Supplementary material

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Table 1 PRISMA Guideline for Systematic Review and Meta-analysis

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	4
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.	4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4, appendix
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.	4, 5
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.	4, 5
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.	4-6
	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.	4-6
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.	5
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.	5-6
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)).	4-6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	5-6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	5-6
	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.	5-6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	5
RESULTS			

Section and Topic	Item #	Checklist item	Location where item is reported
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.	7, appendix
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	7
Study characteristics	17	Cite each included study and present its characteristics.	7, appendix
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	7-9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	7-9
	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.	7-9
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	7-9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10-11
	23b	Discuss any limitations of the evidence included in the review.	11
	23c	Discuss any limitations of the review processes used.	11
	23d	Discuss implications of the results for practice, policy, and future research.	12
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.	4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13
Competing interests	26	Declare any competing interests of review authors.	13
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.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Table 2. Search Strategy

Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to July 17, 2023

Search Strategy:

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1 exp Gastroesophageal Reflux/ or exp Esophagitis/ or exp Barrett esophagus/ or exp Heartburn/ or exp Hernia, Hiatal/ (50841)
2 (GERD or GORD or "gastro?esophageal reflux disease" or "gastro-?esophageal reflux disease" or GER or GOR or "gastro?esophageal reflux" or "gastro-?esophageal reflux" or ?esophagitis or "Barrett* ?esophagus" or reflux* or heartburn or "hiat* hernia*").mp. (98196)
3 1 or 2 (100230)
4 exp Supine Position/ (6609)
5 ("sleep* position*" or "left lateral recumben*" or "left lateral decubitus" or supine or "right lateral recumben*" or "right lateral decubitus").mp. (35217)
6 4 or 5 (35217)
7 3 and 6 (**866**)

Embase 1974 to July 17, 2023

Search Strategy:

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1 exp gastroesophageal reflux/ or exp esophagitis/ or exp Barrett esophagus/ or exp heartburn/ or exp hiatus hernia/ (126759)
2 (GERD or GORD or "gastro?esophageal reflux disease" or "gastro-?esophageal reflux disease" or GER or GOR or "gastro?esophageal reflux" or "gastro-?esophageal reflux" or ?esophagitis or "Barrett* ?esophagus" or reflux* or heartburn or "hiat* hernia*").mp. (185254)
3 1 or 2 (186709)
4 exp supine position/ (27670)
5 ("sleep* position*" or "left lateral recumben*" or "left lateral decubitus" or supine or "right lateral recumben*" or "right lateral decubitus").mp. (59594)
6 4 or 5 (59594)
7 3 and 6 (**1782**)

CENTRAL - The Cochrane Library (Until July 17, 2023)

ID	Search	Hits
#1	MeSH descriptor: [Gastroesophageal Reflux] explode all trees	2566
#2	MeSH descriptor: [Esophagitis] explode all trees	1136
#3	MeSH descriptor: [Barrett Esophagus] explode all trees	370
#4	MeSH descriptor: [Heartburn] explode all trees	612
#5	MeSH descriptor: [Hernia, Hiatal] explode all trees	116
#6	(GERD or GORD or "gastroesophageal reflux disease" or "gastrooesophageal reflux disease" or "gastro-esophageal reflux disease" or "gastro-oesophageal reflux disease"):ti,ab,kw	3217
#7	(GER or GOR or "gastroesophageal reflux" or "gastrooesophageal reflux" or "gastro-esophageal reflux" or "gastro-oesophageal reflux"):ti,ab,kw	5439
#8	((Barrett* NEXT ?esophagus) or reflux* or heartburn or (hiat* NEXT hernia*) or ?esophagitis):ti,ab,kw	11882
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	12367
#10	MeSH descriptor: [Supine Position] explode all trees	979
#11	((sleep* NEXT position*) or (left NEXT lateral NEXT recumben*) or "left lateral decubitus" or supine or (right NEXT lateral NEXT recumben*) or "right lateral decubitus"):ti,ab,kw	10630
#12	#10 or #11	10630
#13	#9 and #12	**167**

Table 3. Study Characteristics – Methodology and Outcome

Study Identifier	Inclusion Criteria of Subjects	Exclusion Criteria of Subjects	Methods of Determining Sleep Position	Outcome Data
Khoury (1999)	10 patients (3 female, 7 male), with mean age of 47.6 years (range 30–67 years) with GERD. Patients were instructed to stop prokinetic agents and all acid suppressive drugs (PPI ≥5 days before; H2RA and anatacids 2 days before study period) and to have a normal nighttime sleep from 11PM to 7 AM in their own bed using only 1 soft pillow. **GERD definition** Distal esophageal recumbent time pH <4 for ≥3% of the time (median 8.2, IQR 5.7–17.5) on previous prolonged pH-metry with a	Patients with sleep disorders, need for sleep medications, or inability to maintain a recumbent position for the entire nighttime were excluded. Acid suppression therapy was not permitted.	Spontaneous sleep posture changes were assessed using a body position sensor taped to the patient's mid-sternum. The position sensor is a mercury switch which records four major sleeping positions: (1) supine, (2) prone, (3) RLD, and (4) LLD. To be recorded, patients must remain in a position for ≥20 seconds. Time spent in between positions or moving is recorded as an artifact.	**Duration of sleep position (%), median (IQR)**: LLD 20 (13-30) vs supine 42 (32-61) vs prone 3 (0-12) vs RLD 35 (22-38). **Acid exposure time (%), median (IQR)**: LLD 0.9 (0-4.5) vs supine 10.6 (5.1-12.5) vs prone 1.4 (0-4.5) vs RLD 18.1 (7.4-44.4) ($p<0.003$). **Acid clearance time, in min/episode, median (IQR)**: LLD 0.4 (0.3-0.7) vs supine 1.8 (1.1-3.5) vs prone 1.6 (range 0.5-14.0) vs RLD 3.1 (2.1-6.6) ($p<0.05$). **Position change reflux event (%)**: LLD 60% vs supine 90% vs prone 50% vs RLD 100% ($p>0.05$). **Number of reflux episodes, per hour, median (IQR)**: LLD 1.2 (0-3.0) vs supine 2.1 (1.6-3.0) vs prone 0 (0-0.27) vs RLD 1.5 (0.9-2.4) ($p<0.04$).

	semidisposable, single channel, antimony pH electrode (Synetics Medical)			
Schuitenmaker (2021)	Adult patients with indication for ambulatory pH-impedance monitoring for reflux evaluation and had an esophageal acid exposure ≥0.5% or higher when in a supine position (nocturnal acid reflux) were included in the study	Patients with a history of esophageal/gastric surgery or esophageal disorders (achalasia and esophageal atresia) were excluded.	Sleep positions were monitored using a sleep position measurement and training device (Side Sleep Technologies B.V., Amsterdam, the Netherlands) in measurement-only mode. The device registers sleep position of patient at 10-second intervals and categorizes into supine (“back”), right, left, prone (“belly”), and upright. The device was placed in mid-sternal with an adhesive sticker and turned on when going to bed. All patients were asked questions about sleep position preference and reflux complaints.	**Duration of sleep position (%), median (IQR)**: LLD 31 (15-48) vs supine 26 (10-48) vs prone 0.4 (0-4) vs upright 1 (0.4-3) vs RLD 27 (14-41). **Acid exposure time (%), median (IQR):** LLD 0.0 (0.0-3.0) vs supine 0.6 (0.0-8.3) vs RLD 1.2 (0.0-7.5) (p=0.022). - Difference was observed in the presence of hiatus hernia (≥2cm), hypotensive LES mean-integrated relaxation pressure over 4 seconds (IRP-4≤5), or reflux esophagitis **Acid clearance time, in sec/episode, median (IQR):** LLD 35 (16-115) vs supine 76 (22-257) vs RLD 90 (26-250) (p=0.007). - Difference more pronounced in ineffective esophageal motility **Total number of reflux episodes per sleep position:** LLD 80 vs supine 102 vs prone 13 vs upright 17 vs RLD 109 (p=0.152).
Schuitenmaker (2022)	Patients with nocturnal symptoms of heartburn and/or acid regurgitation at	Patients with a history of obstructive sleep apnea, esophageal and/or	The electronic position therapy wearable device is a small (40 mm x 40 mm x 7 mm), lightweight (3 g),	**Baseline sleep position (%), intervention vs sham, mean±SD:** LLD 33.2±16.7 vs 31.9±12.0 vs supine 28.1±17.9 vs 29.5±15.6 vs RLD

	least 3 times a week and a total GerdQ score of 8 or higher were included in the study	gastric surgery, or severe and clinically unstable concomitant disease were excluded. Patients with atypical reflux symptoms, predominantly dyspeptic symptoms, PPI nonresponders (if applicable), nightshift workers, and patients who regularly use sleep medication were also excluded.	wearable device with a 3-axis accelerometer (Side Sleep Technologies B.V., Amsterdam, the Netherlands). The device registers the sleep position of a subject at 30-second intervals. It categorizes sleep position as 1 of 5 categories: supine (back), right, left, prone (belly), and upright. The electronic positional therapy–wearable device can be programmed with different vibration modes. Patients were instructed to use the device midsternally with an adhesive sticker and activate when going to bed. - **For baseline measurement**: Device programmed not to vibrate at all and only registers a person's sleeping position - **Intervention group**: The device was programmed to gently vibrate only when the body is in the right lateral decubitus position, with the intention of stimulating the subject to roll over to the left lateral decubitus position. - **Sham group**: The same vibration mode was set, with the restriction that the device only vibrates in the right lateral decubitus during the first 20 minutes of the night.	31.3±13.2 vs 30.6±13.5 **Post-treatment with device (%), intervention vs sham, mean±SD:** LLD 60.9±16.4 vs 38.5±14.3 (p=0.000) vs supine 30.7±16.2 vs 30.2±17.8 (p=0.91) vs RLD 2.2±2.9 vs 23.5±12.3 (p=0.000) **<u>14 days after treatment</u>** Rate of treatment success (≥50% reduction in the N-GSSIQ score) (%), invervention vs sham: 44 vs 24, RD of 20 (95%CI 1.8-38.2, p=0.03) Reflux-free nights, intervention vs sham, median (IQR): 9 (6-11) vs 6 (3-9) (p=0.007) Total number of reflux symptoms, intervention vs sham, median (IQR): 7 (5-13) vs 11 (6-18) (p=0.052) Total N-GSSIQ score after 2 weeks of treatment, intervention vs sham, mean±SD: 18.8±11.6 vs 23.7±11.3 (p=0.04) - Nocturnal GERD symptoms, intervention vs sham, median (IQR): 8.0 (4.5-12.0) vs 12.0 (7.0-16.0) (p=0.01) - Morning Impact of nocturnal GERD, intervention vs sham, median (IQR): 3.0 (1.0-4.5) vs 3.0 (1.0-5.0) (p=0.55) - Concern about nocturnal GERD, intervention vs sham, median (IQR): 5.0 (2.5-10.5) vs 7.0 (5.0-11.0) (p=0.14)

				RDQ questionnaire, intervention vs sham, median (IQR): 0.6 (0.4-1.9) vs 1.1 (0.8-1.8) (p=0.01) Patient-reported treatment success of noctural reflux complaints (%), intervention vs sham: 39 vs 15 (p=0.008) Global score of the PSQI questionnaire, intervention vs sham, median (IQR): 7 (4.5-9.0) vs 7.5 (5.0-9.3) (p=0.46) WPAI-GERD-sleep, intervention vs sham, median (IQR): - Missed work due to GERD-Sleep disturbance: 0 (0-0) vs 0 (0-0) (p=0.98) - Reduced work productivity:10 (0-30) vs 10 (0-30) (p=0.92) - Reduced daily productivity: 20 (0-30) vs 10 (10-30) (p=0.79)

Notes

GERD: Gastroesophageal Reflux Disease; **GerdQ**: GERD Questionnaire; **H2RA**: Histamine-2 Receptor Antagonist; **IQR**: Interquartile Range; **LLD**: Left Lateral Decubitus; **N-GSSIQ**: Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire; **PPI**: Proton Pump Inhibitor; **PSQI**: Pittsburgh Sleep Quality Index; **RDQ**: Reflux Disease Questionnaire; **RLD**: Right Lateral Decubitus

Table 4. Newcastle-Ottawa Quality Assessment Scale (NOS) for Cross-Sectional Studies

Study Identifier	Newcastle-Ottawa Quality Assessment Scale								Overall NOS Score
	Selection				Comparability (Controls for)		Outcome		
	Representativeness of Sample	Sample Size	Non-respondents	Ascertainment of exposure	Age	BMI	Assessment of Outcome	Statistical analysis	
Khoury (1999)	0	0	1	2	0	0	2	1	**6**
Schuitenmaker (2021)	1	0	1	2	1	1	2	1	**9**

Table 5. Cochrane's Risk of Bias 2 (RoB2) Tool for Assessment of Randomized Controlled Trial

Study Identifier	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk of Bias
Schuitenmaker (2022)	Low	Low	Low	Low	Low	**Low**