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Acute Psychological Stress and Pulse Wave Velocity: Meta-Analysis and Recommendations for Future Research

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ABSTRACT

Repeated exposures to acute psychological stress may be associated with cardiovascular disease (CVD) risk, but the mechanisms underlying this relationship are not fully understood. The objective of this meta-analysis was to determine the effect of acute psychological stress on central pulse wave velocity (PWV) compared to pre-stress (baseline) levels in adults free of overt CVD. Electronic databases (PubMed, SPORTDiscus, and Google Scholar) were queried from inception to July 2024. Reference lists of eligible studies and previous relevant reviews were also screened. Studies were included if: (i) a noninvasive measure of PWV was used that included a central (aortic) arterial segment; (ii) participants were adults (≥18 years) free of overt CVD; and (iii) the acute stressor was purely psychological in nature. Appraisal and Synthesis Methods: Effect sizes were calculated as standardized mean differences (SMD) and pooled using a random-effects model. The magnitude of effect was adjudicated as trivial (<0.2), small (0.2), moderate (0.5), or large (0.8). A total of 11,689 studies were identified, from which 7 studies (11 effects, $N = 162$ participants) were eligible for inclusion. Moderate Acute psychological stress induced a moderate (SMD: 0.51, $p < 0.0001$; 95% CI: 0.34, 0.68) increase (detrimental) in central PWV, and there was insubstantial heterogeneity between studies (Cochran's Q (10) = 2.62 ($p = 0.99$)). The small overall number of studies as well as key differences in study methodologies limit the ability to elucidate the magnitude and consistency of stress-induced increases in PWV. Nonetheless, the present findings suggest that acute psychological stress induces significant increases in central PWV among adults free of overt CVD. The acute PWV response to psychological stress likely contributes to elevated CVD risk over time.

1 | Introduction

Psychological stress—the perception that demands to a threat or challenge supersede the ability to cope with those demands (Lazarus 1984)—is an independent and ubiquitous risk factor for cardiovascular disease (CVD) (Brotman et al. 2007; Gill et al. 2023). The physiological reaction to stress is an evolutionary trait that enabled our ancestors—and us—to respond to

situations that are perceived as threats to our wellbeing and/or survival (McEwen 2007). Factors that influence the physiological (and psychological) responses to stress are wide ranging and include genetics, developmental, and contextual (e.g., perceived racial discrimination) factors, lifestyle behaviors (e.g., physical activity levels) past and present stress exposures, as well as intrapersonal factors (e.g., emotion regulation). Regardless of whether a stressor is physical (e.g., pain, cold) or psychological (e.g., public speaking) in nature, the same cascade of physiological reactions generally ensues, mediated largely by two distinct, yet coordinated systems: the sympathetic nervous system (SNS) and the hypothalamic–pituitary–adrenal (HPA) axis.

The SNS—often colloquially termed the "fight-or-flight" response—stimulates the release of catecholamines into the bloodstream, which sharply increases cardiac output and diverts blood flow, and thus oxygen, to essential tissues necessary for immediate survival (e.g., skeletal, cardiac muscle). Though not as fast-acting, the HPA axis similarly serves to increase the metabolic capacity of the body by releasing the catabolic steroid hormone cortisol, which mobilizes energy stores and makes glucose more readily available to tissues in need. While the physiological response to stress is adaptive in the short term, repetitive exposure dysregulates SNS and HPA systems and taxes numerous downstream biological processes, ultimately contributing to systemic inflammation and heightened CVD risk. Though the precise mechanisms are not fully understood, a biologically plausible means by which repetitive exposure to psychological stress increases CVD risk is through the acceleration of biological vascular aging (Chida and Steptoe 2010a; Everson-Rose and Lewis 2005; Steptoe and Kivimäki 2012; Walton et al. 1995).

Biological vascular aging refers to the normal vascular structural and functional (e.g., endothelium-mediated) changes that occur over the lifespan with chronological aging, and is also moderated by CVD risk factors (Kucharska-Newton et al. 2019; Stoner et al. 2023). The most accepted approach for measuring biological vascular aging is arterial stiffness. Reflecting both arterial structure and function, arterial stiffening results in faster propagation of the pulse-pressure wave through one or more segments of the arterial tree (Kucharska-Newton et al. 2019; London and Pannier 2010; Stoner et al. 2023). The time scale of an acute exposure to a psychological stressor is unlikely to affect arterial structure, but rather more plausibly impacts arterial function. Our group has reported that measures of arterial stiffness are sensitive to acute changes in endothelial function (Stoner et al. 2020), while others have similarly demonstrated measures are dependent on nitric oxide (Kinlay et al. 2001; Wilkinson et al. 2002), the primary regulator of endothelial function (Michel and Vanhoutte 2010). Repetitive acute increases in arterial stiffness can lead to structural remodeling, including decreased elastin and increased collagen, and chronically increase arterial stiffness (Stoner et al. 2023).

The gold standard measure of arterial stiffness is pulse wave velocity (PWV) (Laurent et al. 2006; Van Bortel et al. 2012). PWV is defined as distance (length of arterial segment) divided by pulse-transit time (PTT), with a higher (faster) value reflecting increased arterial stiffness and CVD risk (London and Pannier 2010). PWV can be measured repeatedly in a relatively confined timeframe with minimal subject burden. This is a major advantage in the context of acute psychological stress studies, where cardiovascular parameters, including heart rate, blood pressure (BP), and PWV, generally peak within a short-lived window of time (e.g., within ≈1–15 min, with large interindividual variation) before more slowly returning toward resting levels (Gentilin et al. 2023; Lackner et al. 2010; Vlachopoulos et al. 2006). The most established and clinically relevant PWV pathlengths include aortic arterial segments since aortic distensibility directly influences myocardial afterload and transmission of pulse pressure to critical end-organs including the brain and kidneys (Briet et al. 2012; London and Pannier 2010; Pewowaruk et al. 2023). Measurements of PWV encompassing an aortic segment (e.g., carotid-femoral PWV [cfPWV], brachial-ankle [baPWV]) confer superior prognostic capacity than traditional CVD risk factors (Stone et al. 2023; Townsend et al. 2015; Yi et al. 2023). Thus, both aortic and composite (e.g., containing both central and peripheral segments) may be appropriate to investigate in the context of stress exposure and CVD risk.

In this study, we define PWV as a construct that represents a composite measure of arterial structure (i.e., stiffness) and function. A number of studies have reported that acute psychological stressors increase measures of PWV (Dutch and Redman 1983; Gentilin et al. 2023; Jatoi et al. 2014; Kume et al. 2020; Kume et al. 2022a; Logan et al. 2020; Szabo 1993; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009), but the effect magnitude has varied greatly with standardized mean differences (SMD) ranging from 0.01 (trivial) (Szabo 1993) to 0.78 (moderate) (Vlachopoulos et al. 2006). The mixed findings may be attributable, at least in part, to the use of relatively small sample sizes (mean: $n = 31.3$, median: $n = 23$). To bring clarity to the literature, a meta-analytic approach can be used to determine a singular effect size estimate.

1.1 | Objective

The objective of this meta-analysis was to determine the effect of acute psychological laboratory stressors, as compared to baseline (pre-stress) levels, on central PWV, defined herein as including a portion of the aorta, in disease-free adults. Secondarily, we aimed to provide recommendations for future research surrounding the effects of acute psychological stress on central PWV.

2 | Methods

This meta-analysis follows PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines. (Page et al. 2021)

2.1 | Data Sources and Searches

Two authors (GZ and NS) independently searched electronic databases (PubMed, SPORTDiscus, Google Scholar) using key search terms: (psychological stress OR mental stress OR acute stress) AND (arterial stiffness OR pulse wave velocity OR aortic stiffness). The reference lists of identified articles and previous relevant reviews or editorials were also screened. The search

was limited to English language studies published between inception and July 2024.

2.2 | Article Selection

Two researchers (GZ and NS) independently completed the screening process. Conflicts between reviewers were resolved by discussion, or when agreement (consensus) was not reached, by the senior author (LS). The term "article" is used synonymously with study (u), and "trial" (k) is the unit included in the meta-analysis. A given article may have resulted in more than one eligible k if more than one experimental condition (e.g., >1 type of stressor or >1 arterial segment was reported for a given (u). In such cases, data for each estimate were extracted separately. Duplicate studies and repeated publications within the same study (i.e., repeated use of the same dataset) were excluded. The full texts of potentially eligible articles were screened, and a study was included in the meta-analysis if the following criteria were met: (i) a noninvasive measure of PWV was used that included a central (aortic) arterial segment; (ii) participants were adults (mean sample age ≥ 18 years) free of overt CVD and not currently taking vascular-acting medications; and (iii) the stressor was purely psychological—rather than physical or a combination of psychological and physical (e.g., cold pressor task, socially evaluated cold pressor test) (Schwabe and Schachinger 2018).

2.3 | Risk of Bias and Study Quality Assessments

The risk of bias and study quality within studies was independently assessed by two individuals (NS) using the Cochrane Risk-of-Bias 2 (RoB 2 Tools, Beta Version 7) tool (https://sites.google.com/site/riskofbiastool/welcome, 2023) and an adapted version (see Supplement) of the National Heart, Lung, and Blood Institute (NHLBI) Study Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group (NHLBI, NIH, n.d.). In the event of scoring discrepancies, the lead author (GZ) served as the tiebreaker.

2.4 | Data Extraction and Synthesis

Data extracted for each eligible trial included bibliographic information (author, publication year), participant sociodemographic characteristics, details of the stress tasks, and magnitude of effect (mean and SD) in terms of change in PWV from pre (baseline) to post-stress. When mean differences and associated standard deviations were not published, they were requested from the corresponding study author. We were unable to reach the author of one article (Vlachopoulos et al. 2009). Therefore, image analysis software (ImageJ, Version 1.53) was used to extract data from an included figure (Vlachopoulos et al. 2009). The post-stress measurement data point used for analysis was the measurement taken immediately following cessation of the stressor. Due to the fast-acting nature of local (endothelial) and autonomic processes most likely driving PWV responses—and in our attempt to increase the probability of capturing peak responses—when a measure of PWV was not taken immediately following the stressor, the final measurement *during* the stressor was used as the "post" timepoint (Gentilin et al. 2023; Jatoi et al. 2014). When there was no measure taken immediately after OR during the stress exposure, the first post-stress measure was used as the "post" timepoint (5 min post-stress for all) (Kume et al. 2020; Kume et al. 2022b; Logan et al. 2020).

2.5 | Data Analysis

Data were analyzed using the "metafor" (Metafor version 4.4–0) (Viechtbauer 2010) package (R, version 4.2.0). In terms of our comparator, scant experimental studies (e.g., with a true non-stress control condition/group) have assessed acute psychological stress effects on central PWV. To meet what we deemed a minimum article threshold for performing a meta-analysis, we opted to include quasi-experimental studies and as such, baseline levels of PWV were considered the comparator in the current meta-analysis. Outcome measures were expressed as SMD (post-stress PWV minus baseline PWV) rather than weighted mean difference to accommodate structural and functional differences associated with different arterial segments. SMD values <0.2, 0.2–0.49, 0.5–0.8 and >0.8 reflected trivial, small, moderate and large effects, respectively (Cohen 1988). A random-effects model was used and a corresponding forest plot was created. Heterogeneity (τ^2), was estimated with the restricted maximum likelihood method. The Q-test for heterogeneity (Cochran 1954) and the I^2 statistic (Higgins and Thompson 2002) are also reported. Studentized residuals and Cook's distances were used to examine potential outliers and/or influential trials (Viechtbauer and Cheung 2010), using previously published thresholds (Viechtbauer and Cheung 2010). Two authors (GZ, NS) conducted the data extraction and analysis. While the data for this meta-analysis represent a nested structure (i.e., several studies (Kume et al. 2020; Kume et al. 2022a) reported multiple post-stress PWV measurements), alternative multilevel models did not improve model fit or significantly alter the precision of the meta-analysis summary effect. Consequently, we presented results from a more readily interpretable standard (single level) meta-analytic approach.

3 | Results

3.1 | Literature Search and Trial Selection

A total of 11,689 potentially eligible articles were identified. Of these, 35 articles were identified for full-text screening, of which 28 were excluded, leaving 11 trials from 7 studies (Gentilin et al. 2023; Jatoi et al. 2014; Kume et al. 2020; Kume et al. 2022a; Logan et al. 2020; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009) for inclusion (Figure 1).

3.2 | Description of the Included Trials

3.2.1 | Trial Setting and Participants

Included study characteristics are summarized in Table 1. The studies were carried out in the United States ($n=1$) (Logan et al. 2020), Greece ($n=2$) (Vlachopoulos et al. 2006; Vlachopoulos et al. 2009), Japan ($n=2$) (Kume et al. 2020; Kume

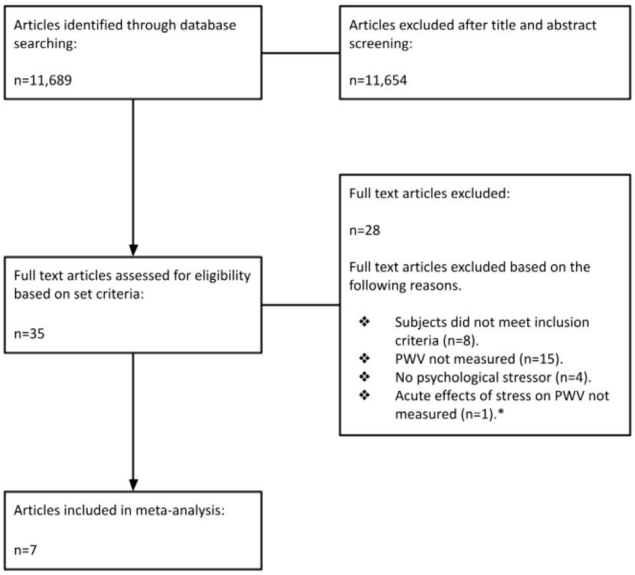

FIGURE 1 | Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart of study selection. Flowchart of study exclusions and selections. *This study (Ellins et al. 2008) was a longitudinal study in which acute stress and PWV were administered and measured 3 years apart, respectively. Abbreviations: n, number of articles; PWV, pulse wave velocity.

et al. 2022a), Italy ($n=1$) (Gentilin et al. 2023), and Ireland ($n=1$) (Jatoi et al. 2014). The number of participants in each study ranged from $N=15$ to $N=85$ (mean: $N=29$ [SD of mean sample sizes: $N=25.0$]; median: $N=19$). One study (Logan et al. 2020) included only female participants and two studies included only male participants (Kume et al. 2020; Kume et al. 2022a). The mean age of the participants ranged from 20.1 to 28.8 years (Gentilin et al. 2023; Jatoi et al. 2014; Kume et al. 2020; Kume et al. 2022a; Logan et al. 2020; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009). Across all of the included studies combined, there were a total of $N=203$ participants (Gentilin et al. 2023; Jatoi et al. 2014; Kume et al. 2020; Kume et al. 2022a; Logan et al. 2020; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009). However, the meta-analysis only included $N=162$ participants (mean age: 24.3 years [SD of mean ages: 3.1 years], 50% female) because 41 participants from Logan et al. (2020) were assigned to a control group that was not exposed to an acute psychological stressor.

3.2.2 | Acute Stressors

A brief description of the acute stress protocols is given in Table 1.

3.3 | Risk of Bias and Study Quality Assessment

3.3.1 | Risk of Bias

Domain S from the ROB 2 tool is specific to crossover trials. Since the studies by Logan et al. (2020) and Gentilin et al. (2023) were not crossover trials, the Domain S criteria were not considered when determining the overall risk of bias. All studies were assessed to have a "low" risk of bias, besides Jatoi et al. (2014) which was rated as having "some concerns" because the stress tasks were not implemented in a randomized order. Risk of bias ratings of included trials are reported in Table 1. Full descriptions of the risk of bias for each study are reported in Table S1.

3.3.2 | Study Quality

Overall, ratings of "good" quality were applied to all studies besides Vlachopoulos et al. (2006) and Jatoi et al. (2014) which were rated as being of "fair" quality because neither reported using a power analysis to determine sample size. Study quality ratings of included trials are reported in Table 1. Full descriptions of study quality ratings for each study are reported in Table S2.

3.4 | Synthesis of the Results

3.4.1 | Measurement and Characterization of the PWV Response

A number of methodological variables likely impacted the PWV responses that were analyzed. In terms of the measurement technology, five of the seven studies reported cfPWV (Gentilin et al. 2023; Jatoi et al. 2014; Logan et al. 2020; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009),with two having used the Complior (Vlachopoulos et al. 2006; Vlachopoulos et al. 2009), one the Sphygmocor (Logan et al. 2020), one the Arteriograph (Jatoi et al. 2014), and one electrocardiogram (ECG)-gated ultrasound (Gentilin et al. 2023). The studies by Kume et al. (2020; Kume et al. 2022a) each measured baPWV, heart–ankle PWV, and heart–brachial PWV using the Vasera device. In terms of measurement timing, there were two studies in which a PWV measurement was not taken immediately following the stressor, in which case the final measurement *during* the stressor was used as the "post" timepoint (Gentilin et al. 2023; Jatoi et al. 2014). In one of these instances (Gentilin et al. 2023), this measurement occurred at minute 10 of a 10-min stressor. The measurement time point was unclear for the other study (Jatoi et al. 2014) (only described as occurring "during" the stressor), and attempts to contact the authors were unsuccessful. However, the stressor duration in this latter study was only 3 min, and thus it is reasonable to assume that the measurement took place approximately 60–120 s into the 3-min stressor.

3.4.2 | Meta-Analytic Results

A total of 11 trials were included in the analysis. The observed outcomes (SMDs) ranged from small to large (0.28–0.78) (Figure 2). The random-effects model produced a moderate effect size SMD (0.51 [95% CI: 0.34, 0.68, $p<0.0001$]), indicating a substantial and significant increase in PWV. Based on the Q-test, there was no evidence of significant heterogeneity ($Q(10)=2.62$, $p=0.99$, $\tau^2=0.00$, $I^2=0.00\%$). Visual inspection of the funnel plot (Figure 3) indicated no evidence of publication bias, and the sensitivity analysis indicated that none of the trials unduly influenced the outcome. While no trials unduly influenced the outcome, the study by Logan et al. (2020) had a relatively large weight compared to the rest of the studies. Subsequent analysis

TABLE 1 | Characteristics of included studies.

Reference	N	Biological sex	Mean Age (years) [SD]	BMI (kg/m^2)	Covariates	Psychological stressor	Duration of stressor (min)	"Post-stress" measurement timing	Arterial segment (Device)	Nonstress control group or condition? (Y/N)	ROB	Quality
Vlachopoulos et al. (2006))	19	F: 10 M: 9	28.5 [0.6]	27.0	Perceived stress, smoking, caffeine	Mental arithmetic	3	Immediately post	cfPWV (Complior)	Yes	Low	Fair
Vlachopoulos et al. (2009))	18	F: 10 M: 8	26.9 [2.6]	NR	Peripheral and central SBP and DBP, peripheral and central AP, AIx, HR, smoking	Distressing Film	30	Immediately post	cfPWV (Complior)	Yes	Low	Good
Jatoi et al. (2014))	23	F: 14 M: 9	23 [3.0]	23.3	SBP, DBP, HR	Mental arithmetic	3	"During" stressor (precise timing un-specified)	cfPWV (Arteriograph)	No	SC	Fair
Logan et al. (2020))	85*	F: 85	28.78 [9.84]	23.48 ± 4.10	SBP, Age, BMI	TSST (speech task + mental arithmetic)	10	5 min post	cfPWV (Sphygmocor)	Yes	Low	Good
Kume et al. (2020))	17	M: 17	20.1 [0.7]	22.7	None	Mental Arithmetic	5	5 min post	baPWV haPWV hbPWV (Vasera VS-1500AN)	Yes	Low	Good
Kume et al. (2022a))	15	M: 15	21.7 [0.3]	21.2 ± 0.5	None	Mental arithmetic	5	5 min post	baPWV haPWV hbPWV (Vasera VS-1500AN)	No	Low	Good
Gentilin et al. (2023))	26	F: 13 M: 13	24.25 [2.85]	F: 21.5 M: 23.7	Sex	Mental arithmetic	10	10th (last) min of stressor	cfPWV (ECG-gated Doppler ultrasound [6.6 MHz linear array])	No	Low	Good

Note: Most BMI standard deviations were not reported. *While Logan et al. (2020) included $n = 85$ total participants, only the experimental group ($n = 44$) were included in the current analysis as the control group did not undergo an acute laboratory stressor.

Abbreviations: AP, augmented pressure; AIx, augmentation index; baPWV, brachial–ankle pulse wave velocity; BMI, body mass index; cfPWV, carotid–femoral pulse wave velocity; DBP, diastolic blood pressure; ECG, electrocardiogram; F, females; haPWV, heart–ankle pulse wave velocity; hbPWV, heart–brachial pulse wave velocity; hfPWV, heart–femoral pulse wave velocity; HR, heart rate; kg, kilogram; M, males; m, meters; MHz, megahertz; Min, minutes; NR, not reported; ROB, risk of bias; SBP, systolic blood pressure; SC, some concerns; TSST, Trier Social Stress Test.

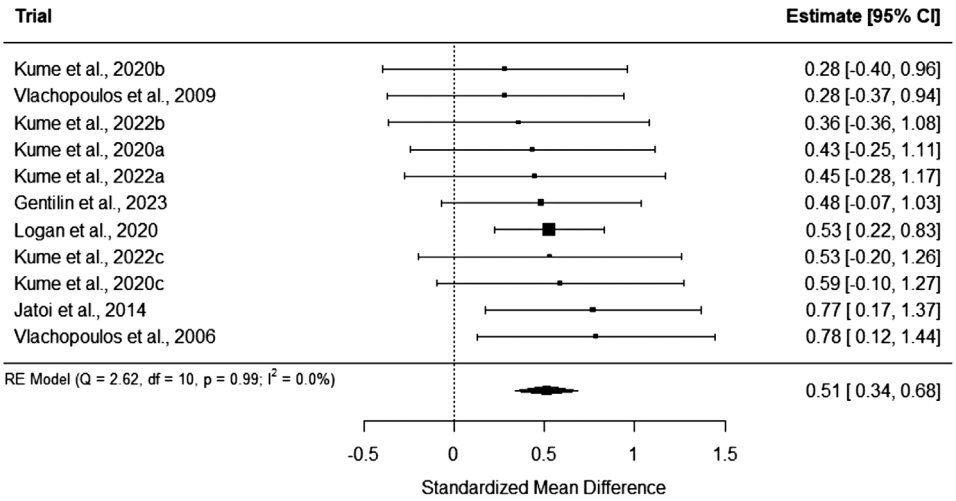

FIGURE 2 | Forest plot showing the observed outcomes and the estimate of the random-effects model. Lower-case letters following study years indicate different trials within a given study (e.g., for differing arterial pathlengths). The random-effects model produced a moderate effect size SMD (0.51 [95% CI: 0.34, 0.68, $p < 0.0001$]), indicating a substantial and significant increase in pulse wave velocity. Based on the Q-test, there was no evidence of significant heterogeneity: ($Q(10) = 2.62$, $p = 0.99$, $\tau^2 = 0.00$, $I^2 = 0.00\%$). Abbreviations: 95% CI, 95% confidence interval; RE, random effects; SMD, standardized mean difference.

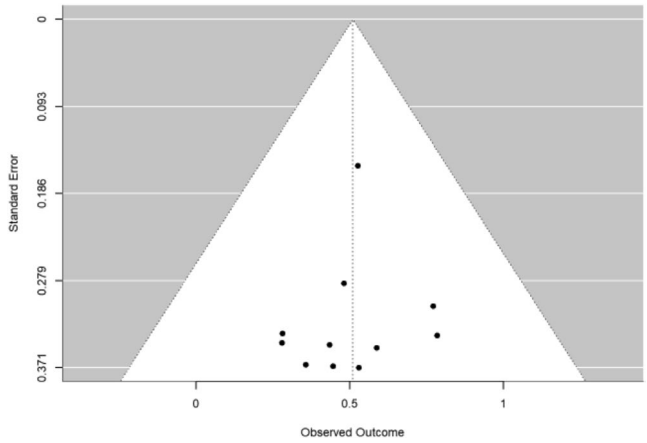

FIGURE 3 | Funnel plot for studies assessing the acute effects of psychological stress on pulse wave velocity. Visual inspection of the funnel plot indicates no evidence of publication bias.

after removing Logan et al. (2020) decreased the observed effect trivially, but it remained statistically significant (SMD = 0.50 [95% CI: 0.29, 0.71, $p < 0.001$]).

4 | Discussion

The objective of this meta-analysis was to determine the effect of acute psychological laboratory stressors versus pre-stress levels on central PWV in disease-free adults. The main findings were that acute exposure to psychological stress resulted in a significant moderate increase in PWV (SMD = 0.51 [95% CI: 0.34, 0.68, $p < 0.0001$]). Below, we summarize our findings in the context of the existing literature and discuss potential physiological mechanisms. We also interrogate the methodological differences across studies to identify possible sources of variance in our pooled effect size estimate, as well as provide recommendations to guide future research. A summary of the study's key findings, implications, and recommendations is outlined in Table 2 and Figure 4.

4.1 | Limitations

Several limitations should be kept in mind when considering the current findings. First, the sample sizes of included trials were generally small (range: $n = 15$ to $n = 85$; median: 19; inter range [IQR]: 9). Trials with greater sample sizes, including those with time-matched, neutral control conditions (or groups) are required to more clearly delineate the impact of acute psychological stress on PWV. Despite the lack of statistically significant heterogeneity, there were clear differences in methodologies which may have influenced the observed outcomes. These differences included varied PWV assessment technologies and arterial segments being assessed, as well as different measurement timepoints relative to the end of the stressor. In terms of the latter point, studies with a greater duration between the end of the stressor and when PWV was next measured are more likely to underestimate true PWV reactivity. Additionally, studies used non-uniform stressors and a wide range of stressor durations, which likely led to inconsistent stress appraisals and therefore responses across participants. Additionally, the majority of trials were mixed sex and, besides Gentilin et al. (2023) did not report sex-stratified results. It remains unclear whether PWV responses to acute psychological stress differ between sexes. Another limitation was that only four of the seven studies compared their results against a neutral or non-stress control group or condition (Kume et al. 2020; Logan et al. 2020; Vlachopoulos et al. 2006; Vlachopoulos et al. 2009). Finally, acute laboratory stressors may elicit different physiological responses to real-world, stress-inducing scenarios (Johnston et al. 1990; Zanstra and Johnston 2011). While the included studies prioritized internal validity using a regimented stress protocol in a laboratory setting, there is equally a need for future studies to examine the acute stress–PWV relationship with a greater emphasis on

TABLE 2 | Key points, implications, and future directions.

What did we know prior to this study?

- Psychological stress is linked to increased CVD risk, likely via vascular and autonomic mechanisms

What did not we know prior to this study?

- Evidence regarding the effects of acute psychological stress on PWV—a key construct reflecting arterial structure (i.e., stiffness) and function—had not yet been systematically reviewed.

What does this study add?

- Across 7 studies, meta-analytic findings demonstrate stress-induced moderate increases in central PWV.

How do we use this new information?

- Findings can inform future studies about the expected effect size for acute psychological stress on central PWV.
- Findings support mechanistic understanding of the link between stress and CVD risk which includes autonomic (central) and local effects on vascular function.

What needs to happen next to move the field forward?

- Given the limited number of studies included, more research is needed with adequate sample sizes obtained via power calculations
- Use of similar and clinically meaningful arterial segments, PWV measurement techniques, standardized laboratory stressors (and associated recovery periods) will enhance comparability of future research.
- Longitudinal studies are needed to determine whether stress-induced increases in central PWV predict future CVD.

external validity. For example, wireless photoplethysmography and/or ambulatory ECG could be employed to track PWV during and following acute stress responses in everyday life (e.g., naturalistic stressors; final examinations, traffic) (Zieff et al. 2023).

4.2 | Comparison With the Literature

We found that acute exposure to psychological stress resulted in a significant and moderate increase (SMD = 0.51) in central PWV. No prior meta-analyses or systematic reviews that we are aware of have summarized the PWV response to acute psychological stress. However, a substantial body of literature has demonstrated that cardiovascular stress reactivity is associated with poor cardiovascular outcomes (Chida and Steptoe 2010b; Moseley and Linden 2006; Sheps et al. 2002; Tabara et al. 2008; Turner et al. 2020; Yuenyongchaiwat 2017). For example, HR and BP reactivity and recovery from acute psychological stress have been associated with HR, BP, and hypertension status 3–10 years later (Carroll et al. 2011; Moseley and Linden 2006). Vascular stress reactivity has also been shown to predict clinical outcomes. Among 569 coronary artery disease patients, the presence of transient endothelial dysfunction in response to acute psychological stress was associated with a 78% increased risk of a 3-year incident major adverse cardiovascular event (Lima et al. 2019). It is also important to acknowledge that not only exaggerated cardiovascular reactivity, but also blunted reactivity, has been implicated in future health outcomes (Turner et al. 2020), and future work should investigate this possibility within the context of PWV responses to stress (Turner et al. 2020). As far as we are aware, no prior studies have assessed how PWV reactivity to psychological stress predicts future CVD. However, a meta-analysis of 17 longitudinal studies (n = 15,877, mean follow-up 7.7 years) indicated that for a 1 m/s increase in cfPWV, the risk of future cardiovascular events increased by 14% and the risk of cardiovascular mortality and all-cause mortality both increased by 15% (Vlachopoulos et al. 2010). In the current study, on average, PWV increased by 0.30 ± 0.25 m/s, and the clinical relevance of findings from acute stress-PWV studies needs to be determined in future research. However, acute stress does not equate to chronic, lifetime stress or the CVD risk associated with chronic stress. Nonetheless, the acute stress-induced increases in central PWV observed in this meta-analysis reflect direct insults to the vasculature, which over time, likely contribute to the progression of CVD risk and may partially explain the well-established relationship between chronic stress and cardiovascular morbidity and mortality.

4.2.1 | Potential Physiological Mechanisms

While the mechanisms underlying the associations between stress reactivity and CVD risk are not fully understood, two potential key players include endothelial and autonomic dysfunction.

Several reviews have investigated the effects of acute stress on endothelial (Xue et al. 2015) and autonomic (Kim et al. 2018) function. This evidence is relevant, given that work from our team has shown that acute laboratory perturbations to vascular endothelial function (Stoner et al. 2020) and autonomic (Zieff et al. 2023) nervous system directly influence PWV. Xue et al. (2015) performed a meta-analysis (8 studies, total n = 164) testing the effects of acute stress on endothelial function, with findings demonstrating a 2.5% stress-induced decrease (worsening) in flow-mediated dilation, the gold standard non-invasive assessment of endothelial function (Stoner et al. 2013). Kim et al. conducted another review (37 studies, total n = 14,298) investigating the effects of stress on heart rate variability (HRV), a widely used technique to assess autonomic regulation (Kim et al. 2018). The most frequently reported changes in HRV were decreases in high-frequency and increases in low-frequency

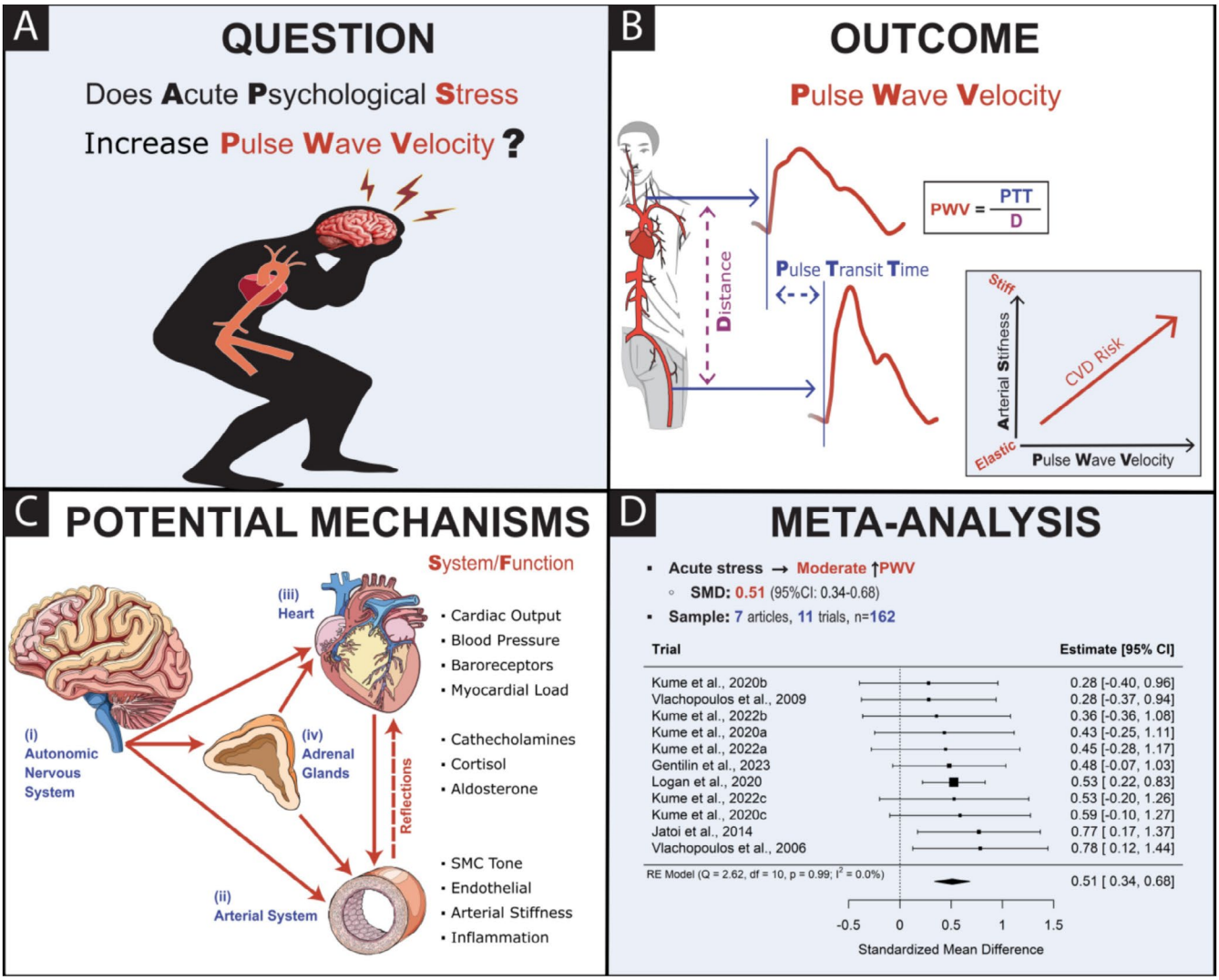

FIGURE 4 | Infographic summarizing meta-analysis: (A) question, (B) methods, (C) potential mechanisms, and (D) results. (A) This meta-analysis investigated the effect of acute psychological stress on central (containing an aortic segment) PWV in disease-free adults. (B) PWV reflects arterial structure (i.e., stiffness) and function and is an established biomarker for CVD risk. PWV is the speed at which the forward pressure waveform is transmitted between a proximal (e.g., carotid) and distal (e.g., femoral) arterial segment, with faster PWV reflecting increased arterial stiffness. (C) Stress-induced increases in PWV may manifest through several pathways. (i) The ANS directly increases sympathetic activity to the arterial system, the myocardium, and the adrenal glands. (ii) Heightened sympathetic activity stimulates SMCs, leading to vasoconstriction. (iii) Increased sympathetic activity at the level of the SA node increases cardiac output, which together with increased SMC tone, raises BP. The hashed red line indicates that increases in PWV also result in quickening and amplification of reflected pressure waves, which increases myocardial burden. (iv) The adrenal glands respond to sympathetic signaling by releasing the primary stress hormones (catecholamines, cortisol) and aldosterone into the bloodstream. The catecholamines promote further increase in SMC tone and cardiac output and promote the release of pro-inflammatory cytokines into the bloodstream. Cortisol has been reported to compromise endothelial function and elevate BP by decreasing baroreflex sensitivity. Aldosterone may further increase BP by increasing sodium and water reabsorption. (D) The literature search identified 7 studies [11 (*k*) effects], with a total of $n = 162$ participants (mean age: 24 ± 3 years). Acute psychological stress led to a moderate (SMD: 0.51 [0.34, 0.68]) increase in PWV. Abbreviations: ANS, autonomic nervous system; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; D, distance; HPA, hypothalamic–pituitary–adrenal; *n*, total sample size; PTT, pulse-transit time; PWV, pulse wave velocity; SA, sinoatrial; SMC, smooth muscle cell; SMD, standardized mean difference.

domains, which reflect reduced parasympathetic activity (Kim et al. 2018). Together, these findings suggest that the effects of psychological stress on PWV are likely mediated by both direct local effects (Ghiadoni et al. 2000) on the vasculature as well as central (e.g., autonomic) mechanisms (Logan et al. 2012) controlling global cardiovascular function.

As mentioned earlier, PWV can be considered a composite measure of arterial structure (i.e., stiffness) and function. Repeated exposure to acute stress over many months or years (e.g., chronic stress) may, in theory, lead to structural changes such as lumen narrowing and/or decreased ratio of elastin to collagen. Acute exposure to psychological stress is unlikely to induce observable changes in arterial structure. Rather, the acute increases in PWV we observed are more likely due to transient changes in autonomic and endothelial function. The mechanisms underlying acute declines in vascular function have not been fully elucidated, but several potential pathways are likely

involved. For example, acute psychological stress may impair vascular endothelial function by inducing an unfavorable ratio of vasodilatory (e.g., nitric oxide) to vasoconstrictive (e.g., endothelin-1) agents (Xue et al. 2015). Acute psychological stress also effects vascular function via central mechanisms, including sympatho-adrenal activation and concomitant vagal withdrawal (Graham 1990; Jayasinghe et al. 2016; Kim et al. 2018; Sloan et al. 1991). Stress-induced increases in autonomic activity directly increase cardiac output (Ring et al. 2002) and aldosterone release (Gideon et al. 2020), two key regulators of BP, which is important because BP is known to impact PWV (London and Pannier 2010), and underscores the need for future studies to control for BP (methodologically or statistically). Additionally, it is imperative to acknowledge that psychological stress impacts systems physiology, and alterations in the function of other (non-cardiovascular) systems have secondary effects on the cardiovascular system which likely impact PWV. For example, acute psychological stress augments HPA release of cortisol (Rimmele et al. 2007), which is also implicated in transient endothelial dysfunction and baroreflex desensitization following stress exposure (Broadley et al. 2005). Figure 4 (Panel C) contains a visual depiction of putative, physiological mechanisms underpinning the relationship between acute psychological stress and PWV.

4.2.2 | Unexpected Findings

While it was not our a priori intention to include only young adult samples, the mean age of participants among included studies ranged from 20.1 to 28.8 years. This was likely a result of investigators utilizing convenience sampling within university settings. Nonetheless, results are most generalizable to young adults free of CVD. As such, our findings represent acute stress-induced increases in PWV among a population relatively unencumbered by age- and chronic disease-related pathophysiological changes to the vascular system.

4.3 | Methodological Considerations: Sources of Variability

We did not observe statistically significant heterogeneity in the pooled effect. It is possible that this lack of significance is an artifact related to the limited number of included studies and a high degree of variance, as illustrated by the wide confidence intervals among included studies (Figure 2). Nevertheless, to inform and improve upon future research testing the effects of acute stress on PWV, it is still worthwhile to critically examine differences in study design that perhaps impacted the magnitude of observed effects. Table 3 summarizes our recommendations for improving future studies.

4.3.1 | Measurement of Pulse Wave Velocity

4.3.1.1 | Differential Arterial Segments. One major between-study difference was the measured arterial segments. These included carotid–femoral, heart–ankle, heart–brachial, and brachial–ankle segments. These segments are correlated (Choo et al. 2014; Lee et al. 2018; Tanaka et al. 2009) but not directly comparable due to differences in

TABLE 3 | Recommendations for minimizing sampling and measurement variance.

	Recommendation	Example
Study Design/Sample	Population driven by research question	Young disease-free adults if interested in avoiding confounds of age and disease-related changes to arterial system
	Sample size driven by power calculation	Based on moderate effect size determined from this meta-analysis
	Use of a control condition or group	Randomized crossover design with a time- and posture-matched neutral control task
Methods	Arterial segment contains an aortic component	Carotid–femoral, brachial–femoral, heart–femoral
	Valid measurement techniques and report lab-specific reliability (e.g., ICC)	Within Day ICC: ≥ 0.90 Between Day ICC: ≥ 0.75
	Well-trained operator (ideally single operator to minimize variance)	Within operator ICC: ≥ 0.90 Between operator ICC: ≥ 0.75
	Use of an established stressor containing social-evaluative threat	Trier Social Stress Test
	Record PWV ≥ 30 min post-stress. More frequent measurements for first 15 min to capture peak response.	Baseline: 2–3 measurements Immediately post: 0, 5, 10, 15 min Recovery: 30, 45, 60 min
Analysis	Adjustments for relevant covariates	Primary: BP Secondary: e.g., BMI, age, medications

Abbreviations: BMI, body mass index; BP, blood pressure; cfPWV, carotid–femoral PWV; ICC, intraclass correlation coefficient; min, minutes; PWV, pulse wave velocity; TSST, Trier Social Stress Test.

structure and function (Fryer et al. 2021; Stone et al. 2021). For example, compared to central arterial segments such as the ascending and descending aorta, the greater concentration of smooth muscle cells in the walls of muscular peripheral arteries makes them more susceptible to changes in tone and diameter via autonomic and vasoactive responses (Leloup et al. 2015). The greater propensity for acute changes in tone and diameter in peripheral arteries may in theory translate to greater stress-induced increases in PWV in these arteries compared to central arteries. Equally important to acknowledge, chronological and biological aging of the vasculature generally accelerates central arterial stiffening relative to stiffening of peripheral arteries, resulting in amplification and quickening of the arterial wave reflection, thereby increasing cardiac afterload and compromising coronary perfusion (Fortier and Agharazii 2016; London and Pannier 2010). As such, age and progression of arterio- and atherosclerotic processes may influence the extent to which central versus peripheral arteries are acutely impacted by psychological stress. Under ideal circumstances with a greater number of included trials, this would normally prompt sensitivity analysis by segment type. Due to the small number of trials ($k = 11$), subgroup analysis by arterial segment was not performed, but will be of interest as additional investigations into stress effects on PWV emerge.

4.3.1.2 | Technique to Determine Pulse Transit Time. The pre-ejection period (PEP) is the electromechanical delay associated with the conversion of electrical signal into the mechanical action of the heart. Some PWV techniques such as ECG-gated Doppler ultrasound, which was used by Gentilin et al. (2023) include this PEP-associated delay, which biases PTT (and subsequently, PWV) estimates. In contrast, Vlachopoulos et al. (2006; Vlachopoulos et al. 2009) used applanation tonometry, which avoids the PEP-related delay. Differences between studies in their ascertainment of PTT impact studies' PWV estimates. We acknowledge that ECG-gated ultrasound is more financially feasible for many researchers. Nonetheless, whenever possible, it is recommended for future studies testing effects of acute stress on PWV to use techniques that truly measure PTT (e.g., from foot of proximal to foot of distal pressure waveforms).

4.3.2 | Type and Duration of Psychological Stressor

4.3.2.1 | Stressor Type. Physiological stress responses can arise from psychological, cognitive, and physical stressors. However, stress responses to these distinct provocations are not necessarily uniform (Finke et al. 2021). For example, cardiovascular effects from the cold-pressor test have been shown to be primarily driven by alpha-adrenergic mechanisms (influencing vasoconstriction), whereas effects from mental arithmetic tasks may be driven more by beta-adrenergic activation (influencing cardiac stimulation and vasodilation) (Montoya et al. 1997). The current meta-analysis excluded physical stressors to help minimize variability and focus on psychological stress as a CVD risk factor. Even among psychological stressors, whether the task incorporates social-evaluative threat can impact the magnitude of physiological reactivity (Schwabe et al. 2008). This point is made clear in a seminal meta-analysis (total $n = 6153$, 208 studies) by Dickerson and Kemeny (Dickerson and Kemeny 2004), which found that, in addition to uncontrollability, social-evaluative threat was a "key ingredient" for acute stressors to be able to reliably induce a robust physiological response.

All but one (Vlachopoulos et al. 2009) of the included studies utilized a mental arithmetic component in their stressor, with various levels of social-evaluative threat incorporated (Gentilin et al. 2023; Jatoi et al. 2014; Kume et al. 2020; Kume et al. 2022a; Logan et al. 2020; Vlachopoulos et al. 2006). Indeed, mental arithmetic is one of the most commonly cited types of stressors utilized in psychophysiological research, and has been reported in the literature for decades including as far back as 1959 by Brod et al. 1959 investigation of hemodynamic effects of stress (Sloan et al. 1991). Cortisol and affective responses to the Trier Social Stress Test (TSST)—which includes a mental arithmetic component—have been shown to significantly and moderately correlate with responses to a naturalistic (oral course exam) stressor on a separate day (Henze et al. 2017). However, parallel research is needed in the context of vascular and autonomic stress biomarkers. Nonetheless, previous findings reported that cardiovascular reactivity to arithmetic tasks predicts future CVD risk (Carroll et al. 2011; Moseley and Linden 2006), and that arithmetic may be a superior stressor in eliciting predictive reactivity responses compared to other types of lab stressors (Yuenyongchaiwat 2017). Future research should also take into account that the most suitable (e.g., robust, ecologically valid) stressors may depend on the population being studied (Allen et al. 2017).

4.3.2.2 | Stressor Duration. Another factor that may influence the PWV response to acute psychological stress is the duration of the stressor. Among the articles included in the present meta-analyses, the stressors ranged in duration from 3 to 30 min (mean: 9.42 min, median: 5 min, IQR: 7 min). Ring et al. (2002) reported that, over the course of a 28-min mental arithmetic task in 30 healthy young adults, cardiac output rose during the first half of the task and then returned to baseline levels, whereas total peripheral resistance increased to a greater extent in the latter portion of the stressor (Ring et al. 2002). These findings suggest that, at least in prolonged mental arithmetic tasks, cardiovascular reactivity may initially be driven by cardiac mechanisms, which then give way to vascular mechanisms as the stressor progresses. To aid comparability among future research examining acute stress effects on PWV, we recommend that future studies use established protocols with standardized protocols (e.g., TSST uses 10-min stressor) and recovery durations.

5 | Conclusions

Chronic psychological stress is a known contributor to elevated CVD risk (Brotman et al. 2007), and severe levels of psychological stress are commonplace in today's society (http://www.apa.org/news/press/releases/stress//snapshot, 2015). A small overall number of studies have examined stress-induced PWV responses using clinically relevant central arterial segments. Results from the current meta-analysis indicate that acute psychological stress causes transient increases in PWV, potentially leading to arterial stiffening and CVD risk over time. However, the magnitude and consistency of stress-induced increases in PWV are not fully clear—particularly given the heterogeneity in stress protocols and arterial pathlengths. Future studies are warranted to investigate (i) the extent to which PWV responses

to laboratory-based stressors are influenced by lifestyle (e.g., exercise, mindfulness, diet, sleep) and lifestyle-associated factors (e.g., resilience, cardiorespiratory fitness), and (ii) how PWV reactivity and/or recovery to acute stressors predicts future CVD risk and outcomes.

Author Contributions

Gabriel Zieff: conceptualization, investigation, writing – original draft, methodology, validation, visualization, writing – review and editing, software, formal analysis, project administration, data curation, resources. **Noora Sharma:** methodology, formal analysis, data curation, validation, visualization, writing – review and editing, investigation. **Keeron Stone:** conceptualization, investigation, writing – original draft, methodology, validation, visualization, writing – review and editing. **Patricia Pagan Lassalle:** investigation, methodology, validation, visualization, writing – review and editing, software, formal analysis. **Aiden J. Chauntry:** writing – review and editing. **Erik D. Hanson:** conceptualization, investigation, methodology, validation, writing – review and editing, supervision. **Michelle L. Meyer:** conceptualization, investigation, writing – review and editing, validation. **Claudio Battaglini:** conceptualization, investigation, validation, writing – review and editing. **Justin B. Moore:** conceptualization, validation, writing – review and editing. **Craig Paterson:** conceptualization, investigation, methodology, validation, writing – review and editing, data curation, software, formal analysis, visualization, writing – original draft. **Lee Stoner:** conceptualization, investigation, writing – original draft, methodology, validation, writing – review and editing, supervision, resources, visualization.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

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