HIGHLIGHTS

- Voluntary slow breathing: VSB; vagally-mediated heart rate variability: vmHRV
- We perform a systematic review and meta-analysis of the effects of VSB on HRV
- Results indicate increases in vmHRV with VSB considering 3 time points
- Time points: during, after 1 session, after a multi-session intervention
- VSB can be advised as prevention and adjunct treatment for many conditions

Effects of voluntary slow breathing on heart rate variability: A systematic review and meta-analysis

ABSTRACT

Voluntary slow breathing (VSB) is used as a prevention technique to support physical and mental health, given it is suggested to influence the parasympathetic nervous system. However, to date, no comprehensive quantitative review exists to support or refute this claim. We address this through a systematic review and meta-analysis of the effects of VSB on heart rate variability (HRV). Specifically, we focus on HRV parameters indexing parasympathetic nervous system (PNS) activity regulating cardiac functioning, referred to as vagally-mediated (vm)HRV: 1) during the breathing session (i.e., DURING), 2) immediately after one training session (i.e., IM-AFTER1), as well as 3) after a multi-session intervention (i.e., AFTER-INT). From the 1842 selected abstracts, 223 studies were suitable for inclusion (172 DURING, 16 IM-AFTER1, and 49 AFTER-INT). Results indicate increases in vmHRV with VSB, DURING, IM-AFTER1, and AFTER-INT. Given the involvement of the PNS in a large range of health-related outcomes and conditions, VSB exercises could be advised as a low-tech and low-cost technique to use in prevention and adjunct treatment purposes, with few adverse effects expected.

Keywords: heart rate variability biofeedback; parasympathetic nervous system; vagus nerve; cardiac coherence; slow breathing; deep breathing; abdominal breathing; diaphragmatic breathing

Effects of voluntary slow breathing on heart rate and heart rate variability: A systematic review and a meta-analysis

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ABSTRACT

Voluntary slow breathing (VSB) is used as a prevention technique to support physical and mental health, given it is suggested to influence the parasympathetic nervous system. However, to date, no comprehensive quantitative review exists to support or refute this claim. We address this through a systematic review and meta-analysis of the effects of VSB on heart rate variability (HRV). Specifically, we focus on HRV parameters indexing parasympathetic nervous system (PNS) activity regulating cardiac functioning, referred to as vagally-mediated (vm)HRV: 1) during the breathing session (i.e., DURING), 2) immediately after one training session (i.e., IM-AFTER1), as well as 3) after a multi-session intervention (i.e., AFTER-INT). From the 1842 selected abstracts, 223 studies were suitable for inclusion (172 DURING, 16 IM-AFTER1, and 49 AFTER-INT). Results indicate increases in vmHRV with VSB, DURING, IM-AFTER1, and AFTER-INT. Given the involvement of the PNS in a large range of health-related outcomes and conditions, VSB exercises could be advised as a low-tech and low-cost technique to use in prevention and adjunct treatment purposes, with few adverse effects expected.

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A systematic review and meta-analysis

1 INTRODUCTION

Breathing is a vital process that functions automatically but can also be voluntarily controlled to reach specific goals, especially preventive and therapeutic ones (Del Negro, Funk, & Feldman, 2018). The voluntary control of breathing, particularly slowing down its rate, has been used for thousands of years as an essential part of most meditative and relaxation practices, stemming from Eastern traditions (Gerritsen & Band, 2018; Russo, Santarelli, & O'Rourke, 2017; Zaccaro et al., 2018). However, if many physical and mental health benefits have been reported from voluntary slow breathing (Lehrer et al., 2020; Russo et al., 2017), its underlying mechanisms remain poorly understood. Several models suggest an implication of the vagus nerve—the main nerve of the parasympathetic nervous system (Brodal, 2016) —in the positive therapeutic effects of voluntary slow breathing (Gerritsen & Band, 2018; Lehrer et al., 2020; Mather & Thayer, 2018; Noble & Hochman, 2019; Sevoz-Couche & Laborde, 2022; Vanderhasselt & Ottaviani, 2022). Heart rate variability (HRV) has been widely used in studies to investigate non-invasively the effects of voluntary slow breathing on cardiac vagal activity and the activity of the vagus nerve regulating cardiac functioning (Berntson et al., 1997; Laborde et al., 2021; Laborde, Mosley, & Thayer, 2017). However, to date, no comprehensive overview has endeavored to synthesize the existing evidence. Consequently, the aim of this systematic review and series of meta-analyses is to investigate the effects of voluntary slow breathing on HRV, as indexed across three time points: while one is performing the slow breathing technique (i.e., DURING), immediately after one session (i.e., IM-AFTER1), and after a multi-session intervention (i.e., AFTER-INT).

Voluntary slow breathing is a technique where breathing is performed at a slower pace (around 6 cycles per minute, cpm) than spontaneous breathing, which is usually comprised between 12 and 20 cycles per minute in adults (Sherwood, 2006), and usually with a higher breathing amplitude (Bernardi et al., 1998). The benefits of voluntary slow breathing have been found at many levels of health and stress-related physiology, including optimizing the functioning of the autonomic nervous system (e.g., baroreflex, respiratory sinus arrhythmia), the functioning of cardiopulmonary and neuroendocrine functions, decreasing anxiety and arousal, and increasing relaxation and resilience (Carnevali, Koenig, Sgoifo, & Ottaviani, 2018; Chaddha, Modaff, Hooper-Lane, & Feldstein, 2019; Herbell & Zauszniewski, 2019; Kennedy et al., 2019; Mahtani, Beinortas, Bauza, & Nunan, 2016; Mahtani, Nunan, & Heneghan, 2012; Noble & Hochman, 2019; Pinter et al., 2019; Russo et al., 2017; Shaffer & Meehan, 2020; Vanderhasselt & Ottaviani, 2022; Yu, Funk, Hu, Wang, & Feijs, 2018; Zaccaro et al., 2018). Regarding the physiological effects of voluntary slow breathing, effects on blood pressure have already received some attention (Chaddha et al., 2019; Landman et al., 2014; Mahtani et al., 2016), showing modest reductions following voluntary slow breathing interventions. A similar systematic investigation is required with parameters reflecting autonomic nervous system activity on the heart, and specifically parasympathetic nervous activity, as indexed with HRV.

HRV represents the change in the time intervals between consecutive R-peaks (Berntson et al., 1997; Laborde et al., 2017). Several HRV parameters can be calculated via time-domain and frequency-domain analyses, which provide an index of underlying physiological mechanisms (Table 1). In other words, while most of the HRV parameters reflect a mixed contribution of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) or other systems related to cardiac functioning, some specific HRV parameters reflect uniquely the PNS contribution to cardiac functioning (referred to as cardiac vagal

activity) (Berntson et al., 1997; Laborde et al., 2017). This PNS contribution is known to be indexed by the root mean square of successive differences (RMSSD) in the time-domain, and in the frequency-domain by either the absolute power in the low-frequency (LF_{abs}) or the high-frequency (HF_{abs}), depending on the breathing frequency. More specifically, cardiac vagal activity will be reflected in HF_{abs} when breathing frequency is comprised between 9 and 24 cpm (Berntson et al., 1997; Laborde et al., 2017), and in LF_{abs} when breathing frequency is lower than 9 cpm (Kromenacker, Sanova, Marcus, Allen, & Lane, 2018). In addition, heart rate reflects many physiological influences and is often used as a non-specific overall marker of global activation (Gordan, Gwathmey, & Xie, 2015).

The following series of meta-analyses aim to investigate the effects of voluntary slow breathing on HRV. All HRV parameters are considered at three time points: DURING, IM-AFTER1, and AFTER-INT.

2 METHODS

The eligibility criteria, outcomes, main and moderator analyses were prespecified and published on PROSPERO (December 2020: CRD42020173255). The methods and results are presented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations, PRISMA (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). The PRISMA flow diagram can be found in Figure 1 and the PRISMA checklist in the Supporting checklist (eTable A). The PICOS parameters and the information regarding data sources and search are reported in Table 2.

2.1 Study Selection

Studies were imported into the reference management software Zotero (version 5.0.89). After removing duplicates, two of the authors (S.L. and C.S.) independently performed the study selection. Differences between the reviewers were resolved through discussion. A full

summary of the characteristics of each study included (eTable2), as well as the list of excluded studies with reasons for exclusion (eTable3), can be found in the Supplementary Material.

2.2 Data Collection and Data Items

The authors developed a data extraction sheet to record information related to the defined PICOS criteria, as well as information related to moderators. For each study, the following characteristics were extracted: study ID, year of publication, study design (within- vs. between-subject design), sample size, sample characteristics (healthy vs. patients; age; gender); characteristics of voluntary slow breathing intervention and control: nose vs. mouth breathing, breathing depth, main locus of breathing (chest vs. abdomen), respiratory frequency, inhalation/exhalation ratio, use of biofeedback, type of breathing pacer (e.g., visual, audio, kinesthetic), intervention length, as well as HRV parameters.

The primary outcomes were HRV parameters related to cardiac vagal activity: RMSSD and LF_{abs} for DURING, and RMSSD for both IM-AFTER1 and AFTER-INT. Given the assumption that LF_{abs} and HF_{abs} reflect cardiac vagal activity depending on the concomitant breathing rate, they could not be considered as standard markers for vmHRV for the time-points IM-AFTER1 and AFTER-INT, due to variations in breathing rates during control conditions across studies. The secondary outcomes were heart rate and the remaining HRV parameters.

2.3 Missing Data

In order to be considered for the meta-analysis, studies needed to present: sample size, mean and standard deviation (SD) during a voluntary slow breathing condition and during a control condition for DURING (or any other statistical information that would allow calculating an effect size related to the difference between the two conditions), and the sample size, mean, and SD at both pre- and post-intervention (or any other statistical information that would allow calculating an effect size related to the difference between the two time points)

for IM-AFTER1 or AFTER-INT. For IM-AFTER1 and AFTER-INT, if multiple time points were available at the end of the intervention, we chose the closest to the end of the intervention. When descriptive statistics were reported in graphs, we used the WebPlotDigitizer version 4.2 (https://automeris.io/WebPlotDigitizer) to extract the data. If the required data was not reported in the paper (for example, incomplete HRV data report), authors were contacted to obtain the missing information. For the papers considered and using the Deep Breathing Test (DBT) – a classical test to assess parasympathetic nervous system functioning – within the Ewing battery (Ewing & Clarke, 1982), authors were contacted for missing data only when at least one HRV parameter was reported[a]. In total, 120 authors were contacted for missing data not reported in the full-text, of which 13 responded with the data required for the meta-analysis. Furthermore, 9 authors sent 11 published papers and 4 datasets of unpublished studies which could be included in the meta-analysis.

2.4 Risk of Bias Assessment

To assess risk of bias, the Cochrane Collaboration's risk-of-bias tool (Rob2) was used (Sterne et al., 2011). This tool considers the presence of bias caused by the randomization process, the deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Articles were independently rated by two of the authors (S.L. and L.S.), in order to compute an inter-rater agreement coefficient. The raters' discrepancies were identified and resolved through discussion. For effects DURING, in the case the DBT was performed, the slow breathing intervention was not the study's main aim, given the DBT is part of a test battery of the autonomic nervous system (Ewing & Clarke, 1982). Nevertheless, those studies were assessed via the Rob2, not considering the primary aim

[a] Given the typical evaluation of the DBT is done only with heart rate, we assumed that if no HRV parameter was presented, HRV analyses were not likely to have been performed. Indeed, these analyses usually require the use of additional software in comparison to heart rate analysis.

for which they have been designed, but specifically regarding the aspects related to the DBT. The full risk of bias assessment is provided in the Supplementary Material (eTable 4).

2.5 Statistical Analysis

All analyses were performed using the software R (version 4.0.4, along with the packages meta and metafor). A total of 23 distinct meta-analyses were performed using the following parameters: HF_{abs}, HF_{nu}, HR, LF_{abs}, LF_{nu}, LF/HF, RMSSD, and SDNN; across the following time points: DURING, IM-AFTER1, and AFTER-INT. The R script as well as all csv files are made publicly available via the Open Science Framework: https://osf.io/jzf2c/.

Changes in HRV parameters were converted to standardized mean differences calculated as Hedges' g. A positive Hedges' g denotes a higher value for the experimental group in comparison to the control group. By convention, effects sizes of 0.2, 0.5, and 0.8 were respectively considered small, medium, and large (Cohen, 1988; Hedges & Olkin, 1985). When required, we created composite scores, as when multiple effect sizes were reported for the same sample (Higgins, Li, & Deeks, 2021; Table 6.5a). Effect sizes across studies were pooled using a random-effects model (Higgins & Thomas, 2019). To identify potential outliers, the standard residuals method was used (Hedges & Olkin, 1985; Viechtbauer & Cheung, 2010). Between-study heterogeneity was measured using tau^2 (variance of true effects) and further assessed using the I^2 statistic which assesses the proportion of between-study variance over total observed variance (Higgins, Thompson, Deeks, & Altman, 2003). An I^2 of 25, 50, and 75% represents respectively small, moderate, and large heterogeneity (Higgins et al., 2003). Small study effects (an indicator of publication bias) was assessed by visually inspecting funnel plots of standardized mean difference against standard error, and using Egger's regression asymmetry test (Duval & Tweedie, 2000; Egger, Davey Smith, Schneider, & Minder, 1997). If evidence for asymmetry was found ($P < 0.1$ on the one-tailed Egger's test), the trim and fill method was used to quantify the magnitude of the effect (Duval & Tweedie, 2000). Potential

causes of heterogeneity were explored via moderator analyses with subgroup analyses for categorical variables (i.e., biofeedback, breathing depth, breathing pacer, design, gender, inhalation/exhalation ratio, locus of breathing, nose/mouth, respiratory frequency, sample, and testing position) and random-effects meta-regressions for continuous moderators (i.e., age and intervention length). The predictive value of continuous moderators was evaluated by the goodness of fit (R^2) and was considered significant at the $P < 0.05$ level. Moderator analyses were performed for each parameter DURING (eTable8) and for each parameter AFTER-INT (eTable9) excluding LF_{nu} and HF_{nu}, due to the small number of studies in these analyses. Moderator analyses were not run for IM-AFTER1 again due to the small number of studies (< 10).

3 RESULTS

3.1 Overview

In total, 223 studies were included in the meta-analyses (172 for DURING, 16 for IM-AFTER1, 49 for AFTER-INT). Ten studies included data available for two of these categories, and two studies included data for all three categories. Table 3 provides a summary of the selected studies. In the following, for space reasons, we present and discuss only the results linked to vagally-mediated HRV. The results and plots concerning other HRV parameters and heart rate, as well as the complete moderator analyses, are presented in the Supplementary Material.

3.2 Risk of Bias

Overall Risk of Bias was high in 215 studies, with some concerns in 5 studies, and low in 1 study[b], with an inter-rater agreement of $\kappa = .95$. For unpublished studies ($k = 4$), data were sent by authors. However, the full text of the papers was not available, and consequently, risk

[b] The risk of bias for the study of Lehrer et al., 2010 was analyzed separately for DURING, IM-AFTER1, and AFTER-INT given the parameters differed among the conditions

of bias could not be assessed for these studies. Nevertheless, unpublished studies were included in the meta-analyses, to address the concern that published studies might display larger effect sizes (Higgins & Thomas, 2019). However, we are also aware that unpublished studies might also be of lower quality, given they have not been subjected to peer-review.

3.3 Effects DURING

For DURING, one potential outlier was found for RMSSD (Valensi et al., 2011) and two for LF_{abs} (Li, Chang, Zhang, & Chai, 2018; Sakakibara, Kaneda, & Oikawa, 2020). Results from the main analysis after outliers' exclusion show a medium effect size 0.530 (95% CI, 0.430 to 0.620) with large general heterogeneity (I^2 = 81%) and moderate variance of the true effect (tau^2 = 0.140) for RMSSD (k = 71), as well as a large effect size 1.490 (95% CI, 1.280 to 1.690), with large heterogeneity (I^2 = 93%; tau^2 = 0.701) for LF_{abs} (k = 57). For RMSSD, visual inspection did not reveal any asymmetry confirmed by a non-significant Egger's test (intercept = 0.580, P = .673). For LF_{abs}, the visual inspection suggested asymmetry that was confirmed by Egger's test (intercept = 0.579, P < .001). However, the Trim and Fill analysis revealed no missing studies. The forest plots can be found in eFigure 5 (LF_{abs}) and eFigure 7 (RMSSD). Funnel plots can be found in Figures 2a and 2b.

3.4 Effects IM-AFTER1

For IM-AFTER1, one outlier was found (Lalitha, Maheshkumar, Shobana, & Deepika, 2020). Results from the main-analysis after outlier's exclusion for IM-AFTER1 show a small effect size of 0.140 (95% CI, 0.030 to 0.240) with no heterogeneity (I^2 = 0%; tau^2 = 0) for RMSSD. We did not perform Egger's test given the small number of studies that reported RMSSD (k = 8), and visual inspection did not suggest any asymmetry. The forest plot can be found in eFigure 14. The funnel plot can be found in Figure 2c.

3.5 Effects AFTER-INT

Results from the main-analysis for AFTER-INT show a small effect size of 0.320 (95% CI, 0.080 to 0.560) with large heterogeneity (I^2 = 79%; tau^2 = 0.219) for RMSSD (k = 22). Visual inspection suggested potential asymmetry that was not confirmed by a non-significant Egger's test (intercept = -0.160, P = 0.620). However, the Trim and Fill analysis revealed no missing studies. The forest plot can be found in eFigure 22. The funnel plot can be found in Figure 2d.

4 DISCUSSION

This paper aimed to investigate the effects of voluntary slow breathing on vagally-mediated HRV. Overall, the data demonstrate an increase in several HRV parameters, specifically those reflecting vagally-mediated HRV, lending support for the theorized action of voluntary slow breathing on the vagus nerve. For DURING, a significant increase was found for RMSSD and LF_{abs}. Additionally, an increase was found for SDNN, LF_{nu}, and LF/HF (see Supplementary Material). For IM-AFTER1, a significant increase was found for RMSSD and LF_{abs}. Finally, for AFTER-INT, a significant increase was found in RMSSD, and for SDNN and LF_{abs} as secondary outcomes (see Supplementary Material).

For clarity and conciseness, the narrative will now mainly focus on HRV parameters reflecting the influence of the parasympathetic nervous system on the heart functioning, cardiac vagal activity: RMSSD and LF_{abs} for DURING, and RMSSD for IM-AFTER1 and AFTER-INT. The rationale for this choice is the following: overall, the interpretation of RMSSD as indexing cardiac vagal activity is considered more straightforward than the frequency-domain markers (such as LF_{abs}) when the respiratory frequency is unknown (Penttila et al., 2001). For DURING, the respiratory frequency is fixed and slow (less than 10cpm, and most of the time around 6cpm), while for IM-AFTER1 and AFTER-INT the measurement is realized at rest and respiratory frequency is spontaneous. Given most studies do not report the spontaneous

breathing frequency during the resting measurements, a clear attribution of cardiac vagal activity to either LF_{abs} or HF_{abs}, in this case, is not achievable.

For all time points considered, DURING, IM-AFTER1, and AFTER-INT, voluntary slow breathing showed a positive influence on vagally-mediated HRV indices (RMSSD and LF_{abs} for DURING, and RMSSD for IM-AFTER1 and AFTER-1). This would confirm that the vagus nerve is likely the common mechanism underlying the positive physical and mental health effects provoked by voluntary slow breathing (Gerritsen & Band, 2018; Noble & Hochman, 2019; Zaccaro et al., 2018). The effects DURING (moderate for RMSSD, and large for LF_{abs}) might reflect a strong stimulation of the vagus nerve afferents by voluntary slow breathing, via its action on the baroreflex, respiratory sinus arrhythmia, pulmonary afferents, emotion regulation networks, which is then reflected in cardiac vagal efferents after integration in the brainstem (Noble & Hochman, 2019). The small increase in RMSSD found for IM-AFTER1 can be explained by the transitory effect that voluntary slow breathing has on stimulating vagus nerve afferents, and that the effects are likely to decrease when voluntary slow breathing stops, as several studies document a return to baseline levels (Lehrer et al., 2020; Rockstroh, Blum, & Göritz, 2019; You et al., 2021).

The small increase in RMSSD found for AFTER-INT could reflect functional changes occurring via repeated stimulation of vagus nerve afferents, which might then be reflected in a chronic increase in vagus nerve efferents (Laborde, Hosang, Mosley, & Dosseville, 2019). These chronic changes might be due to optimizing the functioning of the mechanisms mentioned above, involving both subcortical and cortical functional changes, such as optimizing the baroreflex and respiratory sinus arrhythmia, as well as the functioning of neural networks involved in emotion regulation. Based on the neurovisceral integration model (Thayer, Hansen, Saus-Rose, & Johnsen, 2009), these chronic functional changes could be responsible for the positive outcomes observed on physiological and mental health. Examples

of this include reduction of blood pressure (Chaddha et al., 2019), improvement of the cardio-respiratory functions in patients with bronchial asthma, reduction of perceived stress, improvement of mood, and a reduction of systemic catecholamine and cortisol levels in both clinical and healthy populations (Jayawardena et al., 2020).

The main assets of this work are the large number of included studies and the provision of an overview independent of selective reporting while considering different HRV parameters. However, several limitations need to be considered. The main limitation is that the majority of studies were coded as having a high risk of bias for various reasons. First, many studies reported only partial HRV parameters without systematically providing a convincing rationale for the choice. Thus, we cannot exclude the possibility that reported HRV parameters have been chosen based on significance levels. Second, blinding for participants is not possible with voluntary slow breathing due to the nature of the intervention, which requires participants to voluntarily follow a breathing pacer. Still, participants could be blinded to hypotheses, for example, by testing two breathing conditions (Zucker, Samuelson, Muench, Greenberg, & Gevirtz, 2009). The blinding of data analysts for the DURING category is often compromised due to the obvious graphical display of voluntary slow breathing compared to control conditions, depicting typical sinusoidal oscillations (Shaffer & Meehan, 2020). Third, for DURING, many studies were included, although HRV was not the main outcome or primary goal of these studies, meaning that the studies were not designed for an investigation of the effects of voluntary slow breathing on HRV. In this case, control and experimental conditions were often not randomized, with the control condition often taking place before the experimental condition.

Many of the studies included in this meta-analysis did not report vmHRV parameters (60% did not report LF_{abs} DURING; 58% did not report RMSSD DURING; 44% did not report RMSSD IM-AFTER1; 45% did not report RMSSD AFTER-INT). For this reason, we

encourage further research to provide a full report of HRV parameters, as recommended for HRV research (Laborde et al., 2017), to allow for a better understanding of the effects of voluntary slow breathing on HRV. Moreover, many studies did not report the randomization process, resulting in a high risk of bias. We recommend researchers be more systematic and precise in reporting procedures, methods, and results in breathing intervention studies.

5 CONCLUSION

To conclude, this meta-analysis shows that voluntary slow breathing leads to an increase in the parasympathetic nervous control of the heart, underlined by an increase in RMSSD in all three time points (DURING, IM-AFTER1, AFTER-INT) and LF_{abs} DURING. By considering the importance of the parasympathetic nervous system for health-related issues, stimulating non-invasively the vagus nerve represents a valid target (Gerritsen & Band, 2018; Schmaußer, Hoffmann, Raab, & Laborde, 2022; Sevoz-Couche & Laborde, 2022; Vanderhasselt & Ottaviani, 2022), and these results encourage the implementation of voluntary slow breathing exercises in health-related contexts, given the low-tech and low-cost techniques they require. Moreover, very few adverse effects are reported throughout the studies (e.g., GRADE 1 lightheadedness), providing further support for their use. However, the large majority of studies included present a high risk of bias, which highlights the need for careful interpretation of findings. This cautious approach should encourage researchers to improve the methodological quality of the studies conducted. In particular, this involves measures such as considering pre-registering studies, being more systematic in reporting HRV variables, specifying methodological details, and improving the randomization and blinding aspects. Through these standards, clearer evidence on the protocols and the outcomes expected can be achieved.

Authors contributions

SL, MA, FD, EM have made substantial contributions to the conception and design of the work; SL handled the project administration; SL and CS performed the study selection and data curation; FJ created the R script; SL, CS, LS, FJ, NZ, MI have accessed and verified the data, and have performed the data analysis; SL, LS, FJ realized the interpretation of the data; LS and FJ created the visualization of the data; SL, LS, and FJ have drafted the first version of the work, and MA, UB, FD, TH, MI, EM, NZ, and CS provided critical feedback and substantively edited the manuscript. All authors agreed on the final form of the draft.

Data sharing

The R script as well as all csv files for the 24 meta-analyses are made publicly available via the Open Science Framework: https://osf.io/jzf2c/.

Funding source

There was no funding source for this work.

Conflicts of Interest

None of the authors has any conflict of interest to report.

6 TABLES AND FIGURES

Table 1. Heart rate variability parameters considered in this systematic review and meta-analysis, as well as their underlying physiological mechanisms (Berntson et al., 1997; Laborde et al., 2017; Malik, 1996)

Time-domain indices	**Physiological mechanism**
Standard deviation of R-R intervals (SDNN, ms)	Total variability (both SNS and PNS cardiac contribution)
Root mean square of the successive differences (RMSSD, ms)	Cardiac vagal activity
Frequency-domain indices	
Low-frequency (LF) absolute power (0.04 - 0.15 Hz, ms^2)	When breathing frequency is higher than 9cpm: Both SNS and PNS contribution to cardiac functioning When breathing frequency is lower than 9cpm: Cardiac vagal activity
High-frequency (HF) absolute power (0.15 to 0.40 Hz, ms^2)	Cardiac vagal activity (when breathing frequency is comprised between 9 and 24 cycles per minute)
LF normalized units (LF absolute power / Total power)	Both SNS and PNS contribution to cardiac functioning
HF normalized units (HF absolute power / Total power)	Both SNS and PNS contribution to cardiac functioning
LF/HF	Both SNS and PNS contribution to cardiac functioning

Note: SNS: Sympathetic nervous system; PNS: Parasympathetic nervous system

Table 2a. PICOS parameters (Methley, Campbell, Chew-Graham, McNally, & Cheraghi-Sohi, 2014)

Population	Healthy people and/or patients
Intervention	Voluntary slow breathing intervention (<10cpm)
Comparison	Control condition with breathing frequency higher than 10cpm
Outcomes	Assessment of HRV (at least one parameter reported)
Study design	Within- and between-subject designs

Table 2b. Data sources and search

Databases	Pubmed, Web of Science, ProQuest, PSYCInfo, SCOPUS, Clinicaltrials.gov (for completed but unpublished registered trials), and the Cochrane Library (from inception to June 30th, 2020)
Boolean operators	"AND" and "OR"
Keywords	Related to 1) Breathing: ("breath*" OR "resp*").

	2) Characteristics of slow-paced breathing (AND ("slow" OR "paced" OR "abdominal" OR "diaphragmatic" OR "controlled" OR "deep")). 3) Heart rate variability (AND ("heart rate variability" OR "HRV" OR "parasympathetic" OR "vagal", OR "coherence" OR "biofeedback" OR "SDNN" OR "RMSSD" OR "HF" OR "high-frequency" OR "LF" OR "low-frequency").
Other	Forward citations and reference lists from papers selected for the full-text step as well as from previous reviews and meta-analyses

Table 3. Summary of selected studies

	Number of studies	**Total number of participants**	**Number of studies reporting each parameter**	**Risk of bias**	**Outliers**
DURING	n = 172	n = 7491	HF_{abs} = 69 HF_{nu} = 18 HR = 121 LF_{abs} = 68 LF/HF = 57 LF_{nu} = 17 RMSSD = 72 SDNN = 61	High Risk, n = 168 (4 unpublished studies, full-text not available) Some Concerns, n = 0 Low Risk, n = 0	HF_{abs} = 2 HF_{nu} = 0 HR = 3 LF_{abs} = 2 LF/HF = 1 LF_{nu} = 0 RMSSD = 1 SDNN = 2
IM-AFTER1	n = 16	n = 835	HF_{abs} = 7 HF_{nu} = 2 HR = 9 LF = 6 LF/HF = 5 LF_{nu} = 0 RMSSD = 8 SDNN = 6	High Risk, n = 13 Some Concerns, n = 3 Low Risk, n = 0	HF_{abs} = 0 HF_{nu} = 0 HR = 1 LF = 0 LF/HF = 0 LF_{nu} = 0 RMSSD = 1 SDNN = 0
AFTER-INT	n = 49	n = 2706	HF_{abs} = 19 HF_{nu} = 5 HR = 22 LF = 19 LF/HF = 18 LF_{nu} = 6 RMSSD = 22 SDNN =26	High Risk, n = 46 Some Concerns, n = 2 Low Risk, n = 1	HF_{abs} = 0 HF_{nu} = 0 HR = 1 LF = 1 LF/HF = 2 LF_{nu} = 0 RMSSD = 0 SDNN = 0

Note: SDNN = Standard deviation of R-R intervals; RMSSD = Root mean square of the successive differences; LF = low-frequency; HF = high-frequency: abs = absolute power; nu = normalized units

Figure 1. PRISMA flow chart

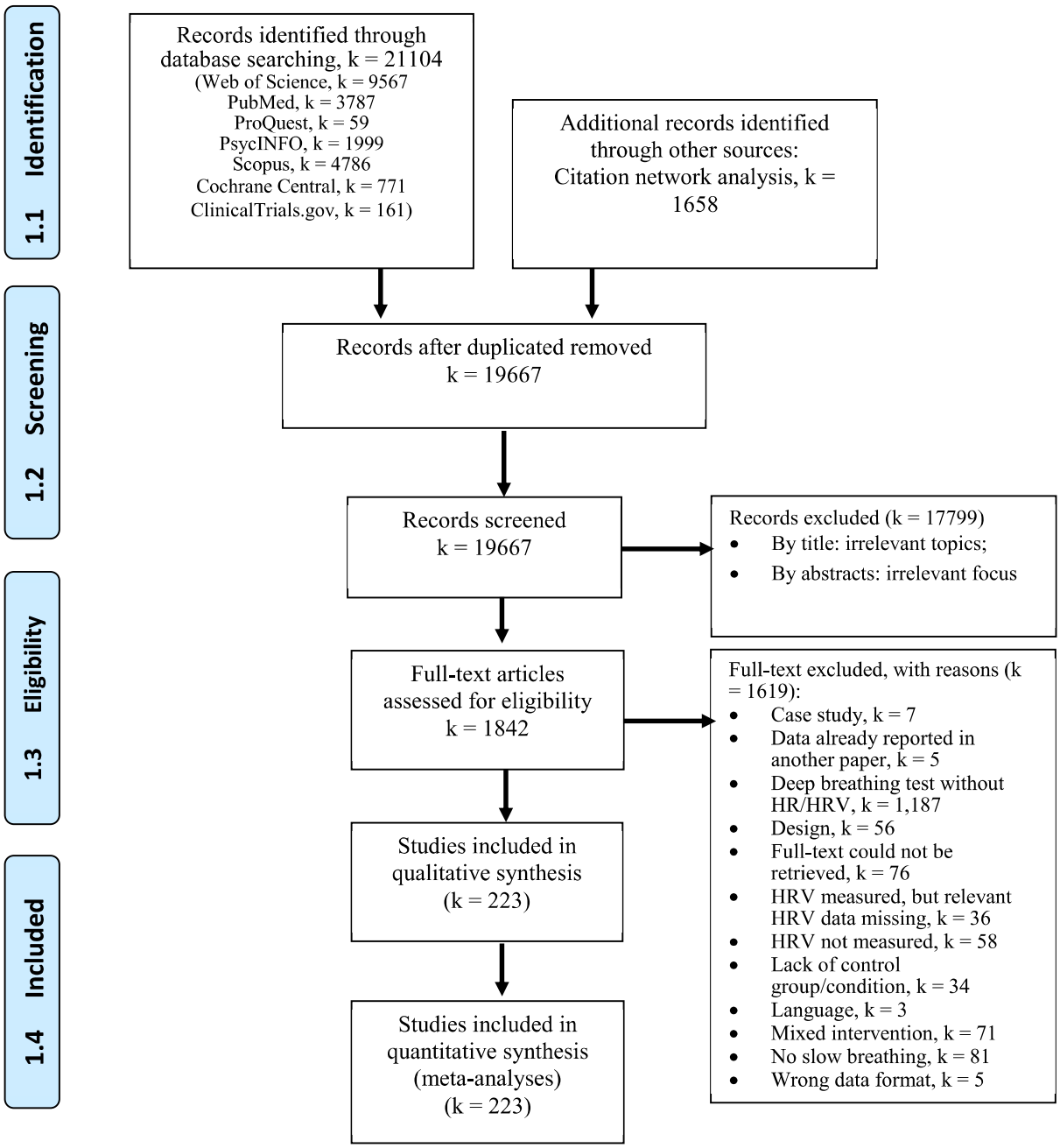
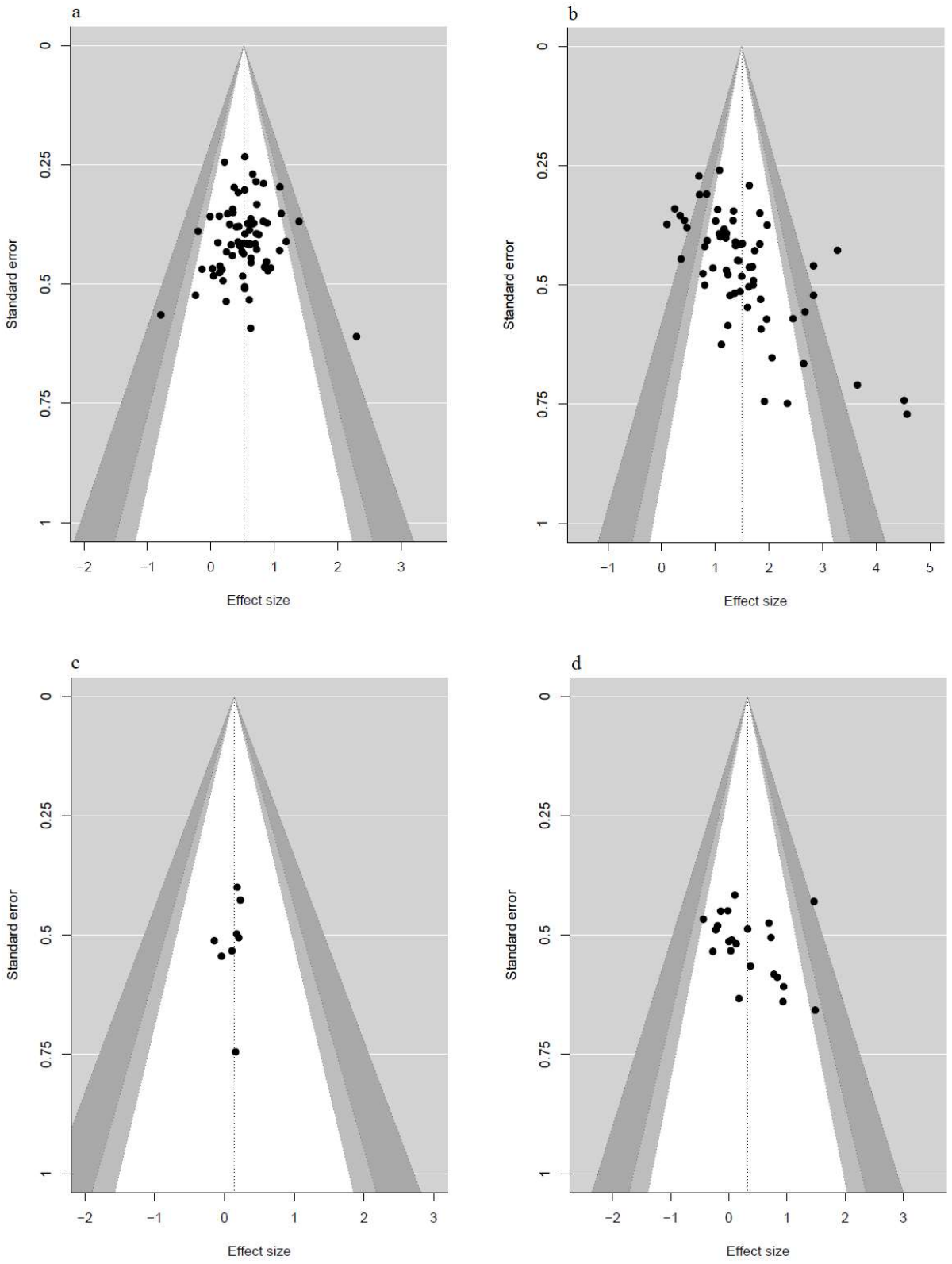


Figure 2. Funnel plots of RMSSD (a) and LF (b) for DURING, RMSSD for IM-AFTER1 (c) and RMSSD for AFTER-INT (d)



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