SUPPLEMENTARY MATERIAL

A systematic review and meta-analysis of cold exposure and cardiovascular health outcomes

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Short title: Meta-analysis of cold exposure and cardiovascular diseases

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Table S1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist[1].

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.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6
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.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	S2
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.	6
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.	7
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.	7
	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.	7
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.	8
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.	7
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)).	7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	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.	8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	8, S6-9
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	8, S9

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
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.	8-9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	9
Study characteristics	17	Cite each included study and present its characteristics.	S4-5
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	12,S16
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.	9,S10-13
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	9,11
	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.	9-11,S15-16
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	11,S15-16
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	11,S14-15
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	S18-22
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	12,17
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	13-14
	23b	Discuss any limitations of the evidence included in the review.	17
	23c	Discuss any limitations of the review processes used.	17
	23d	Discuss implications of the results for practice, policy, and future research.	17
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.	6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	6
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	18
Competing interests	26	Declare any competing interests of review authors.	18
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.	6

Table S2: Search strategy: databases, terms, filters and number of articles for review.

Database	Strategy	Number of hits	Number imported into Endnote
PubMed	#1 weather [MH] OR climate change [MH] OR temperature [TW] OR season [TW] OR cold temperature [TW] OR cold season [TW] OR cold spell [TW] OR cold weather	228,591	

Filters: **English, Human,** **Full text**	[TW] #2 cardiovascular diseases [MH] OR heart diseases [TW] OR vascular diseases [TW] OR hypertensive disease [TW] OR myocardial infarction [TW] OR stroke [TW] OR heart failure [TW] OR arrhythmia [TW] OR cardiac arrest [TW] OR rheumatic heart disease [TW] OR thrombosis [TW] OR thrombotic disease [TW] OR pulmonary heart disease [TW] OR peripheral artery disease [TW] OR aortic aneurysm [TW] OR aortic dissection [TW] #3 epidemiology [MH] OR mortality [TW] OR morbidity [TW] OR incidence [TW] OR prevalence [TW] OR outbreak [TW] OR surveillance [TW] OR occurrence [TW] OR hospital [TW] OR death [TW] #1 AND #2 AND #3	 2,915,117 2,963,121	 9,675
Cochrane **Filters:** **In trails**	#1 ("climate change"):ti,ab,kw OR (temperature):ti,ab,kw OR (season):ti,ab,kw OR ("cold spell"):ti,ab,kw OR ("cold weather"):ti,ab,kw (Word variations have been searched)	35,192	
	#2 MeSH descriptor: [Weather] explode all trees	6,125	
	#3("heart diseases"):ti,ab,kw OR ("vascular diseases"):ti,ab,kw OR ("hypertensive disease"):ti,ab,kw OR ("myocardial infarction"):ti,ab,kw OR (stroke):ti,ab,kw	110,237	
	#4 ("heart failure"):ti,ab,kw OR (arrhythmia):ti,ab,kw OR ("cardiac arrest"):ti,ab,kw	46,428	
	#5("rheumatic heart disease"):ti,ab,kw OR ("thrombotic disease"):ti,ab,kw OR ("pulmonary heart disease"):ti,ab,kw OR ("aortic aneurysm and dissection"):ti,ab,kw OR ("peripheral artery disease"):ti,ab,kw	15,977	
	#6 MeSH descriptor: [Cardiovascular Diseases] explode all trees	118,039	
	#7 (mortality):ti,ab,kw OR (morbidity):ti,ab,kw OR (incidence):ti,ab,kw AND (prevalence):ti,ab,kw AND (outbreak):ti,ab,kw	128,815	
	#8 (surveillance):ti,ab,kw OR (occurrence):ti,ab,kw OR (hospital):ti,ab,kw AND (death):ti,ab,kw	60,131	
	#9 MeSH descriptor: [Epidemiology] explode all trees	42	
	#10 #1 OR #2	36559	
	#11 #3 OR #4 OR #5 OR #6	445,827	
	#12 #7 OR #8 OR #9	171,706	
	#13 #10 AND #11 AND#12		1,733
Scopus **Filters:** **English,** **Article,**	#1 (ALL ("climate change") OR TITLE-ABS-KEY (weather) OR TITLE-ABS-KEY ("low temperature") OR TITLE-ABS-KEY (season) OR TITLE-ABS-KEY ("cold temperature") OR TITLE-ABS-KEY ("cold spell") OR TITLE-ABS-KEY ("cold weather") OR TITLE-ABS-KEY ("cold season")) #2 (ALL ("cardiovascular diseases ") OR TITLE-ABS-KEY ("hypertensive disease") OR TITLE-ABS-KEY ("heart diseases") OR TITLE-ABS-KEY ("vascular diseases") OR TITLE-ABS-KEY (stroke) OR TITLE-ABS-KEY ("myocardial infarction") OR TITLE-ABS-KEY ("heart failure") OR TITLE-ABS-KEY (arrhythmia) OR	2,374,448 3,016,495	

	TITLE-ABS-KEY ("cardiac arrest") OR TITLE-ABS-KEY (“rheumatic heart disease”) OR TITLE-ABS-KEY (“thrombotic disease”) OR TITLE-ABS-KEY (thrombosis) OR TITLE-ABS-KEY (“pulmonary heart disease") OR TITLE-ABS-KEY ("aortic aneurysm”) OR TITLE-ABS-KEY ("aortic dissection”) OR TITLE-ABS-KEY (“peripheral artery disease”)) #3 (ALL (epidemiology) OR TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (morbidity) OR TITLE-ABS-KEY (prevalence) OR TITLE-ABS-KEY (incidence) OR TITLE-ABS-KEY ("hospital admission") OR TITLE-ABS-KEY (occurrence)) #1 AND #2 AND #3	7,885,815	10,316
Total results			21,724

All the included articles[2-160].

Table S3: Rating tool of risk of bias assessment of included study, modified according to the OHAT[161,162].

	Risk of Bias Questions	**Answer**
Key Criteria		
Exposure assessment	Includes measurement error or measurement limitations. List of major considerations: 1) more than one monitoring station per a large geographical area 2) daily ambient temperature measurements were available	-LOW: There is high confidence that the exposure to ambient temperature is the true average population exposure (e.g. using gridded temperature data-interpolated or population weighted temperature). -PROBABLY LOW: There is indirect evidence that suggests low risk of bias, or one of the three listed considerations is not applied (e.g. averaged temperatures from several weather stations). -PROBABLY HIGH: There is insufficient information to permit a judgment of high risk of bias, but there is indirect evidence that suggests high risk of bias. Additionally, two out of the three listed considerations are not applied (e.g. use of single weather station). -HIGH: There is direct evidence of high risk of misclassification bias, or all three of the listed considerations are not applied.
Outcome assessment	Includes blinding, systematic errors, or not comparable outcome measurement across exposure groups. List of major considerations: 1) outcome measurements were not influenced by knowledge of the exposure (data were obtained from different databases) 2) validity of disease classification methods (ICD coding)	-LOW: mortality and morbidity cause classified based on diagnosis standard criteria (International Classification System – ICD code) and provided by a National or Regional Database. -PROBABLY LOW: outcome was assessed based on diagnosis standard criteria (ICD) and collected by researcher, but did not specify the data source. -PROBABLY HIGH: outcome was not assessed based on standard diagnosis criteria. Additionally, there is evidence that suggests the existence of misclassification bias. -HIGH: Outcome was assessed based on self-reports (parents, family) and data

		collected by the researcher. Additionally, there is evidence that suggests the high risk of misclassification bias.
Confounding bias	List of major considerations: 1) study appropriately accounted for all important well studied potential confounders (seasonality, time trends, day of week, relative humidity).4 2) did the authors use an appropriate analysis method or study design that controlled for confounding domains?	-LOW: study accounted for all important confounders which were measured consistently. -PROBABLY LOW: study accounted for most of confounders AND is not expected to introduce bias. -PROBABLY HIGH: study accounted for some but not all confounders AND is expected to introduce bias -HIGH: study did not account for potential confounders OR were inappropriately measured
Other Criteria		
Selection/recruitment bias	List of major considerations: 1) does the selection of participants into the study was done in a manner that might introduce bias in the study? (e.g. study only certain days, and not all days, seasons were included)	-LOW: The descriptions of the studied population were sufficiently detailed to support the assertion that risk of selection effects was minimal (e.g., all relevant mortality and morbidity outcomes in the study setting were reported and included in the study, participants in all exposure levels and with all outcomes had equal opportunity to be included in the study). -PROBABLY LOW: There is insufficient information about population selection to permit a judgment of low risk of bias, but there is indirect evidence that suggests low risk of bias (e.g., participants in all exposure levels may not have equal opportunity to be in the study). -PROBABLY HIGH: There is insufficient information about population selection to permit a judgment of high risk of bias, but there is indirect evidence that suggests high risk of bias (e.g., participants in all exposure levels did not have equal opportunity to be in the study; but not to the extent that seriously bias the effect estimates). - HIGH: There were indications from descriptions of the studied population of high risk of bias (study only included designated high-risk participants, and participants in all exposure levels did not have equal opportunity to be in the study, to the extent that effect estimates were seriously biased).
Incomplete outcome data	List of major considerations: 1) missing data of outcome measures? 2) missing data of exposures?	-LOW: no missing outcome data or missing data are unrelated to true outcome. -PROBABLY LOW: there was insufficient information about incomplete data to judge for low risk, but indirect evidence that suggests low risk of bias (e.g., <10% missing data, or missing data related to outcome or exposure data imputed using appropriate method).

		-PROBABLY HIGH: there was insufficient information about incomplete data to judge for high risk, but indirect evidence that suggests high risk bias (e.g., ≥10% missing data without imputed using appropriate method, while rational for attrition explained in the manuscript with possible methods have been used to properly account for it). -HIGH: missing outcome data are related to true outcome (e.g., substantial missing exposure data (≥10%), rationale for missing data not explained in the manuscript).
Selective reporting	List of major considerations: 1) do the authors report a prior primary and secondary study aims? 2) study reports data analysis over a complete or original database, with no selective reporting of outcomes or analysis	-LOW: all of the studies pre-specified outcomes and findings are reported (i.e., effect estimates presented for all hypothesis tested as per aims) -PROBABLY LOW: there was insufficient information about selective outcome to judge for low risk, but indirect evidence that suggests study was free of selective report (i.e., effect estimates presented for less than all hypotheses tested as per aims; but evidence suggests that effect estimates unlikely to be seriously biased). -PROBABLY HIGH: there was insufficient information about selective reporting to judge for high risk, but indirect evidence suggests that study was not free of selective reporting -HIGH: not all pre-specified outcomes and findings were reported (i.e., effect estimates presented for less than all hypotheses tested as per aims, and with direct evidence suggest that effect estimates likely to be seriously biased)
Conflict of interest	Potential source of bias in reporting through source of funding	-LOW: the study did not receive funding from an entity with financial interest in the outcome of study (e.g. funding source is limited to government or academic grants, authors make a claim denying conflicts of interest) -PROBABLY LOW: there is insufficient information to judge for low risk, but indirect evidence suggests study was free of financial interest -PROBABLY HIGH: there is insufficient information to judge for high risk, but indirect evidence suggests study was not free of financial interest -HIGH: study received support from an entity with financial interest in the outcome of study (e.g., authors/staff from study was employee or otherwise affiliated with an entity with financial interest in the study outcome, authors claim a conflict of interest)
Other sources of bias	Bias due to other problems not covered elsewhere	-LOW: No other sources of bias -PROBABLY LOW: there is insufficient information to judge for low risk, but indirect evidence suggests study was free of other problems

		-PROBABLY HIGH: there is insufficient information to judge for high risk, but indirect evidence suggests study was not free of other problems -HIGH: at least one important risk of bias (e.g., selective reporting of subgroups, a potential source of bias related to the specific study design used, study has been claimed to have been fraudulent)

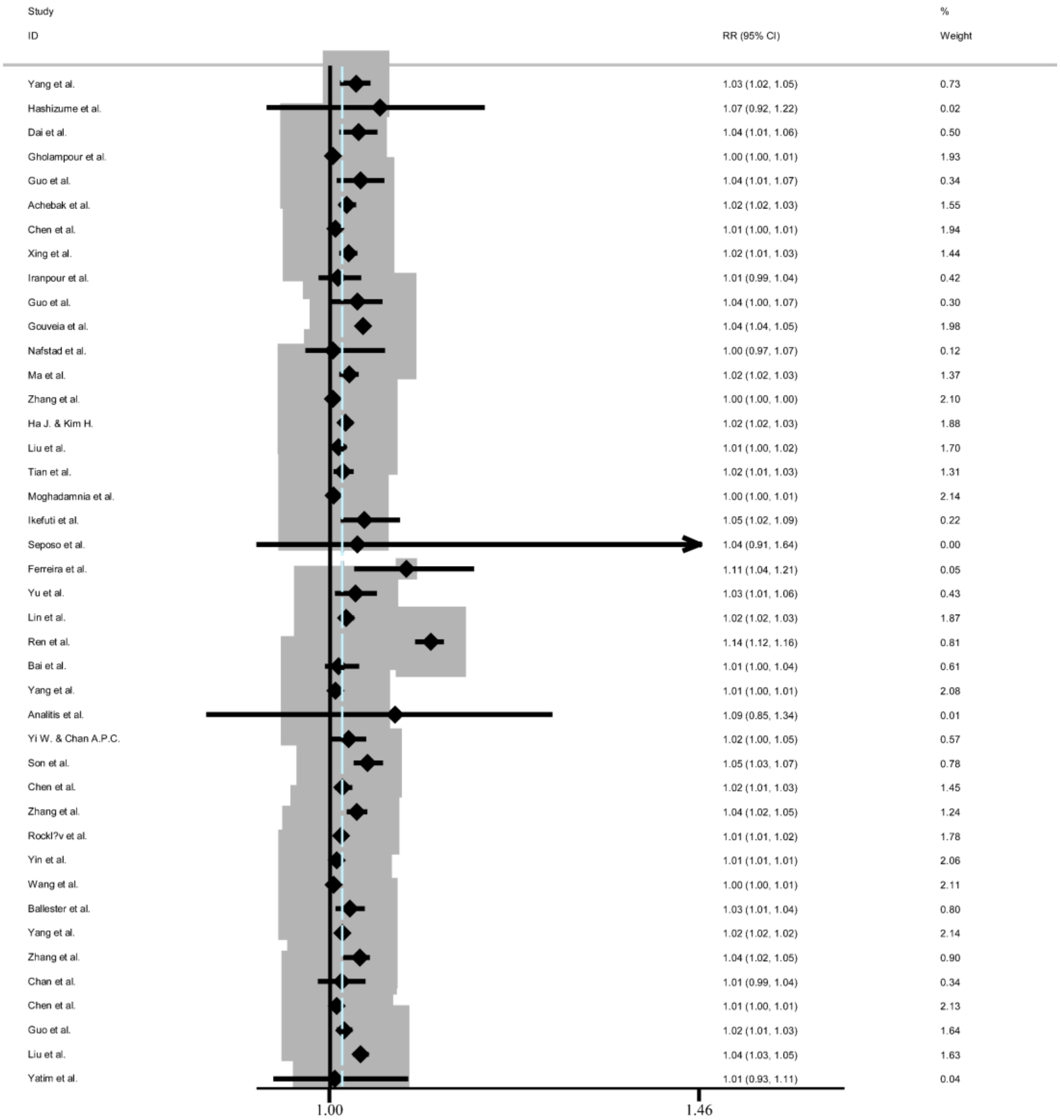
Table S4: Judgement of overall risk of bias rating.

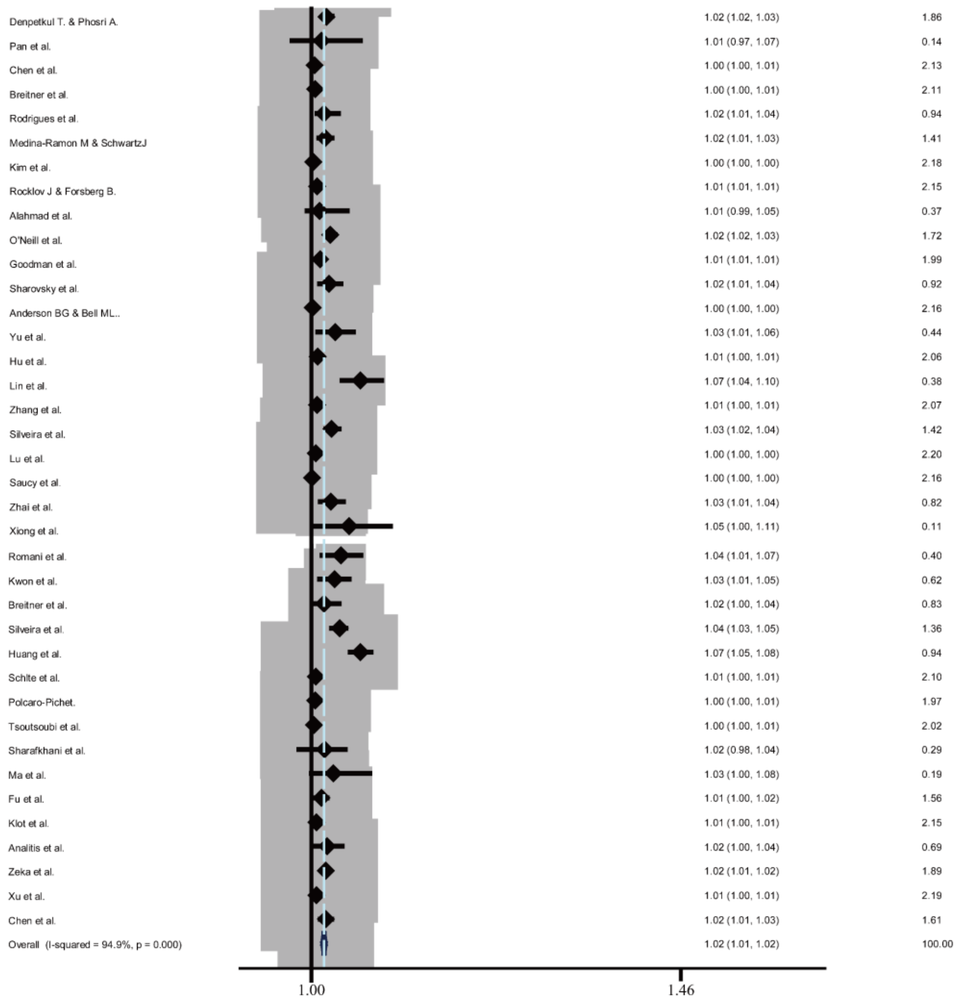
Overall Rating	**Combinations (three key components of exposure assessment, outcome assessment, and confounding bias)**
High (H)	High + High + (High / Probably high / Probably low / Low) High + Probably high + Probably high
Probably high (PH)	High + Probably high + (Probably low / Low) Probably high + Probably high + (Probably high / Probably low / Low)
Probably low (PL)	Probably high + (Probably low / Low) + (Probably low / Low) Probably low + Probably low + Low
Low (L)	Probably low + Low + Low Low + Low + Low

Table S5: Rating tool of evaluation of quality and strength of the body of evidence. According to Johnson et al[163].

Evaluation factors	**Summary of criteria**
Downgrading factors	
Risk of bias	Study limitations include a substantial risk of bias across the body of evidence. Risk of bias was assessed by sensitivity analyses, excluding studies rated "high" and/or "probably high" risk of bias. The quality of body of evidence was downgraded if there was substantial difference between values of sensitivity analysis.
Indirectness	Evidence was not directly comparable to the primary objective of interest i.e., participants, exposure, comparisons, outcome (PECO).
Inconsistency	Estimates of effect in similar populations were widely different (significantly high heterogeneity *I 2* or variability in results). In addition, the evidence was downgraded if the 80% precision interval included unity and was more than twice the random effects meta-analysis confidence interval.
Imprecision	Studies included few participants and small sample sizes (wide confidence interval as judged by reviewers).
Publication bias	Studies were missing from body of evidence, resulting in an over- or underestimate of true effects from exposure. The evidence of publication bias was inspected visually in the funnel plots and egger's test. The *Trim and Fill* procedure was used to estimate potentially missing studies.
Upgrading factors	
Large magnitude of effect	The rating was upgraded if modeling suggested that confounding alone was unlikely to explain associations that were judged to be of large magnitude.
Dose response	Upgraded if consistent relationship between dose and response in one or multiple studies, and/or the dose response across studies.
Confounding minimizes effect	Upgraded if the consideration of all plausible residual confounders or biases would underestimate the effect or suggest a spurious effect when results show no effect.

Figure S1: Forest plot of each study investigating the association between low temperature and cardiovascular disease mortality, with every 1°C decrease in temperature.





Denpetkul T. & Phosri A. 1.02 (1.02, 1.03) 1.86
Pan et al. 1.01 (0.97, 1.07) 0.14
Chen et al. 1.00 (1.00, 1.01) 2.13
Breitner et al. 1.00 (1.00, 1.01) 2.11
Rodrigues et al. 1.02 (1.01, 1.04) 0.94
Medina-Ramon M & SchwartzJ 1.02 (1.01, 1.03) 1.41
Kim et al. 1.00 (1.00, 1.00) 2.18
Rocklov J & Forsberg B. 1.01 (1.01, 1.01) 2.15
Alahmad et al. 1.01 (0.99, 1.05) 0.37
O'Neill et al. 1.02 (1.02, 1.03) 1.72
Goodman et al. 1.01 (1.01, 1.01) 1.99
Sharovsky et al. 1.02 (1.01, 1.04) 0.92
Anderson BG & Bell ML.. 1.00 (1.00, 1.00) 2.16
Yu et al. 1.03 (1.01, 1.06) 0.44
Hu et al. 1.01 (1.00, 1.01) 2.06
Lin et al. 1.07 (1.04, 1.10) 0.38
Zhang et al. 1.01 (1.00, 1.01) 2.07
Silveira et al. 1.03 (1.02, 1.04) 1.42
Lu et al. 1.00 (1.00, 1.00) 2.20
Saucy et al. 1.00 (1.00, 1.00) 2.16
Zhai et al. 1.03 (1.01, 1.04) 0.82
Xiong et al. 1.05 (1.00, 1.11) 0.11
Romani et al. 1.04 (1.01, 1.07) 0.40
Kwon et al. 1.03 (1.01, 1.05) 0.62
Breitner et al. 1.02 (1.00, 1.04) 0.83
Silveira et al. 1.04 (1.03, 1.05) 1.36
Huang et al. 1.07 (1.05, 1.08) 0.94
Schite et al. 1.01 (1.00, 1.01) 2.10
Polcaro-Pichet. 1.00 (1.00, 1.01) 1.97
Tsoutsoubi et al. 1.00 (1.00, 1.01) 2.02
Sharafkhani et al. 1.02 (0.98, 1.04) 0.29
Ma et al. 1.03 (1.00, 1.08) 0.19
Fu et al. 1.01 (1.00, 1.02) 1.56
Klot et al. 1.01 (1.00, 1.01) 2.15
Analitis et al. 1.02 (1.00, 1.04) 0.69
Zeka et al. 1.02 (1.01, 1.02) 1.89
Xu et al. 1.01 (1.00, 1.01) 2.19
Chen et al. 1.02 (1.01, 1.03) 1.61
Overall (I-squared = 94.9%, p = 0.000) 1.02 (1.01, 1.02) 100.00
1.00
1.46

Figure S2: Forest plot of each study investigating the association between low temperature and cardiovascular disease morbidity, with every 1°C decrease in temperature.

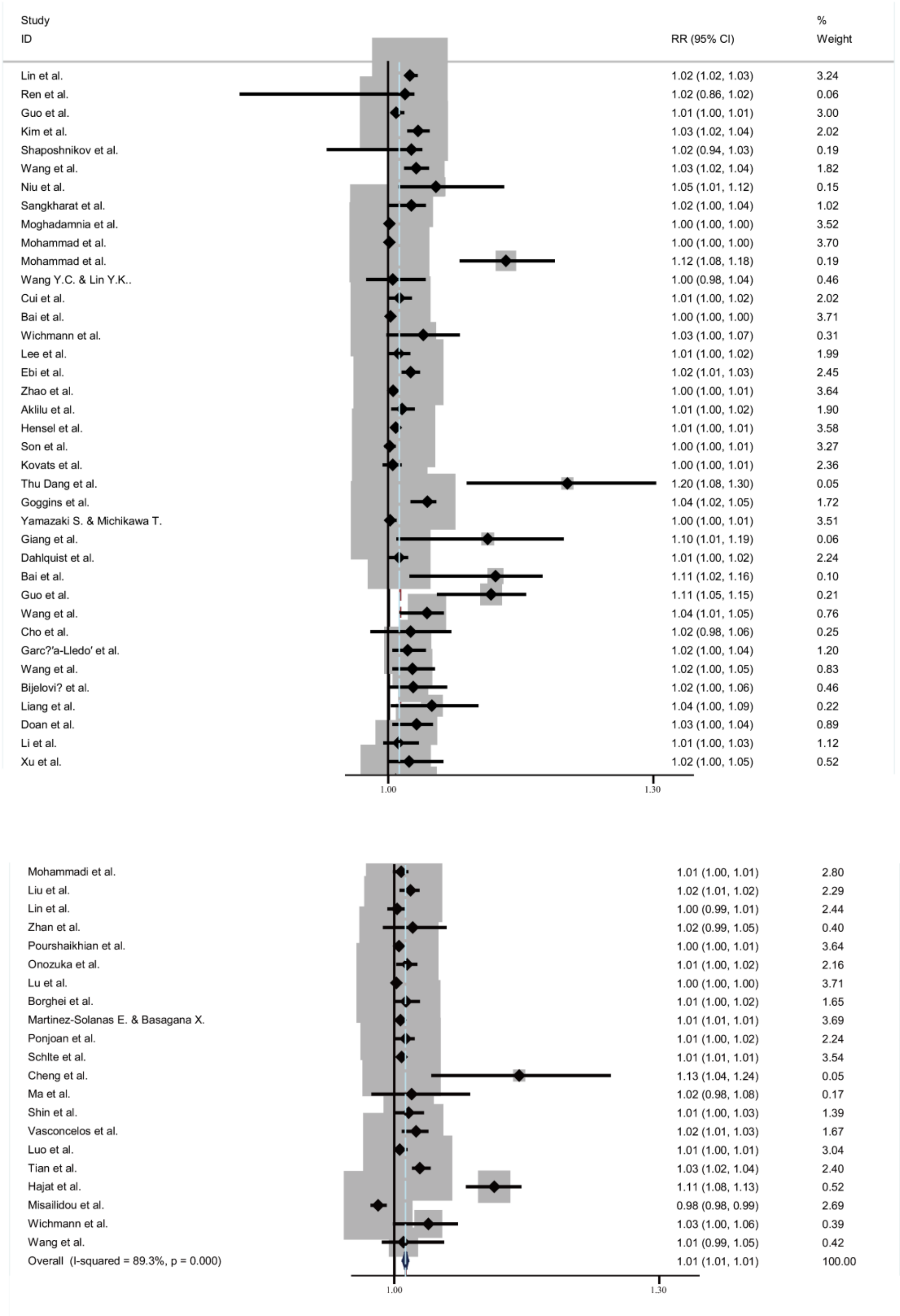


Figure S3: Forest plot of each study investigating the association between cold spells and cardiovascular disease mortality.

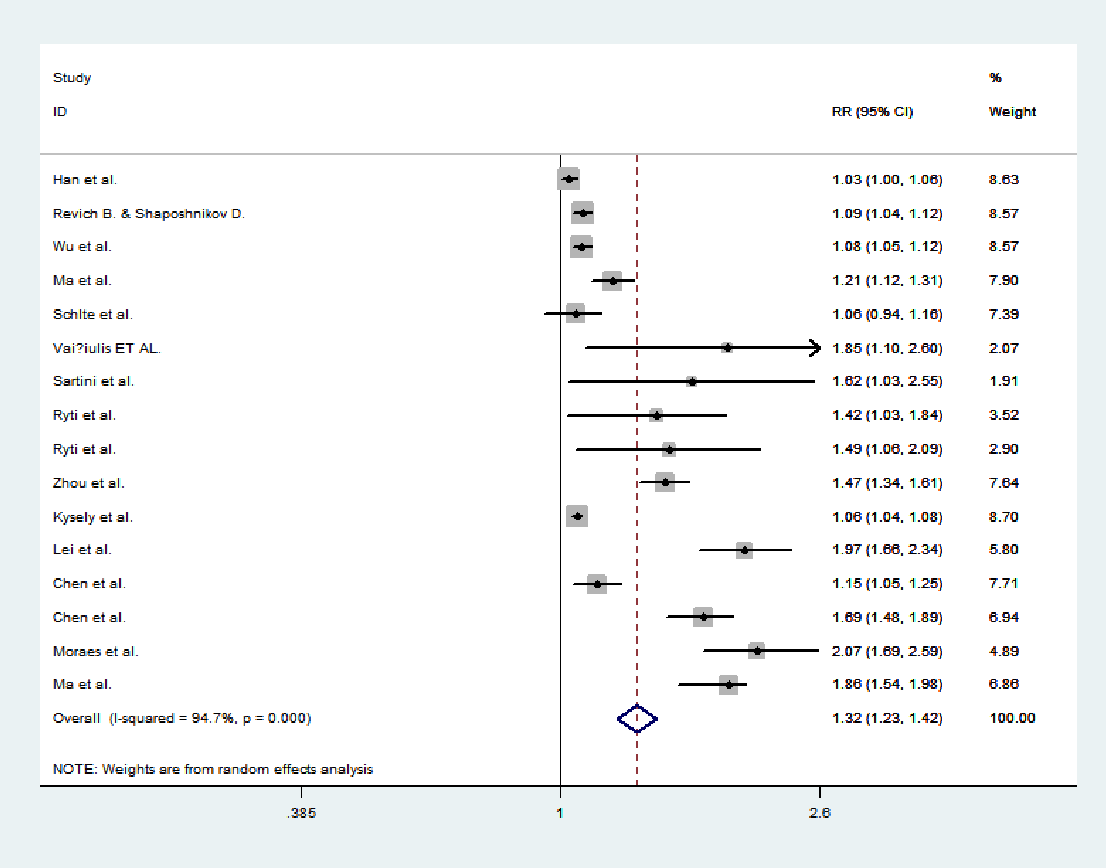


Figure S4: Forest plot of each study investigating the association between cold spells and cardiovascular disease morbidity.

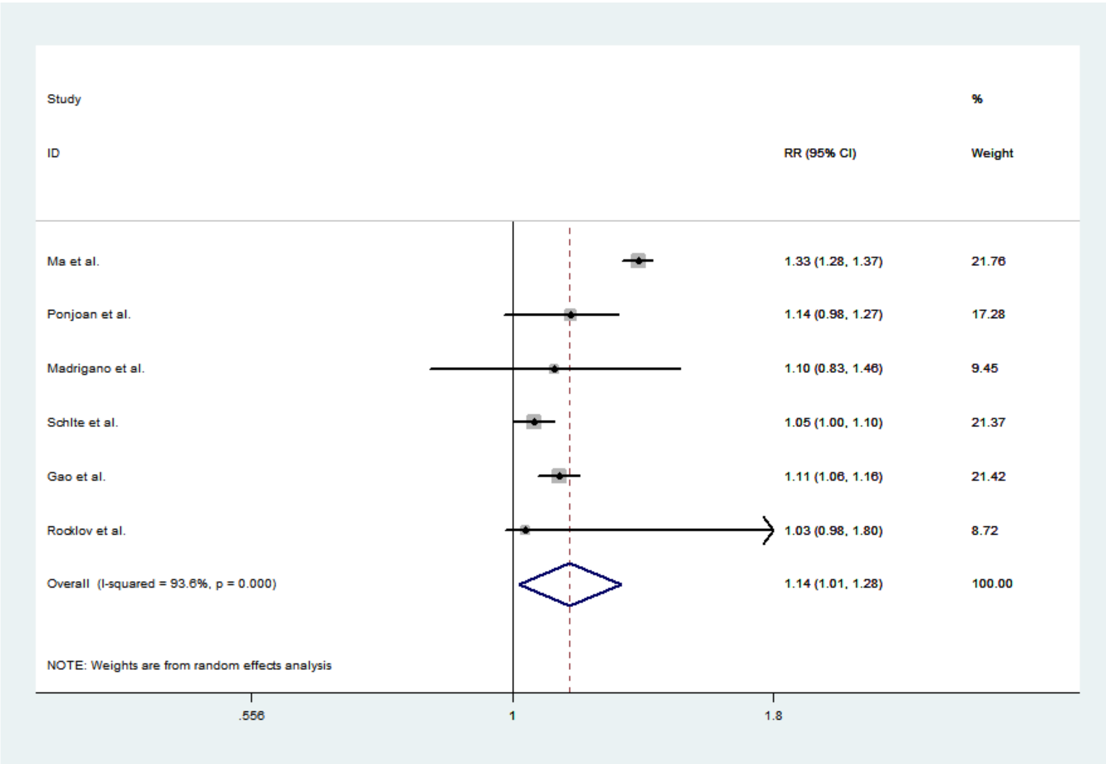


Table S6: Meta-regression model investigating the predictors of log pooled effect sizes for the associations between low temperatures and cardiovascular mortality and morbidity.

Regressors	**Mortality, β (95% CIs,)**
Climate zone (ref = Group A-Tropical)	
Group B-Dry	1.005(0.956-1.057)
Group C-Mediterranean	1.011 (0.967-1.056)
Group C-Oceanic	1.021 (0.981-1.063)
Group C-Subtropical	1.013 (0.989-1.038)
Group D-Continental	1.014 (0.987-1.042)
Group E-Subarctic	1.002 (0.954-1.053)
National income level (ref = high income)	
Upper-middle income	0.993 (0.974-1.014)
Lower-middle income	1.124 (1.035-1.221)*
Annual mean temperature	1.000 (0.998-1.002)
Latitude	1.000 (1.000-1.000)
Longitude	1.000 (1.000-1.000)
Constant	1.013 (0.944-1.086)
Regressors	**Morbidity, β (95% CIs,)**
Climate zone (ref = Group E-Subarctic)	
Group B-Dry	1.005 (0.956-1.057)
Group C-Mediterranean	1.020 (0.976-1.067)
Group C-Oceanic	1.021 (0.981-1.063)
Group C-Subtropical	1.013(0.989-1.038)
Group D-Continental	1.014 (0.987-1.042)
National income level (ref = high income)	
Upper-middle income	0.993 (0.974-1.014)
Lower-middle income	1.124 (1.035-1.221)*
Annual mean temperature	1.000 (0.998-1.002)
Latitude	1.000 (1.000-1.000)
Longitude	1.000 (1.000-1.000)
Constant	1.012 (0.944-1.086)

* , statistically significant (p-value<0·05). 95% CI, 95% Confidence interval.

Table S7: Meta-regression testing for differences between subgroups for the associations between cold spells and cardiovascular mortality and morbidity.

Subgroups	**Mortality (p-value)**	**Morbidity (p-value)**
National income (ref=high income)		
Upper-middle-income	0.49	0.14
Climate zone (ref=Group E-subarctic)		
Group C-Ocean	0.99	..
Group C-Subtropical	0.99	0.25

Group C-Continal	0.97	0.89
Cold spell intensity (ref=high intensity)		
Middle intensity	0.99	0.45
Low intensity	0.89	..

Figure S5: Risk of bias assessment of individual studies.

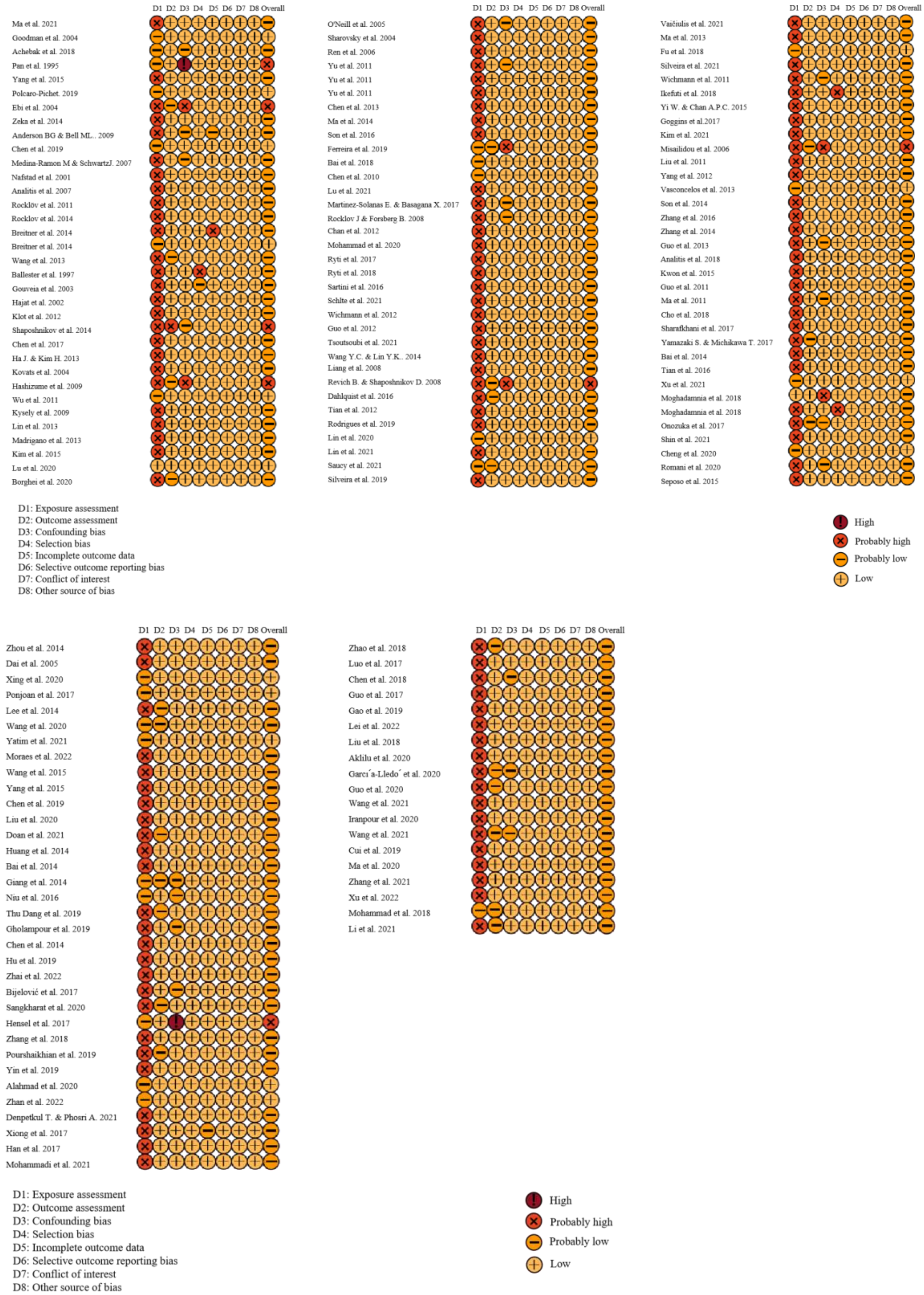


Figure S6: Weighted bar plots of the risk of bias assessment of included studies on low temperatures and cardiovascular disease mortality (A), low temperatures and cardiovascular disease morbidity (B), cold spells and cardiovascular mortality (C), and cold spells and cardiovascular morbidity (D).

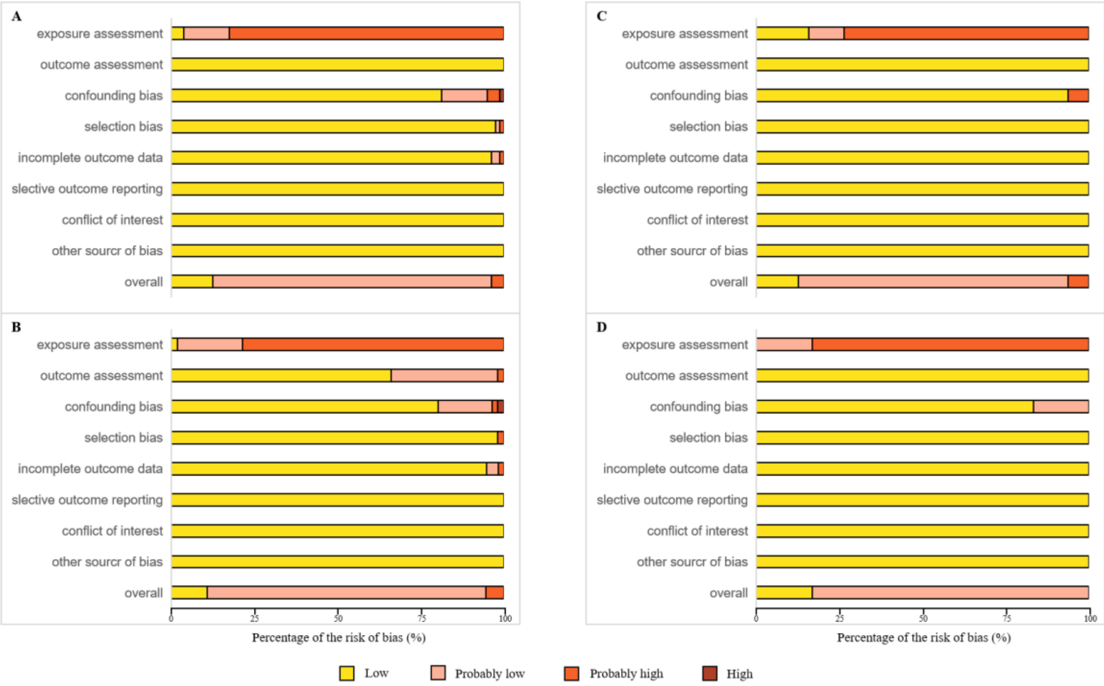


Table S8: Rating of quality and strength of the body of evidence of influence of low temperature and cold spells on cardiovascular mortality and morbidity.

	Low temperature studies		**Cold spell studies**	
	Mortality	**morbidity**	**Mortality**	**morbidity**
Quality of evidence assessment				
Downgrade				
	Rating	**Rating**	**Rating**	**Rating**
-Risk of bias across studies	(0)	(0)	(0)	(0)
-Indirectness	(0)	(0)	(0)	(0)
-Inconsistency	(-1)	(-1)	(-1)	(-1)
-Imprecision	(0)	(0)	(0)	(0)
-Publication Bias	(0)	(0)	(0)	(0)
Upgrade				
-Large magnitude of effect	(0)	(0)	(0)	(0)

-Dose response	(+1)	(+1)	(+1)	(0)
-Confounding minimizes the effect	(0)	(0)	(0)	(0)
Summary of the quality assessment				
-Overall quality of evidence (initial rating is "moderate")	Moderate	Moderate	Moderate	Low

Figure S7: Funnel plots to explore publication bias for studies investigating the association between low temperature and cardiovascular mortality.

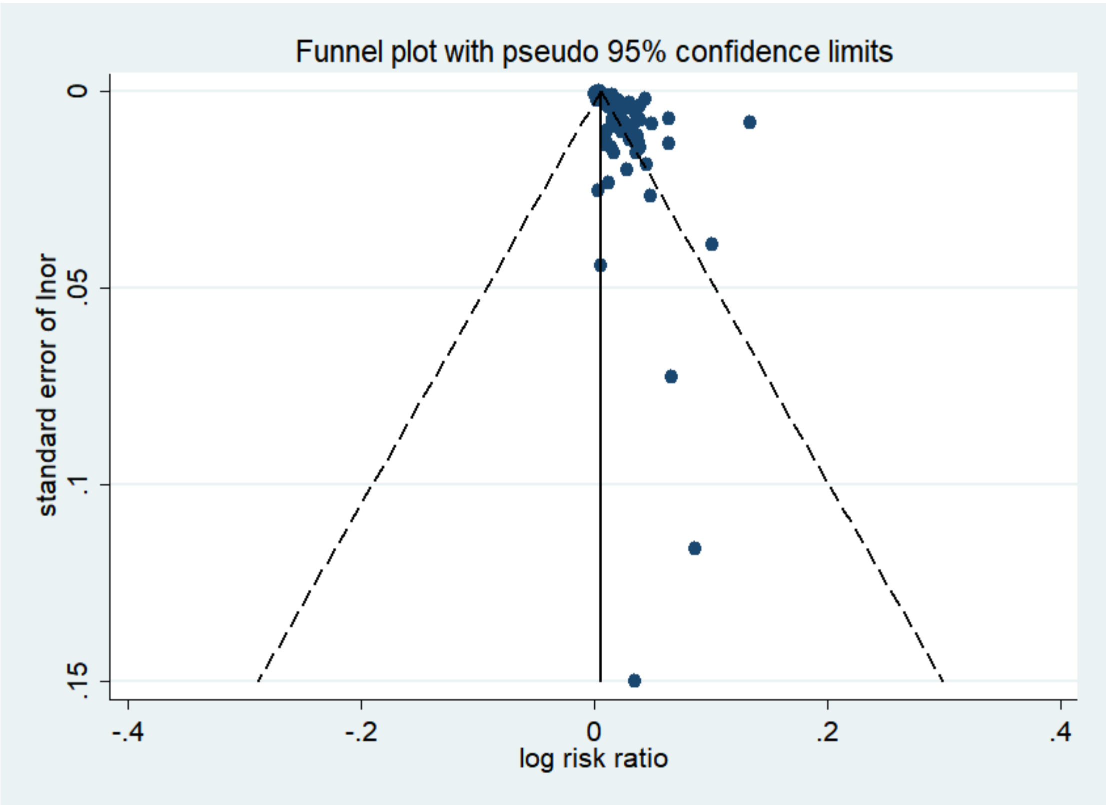


Figure S8: Funnel plots to explore publication bias for studies investigating the association between low temperature and cardiovascular morbidity.

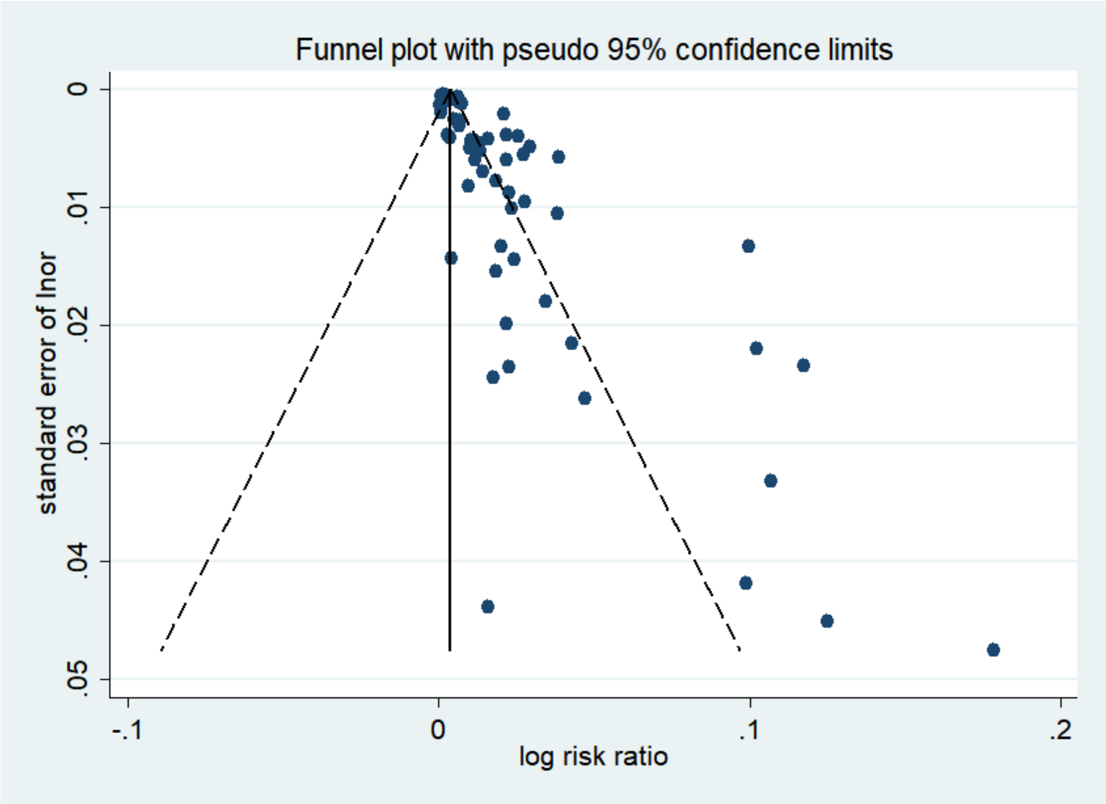


Figure S9: Funnel plots to explore publication bias for studies investigating the association between cold spells and cardiovascular mortality.

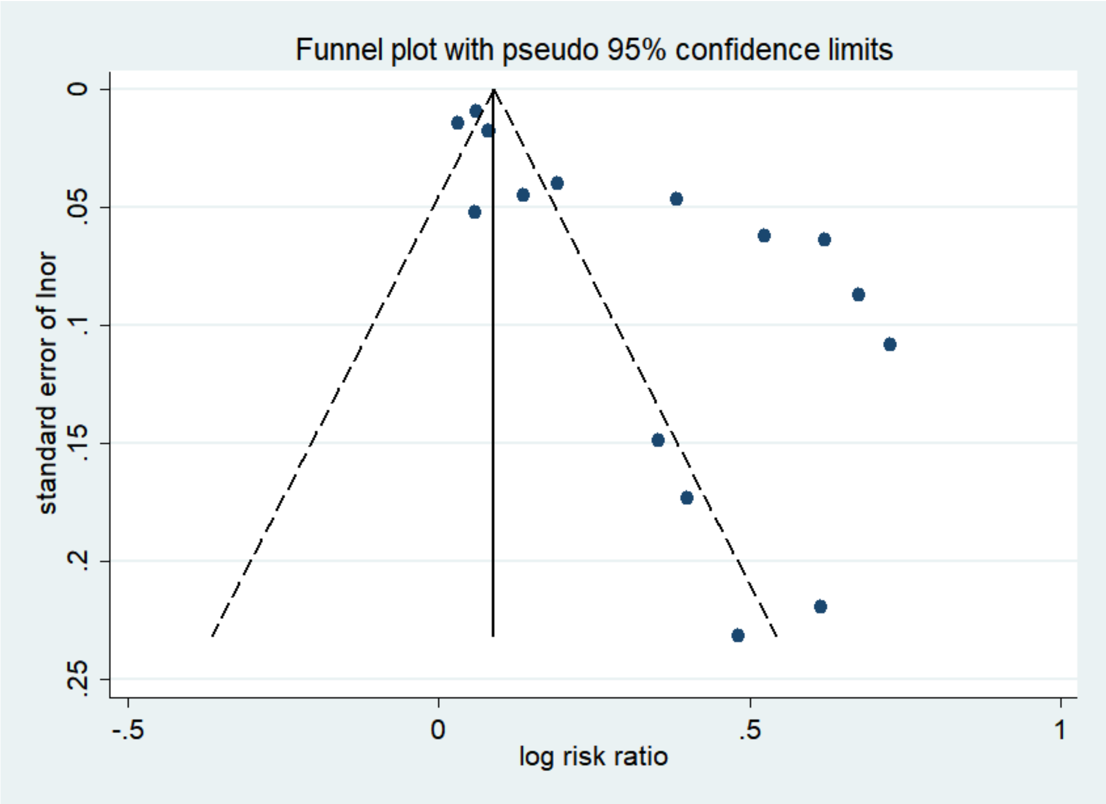


Figure S10: Funnel plots to explore publication bias for studies investigating the association between cold spells and cardiovascular morbidity.

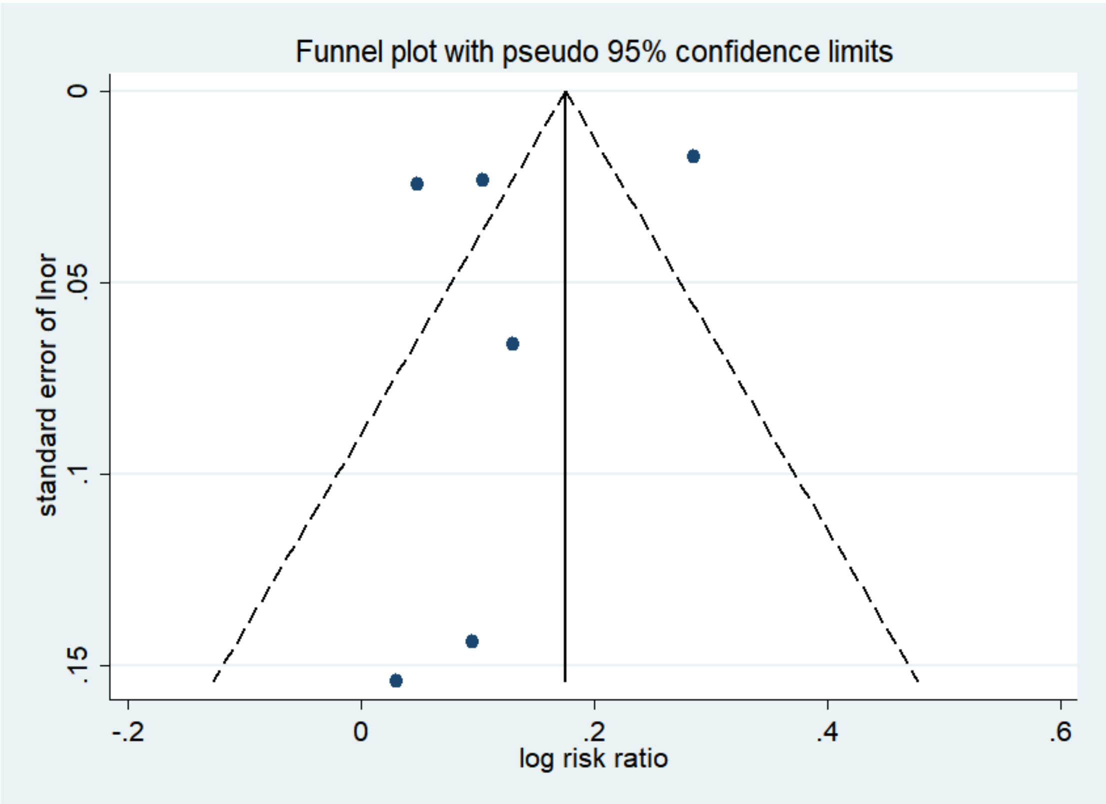


Figure S11: Trim and fill analysis of the studies investigating the association between low temperature and cardiovascular mortality.

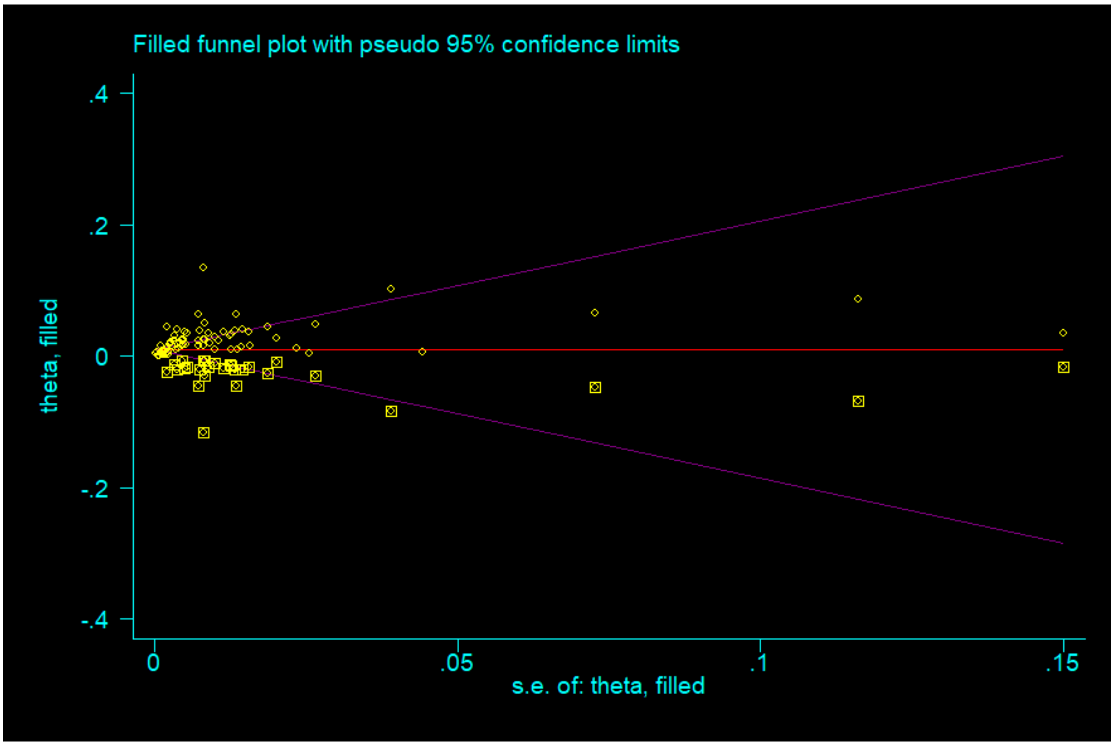


Figure S12: Trim and fill analysis of the studies investigating the association between low temperature and cardiovascular morbidity.

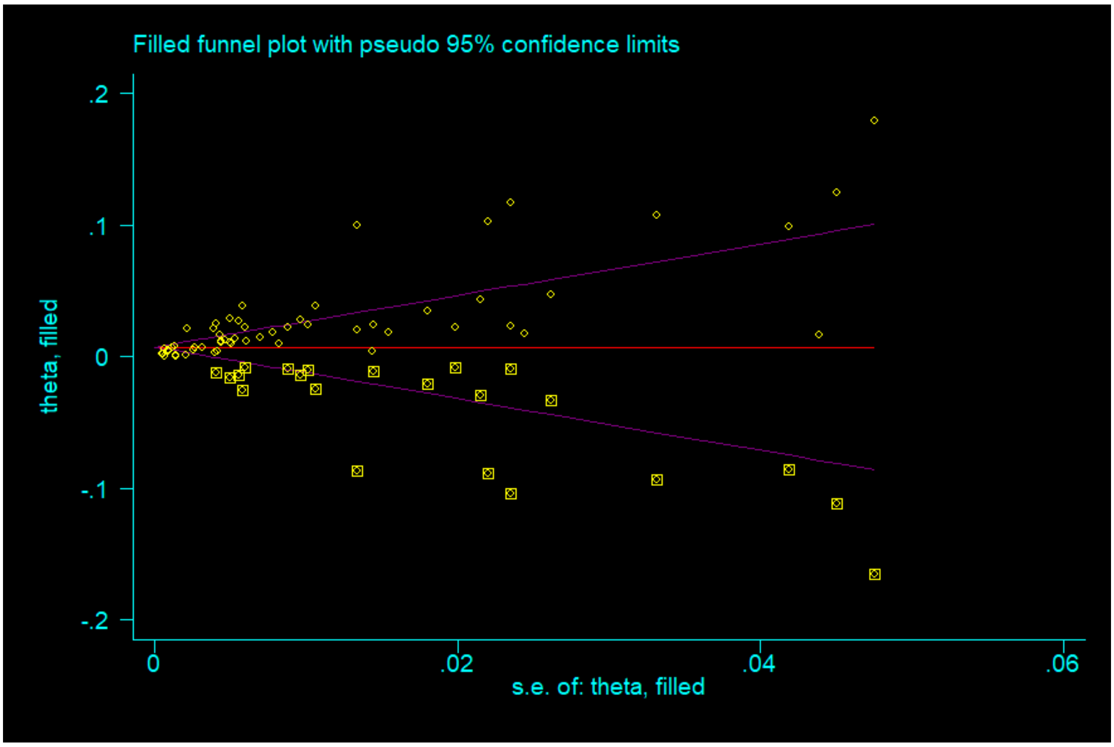


Figure S13: Trim and fill analysis of the studies investigating the association between cold spells and cardiovascular mortality.

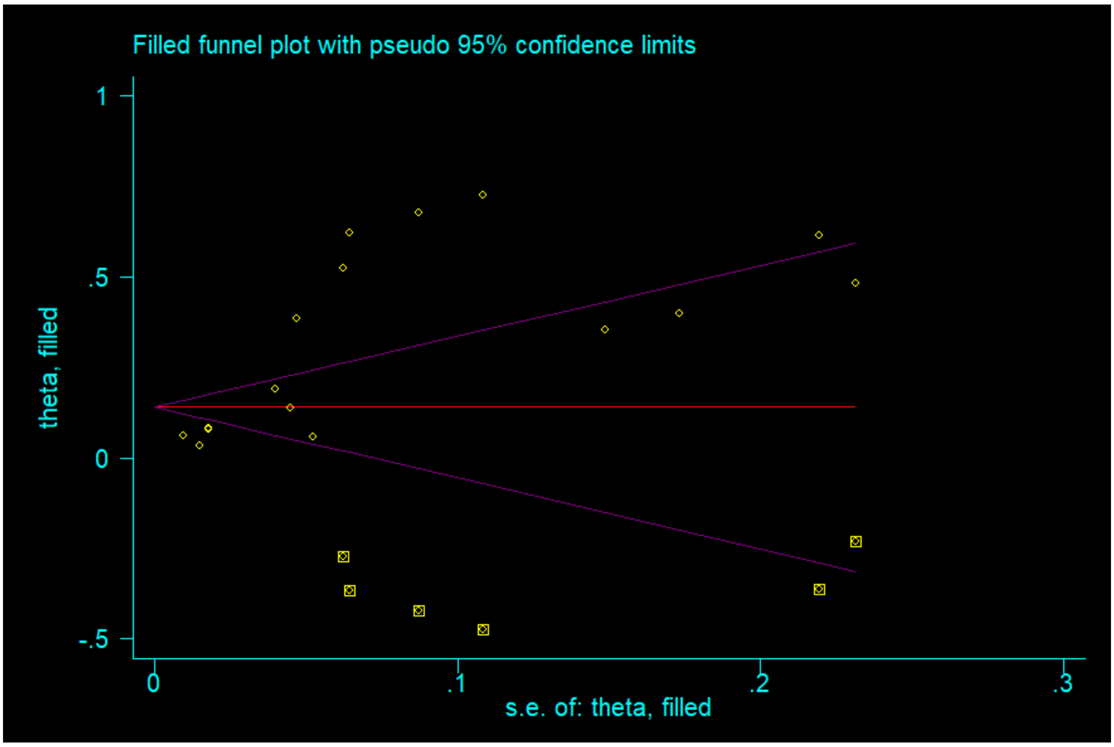


Figure S14: Trim and fill analysis of the studies investigating the association between cold spells and cardiovascular morbidity.

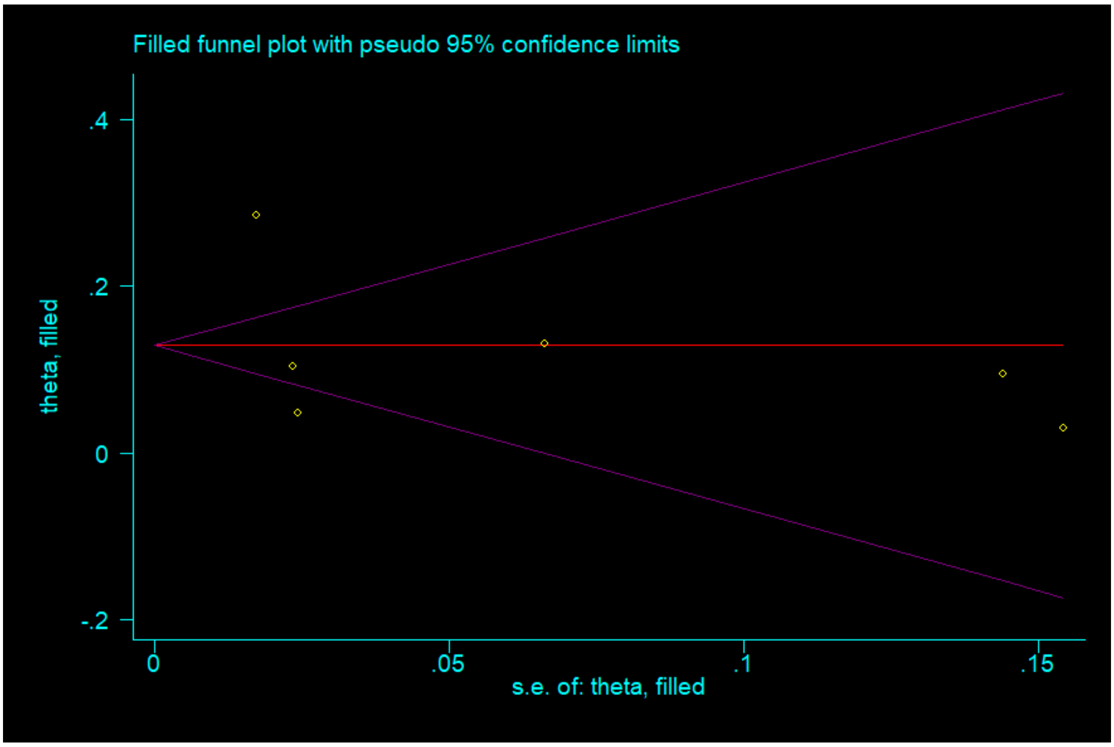


Table S9 Definition of cold spell across studies

Authors	**Study Period**	**Cold Spell Definition**

Ma et al.	1972-2015	2d, meanT< 5nd
Rocklov et al.	1990-2002	2d, meanT<2nd
Wu et al.	1994-2003	24h, minT< 10°C
Kysely et al.	1994-2006	10d, MaxT< 3.5°C
Madrigano et al.	1995-2003	3d, mimT< 5th
Chen et al.	1997-2003	24h, minT< 10°C
Ryti et al.	1998-2011	3d, mimT< 5th
Ryti et al.	1998-2011	3d, mimT< 5th
Sartini et al.	1998-2012	3D, mimT< 10th
Revich B. & Shaposhnikov D.	2000-2006	9d, meanT<3th OR 6d, meanT <1st
Vaičiulis ET AL.	2000-2015	2d, meanT<10th
Ma et al.	2001-2009	7d, MaxT< 3rd
Ma et al.	2005-2008	7d, MaxT< 3rd
Zhou et al.	2006-2010	3d, mimT< 5th
Ponjoan et al.	2006-2013	9d, meanT<5th
Moraes et al.	2006-2015	4d, minT< 3nd
Chen et al.	2007-2013	2d, meanT< 3nd
Han et al.	2011-2014	3d, mimT< 5th
Gao et al.	2013-2015	3d, mimT< 5th

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