The Effects of Cold Exposure (Cold Water Immersion, Whole- and Partial- Body Cryostimulation) on Cardiovascular and Cardiac Autonomic Control Responses in Healthy Individuals: A Systematic Review, Meta-Analysis and Meta-Regression.

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Abstract

Background: Cryostimulation and cold-water immersion (CWI) have recently gained widespread attention due to their association with changes in cardiovascular and cardiac autonomic control responses. Therefore, the aim of the present systematic review and meta-analysis was to identify the global impact of such cold exposures on cardiovascular and cardiac autonomic activity. **Methods:** Three databases (PubMed, Embase, Web-of-Science) were used. Studies were eligible for inclusion if they were conducted on healthy participants using cryostimulation and/or CWI. The outcomes included measurements of blood pressure (BP), heart rate (HR), and heart rate variability (HRV) indices: RR interval (RR), Root mean square of successive RR interval differences (RMSSD), low frequency band (LF), high frequency band (HF), and LF/HF ratio. **Results:** Among the 27 articles included in our systematic literature review, only 24 were incorporated into the meta-analysis. Our results reveal a significant increase in HRV indices: RMSSD (Standardized mean difference (SMD) = 0.61, $p<0.001$), RR (SMD = 0.77, $p<0.001$), and HF (SMD = 0.46, $p<0.001$), as well as significantly reduced LF (SMD = -0.41, $p<0.001$) and LF/HF ratio (SMD = -0.25, $p<0.01$), which persisted up to 15 minutes following cold exposure. Significantly decreased heart rate (SMD = -0.16, $p<0.05$), accompanied by slightly increased mean BP (SMD = 0.28, $p<0.001$), was also observed. These results seem to depend on individual characteristics and the cooling techniques. **Conclusion:** Our meta-analysis suggests that cryostimulation and/or CWI exposure enhance parasympathetic nervous activity. There is scarce scientific literature regarding the effect of individual characteristics on cold-induced physiological responses.

KEYWORDS: Cardiac autonomic control; Autonomic nervous system; Cardiovascular system; cold exposure; Cold water immersion; Partial-body cryotherapy/cryostimulation; Whole-body cryotherapy/cryostimulation.

Introduction

Cold exposure techniques such as whole-body cryostimulation (WBC), partial-body cryostimulation (PBC), and cold-water immersion (CWI) have recently gained widespread attention in the overall context of health and, more specifically recovery after exercise and rehabilitation. Cryostimulation refers to a technique of body cooling, in which individuals are exposed to extremely cold air (usually between −50°C and −160°C) for short periods of time (typically between 2 and 5 minutes). It encompasses two techniques, WBC wherein the individual is entirely exposed to cold air in an environmentally controlled chamber, and PBC, where the individual is similarly exposed, in a barrel-shaped device called cryo-sauna, while excluding the head. While cryotherapy and cryostimulation both refer to the same kind of cold stimulus, they involve patients in the former and healthy individuals in the latter. Cold water immersion entails immersing the entire body, except for the head, or the lower body up to the umbilicus, in water with temperatures typically below 15°C. These techniques are well-reputed for their potential benefits in terms of improved sleep quality and reduced pain, fatigue, inflammation, oxidative stress, and muscle soreness after physical exercise (Douzi et al., 2019b, 2019a; Moore et al., 2023). These features may be directly or indirectly related to changes in cardiovascular and cardiac autonomic control activities.

The autonomic nervous system (ANS) consists of two continuously active and functionally distinct divisions, namely the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). The ANS plays an important role in the control of cardiac activity. At rest, the coordinated activity of the PNS and the SNS helps to maintain stable heart rate (HR) (Yugar et al., 2023). In this regard, heart rate variability (HRV) has been widely recognized as a reliable and noninvasive method for the assessment of autonomic cardiovascular regulation and sympatho-vagal interaction (Mäkinen et al., 2008). HRV is defined as a series of measurements of successive RR interval (intervals between QRS complexes of normal sinus depolarization) variations in the HR record (Sztajzel, 2004; van Ravenswaaij-Arts et al., 1993). HRV assessment can be conducted by means of different methods. The time domain method examines the variability of the RR intervals between consecutive heartbeats such as the root mean square of successive RR interval differences (RMSSD), while the frequency domain approach evaluates the power distribution of HR oscillations across different frequency bands including low-frequency (LF), and high-frequency (HF) bands (Shaffer and Ginsberg, 2017; van Ravenswaaij-Arts et al., 1993). Parasympathetic nervous system effects tend to be more rapid (typically within 1 second) after a stimulus, as - compared to sympathetic activity, which

typically takes more than five seconds (Nunan et al., 2010). Consequently, HF power has been proposed as an indicator of PNS modulation, while LF power predominantly represents SNS modulation (Harinath et al., 2005; Ramaekers, 1998). Of note, the LF/HF ratio is considered to reflect the sympatho-vagal balance (Malik, 1996). More specifically, an increased LF/HF ratio is often interpreted as an indicator of sympathetic dominance, while a decrease is thought to reflect parasympathetic drive. In addition, RMSSD is used as an additional indicator for PNS activity (Hausswirth et al., 2013; Westerlund et al., 2006).

Cold exposure is considered as a highly stressful situation imposed on the human body, which rapidly elicits the deployment of immediate, short-term regulatory mechanisms (Zalewski et al., 2013), most of which are associated with cardiovascular and cardiac autonomic control functions. Notably, a significant increase in plasma noradrenaline levels is observed, reflecting activation of the SNS (Hausswirth et al., 2013). Baroreceptors located in the carotid sinus and aortic arch stimulate autonomic bulb centers to initiate parasympathetic activation in view of restoring physiological homeostasis (Douzi et al., 2020; Pump et al., 2001). Increased parasympathetic activity at rest has long been linked with a better health and a state of well-being, which can be further enhanced through regular physical activity and healthy lifestyle habits (Louis et al., 2015; Udo et al., 2013). In this context, previous works have demonstrated that cryostimulation increases RR intervals, RMSSD and HF power values that correspond to increased PNS activity (Hausswirth et al., 2013; Zalewski et al., 2014b). Consequently, cold exposure may be an efficient intervention to enhance parasympathetic activity.

Numerous studies have investigated the cold exposure effects on blood pressure (Fonda et al., 2014; Muller et al., 2012; Zalewski et al., 2014b), HR (Hausswirth et al., 2013; Sramek et al., 2000; Theurot et al., 2021), and HRV (Louis et al., 2020, 2015; Zalewski et al., 2014b). Nevertheless, it is crucial to note that despite the pertinent findings revealed in individual studies, comprehensive synthesis in this area in the existing literature is still lacking. To the best of our knowledge, there is currently no available meta-analysis having examined the cardiac autonomic control and cardiovascular system responses after cryostimulation and/or CWI exposure. Therefore, a meta-analysis is of importance to fill this gap by providing a more comprehensive overview and robust analysis of the existing literature. The main objective of this review is therefore to identify the real impact of cryostimulation and/or CWI exposure on cardiovascular and cardiac autonomic control activity. Our study also aims to uncover potential moderating factors, such as participant characteristics (age, sex, body mass index and physical level), as well as moderators associated with cold exposure such as cooling technique, and

cooled body areas. Subgroup and meta-regression analysis will be used to provide valuable guidance aimed at personalizing the intervention and at optimizing the use of cold exposure in various settings , including rehabilitation programs and post-exercise recovery . Furthermore, it is worth noting that time course analysis of cold exposure responses with regard to cardiovascular and cardiac autonomic control has not been incorporated into previous studies. Thereby , our meta-analyses may provide more complete and precise assessments of cold exposure effects and help to identify possible variations in physiological responses over time.

Methods

1. Literature search strategy

PubMed, Embase and Web-of-Science databases were searched without time or filter limitations. The search syntax included the following keywords: *[(Whole body cryotherapy) OR (Whole body cryostimulation) OR (partial body Cryotherapy) OR (partial body Cryostimulation) OR (Cryostimulation) OR (Cryotherapy) OR (Cold water immersion)] AND [(Hemodynamic responses) OR (heart rate) OR (heart rate variability) OR (autonomic nervous system) OR (sympathetic activity) OR (parasympathetic activity) OR (arterial blood pressure) OR (blood pressure)]*. All possible medical subject headings (MeSH) terms and synonyms were mapped. Reference lists of the included articles were examined manually to collect further studies not electronically identified. Searches were completed in September 2023.

The search results were imported and processed using Rayyan systematic review software (Ouzzani et al., 2016). Two authors performed the search independently. Retrieved articles were assessed for duplication. After removing duplicates, studies were screened first by title and abstract and then by published full text.

2. Eligibility Criteria

The PECOS (participants, exposure, comparators, outcomes, and study design) model was used to determine the inclusion criteria. Studies were eligible for inclusion if they met the following criteria: (a) the studies were conducted on healthy participants using cold exposure interventions: WBC, wherein individuals are entirely exposed to cold air at temperatures below −50°C; PBC, wherein the body is similarly exposed, while excluding the head; and CWI, which involves immersing the entire body, except for the head, or the lower body up to the umbilicus, in water with temperatures below 15°C. No exposure duration limitation was applied (b) the experimental group results for different measurements before and after intervention were available (c) the studies used validated tests and outcomes regarding MAP, SBP, DBP, HR, R-R, RMSSD, LF, HF and/or LF/HF. Studies were excluded if: (a) the intervention was carried

out on patients or animals; (b) the cold exposure intervention was applied during or after physical exercise. If cold exposure was used before physical activity, specifically for therapeutic purposes or in settings where the measurements were taken after physical exercise, the study was likewise excluded (c) the published works were in the form of books, citations, conference proceedings, systematic reviews, and narrative reviews. Our study protocol was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021). The review protocol was registered in PROSPERO, an international registry for systematic reviews (ID: CRD42023467597).

3. Data Extraction and Coding

Each study was blinded regarding authors, affiliations, and journals. The information were anonymized by a co-author, who was not involved in the data extraction process. The relevant details were revealed only after the data extraction process had been completed. Data were summarized in a spreadsheet (Microsoft Excel software). All included studies were coded using the following moderators: sex, age, body mass index, cold exposure intervention (cryostimulation, CWI), type of cryostimulation (WBC, PBC). The moderators were coded using a nominal scale. Mean and standard deviation were extracted from texts and tables. In cases where data were unavailable, the corresponding authors of the study were contacted. If no response was received, the study was excluded from our analysis. When data were presented in graphs, WebPlot Digitizer (Pacifica, CA, USA, Version: 4.5) was used (Drevon et al., 2017).

4. Methodological quality assessment

The methodological quality of the included studies was evaluated using the 11-item Physiotherapy Evidence Database (PEDro) scale. A score of 1 indicates that the study satisfied the item and a score of 0 indicates that the item was not satisfied (Maher et al., 2003). Two authors independently assessed the methodological quality with discussion and search for consensus over any difference in observed scores. Studies with a score equal or greater than 6 were considered to be high-quality, studies with scores equal to 4 or 5 were considered to be medium-quality, and studies with a score lower than 4 were considered to be low-quality (Maher et al., 2003).

5. Statistical analysis

Standardized mean differences (SMDs) between pre- and post-intervention for each experimental group were calculated using Hedges' g (Hedges, 1981). Since the effect of a cold exposure intervention may differ according to age, BMI, sex, or other moderators we used a random effects model. The SMDs were weighted by the inverse of the variance to calculate an overall effect and its 95% confidence interval (CI). If the CI crosses the value 0, it indicates a

non-statistically significant effect. Conversely, if the CI does not cross 0, it suggests a statistically significant effect (Borenstein et al., 2009). Cohen's classification was used to interpret the magnitude of SMD: < |0.50|: small; |0.50| to |0.80|: moderate; > |0.80|: large (Cohen, 1998). The percentage of variability between studies was assessed using the I^2 statistic, which represents statistical heterogeneity (Borenstein et al., 2009). I^2 values were classified as low (25%) , medium (50%) or high (75%) (Higgins et al., 2003). Subgroup and meta-regression analyses were conducted to identify potential sources of variance and heterogeneity. Meta-regression analysis was carried out for both categorical variables (i.e., sex [men vs women], cryostimulation type [WBC vs PBC]), and continuous variables. For the latter, the means of BMI, body fat %, and age were extracted from data presented in each individual study. The null hypothesis according to which the effect of cold exposure was similar between categories of a moderator variable was tested using a Q test based on analysis of variance (Borenstein et al., 2009). Once the null hypothesis was rejected, pairwise comparisons were performed with a Z test. The statistical significance level was set at $p < 0.05$.

To evaluate possible publication bias, funnel plot potential asymmetry test was used. Stability of the pooled effect size was assessed by sensitivity analyses, which involves removing individual studies from the analysis and calculating the impact of excluding each study on the overall result. All calculations were made with Comprehensive Meta-analysis software (version 3; Biostat, Englewood, NJ, USA).

The level of evidence was established using a specific scale based on methodological quality and statistical heterogeneity (Neal et al., 2016):

- The level of evidence was considered as strong when pooled results were obtained from three or more studies, including at least two high-quality studies that were statistically homogeneous.
- The level of evidence was considered as moderate when pooled results were obtained from multiple studies that were statistically heterogeneous, including at least one high-quality study, or, from multiple medium-quality or low-quality studies that were statistically homogeneous.
- The level of evidence was considered as limited when results were obtained from one high-quality study, or, from multiple medium- or low-quality studies that were statistically heterogeneous. The level of evidence was considered as very limited when it was obtained from one medium-quality study or one low-quality study.

- The level of evidence was considered as very limited when pooled results were not statistically significant and came from multiple studies that were statistically heterogeneous.

Results

1. Overall effect

The flow diagram of the search process is illustrated in Figure 1. The literature search led to the identification of 2669 potential studies eligible for inclusion in our analysis. Over 2000 (2172) articles were screened after removing duplicates, and 40 were assessed for eligibility. Thirteen studies (Barwood et al., 2017; Bonde-Petersen et al., 1992; Damijan and Uhrynski, 2012; Fox et al., 2003; Gregson et al., 2011; Hayward, 1984; Hayward and Eckerson, 1984; O'Brien et al., 2000; Tipton et al., 2000, 1998; Tipton and Golden, 1987; Versteeg et al., 2023; Zhang et al., 2003) were excluded from our analysis. The reasons for exclusion of each study are detailed in Appendix 1 (Supplementary material (SM)). Twenty-seven articles were included in our systematic review. Among them, 3 studies (Mawhinney et al., 2020; Westerlund et al., 2006, 2004) were excluded from the meta-analysis and meta-regression owing to the unavailability of relevant data. Finally, 24 articles were included in the meta-analysis and meta-regression. No additional articles were manually identified by examining the reference lists of the articles included.

A summary of the included studies is presented in Table 1. Additionally, the results of individual studies and pooled effect size are graphically displayed in forest plots (Appendix 2, see SM). Funnel plots used to identify a possible publication bias are presented in Appendix 3 (see SM). Symmetrical distribution of all measures around the mean effect size indicates that the sampling error was random. The results of leave-one-out sensitivity analysis showed that the estimated effect of cold exposure on all cardiovascular and autonomic nervous system variables is robust and not driven by any single study (Appendix 4, see SM). The PEDro scores obtained from each included study are presented in Table 2. The methodological quality average was 6.00 ± 1.06, with scores ranging from 4 to 8. Nine studies were considered of moderate quality, including one that scored 4 and eight that scored 5, while 15 studies were categorized as high quality, with PEDro scores of 6 or higher (Maher et al., 2003).

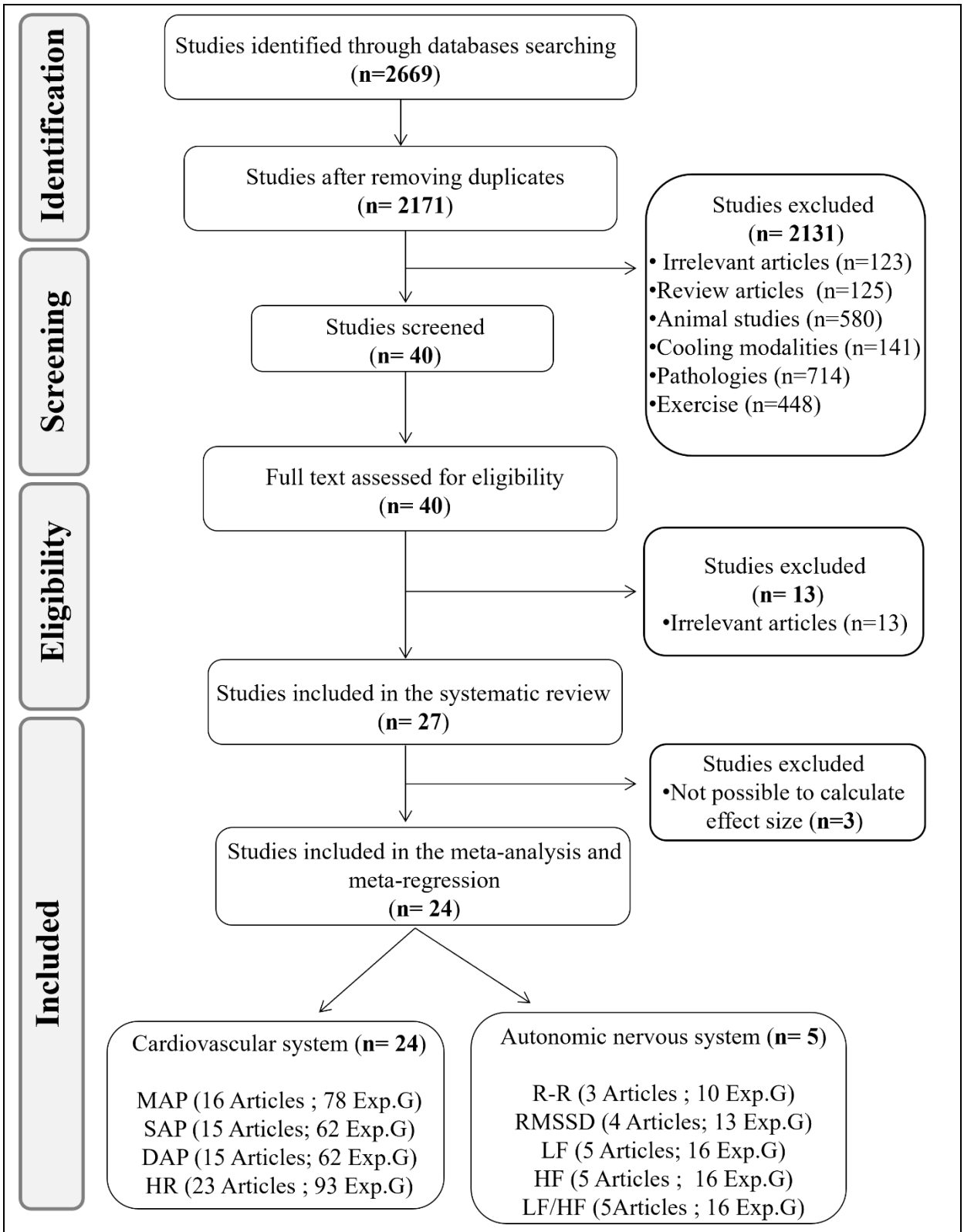

Figure 1. Flowchart of the study selection process.

MAP: Mean Arterial pressure; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; HR: Heart rate; RMSSD: root-mean square difference of successive R–R intervals; R-R: R–R heart rate intervals; High frequency (HF), LF: Low frequency; LF/HF: Ratio of low/high frequency power; EXP.G: Experimental Groups

Table 1. Summary of the included studies investigating the impact of cold exposure on cardiovascular and cardiac autonomic control responses.

Study	Study design	Participant characteristics				Cold exposure characteristics			Main Outcomes
		Sex	Age (years)	BMI (Kg/m^2)	Physical level	Type	Temperature (°C)	Duration (min)	
Theurot et al., 2021	• RCCT	• Men (n=9) • Women (n=9)	• 22.3 ± 1.8 • 22.8 ± 1.4	• 24.6 ± 2.5 • 21.8 ± 2.3	Physically active	PBC	-150	3	• ↘ HR, LF, and LF/HF ratio after PBC in men and women. • ↗ RMSSD and HF after PBC in men and women.
Hausswirth et al., 2013	• nRCT	• Men	• 34.6 ± 11.5 • 33.3 ± 13.8	• 24.2 ± 3.0 • 25.0 ± 3.3	NA	• PBC (n=15) • WBC (n=15)	-160 -110	3	• ↘ HR after WBC and PBC (WBC > PBC) • ↗ RMSSD and HF after PBC and WBC (WBC ≈ PBC) • ↗ SAP and DAP after WBC. • ↘ T°sk for all body regions immediately after WBC and PBC exposure, persisting up to 20 min after the session. • ↘ T°tm only after WBC exposure.
Hammond et al., 2020	• nRCCT	• Men (n=9) • Women (n=8)	• 23.1 ± 3.4 • 26.0 ± 7.0	25.9 ± 2.3 23.3 ± 2.7	Physically active	WBC	-140	3	• → HR and DAP after WBC in men and women • ↗ SAP after WBC in men and women • Men ≈ women for HR SAP and DAP after WBC.
Louis et al., 2015	• RCT	• Men	• 34.7 ± 11.5 • 34.8 ± 9.1	• 24.2 ± 3.0 • 25 ± 5.8	Physically active	• PBC (n=10) • WBC (n=10)	-160 -60	3	• ↘ HR after WBC and PBC (WBC > PBC) • ↗ RMSSD and HF after PBC and WBC (WBC ≈ PBC) • → SAP and DAP after WBC and PBC

								• ↘ T°sk for all body regions immediately after WBC and PBC exposure, persisting up to 20 min after cold exposure. • ↘ Ttm° after WBC and PBC exposure (WBC > PBC).
Dębiec-Bąk et al., 2013	• E P-P	Mixed group • Men (n=103) • Women (n=137)	• 22.74 ± 0.99 • 22.86 ± 0.94	NA	NA	WBC	-60 -60 -100 -100 -120 -120 -140 -140	1 3 1 3 1 3 1 3	• ↗ SAP, and DAP in all examined subgroups. • All measured values remained in physiological range. • ↘ T°sk for all body regions immediately after WBC (Lower limbs > other body area). • The lowest cooling temperatures (120 and 140 °C) and longer exposure time (3 min) caused the greater ↘ in T°sk
Cuttell et al., 2017	• E P-P	• Men (n=10) • Women (n=8)	• 27.7 ± 6.9 • 27.6 ± 6.3	• 23.6 ± 2.4 • 23.2 ± 2.8	Untrained	WBC	-110	3	• ↘ HR in men and women over time until 35 min after WBC (Men ≈ women). • ↘ MAP in men and women over time until 35 min after WBC (Men > women) • ↘ T°c in men and women after 35 min of WBC • ↘ T°sk in men and women immediately, 5 min and 10 min after WBC (Women> men) • ↘ T°tm in men and women after WBC
Fonda et al., 2014	•RnCCT	• Men (n=12)	• 23.9 ± 4.2	• 21.5 ± 2.1	NA	WBC	-140	1.5 2 2.5 3	• → HR, SAP, and DAP after all WBC exposure durations • ↘ T°sk for all body regions immediately after WBC • T°sk significantly lower after longer exposure (2.5 min and 3 min)

Zalewski et al., 2014a	• E P-P	• Men (n=25)	• 30.1 ± 3.7	• 25.9 ± 2.8	NA	WBC	-120	3	• ↘ HR after WBC • →MAP, SAP, and DAP after WB • ↗ LF and HF after WBC then at WBC + 3h and WBC + 6h • ↘ LF/HF ratio after WBC then ↗ at WBC + 3h and WBC + 6h • ↘ T°c 50-60 min following WBC.
Zalewski et al., 2013	• E P-P	• Men (n=30)	• 32.8 ± 6.9	• 25.6 ± 2.9	NA	WBC	-120	3	• ↘ HR after WBC then returned to basal values at WBC + 3h and WBC + 6h • → MAP, SAP, and DAP after WBC
Lubkowska and Suska, 2011	• E P-P	• Men (n=40)	• 22.0 ± 0.7	• 22.3 ± 2.93	NA	WBC	-130	3	• ↗ MAP, SAP, and DAP after WBC then returned to basal values at WBC + 10 min and WBC + 20 min. • ↘ HR after WBC then returned to basal values at WBC + 10 min and WBC + 20 min.
Lubkowska and Szyguła, 2010	• E P-P	• Men (n=25)	• 21.3 ± 0.94	• 23.19 ± 1.9	Physically active	WBC	-130	3	• ↗MAP, SAP, and DAP after WBC then returned to basal values at WBC + 10 min. • ↘HR after WBC then returned to basal values at WBC + 10 min . • → HR, MAP, SAP, and DAP after 15 sessions of WBC.
Louis et al., 2020	• RCT	• Men (n=40)	• 21.3 ± 0.94	• 23.19 ± 1.9	Physically active	WBC	-60 -110	3	• ↗ HR after WBC at -60 °C and at -110 °C. • ↗ SAP and SAP only after WBC at -110 °C. • ↗ RMSSD after WBC at -60 °C and at -110 °C. • ↗ HF only after WBC at -110 °C. • ↘ LF/HF ratio after WBC at -60 °C and at -110 °C.

									• ↘ Tsk° immediately after WBC (-110°C > -60°C), persisting up to 20 min after exposure (only at -110°C) • ↘ T°tm until 20 min after WBC (-110°C > -60°C)
Coppi et al., 2022	•E P-P	• Men (n=10)	• 38.0 ± 12.0	• 19.5 ± 2.0	Physically active	WBC	NA	3	• ↗ HR, SAP, and DAP after WBC • All measured values remained within normal range.
Westerlund et al., 2004	•E P-P	• Women (n=10)	• 38 ± 3	• 24 ± 3	Sedentary	WBC	-60 -110	2	• ↗ SAP after WBC (-110°C > -60 °C) • ↗ DAP after WBC (-110°C ≈ -60 °C)
Westerlund et al., 2006	•E P-P	• Women (n=10)	• 38 ± 3	• 24 ± 3	Moderately physically active	WBC	-60 -110	2	• ↗ RR, RMSSD and HF after CWI • → HF and LF/HF ratio after CWI
Rose et al., 2023	•RCT	• Men	• 23.4 ± 4.6	• 24.4 ± NA	NA	• PBC (n=8) • Head-out CWI (n=9)	• −110 to −140 °C 9 °C	3	• ↗ HR after PBC • ↘ HR after CWI • ↗ SAP and DAP after PBC and CWI
Muller et al., 2012	•RCCT	• Men (n=9)	• 23.0 ± 2.0	• 25.9 ± NA	NA	Lower body CWI	13	60	• ↗ SAP at 10 min and 60 of CWI. • ↗ DAP at 10 min, 40 min, and 60 of CWI. • ↗ SAP at 10, 40 min, 50 min, and 60 of CWI. • ↘ HR at 20 min of CWI. • ↘ Tsk° 15 min, 20 min, 45 min and 60 min of CWI • ↘ T°re at 60 min of CWI.
Sramek et al., 2000	•RCCT	• Men (n=10)	• 22.2 ± 2.4	NA	NA	Head-out CWI	14	60	• ↗ HR, SAP, and DAP after CWI • ↘ Tre° after CWI.
Eimonte et al., 2021	•CRCT	• Men (n=12)	• 23.0 ± 4.0	• 23.67 ± 1.85	Physically active	Head-out CWI	14	10	• ↗ HR after CWI • ↘ Tsk° immediately after CWI persisting up to 1h. • ↘ T°re from 45 to 70 min after CWI

Vogelaere et al., 1995	•E P-P	• Men (n=15)	• 31.2 ± 2.3	• 22.2 ± NA	NA	Head-out CWI	15	60	• ↘ HR at 5 min and 10 min of CWI. • ↗ HR at 20 min of CWI. • → T°re during CWI • ↘ Tsk° from 2 to 60 min following CWI
Jansky et al., 1996	•E P-P	• Men (n=10)	• 22.5 ± 1.8	NA	Physically active	Head-out CWI	14	60	• → HR after the 1st and the 18th sessions of CWI. • ↗ SAP and DAP after CWI • ↘ SAP and DAP after 18th session of CWI compared to the 1st session. • ↘ T°sk during CWI
Kwiecien et al., 2019	•E P-P	• Men (n=11)	• 27.0 ± 7.0	• 24.2 ± NA	Physically active	Lower body CWI	15	15	• ↘ HR after of CWI. • ↗ RMSSD after CWI • → SAP and DAP after CWI • ↘ T°sk and T°c during CWI
Mantoni et al., 2007	•E P-P	• Men (n=13)	• 32.0 ± 7.0	• 25.4 ± NA	NA	Head-out CWI	0	0.5	• ↗ HR after CWI.
Barwood et al., 2014	•E P-P	Mixed group • Men (n=8) • Women (n=4)	• 20.0 ± 1.0	• 23.8 ± NA	NA	Head-out CWI	15	7	• ↗ HR after CWI.
Mantoni et al., 2008	•E P-P	Mixed group • Men (n=5) • Women (n=4)	• 29.0 ± 10.2	NA	NA	Head-out CWI	0	1	• ↗ HR after CWI.
Brazaitis et al., 2014	•E P-P	• Men (n=14)	• 21.6 ± 0.5	• 20.7 ± 1.3	Physically active	Head-out CWI	14	Until the T°re reached 35.5 °C or 170 min had elapsed	• ↗ HR after CWI. • ↘ HR after 17th session of CWI compared to the 1st session. • ↘ T°sk and T°re after CWI

Mawhinney et al., 2020	•E P-P	• Men	•33 ± 8	•24.2 ± NA	Physically active	Lower body CWI	•8 °C (n=10) •15°C (n=10)	•10	• No significant difference was observed between conditions for HR and MAP (8 °C ≈ 15°C) • ↘ T°sk after CWI (8°C) • ↘ Thigh skin temperature after CWI (8°C and 15°C)

↘: Decrease; ↗: Increase; →: no change; > : Greater effect; ≈ : Equal effect; n = sample size; BMI: body mass index; PBC: Partial body cryostimulation; WBC: Whole body cryostimulation; CWI: cold water immersion; HR: Heart rate; RMSSD: root-mean square difference of successive R–R intervals; R-R: R–R heart rate intervals; High frequency (HF), LF: Low frequency; LF/HF: Ratio of low–high frequency power; MAP: Mean Arterial pressure; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; T°sk: Skin temperature; T°tm: Tympanic temperature, T°c: core temperature; RCCT: Randomized controlled crossover trial; nRCT: non-randomized controlled crossover trial; RnCCT: Randomized non-controlled crossover trial; nRCT: non-randomized controlled trial; RCT: Randomized control trial; E P-P: Experimental pre-post design; T°re: Rectal temperature.

Table 2. Methodological quality of included studies.

Study	Item											PEDro Score	Quality
	1	2	3	4	5	6	7	8	9	10	11		
Theurot et al., 2021	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**8**	**High**
Hausswirth et al., 2013	**1**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**
Hammond et al., 2020	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Louis et al., 2015	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Dębiec-Bąk et al., 2013	**0**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**
Cuttell et al., 2017	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Fonda et al., 2014	**0**	**1**	**1**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Zalewski et al., 2014a	**1**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**
Zalewski et al., 2013	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Lubkowska and Suska, 2011	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Lubkowska and Szyguła, 2010	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Louis et al., 2020	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Coppi et al., 2022	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**1**	**4**	**Medium**
Rose et al., 2023	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**6**	**High**
Muller et al., 2012	**0**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**
Sramek et al., 2000	**0**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**
Eimonte et al., 2021	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**8**	**High**
Vogelaere et al., 1995	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Jansky et al., 1996	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Kwiecien et al., 2019	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Mantoni et al., 2007	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Barwood et al., 2014	**1**	**0**	**0**	**1**	**1**	**0**	**0**	**1**	**1**	**1**	**1**	**7**	**High**
Mantoni et al., 2008	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**5**	**Medium**
Brazaitis et al., 2014	**1**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**6**	**High**

2. Cardiovascular responses

The overall SMD shows that cold exposure (cryostimulation and CWI) induces a significant change in cardiovascular outcomes (Table 3). In fact, pooled data showed significantly decreased HR following exposure, with a small negative effect (SMD = - 0.16; 95% CI: -0.04 to -0.28; z = -2.55; I^2 = 39.90; **p = 0.011**) and slightly increased MAP (SMD = 0.28; 95% CI: 0.17 to 0.40; z =-4.94; I^2 = 20.12; **p = 0.000**); in SAP (SMD = 0.37; 95% CI: 0.24 to 0.51; z = 5.36; I^2 = 27.03; **p = 0.000**); and in DAP (SMD = 0.40; 95% CI: 0.29 to 0.52; z = 6.70; I^2 = 19.23; **p = 0.000**). Statistical heterogeneity justified a subgroup analysis with moderator variables, including individual characteristics, as well as cold exposure interventions and cooled body area.

Table 3. Overall effects of cold exposure on cardiovascular responses

	Participants (s)	Experimental groups (n)	Level of evidence	SMD	CI 95 %	p
HR	1234	93	Strong	-0.16	-0.04; -0.28	**0.011**
MAP	1210	78	Strong	0.28	0.17; 0.40	**0.000**
SAP	1066	62	Strong	0.37	0.24; 0.51	**0.000**
DAP	1066	62	Strong	0.40	0.29; 0.52	**0.000**

HR: Heart rate; MAP: Mean Arterial pressure; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; SMD: Standardized mean difference; CI : confidence interval.

2.1. Heart rate

Our results indicate that exposure to cold significantly decreases HR in men (SMD= -0.17; **p = 0.011**) and normal-weight participants (SMD = -0.13; p = **0.031**). Nevertheless, no significant difference between male and female participants or between different BMI categories was observed. Similarly, the meta-regression analysis did not show any significant effect of sex, BMI, body fat percentage, or age on HR changes. Additionally, our findings showed that cryostimulation induces a greater reduction in HR compared to CWI (**p = 0.024**), and that PBC leads to a greater decrease in HR compared to WBC (**p = 0.000**). This finding was supported by the meta-regression analysis, which highlighted a significant impact of cooling technique (CWI: coefficient = 0.35; 95% CI: 0.10 to 0.60; z = 2.73; **p = 0.006**), confirming that cryostimulation has a more substantial effect on HR decrease than CWI. As regards type of cryostimulation, a significant moderating effect (PBC: coefficient = -0.59; 95% CI: -0.92 to -0.25; z = -3.45; **p = 0.001**) was observed, indicating pronounced HR reduction ascribable to PBC intervention.

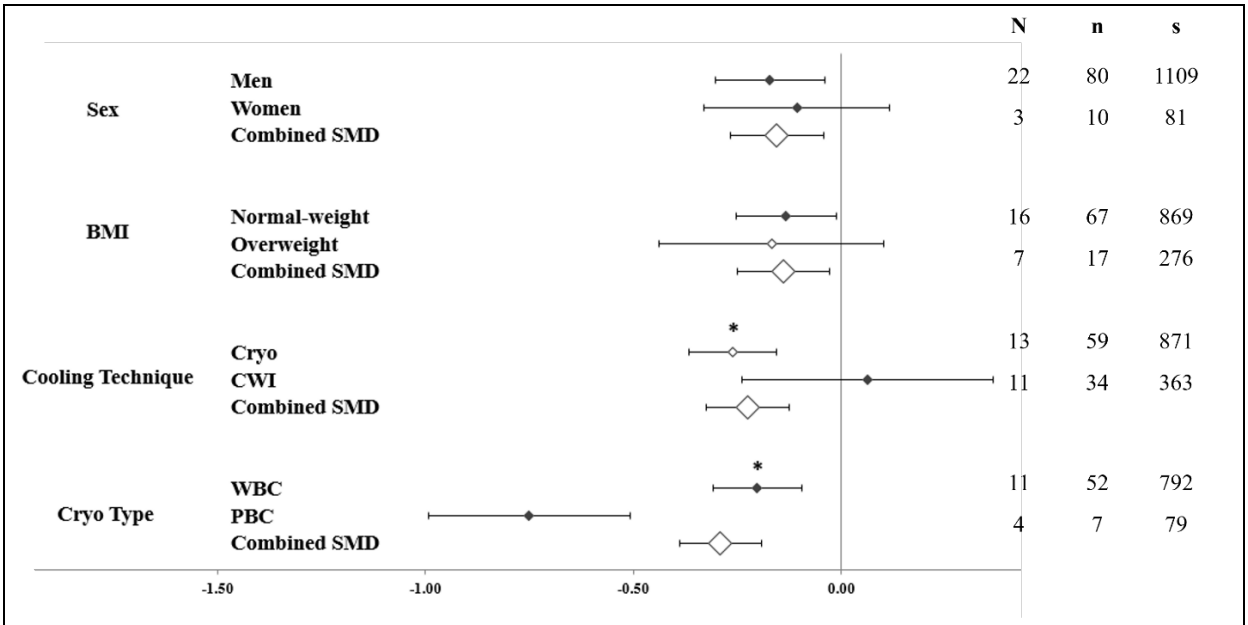

Figure 2. Effect of cold exposure on heart rate magnitude depending on sex, BMI, cooling technique, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; CWI: Cold Water Immersion; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at $p < 0.001$.

2.2. Arterial pressure

Concerning the impact of cold exposure (cryostimulation and CWI) on arterial pressure, our findings revealed slightly increased MAP (SMD = 0.23; **p = 0.001**) (Figure 3), SAP (SMD = 0.31; **p = 0.000**) (Figure 4) and DAP (SMD = 0.32; **p = 0.000**) (Figure 5) in male participants. In addition, there were no significant differences between participants with different BMI categories in terms of MAP, SAP, and DAP. Concerning cooling techniques, our results showed that cryostimulation induced slightly increased MAP (SMD = 0.27; **p = 0.000**), SAP (SMD = 0.40; **p = 0.000**) and DAP (SMD = 0.42; **p = 0.000**). However, there were no differences between the impacts of cooling techniques in terms of MAP, SAP, and DAP. Comparison between the effects of the different types of cryostimulation on arterial pressure showed that exposure to WBC induced a greater increase than the one observed with PBC in MAP (p = **0.035**), SAP (**p = 0.001**) and DAP (**p = 0.025**). Meta-regression analysis was in line with subgroup analysis, indicating no significant impact of age, sex, BMI, body fat percentage or cooling technique on MAP, SAP, and DAP. However, meta-regressions showed a significant

moderating effect of cryostimulation type (PBC: coefficient = -0.60, 95% CI: -1.19 to -0.01; z = -1.98; **p = 0.048**) on SAP.

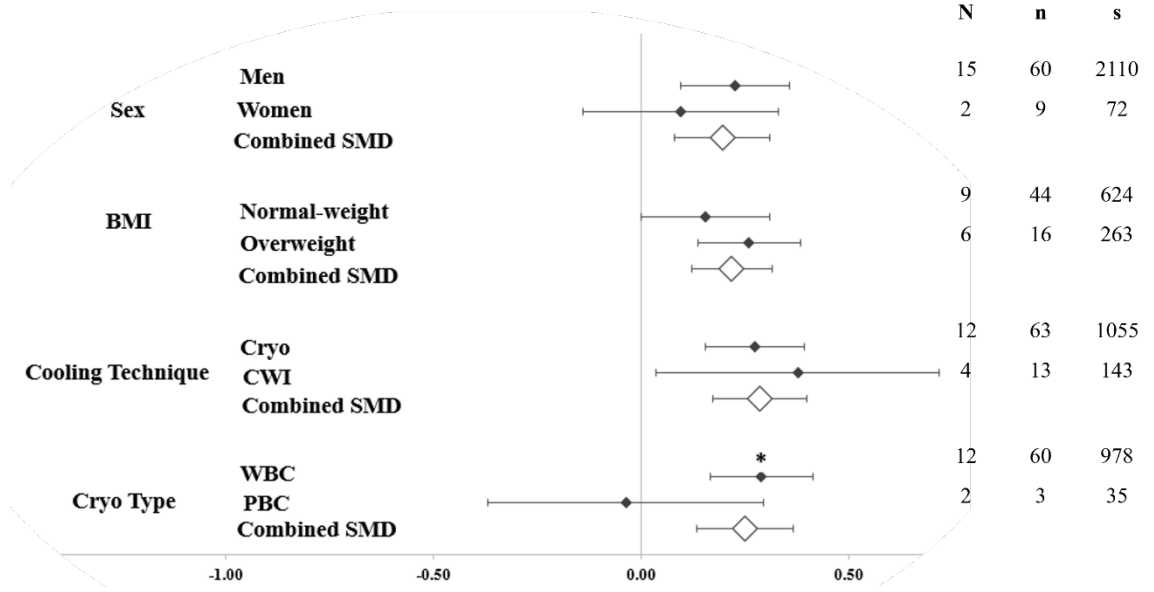

Figure 3. Effect of cold exposure on mean arterial pressure magnitude depending on sex, BMI, cooling technique, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; CWI: Cold Water Immersion; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at p< 0.05.

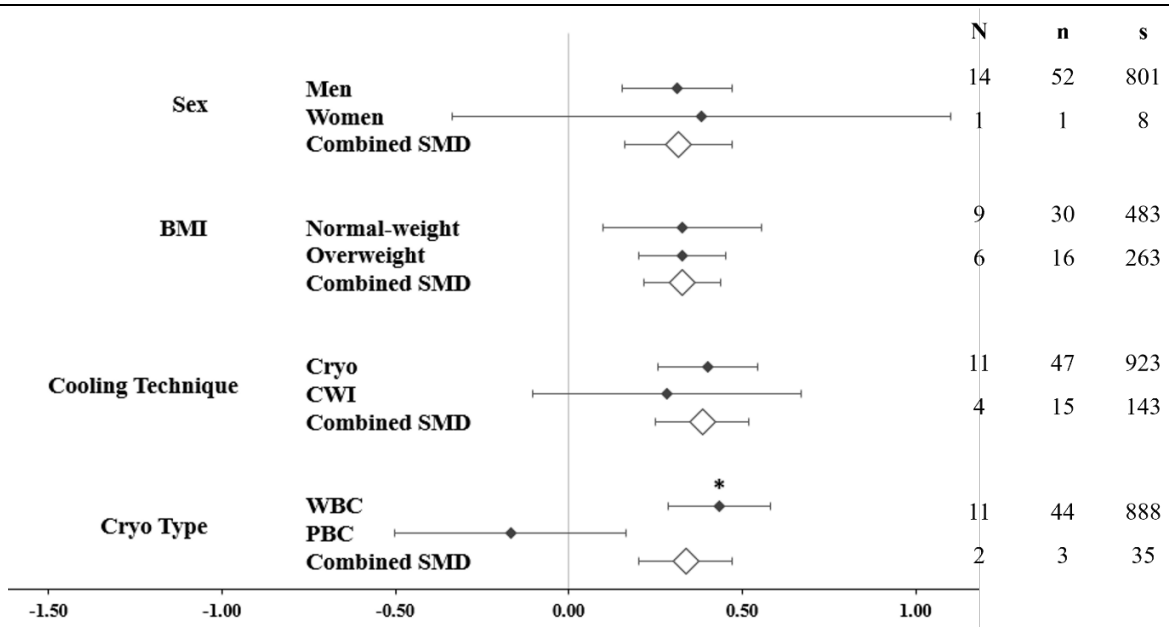

Figure 4. Effect of cold exposure on systolic arterial pressure magnitude depending on sex, BMI, cooling techniques, and cryostimulation type. BMI: Body Mass Index; Cryo: cryostimulation; CWI: Cold Water Immersion; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at p< 0.001

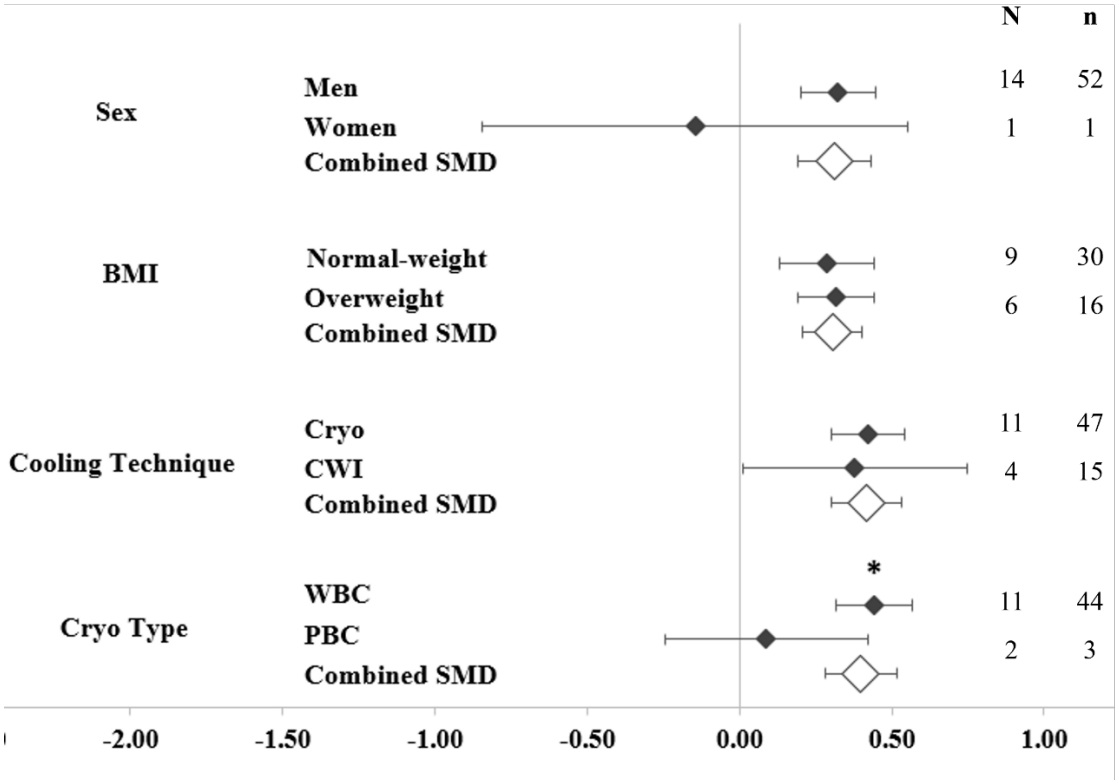

Figure 5. Effect of cold exposure on diastolic arterial pressure magnitude depending on sex, BMI, cooling techniques, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; CWI: Cold Water Immersion; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at $p < 0.05$.

As depicted in Figure 6, time course analysis revealed progressively decreased HR, which remained for 30 min post-exposure (SMD = -0.17; **p = 0.020**). However, the effect dissipated after this time lapse , as indicated by subsequently increased HR until a return to resting values. Additionally, time course analysis revealed a significant gradual decrease in MAP (SMD = 0.33; **p = 0.000**), SAP (SMD = 0.29; **p = 0.002**) and DAP (SMD = 0.45; **p = 0.001**) (Figure 6) for up to 15 min following cold exposure. After 30 min post-exposure, effect size showed a slight increase in SAP (SMD = 0.44; **p = 0.001**), and DAP (SMD = 0.34; **p = 0.000**). However, blood pressure values remained in subclinical ranges (Table 4). Reference intervals for health-related blood pressure values (Master, 1950) are provided in Appendix 5 (see SM).

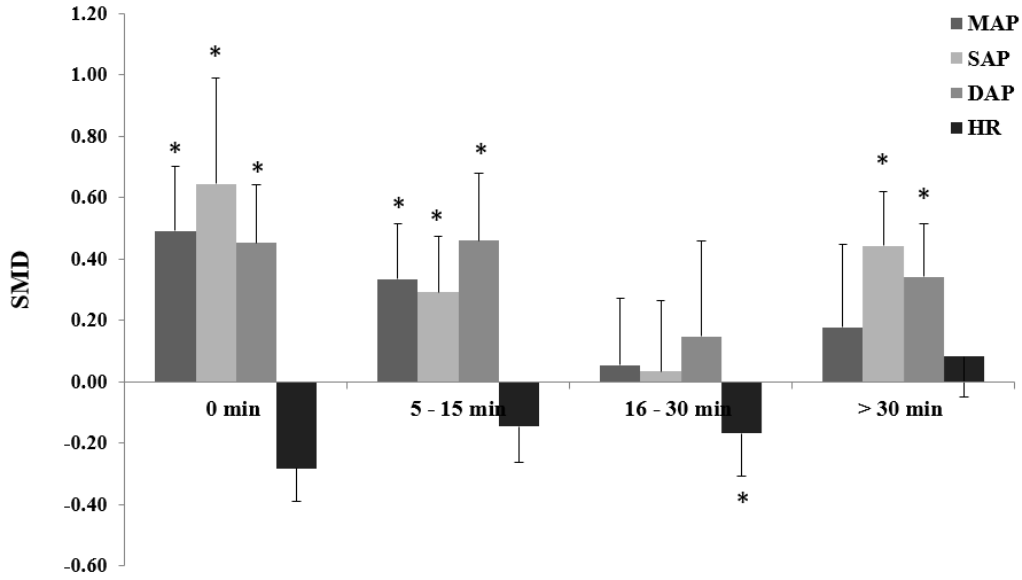

Figure 6. Time course effect of cold exposure on cardiovascular system. SMD: Standardized mean difference; MAP: Mean Arterial pressure; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; *:Significant effect at $p< 0.05$.

Table 4. Arterial pressure magnitude over time after cold exposure

	Before	0 min	5-15 min	15-30 min	> 30 min
MAP (mmHg)	89.28 ± 7.94	94.95 ± 9.83	92.68 ± 9.33	87.81 ± 8.02	87.74 ± 8.32
SAP (mmHg)	122.07 ± 12.42	130.94 ± 13.49	125.29 ± 14.62	121.75 ± 10.10	121.06 ± 11.27
DAP (mmHg)	73.79 ± 7.21	78.24 ± 8.18	78.52 ± 7.41	74.32 ± 7.89	75.74 ± 7.70

MAP: Mean Arterial pressure; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure

3. Cardiac autonomic control

To our knowledge, there have been few if any scientific investigations exploring the effects of CWI on the autonomic nervous system without physical activity intervention. Therefore, we restricted our investigation to whole or partial body cryostimulation. Overall SMD showed that whole /partial body cryostimulation induced a significant change in cardiac autonomic control outcomes (Table 5). More precisely, pooled data showed a significant increase in R-R (SMD = 0.77; 95% CI: 0.55 to 0.98; z = 6.93; $I^2 = 0.00$; **p = 0.000**), RMSSD (SMD = 0.61; 95% CI: 0.43 to 0.79; z = 6.72; $I^2 = 0.00$; **p = 0.000**), and HF (SMD = 0.46; 95% CI: 0.25 to 0.68; z = 4.29; $I^2 = 0.00$; **p = 0.000**), as well as a significant decrease in LF (SMD = -0.41; 95% CI: −0.63 to -0.20; z = -3.82; $I^2 = 4.83$; **p = 0.000**) and LF/HF (SMD = -0.25; 95% CI: −0.42 to -0.09; z = -3.03; $I^2 = 5.12$; **p = 0.002).**

Table 5. Overall effect of Whole/Partial Body cryostimulation on cardiac autonomic control.

	participants (s)	Experimental groups (n)	Level of evidence	SMD	CI 95 %	p
R-R	110	10	Strong	0.77	0.55; 0.98	**0.000**
RMSSD	146	13	Strong	0.61	0.43; 0.79	**0.000**
HF	221	16	Strong	0.46	0.25; 0.68	**0.000**
LF	221	16	Strong	-0.41	-0.63; -0.20	**0.000**
LF/HF	221	16	Strong	-0.25	-0.42; -0.09	**0.002**

RMSSD: root-mean square difference of successive R–R intervals; R-R: R–R heart rate intervals; HR: Heart rate; High frequency (HF), LF: Low frequency; LF/HF: Ratio of low–high frequency power; SMD: Standardized mean difference; CI: confidence interval .

Time course analysis revealed significantly increased RMSSD (SMD = 0.53; **p = 0.000**), RR (SMD = 0.76; **p = 0.000**) and HF (SMD = 0.58; **p = 0.000**) up to 15 min post-exposure (Figure 7). Thirty minutes after exposure, we observed slightly increased LF and decreased HF and LF/HF ratio.

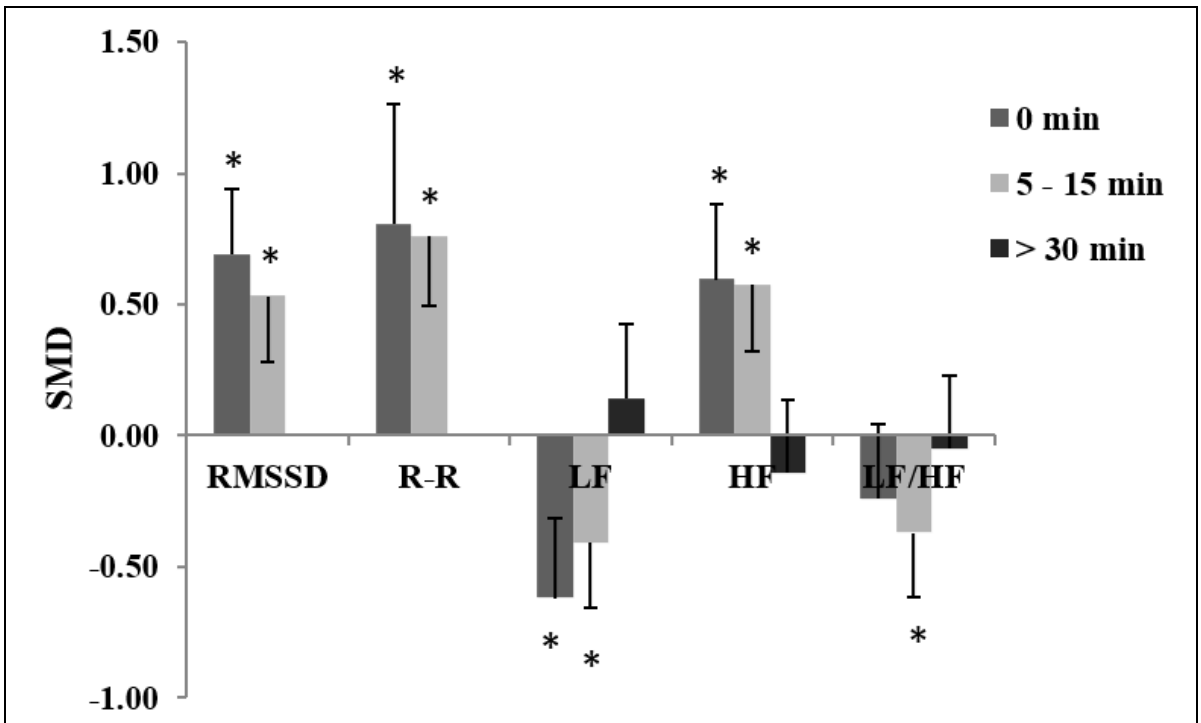

Figure 7. Time course effect of cold exposure on cardiac autonomic control. SMD: Standardized mean difference; RMSSD: root-mean square difference of successive R–R intervals; R-R: R–R heart rate intervals; HR: Heart rate; High frequency (HF), LF: Low frequency; LF/HF: Ratio of low–high frequency power; *:Significant effect at p<0.05.

3.1. R-R intervals

Cryostimulation induced a significant increase in R-R intervals in all BMI categories (normal-weight (SMD = 0.63; **p = 0.000**) and overweight (SMD = 1.18; **p = 0.000**) participants following cryostimulation (WBC (SMD = 0.74; **p = 0.000**) and PBC (SMD = 0.83; **p = 0.000**)) (Figure 8). Regarding BMI categories, there was a significant difference between normal-weight and overweight participants (**p = 0.015**). The meta-regression analysis was aligned with the subgroup findings, indicating that higher BMI (coefficient = 0.56; 95% CI: 0.06 to 1.06; z = 2.18; **p = 0.029**) and elevated body fat percentage (coefficient = 0.82, 95% CI: 0.11 to 1.54; z = 2.26; **p = 0.024**) are linked to a greater increase in R-R intervals following cryostimulation exposure. Of note, meta-regression analysis did not show a significant effect of age in moderating RR interval outcomes. Moreover, the subgroup analysis did not indicate a significant impact of type of cryostimulation on R-R intervals. Meta-regression did not contradict this finding.

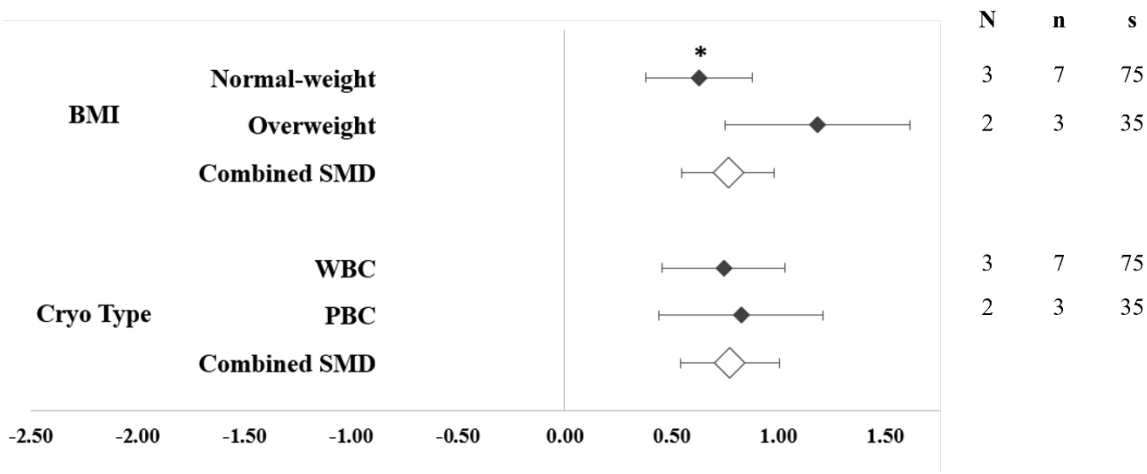

Figure 8. Effect of cold exposure on R-R depending on BMI, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at $p < 0.05$.

3.2. RMSSD

Cryostimulation induced a significant increase in RMSSD across various groups : in men (SMD = 0.57; **p = 0.000**) and women (SMD = 0.90; **p = 0.023**), normal-weight (SMD = 0.63; **p = 0.000**) and overweight (SMD = 0.57; **p = 0.002**) participants, following WBC (SMD = 0.62; **p = 0.000**) and PBC (SMD = 0.61; **p = 0.000**) without any difference between moderators (Figure 9). Meta-regression analysis confirmed these results and showed that the increase in RMSSD was not significantly modulated by age, sex, BMI, body fat percentage, or cryostimulation type.

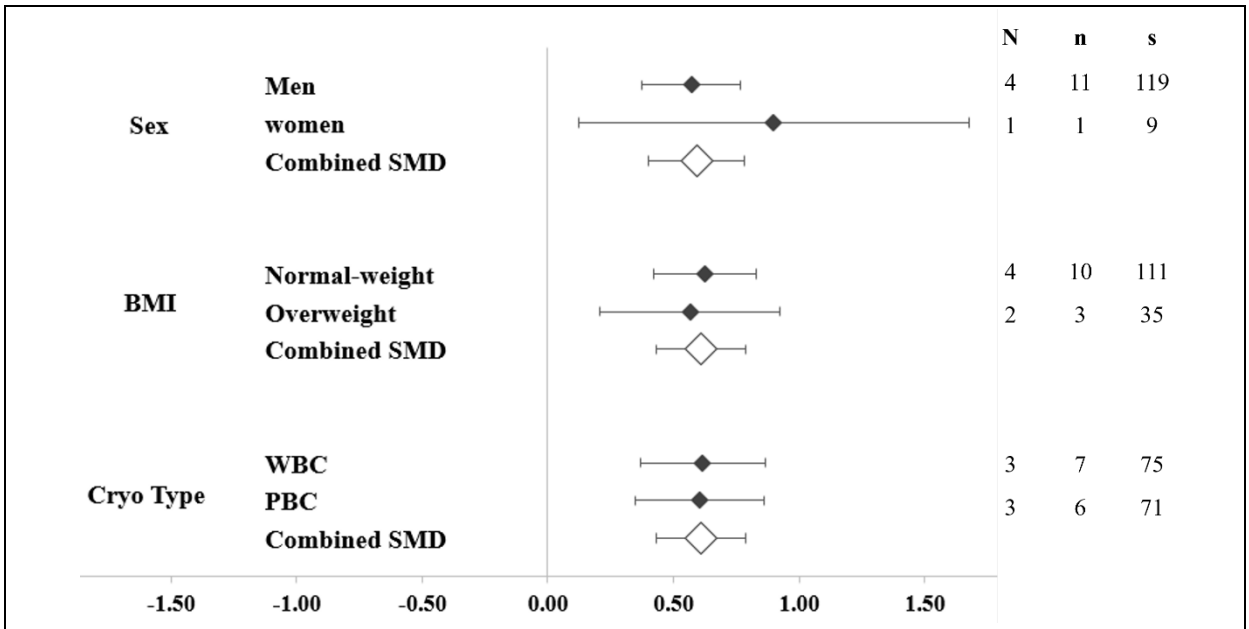

Figure 9. Effect of cold exposure on RMSSD magnitude depending on sex, BMI, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: ~~subjects~~ participants.

3.3. HF

Cryostimulation induced a significant increase in HF in males (SMD = 0.42; **p = 0.000**) and normal-weight participants (SMD = 0.63; **p = 0.000**) (Figure 10). We found a significant difference between BMI categories (**p = 0.021**). Moreover, our results showed a significant increase following both WBC (SMD = 0.28; **p = 0.008**) and PBC (SMD = 0.78; **p = 0.000**). Significant difference between the two cryostimulation types (**p = 0.008**) was also noted. More precisely , a greater increase in HF was found following PBC compared to WBC. Meta-regression analysis confirmed that BMI (Overweight: coefficient = -0.41, 95% CI: -0.78 to -0.05; z = -2.21; **p = 0.027**) and cryostimulation type (PBC: coefficient = 0.48, 95% CI: 0.09 to 0.87; z = 2.42; **p = 0.015**) significantly influenced the magnitude of HF increase. Conversely, age, sex, and body fat percentage did not have a significant effect on HF outcomes after cryostimulation exposure.

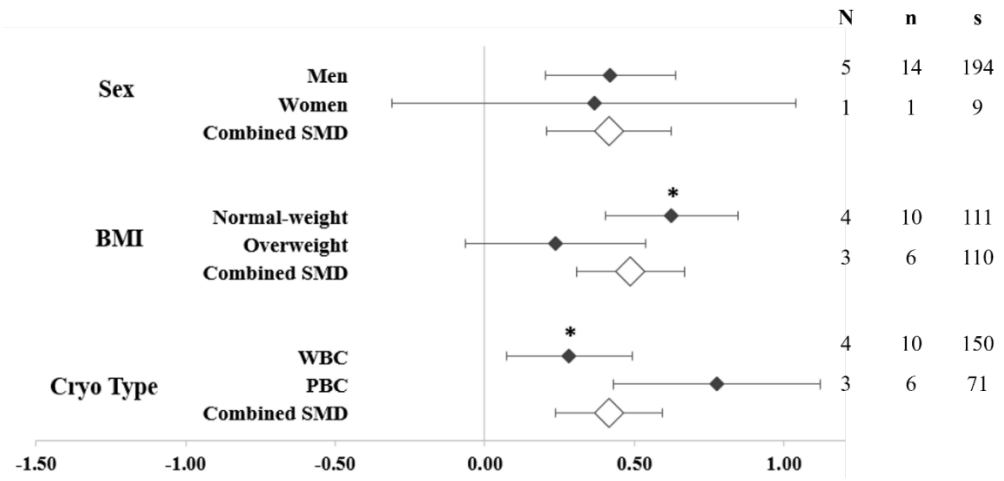

Figure 10. Effect of cold exposure on HF magnitude depending on sex, BMI, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; WBC: Whole Body Cryostimulation; PBC: Partial Body Cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at $p < 0.05$.

3.4. LF

In accordance with the results in HF outcome, a significant decrease in LF was reported following cryostimulation only in men (SMD = -0.36; **p = 0.001**) and in normal-weight participants (SMD = -0.59; **p = 0.000**) (Figure 11). A more pronounced decrease in HF was observed in normal weight compared to overweight participants (**p = 0.012**). On the contrary, no significant differences were found regarding sex. In addition, our results showed a significant decrease in LF following both WBC (SMD = -0.23; **p = 0.020**) and PBC (SMD = -0.74; **p = 0.000**). PBC exposure led to greater reduction in LF compared to the data collected after WBC exposure (**p = 0.014**). Meta-regression analysis supported these results, showing that BMI (Overweight: coefficient = 0.41 , 95% CI: 0.04 to 0.78; z = 2.18; **p = 0.029**) and type of cryostimulation therapy (PBC: coefficient = -0.46 , 95% CI: -0.86 to -0.06; z = -2.27 **p = 0.023**) influenced the LF decrease. However, moderators such as age, sex, and body fat percentage did not show a significant effect on post-cryostimulation HF changes.

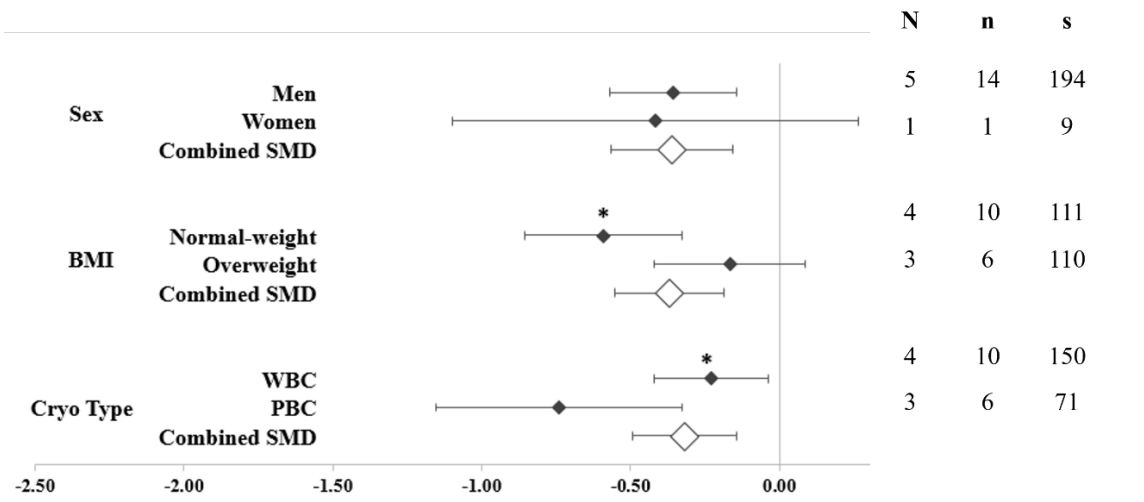

Figure 11. Effect of cold exposure on LF magnitude depending on sex, BMI, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants; *: Significant difference between moderators at $p < 0.05$.

3.5. LF/HF ratio

Our results demonstrated that cryostimulation exposure elicits a significant decrease in men (SMD = -0.23; **p= 0.014**), and in overweight participants (SMD = -0.24; **p = 0.015**) following WBC (SMD = -0.25; **p= 0.010**), as shown in Figure 12. However, we did not observe any significant difference according to sex, BMI, and type of cryostimulation. Consistently, meta-regression analysis showed no significant effect on age, sex, body fat percent, BMI, and type of cryostimulation.

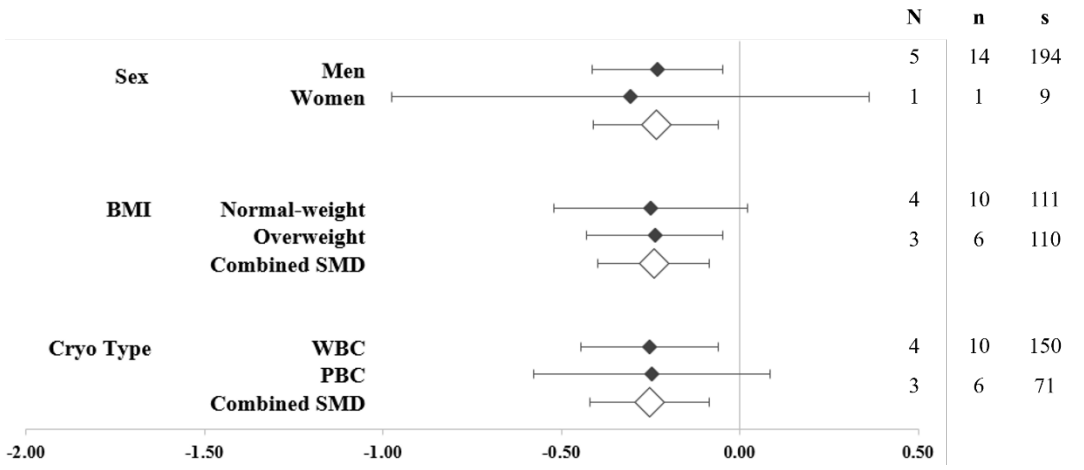

Figure 12. Effect of cold exposure on LF/HF depending on sex, BMI, and cryostimulation type. SMD: Standardized mean difference; BMI: Body Mass Index; Cryo: cryostimulation; WBC: Whole body cryostimulation; PBC: Partial Body cryostimulation; N: Number of articles; n: Number of experimental groups; s: Number of participants

Discussion

The aim of the present meta-analysis is to provide a comprehensive overview of the available scientific literature examining the effects of cold exposure (cryostimulation and CWI) on cardiovascular and cardiac autonomic control responses in healthy participants. Our results suggested enhanced parasympathetic activity and reduced sympathetic nervous activity following cold exposure. These findings are supported by changes in HRV indices, through increased RMSSD, R-R interval, and HF, as well as significantly decreased LF and LF/HF ratio. Furthermore, our results examining cardiovascular responses to cold exposure indicated significantly reduced heart rate, accompanied by a slightly increased blood pressure. Our findings are consistent with the results reported by previous studies (Guolo and Varin, 2017; Hausswirth et al., 2013; Westerlund et al., 2006; Zalewski et al., 2014a). In response to changes in ambient temperature, the cutaneous blood vessels can dynamically dilate or constrict. These mechanisms play a crucial role in the regulation of body temperature by controlling heat loss. When the body is exposed to cold temperatures, the sympathetic α-adrenergic receptors are activated, resulting in the constriction of peripheral blood vessels (Zalewski et al., 2014b). Previous studies have consistently demonstrated that peripheral vasoconstriction inhibits heat loss, leading to a marked reduction in skin capillary perfusion. As a result, blood flow is redirected toward the center, raising arterial pressure (Hausswirth et al., 2013). Our findings are in line with the results of Lubkowska and Szyguła (2010) highlighting that WBC is associated with an elevation in blood pressure along with a compensatory decrease in heart rate. This observation can be explained by the stimulation of baroreceptors located in the carotid sinus and the aortic arch. Specifically, when blood pressure increases, these sensory receptors activate the autonomic bulb centers (Reutersberg et al., 2022). In response to this stimulation, a subsequent parasympathetic reactivation leads to a decrease in heart rate (Pump et al., 2001), as demonstrated in our study's overall cold exposure effect. Additionally, our outcomes regarding the overall effect of cryostimulation on the cardiac autonomic control system are in agreement with the findings reported in previous works (Hausswirth et al., 2013; Westerlund et al., 2006; Zalewski et al., 2014b). It has been shown that cryostimulation effectively increase R-R intervals, RMSSD, and HF bands, which are recognized indicators of enhanced parasympathetic tone activation (Hausswirth et al., 2013; Westerlund et al., 2006; Zalewski et al., 2014a). By initiating parasympathetic activation, baroreceptor stimulation helps to maintain homeostasis by counterbalancing the sympathetic response induced by cold exposure. These observed physiological responses may underlie cold exposure benefits (cryostimulation and

CWI) such as enhanced recovery after exercise, better sympatho-vagal balance, reduced perceived pain, and improved sleep quality (Douzi et al., 2019b, 2019a; Moore et al., 2023). The above findings, particularly increased cardiac parasympathetic activity, have been consistently linked with better overall health and well-being (Louis et al., 2015; Udo et al., 2013). Our results show that parasympathetic activation persists up to 15 min after exposure. To completely comprehend time course analysis of HRV after cold exposure, further research is required. Expanding the number of studies would facilitate exploration of the immediate and prolonged effects of various factors on HRV.

The subgroup and meta-regression analysis results indicate a significant change in cardiovascular and cardiac autonomic control outcomes following cold exposure. The studies included focused primarily on male participants, leading to a significant effect in this subgroup. The small number of female participants in these studies may reduce the statistical power to detect significant effect in this subgroup, which is why it is important to interpret these results cautiously. Without a more extensive body of literature and larger sample sizes, it is challenging to draw a definitive conclusion about the sex-specific effects of cold exposure on cardiovascular and cardiac autonomic control outcomes.

Our findings also showed that while BMI and body fat percentage do not significantly affect cardiovascular variables, they significantly affect heart rate variability, specifically the RR interval. Greater increase in RR interval outcomes was observed in overweight compared to normal weight individuals. This finding may suggest a more pronounced compensatory parasympathetic response, possibly due to different baseline autonomic balance or a different adaptive mechanism to cold stress. In fact, excess body fat, particularly visceral fat, may be associated with pro-inflammatory cytokine secretion, leading to an increased sympathetic tone (Hillebrand et al., 2014). Conversely, normal-weight individuals manifested a more significant effect on HF and LF outcomes post-cryostimulation, with no notable impact of body fat percentage. These contradictory findings highlight that the exact mechanisms through which cryostimulation affects autonomic function, especially in relation to body composition, remain an area of ongoing research. Additionally, we wish to emphasize to highlight that the studies included in our meta-analysis did not specifically focus on examining the interaction between BMI categories. Consequently, the sample sizes for each BMI group may have been insufficient to detect significant differences. A larger sample size and more specific study design could help to provide a clearer understanding of any potential associations between BMI categories and cold exposure effects.

In our meta-analysis, we refrained from conducting a subgroup analysis to investigate the impact of physical level on cold exposure outcomes. It is worth noting that only one of the studies included participants who were untrained. In the other selected works, the volunteers were physically active, or else the relevant information was not available. In addition, our included studies mainly featured young participants, typically under the age of 35. Their homogeneity suggests that age did not emerge as a significant moderator in our analysis. Therefore, limited diversity in physical activity levels and age range restricted exploration of their impact on cold-induced responses. Further research involving more varied participant characteristics is necessary.

Our findings also showed that cryostimulation is more effective than CWI in modifying cardiovascular variables such as BP and HR. Cryostimulation is exposure to extremely low temperatures, often below -100°C, while CWI concerns time of exposure to temperatures below 15°C (Machado et al., 2016). Exposure to very low temperatures may cause a more pronounced physiological reaction, such as vasoconstriction. In this context, Costello et al. (2013) noted that while cryostimulation and CWI were both effective in reducing skin temperature, cryostimulation induced a greater decrease than CWI. It is important to note that scientific studies comparing the impact of CWI and cryostimulation on cardiac autonomic control and cardiovascular responses are lacking.

Additionally, our meta-analysis revealed that compared to PBC, WBC induces significant changes in arterial blood pressure (MAP, SAP, DAP). This finding is consistent with the study by Hausswirth et al. (2013) which confirms that SBP and DBP significantly increase after WBC, but not after PBC. The observed decrease in blood pressure after PBC may be attributed to a reduced level of sympathetic stimulation possibly due to a less pronounced decrease in skin temperature (Hausswirth et al., 2013). Generally, the observed increase in BP is probably associated with a large decrease in HR. In fact, the stimulation of cold trigemino-cardiac reflex receptors located in the face may accentuate the parasympathetic response after WBC by increasing vagal output to the heart (Hausswirth et al., 2013; Louis et al., 2015). Nevertheless, our results showed that compared to WBC, PBC is more effective in reducing HR, increasing HF, and decreasing LF. Additionally, our meta-analysis demonstrated that both WBC and PBC increased RMSSD and decreased LF/HF ratio. Louis et al. (2015) corroborate these findings, as they observed that both cryostimulation techniques effectively stimulated cardiac autonomic control with predominantly parasympathetic drive (Louis et al., 2015). The seemingly contradictory results could be attributed to the limited number of studies using

PBC. It is important to recognize that the inclusion of more research articles utilizing PBC could permit clearer and more consistent understanding of the outcomes.

The thermal outcomes reported in the studies included in our systematic review revealed significant changes in skin, tympanic, core, and rectal temperature in response to WBC, PBC, and CWI exposure. More specifically, WBC and PBC induced a significant and immediate decrease in skin temperature across all body regions, with greater reduction in the lower limbs. The decrease was more pronounced with exposure at lower temperatures and longer exposure times. In some studies, this decrease persisted up to 20 minutes post-exposure (Dębiec-Bąk et al., 2013; Louis et al., 2015).

Skin temperature is a crucial indicator of peripheral vasoconstriction, a key mechanism to reduce heat loss and maintain core body temperature under cold stress (Westerlund et al., 2003). In terms of tympanic temperature, a decrease was observed solely in WBC (Hausswirth et al., 2013), or was found to be more pronounced in WBC compared to PBC (Louis et al., 2020). This discrepancy could be attributed to head exposure during WBC, which does not occur in PBC. Additionally , changes in core body and rectal temperature were observed across various studies involving different durations and CWI and WBC. temperatures Core body temperature was shown to decrease after 35 min (Cuttell et al., 2017) and between 50-60 min (Zalewski et al., 2014a) following WBC. Concerning CWI, rectal temperature (T°re) was reported to decrease at 60 min (Muller et al., 2012) during CWI, and from 45 to 70 min after CWI (Eimonte et al., 2021) . These changes, particularly the afterdrop in core body and rectal temperature, may be attributed to the conduction of cold blood from the periphery to the core of the body.

The methodological quality of the studies included in this meta-analysis, evaluated using the PEDro scale, exhibited scores ranging from 4 to 8. It is noteworthy that a majority were classified as high-quality, which supports the reliability of their findings. However, medium-quality scores in certain studies are indicative of specific methodological limitations that should be considered when interpreting the results. This variability in scores also highlights the diverse research designs and protocols, underscoring a need for careful consideration when generalizing the findings. A common methodological limitation was related to blinding. Nevertheless, it is crucial to note the challenges associated with implementing blinding in interventions involving extreme stimuli like cold exposure. Moreover, issues pertaining to random allocation and participant assignment in some of the included studies could potentially have influenced the study outcomes. In summary, while the results of our systematic review are supported by studies with generally high methodological quality, it is important to note

the limitations, particularly concerning blinding and allocation processes. Addressing these issues in future research may ensure more accurate and reliable interpretations of intervention outcomes.

Conclusion

In conclusion, the present meta-analysis showed that exposure to cryostimulation and CWI induces changes in cardiovascular and cardiac autonomic control activities. These findings revealed enhanced parasympathetic nervous activity leading to reduced HR following cold exposure (CWI and cryostimulation). Overall, the cold-induced cardiac parasympathetic dominance may explain the potential benefits of these cooling techniques, which could consequently be a valuable intervention in the contexts of recovery after physical exercise, therapeutic exigencies , and general wellness practices. Time course analysis is characterized by parasympathetic activation during the initial 15 minutes after exposure, followed by a gradual return to the homeostatic level over the course of 30 minutes. More research is required to completely comprehend the time course analysis of HRV after cold exposure. Our meta-analysis also revealed a noteworthy gap in the current literature regarding the impact of sex, age, BMI, and physical level on cardiovascular and cardiac autonomic control after cold exposure. Filling this gap might provide valuable insights helping to optimize cold exposure strategies and their applications in various contexts.

Strengths, limitations, and perspectives

Our meta-analysis represents the first comprehensive examination of how cold exposure (CWI, WBC, and PBC) affects cardiovascular and cardiac autonomic control responses in healthy individuals. It offers a global overview of existing scientific literature in this field. Importantly, the research was conducted without any language or year restrictions, ensuring a wide-ranging exploration of the available literature. Additionally, the study followed updated PRISMA recommendations. Furthermore, it consisted largely in a time course analysis of HRV, HR and BP revealing the dynamics of autonomic and cardiovascular responses after cold exposure. This temporal perspective enhances comprehension of post-exposure physiological changes. Nevertheless, it is important to acknowledge that additional research is needed to ensure deeper understanding of the immediate and prolonged responses. Another strength is that our study explores the impact of cold exposure according to moderators on the concerned outcomes. While this perspective may help to understand the different reactions of

different groups, it is essential to note that analysis performed in smaller subgroups may reduce our ability to detect statistically significant effects. Consequently, our meta-analysis revealed a noteworthy gap in the current literature regarding the observed changes, according to individual characteristics (sex, age, BMI, body fat percent), in cardiovascular and cardiac autonomic control following cold exposure.

Notwithstanding the scientific interest raised by this meta-analysis, our work is not free of limitations. Given the absence due to the cooling sensation felt by participants of a completely blind procedure, quality assessment using the PEDro scale indicated a maximum score of 8. Furthermore, all included studies presented good to medium methodological quality. In the reviewed articles, only Fonda et al., (Fonda et al., 2014) and Muller al et al., (Muller et al., 2012) conducted their investigation with an a priori power analysis. Therefore, it should be advisable for authors in future studies to estimate appropriate sample size. Additionally, the inclusion criteria in our review seem to be quite specific, focusing only on healthy participants and excluding studies that incorporate physical activity to their protocols. This specificity may limit the diversity of included studies. Due to the limited number of eligible studies, it was necessary to include uncontrolled studies. Lastly, our work relied on data availability, basically means and standard deviations, from the included studies. When studies did not provide such data, they were excluded, limiting the number of included studies in our analysis. Future studies should include information essential to effective data extraction.

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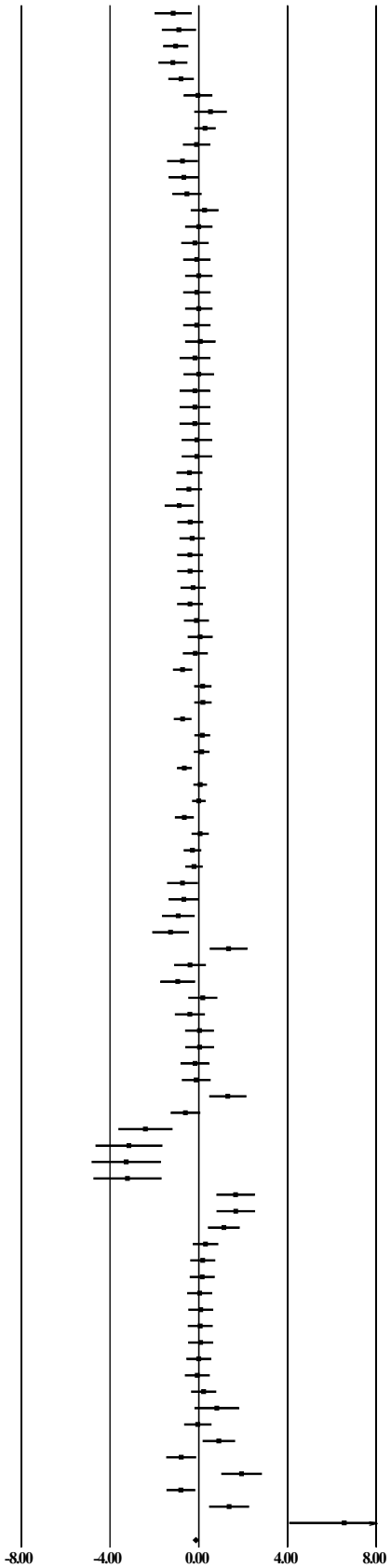
Supplementary Material

Appendix 1. List of excluded articles after full text screening.

Studies	Reasons of exclusion
▪ Damijan and Uhrynski, 2012	▪ Outcomes of interest not addressed
▪ Tipton et al., 2000	▪ Absence of pre- and post-intervention outcome measurements (Measurements was conducted only during cold water immersion).
▪ Tipton et al., 1998	
▪ Barwood et al., 2017	
▪ Bonde-Petersen et al., 1992	
▪ Fox et al., 2003	
▪ O'Brien et al., 2000	▪ Irrelevant cooling technique (cold air exposure at 5°C)
▪ Gregson et al., 2011	▪ Non-continuous cold water immersion technique
▪ Versteeg et al., 2023	▪ Not measured outcomes on acute intervention session
▪ Hayward, 1984	▪ Irrelevant cooling technique (the use of survival suits during cold water immersion)
▪ Hayward and Eckerson, 1984	▪ Absence of post-intervention outcome measurement (Measurement was conducted during cold water immersion).
▪ Tipton and Golden,1987	
▪ Zhang et al., 2003	▪ Irrelevant cooling technique (hand cold-water immersion)

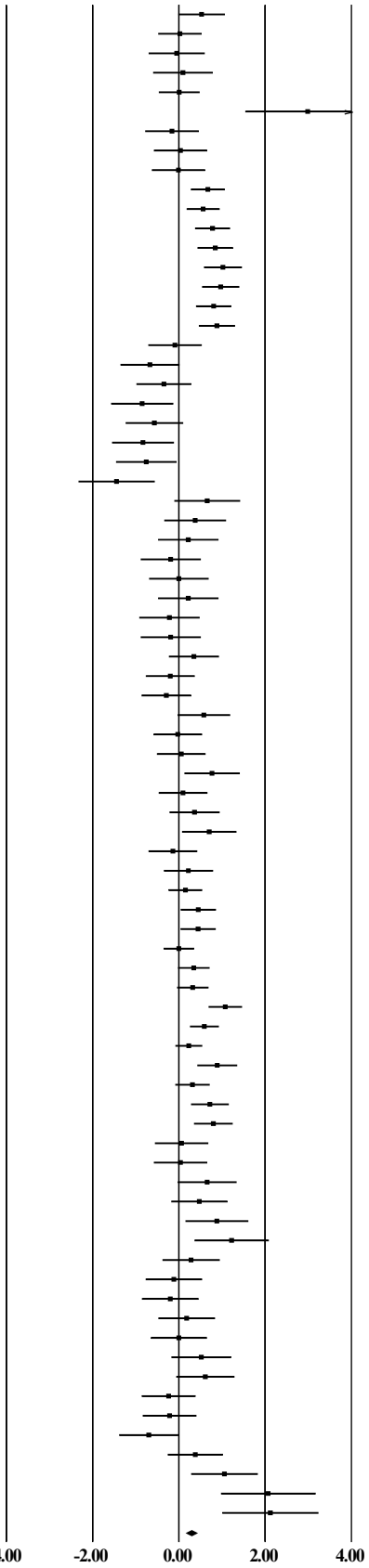
Appendix 2. Forest plots

Study name	Std diff in means	Standard error	Variance	Upper limit	Lower limit	Z-Value	p-Value
Theurot et al., 2021 (1)	-1.154	0.430	0.185	-0.311	-1.997	-2.682	0.007
Theurot et al., 2021 (2)	-0.894	0.394	0.156	-0.121	-1.667	-2.268	0.023
Theurot et al., 2021 (3)	-1.041	0.293	0.086	-0.468	-1.615	-3.557	0.000
Hausswirth et al., 2012 (1)	-1.167	0.335	0.112	-0.511	-1.824	-3.487	0.000
Hausswirth et al., 2012 (2)	-0.799	0.297	0.088	-0.218	-1.380	-2.694	0.007
Hammond et al., 2020 (1)	-0.036	0.333	0.111	0.617	-0.690	-0.109	0.913
Hammond et al., 2020 (2)	0.529	0.378	0.143	1.269	-0.211	1.402	0.161
Hammond et al., 2020 (3)	0.284	0.247	0.061	0.769	-0.201	1.148	0.251
Louis et al., 2015 (1)	-0.100	0.317	0.100	0.521	-0.721	-0.315	0.752
Louis et al., 2015 (2)	-0.734	0.356	0.127	-0.036	-1.432	-2.060	0.039
Louis et al., 2015 (3)	-0.674	0.350	0.123	0.013	-1.360	-1.923	0.054
Louis et al., 2015 (4)	-0.532	0.338	0.114	0.130	-1.194	-1.574	0.116
Cuttell et al., 2017 (1)	0.264	0.322	0.103	0.895	-0.366	0.821	0.412
Cuttell et al., 2017 (2)	0.000	0.316	0.100	0.620	-0.620	0.000	1.000
Cuttell et al., 2017 (3)	-0.173	0.319	0.102	0.451	-0.798	-0.544	0.586
Cuttell et al., 2017 (4)	-0.087	0.317	0.100	0.534	-0.708	-0.274	0.784
Cuttell et al., 2017 (5)	0.000	0.316	0.100	0.620	-0.620	0.000	1.000
Cuttell et al., 2017 (6)	-0.085	0.317	0.100	0.536	-0.706	-0.268	0.789
Cuttell et al., 2017 (7)	0.000	0.316	0.100	0.620	-0.620	0.000	1.000
Cuttell et al., 2017 (8)	-0.089	0.317	0.100	0.532	-0.710	-0.280	0.779
Cuttell et al., 2017 (9)	0.071	0.354	0.125	0.765	-0.623	0.200	0.841
Cuttell et al., 2017 (10)	-0.170	0.356	0.127	0.528	-0.868	-0.476	0.634
Cuttell et al., 2017 (11)	0.000	0.354	0.125	0.693	-0.693	0.000	1.000
Cuttell et al., 2017 (12)	-0.170	0.356	0.127	0.528	-0.868	-0.476	0.634
Cuttell et al., 2017 (13)	-0.170	0.356	0.127	0.528	-0.868	-0.476	0.634
Cuttell et al., 2017 (14)	-0.176	0.356	0.127	0.522	-0.874	-0.494	0.621
Cuttell et al., 2017 (15)	-0.085	0.354	0.125	0.609	-0.779	-0.239	0.811
Cuttell et al., 2017 (16)	-0.082	0.354	0.125	0.612	-0.777	-0.233	0.816
Fonda et al., 2014 (1)	-0.419	0.301	0.091	0.171	-1.010	-1.393	0.164
Fonda et al., 2014 (2)	-0.441	0.302	0.091	0.152	-1.033	-1.458	0.145
Fonda et al., 2014 (3)	-0.878	0.340	0.115	-0.212	-1.544	-2.584	0.010
Fonda et al., 2014 (4)	-0.385	0.299	0.089	0.202	-0.971	-1.286	0.199
Fonda et al., 2014 (5)	-0.298	0.295	0.087	0.281	-0.876	-1.009	0.313
Fonda et al., 2014 (6)	-0.398	0.300	0.090	0.190	-0.985	-1.326	0.185
Fonda et al., 2014 (7)	-0.390	0.299	0.090	0.197	-0.976	-1.301	0.193
Fonda et al., 2014 (8)	-0.257	0.293	0.086	0.318	-0.832	-0.875	0.382
Fonda et al., 2014 (9)	-0.393	0.300	0.090	0.194	-0.980	-1.312	0.190
Fonda et al., 2014 (10)	-0.107	0.289	0.084	0.461	-0.674	-0.368	0.713
Fonda et al., 2014 (11)	0.063	0.289	0.083	0.629	-0.504	0.216	0.829
Fonda et al., 2014 (12)	-0.158	0.290	0.084	0.412	-0.727	-0.542	0.588
P.Zalewski et al., 2014 (1)	-0.731	0.225	0.051	-0.290	-1.172	-3.247	0.001
P.Zalewski et al., 2014 (2)	0.180	0.202	0.041	0.575	-0.215	0.892	0.373
P.Zalewski et al., 2014 (3)	0.188	0.202	0.041	0.583	-0.208	0.931	0.352
Zalewski et al., 2013 (1)	-0.727	0.205	0.042	-0.325	-1.129	-3.541	0.000
Zalewski et al., 2013 (2)	0.158	0.184	0.034	0.519	-0.202	0.863	0.388
Zalewski et al., 2013 (3)	0.131	0.183	0.034	0.490	-0.228	0.715	0.475
Lubkoswka and suska, 2011 (1)	-0.650	0.174	0.030	-0.309	-0.991	-3.733	0.000
Lubkoswka and suska, 2011 (2)	0.065	0.158	0.025	0.375	-0.245	0.410	0.682
Lubkoswka and suska, 2011 (3)	0.000	0.158	0.025	0.310	-0.310	0.000	1.000
Lubkowska and Szygula, 2010 (1)	-0.650	0.220	0.048	-0.218	-1.081	-2.951	0.003
Lubkowska and Szygula, 2010 (2)	0.064	0.200	0.040	0.456	-0.329	0.318	0.751
Lubkowska and Szygula, 2010 (3)	-0.285	0.204	0.042	0.115	-0.685	-1.398	0.162
Lubkowska and Szygula, 2010 (4)	-0.215	0.202	0.041	0.181	-0.612	-1.065	0.287
Louis et al., 2020 (1)	-0.734	0.356	0.127	-0.036	-1.432	-2.060	0.039
Louis et al., 2020 (2)	-0.674	0.350	0.123	0.013	-1.360	-1.923	0.054
Louis et al., 2020 (3)	-0.924	0.378	0.143	-0.184	-1.665	-2.447	0.014
Louis et al., 2020 (4)	-1.272	0.425	0.181	-0.438	-2.105	-2.990	0.003
Coppi et al., 2022	1.346	0.437	0.191	2.201	0.490	3.083	0.002
Rose et al., 2023 (1)	-0.394	0.367	0.135	0.326	-1.113	-1.073	0.283
Rose et al., 2023 (2)	-0.948	0.401	0.161	-0.162	-1.735	-2.363	0.018
Muller et al., 2012 (1)	0.182	0.336	0.113	0.840	-0.477	0.540	0.589
Muller et al., 2012 (2)	-0.400	0.346	0.120	0.279	-1.079	-1.156	0.248
Muller et al., 2012 (3)	0.033	0.333	0.111	0.686	-0.621	0.098	0.922
Muller et al., 2012 (4)	0.037	0.333	0.111	0.691	-0.616	0.112	0.911
Muller et al., 2012 (5)	-0.169	0.336	0.113	0.489	-0.826	-0.502	0.616
Muller et al., 2012 (6)	-0.115	0.334	0.112	0.540	-0.771	-0.344	0.731
Sramek et al., 2000 (1)	1.310	0.431	0.186	2.155	0.465	3.039	0.002
Sramek et al., 2000 (2)	-0.603	0.344	0.118	0.071	-1.276	-1.753	0.080
Sramek et al., 2000 (3)	-2.405	0.624	0.389	-1.182	-3.628	-3.855	0.000
Sramek et al., 2000 (4)	-3.149	0.772	0.596	-1.636	-4.662	-4.080	0.000
Sramek et al., 2000 (5)	-3.272	0.797	0.635	-1.710	-4.835	-4.105	0.000
Sramek et al., 2000 (6)	-3.215	0.785	0.617	-1.676	-4.755	-4.094	0.000
Eimonte et al., 2021 (1)	1.661	0.445	0.198	2.534	0.788	3.730	0.000
Eimonte et al., 2021 (2)	1.672	0.447	0.200	2.548	0.796	3.740	0.000
Eimonte et al., 2021 (3)	1.133	0.370	0.137	1.858	0.408	3.063	0.002
Eimonte et al., 2021 (4)	0.304	0.295	0.087	0.883	-0.274	1.031	0.303
Eimonte et al., 2021 (5)	0.178	0.291	0.085	0.749	-0.392	0.613	0.540
Eimonte et al., 2021 (6)	0.157	0.290	0.084	0.727	-0.412	0.542	0.588
Eimonte et al., 2021 (7)	0.041	0.289	0.083	0.608	-0.525	0.144	0.886
Eimonte et al., 2021 (8)	0.087	0.289	0.084	0.653	-0.480	0.299	0.765
Eimonte et al., 2021 (9)	0.067	0.289	0.084	0.633	-0.500	0.230	0.818
Eimonte et al., 2021 (10)	0.086	0.289	0.084	0.653	-0.480	0.299	0.765
Eimonte et al., 2021 (11)	0.000	0.289	0.083	0.566	-0.566	0.000	1.000
Eimonte et al., 2021 (12)	-0.067	0.289	0.084	0.500	-0.633	-0.231	0.817
Eimonte et al., 2021 (13)	0.220	0.292	0.085	0.793	-0.352	0.754	0.451
Vogelaere et al., 1995	0.814	0.516	0.266	1.826	-0.197	1.578	0.115
Jansky et al., 1996 (1)	-0.043	0.316	0.100	0.577	-0.663	-0.136	0.892
Jansky et al., 1996 (2)	0.907	0.376	0.141	1.644	0.171	2.415	0.016
Kwiecien et al., 2019 (1)	-0.792	0.346	0.119	-0.115	-1.469	-2.292	0.022
Mantoni et al., 2007	1.931	0.469	0.220	2.851	1.011	4.114	0.000
Barwood et al., 2014	-0.808	0.332	0.111	-0.156	-1.459	-2.430	0.015
Mantoni et al., 2008	1.369	0.464	0.215	2.278	0.459	2.951	0.003
Brazaitis et al., 2014	6.562	1.269	1.609	9.049	4.076	5.173	0.000
	-0.157	0.061	0.004	-0.036	-0.277	-2.549	0.011



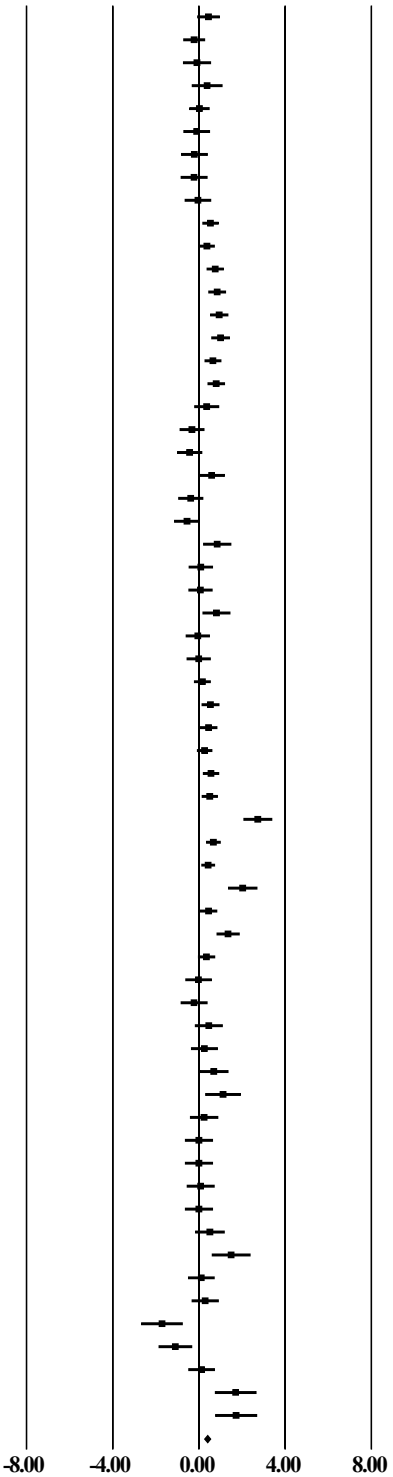
Forest plots of the effect of cold exposure on heart rate

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.527	0.276	0.076	-0.013	1.067	1.912	0.056
Hausswirth et al., 2012 (2)	0.025	0.258	0.067	-0.481	0.531	0.096	0.923
Hammond et al., 2020 (1)	-0.050	0.334	0.111	-0.704	0.604	-0.150	0.880
Hammond et al., 2020 (2)	0.095	0.354	0.126	-0.600	0.789	0.267	0.789
Hammond et al., 2020 (3)	0.009	0.243	0.059	-0.466	0.484	0.038	0.970
Louis et al., 2015 (1)	2.986	0.739	0.546	1.538	4.434	4.042	0.000
Louis et al., 2015 (2)	-0.159	0.318	0.101	-0.782	0.465	-0.499	0.618
Louis et al., 2015 (3)	0.039	0.316	0.100	-0.581	0.659	0.124	0.901
Louis et al., 2015 (4)	-0.009	0.316	0.100	-0.628	0.611	-0.027	0.978
Debiec-Bak et al., 2013 (1)	0.672	0.202	0.041	0.276	1.068	3.323	0.001
Debiec-Bak et al., 2013 (2)	0.562	0.196	0.039	0.177	0.947	2.862	0.004
Debiec-Bak et al., 2013 (3)	0.781	0.209	0.043	0.372	1.190	3.744	0.000
Debiec-Bak et al., 2013 (4)	0.844	0.213	0.045	0.428	1.261	3.971	0.000
Debiec-Bak et al., 2013 (5)	1.022	0.225	0.051	0.580	1.463	4.536	0.000
Debiec-Bak et al., 2013 (6)	0.970	0.221	0.049	0.536	1.404	4.382	0.000
Debiec-Bak et al., 2013 (7)	0.807	0.210	0.044	0.395	1.220	3.841	0.000
Debiec-Bak et al., 2013 (8)	0.882	0.215	0.046	0.461	1.304	4.100	0.000
Cuttell et al., 2017 (1)	-0.090	0.317	0.100	-0.711	0.531	-0.283	0.777
Cuttell et al., 2017 (2)	-0.670	0.350	0.122	-1.356	0.015	-1.916	0.055
Cuttell et al., 2017 (3)	-0.347	0.326	0.106	-0.985	0.291	-1.065	0.287
Cuttell et al., 2017 (4)	-0.850	0.369	0.136	-1.574	-0.127	-2.305	0.021
Cuttell et al., 2017 (5)	-0.567	0.341	0.116	-1.235	0.101	-1.664	0.096
Cuttell et al., 2017 (6)	-0.832	0.367	0.135	-1.551	-0.113	-2.268	0.023
Cuttell et al., 2017 (7)	-0.756	0.359	0.129	-1.459	-0.053	-2.108	0.035
Cuttell et al., 2017 (8)	-1.443	0.452	0.204	-2.329	-0.558	-3.194	0.001
Cuttell et al., 2017 (9)	0.658	0.390	0.152	-0.107	1.422	1.687	0.092
Cuttell et al., 2017 (10)	0.378	0.366	0.134	-0.339	1.095	1.033	0.302
Cuttell et al., 2017 (11)	0.218	0.358	0.128	-0.483	0.919	0.610	0.542
Cuttell et al., 2017 (12)	-0.189	0.357	0.127	-0.888	0.510	-0.530	0.596
Cuttell et al., 2017 (13)	0.000	0.354	0.125	-0.693	0.693	0.000	1.000
Cuttell et al., 2017 (14)	0.218	0.358	0.128	-0.483	0.919	0.610	0.542
Cuttell et al., 2017 (15)	-0.218	0.358	0.128	-0.919	0.483	-0.610	0.542
Cuttell et al., 2017 (16)	-0.189	0.357	0.127	-0.888	0.510	-0.530	0.596
Fonda et al., 2014 (1)	0.349	0.297	0.088	-0.234	0.932	1.174	0.240
Fonda et al., 2014 (2)	-0.198	0.291	0.085	-0.769	0.373	-0.679	0.497
Fonda et al., 2014 (3)	-0.290	0.295	0.087	-0.867	0.288	-0.983	0.326
Fonda et al., 2014 (4)	0.579	0.312	0.097	-0.032	1.190	1.856	0.063
Fonda et al., 2014 (5)	-0.024	0.289	0.083	-0.590	0.541	-0.085	0.932
Fonda et al., 2014 (6)	0.056	0.289	0.083	-0.510	0.622	0.194	0.846
Fonda et al., 2014 (7)	0.770	0.329	0.108	0.125	1.414	2.342	0.019
Fonda et al., 2014 (8)	0.097	0.289	0.084	-0.470	0.664	0.335	0.738
Fonda et al., 2014 (9)	0.364	0.298	0.089	-0.221	0.948	1.220	0.222
Fonda et al., 2014 (10)	0.704	0.322	0.104	0.072	1.336	2.184	0.029
Fonda et al., 2014 (11)	-0.137	0.290	0.084	-0.706	0.431	-0.473	0.636
Fonda et al., 2014 (12)	0.222	0.292	0.085	-0.351	0.795	0.760	0.447
P.Zalewski et al., 2014 (1)	0.153	0.201	0.040	-0.241	0.547	0.761	0.447
P.Zalewski et al., 2014 (2)	0.449	0.210	0.044	0.038	0.861	2.142	0.032
P.Zalewski et al., 2014 (3)	0.446	0.210	0.044	0.035	0.857	2.126	0.034
Zalewski et al., 2013 (1)	0.000	0.183	0.033	-0.358	0.358	0.000	1.000
Zalewski et al., 2013 (2)	0.347	0.188	0.035	-0.022	0.715	1.844	0.065
Zalewski et al., 2013 (3)	0.322	0.187	0.035	-0.045	0.689	1.720	0.085
Lubkoswka and suska, 2011 (1)	1.076	0.199	0.039	0.686	1.465	5.415	0.000
Lubkoswka and suska, 2011 (2)	0.591	0.171	0.029	0.255	0.927	3.448	0.001
Lubkoswka and suska, 2011 (3)	0.230	0.160	0.026	-0.084	0.544	1.437	0.151
Lubkowska and Szygula, 2010 (1)	0.890	0.236	0.056	0.427	1.353	3.766	0.000
Lubkowska and Szygula, 2010 (2)	0.315	0.205	0.042	-0.086	0.717	1.539	0.124
Lubkowska and Szygula, 2010 (3)	0.718	0.224	0.050	0.279	1.158	3.203	0.001
Lubkowska and Szygula, 2010 (4)	0.800	0.230	0.053	0.350	1.250	3.482	0.000
Louis et al., 2020 (1)	0.062	0.317	0.100	-0.558	0.683	0.196	0.844
Louis et al., 2020 (2)	0.039	0.316	0.100	-0.581	0.659	0.124	0.901
Louis et al., 2020 (3)	0.656	0.349	0.122	-0.027	1.340	1.883	0.060
Louis et al., 2020 (4)	0.474	0.334	0.111	-0.180	1.128	1.421	0.155
Coppi et al., 2022	0.881	0.373	0.139	0.151	1.611	2.364	0.018
Rose et al., 2023 (2)	1.223	0.441	0.194	0.359	2.087	2.776	0.006
Muller et al., 2012 (1)	0.283	0.340	0.116	-0.383	0.950	0.834	0.404
Muller et al., 2012 (2)	-0.115	0.334	0.112	-0.771	0.540	-0.345	0.730
Muller et al., 2012 (3)	-0.198	0.337	0.113	-0.858	0.461	-0.589	0.556
Muller et al., 2012 (4)	0.181	0.336	0.113	-0.478	0.840	0.539	0.590
Muller et al., 2012 (5)	0.000	0.333	0.111	-0.653	0.653	0.000	1.000
Muller et al., 2012 (6)	0.521	0.355	0.126	-0.176	1.217	1.465	0.143
Sramek et al., 2000 (1)	0.614	0.345	0.119	-0.062	1.290	1.781	0.075
Sramek et al., 2000 (2)	-0.237	0.321	0.103	-0.865	0.392	-0.738	0.460
Sramek et al., 2000 (3)	-0.214	0.320	0.102	-0.841	0.412	-0.670	0.503
Sramek et al., 2000 (4)	-0.696	0.352	0.124	-1.387	-0.005	-1.974	0.048
Sramek et al., 2000 (5)	0.382	0.328	0.107	-0.260	1.024	1.165	0.244
Sramek et al., 2000 (6)	1.057	0.395	0.156	0.283	1.831	2.677	0.007
Jansky et al., 1996 (1)	2.074	0.561	0.315	0.974	3.174	3.695	0.000
Jansky et al., 1996 (2)	2.121	0.570	0.325	1.004	3.238	3.721	0.000
	0.284	0.058	0.003	0.171	0.397	4.935	0.000



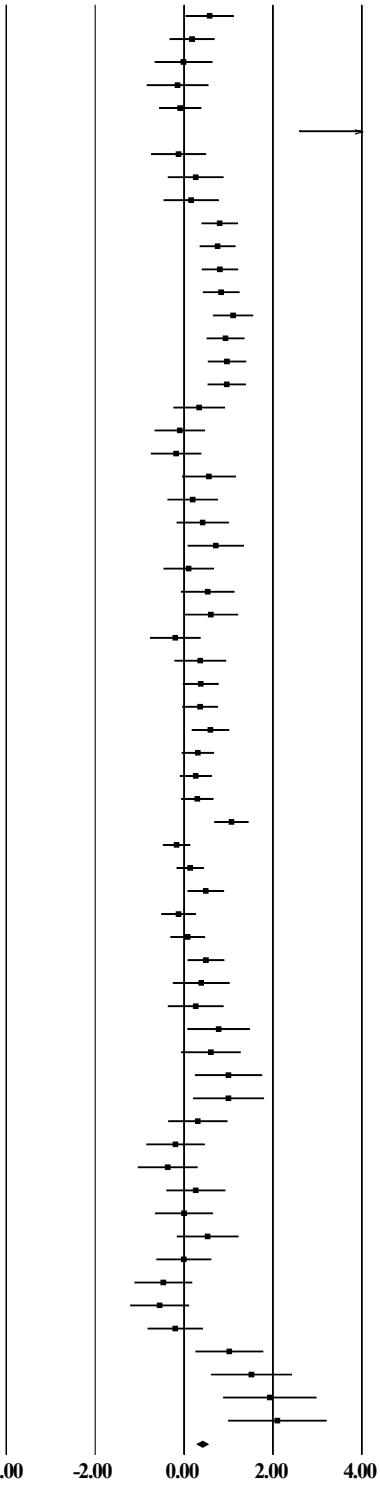
Forest plots of the effect of cold exposure on mean arterial pressure

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.444	0.271	0.073	-0.086	0.975	1.641	0.101
Hausswirth et al., 2012 (2)	-0.222	0.261	0.068	-0.734	0.290	-0.850	0.395
Hammond et al., 2020 (1)	-0.089	0.334	0.112	-0.744	0.565	-0.268	0.789
Hammond et al., 2020 (2)	0.382	0.366	0.134	-0.336	1.100	1.043	0.297
Hammond et al., 2020 (3)	0.024	0.243	0.059	-0.451	0.500	0.100	0.920
Louis et al., 2015 (1)	-0.105	0.317	0.101	-0.726	0.517	-0.330	0.741
Louis et al., 2015 (2)	-0.212	0.320	0.102	-0.838	0.415	-0.662	0.508
Louis et al., 2015 (3)	-0.224	0.320	0.103	-0.852	0.403	-0.701	0.483
Louis et al., 2015 (4)	-0.045	0.316	0.100	-0.666	0.575	-0.144	0.886
Debiec-Bak et al., 2013 (1)	0.535	0.195	0.038	0.152	0.918	2.741	0.006
Debiec-Bak et al., 2013 (2)	0.372	0.189	0.036	0.002	0.742	1.971	0.049
Debiec-Bak et al., 2013 (3)	0.756	0.207	0.043	0.350	1.162	3.652	0.000
Debiec-Bak et al., 2013 (4)	0.847	0.213	0.045	0.430	1.264	3.979	0.000
Debiec-Bak et al., 2013 (5)	0.941	0.219	0.048	0.511	1.371	4.291	0.000
Debiec-Bak et al., 2013 (6)	1.004	0.224	0.050	0.565	1.443	4.485	0.000
Debiec-Bak et al., 2013 (7)	0.650	0.201	0.040	0.256	1.044	3.234	0.001
Debiec-Bak et al., 2013 (8)	0.804	0.210	0.044	0.392	1.215	3.828	0.000
Fonda et al., 2014 (1)	0.359	0.298	0.089	-0.225	0.943	1.205	0.228
Fonda et al., 2014 (2)	-0.323	0.296	0.088	-0.903	0.258	-1.089	0.276
Fonda et al., 2014 (3)	-0.430	0.302	0.091	-1.022	0.161	-1.427	0.154
Fonda et al., 2014 (4)	0.591	0.313	0.098	-0.022	1.204	1.889	0.059
Fonda et al., 2014 (5)	-0.382	0.299	0.089	-0.968	0.204	-1.278	0.201
Fonda et al., 2014 (6)	-0.552	0.310	0.096	-1.159	0.055	-1.782	0.075
Fonda et al., 2014 (7)	0.849	0.337	0.113	0.189	1.509	2.521	0.012
Fonda et al., 2014 (8)	0.087	0.289	0.084	-0.480	0.653	0.299	0.765
Fonda et al., 2014 (9)	0.070	0.289	0.084	-0.497	0.636	0.242	0.809
Fonda et al., 2014 (10)	0.814	0.333	0.111	0.161	1.466	2.443	0.015
Fonda et al., 2014 (11)	-0.052	0.289	0.083	-0.618	0.515	-0.178	0.858
Fonda et al., 2014 (12)	-0.010	0.289	0.083	-0.575	0.556	-0.033	0.974
P.Zalewski et al., 2014 (1)	0.161	0.201	0.041	-0.234	0.555	0.798	0.425
P.Zalewski et al., 2014 (2)	0.538	0.214	0.046	0.118	0.957	2.512	0.012
P.Zalewski et al., 2014 (3)	0.448	0.210	0.044	0.037	0.859	2.136	0.033
Zalewski et al., 2013 (1)	0.263	0.186	0.034	-0.101	0.627	1.414	0.157
Zalewski et al., 2013 (2)	0.559	0.196	0.039	0.174	0.944	2.848	0.004
Zalewski et al., 2013 (3)	0.504	0.194	0.038	0.124	0.884	2.599	0.009
Lubkoswka and suska, 2011 (1)	2.732	0.344	0.118	2.058	3.406	7.943	0.000
Lubkoswka and suska, 2011 (2)	0.672	0.175	0.031	0.329	1.015	3.837	0.000
Lubkoswka and suska, 2011 (3)	0.430	0.165	0.027	0.106	0.754	2.602	0.009
Lubkowska and Szygula, 2010 (1)	2.032	0.350	0.123	1.346	2.718	5.804	0.000
Lubkowska and Szygula, 2010 (2)	0.446	0.210	0.044	0.035	0.857	2.125	0.034
Lubkowska and Szygula, 2010 (3)	1.352	0.277	0.077	0.810	1.895	4.887	0.000
Lubkowska and Szygula, 2010 (4)	0.351	0.206	0.042	-0.053	0.755	1.704	0.088
Louis et al., 2020 (1)	-0.018	0.316	0.100	-0.638	0.602	-0.056	0.955
Louis et al., 2020 (2)	-0.224	0.320	0.103	-0.852	0.403	-0.701	0.483
Louis et al., 2020 (3)	0.459	0.332	0.111	-0.193	1.111	1.381	0.167
Louis et al., 2020 (4)	0.255	0.321	0.103	-0.375	0.884	0.792	0.428
Coppi et al., 2022	0.688	0.352	0.124	-0.001	1.378	1.957	0.050
Rose et al., 2023 (2)	1.120	0.425	0.181	0.286	1.953	2.633	0.008
Muller et al., 2012 (1)	0.240	0.338	0.114	-0.422	0.903	0.710	0.477
Muller et al., 2012 (2)	0.000	0.333	0.111	-0.653	0.653	0.000	1.000
Muller et al., 2012 (3)	0.000	0.333	0.111	-0.653	0.653	0.000	1.000
Muller et al., 2012 (4)	0.080	0.334	0.111	-0.574	0.734	0.240	0.810
Muller et al., 2012 (5)	0.000	0.333	0.111	-0.653	0.653	0.000	1.000
Muller et al., 2012 (6)	0.509	0.354	0.125	-0.185	1.203	1.437	0.151
Sramek et al., 2000 (1)	1.495	0.460	0.212	0.593	2.397	3.249	0.001
Sramek et al., 2000 (2)	0.112	0.317	0.101	-0.510	0.733	0.352	0.725
Sramek et al., 2000 (3)	0.290	0.323	0.104	-0.343	0.923	0.898	0.369
Sramek et al., 2000 (4)	-1.711	0.496	0.246	-2.684	-0.738	-3.447	0.001
Sramek et al., 2000 (5)	-1.092	0.400	0.160	-1.876	-0.309	-2.734	0.006
Sramek et al., 2000 (6)	0.124	0.317	0.101	-0.498	0.747	0.392	0.695
Jansky et al., 1996 (1)	1.706	0.495	0.245	0.735	2.677	3.443	0.001
Jansky et al., 1996 (2)	1.725	0.499	0.249	0.747	2.702	3.458	0.001
	0.372	0.069	0.005	0.236	0.508	5.355	0.000



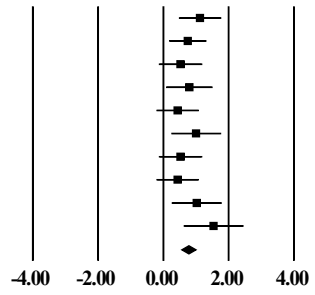
Forest plots of the effect of cold exposure on systolic arterial pressure

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.577	0.279	0.078	0.030	1.123	2.069	0.039
Hausswirth et al., 2012 (2)	0.180	0.260	0.068	-0.330	0.690	0.690	0.490
Hammond et al., 2020 (1)	-0.012	0.333	0.111	-0.665	0.641	-0.036	0.971
Hammond et al., 2020 (2)	-0.146	0.355	0.126	-0.842	0.551	-0.410	0.682
Hammond et al., 2020 (3)	-0.087	0.243	0.059	-0.563	0.390	-0.356	0.722
Louis et al., 2015 (1)	4.757	1.110	1.232	2.582	6.933	4.287	0.000
Louis et al., 2015 (2)	-0.123	0.317	0.101	-0.745	0.499	-0.387	0.699
Louis et al., 2015 (3)	0.263	0.322	0.103	-0.367	0.893	0.817	0.414
Louis et al., 2015 (4)	0.161	0.318	0.101	-0.463	0.785	0.505	0.614
Debiec-Bak et al., 2013 (1)	0.801	0.210	0.044	0.390	1.213	3.819	0.000
Debiec-Bak et al., 2013 (2)	0.754	0.207	0.043	0.349	1.160	3.646	0.000
Debiec-Bak et al., 2013 (3)	0.806	0.210	0.044	0.394	1.218	3.836	0.000
Debiec-Bak et al., 2013 (4)	0.835	0.212	0.045	0.420	1.251	3.939	0.000
Debiec-Bak et al., 2013 (5)	1.103	0.232	0.054	0.649	1.557	4.763	0.000
Debiec-Bak et al., 2013 (6)	0.934	0.219	0.048	0.505	1.363	4.269	0.000
Debiec-Bak et al., 2013 (7)	0.967	0.221	0.049	0.533	1.400	4.372	0.000
Debiec-Bak et al., 2013 (8)	0.960	0.221	0.049	0.528	1.393	4.351	0.000
Fonda et al., 2014 (1)	0.341	0.297	0.088	-0.241	0.923	1.148	0.251
Fonda et al., 2014 (2)	-0.096	0.289	0.084	-0.663	0.471	-0.332	0.740
Fonda et al., 2014 (3)	-0.179	0.291	0.085	-0.750	0.391	-0.617	0.538
Fonda et al., 2014 (4)	0.560	0.311	0.096	-0.048	1.169	1.804	0.071
Fonda et al., 2014 (5)	0.195	0.291	0.085	-0.376	0.766	0.668	0.504
Fonda et al., 2014 (6)	0.421	0.301	0.091	-0.170	1.011	1.396	0.163
Fonda et al., 2014 (7)	0.713	0.323	0.105	0.080	1.347	2.206	0.027
Fonda et al., 2014 (8)	0.104	0.289	0.084	-0.463	0.671	0.360	0.719
Fonda et al., 2014 (9)	0.532	0.308	0.095	-0.072	1.137	1.725	0.084
Fonda et al., 2014 (10)	0.603	0.314	0.098	-0.012	1.218	1.920	0.055
Fonda et al., 2014 (11)	-0.194	0.291	0.085	-0.765	0.377	-0.667	0.505
Fonda et al., 2014 (12)	0.365	0.298	0.089	-0.219	0.950	1.225	0.221
P.Zalewski et al., 2014 (1)	0.376	0.207	0.043	-0.029	0.782	1.819	0.069
P.Zalewski et al., 2014 (2)	0.362	0.206	0.043	-0.043	0.766	1.752	0.080
P.Zalewski et al., 2014 (3)	0.594	0.217	0.047	0.169	1.019	2.738	0.006
Zalewski et al., 2013 (1)	0.310	0.187	0.035	-0.057	0.676	1.657	0.098
Zalewski et al., 2013 (2)	0.264	0.186	0.034	-0.100	0.628	1.422	0.155
Zalewski et al., 2013 (3)	0.299	0.187	0.035	-0.067	0.665	1.602	0.109
Lubkoswka and suska, 2011 (1)	1.067	0.198	0.039	0.679	1.456	5.389	0.000
Lubkoswka and suska, 2011 (2)	-0.168	0.159	0.025	-0.480	0.144	-1.055	0.291
Lubkoswka and suska, 2011 (3)	0.139	0.159	0.025	-0.173	0.450	0.873	0.383
Lubkowska and Szygula, 2010 (1)	0.489	0.212	0.045	0.074	0.903	2.309	0.021
Lubkowska and Szygula, 2010 (2)	-0.123	0.201	0.040	-0.517	0.270	-0.615	0.539
Lubkowska and Szygula, 2010 (3)	0.082	0.200	0.040	-0.310	0.475	0.411	0.681
Lubkowska and Szygula, 2010 (4)	0.493	0.212	0.045	0.078	0.908	2.327	0.020
Louis et al., 2020 (1)	0.387	0.328	0.107	-0.255	1.030	1.181	0.238
Louis et al., 2020 (2)	0.263	0.322	0.103	-0.367	0.893	0.817	0.414
Louis et al., 2020 (3)	0.780	0.361	0.130	0.072	1.488	2.161	0.031
Louis et al., 2020 (4)	0.604	0.344	0.118	-0.070	1.278	1.756	0.079
Coppi et al., 2022	1.000	0.387	0.150	0.241	1.759	2.582	0.010
Rose et al., 2023 (2)	1.000	0.408	0.167	0.200	1.800	2.449	0.014
Muller et al., 2012 (1)	0.311	0.341	0.116	-0.358	0.980	0.911	0.362
Muller et al., 2012 (2)	-0.192	0.336	0.113	-0.851	0.468	-0.569	0.569
Muller et al., 2012 (3)	-0.367	0.344	0.119	-1.041	0.308	-1.064	0.287
Muller et al., 2012 (4)	0.265	0.339	0.115	-0.400	0.930	0.781	0.435
Muller et al., 2012 (5)	0.000	0.333	0.111	-0.653	0.653	0.000	1.000
Muller et al., 2012 (6)	0.530	0.356	0.127	-0.168	1.227	1.488	0.137
Sramek et al., 2000 (1)	-0.005	0.316	0.100	-0.625	0.615	-0.016	0.988
Sramek et al., 2000 (2)	-0.466	0.333	0.111	-1.118	0.187	-1.398	0.162
Sramek et al., 2000 (3)	-0.550	0.339	0.115	-1.215	0.115	-1.620	0.105
Sramek et al., 2000 (4)	-0.198	0.319	0.102	-0.824	0.428	-0.620	0.535
Sramek et al., 2000 (5)	1.019	0.390	0.152	0.255	1.783	2.615	0.009
Sramek et al., 2000 (6)	1.517	0.464	0.215	0.608	2.426	3.271	0.001
Jansky et al., 1996 (1)	1.932	0.535	0.287	0.883	2.981	3.609	0.000
Jansky et al., 1996 (2)	2.101	0.566	0.321	0.991	3.211	3.710	0.000
	0.403	0.060	0.004	0.286	0.521	6.707	0.000



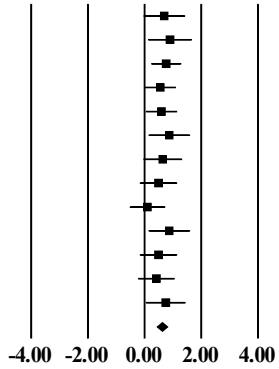
Forest plots of the effect of cold exposure on diastolic arterial pressure

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	1.123	0.330	0.109	0.477	1.769	3.406	0.001
Hausswirth et al., 2012 (2)	0.747	0.292	0.085	0.175	1.320	2.559	0.010
Louis et al., 2015 (1)	0.526	0.337	0.114	-0.136	1.187	1.558	0.119
Louis et al., 2015 (2)	0.795	0.363	0.132	0.084	1.507	2.192	0.028
Louis et al., 2015 (3)	0.439	0.331	0.110	-0.210	1.087	1.324	0.185
Louis et al., 2015 (4)	1.003	0.388	0.150	0.243	1.763	2.588	0.010
Louis et al., 2020 (1)	0.526	0.337	0.114	-0.136	1.187	1.558	0.119
Louis et al., 2020 (2)	0.439	0.331	0.110	-0.210	1.087	1.324	0.185
Louis et al., 2020 (3)	1.024	0.390	0.152	0.259	1.789	2.622	0.009
Louis et al., 2020 (4)	1.538	0.467	0.218	0.622	2.453	3.292	0.001
	0.765	0.110	0.012	0.548	0.981	6.930	0.000



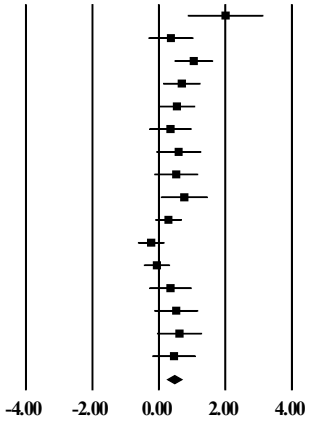
Forest plots of the effect of cold exposure on RR interval

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	0.697	0.372	0.138	-0.031	1.425	1.875	0.061
Theurot et al., 2021 (2)	0.899	0.395	0.156	0.125	1.674	2.277	0.023
Theurot et al., 2021 (3)	0.764	0.268	0.072	0.239	1.289	2.852	0.004
Hausswirth et al., 2012 (1)	0.562	0.278	0.077	0.017	1.107	2.023	0.043
Hausswirth et al., 2012 (2)	0.598	0.280	0.079	0.048	1.147	2.133	0.033
Louis et al., 2015 (1)	0.873	0.372	0.138	0.144	1.601	2.349	0.019
Louis et al., 2015 (2)	0.645	0.348	0.121	-0.036	1.326	1.856	0.063
Louis et al., 2015 (3)	0.493	0.335	0.112	-0.163	1.150	1.473	0.141
Louis et al., 2015 (4)	0.101	0.317	0.101	-0.521	0.722	0.318	0.751
Louis et al., 2020 (1)	0.873	0.372	0.138	0.144	1.601	2.349	0.019
Louis et al., 2020 (2)	0.493	0.335	0.112	-0.163	1.150	1.473	0.141
Louis et al., 2020 (3)	0.420	0.330	0.109	-0.226	1.067	1.274	0.202
Louis et al., 2020 (4)	0.749	0.358	0.128	0.048	1.451	2.094	0.036
	0.611	0.091	0.008	0.433	0.790	6.718	0.000



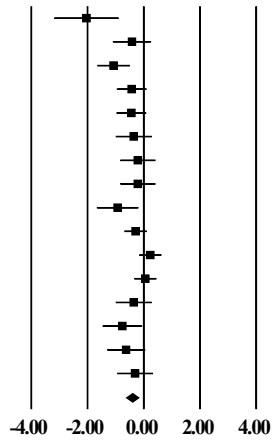
Forest plots of the effect of cold exposure on RMSSD

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	2.007	0.579	0.335	0.873	3.141	3.468	0.001
Theurot et al., 2021 (2)	0.365	0.344	0.119	-0.310	1.040	1.060	0.289
Theurot et al., 2021 (3)	1.051	0.294	0.086	0.475	1.627	3.579	0.000
Hausswirth et al., 2012 (1)	0.693	0.288	0.083	0.129	1.256	2.409	0.016
Hausswirth et al., 2012 (2)	0.544	0.277	0.077	0.002	1.086	1.967	0.049
Louis et al., 2015 (1)	0.350	0.326	0.106	-0.288	0.989	1.075	0.282
Louis et al., 2015 (2)	0.598	0.343	0.118	-0.075	1.271	1.742	0.081
Louis et al., 2015 (3)	0.525	0.337	0.114	-0.136	1.186	1.556	0.120
Louis et al., 2015 (4)	0.766	0.360	0.129	0.061	1.471	2.131	0.033
P.Zalewski et al., 2014 (1)	0.291	0.204	0.042	-0.109	0.691	1.424	0.154
P.Zalewski et al., 2014 (2)	-0.231	0.203	0.041	-0.629	0.166	-1.142	0.253
P.Zalewski et al., 2014 (3)	-0.057	0.200	0.040	-0.450	0.335	-0.286	0.775
Louis et al., 2020 (1)	0.351	0.326	0.106	-0.288	0.989	1.076	0.282
Louis et al., 2020 (2)	0.525	0.337	0.114	-0.136	1.186	1.556	0.120
Louis et al., 2020 (3)	0.622	0.345	0.119	-0.055	1.299	1.800	0.072
Louis et al., 2020 (4)	0.456	0.332	0.110	-0.195	1.108	1.374	0.170
	0.463	0.108	0.012	0.251	0.675	4.286	0.000



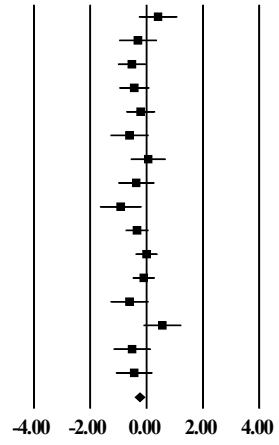
Forest plots of the effect of cold exposure on HF

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	-2.039	0.585	0.342	-3.185	-0.893	-3.486	0.000
Theurot et al., 2021 (2)	-0.417	0.348	0.121	-1.098	0.264	-1.201	0.230
Theurot et al., 2021 (3)	-1.076	0.296	0.088	-1.656	-0.495	-3.633	0.000
Hausswirth et al., 2012 (1)	-0.431	0.270	0.073	-0.960	0.098	-1.596	0.110
Hausswirth et al., 2012 (2)	-0.441	0.270	0.073	-0.971	0.089	-1.629	0.103
Louis et al., 2015 (1)	-0.355	0.326	0.106	-0.994	0.284	-1.088	0.276
Louis et al., 2015 (2)	-0.211	0.320	0.102	-0.838	0.416	-0.660	0.509
Louis et al., 2015 (3)	-0.209	0.320	0.102	-0.836	0.417	-0.654	0.513
Louis et al., 2015 (4)	-0.928	0.378	0.143	-1.669	-0.187	-2.454	0.014
P.Zalewski et al., 2014 (1)	-0.291	0.204	0.042	-0.691	0.109	-1.424	0.154
P.Zalewski et al., 2014 (2)	0.231	0.203	0.041	-0.166	0.629	1.142	0.253
P.Zalewski et al., 2014 (3)	0.057	0.200	0.040	-0.335	0.450	0.286	0.775
Louis et al., 2020 (1)	-0.355	0.326	0.106	-0.994	0.284	-1.088	0.276
Louis et al., 2020 (2)	-0.758	0.359	0.129	-1.461	-0.055	-2.113	0.035
Louis et al., 2020 (3)	-0.626	0.346	0.120	-1.304	0.052	-1.811	0.070
Louis et al., 2020 (4)	-0.307	0.324	0.105	-0.942	0.327	-0.950	0.342
	-0.413	0.108	0.012	-0.625	-0.201	-3.823	0.000



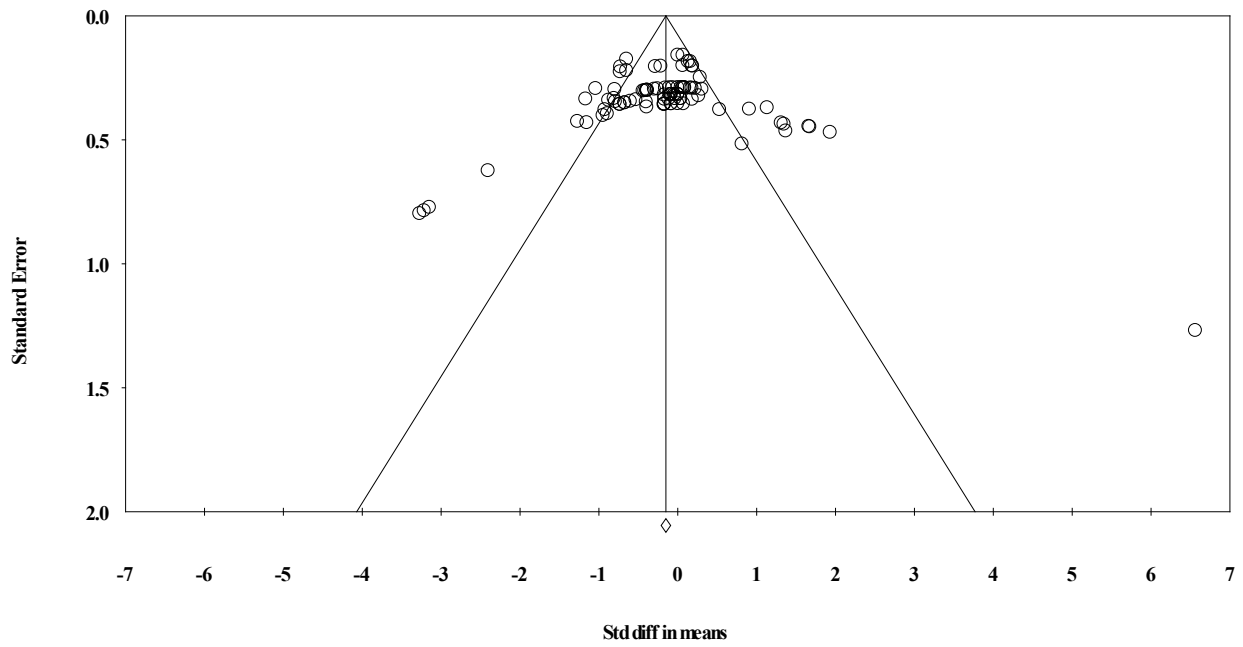
Forest plots of the effect of cold exposure on LF

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	0.411	0.347	0.120	-0.269	1.091	1.184	0.236
Theurot et al., 2021 (2)	-0.305	0.341	0.116	-0.974	0.363	-0.896	0.370
Theurot et al., 2021 (3)	-0.520	0.251	0.063	-1.013	-0.028	-2.072	0.038
Hausswirth et al., 2012 (1)	-0.437	0.270	0.073	-0.967	0.092	-1.618	0.106
Hausswirth et al., 2012 (2)	-0.208	0.261	0.068	-0.720	0.303	-0.797	0.425
Louis et al., 2015 (1)	-0.605	0.344	0.118	-1.279	0.069	-1.758	0.079
Louis et al., 2015 (2)	0.059	0.317	0.100	-0.561	0.680	0.188	0.851
Louis et al., 2015 (3)	-0.365	0.327	0.107	-1.005	0.275	-1.117	0.264
Louis et al., 2015 (4)	-0.918	0.377	0.142	-1.657	-0.179	-2.434	0.015
P.Zalewski et al., 2014 (1)	-0.339	0.206	0.042	-0.742	0.064	-1.647	0.100
P.Zalewski et al., 2014 (2)	0.000	0.200	0.040	-0.392	0.392	0.000	1.000
P.Zalewski et al., 2014 (3)	-0.099	0.200	0.040	-0.492	0.294	-0.493	0.622
Louis et al., 2020 (1)	-0.605	0.344	0.118	-1.279	0.069	-1.758	0.079
Louis et al., 2020 (2)	0.560	0.340	0.116	-0.106	1.227	1.648	0.099
Louis et al., 2020 (3)	-0.515	0.337	0.113	-1.174	0.145	-1.529	0.126
Louis et al., 2020 (4)	-0.438	0.331	0.110	-1.087	0.211	-1.323	0.186
	-0.254	0.084	0.007	-0.418	-0.089	-3.027	0.002

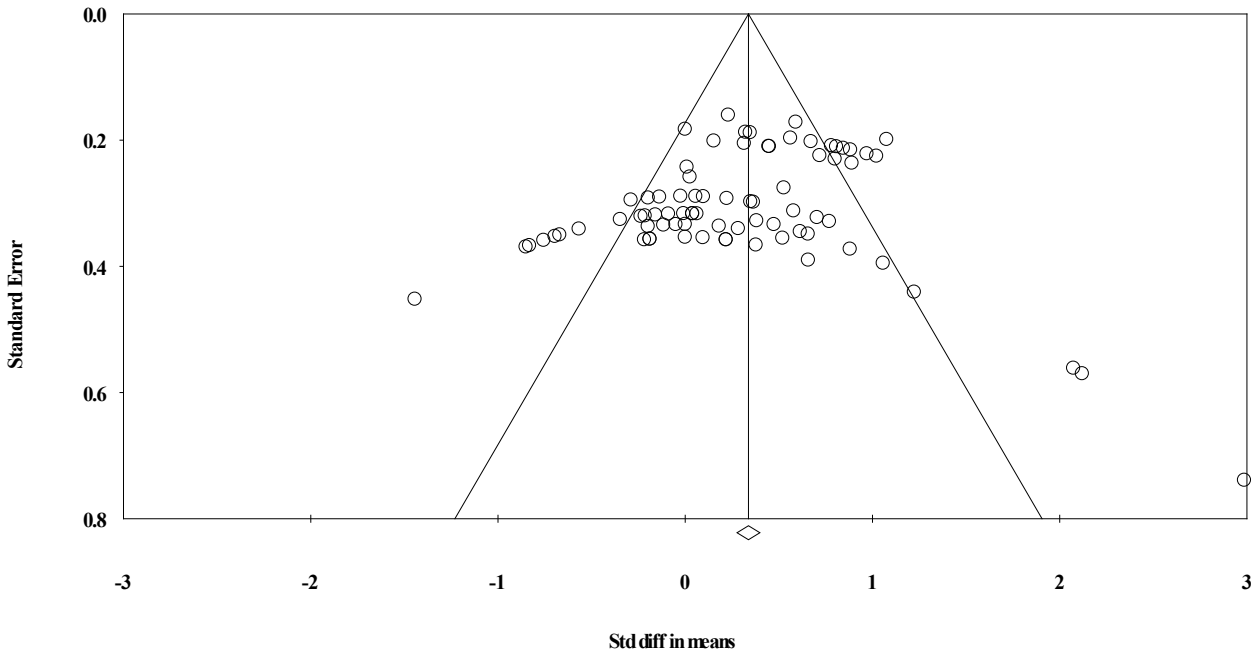


Forest plots of the effect of cold exposure on LF/HF ratio

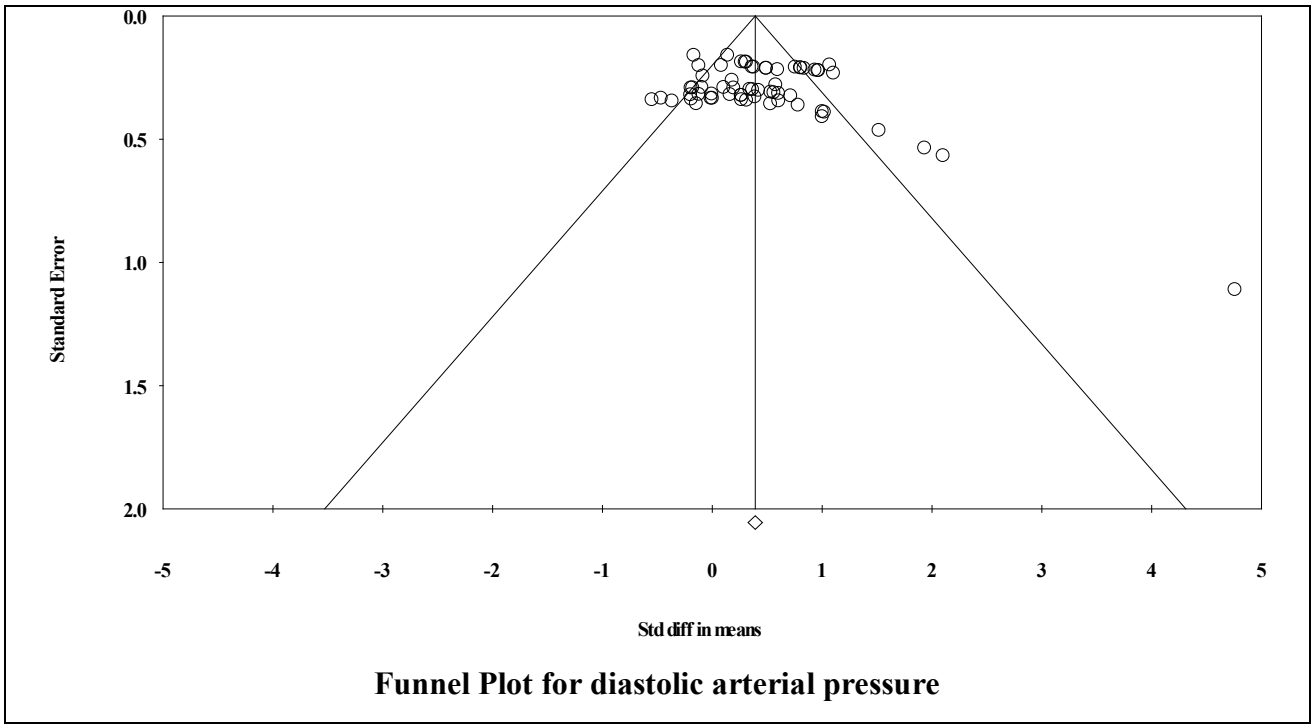
Appendix 3. Funnels Plots



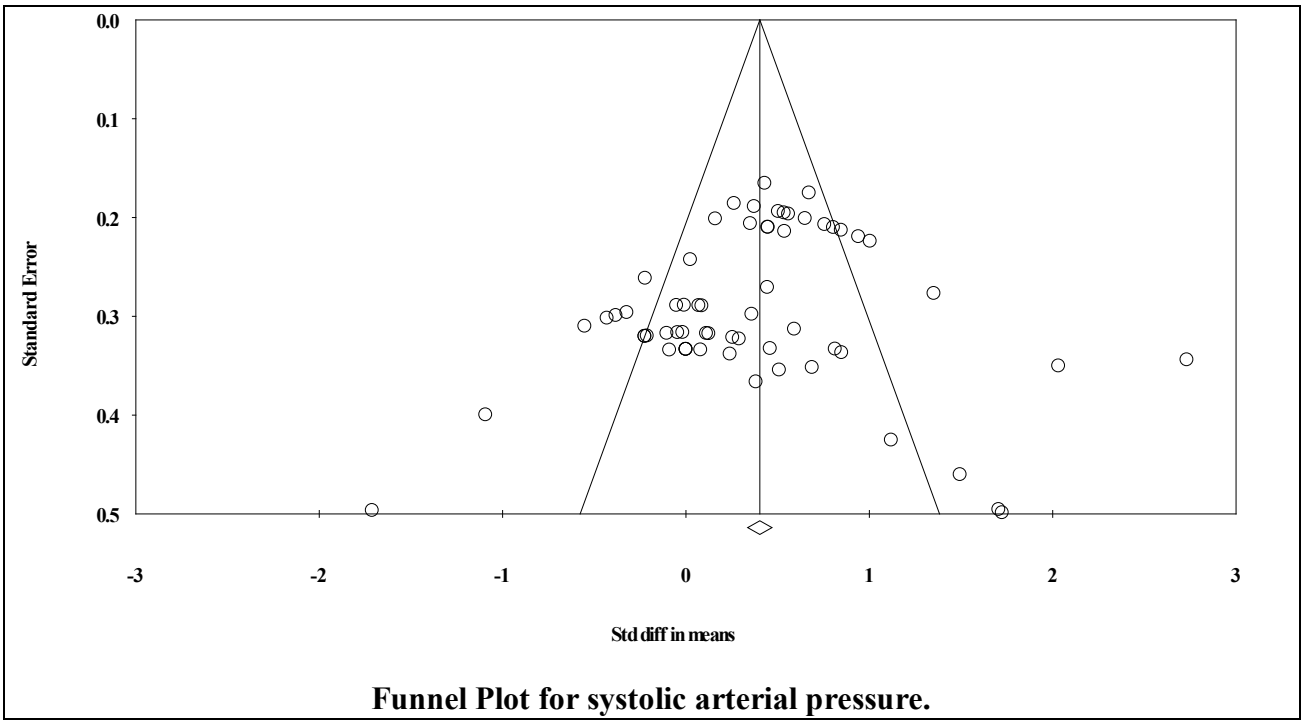
Funnel Plot for heart rate.



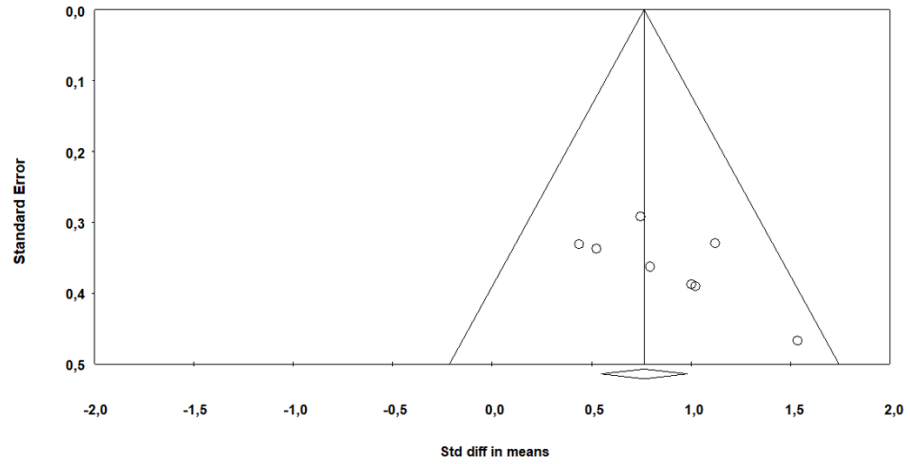
Funnel Plot for mean arterial pressure.



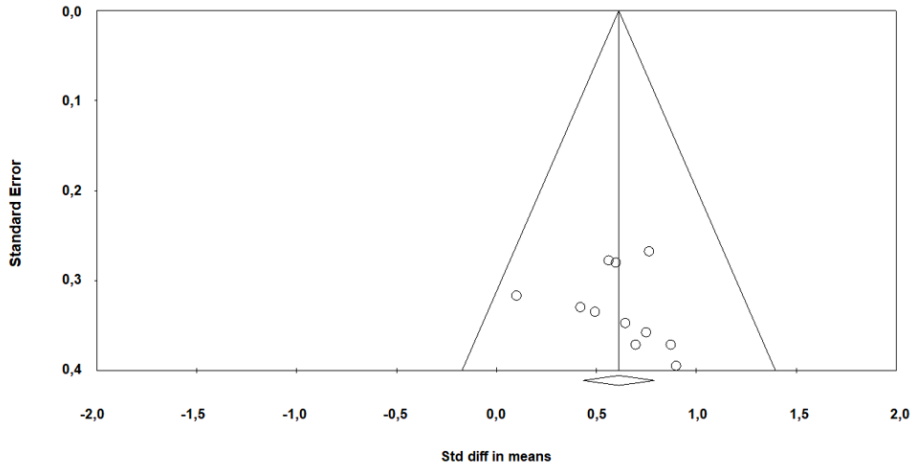
Funnel Plot for diastolic arterial pressure



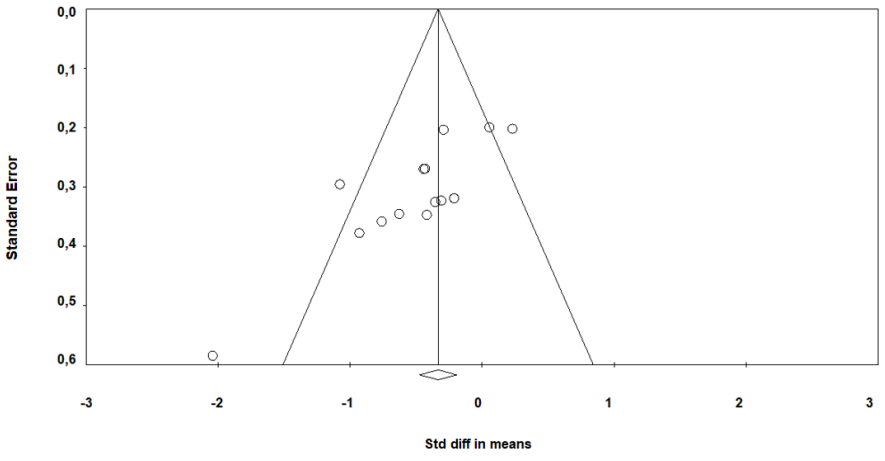
Funnel Plot for systolic arterial pressure.



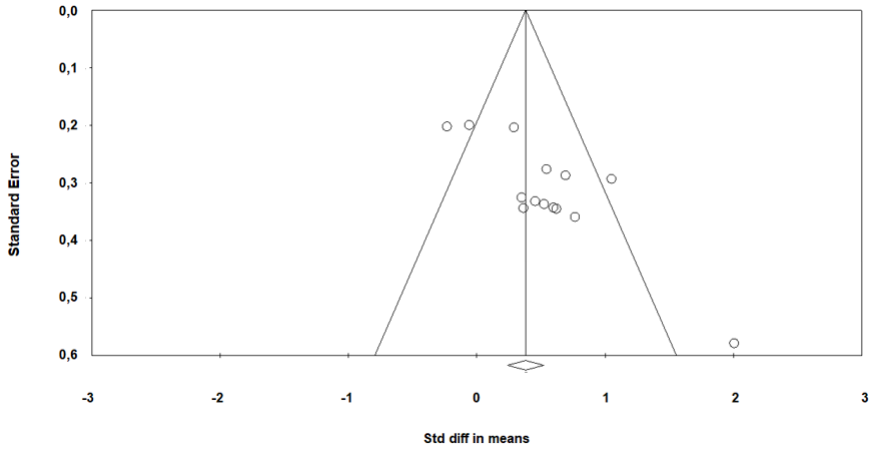
Funnel Plot for R-R interval



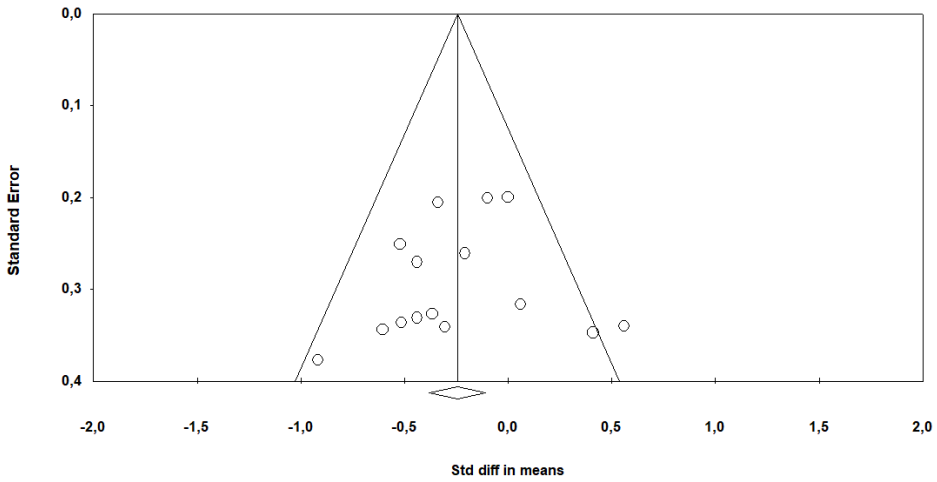
Funnel Plot for RMSSD



Funnel Plot for LF



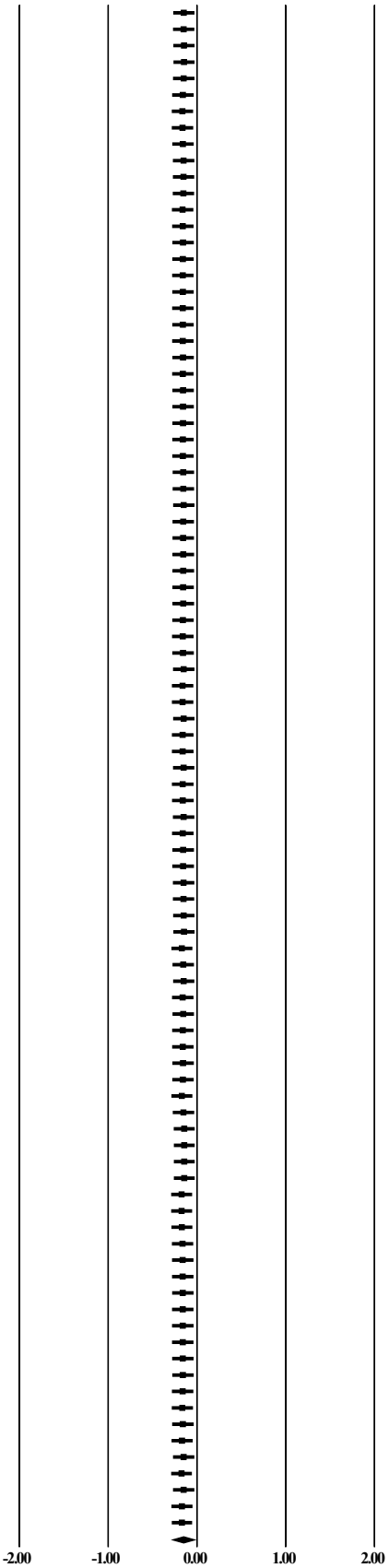
Funnel Plot for HF



Funnel Plot for LF/HF

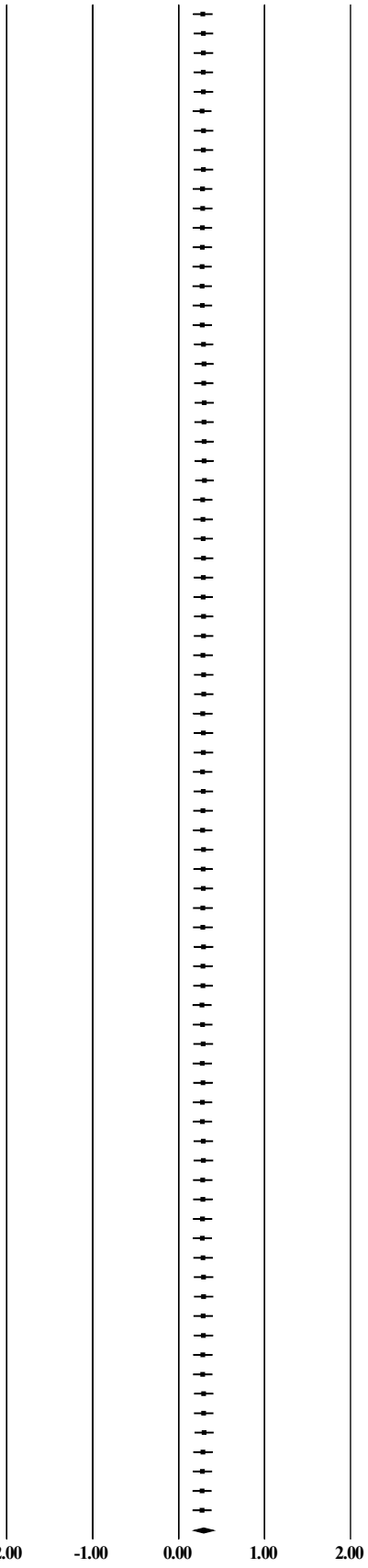
Appendix 4. Leave-one out sensitivity analysis

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	-0.148	0.061	0.004	-0.268	-0.027	-2.403	0.016
Theurot et al., 2021 (2)	-0.149	0.062	0.004	-0.270	-0.029	-2.424	0.015
Theurot et al., 2021 (3)	-0.146	0.061	0.004	-0.266	-0.026	-2.383	0.017
Hausswirth et al., 2012 (1)	-0.145	0.061	0.004	-0.265	-0.026	-2.377	0.017
Hausswirth et al., 2012 (2)	-0.149	0.062	0.004	-0.270	-0.028	-2.416	0.016
Hammond et al., 2020 (1)	-0.158	0.062	0.004	-0.279	-0.036	-2.546	0.011
Hammond et al., 2020 (2)	-0.163	0.062	0.004	-0.284	-0.043	-2.649	0.008
Hammond et al., 2020 (3)	-0.162	0.062	0.004	-0.284	-0.041	-2.617	0.009
Louis et al., 2015 (1)	-0.157	0.062	0.004	-0.279	-0.036	-2.533	0.011
Louis et al., 2015 (2)	-0.150	0.062	0.004	-0.271	-0.029	-2.437	0.015
Louis et al., 2015 (3)	-0.151	0.062	0.004	-0.272	-0.030	-2.444	0.015
Louis et al., 2015 (4)	-0.152	0.062	0.004	-0.274	-0.031	-2.463	0.014
Cuttell et al., 2017 (1)	-0.161	0.062	0.004	-0.283	-0.040	-2.605	0.009
Cuttell et al., 2017 (2)	-0.158	0.062	0.004	-0.280	-0.037	-2.552	0.011
Cuttell et al., 2017 (3)	-0.156	0.062	0.004	-0.278	-0.035	-2.520	0.012
Cuttell et al., 2017 (4)	-0.157	0.062	0.004	-0.279	-0.036	-2.536	0.011
Cuttell et al., 2017 (5)	-0.158	0.062	0.004	-0.280	-0.037	-2.552	0.011
Cuttell et al., 2017 (6)	-0.157	0.062	0.004	-0.279	-0.036	-2.536	0.011
Cuttell et al., 2017 (7)	-0.158	0.062	0.004	-0.280	-0.037	-2.552	0.011
Cuttell et al., 2017 (8)	-0.157	0.062	0.004	-0.279	-0.036	-2.535	0.011
Cuttell et al., 2017 (9)	-0.159	0.062	0.004	-0.280	-0.037	-2.565	0.010
Cuttell et al., 2017 (10)	-0.156	0.062	0.004	-0.278	-0.035	-2.523	0.012
Cuttell et al., 2017 (11)	-0.158	0.062	0.004	-0.280	-0.037	-2.552	0.011
Cuttell et al., 2017 (12)	-0.156	0.062	0.004	-0.278	-0.035	-2.523	0.012
Cuttell et al., 2017 (13)	-0.156	0.062	0.004	-0.278	-0.035	-2.523	0.012
Cuttell et al., 2017 (14)	-0.156	0.062	0.004	-0.278	-0.035	-2.522	0.012
Cuttell et al., 2017 (15)	-0.157	0.062	0.004	-0.279	-0.036	-2.538	0.011
Cuttell et al., 2017 (16)	-0.157	0.062	0.004	-0.279	-0.036	-2.538	0.011
Fonda et al., 2014 (1)	-0.153	0.062	0.004	-0.275	-0.032	-2.475	0.013
Fonda et al., 2014 (2)	-0.153	0.062	0.004	-0.275	-0.032	-2.472	0.013
Fonda et al., 2014 (3)	-0.149	0.062	0.004	-0.269	-0.028	-2.414	0.016
Fonda et al., 2014 (4)	-0.154	0.062	0.004	-0.275	-0.032	-2.481	0.013
Fonda et al., 2014 (5)	-0.155	0.062	0.004	-0.277	-0.033	-2.495	0.013
Fonda et al., 2014 (6)	-0.154	0.062	0.004	-0.275	-0.032	-2.479	0.013
Fonda et al., 2014 (7)	-0.154	0.062	0.004	-0.275	-0.032	-2.480	0.013
Fonda et al., 2014 (8)	-0.155	0.062	0.004	-0.277	-0.034	-2.502	0.012
Fonda et al., 2014 (9)	-0.154	0.062	0.004	-0.275	-0.032	-2.479	0.013
Fonda et al., 2014 (10)	-0.157	0.062	0.004	-0.279	-0.035	-2.530	0.011
Fonda et al., 2014 (11)	-0.159	0.062	0.004	-0.281	-0.037	-2.564	0.010
Fonda et al., 2014 (12)	-0.157	0.062	0.004	-0.278	-0.035	-2.520	0.012
P.Zalewski et al., 2014 (1)	-0.149	0.062	0.004	-0.270	-0.028	-2.413	0.016
P.Zalewski et al., 2014 (2)	-0.161	0.062	0.004	-0.283	-0.039	-2.591	0.010
P.Zalewski et al., 2014 (3)	-0.161	0.062	0.004	-0.283	-0.039	-2.594	0.010
Zalewski et al., 2013 (1)	-0.149	0.062	0.004	-0.270	-0.028	-2.410	0.016
Zalewski et al., 2013 (2)	-0.161	0.062	0.004	-0.283	-0.039	-2.584	0.010
Zalewski et al., 2013 (3)	-0.161	0.062	0.004	-0.283	-0.038	-2.576	0.010
Lubkoswka and suska, 2011 (1)	-0.149	0.062	0.004	-0.271	-0.028	-2.416	0.016
Lubkoswka and suska, 2011 (2)	-0.160	0.063	0.004	-0.283	-0.037	-2.552	0.011
Lubkoswka and suska, 2011 (3)	-0.159	0.063	0.004	-0.282	-0.036	-2.534	0.011
Lubkowska and Szygula, 2010 (1)	-0.150	0.062	0.004	-0.271	-0.029	-2.423	0.015
Lubkowska and Szygula, 2010 (2)	-0.160	0.062	0.004	-0.282	-0.037	-2.560	0.010
Lubkowska and Szygula, 2010 (3)	-0.155	0.062	0.004	-0.277	-0.033	-2.482	0.013
Lubkowska and Szygula, 2010 (4)	-0.156	0.062	0.004	-0.278	-0.033	-2.496	0.013
Louis et al., 2020 (1)	-0.150	0.062	0.004	-0.271	-0.029	-2.437	0.015
Louis et al., 2020 (2)	-0.151	0.062	0.004	-0.272	-0.030	-2.444	0.015
Louis et al., 2020 (3)	-0.149	0.062	0.004	-0.269	-0.028	-2.417	0.016
Louis et al., 2020 (4)	-0.146	0.061	0.004	-0.266	-0.026	-2.389	0.017
Coppi et al., 2022	-0.170	0.061	0.004	-0.289	-0.050	-2.789	0.005
Rose et al., 2023 (1)	-0.154	0.062	0.004	-0.275	-0.033	-2.488	0.013
Rose et al., 2023 (2)	-0.149	0.062	0.004	-0.270	-0.028	-2.419	0.016
Muller et al., 2012 (1)	-0.160	0.062	0.004	-0.282	-0.039	-2.587	0.010
Muller et al., 2012 (2)	-0.154	0.062	0.004	-0.275	-0.033	-2.485	0.013
Muller et al., 2012 (3)	-0.159	0.062	0.004	-0.280	-0.037	-2.558	0.011
Muller et al., 2012 (4)	-0.159	0.062	0.004	-0.280	-0.037	-2.559	0.010
Muller et al., 2012 (5)	-0.156	0.062	0.004	-0.278	-0.035	-2.522	0.012
Muller et al., 2012 (6)	-0.157	0.062	0.004	-0.279	-0.035	-2.531	0.011
Sramek et al., 2000 (1)	-0.169	0.061	0.004	-0.289	-0.050	-2.785	0.005
Sramek et al., 2000 (2)	-0.152	0.062	0.004	-0.273	-0.031	-2.454	0.014
Sramek et al., 2000 (3)	-0.143	0.061	0.004	-0.262	-0.024	-2.361	0.018
Sramek et al., 2000 (4)	-0.143	0.060	0.004	-0.261	-0.025	-2.372	0.018
Sramek et al., 2000 (5)	-0.143	0.060	0.004	-0.261	-0.025	-2.375	0.018
Sramek et al., 2000 (6)	-0.143	0.060	0.004	-0.261	-0.025	-2.373	0.018
Eimonte et al., 2021 (1)	-0.172	0.060	0.004	-0.290	-0.054	-2.849	0.004
Eimonte et al., 2021 (2)	-0.172	0.060	0.004	-0.290	-0.054	-2.850	0.004
Eimonte et al., 2021 (3)	-0.169	0.061	0.004	-0.289	-0.050	-2.784	0.005
Eimonte et al., 2021 (4)	-0.162	0.062	0.004	-0.283	-0.041	-2.617	0.009
Eimonte et al., 2021 (5)	-0.160	0.062	0.004	-0.282	-0.039	-2.589	0.010
Eimonte et al., 2021 (6)	-0.160	0.062	0.004	-0.282	-0.039	-2.584	0.010
Eimonte et al., 2021 (7)	-0.159	0.062	0.004	-0.281	-0.037	-2.560	0.010
Eimonte et al., 2021 (8)	-0.159	0.062	0.004	-0.281	-0.038	-2.569	0.010
Eimonte et al., 2021 (9)	-0.159	0.062	0.004	-0.281	-0.038	-2.565	0.010
Eimonte et al., 2021 (10)	-0.159	0.062	0.004	-0.281	-0.038	-2.569	0.010
Eimonte et al., 2021 (11)	-0.158	0.062	0.004	-0.280	-0.037	-2.551	0.011
Eimonte et al., 2021 (12)	-0.158	0.062	0.004	-0.279	-0.036	-2.538	0.011
Eimonte et al., 2021 (13)	-0.161	0.062	0.004	-0.282	-0.040	-2.598	0.009
Vogelaere et al., 1995	-0.164	0.061	0.004	-0.284	-0.043	-2.663	0.008
Jansky et al., 1996 (1)	-0.158	0.062	0.004	-0.279	-0.036	-2.544	0.011
Jansky et al., 1996 (2)	-0.167	0.061	0.004	-0.287	-0.047	-2.729	0.006
Kwiecien et al., 2019 (1)	-0.150	0.062	0.004	-0.271	-0.029	-2.427	0.015
Mantoni et al., 2007	-0.173	0.060	0.004	-0.291	-0.056	-2.886	0.004
Barwwod et al., 2014	-0.149	0.062	0.004	-0.270	-0.028	-2.422	0.015
Mantoni et al., 2008	-0.169	0.061	0.004	-0.288	-0.050	-2.777	0.005
Brazaitis et al., 2014	-0.169	0.059	0.003	-0.285	-0.053	-2.863	0.004
	-0.157	0.061	0.004	-0.277	-0.036	-2.549	0.011



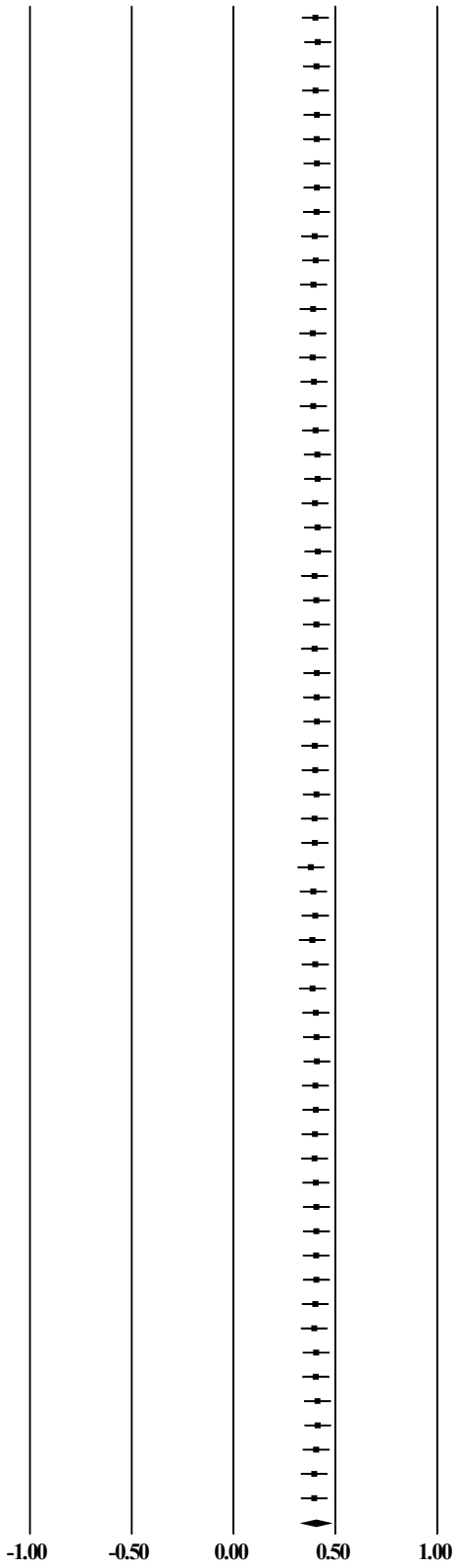
Forest plot of the leave-one-out sensitivity analysis for heart rate

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.281	0.058	0.003	0.167	0.395	4.815	0.000
Hausswirth et al., 2012 (2)	0.288	0.058	0.003	0.174	0.402	4.943	0.000
Hammond et al., 2020 (1)	0.288	0.058	0.003	0.175	0.402	4.963	0.000
Hammond et al., 2020 (2)	0.287	0.058	0.003	0.173	0.401	4.925	0.000
Hammond et al., 2020 (3)	0.288	0.058	0.003	0.174	0.403	4.948	0.000
Louis et al., 2015 (1)	0.273	0.056	0.003	0.162	0.383	4.834	0.000
Louis et al., 2015 (2)	0.290	0.058	0.003	0.176	0.404	4.998	0.000
Louis et al., 2015 (3)	0.287	0.058	0.003	0.173	0.402	4.939	0.000
Louis et al., 2015 (4)	0.288	0.058	0.003	0.174	0.402	4.952	0.000
Debiec-Bak et al., 2013 (1)	0.278	0.058	0.003	0.164	0.392	4.764	0.000
Debiec-Bak et al., 2013 (2)	0.280	0.059	0.003	0.165	0.395	4.776	0.000
Debiec-Bak et al., 2013 (3)	0.277	0.058	0.003	0.163	0.390	4.757	0.000
Debiec-Bak et al., 2013 (4)	0.276	0.058	0.003	0.162	0.389	4.755	0.000
Debiec-Bak et al., 2013 (5)	0.273	0.057	0.003	0.161	0.386	4.754	0.000
Debiec-Bak et al., 2013 (6)	0.274	0.058	0.003	0.161	0.387	4.753	0.000
Debiec-Bak et al., 2013 (7)	0.276	0.058	0.003	0.162	0.390	4.756	0.000
Debiec-Bak et al., 2013 (8)	0.275	0.058	0.003	0.162	0.389	4.754	0.000
Cuttell et al., 2017 (1)	0.289	0.058	0.003	0.175	0.403	4.977	0.000
Cuttell et al., 2017 (2)	0.296	0.057	0.003	0.184	0.408	5.165	0.000
Cuttell et al., 2017 (3)	0.292	0.058	0.003	0.179	0.406	5.060	0.000
Cuttell et al., 2017 (4)	0.297	0.057	0.003	0.186	0.409	5.217	0.000
Cuttell et al., 2017 (5)	0.295	0.057	0.003	0.182	0.407	5.132	0.000
Cuttell et al., 2017 (6)	0.297	0.057	0.003	0.185	0.409	5.212	0.000
Cuttell et al., 2017 (7)	0.297	0.057	0.003	0.185	0.409	5.191	0.000
Cuttell et al., 2017 (8)	0.301	0.056	0.003	0.190	0.411	5.340	0.000
Cuttell et al., 2017 (9)	0.280	0.058	0.003	0.167	0.394	4.827	0.000
Cuttell et al., 2017 (10)	0.283	0.058	0.003	0.169	0.397	4.866	0.000
Cuttell et al., 2017 (11)	0.285	0.058	0.003	0.171	0.399	4.897	0.000
Cuttell et al., 2017 (12)	0.290	0.058	0.003	0.176	0.404	4.999	0.000
Cuttell et al., 2017 (13)	0.288	0.058	0.003	0.174	0.402	4.948	0.000
Cuttell et al., 2017 (14)	0.285	0.058	0.003	0.171	0.399	4.897	0.000
Cuttell et al., 2017 (15)	0.290	0.058	0.003	0.177	0.404	5.007	0.000
Cuttell et al., 2017 (16)	0.290	0.058	0.003	0.176	0.404	4.999	0.000
Fonda et al., 2014 (1)	0.283	0.058	0.003	0.169	0.398	4.858	0.000
Fonda et al., 2014 (2)	0.291	0.058	0.003	0.177	0.405	5.018	0.000
Fonda et al., 2014 (3)	0.292	0.058	0.003	0.179	0.406	5.052	0.000
Fonda et al., 2014 (4)	0.281	0.058	0.003	0.166	0.395	4.817	0.000
Fonda et al., 2014 (5)	0.289	0.058	0.003	0.175	0.403	4.959	0.000
Fonda et al., 2014 (6)	0.287	0.058	0.003	0.173	0.402	4.933	0.000
Fonda et al., 2014 (7)	0.278	0.058	0.003	0.165	0.392	4.794	0.000
Fonda et al., 2014 (8)	0.287	0.058	0.003	0.173	0.401	4.921	0.000
Fonda et al., 2014 (9)	0.283	0.058	0.003	0.169	0.398	4.855	0.000
Fonda et al., 2014 (10)	0.279	0.058	0.003	0.165	0.393	4.801	0.000
Fonda et al., 2014 (11)	0.290	0.058	0.003	0.176	0.404	4.997	0.000
Fonda et al., 2014 (12)	0.285	0.058	0.003	0.171	0.400	4.887	0.000
P.Zalewski et al., 2014 (1)	0.286	0.059	0.003	0.172	0.401	4.887	0.000
P.Zalewski et al., 2014 (2)	0.282	0.059	0.003	0.167	0.397	4.804	0.000
P.Zalewski et al., 2014 (3)	0.282	0.059	0.003	0.167	0.397	4.805	0.000
Zalewski et al., 2013 (1)	0.289	0.058	0.003	0.175	0.404	4.950	0.000
Zalewski et al., 2013 (2)	0.283	0.059	0.003	0.168	0.398	4.817	0.000
Zalewski et al., 2013 (3)	0.284	0.059	0.003	0.168	0.399	4.824	0.000
Lubkoswka and suska, 2011 (1)	0.272	0.057	0.003	0.160	0.384	4.766	0.000
Lubkoswka and suska, 2011 (2)	0.279	0.059	0.003	0.164	0.394	4.757	0.000
Lubkoswka and suska, 2011 (3)	0.285	0.059	0.003	0.170	0.401	4.835	0.000
Lubkowska and Szygula, 2010 (1)	0.275	0.058	0.003	0.162	0.389	4.757	0.000
Lubkowska and Szygula, 2010 (2)	0.284	0.059	0.003	0.169	0.399	4.835	0.000
Lubkowska and Szygula, 2010 (3)	0.278	0.058	0.003	0.164	0.392	4.767	0.000
Lubkowska and Szygula, 2010 (4)	0.277	0.058	0.003	0.163	0.390	4.761	0.000
Louis et al., 2020 (1)	0.287	0.058	0.003	0.173	0.401	4.932	0.000
Louis et al., 2020 (2)	0.287	0.058	0.003	0.173	0.402	4.939	0.000
Louis et al., 2020 (3)	0.280	0.058	0.003	0.166	0.394	4.816	0.000
Louis et al., 2020 (4)	0.282	0.058	0.003	0.168	0.396	4.841	0.000
Coppi et al., 2022	0.278	0.058	0.003	0.164	0.392	4.794	0.000
Rose et al., 2023 (2)	0.276	0.058	0.003	0.163	0.389	4.785	0.000
Muller et al., 2012 (1)	0.284	0.058	0.003	0.170	0.399	4.881	0.000
Muller et al., 2012 (2)	0.289	0.058	0.003	0.175	0.403	4.982	0.000
Muller et al., 2012 (3)	0.290	0.058	0.003	0.177	0.404	5.007	0.000
Muller et al., 2012 (4)	0.286	0.058	0.003	0.171	0.400	4.903	0.000
Muller et al., 2012 (5)	0.288	0.058	0.003	0.174	0.402	4.949	0.000
Muller et al., 2012 (6)	0.282	0.058	0.003	0.168	0.396	4.839	0.000
Sramek et al., 2000 (1)	0.281	0.058	0.003	0.166	0.395	4.821	0.000
Sramek et al., 2000 (2)	0.291	0.058	0.003	0.177	0.405	5.023	0.000
Sramek et al., 2000 (3)	0.291	0.058	0.003	0.177	0.404	5.016	0.000
Sramek et al., 2000 (4)	0.296	0.057	0.003	0.184	0.408	5.173	0.000
Sramek et al., 2000 (5)	0.283	0.058	0.003	0.169	0.397	4.858	0.000
Sramek et al., 2000 (6)	0.277	0.058	0.003	0.163	0.390	4.784	0.000
Jansky et al., 1996 (1)	0.273	0.057	0.003	0.161	0.384	4.791	0.000
Jansky et al., 1996 (2)	0.273	0.057	0.003	0.161	0.384	4.793	0.000
	0.284	0.058	0.003	0.171	0.397	4.935	0.000



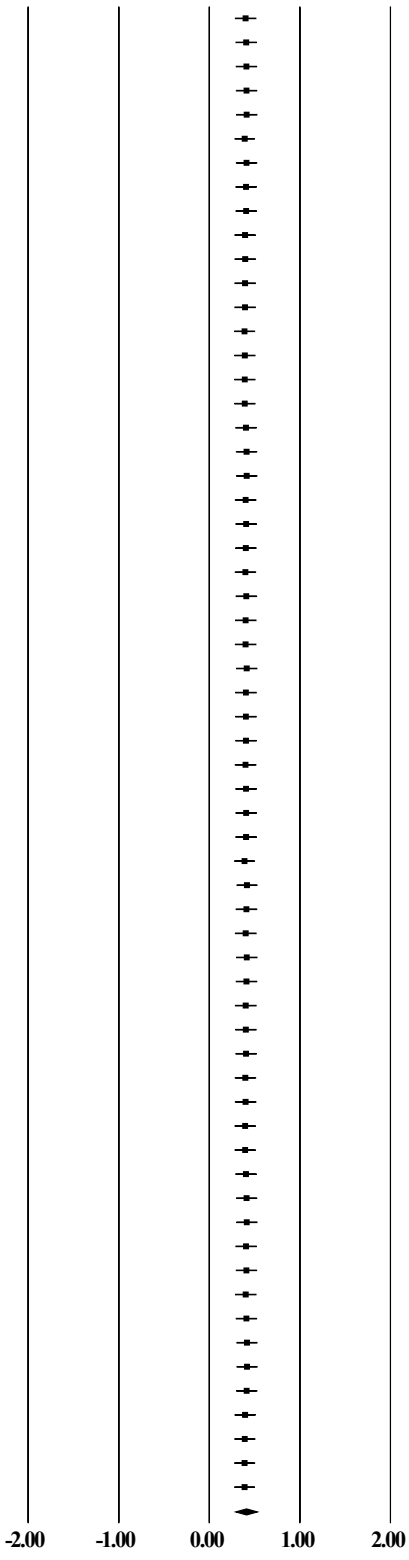
Forest plot of the leave-one-out sensitivity analysis for mean arterial pressure

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.402	0.034	0.001	0.335	0.469	11.791	0.000
Hausswirth et al., 2012 (2)	0.413	0.034	0.001	0.346	0.480	12.116	0.000
Hammond et al., 2020 (1)	0.408	0.034	0.001	0.341	0.474	11.992	0.000
Hammond et al., 2020 (2)	0.403	0.034	0.001	0.336	0.469	11.858	0.000
Hammond et al., 2020 (3)	0.410	0.034	0.001	0.343	0.477	12.007	0.000
Louis et al., 2015 (1)	0.409	0.034	0.001	0.342	0.475	12.007	0.000
Louis et al., 2015 (2)	0.410	0.034	0.001	0.343	0.476	12.041	0.000
Louis et al., 2015 (3)	0.410	0.034	0.001	0.343	0.476	12.045	0.000
Louis et al., 2015 (4)	0.408	0.034	0.001	0.341	0.475	11.988	0.000
Debiec-Bak et al., 2013 (1)	0.399	0.034	0.001	0.331	0.466	11.604	0.000
Debiec-Bak et al., 2013 (2)	0.404	0.034	0.001	0.336	0.471	11.740	0.000
Debiec-Bak et al., 2013 (3)	0.393	0.034	0.001	0.326	0.460	11.461	0.000
Debiec-Bak et al., 2013 (4)	0.391	0.034	0.001	0.324	0.458	11.416	0.000
Debiec-Bak et al., 2013 (5)	0.390	0.034	0.001	0.322	0.457	11.378	0.000
Debiec-Bak et al., 2013 (6)	0.389	0.034	0.001	0.322	0.456	11.356	0.000
Debiec-Bak et al., 2013 (7)	0.395	0.034	0.001	0.328	0.463	11.523	0.000
Debiec-Bak et al., 2013 (8)	0.392	0.034	0.001	0.325	0.459	11.436	0.000
Fonda et al., 2014 (1)	0.403	0.034	0.001	0.337	0.470	11.843	0.000
Fonda et al., 2014 (2)	0.412	0.034	0.001	0.346	0.479	12.107	0.000
Fonda et al., 2014 (3)	0.413	0.034	0.001	0.347	0.480	12.140	0.000
Fonda et al., 2014 (4)	0.400	0.034	0.001	0.334	0.467	11.768	0.000
Fonda et al., 2014 (5)	0.413	0.034	0.001	0.346	0.480	12.126	0.000
Fonda et al., 2014 (6)	0.414	0.034	0.001	0.348	0.481	12.171	0.000
Fonda et al., 2014 (7)	0.398	0.034	0.001	0.332	0.465	11.709	0.000
Fonda et al., 2014 (8)	0.407	0.034	0.001	0.340	0.474	11.951	0.000
Fonda et al., 2014 (9)	0.407	0.034	0.001	0.341	0.474	11.957	0.000
Fonda et al., 2014 (10)	0.398	0.034	0.001	0.332	0.465	11.716	0.000
Fonda et al., 2014 (11)	0.409	0.034	0.001	0.342	0.476	12.007	0.000
Fonda et al., 2014 (12)	0.408	0.034	0.001	0.342	0.475	11.990	0.000
P.Zalewski et al., 2014 (1)	0.410	0.034	0.001	0.342	0.477	11.939	0.000
P.Zalewski et al., 2014 (2)	0.399	0.034	0.001	0.332	0.466	11.653	0.000
P.Zalewski et al., 2014 (3)	0.401	0.034	0.001	0.334	0.469	11.712	0.000
Zalewski et al., 2013 (1)	0.408	0.034	0.001	0.340	0.475	11.844	0.000
Zalewski et al., 2013 (2)	0.398	0.034	0.001	0.331	0.465	11.586	0.000
Zalewski et al., 2013 (3)	0.400	0.034	0.001	0.332	0.467	11.628	0.000
Lubkoswka and suska, 2011 (1)	0.380	0.034	0.001	0.313	0.447	11.176	0.000
Lubkoswka and suska, 2011 (2)	0.392	0.034	0.001	0.325	0.460	11.376	0.000
Lubkoswka and suska, 2011 (3)	0.402	0.035	0.001	0.334	0.469	11.617	0.000
Lubkowska and Szygula, 2010 (1)	0.387	0.034	0.001	0.321	0.454	11.396	0.000
Lubkowska and Szygula, 2010 (2)	0.402	0.034	0.001	0.334	0.469	11.714	0.000
Lubkowska and Szygula, 2010 (3)	0.388	0.034	0.001	0.321	0.455	11.392	0.000
Lubkowska and Szygula, 2010 (4)	0.404	0.034	0.001	0.337	0.471	11.784	0.000
Louis et al., 2020 (1)	0.408	0.034	0.001	0.341	0.474	11.978	0.000
Louis et al., 2020 (2)	0.410	0.034	0.001	0.343	0.476	12.045	0.000
Louis et al., 2020 (3)	0.402	0.034	0.001	0.335	0.469	11.824	0.000
Louis et al., 2020 (4)	0.404	0.034	0.001	0.338	0.471	11.886	0.000
Coppi et al., 2022	0.400	0.034	0.001	0.333	0.467	11.770	0.000
Rose et al., 2023 (2)	0.398	0.034	0.001	0.332	0.465	11.731	0.000
Muller et al., 2012 (1)	0.404	0.034	0.001	0.338	0.471	11.892	0.000
Muller et al., 2012 (2)	0.407	0.034	0.001	0.340	0.474	11.965	0.000
Muller et al., 2012 (3)	0.407	0.034	0.001	0.340	0.474	11.965	0.000
Muller et al., 2012 (4)	0.406	0.034	0.001	0.339	0.473	11.941	0.000
Muller et al., 2012 (5)	0.407	0.034	0.001	0.340	0.474	11.965	0.000
Muller et al., 2012 (6)	0.402	0.034	0.001	0.335	0.468	11.820	0.000
Sramek et al., 2000 (1)	0.397	0.034	0.001	0.330	0.463	11.696	0.000
Sramek et al., 2000 (2)	0.406	0.034	0.001	0.339	0.473	11.934	0.000
Sramek et al., 2000 (3)	0.404	0.034	0.001	0.337	0.471	11.875	0.000
Sramek et al., 2000 (4)	0.413	0.034	0.001	0.346	0.479	12.167	0.000
Sramek et al., 2000 (5)	0.414	0.034	0.001	0.347	0.480	12.179	0.000
Sramek et al., 2000 (6)	0.406	0.034	0.001	0.339	0.473	11.930	0.000
Jansky et al., 1996 (1)	0.397	0.034	0.001	0.330	0.463	11.696	0.000
Jansky et al., 1996 (2)	0.397	0.034	0.001	0.330	0.463	11.696	0.000
	0.403	0.034	0.001	0.336	0.469	11.904	0.000



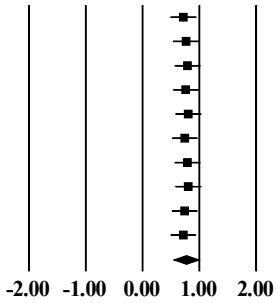
Forest plot of the leave-one-out sensitivity analysis for systolic arterial pressure

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.401	0.061	0.004	0.281	0.520	6.565	0.000
Hausswirth et al., 2012 (2)	0.408	0.061	0.004	0.288	0.527	6.674	0.000
Hammond et al., 2020 (1)	0.410	0.061	0.004	0.291	0.529	6.745	0.000
Hammond et al., 2020 (2)	0.411	0.061	0.004	0.292	0.530	6.789	0.000
Hammond et al., 2020 (3)	0.412	0.061	0.004	0.294	0.531	6.804	0.000
Louis et al., 2015 (1)	0.391	0.058	0.003	0.278	0.505	6.760	0.000
Louis et al., 2015 (2)	0.411	0.061	0.004	0.293	0.530	6.793	0.000
Louis et al., 2015 (3)	0.406	0.061	0.004	0.286	0.525	6.656	0.000
Louis et al., 2015 (4)	0.407	0.061	0.004	0.288	0.527	6.687	0.000
Debiec-Bak et al., 2013 (1)	0.395	0.061	0.004	0.276	0.515	6.505	0.000
Debiec-Bak et al., 2013 (2)	0.396	0.061	0.004	0.277	0.516	6.506	0.000
Debiec-Bak et al., 2013 (3)	0.395	0.061	0.004	0.276	0.514	6.505	0.000
Debiec-Bak et al., 2013 (4)	0.395	0.061	0.004	0.276	0.514	6.505	0.000
Debiec-Bak et al., 2013 (5)	0.389	0.060	0.004	0.272	0.507	6.521	0.000
Debiec-Bak et al., 2013 (6)	0.393	0.060	0.004	0.274	0.511	6.508	0.000
Debiec-Bak et al., 2013 (7)	0.392	0.060	0.004	0.274	0.510	6.510	0.000
Debiec-Bak et al., 2013 (8)	0.392	0.060	0.004	0.274	0.510	6.509	0.000
Fonda et al., 2014 (1)	0.405	0.061	0.004	0.285	0.524	6.628	0.000
Fonda et al., 2014 (2)	0.412	0.061	0.004	0.293	0.530	6.791	0.000
Fonda et al., 2014 (3)	0.413	0.060	0.004	0.294	0.531	6.830	0.000
Fonda et al., 2014 (4)	0.401	0.061	0.004	0.282	0.521	6.580	0.000
Fonda et al., 2014 (5)	0.407	0.061	0.004	0.288	0.527	6.673	0.000
Fonda et al., 2014 (6)	0.403	0.061	0.004	0.284	0.523	6.608	0.000
Fonda et al., 2014 (7)	0.399	0.061	0.004	0.280	0.518	6.558	0.000
Fonda et al., 2014 (8)	0.409	0.061	0.004	0.289	0.528	6.706	0.000
Fonda et al., 2014 (9)	0.402	0.061	0.004	0.282	0.521	6.585	0.000
Fonda et al., 2014 (10)	0.401	0.061	0.004	0.281	0.520	6.573	0.000
Fonda et al., 2014 (11)	0.413	0.060	0.004	0.295	0.531	6.838	0.000
Fonda et al., 2014 (12)	0.404	0.061	0.004	0.285	0.524	6.622	0.000
P.Zalewski et al., 2014 (1)	0.404	0.061	0.004	0.284	0.525	6.581	0.000
P.Zalewski et al., 2014 (2)	0.405	0.061	0.004	0.284	0.525	6.585	0.000
P.Zalewski et al., 2014 (3)	0.400	0.061	0.004	0.280	0.520	6.531	0.000
Zalewski et al., 2013 (1)	0.406	0.062	0.004	0.285	0.527	6.592	0.000
Zalewski et al., 2013 (2)	0.407	0.062	0.004	0.286	0.527	6.612	0.000
Zalewski et al., 2013 (3)	0.406	0.062	0.004	0.285	0.527	6.597	0.000
Lubkoswka and suska, 2011 (1)	0.389	0.060	0.004	0.272	0.506	6.533	0.000
Lubkoswka and suska, 2011 (2)	0.416	0.060	0.004	0.299	0.533	6.960	0.000
Lubkoswka and suska, 2011 (3)	0.410	0.061	0.004	0.289	0.530	6.667	0.000
Lubkowska and Szygula, 2010 (1)	0.402	0.061	0.004	0.282	0.522	6.550	0.000
Lubkowska and Szygula, 2010 (2)	0.414	0.060	0.004	0.296	0.532	6.856	0.000
Lubkowska and Szygula, 2010 (3)	0.410	0.061	0.004	0.290	0.530	6.714	0.000
Lubkowska and Szygula, 2010 (4)	0.402	0.061	0.004	0.282	0.522	6.549	0.000
Louis et al., 2020 (1)	0.404	0.061	0.004	0.284	0.523	6.624	0.000
Louis et al., 2020 (2)	0.406	0.061	0.004	0.286	0.525	6.656	0.000
Louis et al., 2020 (3)	0.398	0.061	0.004	0.279	0.517	6.562	0.000
Louis et al., 2020 (4)	0.401	0.061	0.004	0.281	0.520	6.583	0.000
Coppi et al., 2022	0.396	0.060	0.004	0.277	0.514	6.549	0.000
Rose et al., 2023 (2)	0.396	0.060	0.004	0.278	0.515	6.555	0.000
Muller et al., 2012 (1)	0.405	0.061	0.004	0.286	0.524	6.646	0.000
Muller et al., 2012 (2)	0.412	0.060	0.004	0.293	0.530	6.814	0.000
Muller et al., 2012 (3)	0.414	0.060	0.004	0.296	0.532	6.885	0.000
Muller et al., 2012 (4)	0.406	0.061	0.004	0.286	0.525	6.658	0.000
Muller et al., 2012 (5)	0.409	0.061	0.004	0.290	0.528	6.741	0.000
Muller et al., 2012 (6)	0.402	0.061	0.004	0.283	0.521	6.601	0.000
Sramek et al., 2000 (1)	0.410	0.061	0.004	0.291	0.529	6.745	0.000
Sramek et al., 2000 (2)	0.416	0.060	0.004	0.298	0.533	6.943	0.000
Sramek et al., 2000 (3)	0.417	0.060	0.004	0.300	0.534	6.980	0.000
Sramek et al., 2000 (4)	0.412	0.060	0.004	0.294	0.531	6.824	0.000
Sramek et al., 2000 (5)	0.396	0.060	0.004	0.277	0.514	6.548	0.000
Sramek et al., 2000 (6)	0.392	0.060	0.004	0.275	0.509	6.553	0.000
Jansky et al., 1996 (1)	0.390	0.059	0.004	0.274	0.506	6.576	0.000
Jansky et al., 1996 (2)	0.390	0.059	0.003	0.274	0.505	6.587	0.000
	0.403	0.060	0.004	0.286	0.521	6.707	0.000



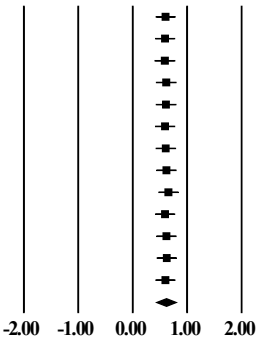
Forest plot of the leave-one-out sensitivity analysis for diastolic arterial pressure

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hausswirth et al., 2012 (1)	0.720	0.117	0.014	0.490	0.949	6.145	0.000
Hausswirth et al., 2012 (2)	0.768	0.119	0.014	0.534	1.001	6.441	0.000
Louis et al., 2015 (1)	0.793	0.117	0.014	0.565	1.022	6.795	0.000
Louis et al., 2015 (2)	0.762	0.116	0.013	0.535	0.989	6.575	0.000
Louis et al., 2015 (3)	0.805	0.117	0.014	0.576	1.035	6.883	0.000
Louis et al., 2015 (4)	0.744	0.115	0.013	0.518	0.969	6.461	0.000
Louis et al., 2020 (1)	0.793	0.117	0.014	0.565	1.022	6.795	0.000
Louis et al., 2020 (2)	0.805	0.117	0.014	0.576	1.035	6.883	0.000
Louis et al., 2020 (3)	0.742	0.115	0.013	0.517	0.968	6.452	0.000
Louis et al., 2020 (4)	0.719	0.114	0.013	0.496	0.942	6.332	0.000
	0.765	0.110	0.012	0.548	0.981	6.930	0.000



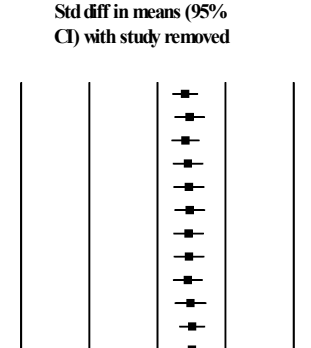
Forest plot of the leave-one-out sensitivity analysis for RR interval

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	0.606	0.094	0.009	0.422	0.790	6.455	0.000
Theurot et al., 2021 (2)	0.595	0.093	0.009	0.412	0.778	6.365	0.000
Theurot et al., 2021 (3)	0.591	0.097	0.009	0.402	0.781	6.113	0.000
Hausswirth et al., 2012 (1)	0.617	0.096	0.009	0.428	0.806	6.409	0.000
Hausswirth et al., 2012 (2)	0.613	0.096	0.009	0.424	0.801	6.371	0.000
Louis et al., 2015 (1)	0.595	0.094	0.009	0.411	0.778	6.336	0.000
Louis et al., 2015 (2)	0.609	0.094	0.009	0.424	0.794	6.457	0.000
Louis et al., 2015 (3)	0.621	0.095	0.009	0.435	0.806	6.565	0.000
Louis et al., 2015 (4)	0.657	0.095	0.009	0.471	0.843	6.918	0.000
Louis et al., 2020 (1)	0.595	0.094	0.009	0.411	0.778	6.336	0.000
Louis et al., 2020 (2)	0.621	0.095	0.009	0.435	0.806	6.565	0.000
Louis et al., 2020 (3)	0.627	0.095	0.009	0.441	0.812	6.623	0.000
Louis et al., 2020 (4)	0.602	0.094	0.009	0.417	0.786	6.396	0.000
	0.611	0.091	0.008	0.433	0.790	6.718	0.000



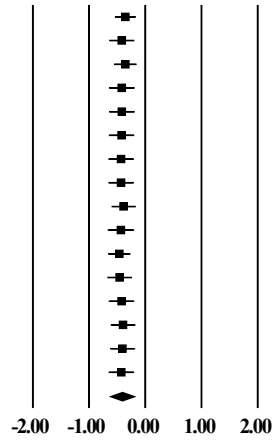
Forest plot of the leave-one-out analysis for RMSSD

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	0.406	0.096	0.009	0.217	0.595	4.214	0.000
Theurot et al., 2021 (2)	0.473	0.115	0.013	0.249	0.697	4.131	0.000
Theurot et al., 2021 (3)	0.412	0.105	0.011	0.206	0.617	3.929	0.000
Hausswirth et al., 2012 (1)	0.449	0.114	0.013	0.226	0.671	3.954	0.000
Hausswirth et al., 2012 (2)	0.461	0.115	0.013	0.235	0.688	3.996	0.000
Louis et al., 2015 (1)	0.475	0.115	0.013	0.249	0.700	4.130	0.000
Louis et al., 2015 (2)	0.458	0.114	0.013	0.235	0.681	4.028	0.000
Louis et al., 2015 (3)	0.463	0.114	0.013	0.239	0.687	4.052	0.000
Louis et al., 2015 (4)	0.447	0.112	0.013	0.228	0.667	3.994	0.000
P.Zalewski et al., 2014 (1)	0.486	0.119	0.014	0.254	0.719	4.095	0.000
P.Zalewski et al., 2014 (2)	0.511	0.097	0.009	0.321	0.701	5.271	0.000
P.Zalewski et al., 2014 (3)	0.508	0.108	0.012	0.296	0.720	4.691	0.000
Louis et al., 2020 (1)	0.475	0.115	0.013	0.249	0.700	4.130	0.000
Louis et al., 2020 (2)	0.463	0.114	0.013	0.239	0.687	4.052	0.000
Louis et al., 2020 (3)	0.457	0.114	0.013	0.234	0.679	4.022	0.000
Louis et al., 2020 (4)	0.468	0.115	0.013	0.243	0.692	4.078	0.000
	0.463	0.108	0.012	0.251	0.675	4.286	0.000



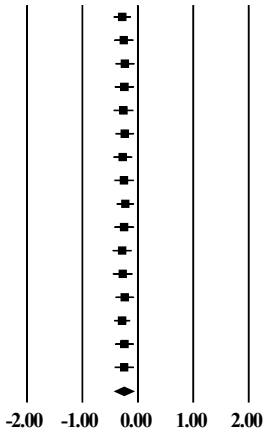
Forest plot of the leave-one-out sensitivity analysis for HF

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	-0.354	0.095	0.009	-0.541	-0.167	-3.716	0.000
Theurot et al., 2021 (2)	-0.417	0.114	0.013	-0.641	-0.193	-3.646	0.000
Theurot et al., 2021 (3)	-0.354	0.103	0.011	-0.555	-0.153	-3.453	0.001
Hausswirth et al., 2012 (1)	-0.417	0.116	0.013	-0.644	-0.189	-3.591	0.000
Hausswirth et al., 2012 (2)	-0.416	0.116	0.013	-0.643	-0.189	-3.586	0.000
Louis et al., 2015 (1)	-0.421	0.115	0.013	-0.646	-0.196	-3.667	0.000
Louis et al., 2015 (2)	-0.430	0.115	0.013	-0.655	-0.205	-3.749	0.000
Louis et al., 2015 (3)	-0.430	0.115	0.013	-0.655	-0.205	-3.751	0.000
Louis et al., 2015 (4)	-0.384	0.109	0.012	-0.598	-0.170	-3.520	0.000
P.Zalewski et al., 2014 (1)	-0.432	0.119	0.014	-0.665	-0.199	-3.630	0.000
P.Zalewski et al., 2014 (2)	-0.460	0.101	0.010	-0.658	-0.263	-4.567	0.000
P.Zalewski et al., 2014 (3)	-0.455	0.111	0.012	-0.672	-0.239	-4.114	0.000
Louis et al., 2020 (1)	-0.421	0.115	0.013	-0.646	-0.196	-3.667	0.000
Louis et al., 2020 (2)	-0.395	0.112	0.012	-0.613	-0.176	-3.537	0.000
Louis et al., 2020 (3)	-0.403	0.113	0.013	-0.625	-0.181	-3.564	0.000
Louis et al., 2020 (4)	-0.424	0.115	0.013	-0.649	-0.199	-3.692	0.000
	-0.413	0.108	0.012	-0.625	-0.201	-3.823	0.000



Forest plot of the leave-one-out sensitivity analysis for LF

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Theurot et al., 2021 (1)	-0.282	0.080	0.006	-0.438	-0.125	-3.535	0.000
Theurot et al., 2021 (2)	-0.252	0.089	0.008	-0.426	-0.078	-2.842	0.004
Theurot et al., 2021 (3)	-0.232	0.088	0.008	-0.404	-0.060	-2.650	0.008
Hausswirth et al., 2012 (1)	-0.241	0.089	0.008	-0.415	-0.067	-2.712	0.007
Hausswirth et al., 2012 (2)	-0.259	0.090	0.008	-0.436	-0.082	-2.863	0.004
Louis et al., 2015 (1)	-0.236	0.086	0.007	-0.405	-0.067	-2.743	0.006
Louis et al., 2015 (2)	-0.272	0.087	0.008	-0.443	-0.102	-3.129	0.002
Louis et al., 2015 (3)	-0.249	0.089	0.008	-0.423	-0.075	-2.803	0.005
Louis et al., 2015 (4)	-0.224	0.080	0.006	-0.382	-0.067	-2.789	0.005
P.Zalewski et al., 2014 (1)	-0.246	0.092	0.008	-0.426	-0.067	-2.687	0.007
P.Zalewski et al., 2014 (2)	-0.282	0.088	0.008	-0.455	-0.109	-3.194	0.001
P.Zalewski et al., 2014 (3)	-0.272	0.091	0.008	-0.450	-0.093	-2.985	0.003
Louis et al., 2020 (1)	-0.236	0.086	0.007	-0.405	-0.067	-2.743	0.006
Louis et al., 2020 (2)	-0.284	0.074	0.005	-0.428	-0.139	-3.848	0.000
Louis et al., 2020 (3)	-0.241	0.087	0.008	-0.412	-0.069	-2.755	0.006
Louis et al., 2020 (4)	-0.245	0.088	0.008	-0.418	-0.072	-2.775	0.006
	-0.254	0.084	0.007	-0.418	-0.089	-3.027	0.002



Forest plot of the leave-one-out sensitivity analysis for LF/HF ratio

Appendix 5. Health-related reference intervals of blood pressure

	Systolic arterial pressure			Diastolic arterial pressure		
Sex/Age	Hypotension upper limit	Normal range	Hypertension lower limit	Hypotension upper limit	Normal range	Hypertension lower limit
Males						
16	98	105-135	145	52	60-86	90
17	98	105-135	145	55	60-86	90
18	98	105-135	145	55	60-86	90
19	98	105-140	150	55	60-88	95
20-24	98	105-140	150	56	62-88	95
25-29	100	108-140	150	60	65-90	96
30-34	100	110-145	155	60	68-92	98
35-39	102	110-145	160	60	68-92	100
40-44	102	110-150	165	60	70-94	100
45-49	104	110-155	170	60	70-96	104
50-54	105	115-160	175	60	70-98	106
55-59	106	115-165	180	60	70-98	108
60-64	108	115-170	190	60	70-100	110
Females						
16	95	100-130	140	55	60-85	90
17	95	100-130	140	55	60-85	90
18	95	100-130	140	55	60-85	90
19	95	100-130	140	55	60-85	90
20-24	95	100-130	140	55	60-85	90
25-29	98	102-130	140	55	60-86	92
30-34	98	102-135	145	55	60.88	95
35-39	100	105-140	150	60	65-90	98
40-44	100	105-150	165	60	65-92	100
45-49	100	105-155	175	60	65-96	105
50-54	105	110-165	180	60	70-100	108
55-59	105	110-170	185	60	70-100	108
60-64	105	115-175	190	60	70-100	110

Blood pressures are represented in millimeters of mercury

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title (p1)
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract (p1)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction (p2-3)
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction (p3-4)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Eligibility criteria (p4)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Literature search strategy (p4)
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Literature search strategy (p4)
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Literature search strategy (p4)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Dara extraction and coding (p5)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Dara extraction and coding (p5)
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Dara extraction and coding (p5)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Statistical analysis (p6)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Statistical analysis (p4)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Literature search strategy (p4)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Statistical analysis (p4)

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Statistical analysis (p6)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Statistical analysis (p6)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	Statistical analysis (p6)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Statistical analysis (p6)
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Statistical analysis (p6)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Statistical analysis (p6-7)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1 (p8)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Appendix 1 (p1 of SM)
Study characteristics	17	Cite each included study and present its characteristics.	Table 1 (p9-14)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 2 (p15)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an estimate effect and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Appendix 2 (p2-7 of SM)
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Overall effect (p7)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results (p15-25)
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results (p15-25)
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Appendix 4 (p12-17 of SM)
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Appendix 3 (p8-11 of SM)

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 3 (p16) Table 5 (p21)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion (p26)
	23b	Discuss any limitations of the evidence included in the review.	Strength limits and perspective (p30-31)
	23c	Discuss any limitations of the review processes used.	Strength limits and perspective (p30-31)
	23d	Discuss implications of the results for practice, policy, and future research.	Strength limits and perspective (p30-31)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Registration (p1)
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Registration (p1)
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Registration (p1)
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding (p1)
Competing interests	26	Declare any competing interests of review authors.	Conflicts of interest (p1)
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data accessibility statement (p1)