The Association Between Ambulatory Blood Pressure Monitoring with Depression, Anxiety and Hostility: A Systematic Review and Meta-Analysis

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Abstract

Elevated systolic blood pressure is the leading cause of death and disability worldwide. There is a growing body of research suggesting an association between hypertension and negative emotions including depression, anxiety and hostility. Hypertension is the main attributable risk factor for cardiovascular disease and is most accurately evaluated using ambulatory blood pressure monitoring. A systematic review and meta-analysis were conducted to evaluate the magnitude of the relationship between depression, anxiety and hostility with systolic and diastolic blood pressures.

Using PubMed, PsycINFO and Scopus, 30 independent eligible studies were identified comprising of 3465 participants. Studies were qualitatively analysed before a random-effects model was used to calculate the weighted standardized mean differences between groups for high versus low levels of depression, anxiety and hostility. The significance of the standardized means was assessed by calculating 95% confidence intervals and heterogeneity.

Significant weak positive effects were obtained for the association between depression and higher levels of both systolic (d= 0.22) and diastolic blood pressure (d= 0.25), whilst similar effects were found for the association between hostility and systolic (d= 0.28) and diastolic blood pressure (d= 0.26). No significant effects were found for anxiety possibly due to high levels of heterogeneity found.

The findings indicate that high levels of depression and hostility are associated with increased blood pressure. There is a need for future research to clarify the strength and causality of these relationships. The results obtained may have significant implications for the diagnosis and management of hypertension and consequent worldwide burden of cardiovascular disease.

Declaration

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Frank Connolly

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Chapter 1

Introduction

1.1 Blood pressure: definition and measurement

Blood pressure can be defined as the product of cardiac output from the heart and total peripheral vascular resistance (Mayet & Hughes, 2003). Simply put, blood pressure can be interpreted as being the pressure exerted by the blood within the arteries. It is assessed by measuring the pressure in in the blood vessels when the hearts beats, known as systolic blood pressure, or it may be assessed by measuring the pressure in the blood vessels between heart beats, commonly referred to as diastolic blood pressure. In healthy individuals, systolic blood pressure should fall within 90-120 millimetres of mercury (mmHg) whilst a normal diastolic blood pressure range falls between 60-80 mmHg. Blood pressure found to be above these ranges represents an increased risk of developing hypertension (high blood pressure) which is clinically diagnosed where systolic blood pressure is above 130 mmHg for systolic and/or 90 mmHg for diastolic recordings (American Heart Association, 2018).

Although there are several methods for measuring systolic and diastolic blood pressure, the most commonly used approach has remained virtually unchanged since the invention of the sphygmomanometer in 1896. Specifically, this method utilises a standard cuff wrapped around a person's upper arm from which the cuff will then inflate until the blood flow in the main artery in the arm ceases. The cuff will then steadily deflate allowing blood flow back into the arm as per normal. The medical professional (typically a doctor or nurse) performing this procedure will then identify signals by listening through a stethoscope or by utilising an automated device. In recent times, the accuracy of this conventional, often clinic or office-based approach has come under scrutiny, particularly in relation to individuals with systolic blood pressure ranging between 120-159 mmHg and diastolic blood pressure between 80-99 mmHg (ranging from pre-hypertensive to hypertensive) (Picone et al., 2017). The accurate

assessment of an individual's blood pressure is vital due the consequences of misdiagnosing them with either high or low blood pressure. A misdiagnosis of low blood pressure may result in a missed opportunity to lower a person's risk of cardiovascular disease (such as stroke, myocardial infarction or kidney disease), whilst a misdiagnosis of high blood pressure may lead to them being prescribed with unnecessary medications. Therefore, it is extremely important that a reliable and accurate approach of measuring blood pressure is utilised.

Ambulatory blood pressure monitoring is the most valid and accurate tool for the diagnosis and treatment of high blood pressure (Otsuka et al., 2004). This form of monitoring records a person's blood pressure at regular intervals (e.g. every 15-45 minutes) for a period of approximately 24-hours. The procedure involves a portable monitor which is attached to a belt around the patient's waste and connects to a standard cuff on their arm. The monitor will automatically detect the individual's systolic and diastolic blood pressure, and heart rate at the prescribed interval using an oscillometric technique. After the 24-hour period has elapsed, the device is connected to a software package which subsequently creates a report for the obtained systolic, diastolic and heart rate data relating to 24-hour, daytime, night-time, sleep and awake recordings. As a consequence, the comprehensive data obtained provides a more realistic representation of an individual's blood pressure during their daily lives. Unlike the conventional clinic approach, ambulatory monitoring reduces the risk of misdiagnosis of hypertension due to phenomena such as the 'white-coat' effect whereby a person's blood pressure becomes higher when taken in a clinical or medical setting rather than at home (Reynolds et al., 2015). Furthermore, ambulatory monitoring is an effective means of establishing which hypertensive patients' blood pressure does not dip as expected. Nocturnal hypertensive 'non-dippers' tend to have a worse prognosis than other hypertensive patients whose blood pressure dips overnight, in terms of cardiovascular conditions and increased risk of end organ damage (Shimada et al., 1992). The ambulatory approach can also be useful in

identifying the lifestyle issues which cause an increase in blood pressure (such as smoking or stress) and evaluating blood pressure during treatment stages (such as the testing of new medication). Lastly, ambulatory monitoring ensures detailed records are kept which can used for long-term follow-up. Despite the benefits of ambulatory monitoring, the conventional method is still more readily utilised (Peixoto, 2015).

1.2 Hypertension: causes and prevalence

Hypertension (also referred to as high blood pressure) is one of the most prevalent conditions worldwide and is identified as one of the most prominent causes of death and disability (second only to childhood malnutrition) (Global Burden of Disease Study, 2017). It is well-established that hypertension is the main attributable risk factor for cardiovascular disease and stroke (Global Burden of Disease Study, 2017). Whilst normotensive individuals evince good blood flow within their vessels, significant vascular changes occur within the vessels of persons with high blood pressure. Initially, a build-up of atherosclerotic plaque will result in the thickening of the arterial vessel wall and vascular resistance. This is followed by an inflammatory response, promoting further plaque build-up, and the development of hypertrophy. These vascular changes result in the narrowing of the lumen and the build-up of pressure such that hypertension occurs (Mayet & Hughes, 2003). Recent data published by The Heart Foundation (2018) provided that nearly one third of all Australians above the age of 18 years (approximately six million people) had experienced high blood pressure during the period of 2013 to 2014. It further outlined that two thirds of the people with high blood pressure (approximately four million people) had unmanaged or uncontrolled blood pressure meaning that they were not taking medication or following any health plan focused on alleviating their condition. Whilst this data outlines that a significant proportion of the Australian population has hypertension, it remains relatively unknown the proportion of people who have pre-hypertension (between 120-140mmHg for systolic and 80-90 mmHg for diastolic pressure).

Research conducted in the USA estimates that one third of American adults have hypertension (75 million people), whilst one third of adults are classified as pre-hypertensive (Nwankwo, Yoon, Burt, & Gu, 2013). Other international studies have reported similar findings for countries including the United Kingdom, Canada and Mexico (Joffres et al., 2013; Rubio-Guerra, 2013). Given the prevalence of hypertension and pre-hypertension within the general population, it is evident that this vast quantity of affected persons warrants greater impetus placed upon conducting more population-based research in relation to this issue.

Whilst the causes of hypertension are not entirely clear, risks factors include obesity, excessive alcohol consumption, diabetes mellitus, metabolic syndrome, high sodium intake, sleep apnoea, dyslipidaemia, old age and family history (DeFronzo & Ferrannini, 1991; Nieto et al., 2000; Parish, Adam, & Facchiano, 2007). Hypertension is either classified as being 'primary' (being a disease in and of itself) or 'secondary' to another related condition. Primary hypertension is typically caused by genetic and lifestyle factors, whilst secondary hypertension may be due to causes such as coagulation of the aorta, hyper aldosteronism, Cushing's syndrome, renal artery stenosis, chronic kidney disease, polycystic kidney disease, nephritic and nephrotic syndrome, obstructive uropathy, hyperthyroidism, obstructive sleep apnoea, chronic alcohol use, use of oral contraceptives, illicit drugs (such as cocaine or methamphetamine) and pre-eclampsia in females. Though most lifestyle and comorbid disease risk factors for hypertension are easily quantified, other risk factors for hypertension, in particular psychosocial risk factors, are more complex. In recent decades, research has increasingly focused its attention on depression, anxiety and hostility as additional potential risk factors for high blood pressure. An overview for the association of each of these negative states with blood pressure is provided below.

1.3 Association between depression and blood pressure

Depression can be defined as a "common and serious medical illness that negatively affects how you feel, the way you think and how you act" (American Psychiatric Association, 2018). Estimates indicate that around 5.8% of males and 9.5% of females will experience a depressive episode at some stage within a 12-month period (Global Burden of Disease, 2017). The World Health Organisation (2017) identifies Major Depressive Disorder as one of the leading causes of disability worldwide. Symptoms of depression may include low mood during most days, having noticeably diminished interest in most activities, weight loss or weight gain not attributable any deliberate dieting or exercise strategies, general lethargy, a slowing of thought or reduction in physical movement, feeling worthless or excessively guilty, increased indecisiveness and difficulty concentrating, recurrent thoughts associated with death or suicide ideation and attempts (American Psychological Association, 2018). For these symptoms to be considered related to major depression, they must not be caused by any other medical conditions or be the result of substance abuse. As per the American Psychiatric Association (2013), an individual will only be clinically diagnosed with depression provided that these symptoms cause significant distress or impairment across a range different situations or areas within a person's life relating to social, professional or any other areas of functioning. In developed countries, it has been estimated that by 2020 depression will rank second only to ischaemic heart disease in relation to disability-adjusted life years lost (World Health Organisation, 2018). Affecting more than 120 million people around the world, depression presents a burden not just to the individual's own ability to function but also affects families, communities and has an economic cost greater than $15 billion in terms of health care in Australian alone (Royal Australian and New Zealand College of Psychiatrists, 2016).

The association between depression and blood pressure is complex and likely bidirectional. Studies suggest that depression increases the risk for developing hypertension,

and conversely, hypertension increases the risk for developing depression (Meng, Chen, Yang, Zheng, & Hui, 2012). In part, this complex association is potentially due to neuroendocrine pathways commonly implicated in depression, especially the hypothalamic-pituitary adrenal axis (also colloquially known as the body's stress response system), as well as behavioural factors such as reduced physical activity, higher likelihood of smoking and alcohol intake (Hu, Chen, Chen, Li, & Li, 2015). Whilst many studies have investigated the relationship between blood pressure and depression much of this research has utilised conventional rather than ambulatory blood pressure monitoring. The association between blood pressure and depression is unclear as many of these conventional studies have reported mixed results. Some studies provide evidence of a significant effect between depression and elevations in blood pressure (Jonas, Franks, & Ingram, 1997; Kahn, Medalie, Neufeld, Riss, & Goldbourt, 1972). Conversely, others have found that depressive symptoms are associated with a decrease in blood pressure (Hildrum, Romild, & Holmen, 2011). Meanwhile, some studies reported no association between depression and blood pressure (Vogt, Pope, Mullooly, & Hollis, 1994; Goldberg, Comstock, & Graves, 1980). Despite the benefits of ambulatory monitoring in providing a more accurate representation of an individual's blood pressure than conventional clinic-based methods, few studies have employed ambulatory methods. Instead, most of the research conducted in this area has been carried out in experimental or artificial environments such as a doctor's office or health clinic, or alternatively, stress induction experiments such as public speaking. As a consequence of the lack of clarity reported by conventional blood pressure studies, an assessment of studies utilising ambulatory methods may provide a clearer picture of the relationship between blood pressure and depression.

1.4 Association between anxiety and blood pressure

Anxiety can be defined as "an emotion characterised by feelings of tension, worried thoughts and physical changes like increased blood pressure" (American Psychological

Association, 2018). Symptoms of anxiety disorders may include recurring intrusive thoughts or concerns, avoidance of certain situations due to worry and physical symptoms such as excessive sweating, dizziness, trembling or rapid heartbeat (American Psychological Association, 2018). Numerous studies have collected data indicating that approximately 30-50% of the population will be affected by an anxiety disorder within their lifetime (Australian Bureau of Statistics, 2008; Bandelow, 2015). Nearly half of the adult population in Australia (45.5%) has experienced an anxiety disorder at some point during their life (Australian Bureau of Statistics, 2008). The high prevalence of anxiety within the population places a significant burden on health care and sufferers are exposed a higher risk of disease (Bandelow, 2015).

The association between anxiety and blood pressure is complex with research providing evidence of a bidirectional relationship (Pan et al., 2015). The association is underpinned by sympathetic activation and endothelial dysfunction as well as behavioural factors such as hypertension awareness (DiBona, 2004; Hamer, Batty, Stamatakis, & Kivimaki, 2010). Whilst many studies have evaluated anxiety and its association with blood pressure, the majority of these studies utilised conventional rather than ambulatory blood pressure recordings. The findings of these conventional studies provide evidence for the association between anxiety and blood pressure. Several studies indicate that anxious individuals are more likely to develop hypertension or clinically meaningful elevations in blood pressure when compared to non-anxious persons (Jonas, Franks, & Ingram, 1997; Markovitz, Mathews, Kannel, Cobb, & D'Agostino, 1993; Perini, Muller, & Buhler, 1991). However, the majority of these studies were conducted in a clinical environment which are notably susceptible to the white-coat effect. Research estimates that between 10-35% of the general population may be affected by white coat hypertension (Myers, Oh, Reeves, & Joyner, 1995; Cobos, Haskard-Zolnierek, & Howard, 2015; Thomas et al., 2016). Therefore, by reviewing studies which employ ambulatory

monitoring, a more accurate representation of the association between anxiety and blood pressure can be obtained.

1.5 Association between hostility and blood pressure

Hostility has been identified as a probable risk factor of coronary heart disease (Barefoot, Dodge, Peterson, & Dahlstrom, 1989; Smith & Ruiz, 2002). The term 'hostility' has not been clearly defined in scientific literature. However, it is typically conceptualised as composed of various components including attitudinal or cognitive, affective and behavioural (Miller, Smith, & Turner, 1996). For the purpose of this investigation, hostility refers to the relatively stable cognitive tendencies of an individual which are characterised by cynical attitudes, suspicion or mistrust, resentment of others and denigrative behaviour (Miller, Smith, & Turner, 1996). Hostility is commonly measured through self-report questionnaires such as the Cook-Medley Hostility Scale and the Spielberger Anger Expression Scale.

Whilst several studies have linked hostility with increased levels of ambulatory blood pressure, the magnitude of this association is not entirely clear. A study utilising the Buss-Durkee inventory (Buss & Durkee, 1957) found that high-hostility hypertensive participants were associated with higher levels of systolic and diastolic blood pressure (Jamner, Shapiro, Hui, Oakley, & Lovett, 1993). Similarly, research using the Cook-Medley Hostility Scale identified that paramedics with high hostility scores were associated with higher levels of daytime and night-time systolic and diastolic blood pressure (Jamner, Shapiro, Goldstein, & Hug 1991). Other studies have obtained results which indicate that male and female university students also follow this trend, whereby higher levels of hostility are associated with higher levels of blood pressure (Benotsch, Christensen, & McKelvey, 1997). By conducting a comprehensive review of the literature, a better understanding of the magnitude of the relationship between hostility and blood pressure may be obtained.

1.6 Summary and Aims

Given that the association between depression, anxiety and hostility with hypertension is most commonly investigated in clinic or experimental settings, it remains unclear the strength of association between depression, anxiety and hostility upon blood pressure in peoples' day-to-day lives. Given the prevalence of hypertension and its prominence as a major cause of death and disability worldwide, a systematic review and meta-analysis would be useful in summarizing the existing research and identifying any inconsistencies regarding the association between depression, anxiety and hostility with an increase in ambulatory blood pressure. A meta-analysis which assesses ambulatory rather than conventional blood pressure in relation to negative emotions would be the first of its kind. By performing a systematic review, the aim was to summarise the existing research base in order to obtain a clearer understanding of the relationship between depression, anxiety and hostility and ambulatory blood pressure. The aim of the meta-analysis was to combine the results of the relevant studies in an attempt to ascertain the magnitude of the association between ambulatory blood pressure and depression, anxiety and hostility, identify heterogeneity in results, and to resolve any inconsistencies in findings between studies. Therefore, the research question was: *What is the association between ambulatory blood pressure with depression, anxiety and hostility?* It was hypothesised that all three negative affect states would have a significant association with increased blood pressure, both systolic and diastolic.

Chapter 2

Method

2.1 Literature search

The three electronic databases of PsycINFO, PubMed and Scopus were searched from their inception (PsychINFO 1967; PubMed 1996; Scopus 1966) until October 2018 for studies that investigated the association of depression, anxiety or hostility with blood pressure as measured by ambulatory monitoring. Studies were sought which examined persons with high levels of either depression, anxiety or hostility relative to an independent control group (low or no depression, anxiety or hostility). This review closely follows the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) and a review protocol was registered on PROSPERO (registration CRD42018103980).

Key depression, anxiety and hostility ('depressive symptoms', 'anxiety disorder', 'anger', 'aggression') and ambulatory blood pressure monitoring ('24-hour blood pressure') terms were developed according to the Thesaurus (PsycINFO), MeSH (PubMed) and Scopus vocabulary (see logic grid, Appendix A). The accuracy of these search terms was confirmed by a research librarian. All studies were evaluated for relevancy regardless of their publication date, thereby maximising the number of included studies. The reference lists of eligible studies were reviewed for further information or new studies. Whilst reviewing the reference lists did not return any new studies, it was invaluable in ensuring that all efforts were made to identify relevant papers.

2.2 Eligibility criteria and study selection

To be included in this review, studies were required to meet certain eligibility criteria. Specifically, the study must have (a) recruited an adult sample, whereby all participants were at least 18 years of age, all of whom showed some symptoms of depression, anxiety or hostility

quantified by either a verified diagnosis of depression or anxiety disorder (e.g. structured interview), or alternatively, persons with high scores on conventional psychometric measures of depression, anxiety and hostility.

Studies were required to have used (b) a validated measure for depression, anxiety or hostility and (c) utilise an independent group design, thereby enabling the comparison of individuals with high levels of depression, anxiety or hostility versus individuals with low or no depression, anxiety or hostility. The comparator group included individuals from the general population, primary care or other population without verified or known depression, anxiety and hostility, or individuals with low scores on conventional psychometric measures of depression, anxiety and hostility.

All studies were required (d) to utilise a recognised and commercially available ambulatory blood pressure monitor which could (e) collect quantifiable and standardised data for systolic or diastolic blood pressure readings in mmHg. In the instance that experimental or naturalistic design studies did not record ABPM for a period of 24 hours, we specified that blood pressure must be recorded for a period of at least 8 hours to be in included in the systematic review analyses. It was essential that studies (f) provided parametric data from which the standardised mean group differences in the form of Cohen's *d* could be calculated, specifically means and their standard deviation or standard error. Lastly, (g) studies were only included if they were peer-reviewed, available in full text and were published in English so that the data, methodological details and study characteristics could be clearly understood and extracted.

Eligible studies included those utilising cross-sectional designs, experimental designs, longitudinal cohort designs, case-control designs and randomised or non-randomised control trials. Prospective and retrospective studies were also eligible. Excluded studies included case

series and case reports, and studies which utilised only office or clinic measures to quantify blood pressure without ABPM.

The initial literature search returned 687 potentially eligible studies. 97 duplicates were identified and removed. The titles and abstracts of the remaining 590 studies were screened for eligibility by two independent reviewers resulting in 38 independent studies remaining. Any disagreements between the two reviewers during the screening process regarding the inclusion of a particular study were resolved by contacting an independent third-party adjudicator, thereby acting to improve interrater reliability. The remaining studies were re-screened against the eligibility criteria resulting in 30 remaining. These remaining 30 studies were independently analysed by a reviewer (P.J.T) to ensure that the selection process was both rigorous and unbiased. There were three studies which were excluded on the basis that more information in regards to their published data was needed in order to impute the means and standard deviations. The authors of two studies were contacted but no response was received (Enkelman et al., 2005; Ewart, Elder, Jorgensen, & Fitzgerald, 2017). The third study by Xu, Xing and Wang (2009) was in the form of a conference abstract without full-text and sufficient data could not be obtained. A PRISMA flow chart was constructed to outline the study selection process and reasons for exclusion (see Figure 1).

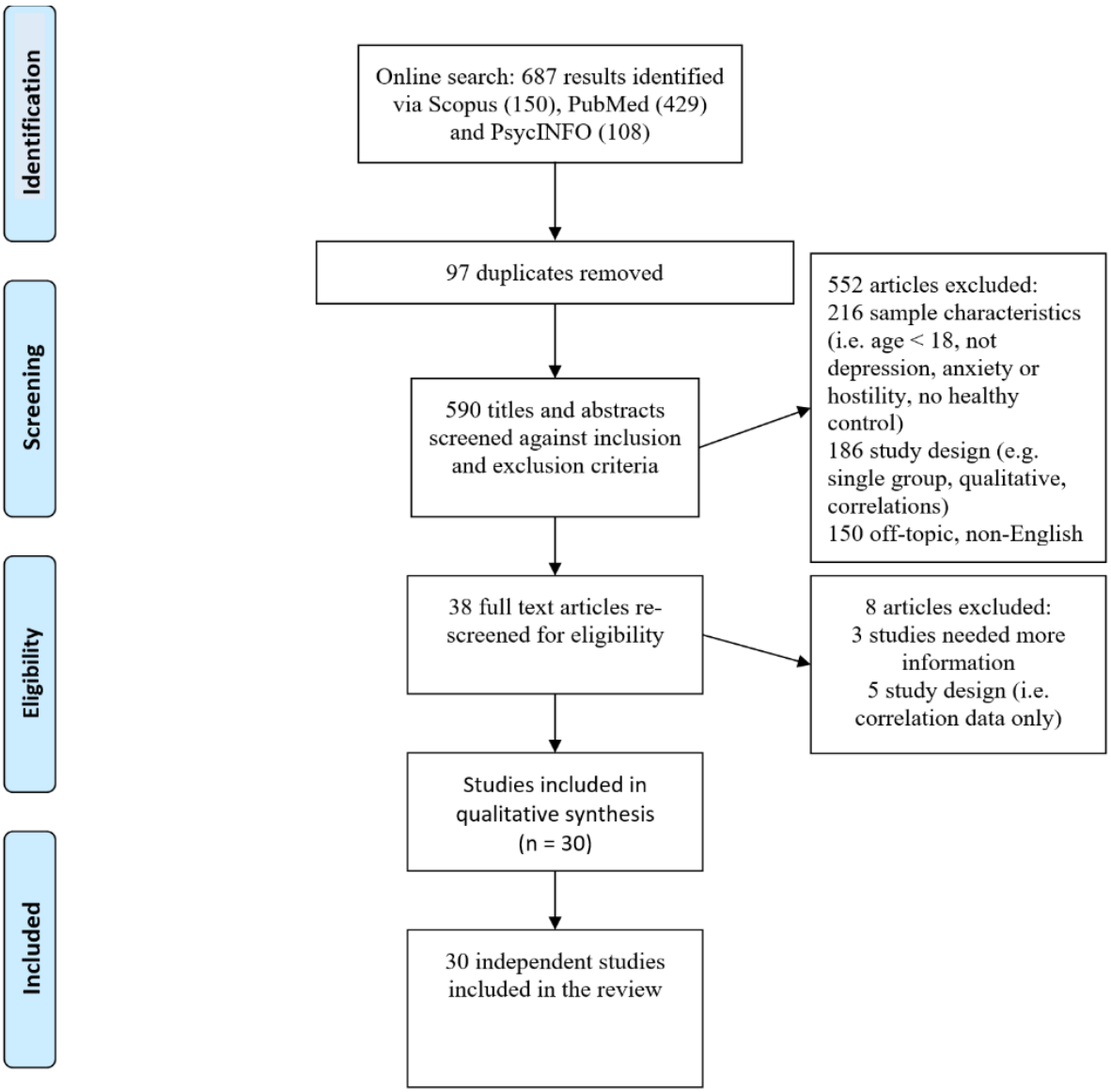


Figure 1. PRISMA flowchart of study selection process.

2.3 Data collection and preparation

In accordance with the PRISMA guidelines, the characteristics of studies (e.g. author, country, design, ABPM type, measure of psychological construct), the sample demographics (e.g. average age, gender, number of participants) and effect size data (e.g. means and standard deviations) were extracted from each study and incorporated into a carefully constructed spreadsheet.

The individual effect sizes of each study were grouped according to their level of depression, anxiety and hostility (high versus low), and according to their measure of blood pressure (systolic and diastolic). As a consequence, an overall effect size for each grouping could be easily obtained and interpreted. If ambulatory blood pressure values were reported for more than two groups, data was extracted from the group with the least severe form of depression, anxiety and hostility (in tertiles, quartiles, quintiles or deciles) and compared to the group with the most severe form of depression, anxiety and hostility. Therefore, this method of data extraction ensured that only one effect size was analysed for each study and that dissimilar groups were not pooled together in analyses. Where possible, correlation data (*r*) was converted to the common metric (*d*) and pooled together with the associated 95% CI. The data collected from each study was assessed by two independent reviewers with the availability of a third-party adjudicator to resolve any disputes which arose.

2.4 Risk of bias assessment

In accordance with the PRISMA guidelines, all studies were analysed for risk of bias and strength of evidence (Moher et al., 2015). Bias tables for each study were constructed in RevMan following the guidelines set out by the Cochrane Risk of Bias Tool (see Appendix C) (Cochrane Handbook for Systematic Reviews of Interventions, 2012). These guidelines were applied to each study as a means of assessing methodological rigour. The risk of bias assessment was undertaken by two independent reviewers with any disagreements being resolved by consensus with an independent third-party. A risk of bias summary and a graphical representation of the results were produced.

2.5 Statistical analysis

The included studies were qualitatively described according to their identification (first author, title, year of publication, country where recruitment occurred), study design and

characteristics (cross-sectional or longitudinal, sample size), patient population (age, gender, hypertension, chronic kidney disease, diabetes mellitus, coronary heart disease, chronic heart failure, stroke), methodology and duration of ABPM, the exposure to either depression or anxiety or hostility and the psychometric measure used, and adjustment for covariates.

The software package, Review Manager 5.3, was used to analyse the study data (The Nordic Cochrane Centre, Copenhagen). Standardised mean group differences were calculated to understand the degree to which systolic and diastolic blood pressure varied between the high versus low group data collected for depression, anxiety and hostility. The means and standard deviations for each study were then pooled so that an overall effect size was obtained for systolic and diastolic data for high versus low depression groups, high versus low anxiety groups and high versus low hostility groups. Therefore, six overall effect sizes were calculated in total for analysis. The effect sizes for the standardized difference between group means were interpreted using the same boundaries outlined by Cohen (Cohen, 1988), whereby an effect size of 0.2 and above is considered small, 0.5 and above is considered moderate and, lastly, an effect size of 0.8 or greater is large.

As many of the studies differed significantly in sample size, greater weighting was given to those studies which utilised larger samples. The weighting was calculated by RevMan using the Generic Inverse Variance Method (GIVM) which employs an estimate and standard error for each exposure effect. The weighting of each individual study was then determined as being the inverse of the variance of the effect estimate (Cochrane, 2018). For each grouping, the confidence intervals (95% CIs) were calculated to ensure the accuracy of both the individual and weighted effect sizes. Between-study heterogeneity was assessed by calculating chi-squared (Chi^2), *p*-values and I-squared (I^2) for the systolic and diastolic data for each of depression, anxiety and hostility. An I^2 value of 30-50% is considered to represent low to moderate heterogeneity and an I^2 value of >50% is considered to represent substantial

heterogeneity. Funnel plots were constructed and used as a visual aid for the detection of systematic heterogeneity and publication bias. In addition, Forrest plots were used to highlight the distribution of the studies' effect sizes.

A random effects model was utilised using the inverse variance method in order to provide a more conservative estimate of effect size. This model was preferred over a fixed effect model given the expectation that the average effect sizes for the studies would all differ in strength and (possibly) direction because they are obtained from differing populations. Furthermore, the fact that the results obtained are intended to be generalised (beyond the included studies) necessitates the use of a random effects model (Field & Gillett, 2010).

Chapter 3

Results

3.1 Study characteristics

Qualitative data was collected from 30 independent cross-sectional studies. The included studies were all published in peer-reviewed journals between the years 1989 and 2018 inclusive (see Table 1). Studies originated predominantly from the USA ($N_{studies}$= 19), however, also originated to a lesser extent from Asia ($N_{studies}$= 7), Europe ($N_{studies}$= 3) and Africa ($N_{studies}$= 1). Overall, data was obtained from 3465 participants for depression, anxiety and hostility with an average sample size of 115.5 participants per study.

For depression, systolic blood pressure data was collected from 412 participants with depressive symptoms and 776 participants without depression or low depression. Diastolic blood pressure results were calculated from 321 depressed participants and 548 non-depressed participants. Systolic blood pressure data in relation to anxiety was obtained from 726 participants with high levels of anxiety versus 1061 participants exhibiting low levels of anxiety. Diastolic data was calculated from 590 anxious persons and 857 non-anxious persons. In regards to hostility, systolic blood pressure data was obtained from 755 high-hostility participants and 756 low-hostility participants. In relation to diastolic blood pressure, data was calculated from 650 and 652 hostile and non-hostile participants respectively. For depression studies, a mean sample size of 124.9 participants per study was calculated, for anxiety-related studies a mean sample size of 161.4 participants was calculated and, lastly, a mean sample size of 94.6 was calculated for hostility-related studies. Across all studies, sample size ranged from the smallest sample of 31 participants (Suarez et al., 1991) to the largest sample of 440 participants (Edmondson et al., 2018).

Table 1.

Study Characteristics

Author ID	Year	Study name	Country of recruitment	Samples size	Design
Benotsch, E.G., Christensen, A.J., & McKelvey, L.	1997	Hostility, social support, and ambulatory cardiovascular activity	USA	48	cross-sectional
Broege, P.	1994	The blood pressure response to daily stress in normotensive female nurses	USA	62	cross-sectional
Brondolo, E., et al.	2009	Trait hostility and ambulatory blood pressure among traffic enforcement agents: The effects of stressful social interactions	USA	73	cross-sectional
Brownley, K.A., Light, K.C., & Anderson, N.B.	1996	Social support and hostility interact to influence clinic, work and home blood pressure in black and white men	USA	129	cross-sectional
Edmondson, D., et al.	2018	The association of post-traumatic stress disorder with clinic and ambulatory blood	USA	440	cross-sectional

		pressure in healthy adults			
Goldstein, I.B., & Shapiro, D.	2000	Ambulatory blood pressure in women: Family history of hypertension and personality	USA	203	cross-sectional
Guyll, M., & Contrada, R.J.	1998	Trait hostility and ambulatory cardiovascular activity: Responses to social interaction	USA	79	cross-sectional
Hamer, M., et al.	2012	Depressive symptons and 24-hour ambulatory blood pressure in Africans: The SABPA study	SAF	190	cross-sectional
Jamner, L.D., Shapiro, D., Goldstein, I.B., & Hug, R.	1991	Ambulatory blood pressure and heart in rate in paramedics: Effects of cynical hostility and defensiveness	USA	33	cross-sectional
Jamner, L.D., et al.	1993	Hostility and differences between clinic, self-determined, and ambulatory blood pressure	USA	45	cross-sectional
Kario, K., Schwartz, J.E., Davidson, K.W., & Pickering, T.G.	2001	Gender differences in associations of diurnal blood	USA	167	cross-sectional

		pressure variation, awake physical activity, and sleep quality with negative affect: The worksite blood pressure study			
Kayano, H., et al.	2012	Anxiety disorder is associated with nocturnal and early morning hypertension with or without morning surge	JAP	120	cross sectional
Lederbogen, F., et al.	2003	Circadian blood pressure regulation in hospitalized depressed patients and non-depressed comparison subjects	GER	78	cross-sectional
Ma, L., Kong, D., Qui, X., & Wang, L.	2008	Generalized anxiety disorder and the circadian rhythm of blood pressure in patients with hypertension	CHN	112	cross-sectional
Ma, L., & Li, Y.	2017	The effect of depression on sleep quality and the circadian rhythm of ambulatory blood pressure in older	CHN	73	cross-sectional

		patients with hypertension			
Okajima, K., et al.	2015	Even mild depression is associated with among-day blood pressure variability, including masked non-dipping assessed by 7-d/24-h ambulatory blood pressure monitoring	JAP	116	cross-sectional
Otsuka, K., et al.	2004	Chromonic community screening reveals about 31% depression, elevated blood pressure and infradian vascular rhythm alteration	JAP	192	cross-sectional
Ozpelit, M.E., et al.	2015	Impact of anxiety level on circadian rhythm of blood pressure in hypertensive patients	TUR	160	cross-sectional
Park, H., et al.	2016	Autonomic nervous system dysfunction in patients with Parkinson disease having depression	KOR	129	cross-sectional
Pasic, J., Shapiro, D., Motivala, S., & Hui, K.	1998	Blood pressure morning surge and hostility	USA	32	cross-sectional

Raikkonen, K., Mathews, K., Flory, J.D., Owens, J.F.	1999	Effects of optimism, pessimism, and trait anxiety on ambulatory blood pressure and mood during everyday life	USA	100	cross sectional
Raikkonen, K., et al.	1999	Effects of hostility on ambulatory blood pressure and mood during daily living in healthy adults	USA	100	cross-sectional
Schneider, R.H., Julius, S., & Karunas, R.	1989	Ambulatory blood pressure monitoring and laboratory reactivity in Type A behaviour and components	USA	33	cross-sectional
Shapiro, D., Goldstein, I.B., & Jamner, L.D.	1996	Effects of cynical hostility, anger out, anxiety and defensiveness on ambulatory blood pressure in black and white college students	USA	144	cross-sectional
Shapiro, D., et al.	2001	Striking a chord: Moods, blood pressure, and heart rate in everyday life	USA	203	cross-sectional
Shear, M.K., et al.	1992	Ambulatory monitoring of blood	USA	47	cross-sectional

		pressure and heart rate in panic patients			
Shinigawa, M., et al.	2002	Seven-day (24-h) ambulatory blood pressure monitoring, self-reported depression and quality of life scores	JAP	54	cross-sectional
Vella, E.J., Kamarck, T.W., & Shiffman, S.	2008	Hostility moderates the effects of social support and intimacy on blood pressure in daily social interactions	USA	172	cross-sectional
Vetrano, D.L., et al.	2015	Association of depressive symptoms with circadian blood pressure alterations in Parkinson's disease	ITA	125	cross-sectional
Suarez, E.C., & Blumenthal, J.A.	1991	Ambulatory Blood Pressure Responses During Daily Life in High and Low Hostile Patients with a recent myocardial infarction	USA	31	cross-sectional

To measure depression (see Table 2), the psychometric measures utilised included the Geriatric Depression Scale (GDS) ($N_{studies}$= 3), Hamilton Depression Rating Scale (HDRS) ($N_{studies}$= 2), Brief Symptom Inventory (BSI) ($N_{studies}$= 1), Patient Health Questionnaire-9 (PHQ-9) ($N_{studies}$= 1) and scales which were specifically constructed for that particular study ($N_{studies}$= 2). The psychometric measures of anxiety used included the State-Trait Anxiety Scale (STAI) ($N_{studies}$= 3), structured clinical interview (SCI) ($N_{studies}$= 1), Brief Symptom Inventory (BSI) ($N_{studies}$= 1), PTSD Checklist Civilian (PCL-C) ($N_{studies}$= 1), mood diary ($N_{studies}$= 1), Taylor Manifest Anxiety Scale (TMAS) ($N_{studies}$= 1), Hospital Anxiety and Depression Scale (HADS) ($N_{studies}$= 1), Zung Self-Rating Anxiety Scale (SAS) ($N_{studies}$= 1) and the Generalised Anxiety Disorder scale (GAD) ($N_{studies}$= 1). The most commonly used psychometric measure of hostility utilised was the Cook Medley Hostility Scale (CMHS) ($N_{studies}$= 7), whilst other measures included the Buss-Durkee Hostility Inventory (BDHI) ($N_{studies}$= 2), structured clinical interview ($N_{studies}$= 2), mood diary ($N_{studies}$= 1) and the Hostile Outlook Scale (HOS) ($N_{studies}$= 1).

Table 2.

Study Ambulatory Characteristics and Psychometric Measures Used

ID	Name of ABPM Monitor	ABPM duration in hours	Average number of BP recordings during ABPM	ABPM during sleep	Separate reporting of sleep and awake blood pressure	Measure used for either depression, anxiety or hostility
Benotsch, E.G., Christensen, A.J., & McKelvey, L.	Accutracker II	8 to 10	N/A	n	n	Cook-Medley Hostility Scale (CMHS)
Broege, P.	Spacelabs 90207	24	56	y	y	Taylor Manifest Anxiety Scale (TMAS)
Brondolo, E., et al.	Accutracker II	16	N/A	n	n	CMHS
Brownley, K.A., Light, K.C., & Anderson, N.B.	Accutracker 103	11 to 13	N/A	n	n	CMHS
Edmondson, D., et al.	Spacelabs 90207	24	48	y	y	PTSD Checklist-Civilian Version (PCL-C)
Goldstein, I.B., & Shapiro, D.	Accutracker	24	N/A	y	y	State Trait Anxiety Inventory (STAI); CMHS
Guyll, M., & Contrada, R.J.	Accutracker II	11.7	N/A	n	n	CMHS

Hamer, M., et al.	Meditech CE-120	24	36	y	y	Patient Health Questionnaire-9 (PHQ-9)
Jamner, L.D., Shapiro, D., Goldstein, I.B., & Hug, R.	Accutracker II	24	72	y	y	CMHS
Jamner, L.D., Shapiro, D., Hui, K., Oakley, M.E., Lovett, M.	Accutracker II	24	N/A	y	n	Buss-Durkee Hostility Inventory (BDHI)
Kario, K., Schwartz, J.E., Davidson, K.W., & Pickering, T.G.	Spacelabs 90207	24	N/A	y	y	Brief Symptom Inventory (BSI)
Kayano, H., et al.	TM-2425	24	48	y	y	Hospital Anxiety Depression Scale (HADS)
Lederbogen, F., et al.	Tonoport II and III	24	68	y	y	Hamilton Depression Scale (HAM-D)
Ma, L., Kong, D., Qui, X., & Wang, L.	Spacelabs 90207	24	62	y	y	Zung Self-Rating Anxiety Scale (SAS); Generalised Anxiety Disorder Scale (GAD)
Ma, L., & Li, Y.	N/A	24	N/A	y	n	HAM-D
Okajima, K., et al.	TM-2431	168	273	y	y	Geriatric Depression Scale (GDS)

Otsuka, K., et al.	TM-2431	168	273	y	y	Depression Screening Scale
Ozpelit, M.E., et al.	BR-102 plus	24	48	y	y	STAI
Park, H., et al.	Mobil-O-Graph	24	N/A	y	y	GDS
Pasic, J., Shapiro, D., Motivala, S., & Hui, K.	Accutracker II	24	48	y	y	BDHI
Raikkonen, K., Mathews, K., Flory, J.D., Owens, J.F.	IBS Model SD-700A	28	56	n	N/A	STAI
Raikkonen, K., et al.	Colin ABPM-630	42	84	n	N/A	CMHS; Structured Clinical Interview (SCI)
Schneider, R.H., Julius, S., Karunas, R.	Del Mar Avionics Pressurometer	24	48	y	y	SCI
Shapiro, D., Goldstein, I.B., & Jamner, L.D.	Accutracker II	24	72	y	y	CMHS
Shapiro, D., et al.	Accutracker II	24	N/A	y	N/A	Mood diary
Shear, M.K., et al.	Del Mar Avionics Pressurometer	24	96	y	y	SCI
Shinigawa, M., et al.	TM-2431	24	39	y	y	Depression Screening Scale and Subjective Quality of Life Scale

Vella, E.J., Kamarck, T.W., & Shiffman, S.	Accutracker II	N/A	N/A	n	y	CMHS
Vetrano, D.L., et al.	Mobil-O-Graph	24	N/A	y	y	GDS
Suarez, E.C., & Blumenthal, J.A	Accutracker II	12 to 14	N/A	n	n	CMHS

3.2 Sample characteristics

The data was calculated from 3465 participants with a mean sample size of 115.5 participants for each study. Participants were recruited from medical clinics, hospitals, universities, communities and the wider general population. The mean age of participants for each study ranged between 18.7 years and 72.7 years, whilst female participation ranged from 0% to 100% across studies. The median age of all the studies was calculated to be 50.2 years whilst the median percentage for female participation was found to be 49.2%. The mean age of participants in depression studies was 57.5 years and the mean percentage of female participation was 49.1%. For anxiety data, the mean age was 46.2 years with 44.5% of the participants being female. Lastly, for the data collected from hostility-related studies, the mean age of participants was 35.5 years with 40.1% of the sample being female.

Where possible, data for each study was obtained in relation the number of participants identified as having hypertension, diabetes mellitus, chronic kidney disease, coronary heart disease, chronic heart failure and stroke. As expected, many studies did not report this information, however, where it was reported, this information was converted to a percentage of the study sample. Overall, of the nine studies which reported information regarding hypertension, a mean of 61.7% was calculated for the percentage of participants with hypertension. Only two studies reported information relating to chronic kidney disease with a mean percentage of 18.7% of the sample experiencing chronic kidney disease. Five studies reported participant information for coronary heart disease with a mean percentage of 36.7% calculated. For chronic heart failure, four studies reported participant information with a mean of 17.7% calculated. Lastly, only two studies reported information whether participants had experienced a stroke with a mean percentage calculated of 9.3%. For the majority of the included studies, the reporting of pertinent medical covariates that are known to influence

blood pressure was inconsistent. Therefore, the estimated prevalence rates of medical covariates are unclear and may not reflect the profile of all included studies.

Table 3.

Characteristics of Study Participants and Covariates

ID	Mean age across groups (SD)	% female	% Hypertension (HT)	% Diabetes Mellitus (DM)	% Chronic Kidney Disease (CKD)	% Chronic Heart Disease (CHD)	% Coronary Heart Failure (CHF)	% with stroke	Adjustment for covariates
Benotsch, E.G., Christensen, A.J., & McKelvey, L.	18.7	50	0	N/A	N/A	0	N/A	N/A	Age, gender, smoking and alcohol usage, weekly exercise.
Broege, P.	34		48.6 (FH)	N/A	N/A	18.38	N/A	N/A	Marital status, number of children, smoking/alcohol consumption, years in position, stress, depression, anger levels
Brondolo, E., et al.	37.84	53	6.9	N/A	N/A	N/A	N/A	N/A	Age, gender, contact with public, race, workday mood
Brownley, K.A., Light, K.C., & Anderson, N.B.	N/A	48.1	0	N/A	0	N/A	0	N/A	Age, gender, ethnicity

Edmondson, D., et al.	52.06	37.9	N/A	N/A	N/A	N/A	N/A	N/A	Age, gender, ethnicity, BMI, depression, BP medication
Goldstein, I.B., & Shapiro, D.	N/A	N/A	0	N/A	N/A	N/A	N/A	N/A	Family history of HT, age, day (work v off).
Guyll, M., & Contrada, R.J.	20.9 (2.4)	49.4	36 (FH)	N/A	N/A	N/A	N/A	N/A	Age, gender, BMI, ethnicity, family history of HT, smoking/coffee consumption.
Hamer, M., et al.	45	45.8	12.64	N/A	N/A	N/A	N/A	N/A	Age, sex, BMI, cholesterol level, glucose level, HT medication usage.
Jamner, L.D., Shapiro, D., Goldstein, I.B., & Hug, R.	27 (median)	n/a	33.3 (FH)	N/A	N/A	33.3 (FH)	N/A	N/A	work context, family history of HT, caffeine/alcohol/smoking consumption.
Jamner, L.D., Shapiro, D., Hui, K., Oakley, M.E., Lovett, M.	49.9	48.9	100	N/A	N/A	N/A	N/A	N/A	Age, gender, BMI, history of HT, BP assessment method, depression, anxiety.
Kario, K., Schwartz, J.E., Davidson, K.W., & Pickering, T.G.	46 (8.9)	46	N/A	N/A	N/A	N/A	N/A	N/A	Age, gender, day, night, physical activity.
Kayano, H., et al.	66 (11)	35.8	100	0	0	N/A	25.8	0	Age, gender, BMI, medication, smoking/alcohol

									consumption, previous cardiovascular events.
Lederbogen, F., et al.	50.67 (av SD)	53.8	0	N/A	N/A	N/A	19	N/A	Day, night, age, gender, BMI, smoking status, cardiovascular disorder, benzodiazepine/hypnotic usage.
Ma, L., Kong, D., Qui, X., & Wang, L.	55 (av SD)	50.1	100	N/A	N/A	N/A	N/A	N/A	Day, night, gender, age, duration of HT, beta blockers and diuretics.
Ma, L., & Li, Y.	67.21(9.27)	41.9	100	N/A	N/A	N/A	N/A	N/A	Age, gender, BMI, duration of HT, sleep quality.
Okajima, K., et al.	59.7 (9.2)	54.3	76.7	N/A	N/A	N/A	N/A	N/A	Age, gender, BMI, HT status.
Otsuka, K., et al.	56.8 (11.3)	60.8	N/A	0	0	0	0	0	Circadian/ circsemiseptan/ circaseptan/ characteristics compared.
Ozpelit, M.E., et al.	55.3 (15.1)	50	100	15.6	16.25	16.25	16.25	16.25	Age, sex, BMI, DM, CVD, duration of HT, beta blocker & diuretic usage.
Park, H., et al.	68.1 (10.4)	61.2	32.6	21.7	N/A	N/A	N/A	N/A	Age, gender, disease duration, smoking status, DM, HT.
Pasic, J., Shapiro, D.,	50.2 (8.7)	43.8	100 (H)	N/A	N/A	N/A	N/A	N/A	Gender, BMI, years of HT.

Motivala, S., & Hui, K.									
Raikkonen, K., Mathews, K., Flory, J.D., Owens, J.F.	36.8 (4.4)	50	0	0	0	0	0	0	Physical activity, posture, location, substance use, interpersonal social interaction.
Raikkonen, K., et al.	36.8 (4.4)	50	0	0	0	0	0	0	Gender, mood.
Schneider, R.H., Julius, S., & Karunas, R.	36.8 (9.1)	0	N/A	N/A	N/A	N/A	N/A	N/A	Work versus non-work, sleep versus awake.
Shapiro, D., Goldstein, I.B., & Jamner, L.D.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Gender, race, BMI, sleep time, posture and activity.
Shapiro, D., et al.	37.7 (6.6)	100	N/A	N/A	N/A	N/A	N/A	N/A	Mood level.
Shear, M.K., et al.	32.9 (5.9)	36.2	18	N/A	N/A	N/A	N/A	N/A	Work versus home versus sleep.
Shinigawa, M. et al.	51.5 (10.8)	46.3	N/A	N/A	N/A	N/A	N/A	N/A	Days of week, quality of life measures.
Vella, E.J., Kamarck, T.W., & Shiffman, S.	60.1 (4.71)	50.7	0	0	N/A	N/A	N/A	N/A	Age, race, BMI, education, gender, posture, physical activity, temperature, recent meal, snack, caffeine/alcohol consumption within last 45 minutes, antihistamine use

									within last 4 hours, smoking habits.
Vetrano, D.L., et al.	72.7 (7.8)	32	60.8	n/a	47.2	15.2	9.6	2.4	Age, gender, smoking habits, current alcohol consumption, anthropometric parameters.
Suarez, E.C., & Blumenthal, J.A.	50	0	N/A	N/A	N/A	100 (MI)	N/A	N/A	Age, myocardial infarction (MI) severity, length of time since MI, usage of non-beta blocker cardiac medicine, resting CV levels.

Note. 'FH'= Family History

3.3 Assessment of bias

The risk of bias assessment was performed by two independent reviewers and provided evidence of low risks of bias across the majority of the included studies (see Figure 2), with good interrater reliability being observed. Performance bias was the most commonly occurring type out of all the biases assessed with a high risk being identified in 23% of the included studies (see Figure 3). Detection bias and attrition bias were identified as the next most prevalent forms of bias with approximately 13% of studies effected. Low risks were observed for reporting bias (3%) and selection bias in the domains of allocation concealment (3%) and random sequence generation (0%). Funnel plots constructed for each of the six associations were all found to be asymmetrical except for the association between hostility and systolic blood pressure (see Appendix B). Therefore, there was a high risk that publication bias had a significant impact on the remaining five associations.

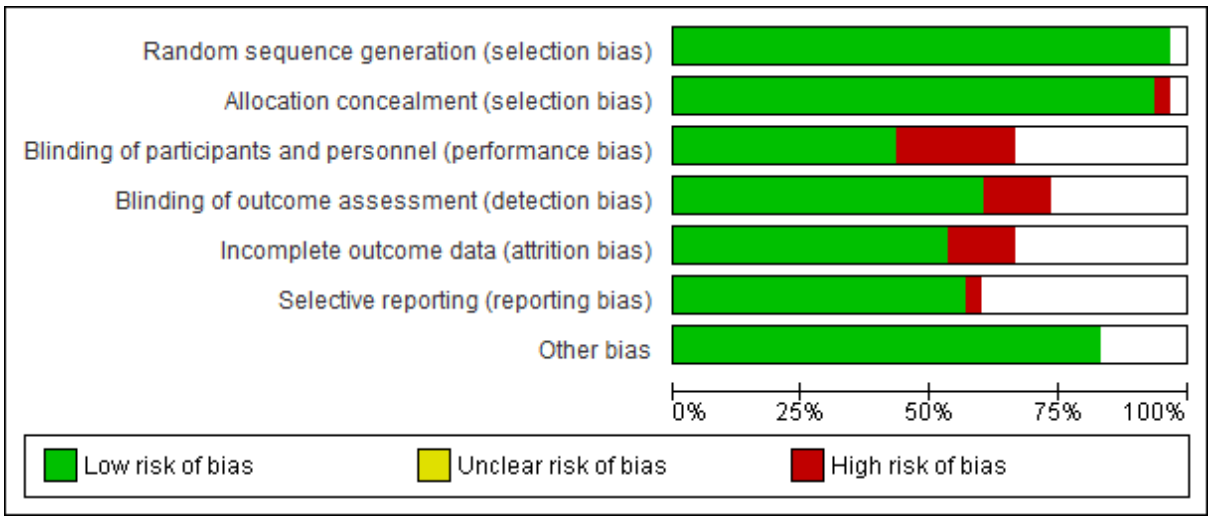


Figure 2. Risk of Bias Graph

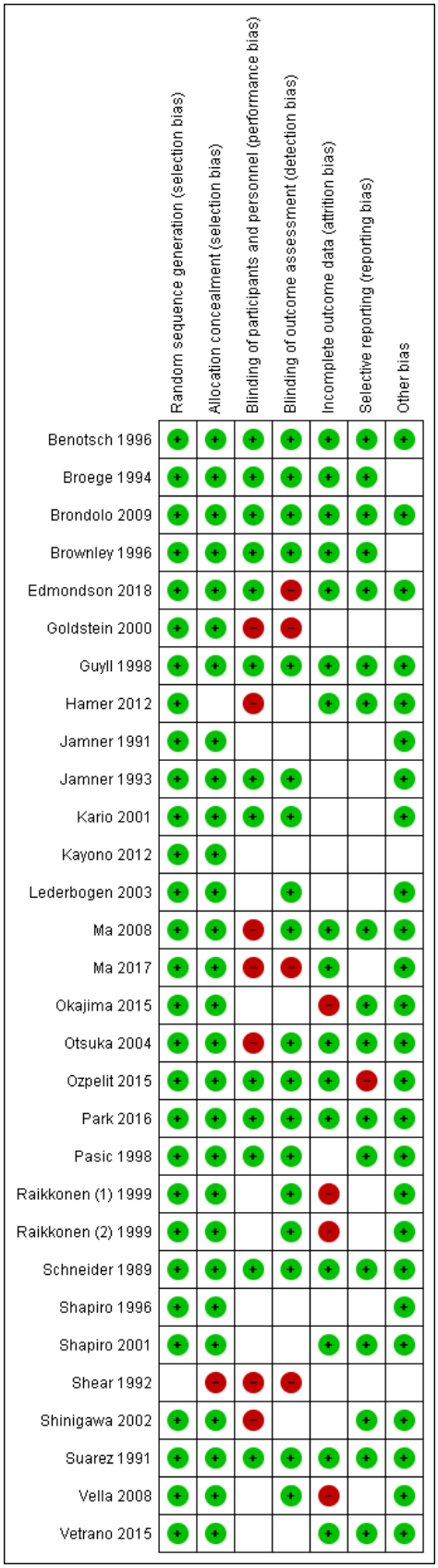


Figure 3. Risk of Bias Summary.

Note. Green= low risk of bias; Red= high risk of bias; Blank= Unknown risk.

3.4 Relationship between depression and systolic blood pressure

Information collected from 11 data sets resulted in a significant overall effect size being obtained for the association between depression and systolic blood pressure, SMD = 0.22 [0.09, 0.34], p= .0007. This finding indicates that there is a weak positive association between depression and systolic blood pressure. Specifically, people in the depressed group experience higher levels of systolic blood pressure.

The effect sizes for each individual study are outlined in Table 4 (see below). Eight out of the 11 included studies reported a small to moderate effect size for the relationship between depression and systolic blood pressure, whilst three studies reported no or minimal effect. The strongest effect size was for the study by Ma et al. (2017) which reported a moderate association between the two variables, 0.47 [-0.01, 0.95]. The weakest effect size was reported by Kario et al. (2001) in relation to male data, -0.01 [-0.48, 0.46]. In calculating the overall effect size, greatest weight (18.4%) was placed on the study by Otsuka et al. (2004) which recorded a weak correlation between the variables of interest, 0.32[0.02, 0.61]. Meanwhile, the least weighting (4.4%) was calculated for studies by Hamer et al. (2012) and Shinigawa et al. (2002). The median weighting of the studies was calculated to be 7%.

The heterogeneity between studies was assessed and found to have low diversity between studies, I^2= 0%. The confidence intervals of each study were reviewed in the Forest plot and all intervals were observed to overlap with each other, thereby supporting the finding of statistical homogeneity between studies.

3.5 Relationship between depression and diastolic blood pressure

Means and standard deviations for depressed groups and non-depressed groups were obtained from eight data sets. A significant overall effect size was observed for the association between depression and diastolic blood pressure, 0.25 [0.00, 0.49], p= .05. Using the

interpretation guidelines outlined for Cohen's d, this effect may be considered small, thereby indicating a weak association between depression and diastolic blood pressure. Specifically, those in the depressed group have higher diastolic blood pressure.

The effect sizes for each individual data set were included in Table 5 (see below). The strongest effect size was reported by Ma et al. (2017), which provided evidence of a moderate correlation between depression and diastolic blood pressure, 0.47[-0.01, 0.95]. Meanwhile, the weakest correlation was reported by Kario et al. (2001) for both males, 0.03[-0.45, 0.51], and females, -0.03[-0.50, 0.44]. In calculating the overall effect, Otsuka et al. (2004) (which also utilised the largest sample) was given the most weighting (18.4%) and reported a small effect size, 0.32[0.02, 0.61]. The study calculated to hold the least weight (9.2%) was Shinigawa et al. (2002). The mean weighting was calculated to be 12.5% whilst the median was found to 11.7%.

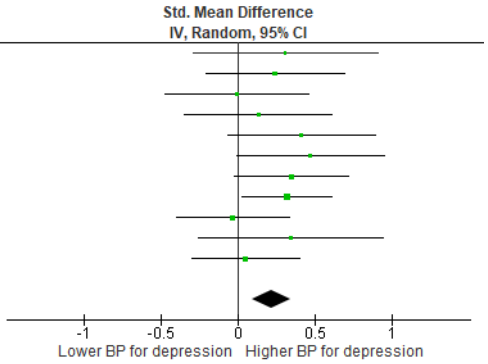
The heterogeneity between the groups was calculated and found to be above the threshold of 60% indicating a high level of diversity between groups, I^2= 62%. The Forest plot was reviewed and it was observed that all studies' confidence intervals overlapped with each other with the exception of Ma et al (2017), 1.10[0.59, 1.61].

Table 4.

Relationship Between Depression and Systolic Blood Pressure.

	Depressed			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Hamer 2012 (1)	127	9.01	12	122.5	15.07	101	4.4%	0.31 [-0.29, 0.91]
Hamer 2012 (2)	136.25	14.79	35	133	12.31	42	7.9%	0.24 [-0.21, 0.69]
Kario 2001 (3)	129.92	10	21	130	10	105	7.3%	-0.01 [-0.48, 0.46]
Kario 2001 (4)	120.33	10	21	119	10	84	7.0%	0.13 [-0.35, 0.61]
Lederbogen 2003	125.5	14.7	52	119.6	13.3	26	7.0%	0.41 [-0.07, 0.89]
Ma 2017	141.06	7.61	28	137.94	5.84	45	7.0%	0.47 [-0.01, 0.95]
Okajima 2015	137	16.9	51	131.4	15.6	65	11.7%	0.34 [-0.03, 0.71]
Otsuka 2004	129.17	13.99	72	124.5	15.17	120	18.4%	0.32 [0.02, 0.61]
Park 2016	118	19.74	44	119	32.45	85	12.0%	-0.03 [-0.40, 0.33]
Shinigawa 2002	136.92	17.38	15	130.53	18.93	39	4.4%	0.34 [-0.26, 0.94]
Vetrano 2015	120.8	13.9	61	120.1	13.8	64	12.9%	0.05 [-0.30, 0.40]
Total (95% CI)			**412**			**776**	**100.0%**	**0.22 [0.09, 0.34]**

Heterogeneity: Tau² = 0.00; Chi² = 6.56, df = 10 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.39 (P = 0.0007)



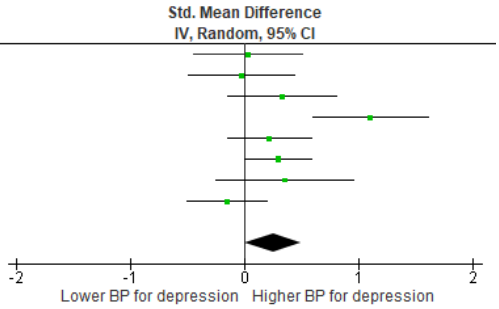
Footnotes
(1) Caucasian
(2) Black
(3) Males
(4) Females

Table 5.

Relationship Between Depression and Diastolic Blood Pressure.

	Depressed			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kario 2001 (1)	78.16	5	21	78	5	84	11.6%	0.03 [-0.45, 0.51]
Kario 2001 (2)	80.86	5	21	81	5	105	11.8%	-0.03 [-0.50, 0.44]
Lederbogen 2003	80.2	9.6	52	77.2	8	26	11.7%	0.33 [-0.15, 0.80]
Ma 2017	92.69	5.98	28	85.5	6.74	45	11.0%	1.10 [0.59, 1.61]
Okajima 2015	82.3	10.4	51	80.3	8.2	65	14.2%	0.22 [-0.15, 0.58]
Otsuka 2004	79.03	8.15	72	76.53	8.66	120	16.0%	0.29 [0.00, 0.59]
Shinigawa 2002	84.02	9.99	15	80.16	11.13	39	9.2%	0.35 [-0.25, 0.95]
Vetrano 2015	71.9	8.4	61	73.3	9.5	64	14.6%	-0.15 [-0.51, 0.20]
Total (95% CI)			**321**			**548**	**100.0%**	**0.25 [0.00, 0.49]**

Heterogeneity: Tau² = 0.07; Chi² = 18.30, df = 7 (P = 0.01); I² = 62%
Test for overall effect: Z = 1.99 (P = 0.05)



Footnotes
(1) Females
(2) Males

3.6 Relationship between anxiety and systolic blood pressure

Data was collected from 11 studies, and the means and standards deviations were calculated for both anxious and non-anxious groups for each study (see Table 6). A non-significant effect was obtained for the relationship between anxiety and systolic blood pressure, 0.14[-0.12, 0.40], p= .29. Therefore, the findings indicate that there is no association between anxiety and systolic blood pressure.

The effect sizes were calculated for each individual anxiety study and effect sizes were noted to vary substantially in both strength and direction. The strongest effect size was reported by Ma et al. (2008), which provided evidence of a strong positive correlation between anxiety and systolic blood pressure, 1.01[0.62, 1.41]. Meanwhile, the weakest effect between the variables of interest was reported by Broege (1994), 0.10[-0.42, 0.62]. Furthermore, negative effect sizes were observed in three studies including Raikkonen et al. (1999) which reported a moderate effect thereby indicating that anxiety and systolic blood pressure are inversely related, -0.68[-1.08, -0.27]. In addition, the weighting of studies was calculated to be relatively even with a mean of 9.1% and median of 9.2% calculated. The study calculated as holding the least weight (6.4%) was Pasic et al. (1998), whilst greatest weight (11%) was placed on the study by Shapiro et al. (2001).

The heterogeneity between the groups was calculated and found to be extremely high, I^2= 83%, reflecting significant differences in effect sizes between studies. Observation of the Forest plot established that the confidence intervals of the studies did not all overlap with each other, thereby confirming the finding of high levels of heterogeneity.

3.7 Relationship between anxiety and diastolic blood pressure

Data was collected from eight data sets and the means and standard deviations were calculated for both the anxiety groups and non-anxiety groups (see Table 7). The overall effect obtained was small, thereby indicating a small positive association between anxiety and diastolic blood pressure, 0.23[-0.01, 0.46], *p*= .06. However, as evidenced by the reported *p*-value, this result was found not to be statistically significant.

In regards to the individual studies, the strongest effect was found for Raikkonen et al. (1999) which provided evidence of a strong positive relationship between anxiety and diastolic blood pressure, 0.81[0.40, 1.22]. The weakest effect was found for Shear et al. (1992) which

evidenced a minimal relationship between the variables, -0.12[-0.69, 0.46]. The weightings of studies were calculated as being the inverse of the variance of their effect estimates and, subsequently, were found to range from 8.7% to 15.5%. The mean weighting was calculated to be 12.5%, whilst the median was 12.4%.

The between groups heterogeneity was calculated and returned significantly high level, I^2= 74%. After further observation of the Forest plot was conducted, it was noted that not all of the studies' confidence intervals overlapped with each other, therefore, acting to confirm the finding of high heterogeneity.

Table 6.

Relationship Between Anxiety and Systolic Blood Pressure.

	Anxious			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Broege 1994	120	9.82	23	119	9.82	39	8.0%	0.10 [-0.42, 0.62]
Edmondson 2018	132	12.8	92	128.7	11.6	348	10.7%	0.28 [0.05, 0.51]
Goldstein 2000	97.9	6.67	98	100.5	6.67	105	10.3%	-0.39 [-0.67, -0.11]
Kario 2001	121	10	21	119	10	84	8.4%	0.20 [-0.28, 0.68]
Kayono 2012	143	13	42	137	14	78	9.4%	0.44 [0.06, 0.82]
Ma 2008	156.6	11	56	143.2	15	56	9.2%	1.01 [0.62, 1.41]
Ozpelit 2015	142.7	14.2	97	139	15	63	10.0%	0.25 [-0.06, 0.57]
Pasic 1998	143	1.03	17	142.67	1.03	15	6.4%	0.31 [-0.39, 1.01]
Raikkonen (1) 1999	114.2	10.56	55	121.4	10.56	45	9.1%	-0.68 [-1.08, -0.27]
Shapiro 2001	121	11.54	203	117	11.54	203	11.0%	0.35 [0.15, 0.54]
Shear 1992	109	12	22	114	12	25	7.4%	-0.41 [-0.99, 0.17]
Total (95% CI)			**726**			**1061**	**100.0%**	**0.14 [-0.12, 0.40]**

Heterogeneity: Tau² = 0.15; Chi² = 59.94, df = 10 (P < 0.00001); I² = 83%
Test for overall effect: Z = 1.05 (P = 0.29)

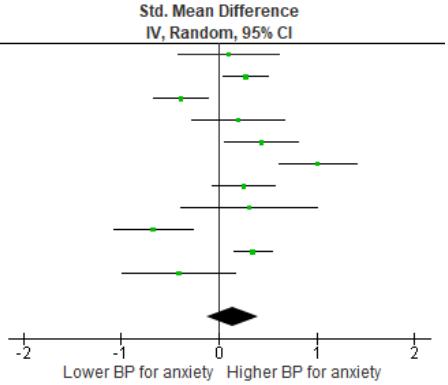
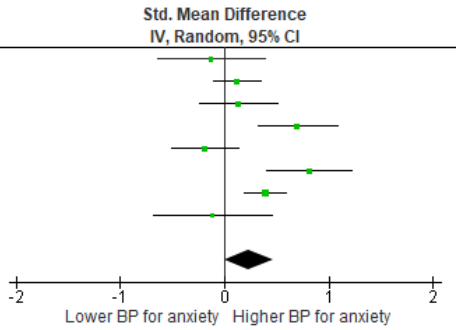


Table 7.

Relationship Between Anxiety and Diastolic Blood Pressure.

	Anxious			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Broege 1994	74	7.63	23	75	7.63	39	9.7%	-0.13 [-0.65, 0.39]
Edmondson 2018	81	9.3	92	80	8.4	348	15.5%	0.12 [-0.11, 0.35]
Kayono 2012 (1)	85	8	42	84	7	78	12.4%	0.13 [-0.24, 0.51]
Ma 2008	101.5	10.1	56	94.1	10.9	56	12.3%	0.70 [0.32, 1.08]
Ozpelit 2015	79.7	9.7	97	81.5	9	63	13.6%	-0.19 [-0.51, 0.13]
Raikkonen (1) 1999	73	7.73	55	66.7	7.73	45	11.7%	0.81 [0.40, 1.22]
Shapiro 2001	73.9	9.74	203	70.1	9.74	203	16.1%	0.39 [0.19, 0.59]
Shear 1992	76	10	22	77	7	25	8.7%	-0.12 [-0.69, 0.46]
Total (95% CI)			**590**			**857**	**100.0%**	**0.23 [-0.01, 0.46]**

Heterogeneity: Tau² = 0.08; Chi² = 27.04, df = 7 (P = 0.0003); I² = 74%
Test for overall effect: Z = 1.91 (P = 0.06)



Footnotes
(1) Diurnal values used

3.8 Relationship between hostility and systolic blood pressure

The means and standard deviations were calculated from 18 data sets for both hostile and non-hostile groups (see Table 8). A significant overall effect was obtained for the relationship between hostility and systolic blood pressure, 0.28[0.11, 0.44], p= 0.001. Using the guidelines outlined earlier, this effect may be considered small, thereby indicating a weak positive association between hostility and systolic blood pressure. More specifically, the findings provide evidence for the notion that persons with high levels of hostility will have higher systolic blood pressure.

The study by Pasic et al. (1998) was found to have the strongest effect size showing a strong positive correlation between hostility and systolic blood pressure, 0.81[0.8, 1.53]. The weakest effect size was found to exist for the study by Schneider et al. (1989) which identified a minimal relationship between the two variables, 0.05[-0.72, 0.82]. The weighting of each study was calculated using the inverse of variance method with weightings found to range from 3% to 10.7%. A mean weighting of 5.6% was calculated, whilst the median was found to be 5.1%.

A substantial degree of heterogeneity was found to exist between the groups, , I^2= 52%. Observation of the Forest plot identified that not all of the studies' confidence intervals crossed over with each other, thereby confirming the finding of heterogeneity.

3.9 Relationship between hostility and diastolic blood pressure

The mean and standards deviations were calculated for hostile and non-hostile groups from 14 sets of data (see Table 9). A significant overall small effect was found, 0.26[0.06, 0.46], p=.009. Therefore, this finding provides evidence of a weak positive association between hostility and diastolic blood pressure. Broadly speaking, the finding indicates that individuals

with high levels of hostility will experience higher diastolic blood pressure when compared to individuals with low levels of hostility.

In regards to the individual studies, the strongest effect size was found for Jamner et al. (1993) which evinced a moderate relationship between hostility and diastolic blood pressure, 0.70[0.10, 1.31]. The weakest effect size was calculated for Suarez et al. (1991) which identified a minimal relationship between the variables of interest, 0.08[-0.62, 0.79]. Utilising the same inverse of variance method as previously outlined for the other results, the weightings for each study were calculated and found to range from 4.2% to 12.5%. The mean weighting for the studies was calculated to be 7.2%, whilst the median was 6.6%.

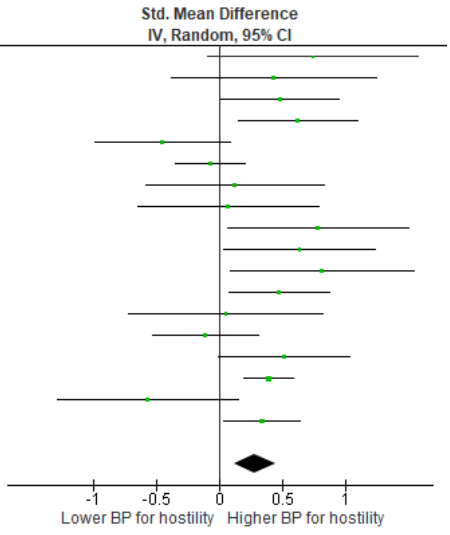
Moderate levels of heterogeneity between the groups was found to exist, I^2= 59%. This finding was confirmed after observation of the Forest plot evinced that not all of the studies' confidence intervals overlapped with each other.

Table 8.

Relationship Between Hostility and Systolic Blood Pressure.

	Hostile/Angry			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Benotsch 1996 (1)	128.2	10.2	12	121.4	7.3	12	3.0%	0.74 [-0.09, 1.57]
Benotsch 1996 (2)	113	8	12	110	5.4	12	3.1%	0.42 [-0.39, 1.24]
Brondolo 2009	140.16	17.03	37	131.98	16.92	36	6.3%	0.48 [0.01, 0.94]
Brownley 1996 (3)	128.3	10.9	36	121.5	10.9	36	6.2%	0.62 [0.14, 1.09]
Brownley 1996 (4)	125	11.37	28	130.2	11.37	28	5.5%	-0.45 [-0.98, 0.08]
Goldstein 2000	116.1	9.85	97	116.8	10.3	106	9.4%	-0.07 [-0.34, 0.21]
Guyll 1998 (5)	114	8.9	16	112.8	10.8	15	3.8%	0.12 [-0.59, 0.82]
Guyll 1998 (6)	125.9	11.3	12	125.3	7.4	20	3.8%	0.06 [-0.65, 0.78]
Jamner 1991	134	6.27	16	129	6.27	17	3.8%	0.78 [0.07, 1.49]
Jamner 1993	148	10.84	23	141	10.84	22	4.7%	0.63 [0.03, 1.23]
Pasic 1998	131.3	14.9	17	120.2	11.4	15	3.7%	0.81 [0.08, 1.53]
Raikkonen (2) 1999	121.1	15.22	49	113.9	15.22	51	7.3%	0.47 [0.07, 0.87]
Schneider 1989	122	11.76	24	121.4	11.4	9	3.4%	0.05 [-0.72, 0.82]
Shapiro 1996 (7)	104.5	8.9	43	105.5	8.9	43	6.9%	-0.11 [-0.53, 0.31]
Shapiro 1996 (8)	112	9.7	29	107	9.7	29	5.6%	0.51 [-0.02, 1.03]
Shapiro 2001	120	6.41	203	117.5	6.41	203	10.7%	0.39 [0.19, 0.59]
Suarez 1991	114.2	17.5	15	122.3	9.4	16	3.7%	-0.57 [-1.29, 0.15]
Vella 2008	131.1	13	86	127.01	11.1	86	8.9%	0.34 [0.04, 0.64]
Total (95% CI)			**755**			**756**	**100.0%**	**0.28 [0.11, 0.44]**

Heterogeneity: Tau² = 0.06; Chi² = 35.06, df = 17 (P = 0.006); I² = 52%
Test for overall effect: Z = 3.28 (P = 0.001)



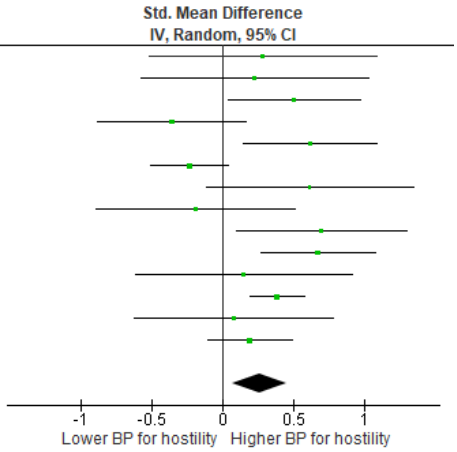
Footnotes
(1) Males
(2) Females
(3) White
(4) Black
(5) Females
(6) Males
(7) White
(8) Black

Table 9.

Relationship Between Hostility and Diastolic Blood.

	Hostile/Angry			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Benotsch 1996 (1)	68.4	4.4	12	67.1	4.5	12	4.2%	0.28 [-0.52, 1.09]
Benotsch 1996 (2)	71.8	5.2	12	70.5	5.9	12	4.2%	0.23 [-0.58, 1.03]
Brondolo 2009	84.49	10.71	37	79	10.74	36	7.9%	0.51 [0.04, 0.97]
Brownley 1996 (3)	78.3	8.76	28	82	11.37	28	7.0%	-0.36 [-0.89, 0.17]
Brownley 1996 (4)	81.1	7.37	36	76.5	7.37	36	7.8%	0.62 [0.14, 1.09]
Goldstein 2000	68.5	4.92	97	69.7	5.15	106	11.2%	-0.24 [-0.51, 0.04]
Guyll 1998 (5)	72.1	4.5	12	68.8	5.6	20	4.8%	0.62 [-0.12, 1.35]
Guyll 1998 (6)	68.3	5.9	16	69.5	6.4	15	5.0%	-0.19 [-0.90, 0.52]
Jamner 1993	88.1	3.64	23	85.5	3.64	22	6.1%	0.70 [0.10, 1.31]
Raikkonen (2) 1999	72.4	8.1	49	66.9	8.1	51	8.9%	0.67 [0.27, 1.08]
Schneider 1989	77.7	9.31	24	76	15.6	9	4.5%	0.15 [-0.62, 0.91]
Shapiro 2001	73.9	8.56	203	70.6	8.46	203	12.5%	0.39 [0.19, 0.58]
Suarez 1991	70.2	11.2	15	69.4	7.6	16	5.0%	0.08 [-0.62, 0.79]
Vella 2008	79.49	7.9	86	78.1	6.5	86	10.7%	0.19 [-0.11, 0.49]
Total (95% CI)			**650**			**652**	**100.0%**	**0.26 [0.06, 0.46]**

Heterogeneity: Tau² = 0.07; Chi² = 31.67, df = 13 (P = 0.003); I² = 59%
Test for overall effect: Z = 2.60 (P = 0.009)



Footnotes
(1) Females
(2) Males
(3) Black
(4) White
(5) Males
(6) Females

Chapter 4

Discussion

4.1 Key Findings

In recent years, ambulatory blood pressure monitoring has increased in popularity given the benefits it provides in relation to diagnosis and treatment (Pellizzari et al., 2008). The overwhelming value of ambulatory monitoring is that it provides a more accurate representation of a person's blood pressure rather than clinically determined blood pressure. Data was collected from 30 independent studies ($N_{participants}$= 3465) and analysed to determine whether increased ambulatory blood pressure is associated with higher levels of negative affect; specifically, depression, anxiety and hostility. For all analyses, the median of the mean ages of each sample was 50.2 years with approximately equal proportions of males and females (49.2% females). The results obtained from this meta-analysis provided significant effects for the association between ambulatory systolic and diastolic blood pressure with depression and hostility. The effects obtained in relation to depression and hostility were both of a similar magnitude and identified the same positive direction of effect which was consistent with the original hypotheses. Meanwhile, the results obtained for the association between anxiety and ambulatory blood pressure indicated a non-significant association. Overall, the findings highlight a weak association between ambulatory blood pressure and negative emotions, whereby individuals with higher levels of depression or hostility are more likely to have higher blood pressure. The findings are analysed in more detail below, with consideration given to the clinical and research implications in addition to a discussion of the methodological limitations of this meta-analysis.

4.2 Association between depression and blood pressure, implications and future research

The review provided an in-depth evaluation of the relationship between depression and blood pressure. As hypothesised, the results obtained evidenced a weak association between depression and both systolic and diastolic blood pressure. Low heterogeneity was found in relation to systolic blood pressure data, thereby indicating that any diversity between studies was unlikely to influence the accuracy of the obtained effect size. However, for diastolic data, a substantial amount of heterogeneity was observed which represented a significant risk of impacting the results. It was noted that two studies, Ma et al. (2017) and Vetrano et al. (2015), appeared to provide outlying effect sizes. Theoretically, the two studies could be excluded on the basis of reporting conflicting results, however, this would introduce bias. One possible reason for such discrepancy is that both of these studies utilised older participants than the other studies, with a mean age of approximately 70 years. Moreover, many of the participants evaluated in the two studies had pre-existing health conditions such as Parkinson's disease, osteoarthritis and hypertension which may have contributed to their divergent results. As a means of addressing the age differences between samples, future research should aim to conduct sub-group analyses according to clinically relevant age ranges such as for populations under 50 years of age versus those over 50 years of age who face an increased risk of developing hypertension (Lionakis, Mendrinos, Sanidas, Favatas, & Georgopolou, 2012).

Although the issue of causality was not resolved by the finding of an association between blood pressure and depression, nonetheless, significant clinical implications still arise. In particular, the findings support the notion that persons with depression may require frequent blood pressure assessments whilst, conversely, individuals with high blood pressure should be evaluated for symptoms of depression given the likely bidirectional association between these conditions (Hu et al., 2015). The consequences of such practices would necessitate increased

interdisciplinary collaboration between professions such as medical doctors and psychologists. Future research should focus on analysing certain groups of people in order to ascertain whether the association between depression and blood pressure is affected by factors such as sex, ethnicity or culture. Likewise, efforts could be made to determine the public's knowledge of the association and initiatives developed aimed at addressing this problem. For example, a partnership between organisations such as The Heart Foundation and Beyond Blue may help to increase awareness of the association between depression and cardiovascular health.

4.3 Association between anxiety and blood pressure, implications and future research

The results obtained indicated a non-significant association between anxiety and both systolic and diastolic blood pressure. Therefore, the findings support the null hypothesis that there would be no association between blood pressure and anxiety. Although the research in this area overwhelmingly indicates an association between anxiety and blood pressure, the majority of this research has utilised conventional clinic-based blood pressure recordings. Therefore, it may be argued that the results obtained in this meta-analysis provide evidence for the superiority of ambulatory blood pressure monitoring over conventional methods in obtaining an accurate representation of an individual's blood pressure, especially among anxious patients susceptible to the white-coat effect. Specifically, the results obtained from the ambulatory studies support the notion that anxiety is not associated with blood pressure which lies in contrast to the current consensus that anxiety is associated with blood pressure largely obtained through conventional methods (Pan et al., 2015). As a consequence, the results of the meta-analysis may reflect the accuracy of ambulatory monitoring in comparison to conventional clinic-based monitoring which may be impacted by the white-coat effect. However, alternatively, the findings may simply highlight the inability of 24-hour ambulatory monitoring to pick-up small spikes in blood pressure caused by anxious episodes. Therefore,

the use of ecological momentary assessment may improve understandings of the association between anxiety and blood pressure (Bishop et al., 2004).

However, central to the interpretation of the anxiety results should be a discussion of the findings of substantial levels of heterogeneity in the data collected for both systolic and diastolic blood pressure readings. The existence of substantial heterogeneity suggests that some of the included studies were not suitable to be combined. Clinical heterogeneity may have occurred due to the variation in mean ages, participant demographics and research settings employed by each study. Similarly, some studies utilised small samples of less than 50 participants which may lead to misestimates of the effect of anxiety on blood pressure, thereby potentially contributing to statistical heterogeneity. However, the underlying reason for the high levels of heterogeneity requires further investigation. To identify and isolate the causes for the heterogeneity, further analyses of the data should be conducted for certain subgroups according to sex, ethnicity and health status. A narrative review of the literature would be useful to comprehend the diversities between the studies in this meta-analysis. Moreover, further longitudinal studies would help to confirm the stability and causality of the association or lack thereof.

4.4 Association between hostility and blood pressure, implications and future research

The effect sizes calculated evinced a weak association between hostility and systolic and diastolic blood pressure. Therefore, the findings supported the original hypothesis that an association existed. The results reflected the current body of scientific literature which proposes that a relationship between the two variables does in fact exist. However, the benefit of performing a meta-analysis in this area was in relation to establishing the magnitude of the association between hostility and blood pressure as quantified by ambulatory monitoring.

The fact that ambulatory rather than conventional blood pressure data was used, should act to confirm the accuracy of the results and their generalisability across other similar populations. The accuracy of the results was further confirmed by heterogeneity scores which indicated that the diversity between the included studies posed only a moderate risk of influencing the overall effect sizes for the association of hostility with systolic and diastolic blood pressure. However, the fact that the majority of studies obtained data from US participants would indicate that the generalisability of findings might be restricted to US populations.

Given the high levels of US civilian involvement in military compared to other countries, and the tendency for military personnel to exhibit increased hostility (Jackson, Thoemmes, Jonkmann, Ludtke, & Trautwein, 2012), future research could be directed at determining whether hostility differs across less militaristic populations and assess the prevalence of hypertension observed in these countries. Furthermore, whilst four studies provided separate data sets according to sex (male versus female) and race (black versus white) the analyses of subgroups should be conducted for all studies to improve understanding of the association between hostility and blood pressure. Ideally, this would ensure that more longitudinal studies are conducted which may help to determine the causality of the association. Lastly, a core component of determining the causality of the association relates to the need for the development of a standardised scientific definition of hostility in the nearby future.

4.5 Methodological limitations

Several methodological limitations were identified as considerations during the interpretation of this systematic review and meta-analysis. Despite the intensive search strategies which were employed, not all of the relevant studies may have been included. Strict eligibility criteria meant that studies which reported correlation data were excluded. Similarly, the fact that all studies were obtained from research databases may increase the risk of

publication bias effecting the results as evidenced by the asymmetry of the obtained Funnel plots. Although a risk of bias assessment was conducted for this meta-analysis, many of the included studies did not clearly outline the methods used to reduce the risk of bias influencing their results. The results of studies employing only one session of ambulatory monitoring (rather than continual assessment across multiple days) may be impacted by novelty effects, particularly in relation to patients who were using an ambulatory device for the first time (Calvo et al., 2003; Murakami et al., 2004).

Recent research indicates that meta-analyses utilising random-effect models with less than five studies may result in power that does not exceed that of the original included studies (Jackson & Turner, 2017). Only seven and eight studies were included for the association between diastolic blood pressure and depression and anxiety respectively. Therefore, the likelihood of an effect being detected for these associations may not enhanced and the probability of making a Type II error may remain the same. Moderator analysis may have been useful to identify true differences between associations; however, no comparisons were conducted in relation to age, sex, education, health status. Therefore, it was unclear whether the obtained outcomes were impacted by between-group variability. The Cochrane Collaboration suggests that a minimum of 10 studies are required for the purpose of subgroup analysis (Fu et al., 2010), which would have made analyses of subgroups possible for three out of the six associations which were assessed in this meta-analysis. However, more recent research proposes that at least 20 studies are necessary for the reliable detection of between-group differences (Rubio-Aparicio et al., 2017), which would mean that any subgroup analyses conducted in this meta-analysis would be extremely unreliable.

The correlational nature of this meta-analysis means that the results obtained cannot be used to demonstrate the direction or causality of the association between the negative states and blood pressure. Whilst speculative suggestions may be proposed, longitudinal studies are

required in order to provide evidence for these proposals. Furthermore, given that the majority of included studies in this meta-analysis originated from the USA and Europe, with most participants being Caucasian, the generalisability of the results should be restricted to Western cultural contexts only.

4.6 Conclusion

The systematic review and meta-analysis provided a valuable overview for the association between negative emotions and blood pressure as quantified through ambulatory monitoring. As expected, a weak association was evidenced between blood pressure and both depression and hostility, whereby high levels of these states was associated with higher levels of blood pressure. Unexpectedly, no association was observed between anxiety and blood pressure possibly due to the considerable findings of heterogeneity impacting upon the results. Nonetheless, the results may have significant implications for people with high levels of depression and hostility as well as for people with high blood pressure. Based on these results, patients with high blood pressure should be screened for depression and hostility whilst, conversely, those with high levels of these negative emotions should have their blood pressure monitored. Future research should focus on developing a universalised scientific definition of hostility to ensure clarity surrounding certain cognitions and behaviours. Lastly, longitudinal studies of the association between negative emotions and ambulatory blood pressure would increase the power of results and aid in understanding the causality of the associations.

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Appendices

Appendix A: Search strategies by database

PsycInfo Logic Grid

AND →

Ambulatory blood pressure monitoring	Depression, Anxiety, Hostility
Ambulatory blood pressure monitor*.tw OR 24-hour blood pressure monitor*.tw OR ABPM*.tw OR Ambulatory monitor*.tw OR	Depression.sh OR depression.tw OR depressive symptom*.tw OR depressive disorder*.tw OR Anxiety.sh OR anxiety*.tw OR anxiety symptom*.tw OR anxiety disorder*.tw OR Hostility.sh OR Hostility.tw OR Anger.sh OR Anger.tw OR Aggression.sh OR Aggression.tw OR Negative emotion*.sh OR Negative emotion*.tw OR Negative affect*.sh OR Negative affect*.tw

PubMed Logic Grid

AND

Ambulatory blood pressure monitoring	Depression, Anxiety, Hostility
Ambulatory blood pressure monitor* OR “ambulatory blood pressure monitor*” OR 24-hour blood pressure monitor* OR “24-hour blood pressure monitor*” OR “ABPM*”	depression OR "depressive symptom*" OR “depressive disorder*” OR Anxiety OR “anxiety symptom*” OR “anxiety disorder*” OR Hostility OR Anger OR Aggression OR “negative emotion*” OR

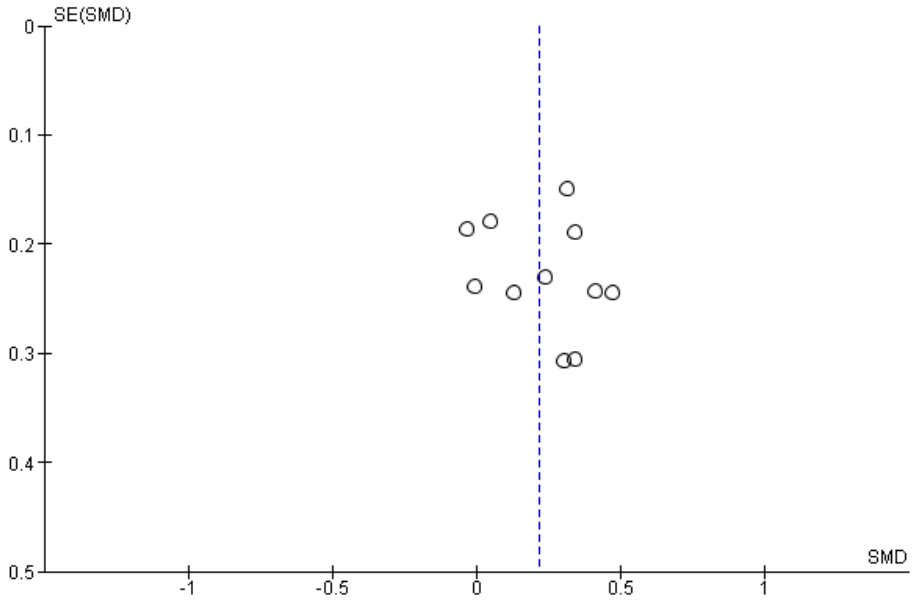
"negative affect*"

Scopus Logic Grid

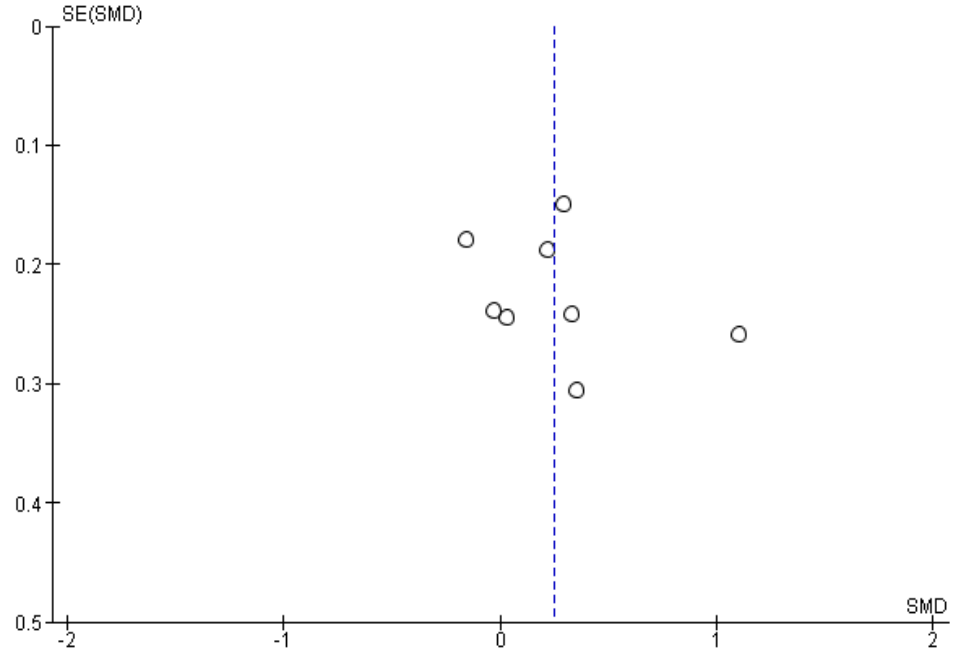
AND►

Ambulatory blood pressure monitoring	Depression, Anxiety, Hostility
Ambulatory blood pressure monitor*[tw] OR 24-hour blood pressure monitor*[tw] OR 24-hour blood pressure monitor*[tw] OR ABPM*[tw] OR	depression [mh:noexp] OR depression [tw] OR depressive symptom*[tw] OR depressive disorder*[tw] OR anxiety [mh:noexp] OR anxiety [tw] OR anxiety symptom*[tw] OR anxiety disorder*[tw] OR hostility [mh:noexp] OR hostility [tw] OR anger [mh:noexp] OR anger [tw] OR aggression [mh:noexp] OR aggression [tw] OR negative emotion*[mh:noexp] OR negative emotion*[tw] OR negative affect*[mh:noexp] OR negative affect*[tw]

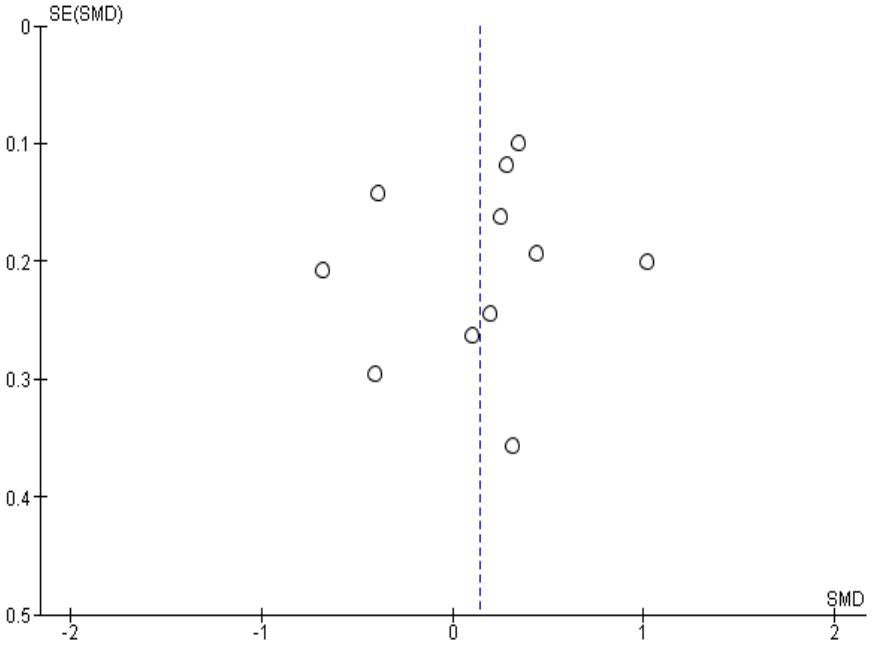
Appendix B: Funnel Plots for each negative state association with blood pressure



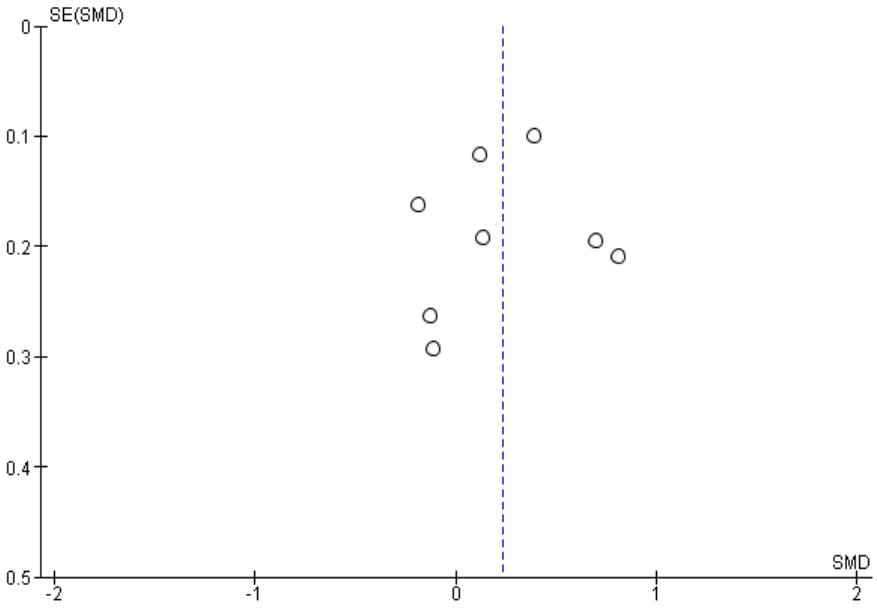
Analysis 1.1. Association between Depression and Systolic Blood Pressure.



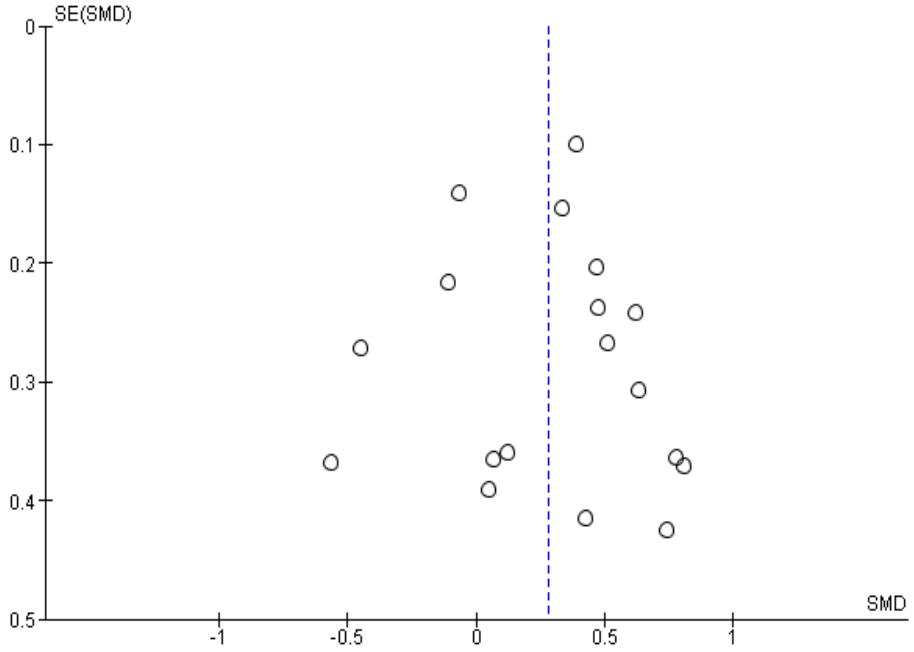
Analysis 1.2. Association between Depression and Diastolic Blood Pressure.



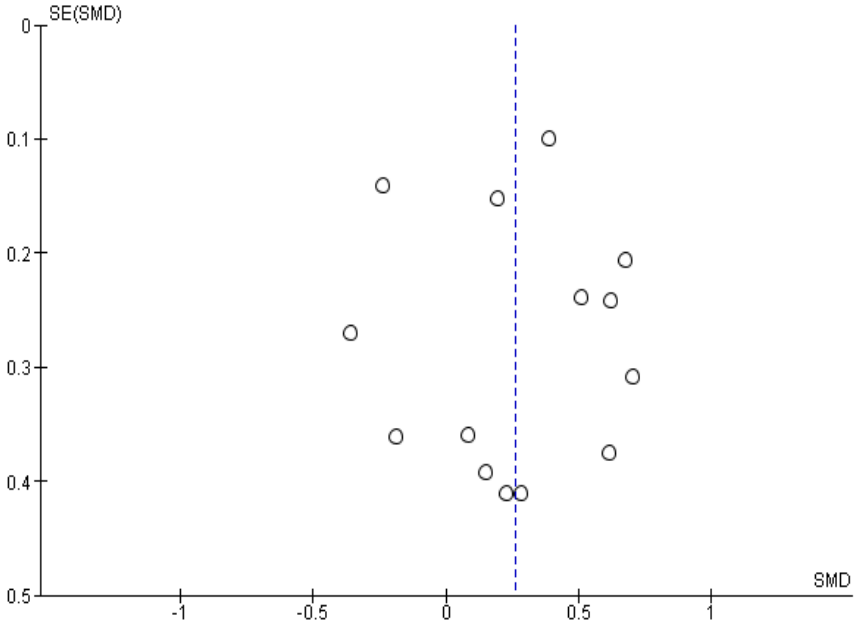
Analysis 2.1. Association between Anxiety and Systolic Blood Pressure.



Analysis 2.2. Association between Anxiety and Diastolic Blood Pressure.



Analysis 3.1. Association between Hostility and Systolic Blood Pressure.



Analysis 3.2. Association between Hostility and Diastolic Blood Pressure.

Appendix C: Cochran's risk of bias tool

AUB KQ1 Risk of Bias Assessment (Reference ID #)

Domain	Description	High Risk of Bias	Low Risk of Bias	Unclear Risk of Bias	Reviewer Assessment	Reviewer Comments
Selection bias ***Random sequence generation***	Described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence	Random sequence generation method should produce comparable groups	Not described in sufficient detail	**High** **Low** **Unclear**	
Selection bias ***Allocation concealment***	Described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrollment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	Intervention allocations likely could not have been foreseen in before or during enrollment	Not described in sufficient detail	**High** **Low** **Unclear**	
Reporting bias ***Selective reporting***	Stated how the possibility of selective outcome reporting was examined by the authors and what was found	Reporting bias due to selective outcome reporting	Selective outcome reporting bias not detected	Insufficient information to permit judgment†	**High** **Low** **Unclear**	
Other bias ***Other sources of bias***	Any important concerns about bias not addressed above*	Bias due to problems not covered elsewhere in the table	No other bias detected	There may be a risk of bias, but there is either insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias	**High** **Low** **Unclear**	

* If particular questions/entries were pre-specified in the study's protocol, responses should be provided for each question/entry.
† It is likely that the majority of studies will fall into this category.
Assess each main or class of outcomes for each of the following. Indicate the specific outcome.

AUB KQ1 Risk of Bias Assessment (Reference ID #)

Outcome:

Domain	Description	High Risk of Bias	Low Risk of Bias	Unclear Risk of Bias	Reviewer Assessment	Reviewer Comments
Performance bias ***Blinding (participants and personnel)***	Described all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.	Blinding was likely effective.	Not described in sufficient detail	**High** **Low** **Unclear**	
Detection bias ***Blinding (outcome assessment)***	Described all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.	Blinding was likely effective.	Not described in sufficient detail	**High** **Low** **Unclear**	
Attrition bias ***Incomplete outcome data***	Described the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. Stated whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported.	Attrition bias due to amount, nature or handling of incomplete outcome data.	Handling of incomplete outcome data was complete and unlikely to have produced bias	Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided)	**High** **Low** **Unclear**	

Example application of Bias Tool in relation to study by Broege (1994).

⊟ Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Anxiety was measured and high versus low group data was created based on the psychometric results.
Allocation concealment (selection bias)	Low risk	Participants were randomly assigned to groups based off of their psychometric scores.
Blinding of participants and personnel (performance bias)	Low risk	Participants were not told of their scores until after the data was collected and analysed.
Blinding of outcome assessment (detection bias)	Low risk	The patients were not aware of the exposure.
Incomplete outcome data (attrition bias)	Low risk	No evidence of risk of attrition bias.
Selective reporting (reporting bias)	Low risk	No evidence of reporting bias found.
Other bias	Unclear risk	