

Table 1. A tabular analysis of all PoTS-related studies within the sample which examined cognitive functioning.

Author	Study Aims	Study Design	Participants	Primary Outcome Measures	Main Findings	Implications / Future Research
Stewart et al. (2012)	To assess postural neurocognitive and neuronal activated cerebral blood flow deficits in response to a n-back test within patients diagnosed with both PoTS & Chronic Fatigue Syndrome (CFS).	Experimental between-subjects	25 patients diagnosed with PoTS & CFS (gender breakdown not provided) 20 healthy controls with similar age, sex, height, weight and BMI	<u>n-back task</u> (with four levels: 0-, 1-, 2-, 3-, 4-back): Number of Correct Responses; Response Time Cerebral blood flow volume (changes) during cognitive task	At a supine posture, there were no significant differences found on each of the four levels of the n-back task between patients and controls. During incremental tilt (15°, 30°, 45°, 60° & 75°) table testing, between-subjects analysis revealed that patients demonstrated significantly longer reaction times and poorer number of correct responses for each level of the n-back task.	Increasing orthostatic stress in PoTS and co-morbid CFS patients decreasing working memory performance. Changes in cerebral blood flow volume changes where unrelated to cognitive functioning during the n-back task.

					Cerebral blood flow volume changes were found to be unrelated to CFS & PoTS patients during the n-back task.	
Anderson et al. (2014)	To assess PoTS patients for psychiatric symptomology, cognitive ability and to measure their health-related quality of life.	Exploratory, comparative between-subjects	15 adult PoTS patients, mean age 30±3 (12 female, 3 male). 30 healthy controls, mean age 32±2 (21 female, 9 male). Age, gender and BMI matched.	Structured clinical interview - Mini International Neuropsychiatric Interview - Anxiety sensitivity profile - Hamilton depression and anxiety rating scale - Wechsler Adult Scale of Intelligence (WASI) – includes some subscales from	PoTS patients scored significantly worse on all SF-36 domains. These scores did not correlate with resting HR or BP. Anxiety sensitivity scores were significantly worse in PoTS patients. PoTS patients performed worse than controls on all examined cognitive domains. Correlational analysis revealed strong associations between cognitive	PoTS patients experienced diminished quality of life. Cognitive deficits in the examined tasks could be predicted by the patients' years spent in education and their depression / anxiety scores (as opposed to PoTS symptomology specifically). Treatment plans for PoTS would benefit from more psychological interventions.

WASI-III including digit span	performance, depression symptomology score and years spent in education.	Specific recommendations by the authors to include stress reduction techniques and providing patients with CBT.
- Short-form Health Survey 36 (HR-QoL)	Following tilt, healthy controls were found to show 15% increased cognitive performance.	
Cogstate computer test battery (prior to, and after, 8 minutes of 60* HUT tilt):		
- Verbal IQ, Non-verbal IQ, Full scale IQ, Digit span – Forward & Back	PoTS patients displayed decreased scores on the cognitive tasks and an increased response. 47% of the variation in response time latency was predicted by Full IQ, SF36 social and physical domains.	
Education (Years)		

Arnold et al. (2015)	To examine whether PoTS patients exhibit	Between-subjects	28 Female PoTS Patients aged 18+	Cognitive Functioning Tests:	PoTS patients had significantly lower years spent in	Deficits found in patients' selective attention,
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deficits on a battery of neuropsychological tests when assessed in a semi-recumbent position (45*)

24 gender/ age matched healthy controls

Estimated Intelligence (Weschler Test of Adult Reading)

education, but did not differ in estimated intelligence from controls.

processing speed and executive functioning may underlie mental cloudiness (brain fog) symptoms.

Selective and sustained attention (RUFF2&7)

Selective attention, cognitive processing speed & executive functioning where significantly worse in PoTS.

Specialised treatments should be developed to specifically target mental cloudiness in PoTS.

Psychomotor Speed (Trails A)

Cognitive processing speed (Symbol Digits Modalities test)

A higher proportion of PoTS patients were found to meet the criteria for clinical impairment in selective attention, processing speed and executive functioning (Stroop), in comparison to controls.

Further work should focus on examining the pathological basis of the identified cognitive deficits patients present.

Memory Function (Randt memory test)

Verbal Fluency (Controlled Oral Word Association)

Sustained attention, psychomotor speed, memory function and verbal

Authors state a limitation of their research is that they did not explore cognitive functioning at altering angles of tilt (only 45* was used for

Executive functioning (Stroop task; Trails B) fluency did not differ between groups. neuropsychiatric assessment).

Psychiatric Measures: Depression scores were higher in PoTS patients.

Depression (Center for Epidemiologic Studies Depression Scale) PoTS patients scored higher only on the somatic (but not cognitive) anxiety items.

Anxiety (Cognitive-somatic Anxiety Questionnaire) Scores on the Subjective Cognitive Impairment scale revealed PoTS patients had more self-perceived cognitive difficulties than controls.

Subjective Cognitive Difficulties (Subjective Cognitive Impairment Scale)

Physiological

BP, HR

Stewart et al. (2015)	To examine whether cognitive impairment in PoTS is due to reduced cerebral blood flow during tilt.	Experimental between-subjects	11 PoTS patients aged 18-26 years old; OI symptoms for 6+ months (9 female; 2 male)	Beat-to-beat BP	PoTS patients display decreased end tidal CO ₂ & increased HR during tilt angles, in comparison to controls.	Evidence suggests that brain fog may be underlined by the interplay of changes in cerebral blood flow during orthostatic challenge and reduced hyperaemia.
	Additional aim of study was to assess the impact of cerebral blood flow velocity changes on neurovascular coupling (hyperaemia).		9 healthy controls aged 17-27 (6 female; 3 male)	HR		
				End tidal CO ₂ , O ₂ saturation		
				Cerebral blood flow volume (CBFv)	PoTS patients displayed a greater, progressive increase in CBFv oscillations as tilt angle increased (not displayed by controls).	Data is evidential of an association between neural coupling and cerebral blood flow oscillations and working memory related neural vascular coupling – future research is needed to develop experimental evidence to examine whether this relationship is causal in nature.
				n-back task (2-levels): Number of correct responses	PoTS patients displayed decreased n-back task accuracy on tilt & were found to have decreased functional hyperaemia during the cognitive task (not displayed by controls).	

Appendix F: Tabular Synthesis – PoTS-Related Sleep Outcome Empirical Research Studies

Table 1 *A tabular analysis of all PoTS-related studies which contain sleep-related outcome measures. N = 5.*

Author	Study Aims	Study Design	Participants	Primary Outcome Measures	Main Findings	Implications / Future Research
Bagai et al. (2013)	To assess sleep quality in POTS patients using wrist actigraphy.	Prospective	36 PoTS patients aged 18 or over (33 female; 3 male) 36 healthy controls with similar ages (33 female)	Actigraphy measures: Total Sleep time (TST), Sleep onset latency, Sleep Efficiency (SE), Wake-time After Sleep Onset (WASO) - HR, BP, Plasma Norepinephrine and Epinephrine concentrations were assessed after overnight rest and again after 30 minutes of standing in subjects with PoTS. Sleep Log: Tiredness, Restless sleep, Average minutes to sleep, average awakenings.	Sleep Log Data: - POTS patients had significantly higher greater number of days (reported as percentage of total days) with restless sleep than healthy control subjects (53% vs. 21%). - Morning tiredness was reported in a greater percentage of days in patients with POTS (75 ± 23%) than control subjects (39 ± 27%). - Average sleep latency was greater in POTS than control subjects (56 ± 66 min vs. 13 ± 9 min). This was also found for the number of awakenings/night	The first study to compare both subjective and objective measures of sleep in POTS patients and controls. Subjects with POTS have sleep pattern changes including poor sleep efficiency and a trend towards increased sleep fragmentation (as measured by WASO). Compared with healthy control subjects, POTS patients have significantly more sleep problems, including subjective complaints of restless sleep and morning tiredness,

reported by POTS patients compared to controls (3 ± 2 vs. 1 ± 1)

perceptions of longer sleep onset latency and greater number of awakenings per night.

Actigraphy Data:

- Sleep efficiency was significantly lower in subjects with POTS ($73 \pm 13\%$) as compared with controls ($79 \pm 6\%$).

- There was a trend towards higher WASO in POTS patients (63 ± 33 min) as compared with controls (50 ± 20 min).

- There was no difference in sleep onset latency between the POTS patients (37 ± 10 min) and control subjects (31 ± 9 min).

- In patients with POTS, there was significant negative correlations between percentage of patients with subjective

					tiredness and sleep efficiency.	
					- Authors also found significant positive correlations between percentage of patients with subjective tiredness and WASO.	
					- There was no significant correlation between subjective tiredness and actigraphic sleep onset latency	
Bagai et al. (2016)	To evaluate sleep quality using overnight polysomnograms in PoTS patients and healthy controls.	Exploratory objective study	16 PoTS Patients aged 18 or over (15 females; 1 male) 15 Healthy Controls (similar age; 13 females & 2 males)	Polysomnograms (Overnight) EEG, Sleep efficiency, Sleep onset latency, quantity of time spent in N1, N2, N3 and REM Sleep, apnea-hypopnea index, periodic leg movement & arousal index. HR, BP, Blood plasma (Norepinephrine and epinephrine concentration), Oxyhemoglobin concentration	- No significant differences were found between PoTS and control groups on sleep efficiency, sleep onset latency, wake time after sleep, amount of time spent in N1, N2, N3 & REM sleep phases, arousal index, apnea-hypopnea index or periodic leg movement. - Within the PoTS group, correlational analyses revealed a negative association between	In regards to the above prior research by the authors, the current study provides further evidence that differences in sleep onset latency between PoTS patients and controls are only detectable by subjective measures. Further research is suggested to explore interventions which

					<p>patient's HR change (due to orthostatic challenge) and sleep efficiency.</p> <p>- Within the PoTS group, correlational analyses revealed a negative association between patient's changes in patients' epinephrine levels (due to orthostatic challenge) and duration of time spent in N2 sleep.</p>	<p>subdue increased sympathetic activity, in the hope that this may improve insomnia in PoTS patients.</p>
Mallien et al. (2014)	To compare subjective and objective sleep quality of PoTS patients with a group of healthy controls	Prospective, Between-Subjects	<p>38 adult PoTS patients</p> <p>31 Healthy Controls (age and gender matched)</p>	<p>Pittsburgh Sleep Quality Index</p> <p>Epworth Sleepiness Scale</p> <p>Sleep Architecture, Heart Rate & Heart rate Variability (over the course of one night's sleep)</p>	<p>- PoTS patients were found to possess significantly lower sleep quality and higher sleepiness than controls</p> <p>- PoTS patients demonstrated significantly lowered HF, LF and HF/LF variability during each sleep phase</p>	<p>Authors suggest that PoTS should be considered as potential differential diagnosis for insomnia.</p>

					- PoTS patients were found to experience a greater proportion of phase II sleep	
Pederson & Brook (2017)	To investigate the prevalence of suicidal ideation, and to explore a possible relationship with this to symptoms of sleep disruption, in postural orthostatic tachycardia syndrome patients.	Online Survey-method; Between-subjects; Correlational (Regression) design	705 PoTS patients over the age of 18 (688 females; 17 males). 170 non-PoTS controls (145 females; 25 males)	Pittsburgh Sleep Quality Index Suicidal Behaviours Questionnaire-Revised	- 98.4% of PoTS Patients were found to possess poor sleep quality - Sleep efficiency in PoTS patients and sleep disturbances due to pain was found to be significantly more impaired in comparison to controls	Conclusion emphasises the importance of prescribing medications and non-pharmacological agents which decrease sympathetic activity to patients in order to improve sleep quality and hygiene. Health care providers should prioritise the treatment of sleep quality issues within PoTS patients in order to decrease suicide risk.
					A significantly higher proportion of PoTS patients were labelled as high-risk suicidal ideation than controls.	
					Regression analysis revealed suicide ideation scores were predicted by sleep scores, age and illness due to PoTS.	

Xu et al. (2016)	To investigated the prevalence of sleep disturbances in POTS patients, in addition to the use of medication and effects on daily life.	Survey-method	30 PoTS patients aged 18-56 years (27 females; 3 males)	<p>In-house survey method containing 22 items which assessed:</p> <ul style="list-style-type: none"> - Sleep Maintenance - Day time Sleepiness - Fatigue - Sleep Quality - Sleep Medication and prescribed treatments - PoTS Symptomology (e.g. Syncope, Low Energy, etc.) - Items concerning psychological symptoms- such as depression, anxiety & stress. 	<p>- The most prevalent sleep disturbances found in PoTS patients included daytime tiredness (96.7%), lack of restfulness when awake (83.3%), dissatisfaction with sleep each night (70%), and trouble falling asleep (63.3%).</p> <p>- Other symptoms associated with sleep disturbance that were reported include fatigue (96.7%), low energy (93.3%), and difficulty with concentration (76.7%).</p> <p>- 20% of patients reported use of over-the-counter medicine to help with sleep.</p> <p>- 23% reported using unspecified type of prescription sleep medication.</p> <p>- 6% of patients used a combination of over-the counter medicine and</p>	<p>Further research is needed to generate a better understanding of the underlying pathophysiological mechanisms which underlie sleep disturbances in PoTS.</p> <p>More consideration needed to explore the effects of commonly used pharmacological treatments for PoTS on sleep quality and hygiene related factors.</p>
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prescription sleep
medication.

- Patients who used
fludrocortisone for PoTS
treatment had more difficulty
with falling asleep.

- Pyridostigmine use was
associated with higher sleep
dissatisfaction.

Appendix G: Tabular Synthesis PoTS Beta-Blocker Empirical Research Studies

Table 1. A tabular analysis of empirical studies within the final review subset which have examined the use of beta-blocker medications for treating PoTS.

Author	Intervention(s) Examined / Research Arms	Study Aims	Study Design	Participants	Primary Outcome Measures	Main Findings	Implications / Future Research
Freitas et al., 2000	<p>Bisoprolol 5 mg, taken once daily - allocated to 10 patients at baseline.</p> <p>Fludrocortisone 0.1 mg, taken once daily - allocated to one co-morbid PoTS & asthmatic patient at baseline & three patients who remained symptomatic at 6 weeks.</p>	<p>Examine the hemodynamic and autonomic profiles of PoTS patients.</p> <p>Assess the effectiveness of bisoprolol and fludrocortisone at a 6 week and 12 week periods.</p>	Prospective, Between- & within-subjects	<p>11 female PoTS patients aged 17-57 (mean age = 31±11)</p> <p>11 healthy age/ gender matched controls who remained un-medicated</p>	<p>Orthostatic symptoms experienced on HUT table test</p> <p>Cardiac Output, Stroke Volume, HR, Systolic BP, Diastolic BP, Baroreceptor Gain, Low-Frequency HRV, High-Frequency HRV</p>	<p>6 Week Stage: 8 patients (including the one patient prescribed fludrocortisone at baseline) were asymptomatic for orthostatic symptoms.</p> <p>12 Week Stage: During HUT, post-treatment patients displayed the following changes from baseline:</p> <ul style="list-style-type: none"> - significantly decreased systolic BP & cardiac output. - increased baroreceptor gain & stroke volume. 	<p>Longitudinal, double-blind placebo study (employing male subjects) needed to confirm study findings.</p> <p>Authors advocate the use of bisoprolol over propranolol to treat hyperadrenergic PoTS patients, as the latter drug is associated with reduced side effects such as fatigue.</p>

- reduced HR increase.

During **HUT**, Systolic BP was significantly lower in the PoTS group than healthy controls within the supine & upright conditions.

Within the **supine condition**, in comparison to baseline scores medicated patients demonstrated:

- decreased heart rate.

- greater high-frequency heart rate variability (RR & ν).

- higher baroreceptor scores following treatment.

- lower cardiac output.

						Post-treatment PoTS patients demonstrated significantly lowered supine resting HR than controls.	
Raj et al., 2009	<p>Propranolol <i>Study (i)</i> – 20 mg</p> <p><i>Study (ii)</i> – 20 mg (Low Dosage Arm) – 80 mg (High Dosage Arm)</p> <p>Placebo <i>Study (i)</i></p>	Compare the effects of a single low propranolol dose on orthostatic symptoms against a placebo [<i>study (i)</i>] & a high propranolol dose [<i>study (ii)</i>] within a sample of PoTS patients	Single Blind Randomized Crossover	<p>Study (i): 54 PoTS patients recruited (Mean Age = 34±10; 49 female)</p> <p>Study (ii): 18 PoTS patients recruited (Mean Age = 33±8; 16 female. Two patients did not complete the 4-hour stage)</p>	<p>Vanderbilt PoTS Symptoms Score</p> <p>HR; Systolic Blood Pressure</p> <p><i>All Measures assessed at baseline, 2 Hours & 4 Hours post-intervention timepoints</i></p>	<p>Study (i) At both the 2 hour and 4 hour stages, Propranolol (20mg) use lead to a significantly reduced standing HR; seated HR; HR change due to orthostatic challenge; seated systolic blood pressure & orthostatic symptom score – in comparison to placebo.</p> <p>Within the 2 hour condition only, Propranolol significantly reduced standing systolic blood pressure in comparison to placebo.</p> <p>Study (ii)</p>	<p>First use of a placebo group to examine beta-blockers in PoTS.</p> <p>Low-dose propranolol outperformed placebo for reducing heart rate and self-reported OI symptoms over a 4 hour period.</p> <p>High dosage propranolol further decreases patients' heart-rates in comparison to low dosage; but changes in OI symptoms did not differ between arms.</p> <p>Limitations mentioned by authors include the lack of</p>

						<p>At both the 2 hour and 4 hour stages, high dosage Propranolol (80mg) use lead to a significantly reduced standing HR & HR change due to orthostatic challenge - in comparison to low dosage.</p> <p>Within the 2 hour condition only, high dosage propranolol significantly reduced standing systolic blood pressure in comparison to low dosage.</p> <p>Other assessed variables did not differ between the 2- and 4-hour stages.</p>	<p>double-blinding used within the study, low sample size for study (ii) & short duration of follow-up period (4 hours).</p> <p>Authors conclude that clinicians should be cautious of prescribing propranolol at high dosages, as this may not lead to a reduction in PoTS symptoms.</p>
Fu et al., 2011	<p>Arm (i): Propranolol - 80 mg per day for 4 weeks.</p> <p><i>Followed by</i></p>	<p>Assess the effects of a combined approach of propranolol and exercise training (<i>compared to an</i></p>	<p>Randomized, Double-blind single-group assignment</p>	<p>19 PoTS patients (Mean Age = 27±9; 18 female) in total</p> <p>10 patients assigned to the</p>	<p>36-SF</p> <p>Plasma Renin-Aldosterone; blood / plasma volume; haemoglobin</p>	<p>Propranolol treatment did not significantly change aldosterone: renin ratio, blood volume,</p>	<p>Exercise training was demonstrated to improve aldosterone: renin ratio and QoL in patients; this was</p>

<p>Exercise Training - Two-four times per week, 4 month period through the use of a bike, rowing or swimming exercise (session duration and intensity gradually increased).</p> <p>- Resistance (Weight) Training once per week for 15-20 minutes (increased gradually to two sessions per week of 30-40 minutes).</p> <p>- Increased salt intake + Water intake</p> <p>Arm (ii): Placebo - Once per day for 4 weeks.</p> <p><i>Followed by</i></p> <p>Exercise Training</p>	<p><i>exercise training only condition</i>) on the hemodynamic response, aldosterone: renin ratio & Quality of Life of PoTS patients</p>	<p>exercise only condition.</p> <p>9 patients assigned to the propranolol + exercise condition.</p> <p>15 healthy controls (Mean Age = 31±10; 14 female)</p>	<p>mass; red blood cell volume.</p> <p>Cardiac Output; Stroke Volume</p>	<p>haemoglobin mass, red blood cell concentration or QoL scores from baseline scores in the patient group.</p> <p>Data trends suggested propranolol lowered blood pressure from baseline during a two-hour standing test, and also decreased standing heart rate.</p> <p>No significant differences were found in relation to the placebo drug on the primary variables of interest.</p> <p>Exercise training led to significantly improved blood volume, haemoglobin mass, red blood cell concentration,</p>	<p>not reflected by the use of propranolol.</p> <p>Further works are needed to examine longer-term exercise interventions in PoTS.</p> <p>Additional further work is needed to examine the effects of the developed exercise programme within a community-based setting.</p>
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		- 4 months as defined above.				QoL scores & lowered upright posture heart rate.	
						A moderate improvement was found in the aldosterone: renin ratios of the patient group.	
Arnold et al., 2013	<p>Propranolol <i>Study (i)</i> - 20 mg (low dose) administered once prior to exercise test.</p> <p><i>Study (ii)</i> – 80 mg (high dose)</p> <p>Metoprolol <i>Study (ii) only</i> – 100mg</p> <p>Placebo <i>Study (i) & (ii)</i></p>	<p><i>Study (i)</i> – Investigate if low-dosage propranolol would increase peak oxygen consumption (VO2 max) against a placebo condition in PoTS patients during a bicycle exercise.</p> <p><i>Study (ii)</i> – Compare the effects of high dose propranolol, metoprolol and a placebo on the exercise capacity in PoTS patients.</p>	<p>Randomized, Double-blind Crossover</p> <p>(Minimum two day “washout” period between study (ii) arms)</p>	<p><i>Study (i)</i> - 11 PoTS females (Mean Age = 32±2)</p> <p>- Control group comprising of 7 healthy females</p> <p><i>Study (ii)</i> - 5 PoTS females (Mean Age = 29±5)</p>	<p>Peak Oxygen Consumption (VO2 Max)</p> <p>Heart-rate variability (Low-Frequency – SBP & RRI; High-Frequency – RRI)</p> <p>HR, SBP & DBP on Autonomic Functioning tests – (for Valsalva Test; Sinus Arrhythmia Ratio; Handgrip & Coldpressor; Supine & Upright postures)</p> <p>Plasma Norepinephrine levels</p>	<p>Study (i) Patients and controls did not significantly differ on exercise measures (VO2max) at the placebo stage.</p> <p>Furthermore, 9 out of 11 patients did not meet the criteria for physical deconditioning (VO2 max < 80%).</p> <p>Propranolol decreased peak heart rate to a similar level to that of controls during exercise.</p>	<p>Findings suggest the effects of propranolol on exercise capacity in PoTS may be dosage-dependent.</p> <p>Low-dose propranolol produced an 11% increase in peak oxygen consumption within patients.</p> <p>Authors state that further works are needed to compare the effects of low-dose propranolol against endurance exercise training, which is known to</p>

						<p>Furthermore, only PoTS patients demonstrated a reduction in VO₂ max within the propranolol condition.</p> <p>Study (ii) Only one of the five patients was found to be deconditioned.</p> <p>Both drugs were found to decrease peak HR during exercise, but were not found to significantly decrease VO₂ max.</p>	decrease upright HR and improve blood volume.
Zhang, Chen, Li & Du, 2014	Metoprolol – 0.5 mg / kg twice a day for a 3 month period.	Examined whether plasma norepinephrine levels could serve as a predictor for the effectiveness of metoprolol in a sample of child Hyperadrenergic PoTS patients.	Prospective between-subjects	27 child PoTS patients aged 6 – 15 years old (Mean Age = 11.0±6; 15 female). 2 patients lost during treatment period due to lose of contact (n = 25).	Plasma Norepinephrine Levels Orthostatic Symptom Severity score	At baseline, greater norepinephrine plasma levels positively correlated with both higher orthostatic symptom severity and orthostatic HR	Prior to the conduction of this study, there was a lack of prior works which had examined the efficacy of beta-blockers for specific subtypes of PoTS.

<p>change on the HUT table test.</p>	<p>Findings suggest that metoprolol is an effective beta-blocker for children who have a plasma norepinephrine level of 3.59 pg/ml or higher.</p>
<p>13 of the patients showed a 50% or greater improvement in orthostatic symptom severity post the 3 month metoprolol treatment (Responders); 12 patients did not (Non-Responders).</p>	<p>Authors identify limitations of the current study due to the low sample size & their decision not to examine the catecholamine levels post-treatment, and for not recruiting a control group of healthy children for further comparison.</p>
<p>Responders and non-responders did not significantly differ between their age, sex, baseline symptom scores, supine blood pressure or orthostatic HR change.</p>	
<p>Responders were found to possess significantly greater levels of baseline norepinephrine</p>	

						than non-responders.	
						ROC curve analysis revealed a moderate predictive value to support the use of plasma norepinephrine levels as an indicator of metoprolol effectiveness within the sample [Sensitivity = 76.9%; Specificity = 91.7%].	
Moon et al., 2018	<p>Arm (i): Propranolol only – 10 mg once per day; increased to 20 mg following 1 month at clinician's discretion.</p> <p>Arm (ii): Bisoprolol only –2.5 mg once per day; increased to 5 mg following 1 month at</p>	Evaluate the efficacy of propranolol, bisoprolol and the effects of each agent alongside pyridostigmine for treating orthostatic symptoms, depression and QoL scores in PoTS patients over a one- and three- month period.	Randomized 2 x 2 mixed factorial	77 PoTS patients (41 females; mean age = 33±12.7) completed the 3 month intervention period [<i>number of patients lost to follow up</i> = 26]	<p>Orthostatic Intolerance Questionnaire [OIQ]</p> <p>Beck Depression Inventory-II [BDI-II]</p> <p>SF-36</p> <p>HR, BP</p>	<p>Both OIQ and BDI-II scores significantly decreased at the 1 month stage, then further decreased at the 3 month stage for all treatment arms (no statistical differences found between treatment arms).</p> <p>Mental and physical</p>	<p>Propranolol and bisoprolol did not differ in their ability to improve health-related QoL, reduce depression and orthostatic symptom severity over a one and three month period.</p> <p>The addition of pyridostigmine to the two beta-blocker</p>

<p>clinician discretion.</p>	<p>- Arm (ii) = 17 patients (8 discontinued) - Arm (iii) = 18 patients (8 discontinued) - Arm (iv) = 23 patients (3 discontinued)</p>	<p>components on the Sf-36 also improved at the 1 month and 3 month stage, regardless of treatment arm.</p>	<p>treatments did not lead to significant improvement in the examined variables. A minor exception to this is the treatment of non-anti-depressant prescribed PoTS patients, who showed greater mental component scores on the SF-36 after a three month period.</p>
<p>Arm (iii): Propranolol + Pyridostigmine - Propranolol dosage same as above. Pyridostigmine dosage 30 mg twice per day; maintained for 3 months.</p>	<p>59 patients used pre-prescribed anti-depressants during the study</p>	<p>Sub-group analysis of patients who were not actively taking anti-depressants revealed that improvements in the BDI-II and OIQ scores at 1 and 3 month periods remained, regardless of treatment arm.</p>	<p>Sub-group analysis indicates the use of antidepressants alongside beta-blocker treatment is unwarranted.</p>
<p>Arm (iv): Bisoprolol + Pyridostigmine - Dosage for both drugs as mentioned above.</p>		<p>Furthermore, sub-group analysis revealed that improvement in the physical component of the SF-36 for both 1 & 3 month periods remained regardless of treatment arm (however, no statistical</p>	<p>Further examination of the included beta-blockers could be conducted to examine changes over longer intervention periods & in comparison to a placebo group.</p>

difference was found between these two time points within Arm iii).

Sub-group analysis also revealed that mental component scores for the SF-36 between the 1 month and 3 month period did not differ for any of the treatments arms.

Sub-group analysis demonstrated that mental component scores at the 3 month stage improved from baseline only within the Propranolol + Pyridostigmine group.

Appendix H: Initial Ocean Breathing Guide



Slow-Paced Breathing for PoTS - Instructional Guide -

This guide will take you through a meditation exercise known as the [Ocean Breath](#).

The Ocean Breath, which has been named after the “wave-like” sound that a person makes during the exercise, is known to induce feelings of calmness & to improve the quality of sleep.

The breathing practice can be performed in either a lying down or in a sitting up position, so please choose the posture which you would find the most comfortable.

Before beginning your practice, it may be a good idea to gently blow your nose beforehand to make sure your airways are clear.

- [Optional Preparation Exercise](#) -

The preparation exercise is an optional step of the practice to perform which aims to increase your awareness of how the body moves as you breathe.

This is a short (2 Minute) exercise, but you are welcome to adapt the length of time you choose to engage with this step to find a pace which you feel most comfortable with.

Breathing as you normally would, we will start by placing one hand on your belly and the other hand on top of your rib cage where the chest is located.

As you gently take each breathe in, keep the hand on your rib cage still and allow only the belly to move with each breath.

As you do this, take a few moments to simply focus on the sensation of the hand on your belly slowly rising & falling.

After we have taken time to reflect on this, we will now try the reverse. This time, keep the hand on your belly still and allow your chest to move in and out with each breath. Once again, the aim here is to focus solely on the sensation of the hand being lifted by the movement of the chest.

When you feel ready to proceed, return both hands back to your side to begin the [Ocean Breathing technique](#) (on the next page).

- [The Ocean Breath](#) -

Ocean breathing works by soothing the ‘fight-or-flight’ pathway of the autonomic nervous system, helping you to feel more refreshed and energised by the end of the practice.

Relax your body and gently close your eyes. Let your mouth drop open slightly. Relax your jaw and your tongue.

1. Slowly and gently inhale and exhale through your mouth. Notice how the air passes through your throat as you do this.
2. As you breathe out, softly whisper the sound “ahhhh,” as you exhale. Imagine that your breath is fogging up a window, or that you are slowly blowing out the candles on a birthday cake.
3. As you are making the “ahhhh” sound, notice that there is a slight constriction in your throat as you do this. As you become comfortable with this sensation as you exhale, we are going to maintain this constriction of the throat during each breath you take in.
4. You will notice your breath making an “ocean” sound, softly moving in and out, like ocean waves. This helps you to establish a steady rhythm – where each inhale takes the same amount of time to perform as each exhale.
5. If you feel comfortable to do so, you may gently close your mouth and begin to breathe only through your nose. You will continue to hear the “ocean” sound as you breathe through your nose. Keep your mouth closed, but your lips soft.
6. Start by practicing steps 1-5 for five minutes. When the ocean breathing practice is complete, release the constriction in your throat and take time just to breathe naturally.

- [Finishing the Practice](#) -

To close your practice, we are going to take a moment to just reflect on this experience.

Keeping your eyes closed, take a moment just to be still and to observe your natural breath entering and leaving your body.

At this moment, focus only on the breath travelling through you. When you feel ready to return back to the present moment, slowly begin to open your eyes.

This concludes your [Ocean Breathing](#) practice.

Appendix I: Interview Schedules

Interview Schedule:

- Patients -

POTS Overview

- (i) What is POTS, and what are your experiences of this?
 - (ii) How long have you been diagnosed with POTS for?
 - (iii) Please could you describe the process of your diagnosis- how was your condition diagnosed, and were there any issues you encountered with this process?
 - Misdiagnosis; understanding of condition by practitioner
 - (iv) What symptoms of POTS do you experience regularly?
 - Fatigue; “brain fog”; dizziness; psychological symptoms
 - (v) How has POTS impacted on your quality of life?
 - Occupation / education; social life and relationships with others; independence
 - (vi) How do you current manage your POTS symptoms?
 - Medication side effects; co-morbidity; fatigue; orthostatic intolerance; intolerance; currently untreated symptoms
-

Prior Experience with Breathing Techniques

- 5) Do you have any previous experience with performing breathing techniques or yoga-related exercises? If so, please can you briefly describe this.
 - If so, how did you learn these breathing techniques? (Self-taught; delivered by clinician)
 - If not, what are your thoughts on these practices?
-

Introduction to the Breathing Technique

The participant is asked to view the following link. If the interview is conducted through Skype or telephone; the researcher will e-mail this to them ahead of time:

<https://www.youtube.com/watch?v=JsbpqW0Baog&t=10s> [Duration: 2.47]

- 6) What are your initial thoughts of the breathing practice?
- 7) Which aspects of the breathing technique would you find interesting to perform and why?
- 8) Are there any aspects of the breathing technique which you may find difficult or challenging to perform? If so, which parts of the technique could present an issue and why?
- 9) How can the breathing practice be altered to alleviate these concerns?
- 10) If asked, would you be prepared to invest the time and effort into learning the technique?
 - Why; Barriers to practice; How can these issues be overcome and alleviated when designing the breathing technique and its delivery?

11) For those of you who have tried or are currently performing breathing techniques, have you discussed this with any healthcare professional who treats you?

- How would you feel about approaching this subject with them?

Instructional Guide

Prior to the session starting, the participant is handed an instructional guide by the researcher and given time to read over this. If the study is conducted via skype / telephone, participants are asked to open this document from an e-mail sent to them by the researcher.

12) What are your thoughts on the instructional guide and its layout?

- Flow, structure, clarity, language, number of steps

13) Are the instructions on the guide sheet clear and easily comprehensible for you to interpret? If not, which elements require further clarification and how could this be done?

14) Which specific steps or terminology within the instructional guide may other patients have

difficulty with understanding? If so, please explain why this may cause an issue.

15) From the instructional guide sheet, is it clear to you what is required of you to

perform the breathing technique, and why you are being asked to do this?

- If not, how can we adapt the instructional guide to make this more clear?

- Delivery & audio instructions

16) By using the instructional guide, would patients be able to feasibly learn and perform the breathing technique on their own, following a short training session with a researcher?

- Why; memorising instructional steps

Mobile Applications [Prana Breath; Breath]

The participant is handed a mobile / tablet by the researcher device which contains two breathing applications on to them. If the interview is being conducted online or by telephone- prior to the study, starting the researcher will send them the following links to two short videos demonstrating the apps:

- Prana Breath:

<https://www.youtube.com/watch?v=S6rqhxAm4tA&feature=youtu.be&fbclid=IwAR1KolsJ40y3sn>

[48HF0HKr4mW0Y_W6SIs8XHXcwfQhrH0hKDyTXImr5aaRk](https://www.youtube.com/watch?v=48HF0HKr4mW0Y_W6SIs8XHXcwfQhrH0hKDyTXImr5aaRk)

- Breath:

<https://www.youtube.com/watch?v=DTIGmjHh7K4&feature=youtu.be&fbclid=IwAR1MPxYoWfL9>

[QUBjmMQ281DL2N6SL5iVup0k7oVVznRz2AjaxtB-zvNRvo4](#)

- 17) What are your initial thoughts of these applications?
- 18) Which aspects do you like about these apps, and why?
- 19) Which app do you prefer to use, and why?
- 20) If you were asked to use this app alongside your practice, how would you feel about this?
- 21) Would a POTS patient encounter any difficulty with using these programmes during a breathing exercise?
- 22) How could the use of a breathing-based application influence participants' compliance with the breathing technique?

Practicalities

23) The research team plans to deliver this breathing technique by providing a single training session, where participants will be guided through the intervention in a step-by-step manner.

What

are your thoughts on this?

24) Would one training session be perceived as sufficient to correctly administer and teach the

technique to patients?

25) If you were to undergo the training session at the same time as other individuals who were

learning the breathing technique, how would you feel about this?

- Supportive environment vs Privacy (one-to-one basis)

- How many individuals would you be willing to learn the technique with? Would you prefer this to undergoing the technique one-to-one with the researcher?

26) If an individual was asked to perform the breathing technique on a daily basis, what factors may determine how successful they are in achieving this?

- Routine; finding the time within the day

27) If you were to regularly undertake the breathing exercise, how might your close family and friends perceive or react to this?

- Supportive network; Barrier to practice

Closing remarks: Anything else you think we should consider in working with this technique with people with POTS?

Interview Schedule:

- Healthcare Professional -

POTS Presentation within Professional Practice

- 1) Please could you describe your involvement with POTS patients within your occupation?
 - CRESTA staff: What role do you play within the team?
 - GPs: Please can you describe the process of diagnosing POTS within a patient?
 - 2) What typical symptoms do patients within your practice usually present?
 - Cognitive; psychological; physiological
 - 3) How are the symptoms of POTs patients managed within your practice?
 - How do patients usually respond to these methods- are they effective?
 - 4) What is the impact of POTS on patients that you see.
 - 5) Within your clinical team, how do you assess / measure the successfulness of these treatments for POTS symptoms?
 - Role of the patient; objective measures
-

Prior Experience with Breathing Techniques

- 5) Do you have any personal experience with performing breathing techniques or yoga-related exercises? If so, please can you briefly describe this.
 - 6) Are any patients within your practice currently using any breathing-related techniques within their treatment regimes?
 - If so, how was this administered? (Self-taught?)
 - How are these methods perceived by these patients?
 - 7) If a patient approached you to say that they were considering performing a breathing technique for managing their POTS symptoms alongside their current treatment plan, how would you feel about this?
 - How would other members of your clinical team feel about this?
-

Introduction to the Breathing Technique

The participant is asked to view the following link. If the interview is conducted through Skype or

telephone; the researcher will e-mail this to them ahead of time:

<https://www.youtube.com/watch?v=t7UXRF1aHdU>

- 8) What are your initial thoughts of the breathing practice?
- 9) In what ways does the breathing techniques differ to other current treatments for POTS?
- 10) In what ways is the breathing technique similar to other treatments for POTS?

11) If the patients you have worked with were asked to perform the breathing technique, how would do you think they might react?

12) Are there any aspects of the breathing technique which patients may find difficult or challenging

to perform? If so, which parts of the technique could present an issue and why?

- Concerns; How can practice be altered to alleviate these

13) Will patients be prepared to invest the time and effort into learning the technique?

- If not, what barriers are likely to hinder the acceptability of this intervention?

- How can these be overcome / alleviated when designing the breathing technique and its delivery to the patient group?

Instructional Guide

Prior to the session starting, the participant is handed an instructional guide by the researcher and

given time to read over this. If the study is conducted via skype / telephone, participants are asked

to open this document from an e-mail sent to them by the researcher.

14) What are your overall thoughts on the instructional guide and its layout?

15) Are the instructions on the guide sheet clear and easily comprehensible for you to interpret? If

not, which elements require further clarification and how could this be done?

16) Which specific steps or terminology within the instructional guide may patients have difficulty

with performing? If so, please explain why this may cause an issue.

17) From the instructional guide sheet, would patients be able to understand what is required of them to perform the breathing technique, and why they are being asked to do this?

18) By using the instructional guide, would patients be able to feasibly learn and perform the breathing technique on their own, following a short training session with a researcher?

- Why do you believe this to be the case?

Perceived Views by the Clinician's Organisational Team

19) If the clinical team within your organisation were also shown this breathing technique, what would their initial impressions of this intervention be?

- Would you expect this to change over time?

20) If the breathing technique were to be administered to patients within clinical practice, how would you feel about this?

Mobile Applications [Prana Breath; Breath]

The participant is handed a mobile / tablet by the researcher device which contains two breathing applications on to them. If the interview is being conducted online or by telephone-prior to the study, starting the researcher will send them the following links to two short videos demonstrating the apps:

- Prana Breath:

<https://www.youtube.com/watch?v=S6rqhxA4tA&feature=youtu.be&fbclid=IwAR1KolsJ40y3sn>

[48HF0HKr4mW0Y_W6SIs8XHXCwfQhrH0hKDYTXImr5aaRk](https://www.youtube.com/watch?v=48HF0HKr4mW0Y_W6SIs8XHXCwfQhrH0hKDYTXImr5aaRk)

- Breath:

<https://www.youtube.com/watch?v=DTIGmjHh7K4&feature=youtu.be&fbclid=IwAR1MPxYoWfL9>

[QUBjmMQ281DL2N6SL5iVup0k7oVVznRz2AjaxtB-zvNRvo4](https://www.youtube.com/watch?v=QUBjmMQ281DL2N6SL5iVup0k7oVVznRz2AjaxtB-zvNRvo4)

21) What are your initial thoughts of these applications?

- Pros / cons; preference for one application or the other

22) If you were asked to use this app alongside during a breathing practice, how would you feel about this?

- Benefits; concerns

23) Would a POTS patient encounter any difficulty with using these programmes during a breathing exercise?

24) How could the use of a breathing-based application influence participants' compliance with the breathing technique?

Issues & Suggested Changes Highlighted by Patient Group

This section will follow from the chief investigator presenting the preliminary findings of stage 1.1 of the study. For each suggested change / issue identified by the patients- the healthcare professional will be asked:

- Their thoughts on each matter and whether they agree with the patient group

- Whether they perceive a suggested change to be effective in alleviating a concern of the patient group, or if this solution is unfeasible and why they believe this.

- For any other alterations which could be made to the breathing technique to overcome foreseen issues, and the methods for implementing this.

Furthermore, in preparation of the **future feasibility trial** (stage 2 of the research), the researcher will present the participants with a number of psychometric outcome measures (such as the autonomic symptom severity index; the hospital anxiety and depression scale;

various quality of life measures, etc) which have been used by past research to assess patients' symptoms. The participant and the researcher will work together to identify the most appropriate outcomes for use within the future stage of the research and the design of the feasibility trial. 25) From the methods discussed today, what support and guidance would a patient need to learn and regularly undertake this breathing practice?

Appendix J: Additional Breathing Guides

BUTEYKO BREATHING

DID YOU KNOW?
Every cell in our body needs a certain concentration of carbon dioxide (CO₂) and oxygen (O₂) in order to function properly. If we breathe in an amount that is too large, the body's needs are not met, and the lungs are not capable of maintaining the correct levels.

SUMMARY
We've been taught that deep breathing is optimal because it allows the most oxygen into the lungs. Strange as it may seem, oxygen deficiency is not caused by lack of oxygen, but by lack of carbon dioxide. If we breathe too much, we actually get less oxygen. Let's see why...

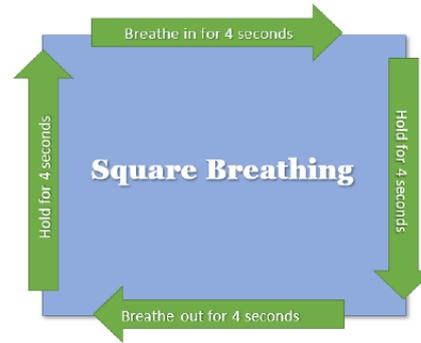
Normal breathing frequency at rest is about 8-12 breaths per minute. Many of us breathe much more, often up to 25 breaths per minute. This breathing habit usually goes unnoticed, but nevertheless causes a low grade form of hyperventilation, upsetting the oxygen and CO₂ balance. For the body to actually use oxygen, it also needs a certain amount of carbon dioxide.

The Buteyko Breathing Method, developed in the 1950's by Russian medical scientist Dr. Konstantin Buteyko, teaches you how to bring your breathing volume back toward normal, or, in other words, reverse what's called chronic hyperventilation, or chronic over-breathing. When your breathing is normal, you have better oxygenation of tissues and organs, including your brain.

HOW TO DO IT
The Buteyko Breathing Technique teaches you how to breathe properly through the nose (not the mouth) and with the diaphragm to improve nitric oxide and carbon dioxide levels in the body. When done properly, Buteyko breathing encourages the activation of the parasympathetic nervous system, resulting in a reduction of blood pressure, a reduction of stress and the strengthening of the immune system. Here are the simple steps to perform this technique.

WHY IT WORKS
Studies have shown that breathing lightly and only through the nose is the ideal technique for education and optimal health. One such study on the effect of Buteyko breathing technique on patients with bronchial asthma showed a significant decrease in asthma related symptoms and a significant improvement in peak respiratory flow rate (PFR).





Square breathing (also known as “box breathing”) is a technique for deep breathing, which has been shown to help relax the nervous system¹.

Deep breathing helps aid the body in many functions such as:

- Calming and regulate the nervous system
- Help the body cope with stress
- Ease panic and worry
- Bring more oxygen to the body

Tips:

- If 4 seconds for each side of the square is too much, you can use 2 or 3 to help you get the hang of it!
- Try saying the numbers in your head if it is hard to find the beat
- Get comfortable! It is easier to relax and breathe when your body is in a relaxed and comfortable position.

Reducing Overwhelm with The STOP Technique

The STOP Technique is a mindfulness-based practice designed to help you defuse stress in the moment.

Creating space in the day to pause, slow down a racing mind, and get back into the present moment has been shown to be incredibly helpful in reducing the negative effects of stress.

Taking a brief pause—even for less than one minute—can help you gain perspective and determine the best possible action you can take next.

Over time and with practice, this way of responding becomes a habit. As Sharon Salzberg says, “Mindfulness isn’t difficult, we just need to remember to do it.”

Stop

Interrupt your thoughts with the command ‘stop!’ and pause whatever you’re doing.



Take a Breath

Notice your breathing for a second. Breathe in slowly through the nose, expanding the belly, and exhale slowly and deeply through pursed lips.



Observe

Become the observer of your thoughts, emotions and physical reactions. What thoughts do you notice? What emotions are present? How does your body feel? Tune in and sit with whatever arises for a few moments.



Proceed

Mindfully consider how you’d like to respond. What’s **one thing** you can focus on right now? What’s your most important and urgent priority? Narrow down your focus and take it one small step at a time.



Diaphragmatic Breathing

Diaphragmatic breathing technique

1. Lie on your back on a flat surface or in bed, with your knees bent and your head supported. You can use a pillow under your knees to support your legs. Place one hand on your upper chest and the other just below your rib cage. This will allow you to feel your diaphragm move as you breathe.



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