UTS UNIVERSITY OF TECHNOLOGY SYDNEY

A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels

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under the supervision of Dr Sean Walsh and Dr Shuai Zheng

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CERTIFICATE OF ORIGINAL AUTHORSHIP

I, Dane Couter, declare that this thesis is submitted in fulfilment of the requirements for the award of Master of Science (Research), in the Science Faculty at the University of Technology Sydney. This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution.

This research is supported by the Australian Government Research Training Program.

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Abbreviations

ACTH	Adrenocorticotropic hormone
AHPRA	Australian Health Practitioner Regulation Agency
ANZCTR	Australian New Zealand Clinical Trials Registry
ASQ	Additional Stress Questionnaire
BDI	Beck Depression Inventory
BL	Bladder (Acupuncture Point/Meridian)
BP	Blood pressure
CEQ	Credibility and Expectancy Questionnaire
CM	Chinese medicine
CMBA	Chinese Medicine Board Australia
CONSORT	Consolidated Standards of Reporting Trials
CRH	Corticotropin releasing hormone
EPDS	Edinburgh Postnatal Depression Scale
fMRI	Functional magnetic resonance imaging
FPI	Fertility Problem Inventory
GB	Gall Bladder (Acupuncture Point/Meridian)
GR	Glucocorticoid receptors
GV	Governor Vessel (Acupuncture Point/Meridian)
HF	High frequency
HPA	Hypothalamic pituitary axis
HR	Heart rate
HREC	Human research ethics committee
HT	Heart (Acupuncture Point/Meridian)

LF	Low frequency
LI	Large Intestine (Acupuncture Point/Meridian)
LISS	Lipp's Inventory of Stress Symptoms
LR	Liver (Acupuncture Point/Meridian)
MR	Mineralcorticoid receptors
MSNA	Muscle sympathetic nerve activity
MYMOP	Measure Your Medical Outcome Profile
NHMRC	National Health and Medical Research Council
PC	Pericardium (Acupuncture Point/Meridian)
PFQ	Participant Final Questionnaire
PIS	Participant information sheet
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
RCT	Randomised controlled trials
REDCap	Research electronic data capture
SP	Spleen (Acupuncture Point/Meridian)
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
ST	Stomach (Acupuncture Point/Meridian)
STAI	State-Trait Anxiety Inventory
STRICTA	Standards for Reporting Interventions in Clinical Trials of Acupuncture
TCM	Traditional Chinese medicine
UCT	Uncontrolled clinical trials
UTS	University of Technology, Sydney

Abstract

Introduction

Stress is a common part of modern life. While it provides a positive stimulus for physiological functions, it may still lead to negative effects when featuring high intensity or duration for an individual. As a population facing many specific challenges, students are often subjected to multiple types of stressors. Limited data exists to show acupuncture as an effective stress reduction intervention, but there is little consensus about treatment protocols. This thesis aims to further inform the possible protocols to be used in subsequent clinical trials.

Aim

The project aims to inform possible further study in acupuncture and stress by refining proposed acupuncture protocols for stress via a Delphi process. Expert consensus was sought regarding diagnosis, syndrome differentiation, signs and symptoms, acupuncture point selection and treatment frequency.

Method

This thesis contains a literature review, a clinical trial protocol and a Delphi process. The literature review highlights the scarcity of acupuncture research specifically about stress. A clinical trial protocol was developed using the literature review results to investigate the impact of acupuncture at different treatment frequencies, focussing on tertiary students as the population group. Finally, a two-round Delphi process seeking expert consensus regarding clinical diagnosis and treatment of stress was undertaken with a threshold level set at 80%.

Results

The literature review found very little evidence of studies using acupuncture for stress (n=11; RCTs n=8, UCTs n=3). There was very little cohesiveness between studies regarding acupuncture dosage (treatment frequency or number of treatments total), acupuncture points used or diagnosis.

The Delphi process showed expert consensus on zangfu relevant to stress diagnoses (Heart and Liver), syndromes relevant to stress diagnoses (qi stasis and zangfu disharmony) and acupuncture

points relevant to stress treatment (Liver 3, Pericardium 6, Heart 7 and Yin Tang). There was no consensus on frequency of treatments or number of treatments preferred.

Conclusion

The clinical trial acupuncture point protocol is valid for future use according to expert consensus. Further research is needed to determine satisfactory acupuncture dosage for use in clinical trials across a range of variables including treatment frequency and total number of treatments.

Chapter 1: Introduction

1.1 Stress

Stress is a complex reaction referring to any type of transient change from a homeostatic baseline or a long-term change for survival, resulting in the development of physical, emotional or psychological reactions and/or behavioural adaptations (World Health Organisation (WHO), 2021). The term can descriptively apply to daily life hassles through to the response to short or long-term exposure to traumatic events and situations. The intensity of symptoms experienced vary between people based on their past experiences, while broader cultural differences modulate the perceived stress and resultant effects (Lee et al., 2022). Stress has both beneficial and pathogenic connotations; while providing a protective response to meet challenges, if left unchecked it can also cause harm. For example, an unexpected event induces a transient rise in blood pressure and heart rate and the stimulation of neural sympathetic activity to induce a fight, fright or flight response to a life threatening situation; yet a sustained elevation of heart rate and blood pressure over time can lead to increased morbidity from stroke and heart disease (McEwen, 2008). Of particular concern are the health and performance impacts of stress on quality of life (QoL) and effects on activities of daily living (ADL), especially when an acute stress response remains unmanaged and contributes to a chronic stress response forming. Chronic stress is sometimes defined as stress which is ongoing for at least six months (Hammen et al., 2009). This pathological stress, the central theme of this thesis, is described as a 'process in which environmental demands tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease.' (p.3) (Cohen et al., 1997). This includes increased cortisol, supressed immune function, and detrimental impacts on performance. There are additional effects on mood and a person's sense of wellbeing (Schneiderman et al., 2005). For example, work related chronic stress can lead to the phenomenon of burnout, an occupational impact resulting in professional disengagement and low empathy, negatively impacting co-workers and family members (Organisation, 2022). In this context, stress is not just an individual experience but resonates into the effected person's inter-personal interactions and their community (Cocker & Joss, 2016).

1.1.2 Epidemiology of Stress

While some populations have been found to be more stressed than others (Mahmoud et al., 2012), stress remains ubiquitous, found across all demographics, peoples and geographical regions. Approximately one in three Americans (37%) report a stress related symptom (such as forgetfulness and difficult making decisions) (American Psychological Association (APA), 2022). Worryingly, younger adults are more affected, with 46% of adults under 35 report being impacted by stress, with

Black adults (56%) being more affected (APA 2022). The South African Stress and Health (SASH) Study additionally reports a high prevalence of moderate (31%) to severe (26%) stress related mental health disorders in a survey sampling of the South African and Nigerian population. Younger adults (18–34 years-old) were reported to be more affected with anxiety related stress, while older adults (> 35 years of age) were more affected by mood disorders and/or poor stress-related behavioural impulse control (Herman et al., 2009)

In Australia, 61% of the population surveyed identified having a significant amount of stress in their life, with 36% reporting this as moderate to extremely severe (Australian Psycholgical Society (APS), 2016) . Stress can also impact people across all timepoints of their life; age is not a barrier to a pathological stress response forming (Mikneviciute et al., 2022). Stress additionally can arise in any of life's domains (Jackson et al., 2016). In Australia, attributable top causes of stress include personal finances (49%), family issues (45%) and personal health (44%), and for younger people (18–25 years of age) this also includes environmental factors. In the Australian workplace alone, increasing stress rates have been calculated to have an associated financial and personal impact, resulting in absenteeism (absence from work or other obligations), work-disconnect and sick leave (the entitlement to paid leave during medical illness) (Camp & Lambert, 2006). This was estimated to impact the economy by $14.81 billion (Medibank Private2008) in 2008, rising to $30.9 billion in 2019 (AMP, 2019). Independent of the workplace, stress is also strongly associated with increasing levels of societal depression and anxiety, with decreasing rates of wellbeing (APS, 2016). Complicating matters further is the trans-migratory nature of stress; while it might arise in one of life's domains, it can cross-over to effect another of life's domains. Consequently, pathological stress is considered both detrimental and insidious, with some segments of the populations more effected than others (Jackson, Kirschbaum & Steptoe, 2016)

1.1.3 Stress and Risk Factors

A stressor is a causal agent that results in changes to perceived or actual stress. Stressors by themselves do not impact a person's bio-psycho-social health outcomes, rather it is the person's perception of, and reaction to, the stressors that can lead to poorer outcomes. These include increased anxiety and depression, decreases in wellbeing and physical and psychological resilience (Barbayannis et al., 2022; Beck & Clark, 1997). That is, while stress is experienced throughout life, whether stress becomes pathological by exceeding the individual's ability to cope depends on multiple variables, including an individual's epistemological framing of an experience.

Critically the response to stressors is heavily affected by a person's past experiences. Positive or negative experiences in a person's romantic, educational or professional life (as examples) will influence the reaction to stressors in a similar situation, such as being abused by a former lover or

having had a supportive supervisor (McEwen, 2008). Early childhood experiences (both negative and positive) have a greater impact, given the core psycho-social-emotional developmental foundations of an individual's early life (Ballantine et al., 2016). The ensuing reaction may lead to taking part in maladjusted coping mechanisms such as eating or drinking too much, poor sleep, lack of exercise, poor social habits or smoking, exacerbating the situation by aggravating the subsequent stress response (McEwen, 2008).

There are many risk factors associated with stress, reflecting it's pervasiveness through life. Mofatteh (2021) divided risk factors for undergraduate students into six themes and further sub-themes: psychological (including self-esteem, personality type and loneliness), academic (workload pressure, exams and assignments), biological (gender, age), lifestyle (smoking, inadequate sleep), social (social networks and support) and financial (lack of income, childhood poverty).

1.1.4 Stress-Induced Physiological Processes

The physiological processes induced by stressors involve multiple systems and mediators. Adrenalin, produced from the adrenal glands, and cortisol, from the adrenal cortex, are the two major "stress hormones", however there are others (McEwen, 2008), including cytokines and catecholamines which have far-reaching effects encompassing functions of the central nervous system, parasympathetic nervous system, cardiovascular function, immune function and metabolism.

These relationships and interactions are complex and non-linear. Changes in one mediator often result in compensatory changes in another (McEwen, 2008), yet clinical trials often measure only one or a few mediators, leaving the inter-relational complexities of the stress response unreported and unaddressed.

The Hypothalamic Pituitary Adrenal Axis (HPA) is an important aspect of stress-related physiology, as it is central to the body's stress response. The hypothalamus is responsible for producing corticotropin releasing hormone (CRH), which stimulates the pituitary to synthesise adrenocorticotropic hormone (ACTH). ACTH then stimulates the adrenal glands to release the stress-related hormone, cortisol. This is one of the main reasons for cortisol measurements to be used in stress-related research, although cortisol levels can be affected by other things such as sleep and metabolism, which reduces it's clinical accuracy somewhat (O'Connor & Vallejo Sefair, 2019).

Similarly, the hypothalamus can stimulate the adrenal medulla to secrete catecholamines (chiefly adrenaline and noradrenaline) in response to stress. This response is generally more short-term in nature (causing effects such as vasoconstriction and increased heart rate), embodying the rapid "fight-or-flight" response to stress and is therefore generally less useful in research into chronic stress related physiological outcomes (O'Connor & Vallejo Sefair, 2019).

These stress responses have been shown to lead to many and varied chronic health outcomes. Stress and the related activation of the sympathetic nervous system has been linked with obesity and sleep apnoea (Malpas, 2010), cardiac and vascular hypertrophy in long-standing hypertension (Mancia et al., 1999) and atherosclerosis leading to chronic heart disease (Rozanski et al., 1999). Sympathetic overactivity has been linked with poorer prognoses in heart failure (Malpas, 2010). Stress has been linked with gynaecological issues such as low birth weights and pre-term birth (Chang et al., 2019). Stress has even been found to alter gene expression involved in the HPA axis (O'Connor & Vallejo Sefair, 2019), thereby affecting the physiological response to stress.

1.1.5 Stress-induced Cognitive Responses

While adrenaline is unable to cross the blood-brain barrier, this not true of the stress hormone cortisol. Corticosteroid receptors called mineralcorticoid receptors (MR) and glucocorticoid receptors (GR) bind cortisol and are generally only partially occupied, but become fully activated when cortisol levels rise, for example in response to a stressor (de Kloet et al., 1999). This binding occupies the prefrontal cortex, amygdala and hippocampus, three regions responsible for memory and cognitive control (Mikneviciute et al., 2022).

Chronic stress and the associated physiological changes (such as increased corticosteroid production) have been linked with multiple negative cognitive health outcomes, including cognitive decline in older people (Aggarwal et al., 2014), increased likelihood of developing Alzheimer's disease (Mikołajewska & Mikołajewski, 2019) and to disruption of memory formation (de Kloet et al., 1999; Sandi, 2013). Chronic stress has also been found to affect cognitive processes involved in appetite and "food addiction" behaviours associated with obesity (Morris et al., 2015).

While chronic stress is generally associated with negative cognitive outcomes, there is evidence to show that acute stress in certain situations and optimal severity *improves* memory formation (Domes & Frings, 2020), that is, when people are subjected to the right amount of stress their performance improves – much like the commonly seen Yerkes-Dodson Law bell curve (Figure 1.1), sometimes referred to as the "stress-performance curve". The Yerkes-Dodson Law shows that performance (shown in multiple animal species including humans) improves and declines according to a bell-shaped curve as the stimulus (in this case stress) increases (Calabrese, 2008; Yerkes & Dodson, 1908), meaning that the right amount of stress, at the right time, is a positive cognitive performance enhancer.

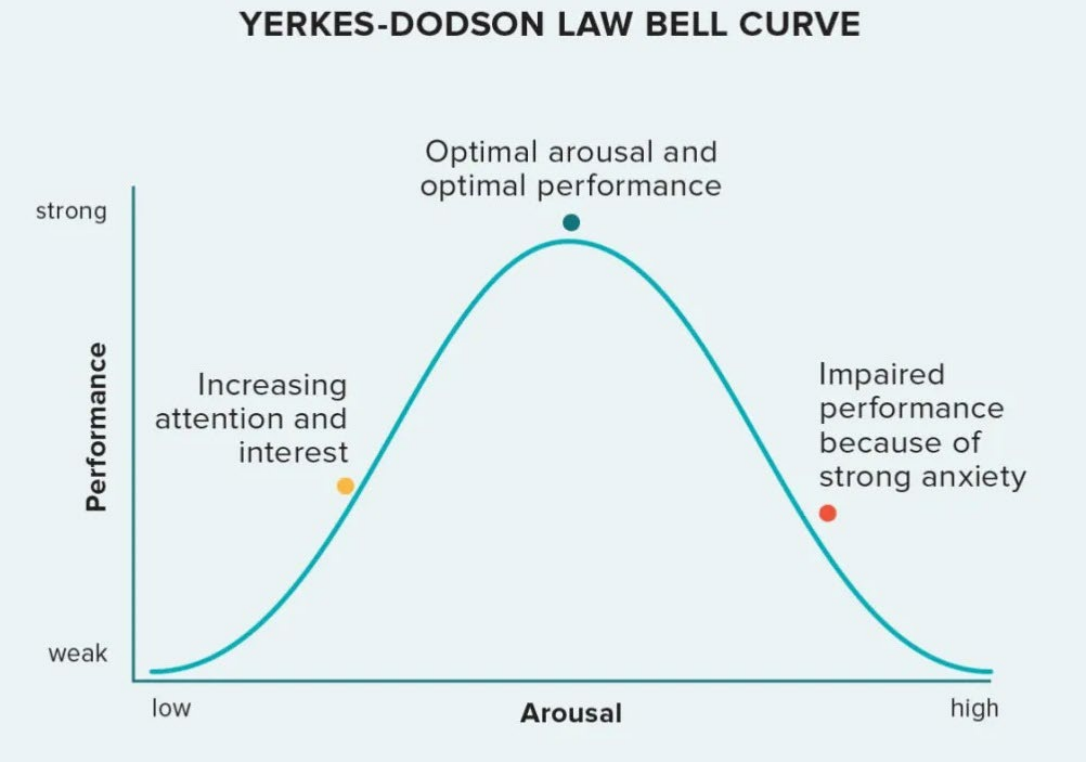


Figure 1.1: The Yerkes-Dodson Law Bell Curve. Reproduced from Healthline (2020)

1.1.6 Stress-related Psychosocial Responses

While stress is ubiquitous, seen through all cultures, the response to stressors from an individual will determine whether that stress will become pathological. It is the degree to which people cope with stressors, relative to social cultural orientations, that will determine their psychological health outcomes (Allen & Leary, 2010). This additionally depends on the individual's 'sense of coherence' and availability of community related coping resources (Braun-Lewensohn, 2014). If resourcing is sufficient, relevant, and accessible then individuals can constructively respond to stress with strategies that aim to build on personal strengths and/or attenuate negative responses (Freire et al., 2020; Rippstein-Leuenberger et al., 2017; Sexton & Adair, 2019; Tugade & Fredrickson, 2007). For example, positive cognitive restructuring to change perspective or address the stressor (Allen & Leary, 2010); affirmative action through building strengths and resilience and dissolve stress and anxiety (Sexton & Adair, 2019); or distraction by engaging in other pleasant activities that extend positive affects (Allen & Leary, 2010; Bryant et al., 2005). Seeking support is often critical when an individual's stress resources no longer assist in coping. Support includes reaching out and engaging with social networks or seeking health professional support (Smallwood et al., 2021).

Avoidance as a coping strategy, that is escaping from the stressor either cognitively or behaviourally, (termed motivational avoidance behaviours), has both concurrent positive and maladaptive consequences, depending on the stressor and strategy (Allen & Leary, 2010). In this context,

maladaptive coping strategies are the result of a coping resource deficit. Such behaviours are often associated with exacerbation of the physiological stress response, forming a positive feedback loop (Jackson et al., 2016). These include behaviours such as substance abuse, destructive physical activities, or consumption of high-sugar foods that may provide perceived subjective benefits, but which ultimately do not address stress or its cause. Increased stress has been associated with multiple negative psychosocial health outcomes. High stress increased likelihood of job dissatisfaction and multi-site pain (Haukka et al., 2011). High stress has been linked to increased depression rates (Sawatzky et al., 2012) and has been shown to increase maladaptive coping behaviours such as risky sexual behaviour and substance use (Reidy et al., 2018), decreased likelihood of smoking cessation (Slopen et al., 2013) and increased appetite and craving of energy-dense comfort foods (Jackson et al., 2016).

1.1.7 Stress in Populations

While stress is pervasive across all people, there are multiple populations at higher risk of elevated stress than others. This can be attributed to various factors, including social relationships, education levels, occupation, economics, gender, and age (as examples).

Increased stress has been associated with discrimination and immigration policies amongst immigrants (Ayón, 2018). Infertile couples utilising assisted reproductive technology (Turner et al., 2013) have reported increased stress levels, while high levels of prenatal stress have been found in groups of low-income pregnant women (Chang et al., 2019). Obese individuals experience long-term elevated cortisol levels, particularly those who have suffered from weight discrimination (Jackson et al., 2016). Increased chronic stress levels have been linked to vulnerable and abused children leading to maladaptive coping behaviours later in life (O'Connor & Vallejo Sefair, 2019). Increased perceived stress levels were reported in newly graduated nurses (Holmes, 2018) and in emergency medical personnel and healthcare workers (Ilczak et al., 2021), while increased academic stress results in poorer student reported wellbeing levels (Barbayannis et al., 2022).

1.1.7.1 Stress and Students

While many groups of society, for a range of reasons and circumstance, may experience on-going stress, of particular concern for this project are the impacts of stress on tertiary education students. Tertiary students are those studying awards spanning Australian Qualifications Framework (AQF) levels 5-10, including diplomas; advanced diplomas; associate degrees; bachelor degrees (including honours); graduate certificates; graduate diplomas; master degrees; doctoral degrees; and higher doctoral degrees (Tertiary Education Quality and Standards Agency (TEQSA), 2022). One report notes stress impacts on mental health and suicide rates and institutional barriers preventing people to

seek assistance, with notable cases being the stress reported by medical students (Rotenstein et al., 2016). In the United States of America, up to 87% of university students reported stress (alongside and further compounded by the COVID-19 pandemic) (American Psychological Association (APA), 2020). This was particularly pronounced in Generation Z students (those aged 18-23 at the time of the survey). It is unsurprising that stress with transition into and with tertiary study, is consequently associated with raised university attrition rates (Engle, 2008).

Tertiary students (and especially those who are recent school-leavers) are subjected to multiple sources of stress arising from both internal (institutional) and external expectations (Reddy et al., 2018). These include adapting to the transition into tertiary study balancing studies with work, familial expectations, and engaging in developing and maintaining collegial inter-student social interactions (Barbayannis et al., 2022; Lee et al., 2022). Academic stress has a subsequent impact on academic success, which in turn can affect motivation to study and stress coping behaviours (Bedewy & Gabriel, 2015; Pascoe et al., 2020; Reddy et al., 2018).

Recent school leavers are particularly vulnerable given their relatively short life experiences, subsequent limited psycho-emotional coping resources, and financial dependency on others, yet expected to act in the role of an adult. This age group is generally referred to as young adulthood, or sometimes emerging adulthood, in reference to the dynamic metamorphic change of societal role as they leave the home they grew up in (Mahmoud et al., 2012). The Australian Psychological Society (2016) report that younger adults (18-25 years-old) generally report lower levels of wellbeing because of stress compared to other older adults. As such, the transitional development stage of young adults also requires evolving skills in independency and self-sufficiency while attempting to develop and maintain relationships, and pressures to fulfil societal roles such as gender and adulthood (Dyson & Renk, 2006). Recent research supports this view, with academic stress levels highest in non-binary identifying students and women more than men (Barbayannis et al. 2022). Independent of gender, students with higher reported levels of academic stress were to have worse reported levels of mental health ($r = 0.53$, $p < 0.001$).

However, there is no single approach to dealing with stress impacts on tertiary students. That is, students are not a homogenous group, with differences in age, sex, gender, culture and socio-economic factors influencing both resilience, coping and sensitivity to a stress response forming (McEwen, 2008). Furthermore, tertiary students are often not only subjected to academic stress, but also financial stress, and the struggle to balance study with extra-curricular commitments (Engle, 2008). Difference in levels of education from school-leavers to postgraduate student are also apparent (Department of Education and Training, 2018), including study modes (part- and full-time), and competing commitments with work and living in a broad range of financial situations, all

contributing to students perceived stress impacts (Crisp et al., 2016). Mature age students, including alumni returning as postgraduate students, will have their own set of stressors, as they will often balance the demands of study with raising children, careers and spouses (Asokan et al., 2022). Students must contend with all of these stressors, combined with academic stress and examination stress, which superimposes acute academic stress on top of chronic stress (Koh et al., 2006).

Post-graduate students have reported further stressors associated with coursework, clinical placement and the associated transition from study to placement, work-life balance and financial pressures (Brooke et al., 2020), publication demands and thesis submissions (Shahnawaz et al., 2021), uncertainty about the research and writing process and difficulties with time management (Silinda & Brubacher, 2016). Undergraduate students report stressors associated with financial pressure (Ahern & Norris, 2011), academic stress and stress associated with clinical placement (Seher Çevik et al., 2021) and balancing work, study and life (Stallman & Hurst, 2016).

One sub-set of students worth mentioning are international students, upon which the Australian tertiary education sector is heavily dependent. The population of international students studying in Australia was estimated at over 400,000 in 2020, delivering more than $36 billion to the Australian economy annually (Fergeson & Sherrell, 2021). These international students must cope with not only all the normal stressors of domestic students, but also additional challenges and stresses associated with immersion in a different culture, language barriers and institutional and government visa bureaucracies (Ayón, 2018; Kristiana et al., 2022; Sullivan & Kashubeck-West, 2015).

Research has identified a strong relationship between extracurricular stresses, financial stress and probability of graduation (Adams et al., 2016; Engle, 2008). Stress has been shown to have an association with poorer academic performance and insomnia (Alsaggaf et al., 2016), and with a higher attrition rate in male nursing students (Kirk, 2020). Long term stress has been shown to have negative impacts on students' mental health and increase the likelihood of developing mental illness (Dyson & Renk, 2006; Susan et al., 2013). Of particular concern is that one in four tertiary students have experienced suicidal thoughts or behaviours (Mortier et al., 2018). High stress amongst college students has been reported, linked to student debt (Chisholm-Burns et al., 2017).

In addition to this, the recent COVID-19 pandemic has contributed an additional, immense stressor on everyone, including students, on a global scale. Yang et al. (2021) found that the COVID-19 pandemic impacted negatively on college students' health, in addition to academic workload and other normal stressors. Barbayannis et al. (2022) also note the COVID19 pandemic response with societal shutdown and school closures forcing students and parents into home schooling could further complicate the stress response.

1.2 Acupuncture

Acupuncture is the insertion of fine filiform needles into specific sites on the body. While having roots in ancient China some thousands of years ago (Flaws, 2004; Liu, 2009a; Unschuld, 2003), the practice of acupuncture continues to flourish, becoming popular in many parts of the world to this day (Leung, 2011).

The traditional philosophy of acupuncture as a therapeutic intervention relies on the concepts of "qi" (energy), "yin" and "yang" (opposing yet intertwined and interdependent energies), "wu xing" (five phases) and "zangfu" (organ systems) (Liu, 2009a). A state of good health relies on the correct flow of qi, the balance of yin and yang, the interplay and constant change of the wu xing and the correct physiological interactions of the zangfu (Liu, 2009a).

Contemporary research endeavours have focused on discovering the various mechanisms of acupuncture. Langevin et al. (2001) showed that needle stimulation of local connective tissues led to transmission of mechanical signals to further distal cells. Acupuncture has been shown to increase the release of endorphins and encephalin, altering the perception of pain (Cabyoglu et al., 2006). Acupuncture affects hormonal levels leading to changes in follicular growth in ovaries (Johansson & Stener-Victorin, 2013). Wenjing Huang et al. (2012) conducted a systematic review into acupuncture trials featuring the use of Functional Magnetic Resonance Imaging (fMRI) which showed that acupuncture affected multiple areas of the brain including somatosensory, cognitive and affective processing. Acupuncture stimulates the somato-autonomic reflex, affecting digestive and cardiovascular function (Cheng, 2014; Takahashi, 2011). While acupuncturists may recognise the somato-autonomic reflex responses as possibly being the foundation for the concepts of yin and yang (Takahashi, 2011) more importantly for this project, the activation of the parasympathetic nervous system holds great potential for understanding the influence of acupuncture on the fright, flight-or-fight response so integral to the body's capability to appropriately respond to stressful events. Conversely, acupuncture has been shown to decrease sympathetic nervous activity (Zhou & Longhurst, 2012), with comparable implications for acupuncture and the stress response.

1.3 Aims and Objectives

Originally, the overall goal of the project was to further contribute and extend the current knowledge of acupuncture treatment for perceived stress levels with a focus on tertiary education students as the population. Since inception of the project, the original project aims have changed due to COVID-19 (discussed further below in section 1.4). The research question being explored in this thesis is to ascertain the feasibility and efficacy of acupuncture in a clinical trial featuring different frequencies of treatments as an intervention for perceived stress levels in tertiary students.

That is, is there a difference or the same dosage effect if acupuncture is delivered over a shorter or longer period? Further, this project aimed to gather expert consensus through a literature review on the reduction of stress using acupuncture relative to Chinese medicine differential diagnosis to inform the development of the treatment protocols. With the onset of COVID19 the thesis objectives were revised. (Please see Section 1.4 below for an explanation of the impact.)

Consequently, the revised goal was to extend the knowledge of acupuncture treatment for perceived stress levels in terms of diagnosis, acupuncture point selection, treatment number and frequency, and diagnostic questionnaires, with a focus on tertiary education students as the population. Specifically, the project works from within the construct and context validation of Chinese medicine pattern diagnosis. Therefore, the project objectives are:

1. Synthesise information from the practice and research literature to identify the critical requirements of acupuncture treatment for perceived stress (further to informing the development of a clinical trial protocol)
2. To develop a clinical trial protocol to assess both feasibility and efficacy. Specifically, this includes: The efficacy of acupuncture to reduce stress; and
3. Evaluate the difference between two different acupuncture protocols featuring high and low frequencies of treatment.
4. Assess feasibility by recruitment, enrolment, retention, and adherence rates; and safety as measured by tolerance and adverse-event frequency.
5. To achieve consensus (via a Delphi process) on diagnosis, syndrome differentiation, signs and symptoms, acupuncture point selection and treatment frequency for the clinical trial protocol.

The current thesis is comprised of three investigative components merging elements of the original pre-COVID-19 study objectives. The first component continues with developing the original literature review, exploring the use of acupuncture in the treatment of stress. Importantly, acupuncture is noted within the validating construct of Chinese medicine and is reviewed within this paradigm. The literature review is used to develop the second component, a clinical trial protocol investigating the use of acupuncture to reduce perceived stress in tertiary students, comparing two different treatment frequency protocols. The third and final component is a two-round Delphi process gathering expert consensus on diagnosis and treatment of stress using acupuncture. The outcomes of the Delphi are consequently used to critique the protocol for additional amendments.

1.4 Impact of COVID-19

The clinical trial investigating the use of acupuncture to reduce stress was developed, received UTS HREC ethics approval in 2020 (ETH20-5098) and registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) (registration number ACTRN12621000598886). COVID-19 lockdown of the UTS campus meant that no recruitment could take place – there were no students on campus. Additionally, the campus suspended all non-essential services including research. Attempts to delay the trial including a leave of absence were taken, unfortunately it became apparent that conducting the trial within the maximum timeframe of the Master's candidature had become impossible. The pivot response was to conduct the Delphi process in order to better inform any possible future development and conduct of acupuncture clinical trials for stress. Ethics approval for the Delphi process was obtained in 2021 (ETH21-6702).

1.5 Structure of Thesis

Chapter 1: Introduction

The introduction includes an overview of the thesis project and structure, as well as a discussion of relevant stress-related topics, acupuncture and the impact of the COVID-19 pandemic.

Chapter 2: Literature Review

An English language literature review of acupuncture and stress. Students and stress are specifically discussed in Chapter 3.

Chapter 3: SPIRIT Trial Protocol

A SPIRIT trial protocol for a feasibility and efficacy trial investigating the use of two different acupuncture treatment frequency protocols for the reduction of perceived stress in tertiary students, based on the literature review, as approved by UTS HREC committee in 2019 and registered with ANZCTR. The protocol provides additional background information about students and stress that should be read with consideration to Chapters 1 and 2.

Chapter 4: Delphi Round 1

An introduction to the Delphi process and development of the Delphi questionnaire, followed by Round 1 results. The results are analysed and discussed, including how Round 1 results informed the development of the Round 2 questionnaire.

Chapter 5: Delphi Round 2

Chapter 5 includes the development of the Round 2 questionnaire, followed by Round 2 results, analysis and discussion.

Chapter 6: Discussion and Future Direction

The outcomes of the literature review and Delphi process are discussed in broader detail, including possible impacts on the trial protocol, and implication for the direction of research and clinical practice in future.

Appendices

Additional information that has been referenced or is pertinent throughout the thesis, including a modified SPIRIT clinical trial protocol as influenced by the Delphi process.

Chapter 2: Literature Review

Chapter 2 is an English-language literature review focussing on stress and acupuncture. This was used to inform the development of the clinical trial protocol using acupuncture to reduce perceived stress levels in tertiary students.

2.1 Aims and Objectives

The purpose of the literature review was to inform the development of a feasibility clinical study to investigate a neuro-modulatory intervention, in the form of acupuncture, as a stress mediation technique as part of a stress intervention program currently being designed in a university setting. Consequently**,** the literature review aimed to audit the reported use of acupuncture as a stress mediator in the research literature. The review objectives were to identify:

- Frequency and type of studies - that is, experimental and clinical studies (randomised and non-randomised);
- Protocols and methods utilised;
- Outcome measures employed;
- Standard of reporting;
- Population demographics; and
- The nature of the stress addressed, that is chronic (on-going, long term) vs acute (induced for the purpose of the study).

2.2 Methodology

A literature search was conducted using five English language databases: ProQuest (Health & Medicine), Medline, AMED, PsycINFO and EMBASE from inception to 2018, using the search terms “acupuncture” AND “stress”. Where applicable, additional limitations included human clinical trials published in the English language literature.

Inclusion criteria were applied to the articles once the initial search outcomes were received. Papers were included if they were randomised controlled trials (RCTs) relating to conventional manual acupuncture treating stress, or using outcome measures relating directly to stress.

Uncontrolled clinical trials (UCTs) were also included to make recommendations for further research however RCTs and UCTs were analysed separately and more weight was given to RCTs to improve the validity of evidence.

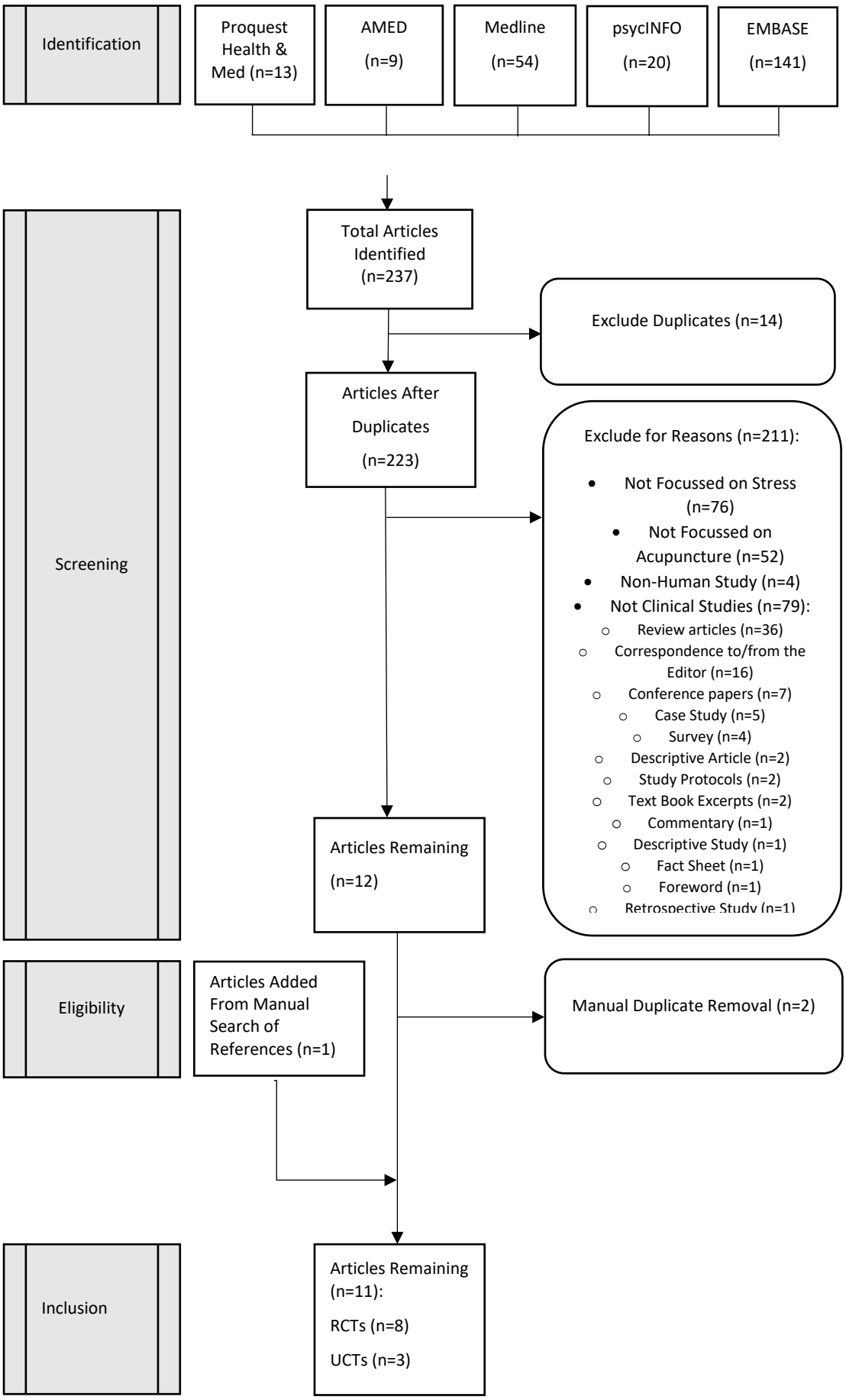
Acupuncture-like interventions, adjunct therapies and electro-acupuncture were excluded, including other methods of neuro-modulation utilising ultrasound (both high and low frequency). References of systematic reviews were also searched for additional studies missed in the database searches.

Studies that passed exclusion and were deemed eligible by the researcher were manually searched for information relevant to the aims and objectives of the literature review. Data was manually entered into excel and analysed for common themes and trends that could be used to develop the clinical trial protocol.

2.3 Results

A total of 237 articles were identified and imported into Endnote X8, where 14 duplicates were removed. A further 211 articles did not meet the inclusion criteria and were consequently removed, leaving 12 articles. Manual searching of the articles located two further duplicates (subsequently removed), and one further article meeting the inclusion criteria. In total, information from 11 articles was consequently imported into Excel 2016 for review analysis. The PRISMA literature review flow chart is shown in Figure 2.1. The full table of results are located in Appendix N. The results are discussed in further detail below.

Figure 2.1 – PRISMA literature review flowchart



2.3.1 Study Characteristics

2.3.1.1 Country of Origin

Three clinical trials were conducted in Brazil (de Oliveira & Scivoletto, 2017; Pavão et al., 2010; Zuppa et al., 2015), the United States of America (Middlekauff et al., 2002; Middlekauff et al., 2001; Schroeder et al., 2017) and the United Kingdom (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012). One trial was reported from Australia (Smith et al., 2011) and one from Hong Kong (Kwong & Yiu, 2010).

2.3.1.2 Study Design

Eight studies were RCTs (Huang et al., 2011; W. Huang et al., 2012; Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001; Schroeder et al., 2017; Smith et al., 2011; Zuppa et al., 2015), three were UCTs (Chan et al., 2002; de Oliveira & Scivoletto, 2017; Pavão et al., 2010)

2.3.1.3 Participant Characteristics

Two studies recruited university staff members (n=18) (Huang et al., 2011; W. Huang et al., 2012). One study recruited university staff, faculty and students (n=62) (Schroeder et al., 2017). One study recruited patients from a voice research laboratory (n=18) (Kwong & Yiu, 2010). One study recruited staff working in a hospice for the terminally ill (n=17) (Chan et al., 2002) and another recruited professionals working with maltreated children in a group shelter (n=19) (de Oliveira & Scivoletto, 2017). One study recruited patients with advanced heart failure (n=15) (Middlekauff et al., 2002) and one study recruited women with a diagnosis of infertility or a history of trying to conceive for 12 months or more (n=32) (Smith et al., 2011). One study recruited subjects from Center for Physical Activities “Terra Brasilis” (n=24) (Pavão et al., 2010). Two studies did not report the population from which the participants were recruited (n=19) (Middlekauff et al., 2001), (n=48) (Zuppa et al., 2015).

2.3.1.4 Quality of Reporting of RCTs

Quality and transparency of reporting varied greatly among the eight RCTs which were assessed according to both the CONSORT and STRICTA reporting guidelines (and are discussed in further in sections 2.3.1.9 to 2.3.1.13).

In terms of the CONSORT and the STRICTA, these refer to the CONSORT (Consolidated Standards of Reporting Trials) checklist, updated in 2010, is a recognised and endorsed means to facilitate critical appraisal of RCTs (Moher et al., 2010). Of the 36 items possible for reporting, the RCTs described: 29 (Smith et al., 2011), 22 (W. Huang et al., 2012), 22 (Schroeder et al., 2017), 19 (Huang et al., 2011), 18 (Kwong & Yiu, 2010), 18 (Middlekauff et al., 2002), 17 (Zuppa et al., 2015) and 16 (Middlekauff et al., 2001).

The STRICTA (Standards for Reporting Interventions in Clinical Trials of Acupuncture) extension replaces one of the CONSORT checklist items. It is designed to improve the quality of reporting of interventions in controlled acupuncture trials (MacPherson et al., 2010). Of the 17 items possible for reporting, the RCTs described: 14 (Smith et al., 2011), 13 (Kwong & Yiu, 2010), 11 (Middlekauff et al., 2002), 11 (Middlekauff et al., 2001), six (Huang et al., 2011), six (Schroeder et al., 2017), five (Zuppa et al., 2015) and three (W. Huang et al., 2012). The variance in reporting standards made some inter-study comparisons difficult to undertake, and questioned the veracity of the studies integrity and design.

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline is a 22-item checklist to assess the transparency of reporting for uncontrolled trials (Cuschieri, 2019). Of the three UCTs, two trials reported 11 items (Chan et al., 2002; Pavão et al., 2010) while one reported three (de Oliveira & Scivoletto, 2017).

2.3.1.5 Outcome Measures

Different outcome measures were used in accordance with the focus of individual studies, as not all the studies were focussed mainly on stress.

Eight of the studies used questionnaires as a primary outcome measure (Chan et al., 2002; de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et al., 2012; Pavão et al., 2010; Schroeder et al., 2017; Smith et al., 2011; Zuppa et al., 2015). Four studies used physiological response markers (see section 2.3.1.7) (W. Huang et al., 2012; Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001). One study used both a questionnaire and a physiological marker relating to stress (W. Huang et al., 2012) and two studies used questionnaires relating to stress and physiological response markers unrelated to stress (Pavão et al., 2010; Zuppa et al., 2015).

2.3.1.6 Questionnaires & Perception Scales

Four studies used three different questionnaires as outcome measures (W. Huang et al., 2012; Pavão et al., 2010; Smith et al., 2011; Zuppa et al., 2015); four studies used a single questionnaire (Chan et al., 2002; de Oliveira & Scivoletto, 2017; W. Huang et al., 2012; Schroeder et al., 2017); and one study used two questionnaires. (Huang et al., 2011)

Four studies used the Perceived Stress Scale (PSS14) (Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017; Zuppa et al., 2015). The State-Trait Anxiety Inventory (STAI)(Pavão et al., 2010; Smith et al., 2011), Beck Depression Inventory (BDI)(Pavão et al., 2010; Zuppa et al., 2015), and Lipp's Inventory of Stress Symptoms for adults (LISS) (de Oliveira & Scivoletto, 2017; Pavão et al., 2010) were also used. Other questionnaires used were: Measure Your Medical Outcome Profile (MYMOP) (Huang et al., 2011), Fertility Problem Inventory (FPI) (Smith et al., 2011), Pittsburgh Sleep

Quality Index (PSQI) (Zuppa et al., 2015) and Edinburgh Postnatal Depression Scale (EPDS) (Chan et al., 2002).

The relevance of the scales used varied greatly. While the PSS14, STAI and LISS are mainly concerned with stress, and MYMOP can be used for self-reporting on any given symptom, other questionnaires had little to do with stress. While this could be expected in studies exploring multiple outcomes that happened to include stress (therefore meeting inclusion criteria in this review), Chan et al. (2002) used the EPDS even though it is not applicable to stress primarily, nor the participant population, but simply because it was user-friendly.

Although few of the studies attempted to define stress in their reporting, three of the studies required a minimum score on the Perceived Stress Scale questionnaire (PSS-14) for participant inclusion (Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017). While this attempts to define a threshold above which a person is "stressed", the PSS-14 scale is a comparative instrument rather than diagnostic (Cohen et al., 1983), and no official threshold exists. The Perceived Stress Scale includes 14 items, each scored from 0 ('never') to 4 ('very often'). After reverse-scoring some items, the scores for all items are summed to create a total score, ranging from 0–56. There is no cut-off score since the tool is not a diagnostic assessment.

While most of the questionnaires are freely available, it is worth noting that the LISS is not free to use, nor readily available in English. This may affect it's lack of widespread use according to this literature review and may also impact current practitioner's awareness, or use of it in practice (see Section 4.3.5).

Table 2.1 summarises the questionnaires used and the components of the questionnaires that are applicable or extraneous to the current project.

Table 2.1: Outcome measure questionnaires

Questionnaire	Pertinent/Applicable Components	Extraneous Components	Authors	Source Reference
PSS14	A reliable and valid tool for the measuring of perceived stress		(Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017; Zuppa et al., 2015)	(Cohen et al., 1983)
STAI	"State" anxiety scale indicates changes in transitory anxiety when subjects are exposed to acute stressors	"Trait" anxiety scale indicates how a subject generally reacts to stressors	(Pavão et al., 2010; Smith et al., 2011)	(Speilberger, 1983)
BDI		A psychometric instrument for discriminating between depressed and non-depressed subjects	(Pavão et al., 2010; Zuppa et al., 2015)	(Wang & Gorenstein, 2013)
LISS	Assesses whether participant has symptoms of stress; in which temporal phase; and whether the stress symptoms are psychological or physical		(de Oliveira & Scivoletto, 2017; Pavão et al., 2010)	(Lipp, 2000)
MYMOP	Can be used as a primary outcome measure that is sensitive to change in any patient-selected symptom.		(Huang et al., 2011)	(Paterson, 1996)
FPI	A reliable measure of perceived infertility-related stress	Measure of stress is focussed entirely on stress as it relates to infertility	(Smith et al., 2011)	(Newton et al., 1999)
PSQI		Measure of sleep quality and disturbance	(Zuppa et al., 2015)	(Buysse et al., 1989)
EPDS		Can assist primary care health professionals in detecting mothers suffering from postpartum depression	(Chan et al., 2002)	(Cox et al., 1987)

2.3.1.7 Physiological Response Markers

Two studies used the same physiological response markers: Muscle Sympathetic Nerve Activity (MSNA), Blood Pressure (BP) and Heart Rate (HR) (Middlekauff et al., 2002; Middlekauff et al., 2001). Two studies used salivary cortisol concentration (W. Huang et al., 2012; Kwong & Yiu, 2010).

MSNA tested the hypothesis that acupuncture would inhibit sympathetic nervous activity in participants during mental stress (Middlekauff et al., 2002; Middlekauff et al., 2001). While valid for determining the mechanism of acupuncture, it is irrelevant to the current project. Changes to BP and HR correlate to mental stress (Nilsen et al., 2007). Saliva2.ry cortisol concentration has been shown to be an accurate indicator of stress (Kirschbaum & Hellhammer, 1994).

2.3.1.8 Acute Versus Chronic Stress

Chronic stress (ongoing, long-term stress) was investigated in nine studies (Chan et al., 2002; de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et al., 2012; Kwong & Yiu, 2010; Pavão et al., 2010; Schroeder et al., 2017; Smith et al., 2011; Zuppa et al., 2015). Two studies investigated acute stress induced by mental stress testing during the trial (Middlekauff et al., 2002; Middlekauff et al., 2001).

2.3.1.9 Diagnostic Methods

This is part of STRICTA item one. Eight studies used standard treatment prescriptions without Chinese Medicine (CM) diagnosis (Chan et al., 2002; Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001; Pavão et al., 2010; Schroeder et al., 2017; Zuppa et al., 2015). Two studies used standard points for all participants with additional points individually prescribed according to Traditional Chinese Medicine (TCM) pathologies diagnosed (Huang et al., 2011; W. Huang et al., 2012). Single studies used either TCM diagnosis (de Oliveira & Scivoletto, 2017) or Causative Factor Diagnosis (Smith et al., 2011) to determine individual point prescriptions.

Diagnoses included Liver qi transforming into Fire (Huang et al., 2011; W. Huang et al., 2012), Liver invading Spleen and Stomach (Huang et al., 2011; W. Huang et al., 2012) and Gallbladder qi deficiency (Huang et al., 2011; W. Huang et al., 2012).

2.3.1.10 Acupuncture Points Used

This is part of STRICTA item two. The most commonly used point was Large Intestine 4 (n=9) (de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et al., 2012; Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001; Pavão et al., 2010; Schroeder et al., 2017; Zuppa et al., 2015). This was followed by Pericardium 6 (n=7) (de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et al., 2012; Middlekauff et al., 2002; Schroeder et al., 2017; Smith et al., 2011; Zuppa et al., 2015), and Liver 3 (n=7) (de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et

al., 2012; Middlekauff et al., 2002; Middlekauff et al., 2001; Schroeder et al., 2017; Zuppa et al., 2015).

Figure 2 shows the total number of uses for the most commonly used acupuncture points according to the literature.

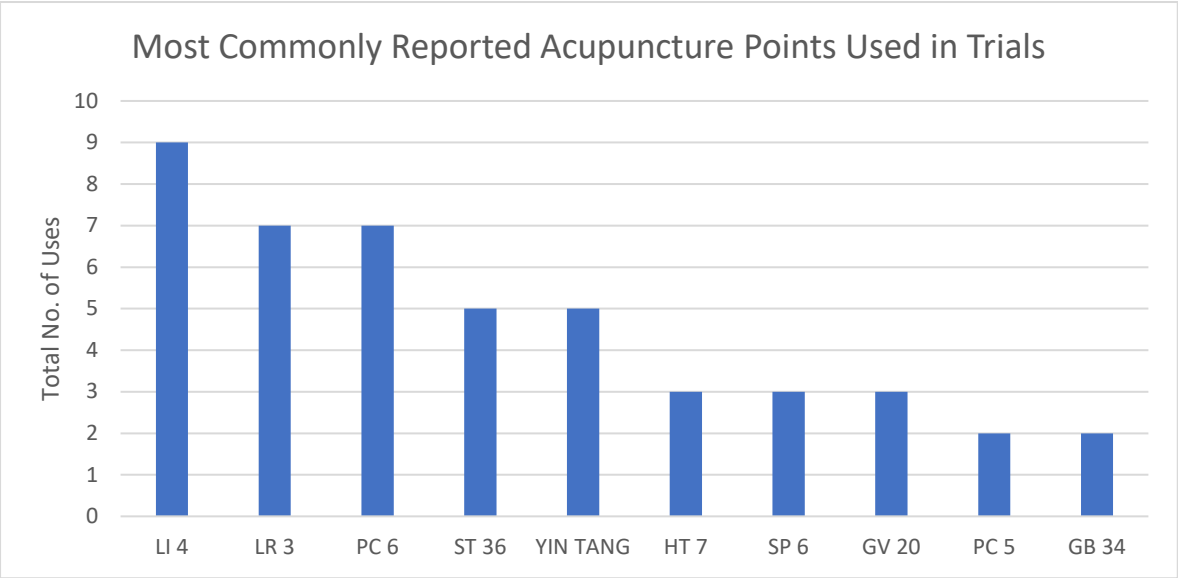


Figure 2.2: Use of individual Acupuncture Points According to the Literature

2.3.1.11 Justification of Point Selection

This is part of STRICTA item 2. Two studies used a standard point prescription with extra individual points based on "Chinese medicine theory, literature review and the practitioner's clinical experience" (Huang et al., 2011; W. Huang et al., 2012). Two studies used points associated with stress reduction (Middlekauff et al., 2002; Middlekauff et al., 2001). One study selected acupuncture points using clinical literature and practitioner experience, integrated with a previous study protocol for vocal pathologies (Kwong & Yiu, 2010; Yiu et al., 2006). One study chose points using individual TCM and Causative Factors diagnosis in response to emotional complaints (Smith et al., 2011). Other studies reported single acupuncture point based on sedative effects (Chan et al., 2002), according to individual traditional energy diagnoses (de Oliveira & Scivoletto, 2017), and previous study protocols (Pavão et al., 2010), although those study protocols had little relevance to stress (Chen & Chen, 2004; Mori et al., 2002; Yamaguchi et al., 2007). Two studies did not justify acupuncture point selection (Schroeder et al., 2017; Zuppa et al., 2015).

2.3.1.12 Number and Frequency of Treatments

This is part of STRICTA item three. Weekly treatment was most commonly reported (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017). (Smith et al., 2011)

administered four treatments weekly then fortnightly. Two studies treated twice weekly (Pavão et al., 2010; Zuppa et al., 2015). One study did not specify frequency (de Oliveira & Scivoletto, 2017).

Overall, three studies administered a single treatment (Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001). Two studies each used six treatments (Pavão et al., 2010; Smith et al., 2011), five treatments (Huang et al., 2011; W. Huang et al., 2012) and ten treatments (de Oliveira & Scivoletto, 2017; Zuppa et al., 2015). Four (Chan et al., 2002) and 12 treatments (Schroeder et al., 2017) were each used in a single study.

2.3.1.13 Comparators Used

This is part of STRICTA item six. Of the controlled studies, this included non-acupuncture point needling (n=3) (Middlekauff et al., 2002; Middlekauff et al., 2001; Zuppa et al., 2015) and wait list control group (n=3) (Huang et al., 2011; W. Huang et al., 2012; Smith et al., 2011). Two studies used an attention-only control group and a waiting list control group (Huang et al., 2011; W. Huang et al., 2012). One study used blunt sham needles at the same points (Kwong & Yiu, 2010), another needled acupuncture points not indicated for stress (Schroeder et al., 2017). This information can be found in Appendix N.

2.3.2 Discussion

The literature review showed the scarcity of acupuncture trials for the treatment of stress. This meant that although trends in trial methodology could be identified, conclusive evidence of best practice protocols could not be positively identified.

There were insufficient studies to support conclusively the treatment of stress with certain acupuncture point combinations. Furthermore, many studies measured stress inclusive of global outcomes, such as depression (Zuppa et al., 2015), or used an experimental model investigating acupuncture's neuro-modulatory mechanisms instead (Middlekauff et al., 2001). These studies included multiple outcome measures not relevant to the current review.

Since the purpose of the literature review was to inform the development of a clinical trial protocol, a further review was undertaken of clinical textbooks to enrich the data using the source texts. This identified similarities but also discrepancies with points used clinical practice compared with research (Figure 2.3) versus clinical practice.

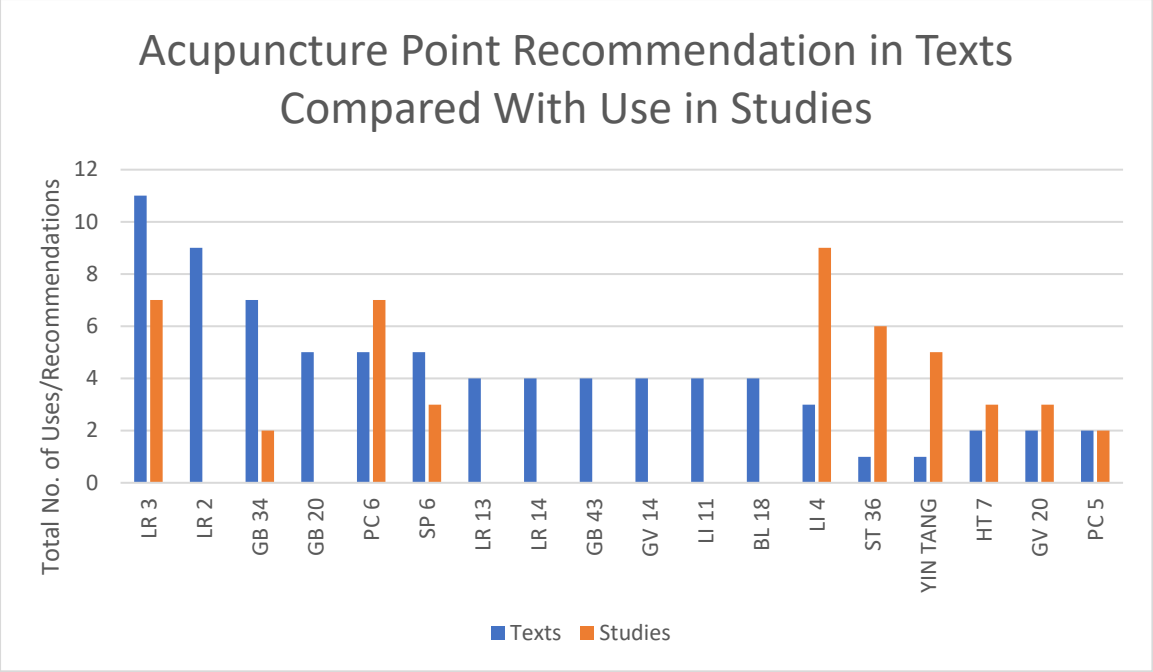


Figure 2.3: Recommendation in Texts Compared with Use in Studies.

The most common acupuncture points in CM texts and research are Liver 3, Liver 2 and Gall Bladder 34. Texts additionally recommend several Liver and Gall Bladder points not yet assessed in controlled conditions. Point use discrepancy may be attributable to addressing acute versus chronic stress, or perhaps differences in diagnosis of stress in CM pathologies (see Section 6.1)

Three studies administered a single acupuncture treatment (Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001). Each of these tested a neuro-modulatory mechanism hypothesis of specific body sites, rather than determining the efficacy of acupuncture to reduce stress. The small sample of studies (n=11) – three of which were non-RCTs – were skewed towards single treatment studies, a consequence of which was to disproportionately alter the perception of efficacy reported in the literature. Since the current project aims to devise a pragmatic treatment strategy to reduce stress, it is possible that those studies, like the non-RCTs, should be given less weight in analysis.

One study (de Oliveira & Scivoletto, 2017) suffered from particularly poor reporting, not reporting particular points used (the study listed 'most commonly used points' only), or treatment frequency. Further detail was requested from the corresponding author with no reply.

It became apparent during analysis that two studies (Huang et al., 2011; W. Huang et al., 2012) were reports of the same study. One of the reports focussed on the use of acupuncture for stress with questionnaire outcomes (PSS-14 and MYMOP) (Huang et al., 2011). The other reported feasibility of salivary cortisol as a stress outcome measure in acupuncture research (W. Huang et al., 2012).

While also recruiting faculty and staff, the only study featuring students and stress (Schroeder et al., 2017) reported promising results. Treatments administered once per week for 12 weeks had statistical significance reducing reported stress. The study did experience high attrition in the control group, which the authors attributed to the study length (approx. 12 weeks), and the inconvenience of attending treatment on campus during holidays.

Universities recognise that student stress is an important issue. Many university websites feature information for students about stress, how to recognise excess stress and possible coping strategies (University of Queensland, 2018; University of Technology Sydney, 2018a; University of Western Sydney, 2018). UTS has initiated programs to recognise the importance of, and improve, the wellbeing of students (University of Technology Sydney, 2018b). International students, particularly those of Asian background, may find acupuncture a more familiar form of treatment than those currently offered.

The evidence to date suggests that acupuncture may be an effective treatment for stress, but more data is needed. Multiple studies showed that acupuncture had a significant effect on the chosen outcome measures. While two studies with higher frequency of treatment showed significant results, there is little evidence to confirm whether high or low frequency treatments affects outcomes. This justifies the proposed study comparing high and low frequency of treatment for acute stress in students.

If successful, the proposed study may provide UTS and other universities a viable and practical intervention to offer students suffering from high stress levels. (See Chapter 3: SPIRIT Protocol)

Chapter 3: SPIRIT Protocol: Students, Acupuncture and Stress – A feasibility study investigating the impact of high and low frequency acupuncture dosage in overall perceived stress changes in tertiary education students

(SAS Study)

The following Chapter contains the SPIRIT clinical trial protocol, as approved by UTS HREC ethics committee.

3.1 Study Details

Trial Identifying Number: Australian New Zealand Clinical Trials Registry (ANZCTR) registration number ACTRN12621000598886

Version Identifier: 1.2

3.1.1 Funded by:

Internal UTS Faculty of Science Funding (HDR grant $5000)

3.1.2 Study Sponsor:

University of Technology Sydney (UTS)

3.1.3 Principal Investigator:

Dane Couter (Master's in candidature), School of Life Sciences, UTS

3.1.4 Co-investigators

Dr Sean Walsh (supervisor), Dr Shuai Zheng (co-supervisor)

3.1.5 Protocol Contributors

- Mr Dane Couter, MSc (in candidature), registered health care practitioner (Ahpra:CMBA)
- Dr Sean Walsh, Supervisor and Senior Lecturer, registered health care practitioner (Ahpra:CMBA)
- Dr Shohreh Razavy, UTS, registered health care practitioner (Ahpra:CMBA)
- Dr Yew Kian Loyeung, External supervisor, Parexel International.

3.1.6 Contact for public queries:

Dane Couter

- **Primary**: University of Technology Sydney, PO Box 123, Broadway NSW 2007, Australia

Contact for scientific queries: **Dane Couter**

3.2 Introduction

3.2.1 Background and Rationale

Stress is “mental, emotional or physical strain or tension” (*Collins Dictionary*, 2018). The term is descriptive, applied to daily life hassles through to major trauma and has both beneficial and pathogenic connotations (McEwen, 2008). Concerning to health and performance in day-to-day activities is the acute stress response that remains unmanaged, and which contributes to a chronic (and pathological) stress response forming often associated with anxiety. This pathological stress is a “process in which environmental demands tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease” (Cohen et al., 1997). This includes increased cortisol, supressed immune function and impact on quality of life and performance.

While many groups of society, for a range of reasons and circumstances, may experience on-going stress, of concern for this study is the impact of stress on students. Recent media reports highlight the impact of stress affecting mental health leading to increased rates of suicide and underreporting of mental health on medical students (as an example) (Rotenstein et al., 2016). Stress additionally has a negative impact on student grades and retention; stress with transition into and with tertiary education are associated with raised university attrition rates (Pritchard & Wilson, 2003). More recently contributing to student stress is the COVID-19 pandemic which has caused individual and community increases in stress- and anxiety-related symptoms (Taylor et al., 2020); up to 70% of university students have reported stress at moderate to severe levels during the pandemic and its associated limits to personal liberties (Husky et al., 2020).

However, there is no single approach to dealing with stress impacts on tertiary students. That is, students are not a homogenous group; differences in age, sex, gender, culture and socio-economic factors influencing both resilience and sensitivity to a stress response forming. In addition to academic stress, tertiary students report financial stress and stress struggling to balance study with extra-curricular commitments (Engle, 2008). That is, competing commitments between study and with work, and living in a broad range of financial situations; all contribute to students’ perceived stress impacts in levels of education. Consequently, stress appears endemic in the tertiary student population, apparent from school-leavers to postgraduate student (Department of Education and Training, 2018), and across study modes (part- and full-time) (Crisp et al., 2016).

The National Tertiary Student Wellbeing Survey reported that 83.2% of 16-25 year olds and 79.8% 26+ year olds found their studies were affected by feeling stressed (Crisp et al., 2016). Research has identified a strong relationship between extracurricular stresses, financial stress and probability of graduation: that higher stress has a negative impact on academic performance (Adams et al., 2016; Engle, 2008; Trombitas, 2012). From a health perspective, long term stress negatively impacts students' mental health and increases the likelihood of developing mental illness, particularly depression and anxiety (Susan et al., 2013). Concerning is that one in four tertiary students have experienced suicidal thoughts or behaviours (Mortier et al., 2018).

Acupuncture has long been used by university students for stress; their views differ from more established (and biased perceptions) of complementary therapies as a threat to public health, instead viewing these as part of an integrative health system meeting diverse community needs, including the students' own (Ellis et al. 2006; Hasan et al. 2011; Amadera et al. 2010). Acupuncture variants such as auricular acupuncture and electro-acupuncture have been trialed with students to reduce exam stress (Klausenitz et al. 2018), anxiety (Vieira et al. 2018) and stress-related symptoms (Dias, Pagnin & Pagnin 2012; Dias et al. 2014).

A literature review of the clinical and biomedical databases with a focus on acupuncture for stress generally, underscored however the scarcity of evidence regarding filiform body acupuncture, (independent of specific conditions and as observed over time), with only 11 studies identified (see Chapter 2). Only one had a focus on students. Of the studies identified, most tested acupuncture using a neuro-modulatory mechanism hypothesis, using needles at specific body sites. Patient perceived change in stress post-treatment and over time were assessed with standardised outcome measures (Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001); while two studies were actually two different reports of the same study: one reporting on acupuncture for treating stress (Huang et al. 2011) and the other reporting on the use of salivary cortisol in acupuncture studies (Huang et al., 2011; W. Huang et al., 2012).

The only study featuring a student population and treatment of stress (Schroeder et al., 2017) reported promising results. The results indicate that 12 treatments administered once per week had statistically significant reduction in stress levels of students as measured by mean PSS14 scores. The study did however experience high attrition in the control group, which the authors attributed to the study length (approx. 12 weeks) and the inconvenience of attending treatment on campus during holidays, making long-term, low treatment frequency acupuncture, a less than feasible approach for this cohort. The authors also pointed out the difficulty of applying the conventional scientific method to acupuncture, particularly in terms of controls used and uniform acupuncture point prescriptions. Further, they indicated that they would have preferred to administer the acupuncture treatments

twice pre week rather than once, although they omit any evidence to support the difference in acupuncture dosage.

3.2.2 Purpose of the study

At present, acupuncture is being utilised by students to assist with their physical and psychological perceptions of stress impacts, including at UTS. The UTS Chinese Medicine Clinic (located in Building 4, Broadway Campus), is a busy clinic with between 6000-7000 patient contacts per year, has a high tertiary education student patient cohort often reporting perceived stress impacting their quality of life and study performance (Meier et al., 2017), in addition to accompanying symptoms of sleep disturbances, reduced motivation, tiredness, headaches and poor concentration.

There is insufficient information regarding acupuncture dosage treatment frequency and potential changes in perceived stress levels in tertiary education students. Further study is required to determine the feasibility and acceptability of acupuncture of different treatment frequencies for stress in tertiary education students. If an acceptable and feasible intervention, it will inform a larger scale cohort study.

Consequently, the study may help inform clinical decision making and perhaps more appropriately target an effective therapeutic acupuncture treatment dosage (White et al. 2008), adding further to an evidence-base; it is a minimally invasive technique with potential benefits for student (and others) well-being, while informing best current clinical practice for acupuncture. It draws on a more medicalized understanding of acupuncture as a neuro-modulatory technique (Hui, Liu & Makris 2000; Napadow, Makris & Liu 2005; White et al. 2008).

3.3 Objectives

3.3.1 Hypothesis

There is a mean difference of perceived stress (PSS14 scores) among stressed students receiving an acupuncture dosage at high treatment frequency compared to students receiving an acupuncture dosage at low treatment frequency, namely that the higher treatment frequency will have a greater effect. Further that certain characteristics are a predictor of perceived stress changes following acupuncture dosage in tertiary students.

3.3.2 Principle Objective

To investigate the impact of high and low frequency acupuncture dosage in overall perceived stress from baseline and at week 12 in tertiary education student participants.

The study proposes comparing high frequency acupuncture dosage (two treatments per week for two weeks) versus low frequency acupuncture dosage (one treatment per week for four weeks).

3.3.3 Secondary Objective

- To observe the magnitude and rate of change in perceived participant stress scores from baseline, and at each treatment (treatments 1-4), and at two (2) weeks and four (weeks) after the last treatment (treatment 4) within and between the high and low frequency acupuncture dosage groups.
- Explore participant socio-demographic responses (such as gender) and stress type characteristics and their relationship to high and low frequency acupuncture dosage response as measured by changes in perceived stress reported using the PSS14.
- Gather participant feedback on perceptions on acupuncture dosage treatment frequency to inform a larger cohort study design (see Participant Final Questionnaire, Appendix H), including safety data.
- Assess feasibility by recruitment, enrolment, retention, and adherence rates; and safety as measured by tolerance and adverse-event frequency.

3.4 Trial Design

This is a 12-week phase II, feasibility and efficacy study - designed as a two arm, randomised study. There are two arms: high frequency acupuncture treatment and low frequency acupuncture treatment. Trial methodology has been informed by the literature review (acupuncture point selection, number of treatments and treatment frequency) and practitioner clinical experience. The study investigates the difference between high or low frequency acupuncture dosage interventions and a participant's perceived stress levels (using the PSS14) before, during and post-treatment intervention. In addition, the study investigates feasibility and acceptability of the treatment measured by recruitment, enrolment, retention, and adherence rates; and safety as measured by tolerance and adverse-event between the two study arms.

All participants will continue with usual standard of care or their usual health and well-being practices - there is not modification nor request to do so as part of this trial.

3.4.1 Methods: Participants, Interventions and Outcomes

3.4.1.1 Study Setting

The study will be carried out on campus at the University of Technology Sydney (UTS) Chinese Medicine Clinic. The clinic is located on the corner of Thomas and Harris Streets at the Broadway campus of the UTS (Building 4). It is an Australian health practitioner regulation agency (Ahpra) accredited teaching and research facility for acupuncture.

3.4.1.2 Participants

Participants will be recruited from the student population at the University of Technology Sydney.

3.4.1.3 Eligibility criteria

3.4.1.3.1 Inclusion Criteria

- Currently enrolled as a tertiary student at UTS
- Aged 18 and over
- Able to provide informed consent
- Self-identify as 'stressed'

3.4.1.3.2 Exclusion Criteria

- Bleeding disorders or any disorder that prohibits the use of acupuncture or certain points specified in this intervention;
- Use of prescribed anti-coagulant medication (such as warfarin) that may interfere with blood clotting
- Use of acupuncture in the 14 days prior to the intervention
- Pregnancy
- Needle phobia
- Unwilling to complete outcome measures or attend the clinic for treatment
- Suicidal ideation*

Participants can withdraw from the study at any time.

*Please refer to the distress protocol regarding suicidal ideation (the protocol was prepared in collaboration with the UTS Student Services: Brett Smout and Sarah Lok), also see below and inserted here in the protocol at the request of Student Services (Boxed).

Participants who report thoughts of suicide or self-harm through the online questionnaire or intake form will be advised immediately:

If you require emergency assistance, contact the Police and/or request an Ambulance by dialling 000.

You may also request assistance by contacting **24-hour crisis phone counselling**:

- Lifeline Counselling Service: 13 11 14
- Suicide Call Back Service: 1300 659 467
- Beyondblue Support Service: 1300 22 4636
- Kids Helpline: 1800 55 1800
- NSW Mental Health Line: 1800 011 511

Please contact UTS student services on (02) **9514 1177 or email at** student.services@uts.edu.au **if you wish to speak to a counsellor or make an appointment.**

Please indicate if you wish to withdraw from the current trial.

3.4.2 Intervention

86 participants will be recruited and first take part in a waiting list baseline group, then randomised into one of two groups:

- High frequency: 4 interventions over 2 weeks (HF)
- Low frequency: 4 interventions over 4 weeks (LF)

All interventions will be performed by individual/s with a Bachelor's degree in Traditional Chinese Medicine/Acupuncture, have 10 years clinical experience, and registered health care practitioners with the Chinese Medicine Board of Australia (Ahpra:CMBA).

Bias is controlled using participant allocation concealment. Clinician administering the treatment will not be involved in the method of randomisation. To control the within treatment reliability with application practises (ie, standardisation), a single practitioner will administer the treatment. This reflects a 'pragmatic' care model but additionally assists with participant's perceptions of continuity of treatment.

All needles used in the study (needle brand 'Balance') are registered as a Medical Device (Class IIa) with the TGA.

3.4.2.1 Waiting List Baseline Group

Each participant will be asked to fill out the PSS-14 once per week for four weeks before beginning acupuncture interventions to establish a baseline measure.

The wait list baseline lead-in length of four weeks was chosen to smooth out the perceived stress variation that might happen due to transient events, and hence calculate a mean score of perceived stress as a better reflection of a baseline measure.

3.4.2.2 Intervention 1 – High Frequency

The patient will be asked to lie supine (face up) on a treatment table. There are four acupuncture points being needled bilaterally, involving a total of 8 needles. The points and order of insertion are: Liver 3, Large Intestine 4, Spleen 6 and Pericardium 6. The needle will be manipulated using a lifting thrusting and rotation method immediately after insertion for a minimum of 10 seconds to illicit a sensation of 'de qi' (numbness, heaviness, dull ache) is reported. The needles will be retained for 20 minutes. The intervention will be performed twice a week for two weeks totalling four treatments.

Needles will be removed in the same order as insertion and immediately placed in a Sharps container.

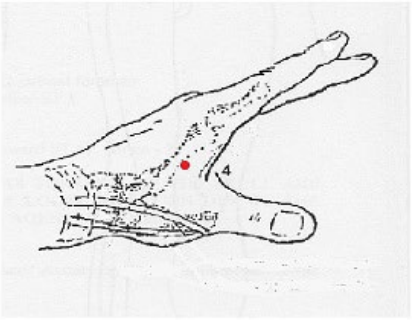
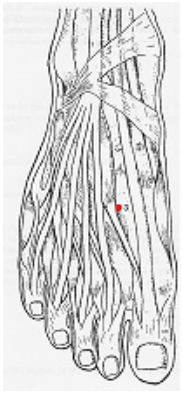
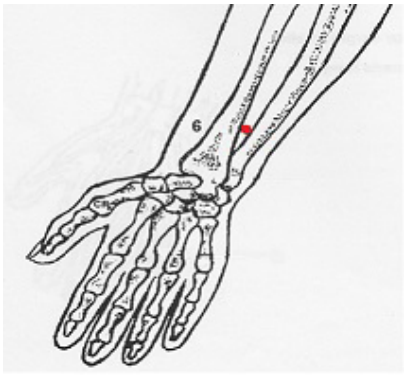
As the acupuncture points are located on distal portions of the arms and legs, no disrobing of the participants is anticipated other than removal of footwear.

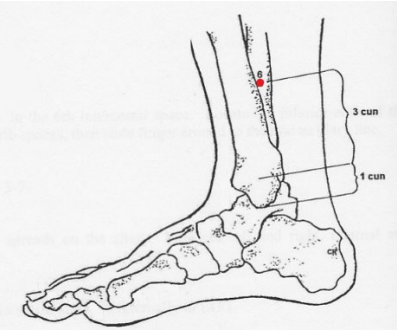
3.4.2.3 Intervention 2 – Low Frequency

As for high frequency but: The intervention will be performed once per week for four weeks for a total of four interventions.

3.4.2.4 Description of Acupuncture Point Locations

The location, needling angle and needling depth will be as follows (Rogers & Rogers, 1995):

Large Intestine 4  **Figure 3.1:** Large Intestine 4	Location: On the dorsum of the hand in the middle of the 2nd metacarpal on the lateral side. At the highest point of the muscle when the thumb and index finger are held close together. Needling Angle: Perpendicular Needling Depth: 5mm Needle Type: Balance, 0.20 x 30mm
Liver 3  **Figure 3.2:** Liver 3	Location: On the dorsum of the foot in the angle formed by the 1st and 2nd metatarsals, just anterior to the articulation with the 1st and 2nd cuneiforms. Needling Angle: Perpendicular Needling Depth: 3mm Needle Type: Balance, 0.20 x 30mm
Pericardium 6  **Figure 3.3:** Pericardium 6	Location: Two anatomical units above the wrist flexure between the tendons of the palmaris longus and the flexor carpi radialis. Needling Angle: Perpendicular Needling Depth: 3mm Needle Type: Balance, 0.18 x 15mm

Spleen 6  **Figure 3.4:** Spleen 6	Location: On the anterior/medial aspect of the leg, 3 anatomical units above the 'tip' (medial extremity) of the medial malleolus, just posterior to the border of the tibia. Needling Angle: Perpendicular Needling Depth: 4 mm Needle Type: Balance, 0.20 x 30mm

3.4.3 Outcomes (endpoints)

The primary outcome is a patient reported outcome measure – the PSS14 (see appendix E for copy). The PSS14 is a self-reported measure which assesses the degree to which the respondent perceives stress specific to their life situation within the last month. That is, it is not diagnostic, but rather about respondent perceptions about how un-predictable, uncontrollable, and overloaded individuals find their life circumstances. There are 14 items, rated using a 5-point Likert scale ranging from 'Never' (0) to 'Very Often' (4). Scoring is a mixed of actual and reverse scoring each item to obtain a score in the range of 0-56.

The mean difference in PSS-14 scores will be compared between pre and post intervention for differences within each acupuncture dosage treatment-frequency group and also between the two groups. The PSS14 has been shown to be a reliable measure of perceived stress (Cohen et al., 1983). It has been trialled previously with a student cohort (Lee 2012), in an Australian population context (Ribeiro et al 2020), and in different completion modes (by mail, in-person, over the phone) Additionally, the relationship between changes in perceived stress as measured by PSS-14 scores; and different causes/types of stress as measured by 10-point scales in the Additional Stress Questionnaire (ASQ) will be analysed (refer to appendix F).

The socio-demographic data will provide descriptive detail and assist with further identification of characteristics that may or may not have influenced acupuncture dosage and treatment-frequency related changes in stress perceptions within a tertiary student framing context (see appendix G for copy of the survey). This includes known poor adaptive coping responses to stress (smoking, drinking, exercise and diet) to provide a framing context specific to individual's entering the study.

The Participant Final Questionnaire (PFQ) comprised 4 questions with 10-point Likert Scale responses, and one open question for feedback on study feasibility.

The Credibility and Expectancy Questionnaire (CEQ) is used to measure treatment expectancy and rationale credibility to allow for possible differences in participants' perception of the intervention and how that may impact observed outcomes (Devilly & Borkovec, 2000). The CEQ consists of four questions using a Likert Scale response from zero to six (see Appendix I).

Secondary outcomes are ASQ, PFQ and CEQ scores; and socio-demographic data as it pertains to PSS-14 scores.

3.4.4 Participant Timeline

Participants who expressed an interest and after conversation with a member of the study team, will be emailed an invite and the PIS, initial consent form for reading – and to organise a meeting for eligibility screening (approximately 30 minutes). With successful screening and signing of the consent form (see Appendices L and M), the sociodemographic survey is then completed (approximately 10 minutes).

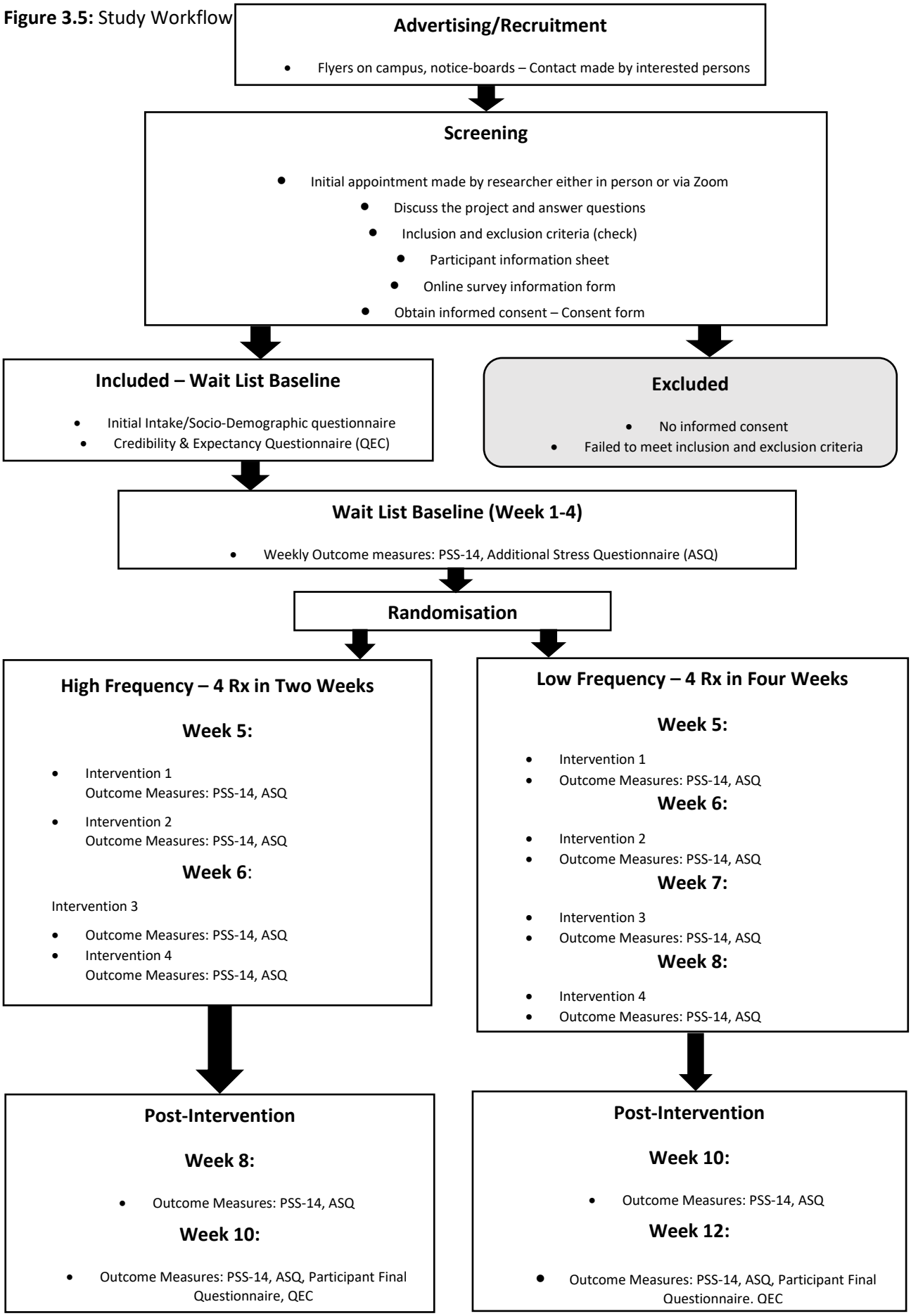
Participants will then go into the wait-list baseline and receive an email invite to the online survey (PSS14 and Additional Stress Questionnaire (ASQ)) weekly, and for an additional three weeks to the end of the wait list baseline period. The PPS14 and ASQ take approximately 5 minutes to complete.

Participants will receive a phone call organising the treatment schedule in Week 4 of the waiting list baseline period. (Approximately 10 minutes)

After each treatment (approximately 40 minutes each), an email invite will immediately be sent to complete the online survey (PSS14, ASQ). Once treatments finish, an email will be sent again at week 2 post treatment and again at week 4 to complete the outcome measures (PSS14 and ASQ). Week 4 will also include the Participant Final Questionnaire (approximately 2 minutes to complete).

Study flowchart below.

Figure 3.5: Study Workflow



3.4.5 Sample Size

The sample size will be 86 participants, randomised into two arms in a 1:1 ratio. This sample size was determined to detect a 20% change (mean PSS14 scores of sham versus verum acupuncture), based on a previous trial featuring stress, acupuncture and students (Schroeder et al., 2017).

3.4.6 Recruitment

The targeted population are university students attending the UTS. Recruitment will take place on UTS city campus using fliers and posters placed in common areas and on UTS public notice boards. A notice will be placed on the Chinese medicine clinic website that informs about research projects (https://www.uts.edu.au/about/faculty-science/chinese-medicine-clinic/our-research), and in the clinics external facing notice boards (Harris Street Foyer, Building 2).

3.5 Methods: Assignment of interventions

3.5.1 Intervention Sequence Allocation

Each participant will be assigned a numerical code, and randomised into the HF or LF acupuncture intervention group using online randomisation software

http://www.graphpad.com/quickcalcs/index.cfm

The randomisation software will be used by a third party to allocate participants.

3.6 Methods: Data Collection, Management and Analysis

3.6.1 Data Collection

Data is collected online via an email invite sent to an online survey (REDCAP). Initial socio-demographic information will be taken once. Primary and secondary outcome measures will be taken at the initial recruitment stage, weekly during the 4-week waiting list baseline group, immediately after each intervention and 2 and 4 weeks post final intervention.

Participants will be emailed reminder notices prior to appointments to improve retention.

Participants who chose to withdraw from the study will be asked if their incomplete data set can be retained and used for analysis.

3.6.2 Data Management

Data management will be according to the *Research Data Management Plan* on UTS Stash.

Data will be entered online by the trial participants using the online survey REDCAP after each treatment. The data will be numerically tagged and exported to Excel and SPSS for analysis. All data will be kept in secure electronic form with back up data on hard-drive, external hard-drives, and OneDrive. Data will only be accessible to the research team.

3.6.3 Statistical Methods

Several statistical tests will be used.

Baseline characterises of participants will be investigated using both t-test and chi square test. If data meet normality assumptions the following statistical tests will be used for different objectives.

- Repeated measure ANOVA→ to investigate mean changes of stress across different intervention measurement time points (I, 2, 3, and 4) in each study group.
- Paired t-test→ to compare baseline measurement with the end of treatment measurement in each study group.
- Independent t-test→ to compare mean differences at each measurement time across the inventions (HF/ LF)
- Pearson correlation → to investigate if there is any relationship between intensity of the perceived stress and other variables from the socio-demographic questionnaire.
- Spearman correlation→ to investigate robustness of the two scale, PSS-14 & ASQ, used to measure stress.
- Feasibility endpoints are recruitment rates and the participation and completion of the study interventions within the stated study periods. Primary outcomes are binary and will be reported as percentages with associated 95% confidence intervals.

3.7 Methods: Monitoring

3.7.1 Data Monitoring

There will be no requirement for a data monitoring committee as this is a small-scale feasibility study and held over a short duration. However, a member of the research team (eg, Dr Sean Walsh), will perform regular entry checks to ensure the data input is accurate and collected at the designated time-points. Data will be exported via software; no data entry needs are anticipated, but exported data will be checked against original data for accuracy before analysis.

3.7.2 Harms

Adverse events will be noted immediately after each intervention when required using the Adverse event reporting form (see Appendix J). Any severe adverse events will cause the interventions to be paused until any possible cause is determined. Participants will be asked to list any adverse events that appear between weekly appointments.

During treatment, there may be slight discomfort on needle insertion (sting), however pain is rare, and will be documented by the research practitioner along with any other adverse events. This data will be reviewed periodically and reported in the final document. Should any findings arise concerning the participants health, physical and/or emotional it will be brought to the attention of the investigation team.

In particular, a detailed distress protocol has been prepared with the UTS Student Services where a student's level of perceived stress is having potential harm to their quality of life or impacting in adverse ways as reported by them to the researcher, then a referral call will be made to Student Services. This is noted in the PIS and Consent form. (Please see appendix K for full detail)

All acupuncture follows the practice guidance by the Chinese Medicine Board Australia (Ahpra: CMBA) and with reference to the document *Infection Prevention and Control Guidelines for Acupuncture* (CMBA 2013), and further to the NHMRC's *Australian guidelines for the prevention and control of infection in healthcare* (NHMRC Guidelines).

For acupuncture, safe clinical practice for the following rare incidents include:

- *Stuck or bent needle:* For muscle spasms, the practitioner will wait a few minutes to allow the muscle to relax. This can be assisted by applying pressure or warmth to the area. If due to patient movement, the practitioner can realign the body to the original position before removing the needle.
- *Broken needle in situ:* Broken above or at skin level, gentle pressure can be applied to the surrounding skin and the needle removed with tweezers or forceps. Broken deep in the tissue the area will be marked with a circle, immobilised and medical attention provided.
- *Needle stick injury:* Needle removed, and the area washed with soap and water, following UTS blood and body fluid exposure procedures. Appropriate medical care and assessment will be provided.
- *Slight bleeding:* Pressure will be applied to the area to stop the bleeding and prevent haematoma.
- *Fainting or dizziness:* Needles will be withdrawn, and the patient will be placed lying down with their legs raised. If there is no response, then first aid with be applied followed by medical assistance.

In the cases of a severe adverse event during treatment the needles will be removed, first aid applied and medical attention provided. In the cases of a severe adverse event between treatments,

appointments will cease, medical attention provided, and the potential causality will be determined, further to reporting event to UTS Ethics.

3.7.3 Auditing

Trial procedures will be audited before trial commencement. Meetings will be scheduled after the first participant to check data entry, and at intermittent time points throughout the trial to ensure proper actions have been taken.

3.8 Ethics and Dissemination

3.8.1 Research Ethics Approval

This trial, SPIRIT protocol and all appendices were approved by UTS Human Research Ethics Committee (HREC), approval number ETH20-5098.

3.8.2 Protocol Amendments

Any large-scale amendments, such as amended study design, objectives or procedures will be reviewed by UTS HREC committee.

Any minor amendments will be agreed on by the trial team, reported to UTS Research and be reported in all post-trial publications.

3.8.3 Consent or Assent

Potential trial participants expressing an interest from advertising, will be emailed an invite to the study, the PIS, an online consent form and details about the research, including normal acupuncture procedures

A baseline meeting (a minimum of one week before the initial baseline PPS14 measure) will take place with the investigator to confirm the participant has a clear understanding of the research and its requirements, complete a finalized check on the inclusion/exclusion criteria, and present the written consent and assent documentation.

Finally, the investigator will further enquire at the initial intervention about any queries or difficulties the participant may have, and confirm the participant's consent to the acupuncture intervention.

3.8.4 Confidentiality

Depersonalised information, linking codes and all gathered data will be stored electronically in a password protected folder in a central location, on an external hard-drive, and on OneDrive. Linking codes will be held separately from data. The folders will only be accessible to the researchers.

Online data will be stored with REDCAP before being exported.

3.8.5 Declaration of Interest

The principle investigators declare no potential conflicts of interest with respect to the research of this trial.

3.8.6 Access to Data

The principal investigators will have sole access to the final trial dataset. A third party may assist with the analysis modelling, but will only have access to depersonalised/anonymised/de-identified data only.

3.8.7 Ancillary and Post-trial Care

Further care needed will be dealt with on a case by case basis, as no serious adverse effects are expected. Possible actions will include referral to UTS Student Services for counselling services.

3.8.9 Dissemination Policy

There are no restrictions on publication. A paper/s will be submitted to an appropriate peer-reviewed journal after final data analysis for publication. Study participants will be invited to receive study results at this time. Additionally, the study protocol may also be published at this time.

Chapter 4: Delphi Round 1 – Introduction, Development, Results

4.1 Introduction

With the onset of COVID-19 and its associated lockdowns, it became apparent that the clinical trial could not be performed within the allocated timeframe of this master's candidature. While the investigational intervention was suspended, the institutional candidature process continued, and it was therefore necessary to identify an alternative data collection approach. The decision was consequently made to pivot to a two-round Delphi, with two research objectives. Firstly, as a check on the veracity of the clinical literature findings on acupuncture and stress (from Chapter 2) and to compare this with real-world clinical perspectives. That is, clinical theory doesn't always translate into clinical practice and identifying what is clinically relevant is key to clinical significance. Secondly, to critique the construct logic of the clinical trial protocol and make refinements, while also gathering practice insights into the diagnosis and treatment of acupuncture and stress through expert consensus.

Consequently, this Chapter first describes and discusses the essential components, properties and features of the Delphi process, the role of the questionnaire tool, and the Delphi's iterative approach to building expert consensus. The discussion extends into the rationale considerations for the questionnaire's development in this study and the Delphi's Round 1 construction process is explained. Finally, responses from the first-round questionnaire will be presented and analyse discussed.

4.1.1 About the Delphi Process

A Delphi process is a widely accepted means of achieving expert consensus on a particular topic using a sequence of specially designed questionnaires(Hsu & Sandford, 2007; Keeney et al., 2011). Precedence exists within the Delphi research literature for its use to inform diagnostic and practice opinions in both Chinese and Western medicine, and in critiquing research protocols and guidelines. Examples include in the development of practice guidelines (Flower et al., 2007), diagnosis(Gadau et al., 2016; Wang et al., 2020), educational approaches (Leach, 2021), research trial design (Witt et al., 2014) and development of meaningfully important differences with effect size calculations for treatment intervention recommendations (Papini et al., 2019).

The Delphi process begins with participants who have subject-related expertise in the topic of interest, and who are then invited to participate in a series of surveys. Consequently, participants are known to the chief investigator, but not to each other. The anonymity of the Delphi process is important. Anonymity reduces the possible bias or conformity accorded to dominant personalities, coercive behaviour or perceived greater expertise (Foth et al., 2016; Hsu & Sandford, 2007; Murry &

Hammons, 1995). For each survey round, other than the first, the participants are given summarised response feedback of all responses to each questionnaire item, and a revised series of questions circulated to determine if participants might individually adjust or change their original response. The process continues until a consensus threshold is reached or the pre-determined number of survey rounds is exhausted. The number of rounds generally vary from a minimum of two and up to four rounds (Hsu & Sandford, 2007). The first round of a Delphi process may feature open-ended questions to develop and refine further survey rounds.

Critical to the Delphi process is the expertise of participants. A participant's 'content-expertise' has a direct impact on the quality of the data obtained. While no exact criteria exists, participants should be considered knowledgeable in the target field, considered competent or highly trained, and be stakeholders or possible users of the research outcomes (Hsu & Sandford, 2007). The participant number should also be manageable. Too few participants limit breadth of expertise and applicability of outcomes, while too many participants impact the Delphi design and increase the number of rounds required for consensus, which in turn increases participants' fatigue and the potential risk of non-completed survey responses rise. Consequently, suggested panel sizes range from a minimum of ten participants (Murry & Hammons, 1995) to a maximum of 50 for projects requiring multiple reference groups (Hsu & Sandford, 2007).

Finally, data analysis of the Delphi outcomes is determined by consensus thresholds. Delphi response thresholds are predetermined minimum levels of response rates required to accept consensus on any given survey outcome. Consensus is considered achieved if a percentage of votes falls within a prescribed range, for example 70% of votes scoring a three or four on a four-point Likert scale (Hsu & Sandford, 2007). The consensus threshold used in the literature varies widely, with examples seen anywhere from 55% to 100% (Powell, 2003), although the median consensus threshold is 75% (Barrios et al., 2021). Generally, the threshold is set according to the specifics of the research requirements: if a broad consensus is acceptable with many data outputs then a lower consensus can be used. Contrarily, if a tight consensus with few data outputs is needed then a higher consensus threshold will be required. Importantly, the threshold should be set a priori so as to specify the agreement required for consensus before initiating the Delphi process (Barrios et al., 2021).

4.2 Development of the Delphi Process

The Delphi process for this research project has the following key features:

- Two rounds;
- A minimum of ten participants with a maximum of 15; and

- An initial consensus threshold of 80%.

The 80% consensus threshold meant that for each response on a 5-point Likert scale (from 1: Not relevant at all, to 5: Extremely relevant), any questions which received a four or higher from 80% of the total respondents met the threshold. For open-ended questions the response would be included if 80% of respondents suggested the additional option. Likewise, response about treatment protocols would meet the threshold if 80% of respondents selected any of the available options.

The methods below describe the Delphi process development for the current study.

4.2.1 Methods

4.2.1.1 Number of Rounds

The number of rounds used in a Delphi process generally varies from two to four rounds (Hsu & Sandford, 2007; Keeney et al., 2011). While less than two rounds obviously give no option for feedback nor increasing consensus; change of opinion decreases or consensus tends to remain stable with three or more rounds. That is, participants have made up their mind by the third round and are unlikely to change (Murry & Hammons, 1995).

The initial round is commonly made of open-ended questions, giving the respondents the freedom of scope to elaborate on the topic and identify issues to be addressed in later rounds (Powell, 2003). However, there are frequent examples of initial questionnaires being pre-shaped by researchers in accordance to previous literature reviews (Flower et al., 2007; Gadau et al., 2016; Leach, 2021; Murry & Hammons, 1995). Using this approach reduces the required number of rounds, as the topics relevant to a research topic (such as acupuncture and stress) have already been identified.

For this project the initial round was based on the literature review (refer to Chapter 2), while also having one open-ended question in each section, providing participants the opportunity to broaden the scope of issues. This meant that two rounds would suffice, while also being a pragmatic number of rounds to complete within the time available.

4.2.1.2 Selection of the Expert Panel

The threshold of what is considered “expert” enough to participate in a Delphi varies in the literature and tends to be context informed. For example, previous studies have required a minimum amount of experience (such as years in practice) (Barrios et al., 2021; Flower et al., 2007; Gadau et al., 2016), others refer to relevant employment positions (Leach, 2021; Murry & Hammons, 1995) or membership of specific research institutions (Wang et al., 2020).

While expertise in a subject-relevant field to the study topic is desirable, it is also encouraged to attempt to have a heterogenous group of experts in order to bring a greater breadth of experience

and backgrounds, and that a more diverse panel of experts will lead to better or more reliable outcomes (Powell, 2003).

Members of the expert panel should be process stakeholders– that is, they should have an interest in the outcomes of the Delphi process, or have an experience of working in a field or having been subjected to the impact of a condition or intervention (Hsu & Sandford, 2007; Powell, 2003).

For this project, participants were identified through professional networks of the researchers. Participants had to be registered with the Chinese Medicine Board Australia. Additionally, participants had to meet a minimum of at least one other of the following criteria:

- A post-graduate qualification in Chinese Medicine; or
- More than five year's clinical practice experience; or
- Currently treating a minimum of twenty patients presenting with stress per month.

It was considered that these inclusion criteria would satisfy the requirements of expertise, while also being pragmatic to ensure assembly of the required panel in the time available. Additionally, the criteria addressed heterogeneity of experts, such as education, qualifications and clinical experience.

4.2.1.3 Number of Participants

The number of participants making up the expert panel in a Delphi process in the literature is varied, with little consensus about what constitutes the "right" number. Generally, there must be enough participants to make a representative pooling of expert opinion on the subject (Hsu & Sandford, 2007), while also taking into account time and resources available to the research team (Powell, 2003). Some authors have decreed that the larger the panel size the better (Black et al., 1999), while others refute this noting that increasing participant numbers increases instability in achieving consensus. Additionally, larger time-related resources are required for larger participant groups, an ethical consideration weighing on both participants and researchers alike (Hsu & Sandford, 2007).

Murry and Hammons (1995) suggests between 10 and 30 participants, while (Black et al., 1999) suggests six to 12 participants. A literature review found expert panels containing up to 1508 participants (Foth et al., 2016). Researchers utilising the Delphi process have used 11 (Flower et al., 2007), 16 (Leach, 2021), 17 (Wang et al., 2020), 26 (Gadau et al., 2016) or 29 (Papini et al., 2019) participants in their expert panel.

The choice of 15 experts to make up the panel was deemed sufficient to be representative of expertise on the subject matter, while also allowing for the project to be concluded within the allotted candidature timeframe.

4.2.1.4 Consensus Threshold

The use of a consensus threshold is an important aspect of the Delphi process, as this determines which responses are retained through subsequent rounds and determines the included data outcomes of the process. While some Delphi processes have not specified a definition of consensus, it is generally considered better to both define consensus, and to define it a priori (Barrios et al., 2021; Diamond et al., 2014). Higher consensus thresholds will indicate a greater agreement amongst experts regarding the outcomes but will also reduce the possible data outcomes while possibly extending the time the process takes to achieve consensus.

Reported consensus thresholds used for Delphi studies have varied greatly, from as low as 55% up to 100% (Powell, 2003). Examples found in the literature include 51% according to a Content Validity Index (CVI) (Gadau et al., 2016), a median score of five or more on a seven-point Likert scale (Flower et al., 2007), and 75% of respondents rating four or five on a five-point Likert scale (Guan et al., 2019). One review of Delphi processes in the literature determined that the median Delphi consensus threshold was 75% (Diamond et al., 2014).

As the total number of participants equalled 15, a 75% threshold would require 11.25 participants responses, a nonsensical number. Therefore, the threshold could be set at either slightly above (80%) or slightly below (73.3%) the median threshold. It was decided that a higher threshold was desirable, in order to produce a small number of data outcomes that were highly agreed upon by the expert panel. The threshold was set at 80%, therefore consensus was reached if 12 out of 15 participants rated the question as four (very relevant) or five (extremely relevant) on a five-point Likert scale.

4.2.2 Construction of the Delphi

The Delphi process takes several steps to complete. Detailed below are the steps in reference to the two-round Delphi process utilised:

1. *Identification of experts:* Invitees (n=42) were identified through professional networks of the researchers, including clinicians, academics and postgraduate research students (who were also registered Chinese medicine practitioners). A total of 18 people responded to the invite to participate. Of these, three people did not complete the first-round questionnaire, leaving a total of 15 experts who completed both Rounds 1 and 2.
2. *Development of round 1 questionnaire:* Questions were constructed from the literature review conducted for this master's project (see Chapter 2), validated stress-based questionnaires, and CM clinical texts. Each section of the questionnaire also contained one open-ended question to allow further input from the experts. The questionnaire also included inclusion and exclusion criteria to eliminate "unwanted lack of expertise" which

could potentially occur due to the anonymity programmed into the online Delphi process to address ethical considerations relating to recruitment.

3. *Invitation*: Participants were invited via email containing information about the Delphi process and a link to the first online survey. A reminder email was re-sent twice during the first round; at the mid-point and one week from Round 1 closure
4. *Round 1 data collection and analysis:* The results from Round 1 were exported to Excel and manually analysed by the researcher.
5. *Development of Round 2 questionnaire:* Responses that met threshold (80%) were retained for round 2. Popular additional responses from open-ended questions were included where appropriate, as were items of interest (see Chapter 4: Round 1 Results, and Chapter 6: Discussion). The Round 2 survey also featured exclusion criteria to ascertain that the respondent had completed round 1.
6. *Invitation for Round 2:* The same 42 invitees were invited to take part in round 2, provided they had taken part in round 2. All 42 invitees had to be re-invited due to the anonymity intrinsic in the Delphi process design – the researchers had no way of knowing who had responded out of all the invitees. Reminder emails were sent twice during round 2.
7. *Round 2 data collection and analysis:* The results from round 2 were exported to Excel and manually analysed by the researcher. (See Chapter 5)

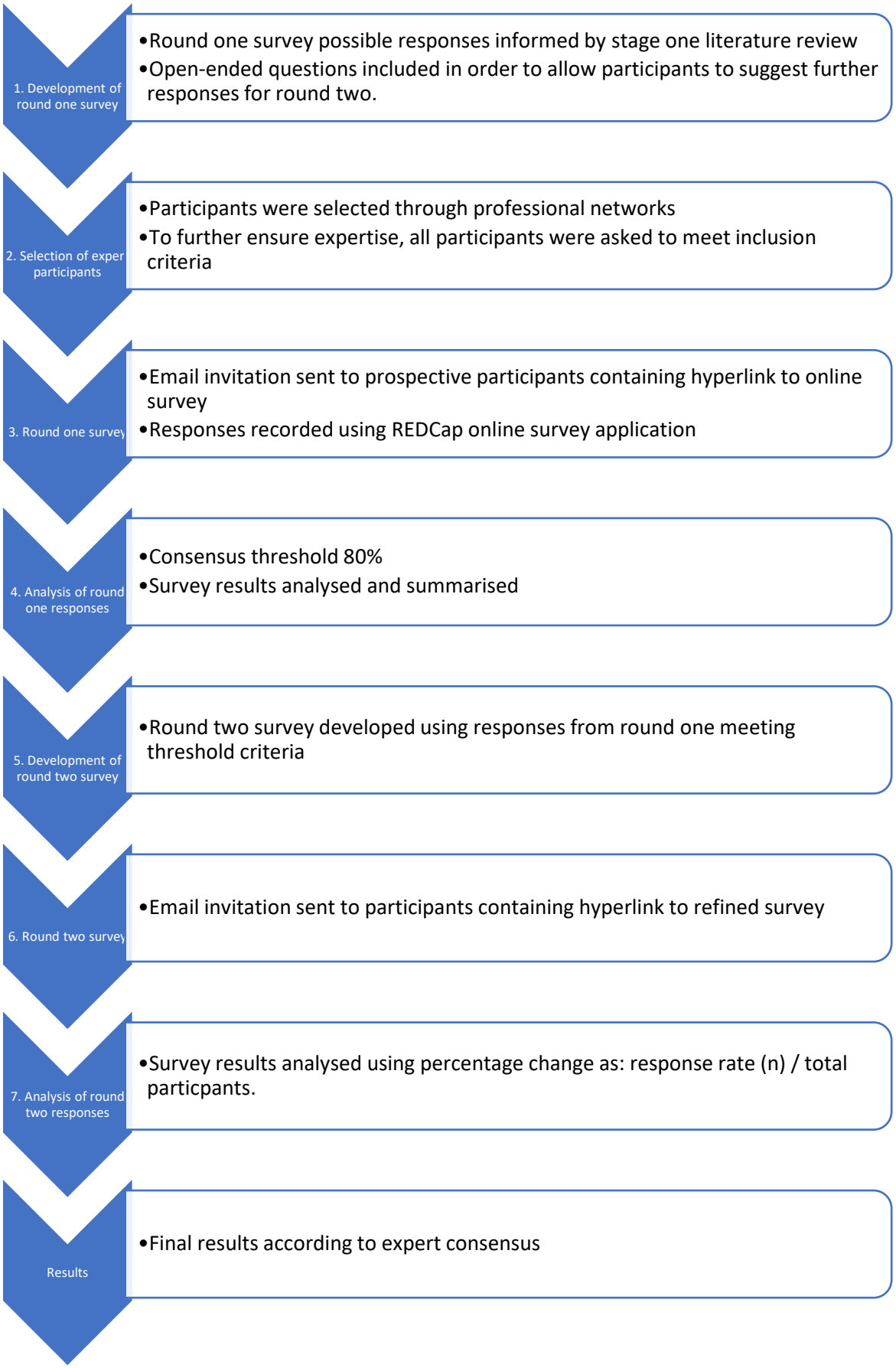


Figure 4.1. Delphi process workflow

4.2.3 Ethical Considerations

Prior to commencement of the study, ethical approval was obtained from the Human Research Ethics Committee at the University of Technology Sydney (reference number ETH21-6702). Participation in the Delphi process was completely voluntary. Consent information was included in the beginning of the round 1 survey, with completion of the survey indicating consent.

4.2.4 Survey Distribution

Potential participants were contacted by email to enquire about interest in participation (n=42). Participants were emailed an invitation with a hyperlink to the online survey (see appendix O). Participant responses were completely anonymous – no identifying information was collected, nor was the response attached to any email address. Distribution began in October 2021 and carried through to April 2022. Of the 42 invites, 18 experts began the round 1 questionnaire, while three respondents did not complete round 1, leaving a total of 15 participants completing both rounds 1 and 2.

4.2.5 Questionnaire Construction

The survey was constructed using the online survey application REDCap. The initial survey consisted of 82 questions in six parts. The full questionnaire is located in the appendix A, with a brief explanation of each of the six parts listed below. These included:

- Part One – About you: This section formed the inclusion/exclusion criteria, demographic information and consent information.
- Part Two – Diagnosis – Zangfu: Asked questions about the relevance of various *zangfu* (organs) in a diagnosis of stress
- Part Three – Diagnosis – Syndromes: Asked about the relevance of syndromes in a diagnosis of stress
- Part Four – Diagnosis – Signs and Symptoms: Asked about the relevance of signs and symptoms in a diagnosis of stress
- Part Five – Treatment - Acupuncture Points: Asked about the relevance of various acupuncture points in a treatment of stress
- Part Six – Treatment Protocols: Asked about number and frequency of acupuncture treatments expected to be needed for clinically significant results and the use of diagnostic questionnaires in practice.

4.2.5.1 Part One – About You

This section asked about the respondents' years of practice, highest qualification completed and number of stressed patients treated. This formed the inclusion/exclusion criteria as per the requirements for the expert panel. Respondents who did not meet the inclusion criteria were

immediately redirected to a message informing them of their ineligibility and thanking them for their time. REDCap did not retain any data from these responses.

The inclusion/exclusion criteria were required in this section in response to the anonymity designed into the Delphi process. The email contained a hyperlink to the survey and both the email and link were not specific to an individual. While advantageous in terms of ease of access to the survey, it also meant invitees were requested not to forward the link and to keep it confidential. Despite this request, and due to the anonymity design, the expertise of any possible respondent still needed to be confirmed.

This section also included the research consent information as approved by UTS HREC committee, with completion of the questionnaire indicating consent.

4.2.5.2 Part Two: Diagnosis – Zangfu

This section asks respondents to indicate their opinion about the clinical relevance of various zangfu in a diagnosis of stress, as indicated on a five-point Likert scale from one (not relevant at all) to five (extremely relevant).The zangfu were sourced from the Chapter 2 literature review carried, where the literature had indicated a zangfu diagnosis (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012), and CM clinical texts (Deadman & Al-Khafaji, 2001; Maciocia, 2006; Rossi, 2007). An open-ended question allowed participants to nominate any further zangfu they considered relevant.

4.2.5.3 Part Three: Diagnosis – Syndromes

This section asks respondents to indicate their opinion about the clinical relevance of various syndromes in a diagnosis of stress, as indicated on a five-point Likert scale from one (not relevant at all) to five (extremely relevant). Syndromes were sourced from the literature review (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012), further literature from recent stress-related research (Zheng et al., 2017) and CM clinical texts (Deadman & Al-Khafaji, 2001; Maciocia, 2006; Rossi, 2007). Syndromes were included from clinical texts if they were indicated for the diagnosis of stress. An open-ended question allowed participants to nominate any further syndrome they considered relevant.

4.2.5.4 Part Four: Diagnosis – Signs and Symptoms

This section asks respondents to indicate their opinion about the clinical relevance of various signs and symptoms in a diagnosis of stress, as indicated on a five-point Likert scale from one (not relevant at all) to five (extremely relevant). Signs and symptoms were sourced from CM clinical texts (Deadman & Al-Khafaji, 2001; Liu, 2009b; Maciocia, 2004, 2006; Rossi, 2007) and stress-related

questionnaires (Cohen et al., 1983; Zheng et al., 2017). An open-ended question allowed participants to nominate any further syndrome they considered relevant.

4.2.5.5 Part Five: Treatment – Acupuncture Points

This section asks respondents to indicate their opinion about the clinical relevance of various acupuncture points in a treatment of stress, as indicated on a five-point Likert scale from one (not relevant at all) to five (extremely relevant). Acupuncture points were sourced from the literature review (Chan et al., 2002; de Oliveira & Scivoletto, 2017; Huang et al., 2011; W. Huang et al., 2012; Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001; Pavão et al., 2010; Schroeder et al., 2017; Smith et al., 2011; Zuppa et al., 2015) and CM clinical texts (Deadman & Al-Khafaji, 2001; Liu, 2009b; Maciocia, 2006; Rogers & Rogers, 2006; Rossi, 2007). Acupuncture points were chosen if they were indicated in the treatment of any of the symptoms or syndromes from parts three and four. An open-ended question allowed participants to nominate any further acupuncture points they considered relevant.

4.2.5.6 Part Six: Treatment – Treatment Protocols

This section asked about the use of stress-related questionnaires in clinical practice. Respondents were asked to indicate yes or no to the use of several questionnaires. These questionnaires were sourced from the literature review (Cohen et al., 1983; Lipp, 2000; Paterson, 1996; Speilberger, 1983). An open-ended question allowed the respondents to nominate any other stress-based questionnaire used in clinical practice.

Section six also asked respondents two further questions: How many treatments per week would they prefer to administer to achieve clinically relevant results (choices from one to seven), and how many total number of treatments would they normally expect to administer to achieve clinically relevant results (choices from one to 12+).

4.3: Delphi Round 1 Results

The complete set of survey results can be found in appendix C. This Chapter discusses the results from Round 1 and additions and changes to the questionnaire for Round 2.

4.3.1 Profile of Participants

The selection of the experts to be involved in the Delphi process is important for the validity of the Delphi outcomes (see Subheading 4.1). Thus, participant responses to the first three questions were used as inclusion/exclusion criteria. If a respondent did not meet the inclusion criteria the survey was immediately and automatically terminated, and any data taken up to that point was not retained.

In total, 100% (n=15) of respondents satisfied the criteria of being a registered health practitioner with the CMBA, and at least two of the other inclusion criteria. This is summarised below in Table 4.1 with further discussion following below.

Table 4.1: Summary of participant reported inclusion criteria characteristics by frequency count.

Characteristics	All participants n (%)
Years in clinical practice:	**15**
<5	1 (6.7)
5-10	3 (20.0)
11-15	4 (26.7)
16-20	2 (13.3)
20+	5 (33.3)
Stressed patients treated / month:	**15**
5-10	5 (33.3)
11-20	2 (13.3)
21-30	2 (13.3)
31-40	2 (13.3)
41+	4 (26.7)
What is your highest qualification:	**15**
Undergraduate (Bachelor's degree)	6 (40.0)
Postgraduate (Master's)	5 (33.3)
Postgraduate (Doctorate)	4 (26.7)

4.3.1.1 Years of Clinical Practice

Overall, 33% of participants had 20 or more years of clinical practice in Chinese Medicine (n=5), and 27% of participants had between 11 and 15 years of experience (n=4). In total, 93% of participants had more than five years of clinical experience (n=14).

It was noticed after completion of the Delphi process that there was a possible overlap in years in clinical practice. That is, a participant with 20 years of experience could select either 16-20 or 20+. However, as both options more than satisfied inclusion criteria it was deemed that the error was inconsequential.

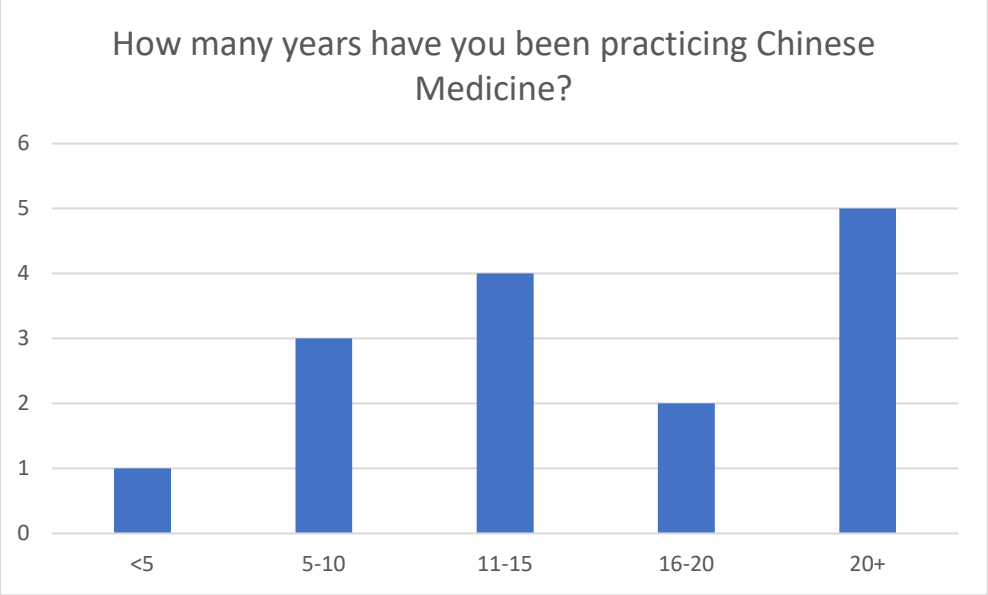


Figure 4.2: Participant Profile – Years of Practice. The figure shows the frequency count of years in practice as reported by participants.

4.3.1.2 Stressed Patients per Month

Over one third (40%) of participants treated between five and ten stressed patients per month (n=6) and 26% of participants treated forty or more stressed patients per month (n=4). In total, 53% of participants treated 20 or more stressed patients per month (n=8).

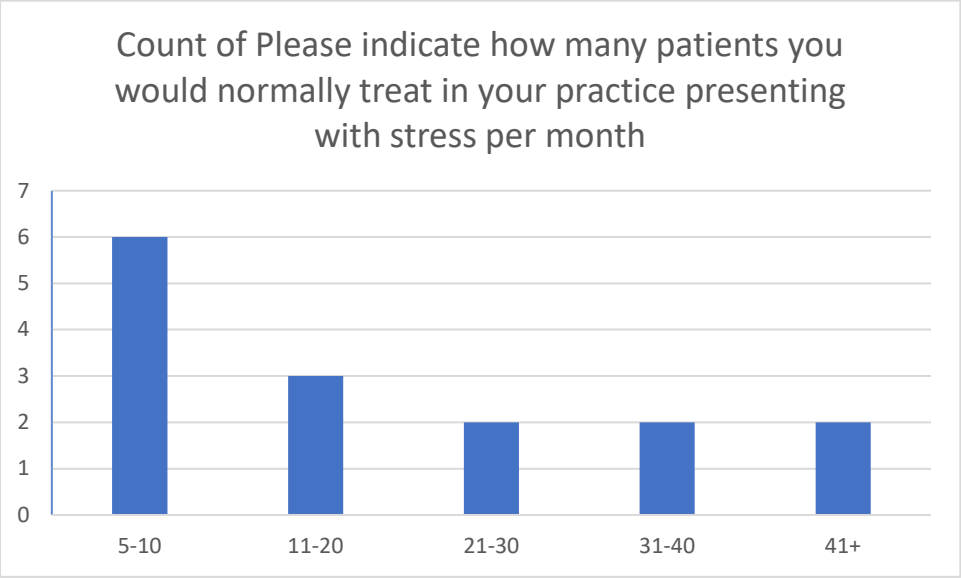


Figure 4.3: Participant Profile – Number of Stressed Patients per Month. The figure shows the frequency count of treatments as reported by participants.

4.3.1.3 Participant Qualifications

40% of participants held an undergraduate degree as their highest qualification (n=6). 33% of participants had a postgraduate Master's degree (n=5). In total, 73% of participants had postgraduate qualification in Chinese Medicine (n=11).

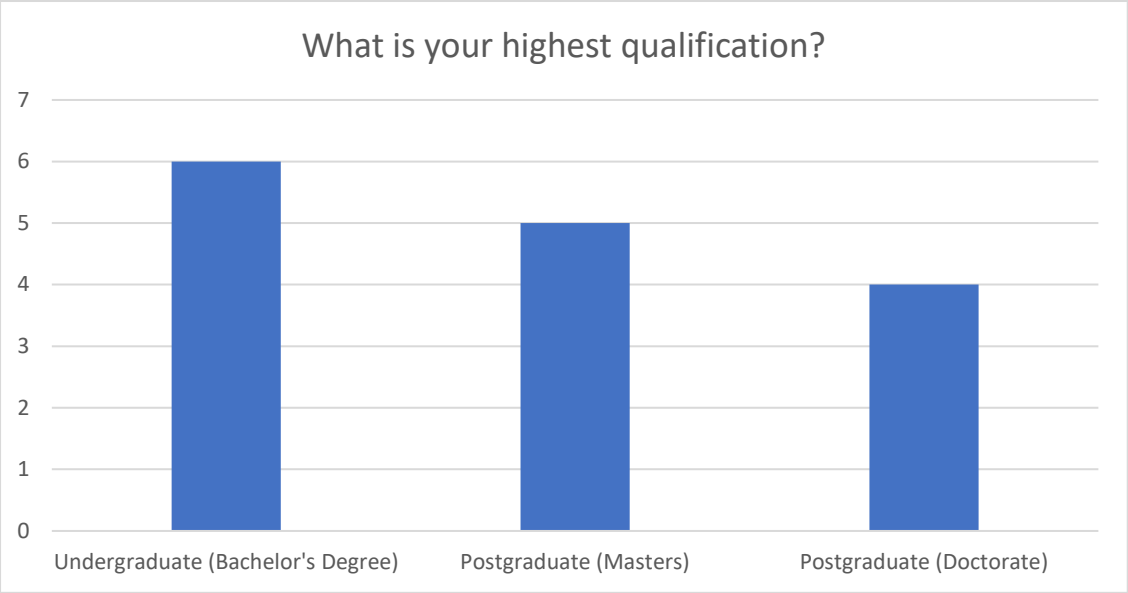


Figure 4.4: Participant Profile - Highest Qualification. The figure shows the frequency count by highest qualification reported by participants.

4.3.2 Zangfu Clinically Relevant to a Diagnosis of Stress

All participants (100%) rated the Liver as clinically relevant to a diagnosis of stress (n=15) and 80% of participants rated the Kidney as relevant (n=12). No other Zangfu made threshold for Round 2. The open-ended question gave participants the option to nominate additional Zangfu not yet mentioned. Although no participant suggestions made threshold, the Gall Bladder was the most popular suggestion (40%, n=6). This was subsequently added to the second round of the Delphi.

Zheng et al. (2017) developed a novel CM questionnaire for the diagnosis of patterns based on self-reported symptoms. The questionnaire features 70 signs and symptoms associated with stress, which correlate to 14 different stress-related CM diagnostic patterns. A total of 33 participants who self-reported as stressed completed the questionnaire and the most common pattern diagnoses were calculated. According to Zheng et al. (2017) the most common zangfu diagnoses based on self-reported symptoms for men were (in descending order) Heart Qi deficiency, Liver Blood deficiency followed by Heart Blood deficiency. For women, these patterns were Heart Qi deficiency, Heart Blood deficiency and Liver Blood deficiency/Liver Blood stasis.

Zheng et al., (2017) findings challenge the common perceptions of stress-related CM patterns reported in the CM clinical literature (noted in chapter 2) as relating to a CM pattern diagnosis of Liver Qi stasis, also consistent with participants Round 1 Delphi results noting Liver Qi stasis.

Despite the Heart zang being the most dominant of the zangfu when relying on self-reported symptoms, the Heart did not make threshold (73.3%, n=11) in the Round 1 Delphi. Given this apparent paradox, a further two zangfu questions were added to Round 2. These were:

- The most popular zangfu answer from Round 1 that did not make threshold was Heart (73.3%). Does knowing this make you reconsider the Heart in a diagnosis of stress?
- Keeping your response to the previous question in mind, Zheng et al. (2017) found that the most common diagnoses for stress, when based on self-reported symptoms, were Heart zangfu pathologies. Does this change your opinion about the relevance of the Heart zang in diagnosis for stress?

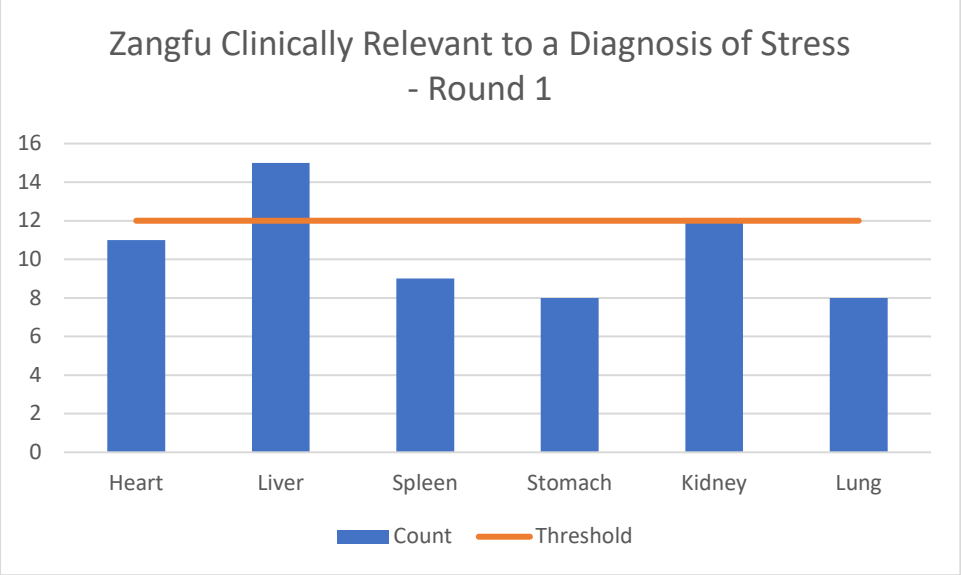


Figure 4.5: Diagnosis - Zangfu Clinically Relevant to a Diagnosis of Stress. The figure shows the count of participants who rated the Zangfu as four or five out of five on a Likert Scale. (Threshold =80%, or n=12)

4.3.3 Syndromes Clinically Relevant to a Diagnosis of Stress

All participants (100%) rated Qi Stasis as clinically relevant to stress (n=15). No other syndrome made threshold, although Zangfu Disharmony/Mutual Insult was the closest at 73.3% (n=11). As this was very close to threshold, it was included in Round 2 to see if threshold would be achieved if there were fewer choices available to participants.

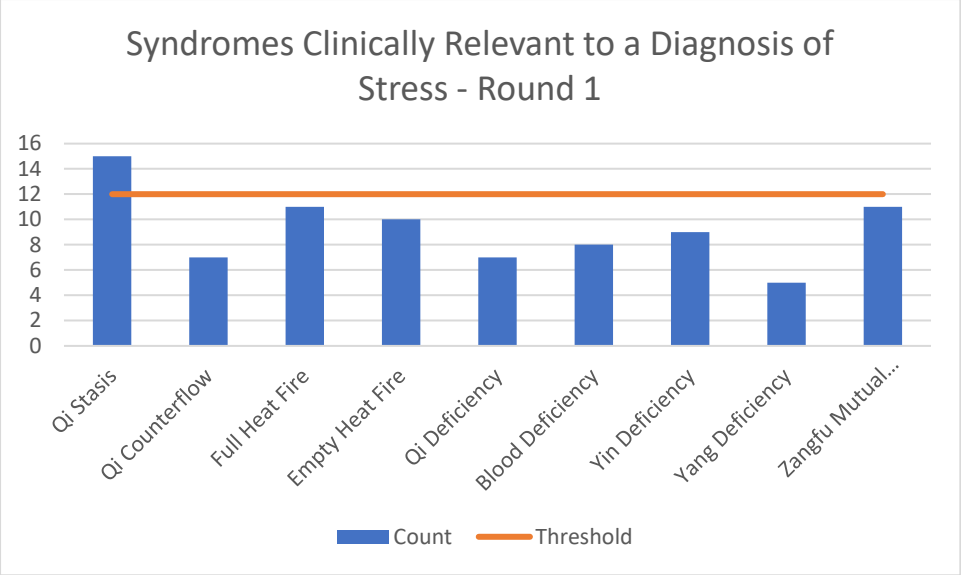


Figure 4.6: Diagnosis - Syndromes Clinically Relevant to a Diagnosis of Stress. The figure shows the count of participants who rated the syndrome as four or five out of five on a Likert Scale. (Threshold =80%, or n=12)

4.3.4 Symptoms Clinically Relevant to a Diagnosis of Stress

All participants (100%) rated both "Irritability or short tempered" and "Agitation or inability to relax" as clinically relevant to stress (n=15). Other symptoms to make threshold included "Anxious or racing thoughts" (93.3%, n=14), "Constant worrying" (86.6%, n=13), "Insomnia or other sleep disturbances" (86.6%, n=13), "feeling unable to cope with all the things you must do" (86.6%, n=13) and "Feeling unable to deal with life hassles" (86.6%, n=13).

Several most common self-reported symptoms of stress from the novel pattern diagnostic questionnaire (Zheng et al., 2017) made threshold, including:

- "Anxious or racing thoughts" (93%, n=14)
- "Constant worrying" (86.6%, n=13)
- "Irritability or short temper" (100%, n=15)
- "Agitation or inability to relax" (100%, n=15)
- "insomnia or other sleep disturbances" (86.6%, n=13)

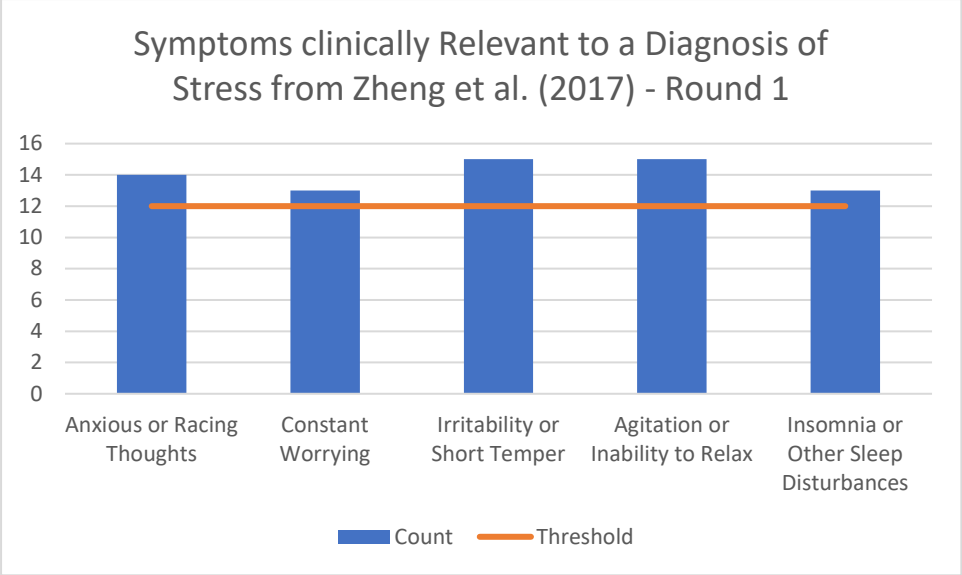


Figure 4.7: Diagnosis - Symptoms Clinically Relevant to a Diagnosis of Stress, from Zheng et al (2017)**.** The figure shows the count of participants who rated the symptom as four or five out of five on a Likert Scale. (Threshold =80%, or n=12)

Interestingly, those self-reported symptoms most common amongst males in the findings of Zheng et al. (2017) were more likely to make threshold than those self-reported by females. For instance, the third most common symptom self-reported by females according to Zheng et al. (2017) was "Easily fatigued" (60%, n=9), while the fourth most common was "Inability to concentrate" (53.3%, n=8).

To further explore this, further questions were included to explore how gender or sex may be an influencing characteristic considered by practitioners:

- When thinking about your response to the previous questions (symptoms), did you consider the sex of the patient? (Sex is referring to the patient's sex assigned at their birth)
- When thinking about your response to the previous questions (symptoms), did you consider the patient's self-defined gender identity? (Gender refers to the norms, behaviours and roles associated with socially constructed identity.)
- In your opinion, would you expect to see different symptoms for stress presenting in patients of different sexes (for example, different symptoms in males vs females)?
- In your opinion, would you expect to see different symptoms for stress presenting in patients of different genders (for example, different symptoms in patients identifying as male vs female)?

No pulse qualities or tongue signs made threshold. The highest rated pulse quality was "Wiry" (73.3%, n=11) and the highest rated tongue sign was "Red tongue tip" (60%, n=9). This was

surprising considering the traditional importance given to pulse and tongue qualities. Consequently, to explore this further by possibly eliciting some form of consensus in Round 2, the closed questions from Round 1 were replaced with an open-ended question and included in Round 2:

- Please list any pulse qualities that you believe would be clinically relevant to a diagnosis of stress.

The four symptoms listed in Round 1 that were taken from the PSS14 (Cohen et al., 1983), all made threshold:

- Feeling Unable to Control Important Things in Life (80%, n=12)
- Feeling Unable to Cope With All the Things You Must Do (86.6%, n=13)
- Feeling Unable to Control Irritations in Life (80%, n=12)
- Feeling Unable to Deal Well With Life Hassles (86.6%, n=13)

Yet only two participants indicated its use in practice. To explore this further, Round 2 included an additional question:

- The previous four signs and symptoms were taken from the Perceived Stress Scale (PSS). The PSS is a clinical questionnaire which is a validated, global measure of stress using patient's self-reported symptoms. All symptoms from the PSS were included in Round 1 and reached agreement threshold. These items are included in Round 2 of the study (this survey). However, very few respondents (13.3%) from Round 1 indicated using the PSS in their clinical practice. Considering this information about the PSS, would you now consider incorporating the PSS into your clinical practice?

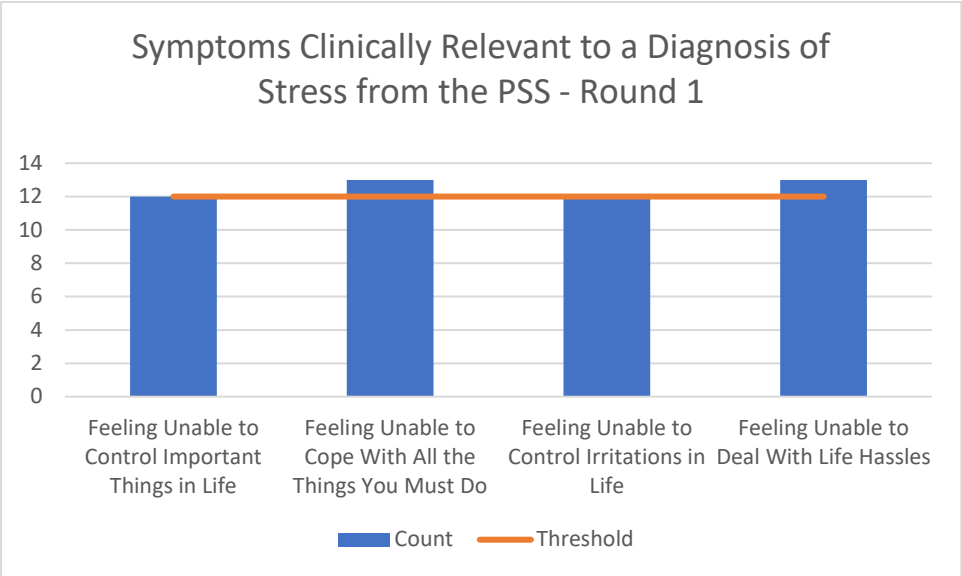


Figure 4.8: Diagnosis – Symptoms Clinically Relevant to a Diagnosis of Stress, from the PSS. The figure shows the count of participants who rated the symptom as four or five out of five on a Likert Scale. (Threshold =80%, or n=12)

4.3.5 Use of Validated Stress Questionnaires

No count of the use of validated stress questionnaires made threshold. The highest rated questionnaire was the MYMOP questionnaire (26.6%, n=4). This might be accounted by the fact that it is used for many different clinical purposes, and not just stress. However, as discussed above, the symptoms taken from the PSS14 all made threshold. That is, while participants may not have recognised the PSS14 as a stress-specific questionnaire, they did however recognise the clinical presentation of stress described in the PSS14. To explore this further, questions regarding the use clinically validated questionnaires and use in Chinese medicine were included in Round 2

- ROUND 1 of this study included a question about the use of five (5) stress-related questionnaires. Please indicate whether you had previously been aware of the following specific stress-related questionnaires:
    - Perceived Stress Scale (PSS)
    - State-Trait Anxiety Scale (STAI)
    - Lipp's Inventory for Stress Symptoms (LISS)
    - Measure Yourself Medical Outcome Profile (MYMOP)
- If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in practice?
- If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in clinical practice (to assist in diagnosis)?
- If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you use it as an outcome measure (to assess the effects of treatment and changes in stress over time)?

4.3.6 Acupuncture Points

There were 19 acupuncture points listed in Round 1 for participants to rate. Of these, Yin Tang (an extra point) was the highest rated acupuncture point (93.3%, n=14). Other points to make threshold includes Liver 3 (Taichong), Gallbladder 34 (Yanglingquan), Pericardium 6 (Neiguan), Governor Vessel 20 (Baihui) (all 86.6%, n=13) and Heart 7 (Shenmen) (80%, n=12). No other suggested acupuncture points made threshold. Acupuncture points that did make threshold were carried over to the Round 2 survey.

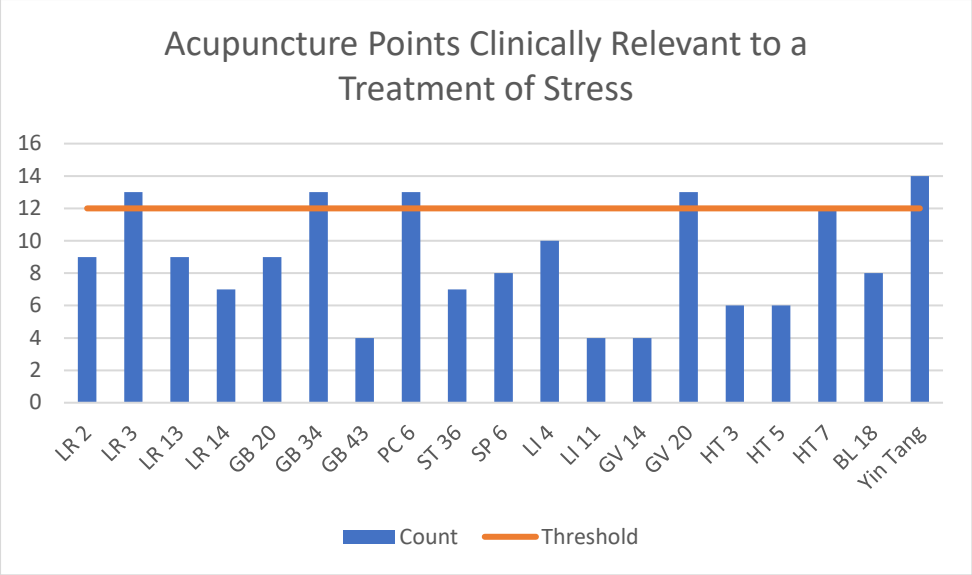


Figure 4.9: Treatment - Acupuncture Points Clinically Relevant to a Treatment of Stress. The figure shows the count of participants who rated the acupuncture point as four or five out of five on a Likert Scale. (Threshold =80%, or n=12)

4.3.7 Treatment Frequency

No treatment frequency met threshold. The closest to threshold was two treatments per week (73.3%, n=11).

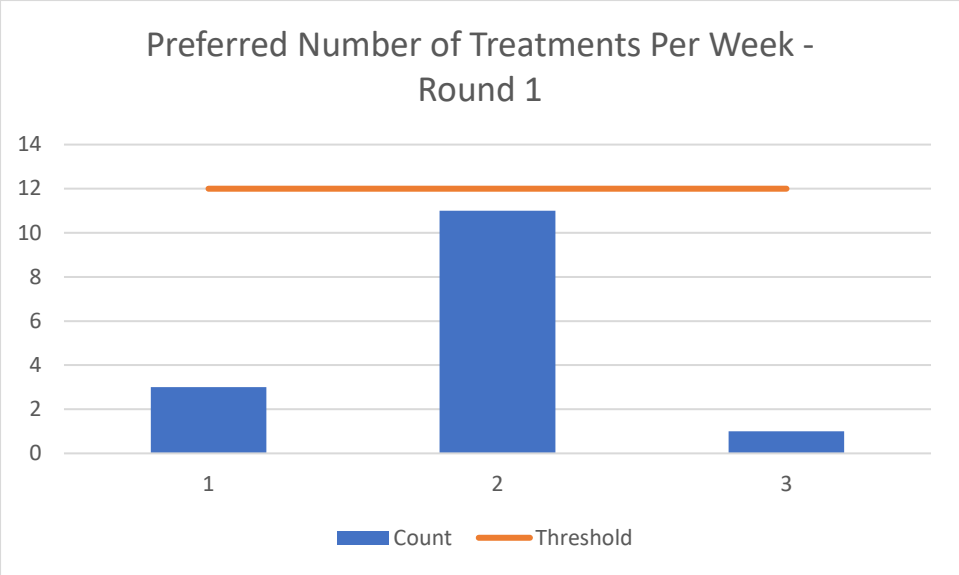


Figure 4.10: Treatment - Preferred Number of Treatments per Week. The figure shows the count of participants who nominated a set number of treatments per week. (Threshold =80%, or n=12)

4.3.8 Total Number of Treatments

No total number of treatments made threshold. The closest to threshold was eight (33.3%, n=5).

Frequency of treatments and total number of treatments are discussed further in Chapter 6.

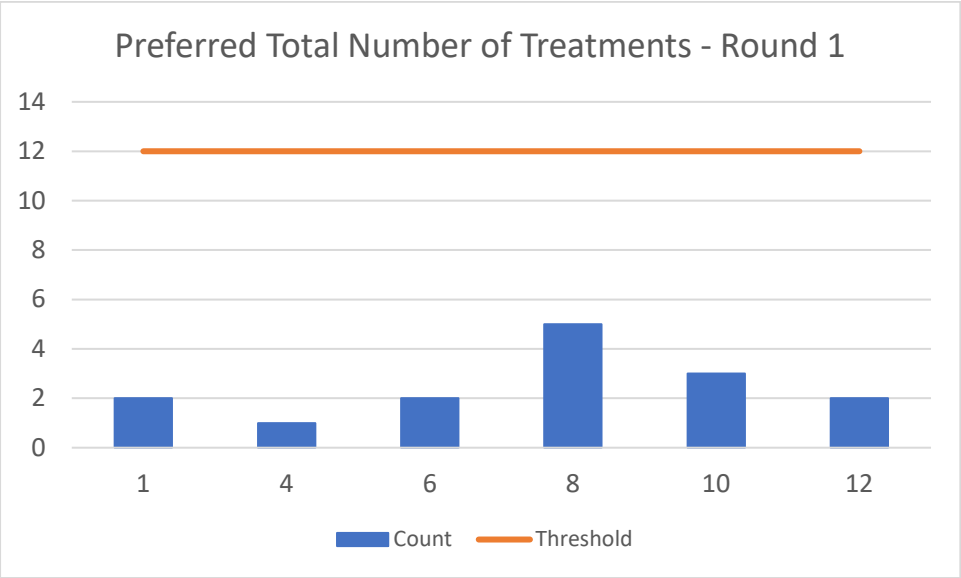


Figure 4.11: Treatment - Preferred Total Number of Treatments. The figure shows the count of participants who nominated a set number of total treatments. (Threshold =80%, or n=12)

Chapter 5: Delphi Round 2 – Results, Discussion

The complete results from Round 2 can be found in appendix D. This Chapter discusses the results from Round 2. The full round 2 questionnaire can be found in Appendix B.

Participants completing Round 1 were invited by email to complete Round 2. Participants were emailed an invitation with a hyperlink to the online survey (see appendix O). Of the original number of Round 1 questions, only 18 remained and which were supplemented by additional questions identified from the Round 1 results (and as discussed in Chapter 4). The results of the second and final Delphi survey round (Round 2) are presented below along with discussion.

5.1 Zangfu Clinically Relevant to a Diagnosis of Stress

The only Zangfu to achieve the consensus threshold of 80% was the Liver (93.3%, n=14). Kidney (66.6%, n=10) and Gallbladder (66.6%, n=10) were both rated lower than the consensus threshold.

Traditionally in CM the Liver has the function of ensuring the smooth flow of qi (Maciocia, 2005). This is seen as being not only important on a physical level, but also psychologically – the smooth flow of qi is also required to maintain a balanced emotional state (Rossi, 2007). Physically, Liver qi stasis manifests as frequent sighing, nausea, or abdominal distension, while emotionally it may be indicated by depression, irritability or moodiness (Maciocia, 2005); and these symptoms can be associated with stress from a biomedical point of view. Stress is believed to impair the functioning of the Liver (Chen, 2004) and so this may cause something of a feedback loop – the Liver is unable to ensure the flow of qi, leading to qi stagnation, which in turn disrupts the emotional balance, leading to further stress.

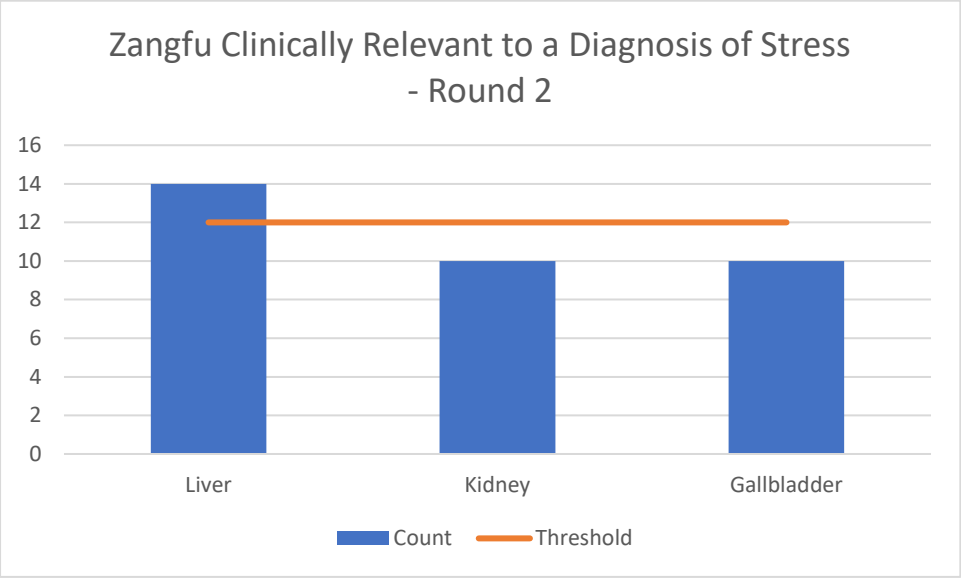


Figure 5.1: Diagnosis - Zangfu Clinically Relevant to a Diagnosis of Stress. The figure shows the count of participants who rated the Zangfu as four or five out of five on a Likert Scale. (Consensus =80%, or n=12)

5.2 The Heart Zang

When made aware that the Heart was the most popular zangfu that did not make threshold, 53.3% (n=8) of participants said that this did make them reconsider their response to Round 1.

When made aware that in Zheng et al (2017) the most common zangfu involved in stress diagnoses according to self-reported patient symptoms was the Heart, 46.6% (n=7) of participants said that it did change their opinion about the Heart in a diagnosis of stress.

Subsequently, 100% (n=15) of participants rated the Heart as relevant to a diagnosis of stress.

The Heart is often considered one of the most important zangfu when discussing emotional or psychological states, due to its function of housing the Shen (sometimes translated as “soul” or “mind”). The Shen harmonises the emotions and governs consciousness and perception (Rossi, 2007), and people who are suffering from altered psychological states such as mania are often diagnosed as having a disturbed Shen (Maciocia, 2005). Heart zang symptoms which may be associated with stress include palpitations, timidity, anxiety, insomnia or poor memory (Chen, 2004; Rossi, 2007).

The high rating of the Heart in the Delphi Round 2 may indicate two things. One is that the respondents may agree, on reflection, that the Heart is highly relevant to a diagnosis of stress, if it has been brought to their attention in some way. The second is that the respondents may accord high importance to evidence-based practice. That is, when made aware of academic literature showing evidence that the Heart zang is relevant, respondents are more likely to concur with the literature and rate the Heart accordingly. It is worth noting that the nature of the Delphi process, specifically giving feedback between rounds, has been shown to influence opinions of the participants (Barrios et al., 2021; Foth et al., 2016) and therefore the inclusion of information from Zheng et al. (2017) cannot be ruled out as an influence (see also subheading 6.4).

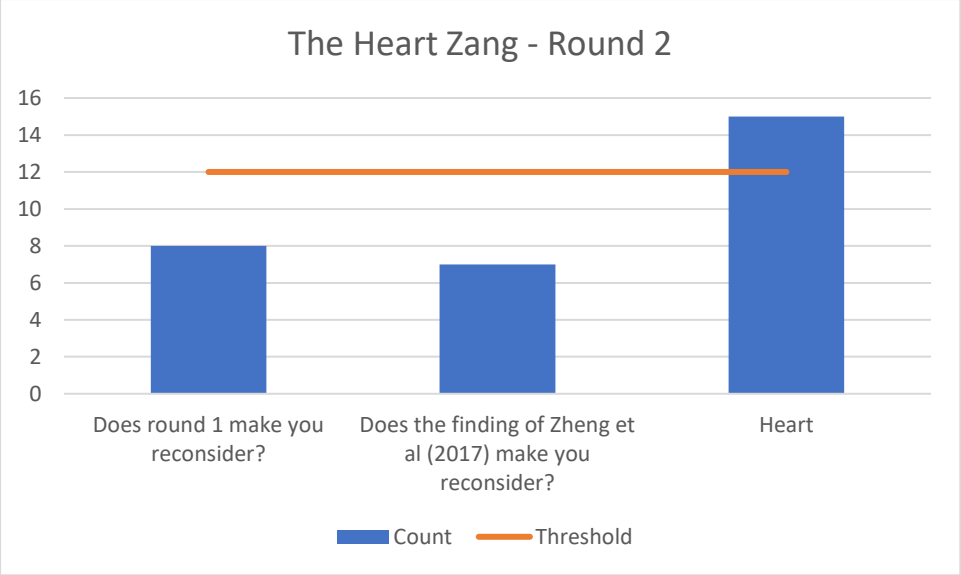


Figure 5.2: Diagnosis – The Heart zang. The figure shows the count of participants who chose "yes" to questions regarding their changed opinion of the Heart, and the count of participants rated the Heart as four or five out of five on a Likert Scale. (Consensus =80%, or n=12)

5.3 Zangfu Disharmony/Mutual Insult

When presented with a single choice of syndrome in round 2, 93.3% (n=14) of participants rated Zangfu disharmony/mutual insult as relevant to a diagnosis of stress.

The syndrome of zangfu disharmony refers to the inter-organ relationships that are foundational for good health according to CM. Each zangfu has interdependent actions, functions and processes that are woven together in particular symbiotic activities between zangfu.

The wuxing are five elements (or phases) according to Chinese philosophy: fire, earth, metal, water and wood. Each element is associated with concordances found in the world, such as colours, flavours, compass directions and so on. Each zangfu is related to one of the five elements. (Please refer to Table 5.1)

Table 5.1: The zangfu and their associated elements.

Zangfu	Element
Heart, Small Intestine, Pericardium	Fire
Spleen, Stomach	Earth
Lung, Large Intestine	Metal
Kidney, Bladder	Water
Liver, Gallbladder	Wood

The interactions between the elements are determined by different cycles, known as the Sheng and Ke cycles. The Sheng cycle is one of creation and generation, while the Ke cycle is one of controlling. The two cycles are complimentary of one another, so that the generation and controlling maintains a balance between the elements.

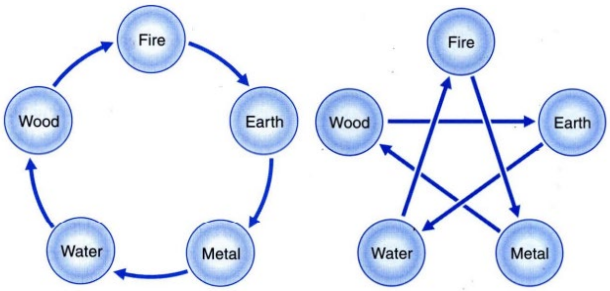


Figure 5.3: The Sheng and Ke Cycles. Reproduced from (Maciocia, 2005)

As the zangfu are assigned each to an element, the Sheng and Ke cycles also apply to the relationships between the zangfu in accordance with the wuxing. In order to have optimal health, the zangfu self-regulate a homeostatic balance between Sheng and Ke cycles. The syndrome of zangfu disharmony or mutual insult indicates that the zangfu relationships are not functioning normally.

5.4 Symptoms Clinically Relevant to a Diagnosis of Stress from (Zheng et al 2017)

All symptoms from (Zheng et al 2017) that featured in Round 2 made the consensus threshold. Highest rated were “Anxious or racing thoughts” (100%, n=15) and “Constant worrying” (100%, n=15). “Irritability or short temper” (93.3%, n=14), “Agitation or inability to relax” (93.3%, n=14) and “Insomnia or other sleep disturbances” (93.3%, n=14) were also rated very highly.

The high consensus rating of the symptoms from (Zheng et al., 2017) may indicate that the participants accept the validity of the questionnaire. That is, expert opinion agrees that the symptoms featured in the questionnaire were, indeed, indicative of stress.

Of the five symptoms to make consensus, three of those are associated with the Heart: “Anxious or racing thoughts”, “Constant worrying” and “Insomnia or other sleep disturbances”. This may indicate that expert consensus also validates, to a degree, the findings of the article, namely that the Heart zang is highly relevant to a diagnosis of stress.

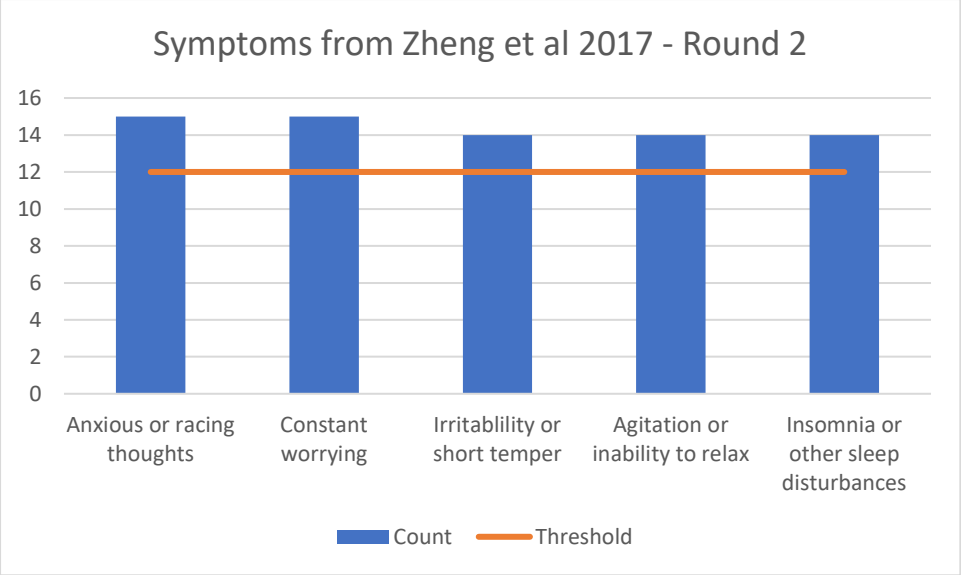


Figure 5.4: Diagnosis - Symptoms Clinically Relevant to a Diagnosis of Stress from Zheng et al (2017). The figure shows the count of participants who rated the symptom as four or five out of five on a Likert Scale. (Consensus =80%, or n=12)

5.5 Symptoms – Sex and Gender

When queried about whether they had considered the sex or gender of the patient when answering previous questions about symptoms, 40% (n=60) of participants had considered sex, while 33.3% (n=5) had considered gender.

Subsequently, when asked if they would expect to see different symptoms for stress presenting in different sexes or genders, 80% (n=12) of participants indicated they would expect differences between sexes, while 66.6% (n=9) of participants indicated they would expect differences between genders.

CM has a long history of gynaecological medical writings, with writings from over 2000 years ago detailing specific issues relating to female anatomy, diagnosis, fertility and gynaecology (West, 2002). The treatment of female infertility and using acupuncture with assisted reproductive technological advancements have been frequently discussed in modern texts and literature in recent years (Bovey et al., 2010; Cochrane et al., 2016; Li et al., 2020; Lyttleton, 2004). Therefore, it is not surprising that experts agree that symptoms would be different between sexes.

It is also worth noting that the Round 1 Delphi process questionnaire did feature specific gynaecological symptoms such as dysmenorrhoea and irregular menstruation (full details of the questionnaire can be found in appendix A). This makes it somewhat more surprising that over half of the expert panel had not considered sex or gender when answering symptom-related questions.

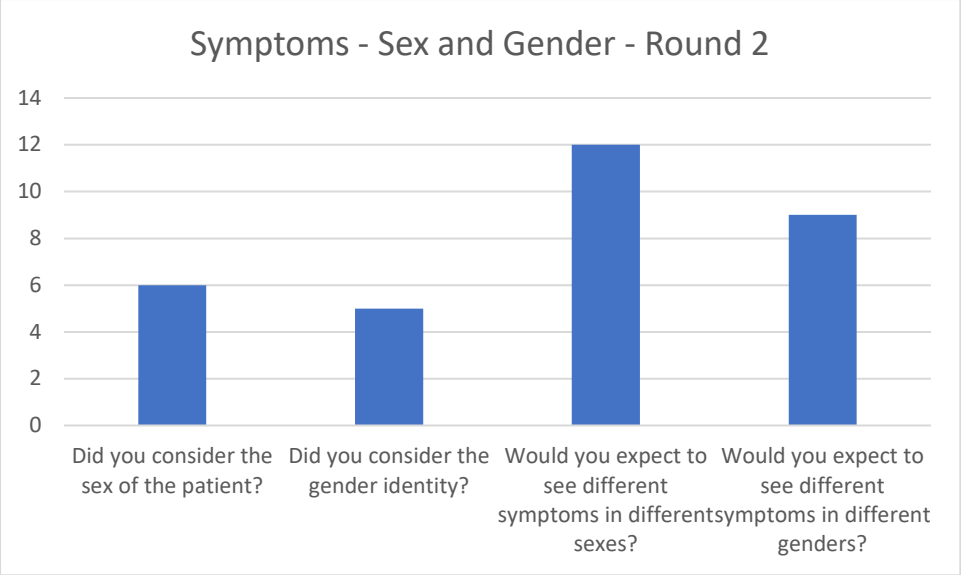


Figure 5.5: Symptoms – Sex and Gender. The figure shows the count of participants who chose "yes" to questions regarding their consideration of, and expectations for, symptoms according to sex and gender.

5.6 Awareness of Stress-Based Questionnaires

Most participants were previously aware of both the PSS (80%, n=12) and the STAI (80%, n=12). Fewer participants were aware of the MYMOP (60%, n=8) and LISS (13.3%, n=2) questionnaires.

The PSS and the STAI are both well known within the stress research community and are popular outcome measures for stress-related investigations (Grös et al., 2007; Schmidt et al., 2020). This shows that the responses from the expert panel were as expected. The LISS is not as well known, particularly in the English-speaking research community, as it was developed in Brazil and originally written in Portuguese (Lipp, 2000). For this reason, the participants' responses were also in line with expectations.

The MYMOP questionnaire is a patient-reported health status instrument that can be applied to any symptom and can be used as an outcome measure for almost any symptom (Paterson, 1996). For this reason, a higher awareness of the MYMOP questionnaire was expected, simply due to it's broad applicability, rather than being explicitly stress-based.

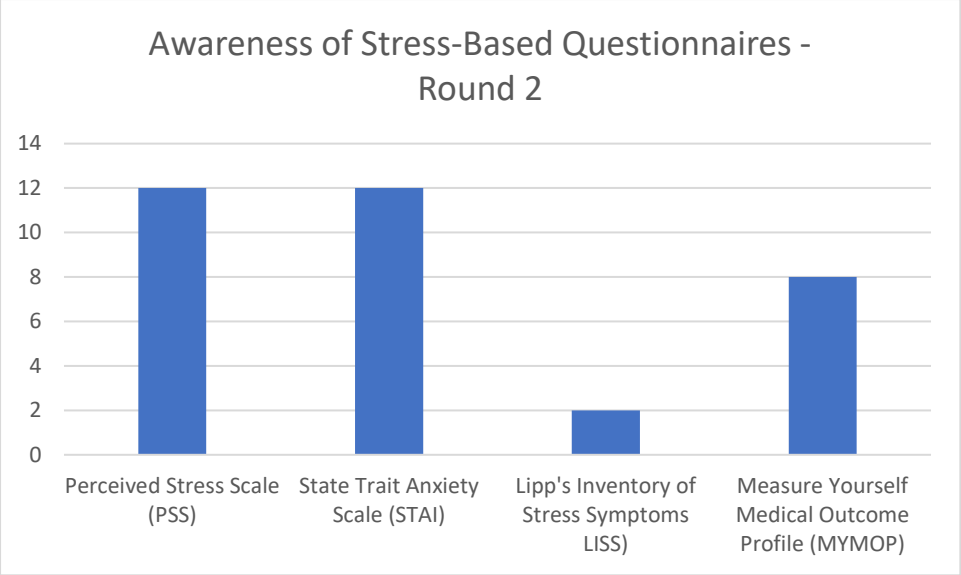


Figure 5.6: Awareness of Stress-Based Questionnaires. The figure shows the count of participants who chose "yes" to questions about their awareness of stress-based questionnaires.

5.7 Symptoms Clinically Relevant to a Diagnosis of Stress from the PSS Questionnaire

All symptoms from the PSS questionnaire made the consensus threshold. "Feeling unable to cope with all the things you must do" (100%, n=15) and "Feeling unable to control irritations in life" (100%, n=15) were the highest rated, followed closely by "Feeling unable to control important things in life" (93.3%, n=14) and "Feeling unable to deal well with life hassles" (93.3%, n=14).

The high rating given to the PSS symptoms implies that the PSS is considered valid by a CM expert panel. Further, this also suggests that CM experts can recognise and appreciate terminology used in questionnaires as it applies to stress, even seen through a western biomedical paradigm and removed from CM jargon. This will be discussed further in Chapter 6.

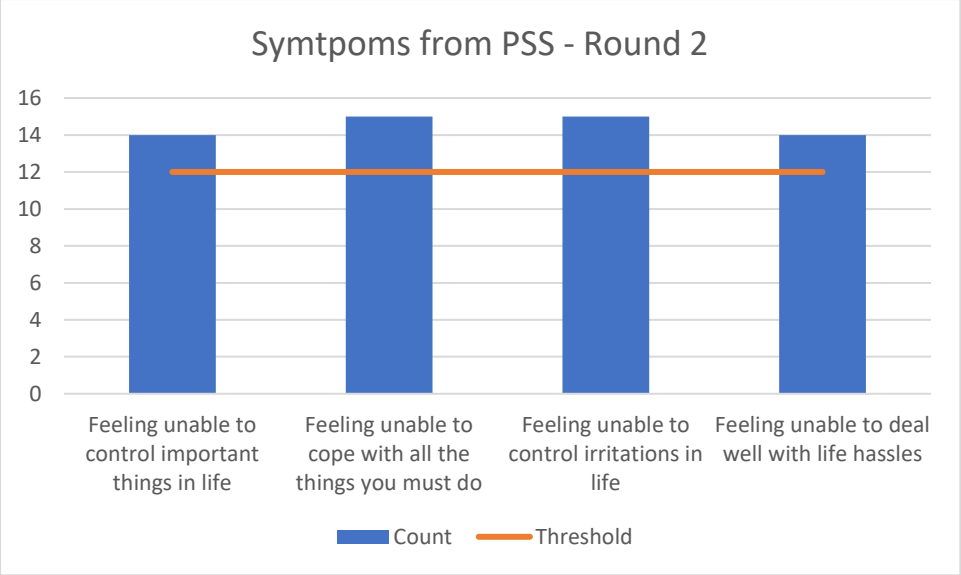


Figure 5.7: Diagnosis - Symptoms Clinically Relevant to a Diagnosis of Stress from the PSS questionnaire. The figure shows the count of participants who rated the symptom as four or five out of five on a Likert Scale. (Consensus =80%, or n=12)

5.8 Use of questionnaires in Practice

Participants were made aware of the source of the PSS symptoms, and that they had all made threshold (see Chapter 4: Round 1 results and discussion). When asked if this made them reconsider incorporating the PSS into their practice, 66.6% (n=10) of participants chose “yes”.

When asked if they were made aware of a Chinese Medicine based stress questionnaire, would they consider using it in practice, 73.3% (n=11) of participants chose “yes”. Further to this, 66.6% (n=10) of participants indicated they would use it to assist in diagnosis, while 73.3% (n=11) of participants indicated they would use a Chinese Medicine based stress questionnaire as an outcome measure.

s. This will be discussed further in Chapter 6.

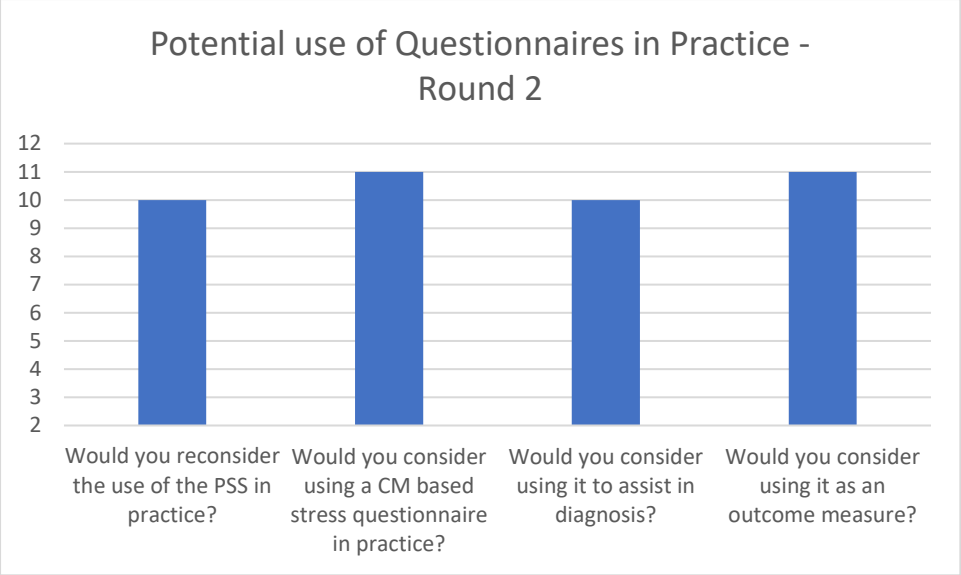


Figure 5.8: Potential Use of Questionnaires in Practice. The figure shows the count of participants who chose "yes" to questions about their potential use of stress-based questionnaires in practice.

5.9 Pulse Qualities

When given a single open-ended question to nominate pulse qualities clinically relevant to a diagnosis of stress, the highest nominated pulse quality was wiry (73.3%, n=11). No other pulse quality was nominated as frequently, with the next closest being weak (26.6%, n=4) and choppy (26.6%, n=4).

The pulse is often considered to be fundamental to CM diagnosis and has been discussed as far back as the classic CM text the *Nan Jing* (Classic of Difficulties) in the first or second century (Flaws, 2004). A wiry pulse is classically associated with Liver qi stasis (Walsh & King, 2007) and this may go some way to explaining the connection of Liver qi stasis and the western biomedical concept of stress, particularly as the wiry pulse commonly signifies hypertension (Walsh & King, 2007). This will be further discussed in Chapter 6.

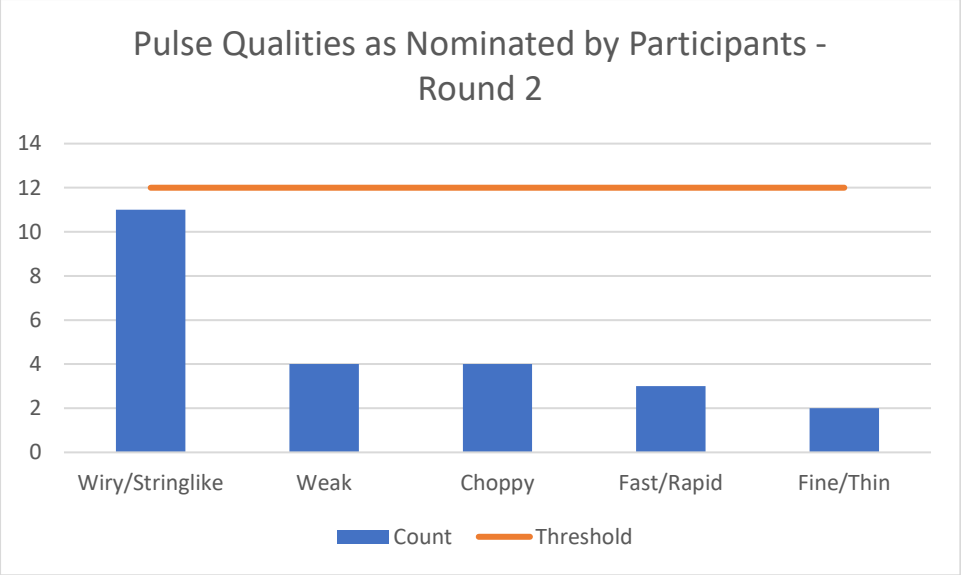


Figure 5.9: Pulse Qualities as Nominated by Participants. The figure shows the count of pulse qualities that were nominated by participants when presented with a single, open-ended question.

5.10 Acupuncture Points Clinically Relevant to a Treatment of Stress

Yin Tang (93.3%, n=14) and Pericardium 6 (93.3%, n=14) were the two highest rated acupuncture points. Also making the consensus threshold were Liver 3 (Taichong) (86.6%, n=13) and Heart 7 (Shenmen) (80, n=12).

According to CM texts:

- Liver 3 is the “yuan” (source) point for the Liver channel and is considered the major point to spread the Liver qi and relieve qi stagnation;
- Pericardium 6 regulates qi in the chest, regulates the Heart and calms the Shen;
- Heart 7 is the yuan point for the Heart and calms the Shen;
- Yin Tang is an extra point not associated with any zangfu or channel; it calms the Shen (Deadman & Al-Khafaji, 2001; Maciocia, 2005, 2007; Rossi, 2007).

From this group of acupuncture points that achieved consensus it can be seen that there is an emphasis firstly on Shen-calming points (a function associated with Heart) and secondly qi-regulating points (a function of the Liver). This could be considered somewhat unexpected when it is considered that in the Delphi Round 1 only Liver and Qi stasis made threshold. This will be discussed further in Chapter 6.

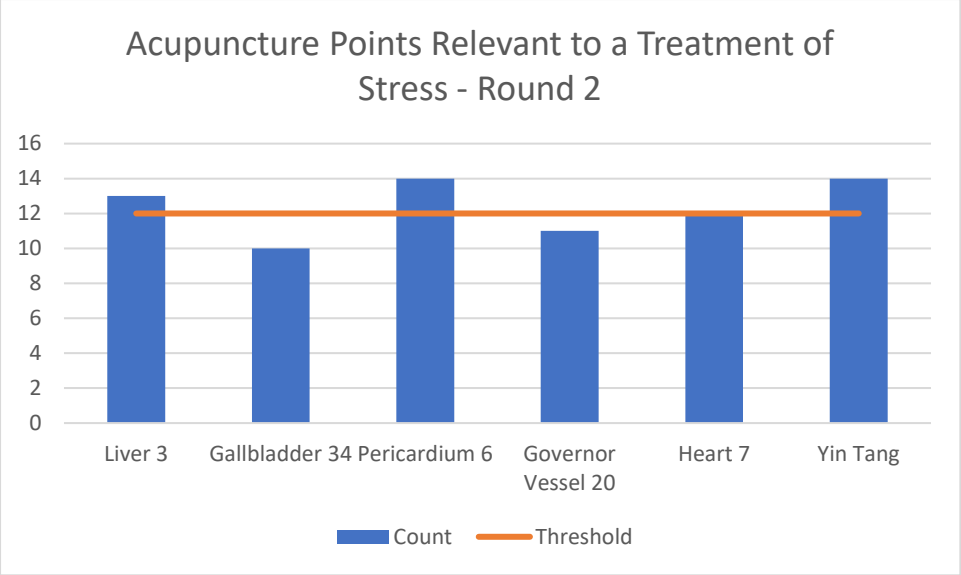


Figure 5.10: Treatment – Acupuncture Points Clinically Relevant to a Treatment of Stress. The figure shows the count of participants who rated the acupuncture point as four or five out of five on a Likert Scale. (Consensus =80%, or n=12)

Chapter 6: Discussion and Future Direction

Chapter 6 features a general discussion about the results of the Delphi process and what they might infer, including how the clinical trial protocol may be reviewed and modified and possible future research directions.

6.1 Heart vs Liver Pathologies

6.1.1 From the Literature Review

The literature review carried out for this project attempted to identify Chinese medicine pattern diagnoses featured in clinical trials, where reported. Only two trials reported a diagnosis (Huang et al., 2011; W. Huang et al., 2012), although it is possible that these were two reported articles from one study (see Chapter 2: Literature Review). The three diagnoses reported were:

- Liver qi stasis with Fire
- Liver and Spleen Disharmony
- Gallbladder qi deficiency

In addition to this, one study used a single acupuncture point (Heart 7) based on the actions of calming the Spirit and pacify the Heart (Chan et al., 2002). From this is inferred a possible diagnosis of a disturbed Shen – commonly resulting in insomnia or anxiety (see Chapter 5.2: The Heart Zang).

The lack of diagnoses in the literature may reflect one of the difficulties in carrying out acupuncture research, namely, that in order to be methodologically sound when using the standard RCT design, all participants should receive the same intervention, meaning all participants should be needled at the same acupuncture points. However, from a CM perspective applying a single acupuncture point prescription to multiple patients who, while all identifying as stressed, show different signs and symptoms, would be considered sub-optimal treatment. Research which fails to consider the validating construct of acupuncture may fail to identify a statistically significant positive effects on people's perception of stress. That is, the increase chances of making a Type II error. Further, given the complex nature of stress as a construct, this requires further differentiation and reporting in the literature if it is to be firstly, adequately assessed with acupuncture; and secondly findings of research to have relevancy to the clinical practice of acupuncture. In effect, the PSS14, as an example, may not be sufficient to the task of identifying the construct of stress in a Chinese medicine context. This means further Chinese medicine-based differentiation measures should be developed to facilitate construct and context relevant investigations.

What can be taken from the research literature, while based on meagre data, reflects general CM diagnosis for stress: Liver qi stasis, Zangfu disharmony, and Gallbladder and (to a lesser extent) Heart pathologies.

6.1.2 From the Delphi Process

The Liver and Heart zang both made the consensus threshold of the Delphi process. Qi stasis and zangfu mutual disharmony also both made consensus. From this, although the two were not explicitly linked we may infer that, according to the expert panel, Liver qi stasis is the most relevant diagnosis of stress, so this agrees with the literature (Huang et al., 2011; W. Huang et al., 2012). Zangfu mutual disharmony may be indicative of Liver and Spleen disharmony (See Chapter 5.3: Zangfu Disharmony/Mutual Insult) and this is also reflected in the literature (Huang et al., 2011; W. Huang et al., 2012). The Heart zang made the consensus threshold as well, and can be found in the literature data (Chan et al., 2002).

Symptoms that made the consensus threshold were also associated either with Heart (anxious or racing thoughts, constant worrying and insomnia or other sleep disturbances) or Liver pathologies (irritability or short temper and agitation or inability to relax). This reinforces the findings of the Delphi process and literature review in terms of diagnosis.

6.1.3 Diagnoses From the Literature Review and CM Texts by Acupuncture Point Function

Due to the lack of available data regarding diagnosis in the literature, further analysis may be required. By examining the functions of the acupuncture points found to be most popular in both CM texts and the literature review (see Chapter 2.3.1.10: Acupuncture Points Used) an attempt can be made to “reverse engineer” a likely set of diagnoses. That is, if the functions of the acupuncture points are collated, the most common functions may indicate the intended diagnoses to be treated.

The most popular acupuncture points combined from the literature review and CM texts with their functions pertinent to this review can be found in table 6.1.

Table 6.1: Acupuncture point functions relative to stress. Acupuncture point functions are from (Deadman & Al-Khafaji, 2001; Maciocia, 2005, 2007; Rossi, 2007)

Acupuncture Point	Function Relative to Stress
Liver 3	Spread the Liver qi Regulate qi
Large Intestine 4	Regulate qi (especially combined with Liver 3)
Pericardium 6	Regulate qi Regulate the Heart Calm the Shen
Spleen 6	Calm the Shen Regulate qi
Stomach 36	Tonify qi Regulate qi
Yin Tang	Calm the Shen

From this it can be seen that the predominant functions of the acupuncture points pertain to the Liver, particularly to qi stasis, while also addressing the Heart and it's function of housing the Shen. This implies that, while not explicitly diagnosing participant's syndromes, the researchers were applying acupuncture points to address predominantly Liver pathologies, and to a lesser degree Heart pathologies.

There is also some overlap in acupuncture point selection between the literature and the expert panel, namely that the four acupuncture points determined to be relevant to stress (Yin Tang, Pericardium 6, Liver 3 and Heart 7) were all within the six most popular acupuncture points in the literature and all of these points have functions associated with Heart and to a lesser extent, Liver pathologies.

6.1.4 Diagnosis and Definition of Stress

A further complicating factor in the diagnosis of stress according to CM is the lack of definitive diagnostic criteria for "stress", either in western medicine (Organisation, 2022) or in CM (Zheng et al., 2014). Researchers must therefore rely on participants' self-reported perception of stress (Schroeder et al., 2017; Zheng et al., 2017), or minimum scores on a measure such as the PSS (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017).

In CM there is a tradition of referring back to the "classics", a series of foundational texts upon which modern CM is built, such as the *Huang Di Nei Jing Su Wen* (The Yellow Emperor's Classic). This assists

practitioners to attempt to ascertain the “original” thoughts about a particular sign or symptom. Unfortunately, the term “stress” is a modern term that has no ready translation in the classics (Zheng et al., 2017), so this strategy cannot be employed.

Overall, this indicates some points for consideration. Firstly, diagnosis of stress in CM is varied, although both the literature review and the expert panel tend towards Liver (particularly Liver qi stasis) and Heart pathologies. This is also echoed in CM texts when discussing the importance of the Liver and Heart in emotional illnesses.

Secondly, questionnaires such as the CM stress-based questionnaire developed by (Zheng et al., 2017) could provide a useful tool for stress-based research in CM, and also in practice for assistance in diagnosis.

Thirdly, so long as the research is based on western biomedical diagnostic terms, the CM diagnosis of those terms when used in research will continue to be problematic.

6.2 Acupuncture Dosage

Acupuncture dosage, in terms of frequency and total number of treatments, is an important aspect of acupuncture research.

6.2.1 Dosage in the Literature Review

Total number of treatments found in the literature varied greatly, from one treatment (Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001) to 12 (Schroeder et al., 2017). While the studies conducting singular treatments were investigating the use of acupuncture and using real-time measurements such as salivary cortisol levels (Kwong & Yiu, 2010) and Muscle Sympathetic Nervous Activity (MSNA) (Middlekauff et al., 2002; Middlekauff et al., 2001), thus justifying the use of a single treatment, this low dose of acupuncture adds to the evidence base for acupuncture, for better or worse, whether or not it is representative of acupuncture as it is commonly treated.

Treatment frequency in the literature was less varied, with a majority administering acupuncture treatments weekly (Chan et al., 2002; Huang et al., 2011; W. Huang et al., 2012; Schroeder et al., 2017; Smith et al., 2011).

6.2.2 Dosage in the Delphi Process

Total number of treatments in the Delphi process were also varied, from one to 12. While not making consensus, the most popular total number was eight (n=5).

Treatment frequency was less varied, and while also not quite making consensus, the majority of respondents (n=11) preferred twice-weekly treatments.

6.2.3 Dosage discussion

Acupuncture dosage in the literature is highly variable and poorly reported (White et al., 2008). The Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) were developed as an extension to the Consolidated Standards of Reporting Trials (CONSORT) to assist the development and standardisation of reporting acupuncture trials (MacPherson et al., 2010). It replaces Item four of the CONSORT statement which relates to the intervention.

The six items in STRICTA are:

1. Acupuncture rationale
2. Details of needling
3. Treatment regimen
4. Other components of treatment
5. Practitioner background
6. Control or comparator interventions (MacPherson et al., 2010).

While the STRICTA items aid transparency and accuracy in reporting of trials, the adherence to the STRICTA guidelines is not universal. In the literature review for this project the STRICTA reporting varied from three (W. Huang et al., 2012) to 14 (Smith et al., 2011) out of a possible 17 items.

Regardless of reporting, there is still no indication as to what an adequate dose of acupuncture actually *is* (Bauer et al., 2020), making any treatment protocol highly subjective in nature. Recently there have been some attempts to answer this question, with mixed success. Harris et al. (2005) found that three treatments per week had a greater effect than one. Kim et al. (2018) found that two or three treatments per week were optimal, but that increasing frequency higher than that did not deliver better results. Some researchers have attempted to define “high” or “low” doses and found correlations between better outcomes and higher dosage, but these definitions are essentially arbitrary, generally based on individual researchers’ experience (Lin et al., 2016; Schwehr et al., 2018; Sun et al., 2019).

It is inconceivable that this would happen in many health-related schools of research. For example, no pharmaceutical company would proceed with clinical trials of a new chemical compound without having a clear and concise definition of what an adequate, effective or sufficient dose is required. For acupuncture, as a whole, to proceed blindly as has been done thus far is unreasonable. This project has discussed dosage only in terms of treatment numbers and frequency, but dosage as a whole may include number of needles, time of needle retention, method of stimulation, depth of needling (as examples). The investigation into acupuncture dosage is an urgent matter, but is out of the scope of this master’s project. There is a lack of agreement in the clinical research literature

about the most appropriate acupuncture treatment frequency for stress, and experts did not reach a consensus on the most appropriate treatment frequency. In the absence of such agreement, the trial protocol (i.e., comparing high frequency with low frequency) would provide further information about the most effective and feasible treatment approach.

6.3 Questionnaires

According to the Delphi process the use of questionnaires by clinicians was minimal, and awareness of questionnaires was also generally low. However, the expert panel showed that they could recognise questionnaire accuracy, as indicated by the high consensus rate to stress-related symptoms sourced from questionnaires in the Delphi process. This recognition occurred across medical paradigms, as experts rated symptoms from both western biomedical and CM questionnaires highly. It is worth noting that not all questionnaires are readily available nor free to use, and this could reduce both awareness and use of questionnaires in practice.

The general acceptance of future CM based questionnaires for stress by the expert panel shows that there is scope for the development of questionnaires for use in practice, both as an assistance for diagnosis such as Zheng et al. (2017) and also as an outcome measure to gauge severity of symptoms and/or treatment progression, such as the PSS.

6.4 Confounding Elements & Limitations

The obvious limitations to this study are particularly those of the Delphi process relating to feedback and question format influencing consensus and the size and makeup of the expert panel.

While feedback is an important aspect of the Delphi process, it has been shown that the feedback itself can influence participants' responses, both negatively and positively (Barrios et al., 2021), to some degree. While consensus is important (in fact it is the desired outcome), the degree in which the participants are influenced by feedback and format of questioning can't be overlooked. For example, the questions in the Delphi process round 2 regarding acupuncture point selection were asked close to the end of the survey, after questions about involvement of the Heart zang in stress-based pathologies. This may have influenced the respondent's choice of acupuncture points. Furthermore, wording of questions included in the survey such as those regarding the Heart zang may have influenced the expert's responses.

Theoretically any bias or influence could be diminished by increasing the size of the expert panel larger, however this project had to be pragmatic in panel size in order to complete the project within the allowed timeframe of the candidature (data collection took time even with a comparatively small panel size), and also allows for manual analysis of the data. Future Delphi processes could include larger panel sizes – this would also help ensure heterogeneity of the experts' background

and experience, although the use of several “OR” inclusion criteria allowed for the panel of this Delphi process to include quite diverse backgrounds and experience.

Furthermore, while the inclusion and exclusion criteria used was intended to avoid homogeneity, there was no information taken on where the experts’ foundational location of their CM training and education. Since the initial point of contacting potential participants was through professional networks of the researchers, there may be a majority of experts with similar training and educational backgrounds, learning from similar schools of CM theory and therefore having similar approaches to the diagnosis and treatment of stress. This could be avoided by recruiting experts on an intentionally international, multi-school basis.

The cultural or socio-economic aspects to stress were also not addressed in this study. It may be possible that signs and symptoms associated with stress may be different among cultures or across socio-economic backgrounds. For example, perhaps a Korean patient may report different symptoms to one from Australia, and likewise perhaps a patient who can afford access to acupuncture is likely to report milder signs and symptoms of stress than those who cannot, or vice versa.

Based on the Delphi feedback with consideration to the protocol, the calculation of the sample size would be amended to account for a different set of assumptions, including accounting for larger attrition rates given the burden of people committing to a clinical trial who are already perceived themselves stressed. The estimated sample size calculation is based on a 0.9 probability to detect a difference between the groups and to statistically reject the null hypothesis on a basis of $P < 0.05$. To detect a moderate clinical stress response difference of 0.5 standard deviations between dosage groups after the intervention (or a 20% difference in scores as measured by the PSS14 and on the basis of work undertaken by Schroeder et al., 2017), a total of 172 participants (or 86 per group) will need to complete the trial. Allowing for 15% withdrawal rate we will need to recruit 202 participants to assess the dosage according to the primary outcome.

In addition, the literature review used to inform the Delphi process was limited to studies published in English. There may be a wealth of information on the use of acupuncture to reduce stress in other languages, but that is outside the remit of this project.

6.5 Future Direction

The clinical trial protocol as developed for this project is valid, with only the minor modification of acupuncture points to be used, further to amendment to the sample size (See Appendix P). Previous trials using acupuncture to reduce stress have shown some promise, but more research is needed to look at the construct of stress and explore socio-demographic and cultural profiles of participants

and outcomes from treatments. This would involve larger (Stage III) multi-centre studies developed from the results of the current proposed study presented in this thesis. This includes calculating an effect size from the current proposed study along with future study hypotheses. Stress has been linked to multiple poorer health outcomes, acupuncture could become a useful tool in any stress management strategy.

The current study protocol is only the first step to a larger series of studies to investigate acupuncture, stress, and treatment dosage. There are some limitations in the current study design which can be addressed in future studies. This includes practitioner and patient concealment to address bias. For example, practitioner concealment can be addressed in larger studies with multiple practitioners who are blinded to the treatment frequency protocol by not always treating the same participant as well as being blinded to the outcome measure scores. Participant concealment can be partially addressed in a larger study by having a non-active treatment incorporated into the low-treatment frequency group. This would mean all participants in both groups are having the same frequency of clinical contacts, but the low frequency group receives a difference in dosage by incorporating a non-active treatment mixed along with the active treatments as described in the protocol.

While the focus of clinical trials has previously been on the efficacy of acupuncture in the reduction of stress, the trial protocol developed for this project also compares different acupuncture dosages (in the form of treatment frequency). As shown in both the literature review and the Delphi process contained in this thesis, there is very little consensus on how an effective 'dose' of acupuncture is defined. Until more research in this field is undertaken, any conclusions made about the efficacy of acupuncture could be considered invalid. Further researchers must accurately define acupuncture dosage in multiple forms, including treatment frequency, total number of treatments, number of acupuncture points used and needling depth. Once this is determined, a revision of previous research conclusions will be needed in order to reassess both the validity of previous outcomes and, potentially, the evidence base for acupuncture as it stands. This is a large area of potential future acupuncture research which will require a significant amount of effort and resources from those who wish to pursue it.

6.6 Conclusion

While the initial focus of this project was unable to be achieved due to the impact of COVID-19 (See Chapter 1.4), there are still several conclusions to be drawn.

The use of acupuncture to reduce stress may be effective, but more research is needed. Stress has become so common in today's society that is considered ubiquitous, yet it has been shown to cause

multiple negative health outcomes (mental, cognitive, psychosocial and physical inclusive) and is therefore a valid focal point of acupuncture research.

There is some consensus amongst experts and scientific literature about the diagnosis of stress according to CM principles, namely that it involves Heart and Liver pathologies. However, this may be somewhat influenced by the difficulty in translating of terms from ancient Chinese to modern English, particularly when considering 'stress' is a modern concept.

Acupuncture research and treatment lacks consensus on appropriate dosage of acupuncture and this also requires further research. This thesis, through both a literature review and Delphi process, has demonstrated the design and modification of a clinical trial protocol to assess efficacy of acupuncture to reduce stress, and to also compare the effects of two different acupuncture frequency dosages.

Appendices

Appendix A: Literature Review: Summary of RCTs and UCTs Relating to Acupuncture and Stress

Study Type & Participant Characteristics

First Author (Year)	Study Design	Country of Origin	Sample Size/n (Attrition Rate/ Completed)	Demographic, Mean Age (SE)	Intervention/Control Group	Control Used	Key
Huang, W. (2011)	RCT Pilot	United Kingdom	149/n=18 (0/18)	Thames Valley University Staff, A:46.0 (3.8) B:45.3 (4.8) C:35.5 (4.9)	A:TCA (n=6), B:ATT (n=6), C:CT (n=6)	Attention Only & Waiting List	TCA: Traditional Chinese Acupuncture, ATT: Attention Only Group, CT: Control Group
Huang, W. (2012)	RCT Pilot	United Kingdom	n=18 (1/17)	Thames Valley University Staff, A:46.0 (3.8) B:45.3 (4.8) C:35.5 (4.9)	A:TCA (n=6), B:ATT (n=6), C:CG (n=6)	Attention Only & Waiting List	TAC: True Acupuncture Group, ATT: Attention Only Group, CG: Control Group
Kwong, E. (2010)	RCT	Hong Kong	n=18 (0/18)	Recruited patients from the Voice Research Laboratory at the University of Hong Kong, A:33.56 (10.08) B:31.78 (4.87)	A:EG (n=9), B:PG (n=9)	Blunt Needle Sham at same points.	EG: Experimental Group, PG: Placebo Group
Middlekauff, H.R. (2001)	RCT	USA	n=19 (0/19), some assigned 2 protocols	Not Reported, 40+/-3.5	A:RA (n=12), B:NA(n=11), C:CA(n=7)	Non-acupoint (ant.Deltoid Muscle) acupuncture/ Non-needle acupuncture (guide tube tap)	RA:Real Acupuncture, NA: Non-Acupoint Acupuncture, CA: Control Acupuncture
Middlekauff, H.R. (2002)	RCT	USA	15/n=30 (0/30), randomly assigned into 2 of 3 protocols	Not reported, 43+/-11	A: RA (n=10), B:NA (n=10), C:CA (n=10)	Non-acupoint (ant.Deltoid Muscle) acupuncture/ Non-needle acupuncture (guide tube tap)	RA:Real Acupuncture, NA: Non-Acupoint Acupuncture, CA: Control Acupuncture

Schroeder, S. (2017)	RCT	USA	n=111 (49/62)	College students, faculty, and staff at a large public university in the south-western United States	A:VA (n=36), B:SA (n=26)	Acupuncture at non-stress related points	VA:Verum Acupuncture, SA:Sham Acupuncture
First Author (Year)	**Study Design**	**Country of Origin**	**Sample Size/n (Attrition Rate: Completed)**	**Demographic, Mean Age (SE)**	**Intervention/Control Group**	**Control Used**	**Key**
Smith, C.A. (2011)	RCT	Australia	124/n=32 (2/30)	Not reported, A:35.1 (4.2) B:34.1 (5.2)	A: TG (n=16), CG (n=14)	Waiting List	TG: Treatment Group, CG:Control Group
Zuppa, C. (2015)	RCT	Brazil	n=48 (0/48)	Elderly, A:67.13 (4.9) B:65.75 (3.8)	A:TA (n=24), B:SA (n=24)	Non-acupoint: Points far from true acupuncture points	TA: True Acupuncture, SA: Sham Acupuncture
Chan, J. (2002)	Uncontrolled Pilot Study	United Kingdom	n=17 (0/17)	Staff in hospice caring for the terminally ill, 43 (Range 24-58)	1 group (n=17)	n/a	
de Oliveira, C.C.C. (2017)	Uncontrolled Clinical Trial	Brazil	n=19 (0/19)	Professionals working with maltreated children in a group shelter in São Paulo, Brazil, 40.6 (8.59)	1 group (n=19)	n/a	
Pavao, T.S. (2010)	Uncontrolled Clinical Trial	Brazil	n=24 (0/24)	Not reported, A:27.6 (Range 23-38) B:65.6 (Range 60-81)	Young:Old 12:12	n/a	

Outcomes

First Author (Year)	Outcome Measures	Pre/Post Treatment Difference	Intergroup Difference	Key
Huang, W. (2011)	PSS-14, MYMOP	Mean (SE), *=p<0.05: PSS-14: A:28.67 (1.80)/24.67 (3.04), B:32.50 (2.28)/26.33 (1.69), C: 35.17 (1.85)/33.83 (2.57), MYMOP: A: 3.71 (0.29)/2.00 (0.21)*, B:4.54 (0.22)/3.25 (0.25)*, C: 4.42 (0.35)/3.96 (0.30)	PSS-14: A vs B: z=0.645 p=>0.05, A vs C: z=0.723 p=>0.05, B vs C: z=1.286 p=>0.05, MYMOP: A vs B: z=2.18 p<0.05, B vs C: z=2.10 p=<0.05, A vs B: z=0.24 p=>0.05	PSS-14: Perceived Stress Scale 14, MYMOP: Measure Yourself Medical Outcome Profile
Huang, W. (2012)	PSS-14, Salivary Cortisol	Mean (SE), Waking/30 Min After/3 Hrs After/12 Hrs After, TCA Pre: 12.35 (2.92)/19.3 (2.39)/4.19 (1.08)/2.18 (0.51), TCA Week 5: 12.93 (1.93)/18.79 (1.74)/6.44 (1.58)/1.26 (0.25), ATT Pre: 21.99 (12.42)/19.88 (10.37)/4.71 (0.71)/2.44 (1.00), ATT Week 5: 7.75 (1.53)/14.30 (3.96)/2.36 (0.58)/1.85 (0.44), CG Pre:7.75 (1.02)/11.51 (2.48)/3.96 (1.08)/2.36 (0.95), CG Week 5:10.49 (2.52)/12.23 (3.38)/2.79 (0.90)/1.15 (0.08)	No significant intergroup difference	PSS-14: Perceived Stress Scale 14, TAC: True Acupuncture Group, ATT:Attention Only Group, CG: Control Group
Kwong, E. (2010)	Salivary Cortisol Concentration	Mean (SD) *=p<0.05: Pre/Mid/Post-0/Post-10, A:2.19 (1.92)/1.28 (0.51)*/2.41 (2.09)/2.30 (2.11), B: 2.87 (2.60)/1.72 (1.75)*/1.77 (1.29)/1.80 (1.68)	No significant intergroup difference	
Middlekauff, H.R. (2001)	Muscle Sympathetic Nerve Activity (MSNA), Blood Pressure (BP), Heart Rate (HR)	A: acupuncture at known acupoints significantly attenuates the increase in MAP during mental stress (overall time effect, p = 0.001). Pointwise comparisons revealed greater attenuation of MAP at minute 2 (p = 0.01) and minute 3 (p = 0.001) of mental stress. B: acupuncture at nonacupoints significantly attenuates the increase in MAP during mental stress (overall time effect, p= 0.0003)	No significant intergroup difference	
Middlekauff, H.R. (2002)	Muscle Sympathetic Nerve Activity (MSNA), Blood Pressure (BP), Heart Rate (HR)	Mean (SD), *=p<0.05, MSNA A: Min1: –10(54)/ –63(37), Min2: 122 (65)/ –54(34), Min3:447(57)*/ –289(67), Min4:37(85)/–271(85) Overall p=0.03	Pre/Post MSNA, Mean (SEM) at Min 3, *=p<0.05: A:447 (57)*/ –289 (67), B: 215 (95)/0.1 (121), C: 911 (95)/ 857 (70)	
Schroeder, S. (2017)	PSS-14	Mean (SD) *=p<0.05: Pre/Week12/Week24, A: 35.8 (6.4)/19.4 (6.2)*/ 21.4 (8.5)*, B:34.5 (5.5)/20.6 (6.9)*/26.2 (9.1)*	Mean (SD) Week 12, A: 19.4 (6.2), B: 20.6 (6.9), p<0.05	

First Author (Year)	Outcome Measures	Pre/Post Treatment Difference	Intergroup Difference	Key
Smith, C.A. (2011)	State–Trait Anxiety Inventory (STAI), Fertility Problem Inventory (FPI), Infertility Self-Efficacy Scale (ISE)	No significant difference reported	MD, *=p<0.05 STAI: -2.54, ISE: 11.9, FPI: 1:-3.75, 2:-2.50 3:-3.66* 4:-0.26, 5:-1.38*	MD:Mean Difference (TG-CG), FPI: 1:Social Concern, 2: Sexual Concern, 3: Relationship Concern, 4:Rejection of childfree lifestyle, 5: Need for parenthood
Zuppa, C. (2015)	Beck depression inventory (BDI), perceived stress scale (PSS),Pittsburgh sleep quality index (PSQI). (Also Immunophenotyping & Plasma BDNF levels)	No significant difference reported	Acupuncture significantly reduced PSQI scores (−53.23%;p< 0.01). True acupuncture was effective in attenuating stress (−25.46%; p< 0.01) and depression scores (−48.41%; p< 0.01)	
Chan, J. (2002)	Edinburgh Postnatal Depression Scale (EPDS)	Repeated measures analysis of variance (ANOVA) indicated that a significant change had occurred over the course of the study (p=0.001). Using a paired t test for the analysis there was a significant reduction in EPDS scores from baseline to the second time point (p=0.002) and to each subsequent time point (p<0.001)	n/a	
de Oliveira, C.C.C. (2017)	Lipp's inventory of stress symptom scale (LISS)	Mean (SD): Pre:20.6 (8.9), Post: 13.6 (8.2), p=0.0011	n/a	
Pavao, T.S. (2010)	Lipp's Inventory of Stress Symptoms for adults (LISS), State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), (Also T-Cell Proliferation via Blood Samples)	Reduced Stress (p<0.0001), anxiety (p<0.0001), depression (p<0.0001)	n/a	

Acupuncture Protocols

First Author (Year)	No. of Treatments/Frequency	Diagnosis Protocol/Points Used	Chronic/Acute Stress	CONSORT/STRICTA	Comments
Huang, W. (2011)	5/Weekly	TCM Diagnosis/DU20, DU24, EX-HN3, LI4, PC6, ST36, and LR3 Plus According to Diagnosis:LR2, PC5; ST25, RN12; GB34, ST40	Chronic	19/06	A: Significant Improvement, also improvements in other symptoms. B: Significant Improvement. C: No significant.
Huang, W. (2012)	5/Weekly	TCM Diagnosis/DU20, DU24, EX-HN3, LI4, PC6, ST36, and LR3 Plus According to Diagnosis:LR2, PC5; ST25, RN12; GB34, ST40	Chronic	22/03	No significant improvement or intergroup differences, however author notes a general trend of improvement but too low sample size. Suggests salivary cortisol profile is useful as chronic stress objective outcome measure. Does not report on PSS-14 scores with any detail.
Kwong, E. (2010)	1/Singular	Standard Treatment/LI4, LU7, CV23, ST9, KD 6	Chronic	18/13	Significant reduction of salivary cortisol at MID time point (true and sham), which did not sustain.
Middlekauff, H.R. (2001)	1/Singular	Standard Treatment: Right LI4, Right LR3, Left SP6	Acute	16/11	1) acupuncture at acupoints Li4, P6, and Liv3, at nonacupoints, and "no-needle" acupuncture does not modulate resting MSNA or MSNA responses to mental stress in normal humans; 2) acupuncture at acupoints Li4, P6, and Liv3 significantly attenuates the blood pressure response to mental stress; 3) acupuncture at nonacupoints also significantly decreases the blood pressure response to mental stress, although perhaps to a lesser degree 4)microneurography had an "acupuncture-like" effect, because the increase in mean arterial pressure during mental stress before acupuncture was significantly greater in the absence compared with the presence of microneurography
Middlekauff, H.R. (2002)	1/Singular	Standard Treatment: Right LI4, Right LR3, Left PC6	Acute	18/11	sympathetic activation during mental stress is virtually eliminated after acupuncture at Li4, P6, and Liv3, No other significant changes
Schroeder, S. (2017)	12/Weekly	Standard Treatment/ GV 20, HT 7, PC 6, Yintang, Four Gates, CV 17, CV 6, ST36 and auricular points: Shen Men, Liver, Point 0, and Heart	Chronic	22/06	Both groups showed significant reduction, but with a significant difference between groups (verum>sham) at week 12

First Author (Year)	No. of Treatments/Frequency	Diagnosis Protocol/Points Used	Chronic/Acute Stress	CONSORT/STRICTA	Comments
Smith, C.A. (2011)	6/Weekly (n=4) then Fortnightly (n=2)	Causative Factor & TCM Diagnosis/ Common points used included the Kidney Chest points and PC6, PC5, HT5, HT7	Chronic	29/14	Significant changes in 1 domain in the FPI
Zuppa, C. (2015)	10/Twice Weekly	Standard Treatment: SP6, LI4, ST36, LR3, PC6, Yin Tang	Chronic	17/05	Acupuncture significantly reduced PSQI scores, indicating a significant improvement in sleep quality, true acupuncture was effective in attenuating stress and depression scores. No significant changes were observed in the placebo group.
Chan, J. (2002)	4/Weekly	Standard Treatment: HT7 (Manipulation for 2 seconds; No needle retention)	Chronic	n/a	No needle retention. Significant improvements from baseline to finish (1 week post last treatment), and also between treatments
de Oliveira, C.C.C. (2017)	10/Not shown	Traditional Energy Diagnosis: n=34, top 10 by frequency used: ST36, Yin Tang, LR3, BL62, PC6,SP6, LI4, CV4, KD3, GB34	Chronic	n/a	
Pavao, T.S. (2010)	6/Twice Weekly	Standard Treatment: SP6, LI4,ST36	Chronic	n/a	Young vs Elderly groups. Very significant results in both groups, with Elderly also increasing T-cell proliferation.

Appendix B: Participant Final Questionnaire (PFQ)

PARTICIPANT FINAL QUESTIONNAIRE

UTS APPROVAL NUMBER ETH20-5098

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

Please indicate by ticking the response box that best reflects how strongly you agree or disagree with each of the following statements:

1. The stress of attending the acupuncture treatments outweighed any benefits I feel I may have gained from the treatment

Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
☐	☐	☐	☐	☐

2. I feel that attending the acupuncture treatments reduced my stress levels

Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
☐	☐	☐	☐	☐

3. I would have preferred to attend the acupuncture treatments more frequently

Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
☐	☐	☐	☐	☐

4. I would have preferred to attend the acupuncture treatments less frequently

Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree

☐ ☐ ☐ ☐ ☐

Are there any comments or feedback you would like to add about the trial you completed?

Appendix C: Perceived Stress Scale 14

The questions in this scale ask you about your feelings and thoughts during the LAST MONTH. In each case, you will be asked to indicate your response by checking the box representing HOW OFTEN you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

1. In the last month, how often have you been upset because of something that happened unexpectedly?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

2. In the last month, how often have you felt that you were unable to control the important things in your life?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

3. In the last month, how often have you felt nervous and "stressed"?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

4. In the last month, how often have you dealt successfully with day to day problems and annoyances?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

5. In the last month, how often have you felt that you were effectively coping with important changes that were occurring in your life?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

6. In the last month, how often have you felt confident about your ability to handle your personal problems?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

7. In the last month, how often have you felt that things were going your way?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

8. In the last month, how often have you found that you could not cope with all the things you had to do?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

9. In the last month, how often have you been able to control irritations in your life?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

10. In the last month, how often have you felt that you were on top of things?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

11. In the last month, how often have you been angered because of things that happened that were outside of your control?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

12. In the last month, how often have you found yourself thinking about things that you have to accomplish?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

13. In the last month, how often have you been able to control the way you spend your time?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

Never	Almost Never	Sometimes	Fairly Often	Very Often
☐	☐	☐	☐	☐

Appendix D: Additional Stress Questionnaire (ASQ)

UTS APPROVAL NUMBER ETH20-5098

On the following scales of 1-10, please indicate your level of each type of stress, where 1 = No stress, and 10 = Maximum stress

1. Emotional Stress

1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

2. Financial Stress

1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

3. Academic Stress

1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

4. Occupational Stress

1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

5. On the following scale of 1-10, please indicate your overall level of stress you feel right now, where 1 = No stress, and 10 = Maximum stress

1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

6. Please tick this box if you have experienced any thoughts of suicide or self-harm

Appendix E: Sociodemographic Questionnaire

UTS APPROVAL NUMBER ETH20-5098

Stress, Acupuncture and Students (SAS) Study - QUESTIONNAIRE

The information that you provide will remain strictly anonymous. Please answer every question you can. If you are unsure about how to answer a question mark the response for the closest answer to how you feel.

1. Age (in years):

☐ 19 – 24 ☐ 25 – 29 ☐ 30 – 34 ☐ 35 – 39 ☐ 40 – 44 ☐ 45 – 49
☐ 50 – 54 ☐ 55 – 59 ☐ 60 – 64 ☐ 65 – 69 ☐ 70 – 74 ☐ 75 – 79
☐ 80+

2. Partnership Status:

☐ Single ☐ Never married ☐ Partnered ☐ De facto
☐ Married ☐ Divorced or separated ☐ Widowed

3. Who lives with you?

☐ I live alone ☐ Partner/spouse ☐ Own children ☐ Someone else's children
☐ Parents ☐ Other adults (non-tertiary students) ☐ Other adults (and are tertiary students)

4. ☐ Female ☐ Male ☐ Other ☐ Prefer not to say

5. What is your country of birth: _____

What year did you move to Australia (if applicable): _____

6. Are you classified by the university as a:

☐ Local student
☐ International student

7. Are you CURRENTLY enrolled as a:

☐ Part-time student (1- 2 subjects or ≤ 12 credit points equivalent)
☐ Full-time (3 subjects or 18 credit points equivalent)
☐ Full-time (4 subjects or 19-24 credit points equivalent)

☐ Above Load (5 or more subjects or >25 credit points equivalent)

8. Have you previously studied at university – please select the most appropriate to your circumstances:

☐ First time studying at university

☐ Previous attempted university but never finished

☐ Completed previous studies at university. If selecting this option, please also indicate your previous study-type from the following list. Select all relevant descriptors to your circumstance:

- ☐ Non-award
- ☐ Bachelor degree
- ☐ Post-graduate course-work program (Grad-Cert, Grad-Dip, Master's)
- ☐ Post-graduate research degree (Master's (by thesis), PhD)

9. How many years have you been at university in your CURRENT degree

☐ First year

☐ Second year

☐ Third year

☐ Fourth year

10. What is your current occupational status:

☐ Employed full-time (35 hrs per wk)

☐ Employed part-time (between 21-34 hrs per wk)

☐ Unemployed

☐ Employed part-time (≤ 20 hrs per wk)

☐ Retired

☐ Casual employment

☐ Homemaker

☐ Not working due to ill health

☐ Other (please specify): _____

11. If relevant, was your current working hours effected by the COVID19 emergency response?

☐ No, working hours remained the same

☐ Yes, work hours increased (working more)

☐ Yes, work hours decreased (working less)

☐ Yes, had to find new employment

12. Have you ever smoked? ☐ Yes ☐ No

Do you still smoke? ☐ Yes ☐ No If so, how many cigarettes a day: _____

13. Approximately how many **times a week** do you do the following kinds of exercise for MORE than 15 minutes:

Mild/light exercise (minimal effort): _____

Moderate leisure activity (not exhausting): _____

Vigorous exercise (heart beats rapidly): _____

14. How many caffeinated beverages do you drink a day (coffee, tea, hot chocolate, coke): _____

How many alcoholic drinks do you drink a week? ☐ None Wine: ___ Beer: _____

Spirits: ____

How many days a week do you drink alcohol (if applicable)? _____

15 Please indicate if you are currently having treatment/support (therapy or medication) with another health care practitioner for a diagnosed mental health condition. Please select the all relevant from the following list.

- Mood (including depression) condition
- Anxiety condition
- Bipolar condition
- Eating disorder
- Psychosis
- Stress
- Other _____ (Please note)

Appendix F: Credibility and Expectancy Questionnaire (CEQ)

CREDIBILITY AND EXPECTANCY QUESTIONNAIRE

UTS APPROVAL NUMBER ETH20-5098

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

Please indicate on a scale of 0-6 that best reflects your answer, where 6 = very confident and 0 = not confident at all:

1. How confident are you that this treatment can alleviate your complaint?

0	1	2	3	4	5	6
☐	☐	☐	☐	☐	☐	☐

Please indicate on a scale of 0-6 that best reflects your answer, where 6 = very logical and 0 = not logical at all:

2. How logical does this treatment seem to you?

0	1	2	3	4	5	6
☐	☐	☐	☐	☐	☐	☐

Please indicate on a scale of 0-6 that best reflects your answer, where 6 = very confident and 0 = not confident at all:

3. How confident would you be in recommending this treatment to a friend who suffered the same complaint?

0	1	2	3	4	5	6
☐	☐	☐	☐	☐	☐	☐

Please indicate on a scale of 0-6 that best reflects your answer, where 6 = very successful and 0 = not successful at all:

4. How successful do you think this treatment would be in alleviating other complaints?

0	1	2	3	4	5	6
☐	☐	☐	☐	☐	☐	☐

Appendix G: Online Survey Information Sheet

INFORMATION SHEET AND CONSENT FORM FOR ONLINE SURVEYS

UTS APPROVAL NUMBER ETH20-5098

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

What is the research study about?

This research will investigate the use of acupuncture to treat stress in university students. There is some evidence to support the use of acupuncture to reduce stress, but more research is needed. As they have been identified as a socio-demographic group prone to heightened stress levels, university students may be able to improve their well-being through the use of acupuncture.

I'm seeking university students at UTS to take part in a clinical trial. No previous experience with acupuncture is necessary.

You have been invited to participate in this study because you are a student at UTS.

Who is conducting this research?

My name is Dane Couter. I am a Higher Degree Research candidate at the University of Technology Sydney (UTS) and registered with AHPRA as a qualified health practitioner in Acupuncture and Chinese Herbal Medicine. My supervisor is Dr Sean Walsh, Academic Research Supervisor and Senior Lecturer in the School of Life Science, UTS.

Inclusion/Exclusion Criteria

Before you decide to participate in this research study, we need to ensure that it is ok for you to take part.

You must be currently enrolled at UTS.

You must be aged 18 years or over.

You must not be pregnant.

You must not have haemophilia or any disorder or be taking any medication that may interfere with blood clotting.

You must not have a needle phobia.

Do I have to take part in this research study?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part.

If you decide to participate, I (Dane Couter) will invite you as a participant patient to:

- Receive 4 acupuncture treatments by a qualified and registered health practitioner, 1-2 times a week over a period of 2-4 consecutive weeks, at the UTS Chinese Medicine Clinic, located on the UTS City Campus, on the corner of Harris and Thomas Streets (opposite the ABC Ultimo Centre on Harris St).
- You will be asked (via email) to fill out an online survey before beginning treatment and at set times during the trial. The survey is expected to take only a few minutes of your time.

You can change your mind at any time and stop completing the surveys without consequences.

Are there any risks/inconvenience?

This study has been carefully designed but there may be possible risks and inconvenience:

- The acupuncture treatment will be only administered on the four limbs (i.e. hands, feet, lower legs, lower arms). You will not have to disrobe, other than shoes/socks.
- Some people might experience some discomfort or reactions to acupuncture more than others. You might feel discomfort from needle insertion on the surface and skin reactions on the needling site (e.g. bruising, redness, pain), which will be transient, disappearing in a day or two, but bruising may persist for longer (several days).
- You may temporarily feel some discomfort such as light-headedness, or a vaso-vagal response resulting in nausea.
- You might be concerned about potential related risks of infection (e.g. contamination of needles, etc.). To ensure the safe practice of acupuncture at UTS TCM clinic, every procedure and situation which has potential of exposure to blood, body fluids and other contaminated material will follow the principles embodied in standard precautions, including the correct disposal of containment material (sharps and non-sharps) into the appropriately marked containment facilities provided in the clinic, appropriate hand hygiene procedures, use of barrier protection, clinical management of patients with contagious infections under the guidelines of UTS Clinical Procedures and Safe Clinical Practice, and Infection Prevention.

- You might be concerned about the exposure of your identity in the publications. I can assure you, however, that your name will not be used in any data sets or publications. Any identifying information will be removed from the data as it is entered into the online survey.
- You might find some minor inconvenience in filling in the forms and questionnaires in each treatment session. You will be sent an individual link to the online survey at set times throughout the trial. The survey is expected to take only a few minutes of your time.
- Your time and schedule are highly respected, and I'll pre-arrange the treatment sessions with you. All treatment sessions will be conducted with sensitivity and confidentiality.
- If you're not happy due to distress, dissatisfaction or complaints from the treatment, or for reasons outside of your control that impact participation, you have right to withdraw from the research any time.

What will happen to information about me?

Access to the online questionnaire is via a direct weblink that will be emailed to you. Submission of the online questionnaire/s is an indication of your consent. By clicking the weblink you consent to the research team collecting and using personal information about you for the research project. All this information will be treated confidentially.

The security of data will be in compliance with the Stash Research Data Management Plan and the Guidelines for the Management of Research Data (UTS, 2019). Data collected from this project is classified into four categories: source data, link data, de-identified primary data, and analysis data. To ensure the security of data, the project will comply with the Guidelines for the Management of Research Data (UTS, 2019) and Stash Research Data Management Plan.

The Data security strategy for the four categories of project data is as follows:

- Source data includes hard copies collected in paper form and online data entered into the online survey. All source data will display a unique participation identification number (UPIN) on it. Hard copies will be stored in a locked UTS filing cabinet to which only the researcher has a key.
- Link data is an electronic linking file containing both participant identification information and UPIN. The linking file will be encrypted and securely stored under a specific folder in the eResearch file share, locked with a password and authorised access control.
- De-identified primary data includes electronic files created based on hard copies of source data. All primary data contains UPIN only (i.e. de-identified). Primary data (de-identified data) will be stored in an encrypted folder on the researcher's password-protected laptop and on the UTS OneDrive (approved for health data). All primary data will display a unique participation identification number (UPIN) on it.
- Analysis data includes electronic files derived from various data analysis processes. Analysis data will be stored in an encrypted folder on researcher's password protected laptop, on the UTS One Drive, and in an encrypted folder on a hard drive with password protection for back-up only.
- To protect the confidentiality and privacy of the participants, each participant's data will only be identified by a unique participant identification code (UPIN) as pseudonym. The linking file will be encrypted and securely stored, separately from the source data and the primary data (de-identified).

When the research is complete (journal articles published and thesis approved), all source data (hard-copies and survey results) and linking files, de-identified primary data and analysis data will be archived and moved to the eResearch fileshare and kept for 5 years in accordance with the UTS Guidelines for the Management of Research Data and the Stash RDMP. Participant information will not be shared with others as defined in the Confidentiality/Privacy section of the Participant Informed Consent form. The research practitioner and supervisor will ensure participant privacy and confidentiality as outlined in the associated ethics application.

Your information will be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. We plan to publish the results in journal articles and dissertations. Information will be provided in such a way that you cannot be identified in any publication, including books, conference papers, electronic publication, media, and reports. In all instances your information will be unidentifiable and treated confidentially.

In case of emergency some of your personal details (Name, Student Number, Contact Details) may be shared with the UTS Student Services Counselling in order to carry out UTS' duty of care. Student Services Counselling are bound by normal privacy and confidentiality constraints and will not share your information with any other party.

What if I have concerns or a complaint?

If you have concerns about the research that you think my supervisor or I can help you with, please feel free to contact me at dane.couter@student.uts.edu.au, or my supervisor Sean Walsh at sean.walsh@uts.edu.au or by phone on 9514 7864.

If you would like to talk to someone who is not connected with the research, you may contact the Research Ethics Officer on 02 9514 9772 or Research.ethics@uts.edu.au and quote this number **ETH20-5098**

Appendix H: Participant Information Sheet & Consent Form

PARTICIPANT INFORMATION SHEET

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

HREC APPROVAL NUMBER ETH20-5098

WHO IS DOING THE RESEARCH?

My name is Dane Couter. I am a Higher Degree Research candidate at the University of Technology Sydney (UTS) and registered with AHPRA as a qualified health practitioner in Acupuncture and Chinese Herbal Medicine. My supervisor is Dr Sean Walsh, Academic Research Supervisor and Senior Lecturer in the School of Life Science, UTS.

WHAT IS THIS RESEARCH ABOUT?

This research will investigate the use of acupuncture to treat stress in university students. There is some evidence to support the use of acupuncture to reduce stress, but more research is needed. As they have been identified as a socio-demographic group prone to heightened stress levels, university students may be able to improve their well-being through the use of acupuncture.

I'm seeking university students at UTS to take part in a clinical trial. No previous experience with acupuncture is necessary.

WHY HAVE I BEEN ASKED?

You have been invited to participate in this study because you are a student at UTS.

IF I SAY YES, WHAT WILL IT INVOLVE?

If you decide to participate, I (Dane Couter) will invite you as a participant patient to:

- Receive 4 acupuncture treatments by a qualified and registered health practitioner, 1-2 times a week over a period of 2-4 consecutive weeks, at the UTS Chinese Medicine Clinic, located on the UTS City Campus, on the corner of Harris and Thomas Streets (opposite the ABC Ultimo Centre on Harris St).
- You will be asked (via email) to fill out an online survey before beginning treatment and at set times during the trial. The survey is expected to take only a few minutes of your time.

Please refer to the detailed explanation of procedures in the appendix section of this document.

ARE THERE ANY RISKS/INCONVENIENCE?

This study has been carefully designed but there may be possible risks and inconvenience:

- The acupuncture treatment will be only administered on the four limbs (i.e. hands, feet, lower legs, lower arms). You will not have to disrobe, other than shoes/socks.
- Some people might experience some discomfort or reactions to acupuncture more than others. You might feel discomfort from needle insertion on the surface and skin reactions on the needling site (e.g. bruising, redness, pain), which will be transient, disappearing in a day or two, but bruising may persist for longer (several days).
- You may temporarily feel some discomfort such as light-headedness, or a vaso-vagal response resulting in nausea.
- You might be concerned about potential related risks of infection (e.g. contamination of needles, etc.). To ensure the safe practice of acupuncture at UTS TCM clinic, every procedure and situation which has potential of exposure to blood, body fluids and other contaminated material will follow the principles embodied in standard precautions, including the correct disposal of containment material (sharps and non-sharps) into the appropriately marked containment facilities provided in the clinic, appropriate hand hygiene procedures, use of barrier protection, clinical management of patients with contagious infections under the guidelines of UTS Clinical Procedures and Safe Clinical Practice, and Infection Prevention.
- You might be concerned about the exposure of your identity in the publications. I can assure you, however, that your name will not be used in any data sets or publications. Any identifying information will be removed from the data as it is entered into the online survey.
- You might find some minor inconvenience in filling in the forms and questionnaires in each treatment session. You will be sent an individual link to the online survey at set times throughout the trial. The survey is expected to take only a few minutes of your time.
- Your time and schedule are highly respected, and I'll pre-arrange the treatment sessions with you. All treatment sessions will be conducted with sensitivity and confidentiality.
- If you're not happy due to distress, dissatisfaction or complaints from the treatment, or for reasons outside of your control that impact participation, you have right to withdraw from the research any time.

DO I HAVE TO SAY YES?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part.

WHAT WILL HAPPEN IF I SAY NO?

If you decide not to participate, it will not affect your relationship with the researchers or the University of Technology Sydney. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason, by contacting the researcher Dane Couter by email at dane.couter@student.uts.edu.au or the supervisor Dr Sean Walsh at sean.walsh@uts.edu.au or 02 9514 7864.

If you withdraw from the study, we will not collect additional data from you but would be interested in a reason if you are willing to provide one.

If you decide to leave the research project, we will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

CONFIDENTIALITY

By signing the consent form, you consent to the research team collecting and using personal information about you for the research project. All this information will be treated confidentially. All participant patients' data will be de-identified and the information will not be shared with others as defined in the Confidentiality/Privacy section of the participant informed consent form and the UTS ethics application.

The security of data will be in compliance with the Stash Research Data Management Plan and the Guidelines for the Management of Research Data (UTS, 2019). Data collected from this project is classified into four categories: source data, link data, de-identified primary data, and analysis data. To ensure the security of data, the project will comply with the Guidelines for the Management of Research Data (UTS, 2019) and Stash Research Data Management Plan.

The Data security strategy for the four categories of project data is as follows:

- Source data includes hard copies collected in paper form and online data entered into the online survey. All source data will display a unique participation identification number (UPIN) on it. Hard copies will be stored in a locked UTS filing cabinet to which only the researcher has a key.
- Link data is an electronic linking file containing both participant identification information and UPIN. The linking file will be encrypted and securely stored under a specific folder in the eResearch file share, locked with a password and authorised access control.
- De-identified primary data includes electronic files created based on hard copies of source data. All primary data contains UPIN only (i.e. de-identified). Primary data (de-identified data) will be stored in an encrypted folder on the researcher's password-protected laptop and on the UTS OneDrive (approved for health data). All primary data will display a unique participation identification number (UPIN) on it.
- Analysis data includes electronic files derived from various data analysis processes. Analysis data will be stored in an encrypted folder on researcher's password protected laptop, on the UTS One Drive, and in an encrypted folder on a hard drive with password protection for back-up only.
- To protect the confidentiality and privacy of the participants, each participant's data will only be identified by a unique participant identification code (UPIN) as pseudonym. The linking file will be encrypted and securely stored, separately from the source data and the primary data (de-identified).

When the research is complete (journal articles published and thesis approved), all source data (hard-copies and survey results) and linking files, de-identified primary data and analysis data will be archived and moved to

the eResearch fileshare and kept for 5 years in accordance with the UTS Guidelines for the Management of Research Data and the Stash RDMP. Participant information will not be shared with others as defined in the Confidentiality/Privacy section of the Participant Informed Consent form. The research practitioner and supervisor will ensure participant privacy and confidentiality as outlined in the associated ethics application.

Your information will be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. We plan to publish the results in journal articles and dissertations. Information will be provided in such a way that you cannot be identified in any publication, including books, conference papers, electronic publication, media, and reports. In all instances your information will be unidentifiable and treated confidentially.

In case of emergency some of your personal details (Name, Student Number, Contact Details) may be shared with the UTS Student Services Counselling in order to carry out UTS' duty of care. Student Services Counselling are bound by normal privacy and confidentiality constraints and will not share your information with any other party.

WHAT IF I HAVE CONCERNS OR A COMPLAINT?

If you have concerns about the research that you think I or my supervisor can help you with, please feel free to contact me by email at Dane.Couter@student.uts.edu.au or my supervisor at Sean.Walsh@uts.edu.au or by phone on 9514 7864.

You will be given a copy of this form to keep.

NOTE:

This study has been approved in line with the University of Technology Sydney Human Research Ethics Committee [UTS HREC] guidelines. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat on ph.: +61 2 9514 2478 or email: Research.Ethics@uts.edu.au], and quote the UTS HREC reference number. Any matter raised will be treated confidentially, investigated and you will be informed of the outcome.

CONSENT FORM

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

HREC APPROVAL NUMBER ETH20-5098

I _____, agree to participate in the research project *Students, Acupuncture and Stress – a feasibility study comparing treatment frequency and reported change in stress UTS HREC approval number ETH20-5098* being conducted by Dane Couter (Dane.Couter@student.uts.edu.au).

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research as described in the Participant Information Sheet.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time without affecting my relationship with the researchers or the University of Technology Sydney.

I understand that I will be given a signed copy of this document to keep.

I agree that the research data gathered from this project may be published in a form that:

☐ Does not identify me in any way

☐ May be used for future research purposes

I am aware that I can contact Dane Couter if I have any concerns about the research.

_____ ____/____/____

Name and Signature [participant] Date

_____ ____/____/____

Name and Signature [researcher or delegate] Date

Appendix I: Serious Adverse Event Report Form

UTS HUMAN RESEARCH ETHICS COMMITTEE

SERIOUS ADVERSE EVENT (SAE) AND

SERIOUS UNEXPECTED SUSPECTED ADVERSE REACTION (SUSAR) REPORT

Students, Acupuncture and Stress – A feasibility study into acupuncture treatment frequency and self-reported changes in perceived stress in university students

(ETH20-5098)
INSTRUCTIONS for completing the report

This report is to be completed only when UTS HREC is the **main committee** approving the study. Where the UTS HREC has provided ratification of an HREC approval from another institution, SAE/SUSAR should be reported to UTS HREC **only** if they have occurred at local or UTS affiliated institutions participating in the research. For multi-centre research projects, the Principal Investigator is responsible for reporting SAE/SUSAR occurring at their site directly to the main HREC that approved the research.

1. Serious Adverse Events must be reported to the UTS HREC within 24-72 hours of the researchers becoming aware of the event, using the form below.
2. Please complete this form electronically before printing.
3. Enter one adverse event/reaction per form.
4. Each form must be signed by the Principle Investigator and submitted electronically and in hard copy to the UTS Ethics Secretariat.

Project Details	
UTS HREC approval number	**ETH19-3716**
Project title	Students, Acupuncture and Stress – A feasibility study into acupuncture treatment frequency and self-reported changes in perceived stress in university students
Name of Principal investigator	Dr Sean Walsh
Name of UTS affiliated investigator	Mr Dane Couter

Adverse Event Details	
Participant study number	
Site where participant was consented	

Date event occurred	
Date event resolved	
Description of event (please attach supporting documentation)	
Investigator's opinion about the relationship of the adverse event to the study	☐ Not related ☐ Possibly related ☐ Directly related
Likely cause of event	☐ Study drug/treatment/intervention ☐ Standard treatment/intervention ☐ Progressive disease ☐ Concurrent medication ☐ Concurrent disorder ☐ Other (please specify) _____ _____ _____
Outcome	☐ Permanent or significant disability/incapacity ☐ Required hospitalisation ☐ Life threatening ☐ Fatal
Was this adverse event anticipated in the original research protocol?	☐ Yes ☐ No
Was it described in the Participant Information sheet?	☐ Yes ☐ No
Has this event been reported to the sponsor?	☐ Yes ☐ No If No, please explain _____ _____ _____
Will there be any changes to the conduct of the study as a result of this event?	☐ Yes ☐ No
Additional information	

Principal Investigator: (Print name)	
Signature:	
Date:	

Contact details for enquiries relating to this report:	

UTS HREC Ethics Secretariat use only	
Date reviewed:	
Name:	
Signature:	

Appendix J: Distress Protocol

DISTRESS/SUICIDAL IDEATION PROTOCOL

STUDENTS, ACUPUNCTURE AND STRESS – A FEASIBILITY STUDY COMPARING TREATMENT FREQUENCY AND REPORTED CHANGE IN STRESS

HREC APPROVAL NUMBER ETH20-5098

Participant Distress Protocol:

The following protocol will be put in place should a participant exhibit signs of distress during the acupuncture treatment session. Prior to commencement participants will be provided sufficient information regarding possible risks and benefits in order to make informed decisions regarding their involvement.

1. The clinician will pause the acupuncture treatment and provide verbal support.
2. Ask the participant if they wish to end the acupuncture session or continue.
3. If the participant wishes this, the acupuncture session will be terminated.
4. Encourage the participant to contact their GP, mental health provider and/or Student Services Counselling.
5. If the distressed episode occurs during business hours, offer to escort the participant, with their consent, to student services counselling. Alternatively, contact Student Services Counselling by phone to inquire about counselling availability.
6. If the participant mentions hopelessness/suicidal ideation then contact will be made with Student Services Counselling by the researcher for referral.
7. If the participant is deemed at risk of suicide/requiring emergency assistance then the researcher will contact UTS security or 000.
8. Follow up the next business day with a phone call enquiring about the participant's well-being.
9. Determine if further involvement in the study is feasible.

Online Suicidal Ideation Protocol:

At the conclusion of the online survey the participant will be asked if they have had any thoughts of suicide or self-harm. If the participant chooses the "yes" option the following message will appear (from UTS Student Services online intake form):

https://www.uts.edu.au/current-students/support/health-and-wellbeing/counselling-service-and-self-help/first-visit

Please be aware that the information submitted in this online questionnaire will not be seen by the researchers immediately.

If you require emergency assistance, contact the Police and/or request an Ambulance by dialling 000.

You may also request assistance by contacting **24-hour crisis phone counselling**:

- Lifeline Counselling Service: 13 11 14
- Suicide Call Back Service: 1300 659 467
- Beyondblue Support Service: 1300 22 4636
- Kids Helpline: 1800 55 1800
- NSW Mental Health Line: 1800 011 511

Please contact the UTS Student Services Counselling Service on:

Phone: +61 2 9514 1177

Fax: +61 2 9514 1172

Email: student.services@uts.edu.au

Location: CB01.6 (Level 6) Building 1, 15 Broadway, Ultimo, NSW 2007 (view map)

An email will be automatically generated and sent to notify both the researcher (Dane Couter) and the supervisor (Sean Walsh).

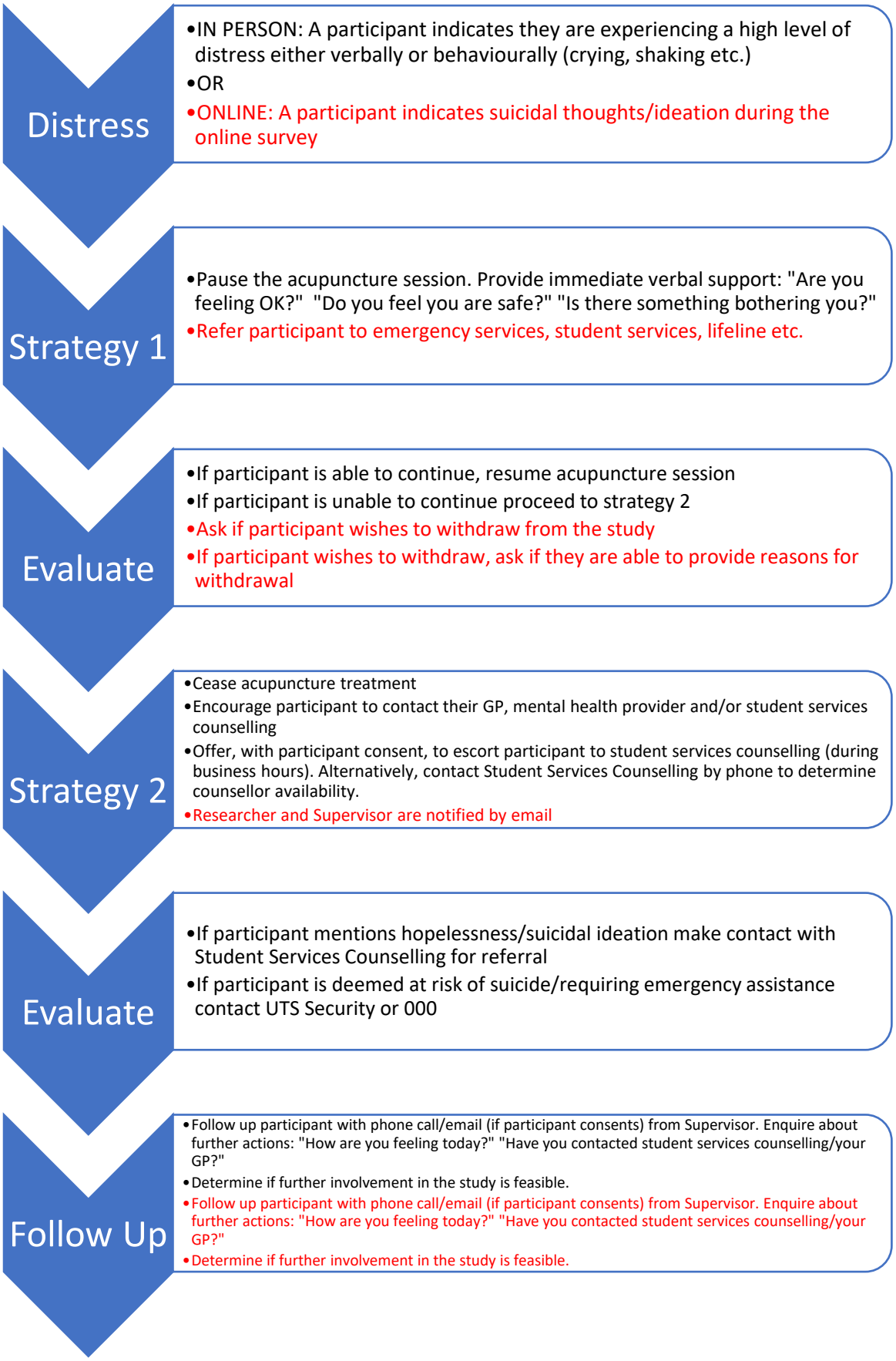
The supervisor will make a follow-up contact (either by email or phone) the next business day to inquire about the welfare of the participant and to determine if any further involvement in the study is feasible.

The supervisor will contact student services the next business day to ensure that the participant has made contact.

If either the researcher or supervisor are unable to perform these duties (on leave, illness etc.) then the co-supervisor (Shuai Zheng) will be notified via email.

Both the participant and researchers will determine if continuing participation in the study is feasible.

Participants' Distress/Suicidal Ideation Protocol:



Appendix K: Delphi Invitation Email

A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels

My name is Dane Couter and I am a Master's (Research) student at the University of Technology Sydney (UTS). My supervisors are Dr Sean Walsh and Dr Shuai Zheng in the School of Life Science, Faculty of Science.

I am contacting you to invite you to participate in an online Delphi survey. No identifying information will be collected and it will take approximately 15 minutes to complete.

The survey is in three parts. Part one is about diagnosis of stress according to Chinese Medicine (CM). The second is about acupuncture point selection. The third is about treatment protocols such as treatment frequency.

The survey aims to inform a proposed clinical trial using acupuncture to reduce perceived stress levels.

If you are interested and willing to take part in the survey, please click on the link contained in this email:

Thank you in advance for donating your valuable time and expertise.

Dane Couter

Master's (Research) student, UTS

Appendix L: Delphi Process Survey, Round 1

A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels

My name is Dane Couter and I am a Masters (Research) student at the University of Technology Sydney (UTS). My supervisors are Dr Sean Walsh and Dr Shuai Zheng in the School of Life Science, Faculty of Science.

I am contacting you to invite you to participate in an online Delphi survey. No identifying information will be collected and it will take approximately 15 minutes to complete.

The survey is in three parts. Part one is about diagnosis of stress according to Chinese Medicine (CM). The second is about acupuncture point selection. The third is about treatment protocols such as treatment frequency.

The survey aims to inform a proposed clinical trial using acupuncture to reduce perceived stress levels.

Please take your time to consider each question consider all possible answers before selecting the one you believe is the most accurate.

Thank you for your participation.

ONLINE SURVEY INFORMATION SHEET

[UTS APPROVAL NUMBER ETH21-6702] - A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels

WHO IS CONDUCTING THIS RESEARCH?

My name is Dane Couter and I am a student at UTS. My supervisors are Sean Walsh and Shuai Zheng.

WHAT IS THE RESEARCH ABOUT?

The purpose of this research is to gain expert consensus into the diagnosis and treatment of stress using acupuncture, in order to develop a clinical trial.

You have been invited to participate because you may have expertise in this field and can help to shape future research.

Before you decide to participate in this research study, we need to ensure that it is ok for you to take part. You must have at least five years of clinical experience as a registered acupuncturist OR currently treating greater than five patients presenting with stress per month OR have a postgraduate qualification in the Chinese Medicine field.

WHAT DOES MY PARTICIPATION INVOLVE?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part.

If you decide to participate, I will invite you to take part in two online surveys. The surveys ask questions about diagnosis and treatment of stress according to Chinese Medicine. Each survey may take up to 15 minutes to complete.

You can change your mind at any time and stop completing the survey/s without consequences.

ARE THERE ANY RISKS/INCONVENIENCE?

We don't expect this questionnaire to cause any harm or discomfort. However, if you experience discomfort or distress answering the questions please contact your family doctor or physician.

WHAT WILL HAPPEN TO INFORMATION ABOUT ME?

Access to the online questionnaire is via a weblink in an email sent to you. Submission of the online questionnaire/s is an indication of your consent.

The results of this research may also be shared through open access (public) scientific databases, including internet databases. This will enable other researchers to use the data to investigate other important research questions. Results shared in this way will always be de-identified by removing all personal information (e.g. your name, address, date of birth etc.).

AND

In accordance with relevant Australian and/or NSW Privacy laws, you have the right to request access to the information about you that is collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please inform the research team member named at the end of this document if you would like

to access your information.

WHAT IF I HAVE ANY QUERIES OR CONCERNS?

If you have concerns about the research that you think I or my supervisor can help you with, please feel free to contact me: dane.couter@student.uts.edu.au, or sean.walsh@uts.edu.au

If you would like to talk to someone who is not connected with the research, you may contact the Research Ethics Officer on 02 9514 9772 or Research.ethics@uts.edu.au and quote this number ETH21-6702.

How many years have you been practicing Chinese Medicine?	◯ < 5 ◯ 5-10 ◯ 11-15 ◯ 16-20 ◯ 20+
Please indicate how many patients you would normally treat in your practice presenting with stress per month	◯ < 5 ◯ 5-10 ◯ 11-20 ◯ 21-30 ◯ 31-40 ◯ 41+
What is your highest qualification?	◯ Diploma/Certificate ◯ Undergraduate (Bachelor's degree) ◯ Postgraduate (Masters) ◯ Postgraduate (Doctorate)
What is your highest qualification?	◯ Diploma/Certificate ◯ Undergraduate (Bachelor's degree) ◯ Postgraduate (Masters) ◯ Postgraduate (Doctorate)

Diagnosis

Please complete the survey below.

Thank you!

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following zangfu to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Heart	○	○	○	○	○
Liver	○	○	○	○	○
Spleen	○	○	○	○	○
Stomach	○	○	○	○	○
Kidney	○	○	○	○	○
Lung	○	○	○	○	○

Are there any other zangfu you believe would be clinically relevant to a diagnosis of stress?
○ Yes
○ No

If yes, please specify

_____

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following syndromes to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Qi Stasis	○	○	○	○	○
Qi Counterflow	○	○	○	○	○
Full Heat/Fire	○	○	○	○	○
Empty Heat/Fire	○	○	○	○	○
Qi Deficiency	○	○	○	○	○
Blood Deficiency	○	○	○	○	○
Yin Deficiency	○	○	○	○	○
Yang Deficiency	○	○	○	○	○
Zangfu Disharmony/Mutual Insult	○	○	○	○	○

Are there any other syndromes you believe would be clinically relevant to a diagnosis of stress?
○ Yes
○ No

If yes, please specify

_____

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following signs and symptoms to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Anxious or Racing Thoughts	○	○	○	○	○
Constant Worrying	○	○	○	○	○
Inability to Concentrate	○	○	○	○	○
Irritablility or Short Temper	○	○	○	○	○
Agitation or Inability to Relax	○	○	○	○	○
Insomnia or Other Sleep Disturbances	○	○	○	○	○
Moodiness	○	○	○	○	○
Easily Fatigued	○	○	○	○	○
Poor Memory	○	○	○	○	○
Listlessness	○	○	○	○	○
Thirst	○	○	○	○	○
Depression	○	○	○	○	○
General Unhappiness	○	○	○	○	○
Frequent Sighing	○	○	○	○	○
Wiry Pulse	○	○	○	○	○
Rapid Pulse	○	○	○	○	○
Tight Pulse	○	○	○	○	○
Irregular/Choppy Pulse	○	○	○	○	○
Headache	○	○	○	○	○
Neck/Shoulder Tension	○	○	○	○	○
Abdominal Tension	○	○	○	○	○
Tightness/Opression of the Chest	○	○	○	○	○
Indigestion	○	○	○	○	○
Constipation	○	○	○	○	○
Faltulence	○	○	○	○	○
Nausea and Vomiting	○	○	○	○	○
Palpitations	○	○	○	○	○
Cough	○	○	○	○	○
Hypertension (High Blood Pressure)	○	○	○	○	○
Red Tongue Body	○	○	○	○	○
Purple Tongue Body	○	○	○	○	○
Yellow Tongue Coating	○	○	○	○	○
Peeled Tongue Coating	○	○	○	○	○

Red Tongue Tip	○	○	○	○	○
Pale Tongue Body	○	○	○	○	○
Bitter Taste in Mouth	○	○	○	○	○
Weak Voice	○	○	○	○	○
Pale Complexion	○	○	○	○	○
Dysmenorrhea/Painful Menstruation	○	○	○	○	○
Irregular Menstruation	○	○	○	○	○
Premenstrual Tension	○	○	○	○	○
Feeling Unable to Control Important Things in Life	○	○	○	○	○
Feeling Unable to Cope With All the Things You Must Do	○	○	○	○	○
Feeling Unable to Control Irritations in Life	○	○	○	○	○
Feeling Unable to Deal Well With Life Hassles	○	○	○	○	○

Are there any other syndromes you believe would be clinically relevant to a diagnosis of stress?

○ Yes
○ No

If yes, please specify

_____

Treatment Protocols

Please complete the survey below.

Thank you!

Please indicate in the following scale of 1-5 how clinically relevant you would consider the following acupuncture points to a treatment of stress, where 1 = not relevant at all, and 5 = extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Liver 3	○	○	○	○	○
Liver 2	○	○	○	○	○
Gallbladder 34	○	○	○	○	○
Gallbladder 20	○	○	○	○	○
Pericardium 6	○	○	○	○	○
Stomach 36	○	○	○	○	○
Spleen 6	○	○	○	○	○
Liver 13	○	○	○	○	○
Liver 14	○	○	○	○	○
Gallbladder 43	○	○	○	○	○
Governor Vessel 14	○	○	○	○	○
Governor Vessel 20	○	○	○	○	○
Large Intestine 11	○	○	○	○	○
Large Intestine 4	○	○	○	○	○
Bladder 18	○	○	○	○	○
Heart 7	○	○	○	○	○
Heart 5	○	○	○	○	○
Heart 3	○	○	○	○	○
Yin Tang	○	○	○	○	○

Are there any other acupuncture points you believe would be clinically relevant to a treatment of stress?

○ Yes
○ No

If yes, please specify

_____

Please indicate if you use any of the following questionnaires as a diagnostic tool or outcome measure for stress in your practice:

☐ Perceived Stress Scale (PSS)
☐ State-Trait Anxiety Scale (STAI)
☐ Lipp's Inventory for Stress Symptoms (LISS)
☐ Measure Yourself Medical Outcome Profile (MYMOP)
☐ Other
☐ None of the above

If other, please specify

_____

Please indicate how many acupuncture treatments per week you would prefer to administer in order to achieve clinically relevant results in a treatment protocol for stress:	○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7
Please indicate the total number of acupuncture treatments you would normally expect to administer to achieve a clinically relevant reduction in perceived stress levels:	○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ 11 ○ 12+

Appendix M: Complete Delphi Process Results, Round 1

For raw data in the form of excel spreadsheets, please contact the thesis writer (Dane Couter).

1. Years of Practice

Years of Practice	<5	5-10	11-15	16-20	20+
Count	1 (7%)	3 (20%)	4 (26.7%)	2 (13.3%)	5 (33.3%)

2. Number of stressed patients per month

Stressed patients per month	5-10	11-20	21-30	31-40	40+
Count	6 (40%)	3 (20%)	2 (13.3%)	2 (13.3%)	2 (13.3%)

3. Highest Qualification

Highest Qualification	Undergraduate (Bachelor's Degree)	Postgraduate (Master's)	Postgraduate (Doctorate)
Count	6 (40%)	5 (33.3%)	4 (26.7%)

4. Zangfu relevant to a diagnosis of stress

Zangfu	Heart	Liver	Spleen	Stomach	Kidney	Lung
4/5 Count	11 (73.3%)	15 (100%)	9 (60%)	8 (53.3%)	12 (80%)	8 (53.3%)

Zangfu Open-ended Responses
Gall Bladder
San Jiao and GB
Pericardium, San Jiao, Small Intestine, Gall Bladder, Large Intestine
Bladder Large intestine
gallbladder
LI and SI
Gall bladder
gallbladder

5. Syndromes relevant to a diagnosis of stress

Syndrome	Qi Stasis	Qi Counterflow	Full Heat/ Fire	Empty Heat/Fire	Qi Deficiency	Blood Deficiency	Yin Deficiency	Yang Deficiency	Zangfu Disharmony/Mutual Insult
4/5 Count	15 (100%)	7 (46.7%)	11 (73.3%)	10 (66.7%)	7 (46.7%)	8 (53.3%)	9 (60%)	5 (33.3%)	11 (73.3%)

Syndromes Open-ended Responses
The Qi Deficiency may be related to a specific organ eg HT Qi deficiency rather than a generalised Qi Deficiency
damp phlegm obstruction patterns
phlegm / damp (heat / cold types) static blood
Damp heat
Heat in the Blood

6. Symptoms relevant to a diagnosis of stress

Symptom	4/5 Count
Agitation or Inability to Relax	15 (100%)
Irritability or Short Temper	15 (100%)
Anxious or Racing Thoughts	14 (93.3%)
Constant Worrying	13 (86.7%)
Insomnia or Other Sleep Disturbances	13 (86.7%)
Feeling Unable to Cope With All the Things You Must Do	13 (86.7%)
Feeling Unable to Deal Well With Life Hassles	13 (86.7%)
Feeling Unable to Control Important Things in Life	12 (80%)
Feeling Unable to Control Irritations in Life	12 (80%)
Moodiness	11 (73.3%)
Wiry Pulse	10 (66.7%)
Depression	10 (66.7%)
Easily Fatigued	9 (60%)
Poor Memory	9 (60%)
General Unhappiness	9 (60%)
Palpitations	9 (60%)
Red Tongue Tip	9 (60%)
Inability to Concentrate	8 (53.3%)
Frequent Sighing	8 (53.3%)
Rapid Pulse	8 (53.3%)
Irregular/Choppy Pulse	8 (53.3%)
Neck/Shoulder Tension	8 (53.3%)
Tightness/Oppression of the Chest	8 (53.3%)
Tight Pulse	7 (46.7%)
Premenstrual Tension	7 (46.7%)
Abdominal Tension	6 (40%)
Purple Tongue Body	6 (40%)
Listlessness	5 (33.3%)
Hypertension (High Blood Pressure)	5 (33.3%)
Red Tongue Body	5 (33.3%)
Bitter Taste in Mouth	5 (33.3%)
Headache	4 (26.7%)
Indigestion	4 (26.7%)
Constipation	4 (26.7%)
Peeled Tongue Coating	4 (26.7%)
Pale Tongue Body	4 (26.7%)
Dysmenorrhea/Painful Menstruation	4 (26.7%)
Thirst	3 (20%)
Flatulence	3 (20%)
Yellow Tongue Coating	3 (20%)
Irregular Menstruation	3 (20%)
Nausea and Vomiting	2 (13.3%)
Pale Complexion	2 (13.3%)
Cough	1 (6.7%)
Weak Voice	1 (6.7%)

Symptoms Open-ended Responses
Motivation to hygiene and time, deadlines
signs: - talking and speech (excess, taciturn, confused) - laughing (excess, inappropriate, absent) - emotional lability, extremes, unemotional - distorted perceptions (e.g. hyper-sensitivity to smells, noises, tastes, etc.) - eyes (dull, downcast, staring, unseeing)
tearfulness, impatience, poor eating habits (skipped meals or meals eaten on the run or late at night), poor self-care in general including quality of diet and fluid intake, and poor appointment time-keeping.
Acne, eczema, dermatitis, general skin irritations

i. Acupuncture points relevant to a treatment of stress

Acupuncture Point	Liver 3	Liver 2	Gallbladder 34	Gallbladder 20	Pericardium 6	Stomach 36	Spleen 6	Liver 13	Liver 14	Gallbladder 43
4/5 Count	13 (86.7%)	9 (60%)	13 (86.7%)	9 (60%)	13 (86.7%)	7 (46.7%)	8 (53.3%)	9 (60%)	7 (46.7%)	4 (26.7%)
Acupuncture Point	Governor Vessel 14	Governor Vessel 20	Large Intestine 11	Large Intestine 4	Bladder 18	Heart 7	Heart 5	Heart 3	Yin Tang	
4/5 Count	4 (26.7%)	13 (86.7%)	4 (26.7%)	10 (66.7%)	8 (53.3%)	12 (80%)	6 (40%)	6 (40%)	14 (93.3%	

Acupuncture Points Open-ended Responses
PC3 & PC7 PC9 & PC5 HT9 & HT4 HT3 & HT7 SI1 & SI3 SI2 & SI8 TE1 & TE3 TE2 & TE10
KI 6, Ki 2, KI 26, 25, 24; LR8, SJ 5, SJ3, GB 41, CV14, CV 15, CV 17, DU 24, GB 25, GB 38, ST 43,
ear, TE points, Tai Yang
too many possibilities to list them all, based on individual presentations and changes
Dozens, I'm afraid, depending on the differential diagnosis of stress responses in the individual patient (many on the GB channel, some Pericardium points, all the Extraordinary Vessels, all the Back Shu points...). But as points for primary stress, I find auricular points very useful, particularly those in the concha of the ear triggering the auricular branch of the vagus nerve, such as Thalamus and Point Zero; will occasionally do 3-4 points bilaterally from NADA protocol for destress. (Ear) Shen Men useful for ear seeds or magnets.
Auricular acupuncture points Relaxation Tranquilizer Master cerebral
Anmian
Ear Shenmen
Gb14, Gb41, LR4
GB21, 40, 41 BL14, 15, 19, 44, 45, 47, 62, 66 GV8, 9, 11, 12, 20, 24 CV6, 14, 15, 17...and too many more
BL 13,15 18 20 23 BL 42 44 46

7. Use of stress questionnaires in practice

Questionnaire	Perceived Stress Scale (PSS)	State-Trait Anxiety Scale (STAI)	Lipps Inventory for Stress Symptoms (LISS)	Measure Yourself Medical Outcome Profile (MYMOP)	Other	None of the above
"Yes" Count	2 (13.3%)	3 (20%)	1 (6.7%)	4 (26.7%)	1 (6.7%)	8 (53.3%)

Questionnaire Open-ended Response
VAS

8. Preferred number of treatments per week

Treatments per week	1	2	3
Count	3 (20%)	11 (73.3%)	1 (6.7%)

9. Preferred number of total treatments

Total number of treatments	1	4	6	8	10	12
Count	2 (13.3%)	1 (6.7%)	2 (13.3%)	5 (33.3%)	3 (20%)	2 (13.3%)

Appendix N: Complete Delphi Process Results, Round 2

For raw data in the form of excel spreadsheets, please contact the thesis writer (Dane Couter).

1. Zangfu relevant to a diagnosis of stress

Zangfu (Round 1 Feedback)	Liver (100%)	Kidney (80%)	Gall Bladder (40%)
Count	14 (93.3%)	10 (66.7%)	10 (66.7%)

2. The Heart zang

Question	The most popular zangfu answer from Round 1 that did not make threshold was Heart (73.3%). Does knowing this make you reconsider the Heart in a diagnosis of stress?	Keeping your response to the previous question in mind, Zheng et al. (2017) found that the most common diagnoses for stress, when based on self-reported symptoms, were Heart zangfu pathologies. Does this change your opinion about the relevance of the Heart zang in diagnosis for stress?	Heart (73.3%)
"Yes" Count	8 (53.3%)	7 (46.7%)	15 (100%)

3. Syndrome relevant to a diagnosis of stress

Syndrome (Round 1 Feedback)	Zangfu Disharmony/Mutual Insult (73.3%)
Count	15 (100%)

4. Symptom relevant to a diagnosis of stress, from the Zheng et al 2017

Symptom (Round 1 Feedback)	Anxious or Racing Thoughts (93.3%)	Constant Worrying (86.7%)	Irritability or Short Temper (100%)	Agitation or Inability to Relax (100%)	Insomnia or Other Sleep Disturbances (86.7%)
Count	15 (100%)	15 (100%)	14 (93.3%)	14 (93.3%)	14 (93.3%)

5. Awareness of questionnaires

Questionnaire	Perceived Stress Scale (PSS)	State-Trait Anxiety Scale (STAI)	Lipp's Inventory for Stress Symptoms (LISS)	Measure Yourself Medical Outcome Profile (MYMOP)
"Yes" Count	12 (80%)	12 (80%)	2 (13.3%)	8 (53.3%)

6. Symptoms relevant to a diagnosis of stress, from the PSS

Symptom (Round 1 Feedback)	Feeling Unable to Control Important Things in Life (80%)	Feeling Unable to Cope With All the Things You Must Do (86.7%)	Feeling Unable to Control Irritations in Life (80%)	Feeling Unable to Deal Well With Life Hassles (86.7%)
Count	14 (93.3%)	15 (100%)	15 (100%)	14 (93.3%)

7. Possible use of questionnaires in practice

Question	The previous four signs and symptoms were taken from the Perceived Stress Scale (PSS). The PSS is a clinical questionnaire which is a validated, global measure of stress using patient's self-reported symptoms. All symptoms from the PSS were included in Round 1 and reached agreement threshold. These items are included in Round 2 of the study (this survey). However, very few respondents (13.3%) from Round 1 indicated using the PSS in their clinical practice. Considering this information about the PSS, would you now consider incorporating the PSS into your clinical practice?	If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in practice?	If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in clinical practice (to assist in diagnosis)?	If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you use it as an outcome measure (to assess the effects of treatment and changes in stress over time)?
"Yes" Count	10 (66.7%)	11 (73.3%)	9 (66.7%)	11 (73.3%)

8. Acupuncture points relevant to a treatment of stress

Acupuncture point (Round 1 Feedback)	Liver 3 (86.7%)	Gallbladder 34 (86.7%)	Pericardium 6 (86.7%)	Governor Vessel 20 (86.7%)	Heart 7 (80%)	Yin Tang (93.3%)
Count	13 (86.7%)	10 (66.7%)	14 (93.3%)	11 (73.3%)	12 (80%)	14 (93.3%)

Appendix O: Delphi Process Survey, Round 2

A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels ROUND 2

My name is Dane Couter and I am a Masters (Research) student at the University of Technology Sydney (UTS). My supervisors are Dr Sean Walsh and Dr Shuai Zheng in the School of Life Science, Faculty of Science.

I am contacting you to invite you to participate in the second round (Round 2) of an online Delphi survey. No identifying information will be collected, and it will take approximately 10 minutes to complete.

The survey results will inform a proposed clinical trial using acupuncture to reduce perceived stress levels.

Please take your time to consider each question, all possible answers before selecting the response option you believe is the most accurate.

Thank you for your participation.

ONLINE SURVEY INFORMATION SHEET

[UTS APPROVAL NUMBER ETH21-6702] - A Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress Levels - ROUND 2

WHO IS CONDUCTING THIS RESEARCH?

My name is Dane Couter and I am a research student at the University of Technology Sydney (UTS). My supervisors are Dr Sean Walsh and Dr Shuai Zheng.

WHAT IS THE RESEARCH ABOUT?

The purpose of this research is to gain an expert consensus into the diagnosis and treatment of stress using acupuncture. The results will be used to develop a clinical trial.

You have been invited to participate because you may have expertise and been identified as an expert in this field and can help to shape future research.

Before you decide to participate in this research study, we need to ensure that it is ok for you to take part. This is ROUND 2 of a Delphi study. You must have already been involved in ROUND 1 to take part in this survey.

WHAT DOES MY PARTICIPATION INVOLVE?

Participation in this study is voluntary. It is completely your choice whether or not you decide to participate. If you participated in Round 1 then your response to Round 2 is critical. This is to ensure any consensus reliably builds on the same experts responding in both survey rounds.

If you decide to participate in Round 2, there is a short survey to complete online. This will be the second and final survey in the study. The Round 2 surveys ask questions about diagnosis and treatment of stress according to Chinese Medicine. This survey may take up to 10 minutes to complete.

You can change your mind at any time and stop completing the survey/s without consequences.

ARE THERE ANY RISKS/INCONVENIENCE?

We don't expect the Round 2 survey questions to cause any harm or discomfort. However, if you experience discomfort or distress answering the questions, please contact your family doctor or physician.

WHAT WILL HAPPEN TO INFORMATION ABOUT ME?

Access to the online questionnaire is via a weblink sent to you in an email. If the link is not activated for you, please contact me and I can resend the link to you. (I can be contacted at dane.couter@student.uts.edu.au). Submission of the online questionnaire/s is an indication of your consent to participate.

The results of this study will contribute to a research thesis, and shared through open access (public) scientific databases, including internet databases as publications. This will enable other researchers to use the data to investigate other important research questions about Chinese Medicine and stress. Results shared in this way will always be de-identified. There is no personal information collected that can identify you (e.g. your name, address, date of birth etc.), and all results are aggregated. This means only the summarised results are published, not individual responses.

AND

In accordance with relevant Australian and/or NSW Privacy laws, you have the right to request access to the information about you that is collected and stored by the research team (Please note that submitted survey responses in this study are completely anonymous and cannot be linked to participants. Only the aggregated responses are available). You also have the right to request that any information with which you disagree be corrected. Please inform the research team member named at the end of this document if you would like to access the information.

WHAT IF I HAVE ANY QUERIES OR CONCERNS?

If you have concerns about the research that you think I or my supervisor can help you with, please feel free to contact me: dane.couter@student.uts.edu.au, or sean.walsh@uts.edu.au

If you would like to talk to someone who is not connected with the research, you may contact the Research Ethics Officer on 02 9514 9772 or Research.ethics@uts.edu.au and quote this number ETH21-6702.

Did you respond to and complete the ROUND 1 of this study titled: Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived Stress?	◯ Yes ◯ No
How many years have you been practicing Chinese Medicine?	◯ < 5 ◯ 5-10 ◯ 11-15 ◯ 16-20 ◯ 20+
Please indicate how many patients you would normally treat in your practice presenting with stress per month	◯ < 5 ◯ 5-10 ◯ 11-20 ◯ 21-30 ◯ 31-40 ◯ 41+
What is your highest qualification?	◯ Diploma/Certificate ◯ Undergraduate (Bachelor's degree) ◯ Postgraduate (Masters) ◯ Postgraduate (Doctorate)
What is your highest qualification?	◯ Diploma/Certificate ◯ Undergraduate (Bachelor's degree) ◯ Postgraduate (Masters) ◯ Postgraduate (Doctorate)

Diagnosis

This is Round 2 a Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived stress.

Responses that made consesnus from ROUND 1 are returned for your review in ROUND 2. These results from ROUND 1show agreement levels expressed as a percentage. Only those responses that reached a pre-set consensus threshold of agreement are shown. The agreement level is shown in parenthesis for each item. For example, 'Liver (100%)' indicates that 100% of respondents indicated that the organ was relevant (a rating of four) or extremely relevant (a rating of five) on a five-point scale indicated in the questions below.

On the basis of results from ROUND 1 and your expert opinion, you are now being asked to respond to each question again. Your response can be the same, or it may differ from your response to ROUND 1.

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following zangfu to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Liver (100%)	○	○	○	○	○
Kidney (80%)	○	○	○	○	○
Gall Bladder (40%)	○	○	○	○	○

The most popular zangfu answer from Round 1 that did not make threshold was Heart (73.3%). Does knowing this make you reconsider the Heart in a diagnosis of stress?

○ Yes
○ No

Keeping your response to the previous question in mind, Zheng et al. (2017) found that the most common diagnoses for stress, when based on self-reported symptoms, were Heart zangfu pathologies.

Does this change your opinion about the relevance of the Heart zang in diagnosis for stress?

○ Yes
○ No

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following zangfu to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1: Not relvant at all	2	3	4	5: Extremely relevant
Heart (73.3%)	○	○	○	○	○

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following syndromes to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1-Not relevant at all	2	3	4	5- Extremely relevant

Zangfu Disharmony/Mutual Insult (73.3%)	○	○	○	○	○

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following signs and symptoms to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Anxious or Racing Thoughts (93.3%)	○	○	○	○	○
Constant Worrying (86.6%)	○	○	○	○	○
Irritablility or Short Temper (100%)	○	○	○	○	○
Agitation or Inability to Relax (100%)	○	○	○	○	○
Insomnia or Other Sleep Disturbances (86.6%)	○	○	○	○	○

When thinking about your response to the previous questions (symptoms), did you consider the sex of the patient? (Sex is referring to the patient's sex assigned at their birth)	○ Yes ○ No
When thinking about your response to the previous questions (symptoms), did you consider the patient's self-defined gender identity? (Gender refers to the norms, behaviours and roles associated with socially constructed identity.)	○ Yes ○ No
In your opinion, would you expect to see different symptoms for stress presenting in patients of different sexes (for example, different symptoms in males vs females)?	○ Yes ○ No
In your opinion, would you expect to see different symptoms for stress presenting in patients of different genders (for example, different symptoms in patients identifying as male vs female)?	○ Yes ○ No

ROUND 1 of this study included a question about the use of five (5) stress-related questionnaires. Please indicate whether you had previously been aware of the following specific stress-related questionnaires:

	Yes	No
Perceived Stress Scale (PSS)	○	○
State-Trait Anxiety Scale (STAI)	○	○
Lipp's Inventory for Stress Symptoms (LISS)	○	○

Measure Yourself Medical Outcome Profile (MYMOP)	○	○

Please indicate on the following scale of 1-5 how clinically relevant you would consider the following signs and symptoms to a diagnosis of stress, where 1=not relevant at all, and 5=extremely relevant:

	1: Not relvant at all	2	3	4	5: Extremely relevant
Feeling Unable to Control Important Things in Life (80%)	○	○	○	○	○
Feeling Unable to Cope With All the Things You Must Do (86.6%)	○	○	○	○	○
Feeling Unable to Control Irritations in Life (80%)	○	○	○	○	○
Feeling Unable to Deal Well With Life Hassles (86.6%)	○	○	○	○	○

The previous four signs and symptoms were taken from the Perceived Stress Scale (PSS). The PSS is a clinical questionnaire which is a validated, global measure of stress using patient's self-reported symptoms. All symptoms from the PSS were included in Round 1 and reached agreement threshold. These items are included in Round 2 of the study (this survey). However, very few respondents (13.3%) from Round 1 indicated using the PSS in their clinical practice.

Considering this information about the PSS, would you now consider incorporating the PSS into your clinical practice?

○ Yes
○ No

If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in practice?

○ Yes
○ No

If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you consider using it in clinical practice (to assist in diagnosis)?

○ Yes
○ No

If you were aware of a Chinese Medicine-based clinical questionnaire about stress would you use it as an outcome measure (to assess the effects of treatment and changes in stress over time)?

○ Yes
○ No

Please list any pulse qualities that you beleive would be clinically relevant to a diagnosis of stress.

_____

Treatment Protocols

This is a Delphi Process to Inform a Clinical Trial Using Acupuncture to Reduce Perceived stress ROUND 2.

Responses that made threshold from ROUND 1 are returned for ROUND 2. Results from ROUND 1 as a percentage of responses meeting threshold are shown in parenthesis for each item, for example, Liver (100%) indicates that 100% of respondents indicated a 4 or 5 on a 5 point scale.

On the basis of results from ROUND 1 and your own opinion, you are asked to respond to each question again. Your response can be the same, or a different response to ROUND 1.

Please indicate in the following scale of 1-5 how clinically relevant you would consider the following acupuncture points to a treatment of stress, where 1 = not relevant at all, and 5 = extremely relevant:

	1:Not relevant at all	2	3	4	5: Extremely Relevant
Liver 3 (86.6%)	○	○	○	○	○
Gallbladder 34 (86.6%)	○	○	○	○	○
Pericardium 6 (86.6%)	○	○	○	○	○
Governor Vessel 20 (86.6%)	○	○	○	○	○
Heart 7 (80%)	○	○	○	○	○
Yin Tang (93.3%)	○	○	○	○	○

Appendix P: Modified Clinical Trial Protocol

SPIRIT Protocol: Students, Acupuncture and Stress – A feasibility study investigating the impact of high and low frequency acupuncture dosage in overall perceived stress changes in tertiary education students

(SAS Study)

1. Study Details

Trial Identifying Number: Australian New Zealand Clinical Trials Registry (ANZCTR) registration number ACTRN12621000598886

Version Identifier: 2.0

1.1 Funded by:
Internal UTS Faculty of Science Funding (HDR grant $5000)

1.2 Study Sponsor:
University of Technology Sydney (UTS)

1.2 Principal Investigator:
Dane Couter (Master's in candidature), School of Life Sciences, UTS

1.4 Co-investigators
Dr Sean Walsh (supervisor), Dr Shuai Zheng (co-supervisor)

1.5 Protocol Contributors

- Mr Dane Couter, MSc (in candidature), registered health care practitioner (Ahpra:CMBA)
- Dr Sean Walsh, Supervisor and Senior Lecturer, registered health care practitioner (Ahpra:CMBA)
- Dr Shohreh Razavy, UTS, registered health care practitioner (Ahpra:CMBA)
- Dr Yew Kian Loyeung, External supervisor, Parexel International.

1.6 Contact for public queries:

Dane Couter

Dane.Couter@uts.edu.au

- **Primary**: University of Technology Sydney, PO Box 123, Broadway NSW 2007, Australia

Contact for scientific queries: **Dane Couter**

2. Introduction

2.1 Background and Rationale

Stress is “mental, emotional or physical strain or tension” (*Collins Dictionary*, 2018). The term is descriptive, applied to daily life hassles through to major trauma and has both beneficial and pathogenic connotations. For example, the body’s response to an unexpected event induces a rise in blood pressure and heart rate to assist with an affective response, yet chronic elevation of heart rate and blood pressure can over time lead to stroke and heart disease (McEwen, 2008). Concerning to health and performance in day-to-day activities is the acute stress response that remains unmanaged, and which contributes to a chronic (and pathological) stress response forming often associated with anxiety. This pathological stress is a “process in which environmental demands tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease” (Cohen et al., 1997). This includes increased cortisol, supressed immune function and impact on quality of life and performance.

While many groups of society, for a range of reasons and circumstances, may experience on-going stress, of concern for this study is the impact of stress on students. Recent media reports highlight the impact of stress affecting mental health leading to increased rates of suicide and underreporting of mental health on medical students (as an example) (Rotenstein et al., 2016). Stress additionally has a negative impact on student grades and retention; stress with transition into and with tertiary education are associated with raised university attrition rates (Pritchard & Wilson, 2003). More recently contributing to student stress is the COVID-19 pandemic which has caused individual and community increases in stress- and anxiety-related symptoms (Taylor et al., 2020); up to 70% of university students have reported stress at moderate to severe levels during the pandemic and its associated limits to personal liberties (Husky et al., 2020).

However, there is no single approach to dealing with stress impacts on tertiary students. That is, students are not a homogenous group; differences in age, sex, gender, culture and socio-economic factors influencing both resilience and sensitivity to a stress response forming. In addition to academic stress, tertiary students report financial stress and stress struggling to balance study with extra-curricular commitments (Engle, 2008). That is, competing commitments between study and with work, and living in a broad range of financial situations; all contribute to students’ perceived stress impacts in levels of education. Consequently, stress appears endemic in the tertiary student population, apparent from school-leavers to postgraduate student (Department of Education and Training, 2018), and across study modes (part- and full-time) (Crisp et al., 2016).

The National Tertiary Student Wellbeing Survey reported that 83.2% of 16-25 year olds and 79.8% 26+ year olds found their studies were affected by feeling stressed (Crisp et al., 2016). Research has

identified a strong relationship between extracurricular stresses, financial stress and probability of graduation: that higher stress has a negative impact on academic performance (Adams et al., 2016; Engle, 2008; Trombitas, 2012). From a health perspective, long term stress negatively impacts students' mental health and increases the likelihood of developing mental illness, particularly depression and anxiety (Susan et al., 2013). Concerning is that one in four tertiary students have experienced suicidal thoughts or behaviours (Mortier et al., 2018).

Acupuncture has long been used by university students for stress; their views differ from more established (and biased perceptions) of complementary therapies as a threat to public health, instead viewing these as part of an integrative health system meeting diverse community needs, including the students' own (Ellis et al. 2006; Hasan et al. 2011; Amadera et al. 2010). Acupuncture variants such as auricular acupuncture and electro-acupuncture have been trialed with students to reduce exam stress (Klausenitz et al. 2018), anxiety (Vieira et al. 2018) and stress-related symptoms (Dias, Pagnin & Pagnin 2012; Dias et al. 2014).

A literature review of the clinical and biomedical databases with a focus on acupuncture for stress generally, underscored however the scarcity of evidence regarding filiform body acupuncture, (independent of specific conditions and as observed over time), with only 11 studies identified (See chapter 2). Only one had a focus on students. Of the studies identified, most tested acupuncture using a neuro-modulatory mechanism hypothesis, using needles at specific body sites. Patient perceived change in stress post-treatment and over time were assessed with standardised outcome measures (Kwong & Yiu, 2010; Middlekauff et al., 2002; Middlekauff et al., 2001); while two studies were actually two different reports of the same study: one reporting on acupuncture for treating stress (Huang et al. 2011) and the other reporting on the use of salivary cortisol in acupuncture studies (Huang et al., 2011; W. Huang et al., 2012).

The only study featuring a student population and treatment of stress (Schroeder et al. 2017) reported promising results. The results indicate that 12 treatments administered once per week had statistically significant reduction in stress levels of students as measured by mean PSS14 scores. The study did however experience high attrition in the control group, which the authors attributed to the study length (approx. 12 weeks) and the inconvenience of attending treatment on campus during holidays, making long-term, low treatment frequency acupuncture, a less than feasible approach for this cohort. The authors also pointed out the difficulty of applying the conventional scientific method to acupuncture, particularly in terms of controls used and uniform acupuncture point prescriptions. Further, they indicated that they would have preferred to administer the acupuncture treatments twice pre week rather than once, although they omit any evidence to support the difference in acupuncture dosage.

2.2 Purpose of the study

At present, acupuncture is being utilised by students to assist with their physical and psychological perceptions of stress impacts, including at UTS. The UTS Chinese Medicine Clinic (located in Building 4, Broadway Campus), is a busy clinic with between 6000-7000 patient contacts per year, has a high tertiary education student patient cohort often reporting perceived stress impacting their quality of life and study performance (Meier et al., 2017), in addition to accompanying symptoms of sleep disturbances, reduced motivation, tiredness, headaches and poor concentration.

There is insufficient information regarding acupuncture dosage treatment frequency and potential changes in perceived stress levels in tertiary education students. Further study is required to determine the feasibility and acceptability of acupuncture of different treatment frequencies for stress in tertiary education students. If an acceptable and feasible intervention, it will inform a larger scale cohort study.

Consequently, the study may help inform clinical decision making and perhaps more appropriately target an effective therapeutic acupuncture treatment dosage (White et al. 2008), adding further to an evidence-base; it is a minimally invasive technique with potential benefits for student (and others) well-being, while informing best current clinical practice for acupuncture. It draws on a more medicalized understanding of acupuncture as a neuro-modulatory technique (Hui, Liu & Makris 2000; Napadow, Makris & Liu 2005; White et al. 2008).

3. Objectives

3.1. Hypothesis

There is a mean difference of perceived stress (PSS14 scores) among stressed students receiving an acupuncture dosage at high treatment frequency compared to students receiving an acupuncture dosage at low treatment frequency, namely that the higher treatment frequency will have a greater effect. Further that certain characteristics are a predictor of perceived stress changes following acupuncture dosage in tertiary students.

3.2 Principle Objective

To investigate the impact of high and low frequency acupuncture dosage* in overall perceived stress from baseline and at week 12 in tertiary education student participants.

The study proposes comparing high frequency acupuncture dosage (two treatments per week for two weeks) versus low frequency acupuncture dosage (one treatment per week for four weeks).

3.3 Secondary Objective

- To observe the magnitude and rate of change in perceived participant stress scores from baseline, and at each treatment (treatments 1-4), and at two (2) weeks and four (weeks) after

the last treatment (treatment 4) within and between the high and low frequency acupuncture dosage groups.

- Explore participant socio-demographic responses (such as gender) and stress type characteristics and their relationship to high and low frequency acupuncture dosage response as measured by changes in perceived stress reported using the PSS14.
- Gather participant feedback on perceptions on acupuncture dosage treatment frequency to inform a larger cohort study design (see Participant Final Questionnaire), including safety data.

4. Trial Design

This is a 12-week phase II, feasibility study - designed as a two arm, randomised study. There are two arms: high frequency acupuncture treatment and low frequency acupuncture treatment. Trial methodology has been informed by the literature review (acupuncture point selection, number of treatments and treatment frequency) and practitioner clinical experience. The study investigates the difference (if any) between high or low frequency acupuncture dosage interventions and a participant's perceived stress levels (using the PSS14) before, during and post-treatment intervention. In addition, the study investigates feasibility and acceptability of the treatment and frequency difference by a tertiary student cohort.

All participants will continue with usual standard of care or their usual health and well-being practices - there is not modification nor request to do so as part of this trial.

4.1 Methods: Participants, Interventions and Outcomes

4.1.1 Study Setting

The study will be carried out on campus at the University of Technology Sydney (UTS) Chinese Medicine Clinic. The clinic is located on the corner of Thomas and Harris Streets at the Broadway campus of the UTS (Building 4). It is an Australian health practitioner regulation agency (Ahpra) accredited teaching and research facility for acupuncture.

4.1.2 Participants

Participants will be recruited from the student population at the University of Technology Sydney.

4.1.3 Eligibility criteria

Inclusion Criteria

- Currently enrolled as a tertiary student at UTS
- Aged 18 and over
- Able to provide informed consent
- Self-identify as 'stressed'

Exclusion Criteria

- Bleeding disorders or any disorder that prohibits the use of acupuncture or certain points specified in this intervention;
- Use of prescribed anti-coagulant medication (such as warfarin) that may interfere with blood clotting
- Use of acupuncture in the 14 days prior to the intervention
- Pregnancy
- Needle phobia
- Unwilling to complete outcome measures or attend the clinic for treatment
- Suicidal ideation*

Participants can withdraw from the study at any time.

*Please refer to the distress protocol regarding suicidal ideation (the protocol was prepared in collaboration with the UTS Student Services: Brett Smout and Sarah Lok), also see below and inserted here in the protocol at the request of Student Services (Boxed).

Participants who report thoughts of suicide or self-harm through the online questionnaire or intake form will be advised immediately:

If you require emergency assistance, contact the Police and/or request an Ambulance by dialling 000.

You may also request assistance by contacting **24-hour crisis phone counselling**:

- Lifeline Counselling Service: 13 11 14
- Suicide Call Back Service: 1300 659 467
- Beyondblue Support Service: 1300 22 4636
- Kids Helpline: 1800 55 1800
- NSW Mental Health Line: 1800 011 511

Please contact UTS student services on (02) **9514 1177 or email at** student.services@uts.edu.au **if you wish to speak to a counsellor or make an appointment.**

Please indicate if you wish to withdraw from the current trial.

4.2 Intervention

202 participants will be recruited and first take part in a waiting list control group, then randomised into one of two groups :

- High frequency: 4 interventions over 2 weeks (HF)
- Low frequency: 4 interventions over 4 weeks (LF)

All interventions will be performed by individual/s with a Bachelor's degree in Traditional Chinese Medicine/Acupuncture, have 10 years clinical experience, and registered health care practitioners with the Chinese Medicine Board of Australia (Ahpra:CMBA).

Bias is controlled using blinding and participant allocation concealment, including method of randomisation, from the individuals delivering the acupuncture.

4.2.1 Waiting List Control Group

Each participant will be asked to fill out the PSS-14 once per week for four weeks before beginning acupuncture interventions to establish a baseline measure.

The wait list control lead-in length of four weeks was chosen to smooth out the perceived stress variation that might happen due to transient events, and hence calculate a mean score of perceived stress as a better reflection of a baseline measure.

4.2.2 Intervention 1 – High Frequency

The patient will be asked to lie supine (face up) on a treatment table. There are four acupuncture points being needled bilaterally, involving a total of 8 needles. The points and order of insertion are: Liver 3, Pericardium 6, Heart 7 and Yin Tang. The needle will be manipulated using a lifting thrusting and rotation method immediately after insertion for a minimum of 10 seconds to illicit a sensation of *de qi* (numbness, heaviness, dull ache) is reported. The needles will be retained for 20 minutes. The intervention will be performed twice a week for two weeks totalling four treatments.

All needles used in the study (needle brand 'Balance') are registered as a Medical Device (Class IIa) with the TGA. Needles will be removed in the same order as insertion and immediately placed in a Sharps container.

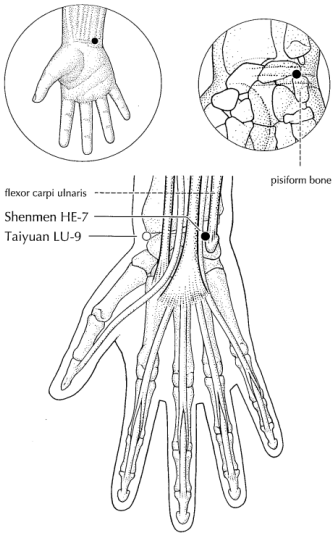
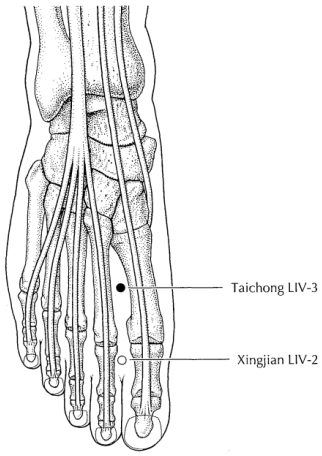
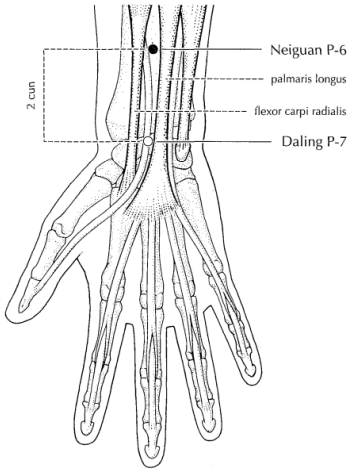
As the acupuncture points are located on the forehead and distal portions of the arms and legs, no disrobing of the participants is anticipated other than removal of footwear.

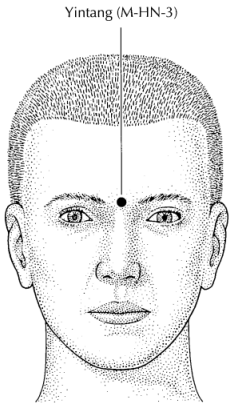
4.2.3 Intervention 2 – Low Frequency

As for high frequency but: The intervention will be performed once per week for four weeks for a total of four interventions.

4.2.4 Description of Acupuncture Point Locations

The location, needling angle and needling depth will be as follows (Deadman & Al-Khafaji, 2001):

Heart 7  **Figure 1**: Large Heart 7	Location: At the wrist joint, on the radial side of flexor carpi ulnaris, in the depression at the proximal border of the pisiform bone Needling Angle: Perpendicular Needling Depth: 0.5 cun Needle Type: Balance, 0.18 x 15mm
Liver 3  **Figure 2:** Liver 3	Location: On the dorsum of the foot, in the hollow distal to the junction of the first and second metatarsal bones. Needling Angle: Perpendicular Needling Depth: 0.5 cun Needle Type: Balance, 0.20 x 30mm
Pericardium 6  **Figure 3:** Pericardium 6	Location: On the flexor aspect of the forearm, 2 cun proximal to Daling P-7, between the tendons of palmaris longus and flexor carpi radialis. Needling Angle: Perpendicular Needling Depth: 0.5 cun Needle Type: Balance, 0.18 x 15mm

Yin Tang  **Figure 4:** Yin Tang	Location: At the glabella, at the midpoint between the medial extremities of the eyebrows. Needling Angle: In an inferior direction Needling Depth: 0.3 cun Needle Type: Balance, 0.20 x 30mm

4.3 Outcomes (endpoints)

The primary outcome is a patient reported outcome measure – the PSS14 (see appendix E). The PSS14 is a self-reported measure which assesses the degree to which the respondent perceives stress specific to their life situation within the last month. That is, it is not diagnostic, but rather about respondent perceptions about how un-predictable, uncontrollable, and overloaded individuals find their life circumstances. There are 14 items, rated using a 5-point Likert scale ranging from 'Never' (0) to 'Very Often' (4). Scoring is a mixed of actual and reverse scoring each item to obtain a score in the range of 0-56.

The mean difference in PSS-14 scores will be compared between pre and post intervention for differences within each acupuncture dosage treatment-frequency group and also between the two groups. The PSS14 has been shown to be a reliable measure of perceived stress (Cohen et al., 1983). It has been trialled previously with a student cohort (Lee 2012), in an Australian population context (Ribeiro et al 2020), and in different completion modes (by mail, in-person, over the phone) Additionally, the relationship between changes in perceived stress as measured by PSS-14 scores; and different causes/types of stress as measured by 10-point scales in the Additional Stress Questionnaire (ASQ) will be analysed (see appendix F).

The socio-demographic data will provide descriptive detail and assist with further identification of characteristics that may or may not have influenced acupuncture dosage and treatment-frequency related changes in stress perceptions within a tertiary student framing context (see appendix G). This includes known poor adaptive coping responses to stress (smoking, drinking, exercise and diet) to provide a framing context specific to individual's entering the study.

The Participant Final Questionnaire comprised 4 questions with 10-point Likert Scale responses, and one open question for feedback on study feasibility.

The Credibility and Expectancy Questionnaire (CEQ) is used to measure treatment expectancy and rationale credibility to allow for possible differences in participants' perception of the intervention and how that may impact observed outcomes (Devilly & Borkovec, 2000). The QEC consists of four questions using a Likert Scale response from zero to six (see Appendix I).

Secondary outcomes are ASQ, PFQ and CEQ scores; and socio-demographic data as it pertains to PSS-14 scores.

4.4 Participant Timeline

Participants who expressed an interest and after conversation with a member of the study team, will be emailed an invite and the PIS, initial consent form for reading – and to organise a meeting for eligibility screening. With successful screening and signing of the consent form, the sociodemographic survey is then completed (approximately 10 minutes).

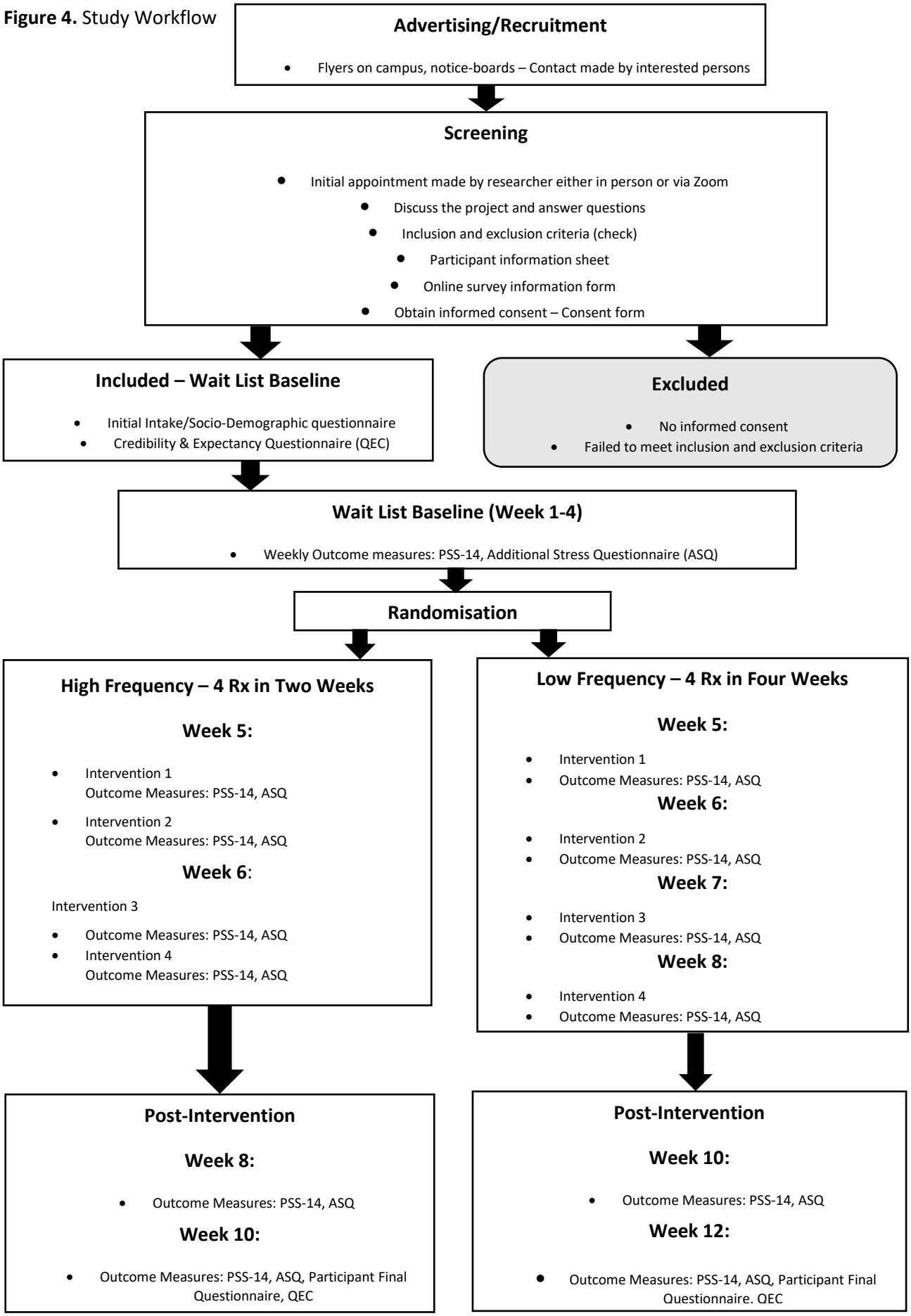
Participants will then go into the wait-list control and receive an email invite to the online survey (PSS14 and Additional Stress Questionnaire (ASQ)) weekly, and for an additional three weeks to the end of the wait list control period.

Participants will receive a phone call organising the treatment schedule in Week 4 of the waiting list control period.

After each treatment, an email invite will immediately be sent to complete the online survey (PSS14, ASQ). Once treatments finish, an email will be sent again at week 2 post treatment and again at week 4 to complete the outcome measures (PSS14 and ASQ). Week 4 will also include the Participant Final Questionnaire.

Study flowchart below.

Figure 4. Study Workflow



4.5 Sample Size

The sample size will be 86 participants, randomised into two arms in a 1:1 ratio. This sample size was determined to detect a 20% change (mean PSS14 scores of sham versus verum acupuncture), based on a previous trial featuring stress, acupuncture and students (Schroeder et al., 2017).

4.6 Recruitment

The targeted population are university students attending the UTS. Recruitment will take place on UTS city campus using fliers and posters placed in common areas and on UTS public notice boards. A notice will be placed on the Chinese medicine clinic website that informs about research projects (https://www.uts.edu.au/about/faculty-science/chinese-medicine-clinic/our-research), and in the clinics external facing notice boards (Harris Street Foyer, Building 2).

5. Methods: Assignment of interventions

Intervention Sequence Allocation

Each participant will be assigned a numerical code, and randomised into the HF or LF acupuncture intervention group using online randomisation software http://www.graphpad.com/quickcalcs/index.cfm

The randomisation software will be used by a third party to allocate participants

6. Methods: Data Collection, Management and Analysis

6.1 Data Collection

Data is collected online via an email invite sent to an online survey (REDCAP). Initial socio-demographic information will be taken once. Primary and secondary outcome measures will be taken at the initial recruitment stage, weekly during the 4-week waiting list control group, immediately after each intervention and 2 and 4 weeks post final intervention.

Participants will be emailed reminder notices prior to appointments to improve retention.

Participants who chose to withdraw from the study will be asked if their incomplete data set can be retained and used for analysis.

6.2 Data Management

Data management will be according to the *Research Data Management Plan* on UTS Stash.

Data will be entered online by the trial participants using the online survey REDCAP after each treatment. The data will be numerically tagged and exported to Excel and SPSS for analysis. All data will be kept in secure electronic form with back up data on hard-drive, external hard-drives, and OneDrive. Data will only be accessible to the research team.

6.3 Statistical Methods

Several statistical tests will be used.

Baseline characterises of participants will be investigated using both t-test and chi square test.

If data meet normality assumptions the following statistical tests will be used for different objectives.

- Repeated measure ANOVA→ to investigate mean changes of stress across different intervention measurement time points (I, 2, 3, and 4) in each study group.
- Paired t-test→ to compare baseline measurement with the end of treatment measurement in each study group
- Independent t-test→ to compare mean differences at each measurement time across the inventions (HF/ LF).
- Pearson correlation → to investigate if there is any relationship between intensity of the perceived stress and other variables from the socio-demographic questionnaire.
- Spearman correlation→ to investigate robustness of the two scale, PSS-14 & ASQ, used to measure stress.

7. Methods: Monitoring

Data Monitoring

There will be no requirement for a data monitoring committee as this is a small-scale feasibility study and held over a short duration. However, a member of the research team (eg, Dr Sean Walsh), will perform regular entry checks to ensure the data input is accurate and collected at the designated time-points. Data will be exported via software; no data entry needs are anticipated, but exported data will be checked against original data for accuracy before analysis.

Harms

Adverse events will be noted immediately after each intervention when required using the Adverse event reporting form. Any severe adverse events will cause the interventions to be paused until any possible cause is determined. Participants will be asked to list any adverse events that appear between weekly appointments.

During treatment, there may be slight discomfort on needle insertion (sting), however pain is rare, and will be documented by the research practitioner along with any other adverse events. This data will be reviewed periodically and reported in the final document. Should any findings arise concerning the participants health, physical and/or emotional it will be brought to the attention of the investigation team.

In particular, a detailed distress protocol has been prepared with the UTS Student Services where a student's level of perceived stress is having potential harm to their quality of life or impacting in adverse ways as reported by them to the researcher, then a referral call will be made to Student Services. This is noted in the PIS and Consent form. (Please see the distress protocol for full detail)

All acupuncture follows the practice guidance by the Chinese Medicine Board Australia (Ahpra: CMBA) and with reference to the document *Infection Prevention and Control Guidelines for Acupuncture* (CMBA 2013), and further to the NHMRC's *Australian guidelines for the prevention and control of infection in healthcare* (NHMRC Guidelines).

For acupuncture, safe clinical practice for the following rare incidents include:

- *Stuck or bent needle:* For muscle spasms, the practitioner will wait a few minutes to allow the muscle to relax. This can be assisted by applying pressure or warmth to the area. If due to patient movement, the practitioner can realign the body to the original position before removing the needle.
- *Broken needle in situ:* Broken above or at skin level, gentle pressure can be applied to the surrounding skin and the needle removed with tweezers or forceps. Broken deep in the tissue the area will be marked with a circle, immobilised and medical attention provided.
- *Needle stick injury:* Needle removed, and the area washed with soap and water, following UTS blood and body fluid exposure procedures. Appropriate medical care and assessment will be provided.
- *Slight bleeding:* Pressure will be applied to the area to stop the bleeding and prevent haematoma.
- *Fainting or dizziness:* Needles will be withdrawn, and the patient will be placed lying down with their legs raised. If there is no response, then first aid with be applied followed by medical assistance.

In the cases of a severe adverse event during treatment the needles will be removed, first aid applied and medical attention provided. In the cases of a severe adverse event between treatments, appointments will cease, medical attention provided, and the potential causality will be determined, further to reporting event to UTS Ethics.

Auditing

Trial procedures will be audited before trial commencement. Meetings will be scheduled after the first participant to check data entry, and at intermittent time points throughout the trial to ensure proper actions have been taken.

8. Ethics and Dissemination

Research Ethics Approval

This trial, SPIRIT protocol and all appendices were approved by UTS Human Research Ethics Committee (HREC), approval number ETH20-5098.

Protocol Amendments

Any large-scale amendments, such as amended study design, objectives or procedures will be reviewed by UTS HREC committee.

Any minor amendments will be agreed on by the trial team, reported to UTS Research and be reported in all post-trial publications.

Consent or Assent

Potential trial participants expressing an interest from advertising, will be emailed an invite to the study, the PIS, an online consent form and details about the research, including normal acupuncture procedures

A baseline meeting (a minimum of one week before the initial baseline PPS14 measure) will take place with the investigator to confirm the participant has a clear understanding of the research and its requirements, complete a finalized check on the inclusion/exclusion criteria, and present the written consent and assent documentation.

Finally, the investigator will further enquire at the initial intervention about any queries or difficulties the participant may have, and confirm the participant's consent to the acupuncture intervention.

Confidentiality

Depersonalised information, linking codes and all gathered data will be stored electronically in a password protected folder in a central location, on an external hard-drive, and on OneDrive. Linking codes will be held separately from data. The folders will only be accessible to the researchers.

Online data will be stored with REDCAP before being exported.

Declaration of Interest

The principle investigators declare no potential conflicts of interest with respect to the research of this trial.

Access to Data

The principle investigators will have sole access to the final trial dataset. A third party may assist with the analysis modelling, but will only have access to depersonalised/anonymised/de-identified data only.

Ancillary and Post-trial Care

Further care needed will be dealt with on a case by case basis, as no serious adverse effects are expected. Possible actions will include referral to UTS Student Services for counselling services.

Dissemination Policy

There are no restrictions on publication. A paper/s will be submitted to an appropriate peer-reviewed journal after final data analysis for publication. Study participants will be invited to receive study results at this time. Additionally, the study protocol may also be published at this time.

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