Supplementary files

Supplementary Formula-1. standard deviation (SD) for change in outcome measures (SD_{diff}) were imputed using the SD from baseline (SD_{bl}) and SD from post-intervention (SD_{pi}) with the conservative value of r=0.5 used.

$$SD_{diff} = \sqrt{SD_{bl}^{\ 2} + SD_{pi}^{\ 2} - 2 \times r \times SD_{bl} \times SD_{pi}}$$

Supplementary Tables (P3-4)

Supplementary Figures (P5-11)

Supplementary Figure 8. (A) Forest plot of incidence of rescue medications; (B) Forest plot of incidence of medication discontinuance.

Supplementary Figure 9 Funnel plot depicting the publication bias of effect sizes in knee pain by subgroup of comparators

Supplementary Figure 10. Funnel plot depicting the publication bias of effect sizes in knee function by subgroup of comparators

Supplementary Figure 11. Funnel plot depicting the publication bias of risk difference of adverse events by subgroup of comparators

Protocol (P12-14)

PRISMA checklist (P15-16)

Inclusion/Exclusion Form for Primary Studies (P17)

Risk-of-Bias Form (P18)

Data Extraction Form (P19-20)

Supplementary Tables (P3)

Supplementary Table 1 Outcome measures and details of intervention of trials included in the analysis by year of publication (if NSAIDs (ibuprofen or diclofenac) is given in both experiment and comparator arms, the trial is considered as placebo-controlled)

Trial No.	Author, Year, Country	Outcome Measure	Details of Intervention and dose
1	Kuptniratsaikul et al, 2009, Thailand	Pain on level walking and on stairs; Knee function; Adverse events	*C. domestica* extract 2000 mg/d; Ibuprofen 800 mg/d
2	Moharamzad et al, 2011, Iran (Unpublished)	WOMAC, VAS, QOL: LPFI Physician and patient global assessment	Curcumin capsule 600 mg/d
3	Kertia et al, 2012 Indonesiana	VAS, synovial fluid leucocyte count and MDA level, and ROI Secretion	Curcuminoids 90 mg/d; Diclofenac 75 mg/d
4	Pinsornsak et al, 2012 Thailand	VAS, KOOS	Diclofenac 75 mg/d with curcumin 1000 mg/d; Diclofenac with placebo
5	Madhu et al, 2013 India	VAS, WOMAC, CGIC, Adverse events	T_a: NR-INF-02 (Turmacin®, *C. longa* extract, containing 12.6% w/w polysaccharides) 1000 mg/d; P_a: placebo (Microcrystalline cellulose) 800 mg/d; T_b: T_a+ glucosamine (1500 mg/d); P_b: glucosamine (1500 mg/d)
6	Kuptniratsaikul et al, 2014 Thailand	WOMAC, 6-min walk, adverse events	*C. domestica* extract 1500 mg/d; Ibuprofen 1200 mg/d
7	Nakagawa et al, 2014 Japan	JKOM, JOA, VAS, Adverse events, blood biochemistry tests: triglyceride, creatinine, uric acid, amylase, red blood cells	Theracurmin® (surface-controlled water-dispersible cucumin)180 mg/d
8	Panahi et al, 2014[a] & Panahi et al, 2015[a] Iran Rahimnia et al, 2015[a] Iran	WOMAC, VAS, QOL: LPFI Adverse events; serum MDA serum levels of IL-4, IL-6, TNF-α, TNF-β, hs-CRP, ESR	Curcuminoids (C3 complex®) 1500 mg/d with 15 mg/d Bioperine® to enhance oral bioavailability
9	Srivastava et al, 2016 India	WOMAC, VAS, Adverse events, IL-1β, MDA	*C. longa* 500 mg/d with Diclofenac 50 mg/d; placebo with Diclofenac 50 mg/d
10	Haroyan et al, 2018 Armenia	WOMAC, physical function performance, inflammation sensitive hematological measures: ESR, CRP	CuraMed® (curcuminoid complex extract from turmeric rhizome with turmeric volatile oil) 1500 mg/d
11	Panda et al, 2018 India	VAS, WOMAC, and laboratory parameters to evaluate safety haemoglobin, platelet count, etc.	Curene® (turmeric *C. longa* extract comprising bioavailability enhanced curcuminoids) 500 mg/d
12	Gupte et al, 2019 India	VAS, WOMAC, inflammatory markers, TNF-α, IL6, IL1β and CTX II.	Longvida® (solid curcumin particle encapsulates the free curcumin in a tri-lipid matrix) 160 mg/d; Ibuprofen 400 mg/d
13	Henrotin et al, 2019 Belgium	KOOS, VAS, serum coll-2, PGADA assessed with a VAS	T_a: FLEXOFYTOL® (*C. longa* extract) 280 mg/d; T_b: FLEXOFYTOL® 187 mg/d
14	Shep et al, 2019 India	VAS, KOOS, adverse events and laboratory-based evaluations of safety: hemoglobin, serum creatinine, etc.	T_a: Curcumin 1000 mg/d + Diclofenac 100 mg/d; T_b: BCM-95® (curcuminoids and essential oil of turmeric complex) 1500 mg/d; D: Diclofenac 100 mg/d
15	Hashemzadeh et al, 2020 Iran	WOMAC, direct and total bilirubin, platelet count, and serum creatinine	SinaCurcumin™ (nanocurcumin, nanomicelle curcuminoids) 80 mg/d
16	Wang et al, 2020 Australia	VAS, WOMAC, physical function, effusion synovitis, cartilage relaxation times, QOL, adverse events	*C. longa* extract (80% turmerosaccharides and 20% curcuminoids [Turmacin Plus]) 1000 mg/d

Abbreviations: IA, Intra-Articular; NR, Not Reported; NRS, Numerical Rating Scale; VAS, Visual Analog Scale; WOMAC,Western Ontario and McMaster Universities Osteoarthritis Index; KOOS, Knee Injury and Osteoarthritis Outcome Score; QOL, Quality of life; LPFI, Lequesne Pain-Function Index; CGIC, The Clinician Global Impression of Change; JKOM, Japanese Knee Osteoarthritis Measure; JOA, Japanese Orthopedic Association; PGADA, Patient Global Assessment of Disease Activity; hs-CRP, high-sensitivity C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; MDA, malondialdehyde; ROI, Reactive Oxygen Intermediates; coll-2, Collegen-2; CTX II, C-Terminal telopeptides of type II Collagen.

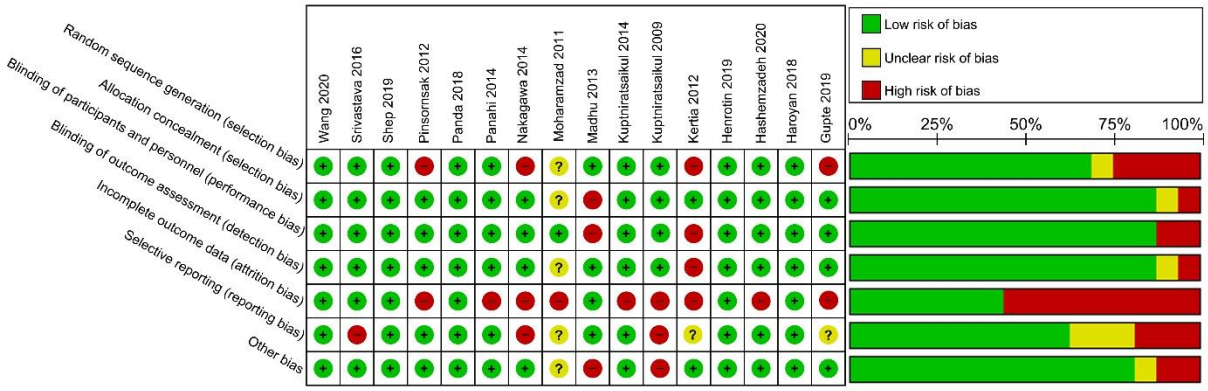
[a] The Panahi et al. 2014 & 2015 and Rahimnia et al, 2015 reported results from the same trial conducted at Baqiyatallah University of Medical Sciences, Tehran, Iran.

Supplementary Table 2. Variance and adjusted R^2 values from meta-regression of pain and physical function effect size on continuous study-level characteristics among RCTs comparing turmeric extracts and placebo.

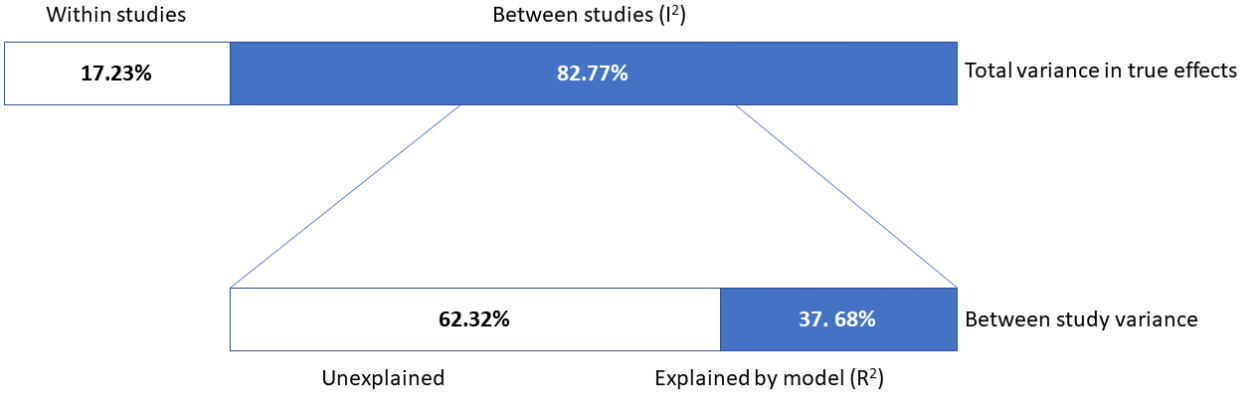
Outcome / Moderator	No. of comparisons	No. of participants	Coefficient (95% CI)	*P* value	I^2 residual (%)	Adjusted R^2(%)
Pain						
BMI (kg/m^2)	10	739	0.26 (0.04 to 0.48)	0.023	82.77	37.68
Age (years)	12	916	0.07 (-0.01 to 0.14)	0.087	85.34	17.94
Female proportion (%)	12	954	1.17 (-0.72 to 3.05)	0.225	81.16	5.20
Duration (weeks)	14	1071	0.06 (-0.05 to 0.16)	0.272	85.77	0.51
Physical Function						
BMI (kg/m^2)	9	729	0.48 (0.21, 0.74)	<0.001	81.67	67.24
Age (years)	11	906	0.08 (-0.04, 0.20)	0.174	90.16	7.42
Female proportion (%)	10	856	0.52 (-0.97 to 2.01)	0.491	73.09	0.00
Duration (weeks)	12	973	0.04 (-0.08, 0.17)	0.473	90.39	0.00

* I^2 residual (%) denotes the proportion of the between-study variance in total variance in true effects; Adjusted R^2 (%) denotes the proportion of variance explained by meta-regression moderators in the between-study variance.

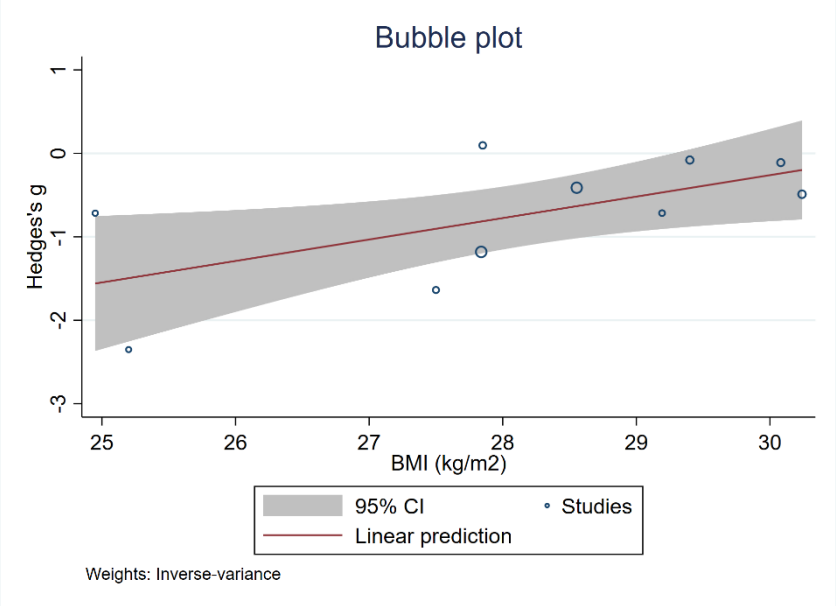
Supplementary Figures (P5)



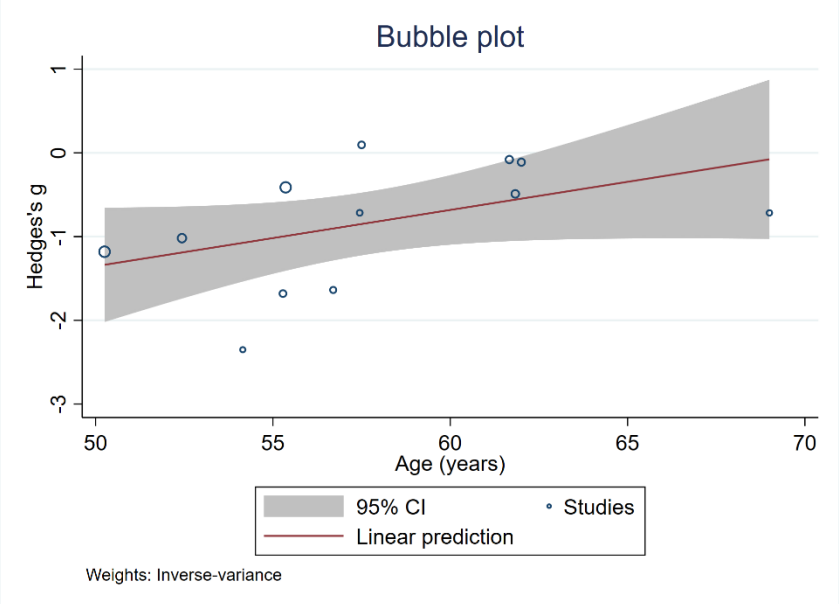
Supplementary Figure 1. Risk of bias assessment



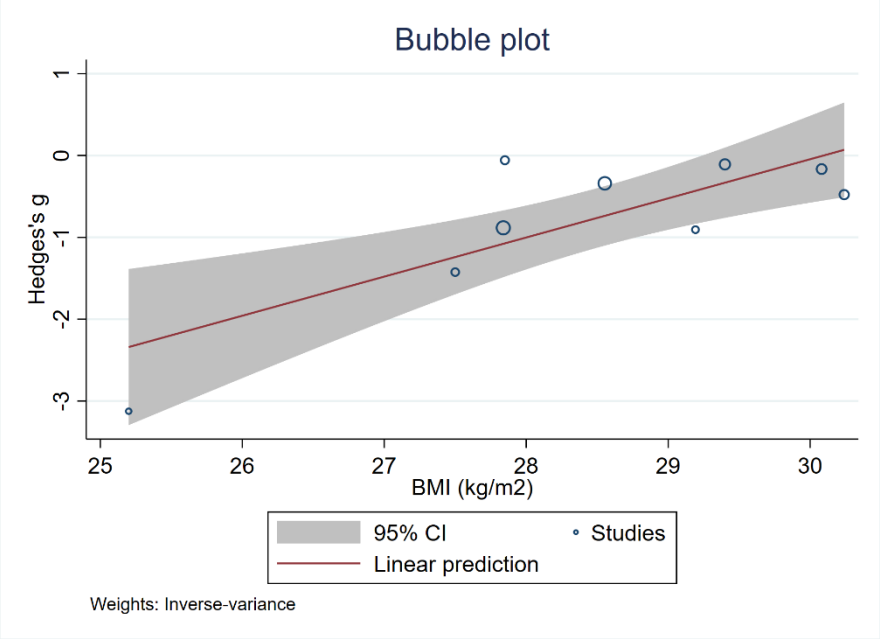
Supplementary Figure 2. Meta-regression analyses (REML): proportion of heterogeneity and variance illustrated for BMI as a covariate for studies assessing knee pain.



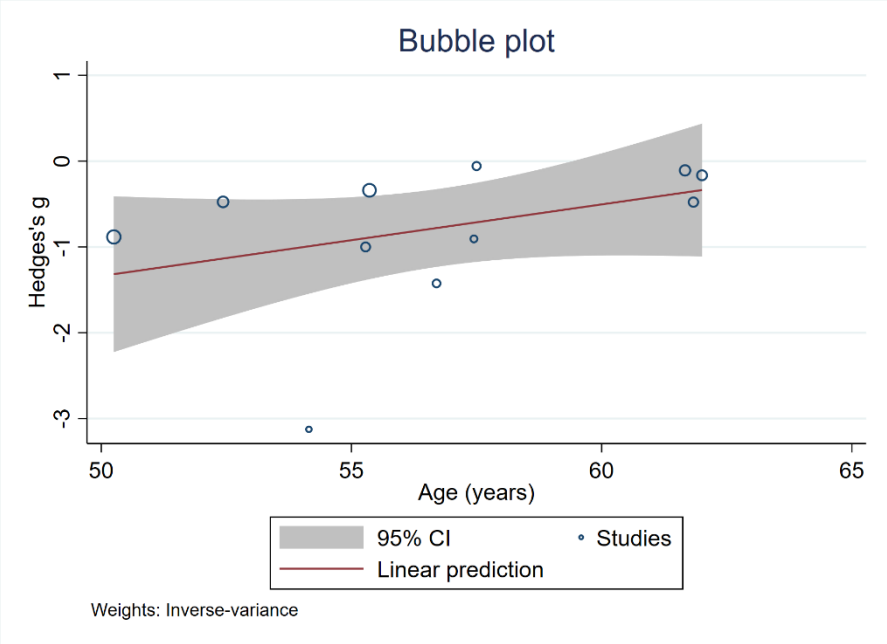
Supplementary Figure 3. Meta-regression analyses (REML): standardised mean differences (SMD) of the individual studies according to pain at different study-level BMI of trial participants



Supplementary Figure 4. Meta-regression analyses (REML): standardised mean differences (SMD) of the individual studies according to pain at different study-level age of trial participant

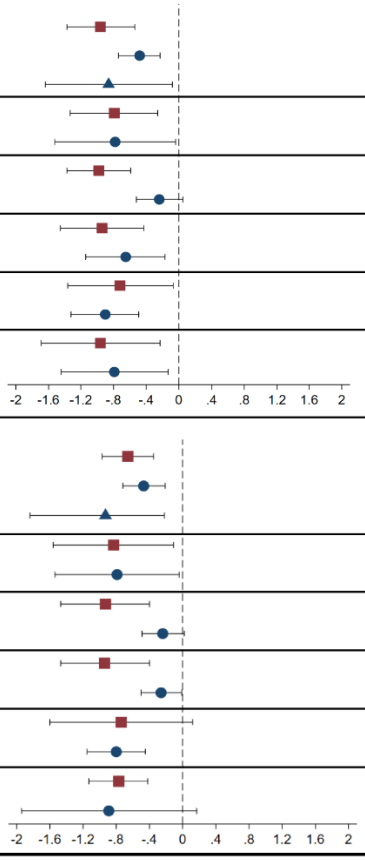


Supplementary Figure 5. Meta-regression analyses (REML): standardised mean differences (SMD) of the individual studies according to physical function at different duration of study-level BMI of trial participants

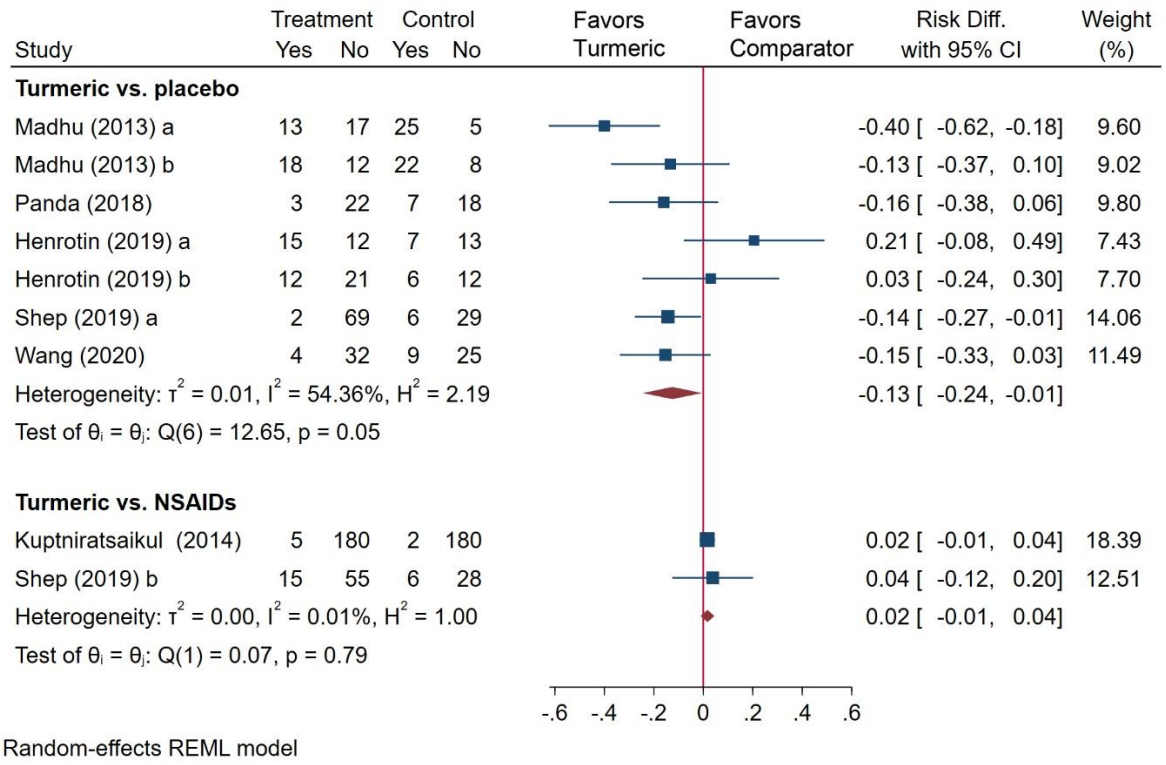


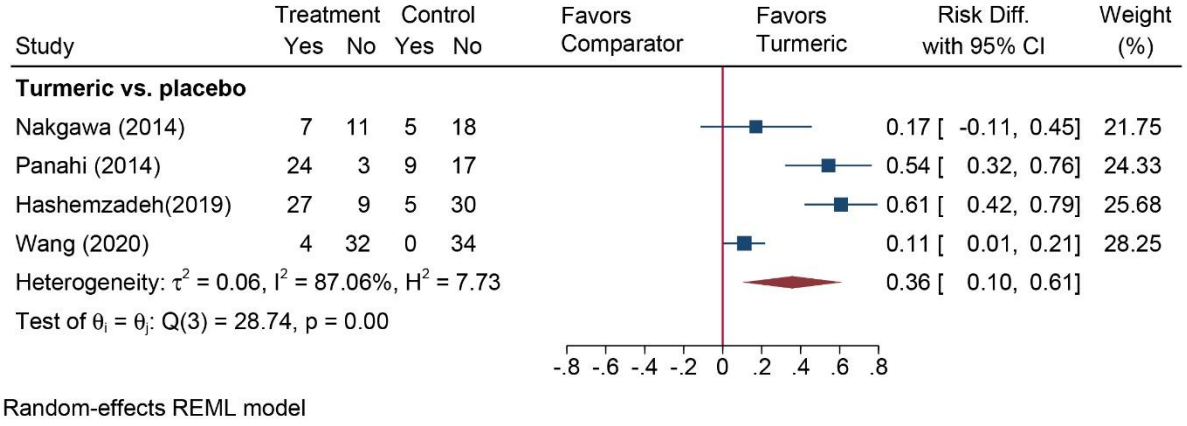
Supplementary Figure 6. Meta-regression analyses (REML): standardised mean differences (SMD) of the individual studies according to physical function at different study-level age of trial participant

Outcome / Moderator	Subgroup	N. of comparisons	N. of participants	Mean difference (95% Confidence Interval)	Favours turmeric extract	Favours Placebo	*P* values for between group difference
Pain							
formulation types	curcumin	5	367	-0.96 (-1.37 to -0.54)			0.14
	curcuminoids	3	244	-0.48 (-0.74 to -0.23)			
	holistic extract	6	460	-0.86 (-1.64 to -0.08)			
bio-enhancer	enhanced	8	540	-0.79 (-1.33 to -0.26)			0.97
	no enhancer	4	358	-0.78 (-1.52 to -0.04)			
trial location	asian	11	861	-0.98 (-1.37 to -0.59			<0.01
	not asian	3	210	-0.24 (-0.52 to 0.05)			
type of pain measures	VAS	8	619	-0.94 (-1.45 to -0.43)			0.42
	other	6	452	-0.65 (-1.14 to -0.17)			
study quality	high	6	500	-0.72 (-1.36 to -0.07)			0.63
	low	8	571	-0.90 (-1.32 to -0.49)			
funding	investigator-initiated	3	181	-0.96 (-1.69 to -0.23)			0.73
	industry	6	519	-0.79 (-1.44 to -0.13)			
Physical function							
formulation types	curcumin	3	244	-0.66 (-0.97 to -0.35)			0.46
	curcuminoids	3	244	-0.47 (-0.72 to -0.21)			
	holistic extract	6	458	-0.93 (-1.84 to -0.22)			
bio-enhancer	enhanced	7	530	-0.83 (-1.56 to -0.11)			0.93
	no enhancer	3	270	-0.79 (-1.54 to -0.04)			
trial location	asian	9	738	-0.93 (-1.47 to -0.40)			0.02
	not asian	3	235	-0.24 (-0.49 to 0.02)			
type of function measures	WOMAC	9	702	-0.94 (-1.47 to -0.40)			0.02
	other	3	271	-0.26 (-0.50 to -0.01)			
study quality	high	6	525	-0.74 (-1.60 to 0.12)			0.90
	low	6	448	-0.80 (-1.15 to -0.45)			
funding	investigator-initiated	3	181	-0.77 (-1.13 to -0.42)			0.84
	industry	5	509	-0.89 (-1.94 to 0.17)			

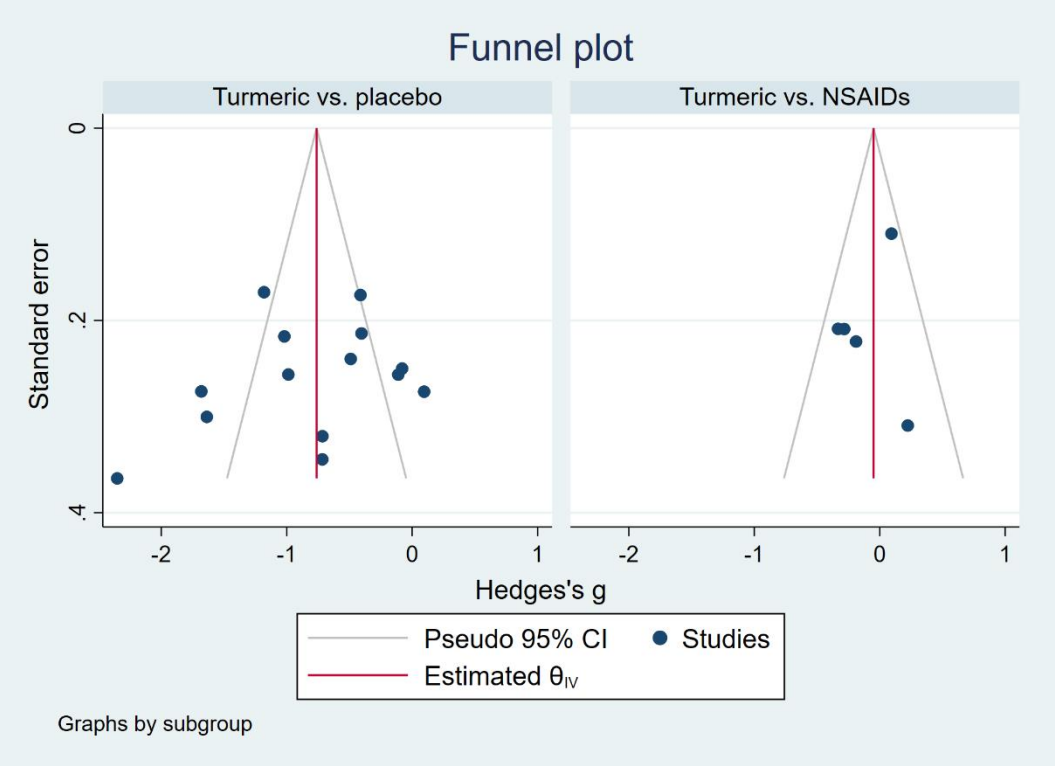


Supplementary Figure 7. Subgroup analysis of pain and physical function for categorical study-level characteristics comparing turmeric extract with placebo. (VAS, Visual Analog Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index)



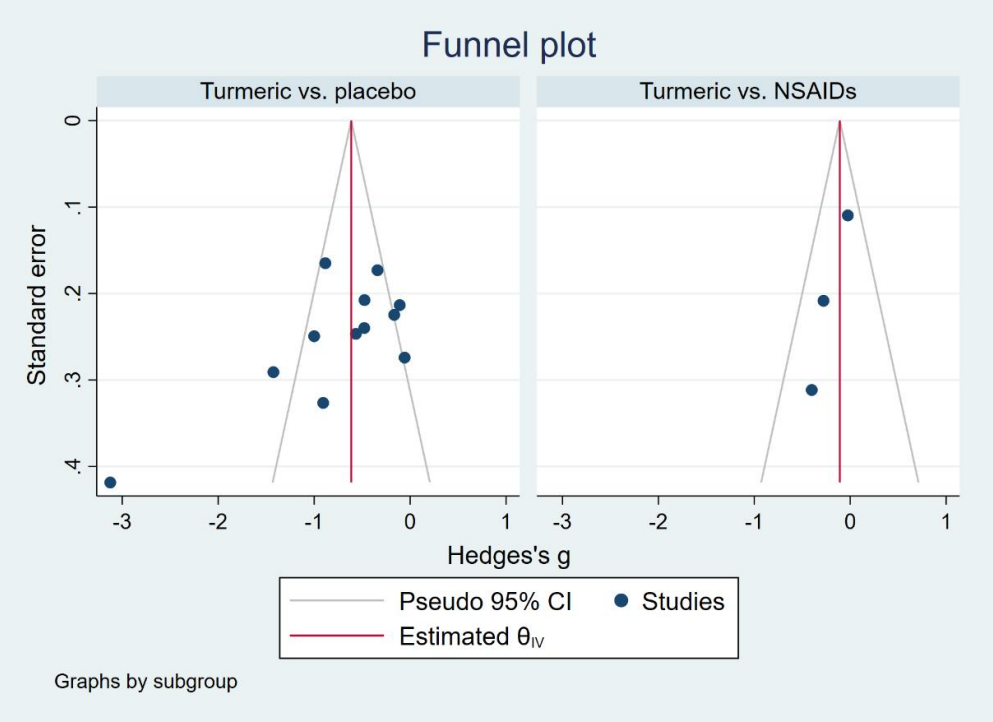


Supplementary Figure 8. (A) Forest plot of incidence of rescue medications; (B) Forest plot of incidence of medication discontinuance.

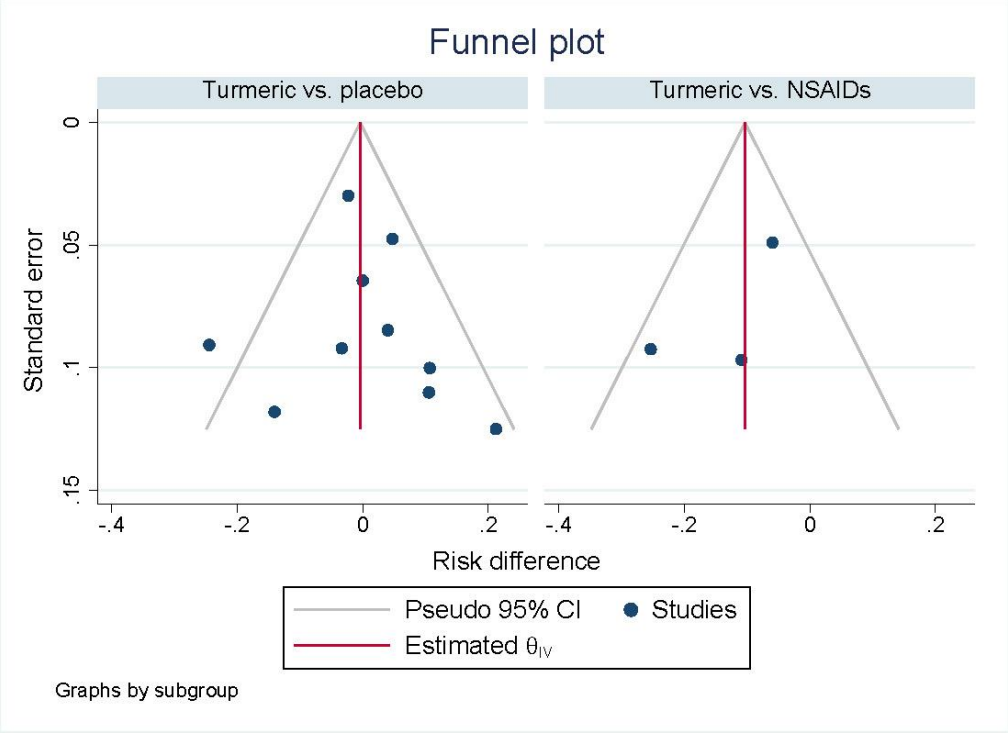


Funnel plot is provided for subgroups analysed (i.e. placebo and NSAIDs); however, we acknowledge that NSAIDs subgroups has fewer studies than recommended for a funnel plot.

Supplementary Figure 9. Funnel plot depicting the publication bias of effect sizes in knee pain by subgroup of comparators



Supplementary Figure 10. Funnel plot depicting the publication bias of effect sizes in knee function by subgroup of comparators



Supplementary Figure 11. Funnel plot depicting the publication bias of risk difference of adverse events by subgroup of comparator

Protocol

Efficacy and safety of turmeric extracts in knee osteoarthritis: protocol for a systematic review and meta-analysis of randomised controlled trials

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[ξ] *equal first authors*

Background and rationale

Knee osteoarthritis (OA) is a common chronic disease that causes joint pain and knee function loss.[1] There are currently no approved disease-modifying drugs available to treat OA. The options for pharmacological management of OA is limited to analgesics, intra-articular corticosteroids, and NSAIDs.[2] These medications only have a mild to moderate effect on pain, which results in patient dissatisfaction. Moreover, these drugs are associated with gastrointestinal, renal, and cardiovascular complications.[3] These medications and are often contraindicated in patients with comorbidities, which is a common feature in OA patients.

Turmeric extracts, or *Curcuma longa* extracts, has been used as a remedy for treating arthritis in traditional medicine. Preclinical and clinical evidence suggests that *C. longa* extracts are effective and safe for the treatment of OA. The safety profile of the drug makes it an ideal option for long-term treatment for OA patients who often have comorbidities. Recent years have witnessed the rise of different extracts from Turmeric and the randomised clinical trials (RCTs) evaluating the efficacy and safety of these extracts for the treatment of knee OA.

Objectives

We aim to systematically review and meta-analyse the evidence from RCTs on efficacy and safety of turmeric extracts for knee OA, in terms of pain and physical function improvement, change in biomarkers, and adverse events.

Methodology

Eligibility criteria

According to the criteria proposed by the PRISMA Extension Statement for Reporting of Systematic Reviews, the selection of studies will be based on the specific definition of PICOS items: Participants, Interventions, Comparators, Outcomes, and Study design.[4]

Characteristics of participants (P)

The population of interest will include adult participants, at least 40 years old, of any sex and with a confirmed diagnosis of knee OA, possibly according to the criteria proposed by the American College of Rheumatology or similar.[5] Moreover, studies involving mixed samples of patients with OA of the knee and/or hip may also be included, if found appropriate as per the inclusion criteria.

Characteristics of interventions (I)

This study will focus on turmeric extracts from different *Curcuma* species (*C. longa*, *C. zedoaria*, *C. Domestica*), turmerosacchrides, Curcuminoids, curcumin, jiang huang (Chinese name of *C. longa*), and such other formulations. RCTs evaluating combination therapy of turmeric as adjuvant or complementary to conventional drugs (eg. Paracetamol or NSAIDs) will be included, if the comparator group also received the same drugs. We will exclude trials with multi-herbal formulations. However, any turmeric extract formulation which includes bioavailability enhancing product will be included. For instance, piperine combined with turmeric will be included as previous trials suggest it enhances the bioavailability of curcumin.[6]

Characteristics of comparators (C)

We will include the studies comparing turmeric extracts with active control (eg. but not limited to, NSAIDs) or placebo for the treatment of knee OA.

Characteristics of outcomes (O)

The studies reporting data for at least one of the following outcomes: pain, physical function, imaging biomarkers (x-ray joint space narrowing, MRI structural measures), biochemical markers, medication change, and adverse events will be included in the analysis.

For each outcome, data on baseline and follow-up values and/or mean change from baseline will be extracted. If the data are expressed in the graphical information, the numerical data will be extracted from graphs using the procedure (adapted) suggested by Guyot et al.[7] If the studies do not provide complete data, authors of primary studies will be contacted through email to provide missing or additional data.

Characteristics of study design (S)

Papers will be included if they used a randomised, quasi-randomised, controlled, blinded or non-blinded design. Observational and non-randomised studies will be excluded.

Primary and secondary outcomes

Our primary outcome will be to evaluate the effectiveness of turmeric extracts on knee pain. Moreover, we will consider physical function loss, change in biochemical markers and imaging biomarkers as the secondary outcome.

Information sources and search procedure

The search procedure will be implemented consistently with the following criteria.

Electronic source and search strategy

Studies will be retrieved through a systematic search of the biomedical databased for the currently available literature on the use of turmeric extracts for knee OA. We will search online databases such as PubMed, Scopus, Embase, Web of Science and Cochrane Central Register of Controlled Trial, Google scholar, etc. from inception to April 2020. Both published and unpublished trials will be included, with the latter including e.g. abstracts, conference proceedings and posters with available data. Studies that have compared interventions of interest and reported extractable data for at least one measure of pain, physical function, imaging biomarkers, biochemical markers, medication change, and adverse events will be included.

Hand-searching

Abstract booklet from conference proceedings, abstracts, and poster sessions will be hand searched using the online sources of major international association involved in OA research: European League Against Rheumatism (EULAR), Osteoarthritis Research Society International (OARSI), American Academy of Orthopaedic Surgeons (AAOS) and American College of Rheumatology (ACR). Moreover, references retrieved from relevant meta-analysis and review articles will be hand-searched and analysed for inclusion as per the eligibility criteria.

Study selection

Study selection will be performed by two reviewers, independently, and each potential discrepancy will be discussed and solved through consensus with other authors and independent expert consultation.

Assessment of risk of bias

The methodological quality of the selected studies will be evaluated using the Cochrane risk of bias tool.[8] Each article will be evaluated independently in a blind method by two researchers using the Cochrane risk of bias tool. This double-check method will reduce the probability of an incorrect or inaccurate judgment risk of bias. The Cochrane risk of bias tool considers characteristics of the following items: sequence generation, allocation concealment, blinding of participants, study personnel and outcome assessors, incomplete outcome data, selective outcome reporting and other potential sources of bias. At the end of quality assessment, a consensus on final evaluation will be reached; any disagreements will be resolved by the discussion with senior authors.

Data extraction

Two reviewers will extract data independently from the included studies for the following information: study design, characteristics of the population (age, sex, and BMI), sample size, intervention details and dosage, duration of follow-up, type of placebo or other control, outcome measurements, mean change values of the relevant outcome, and the number of adverse event report and medication change. Intention-to-treat data will be used whenever available.

Statistical analysis

The fixed-effect model will be used if included studies are homogeneous, otherwise, the random-effect model with a restricted maximum-likelihood will be employed for the meta-analysis of both continuous and binary outcomes.[9] The heterogeneity of the effect size across the trials will be tested using the Q statistics ($P<0.05$ was considered heterogeneous) and I^2 statistic (I^2 >50% will be considered heterogeneous).[9] Due to different outcome measures, the change from baseline to follow-up scores will be translated into standard mean differences (SMD) using Hedges' g effect sizes, as per the data availability. Statistical analysis will be performed using STATA version 16 (STATA Corp., Texas, USA). and Review Manager 5 (RevMan 5.3) (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

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3. Hunter DJ. Pharmacologic therapy for osteoarthritis-the era of disease modification. Nature Review Rheumatology 2011; 7:13-22.
4. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations. Annals of Internal Medicine. 2015; 162(11):777.
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9. Singh A, Hussain S, Najmi AK. Number of studies, heterogeneity, generalisability, and the choice of method for meta-analysis. Journal of the Neurological Sciences. 2017; 381:347

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7,8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7,8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8 Figure1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9 Table1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-16
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, 16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	14,15
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16,17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Inclusion/Exclusion Form for Primary Studies

Study ID:
Reviewer:
Date:

Identification Details

Author	Year	Journal/ Conference	Source

On Endnote database .....Yes/ No

Full text availability ……..Yes/ No

Study Eligibility

Study design is one of the following:
Randomised clinical trial..... Yes/ No
The study concerns osteoarthritis..... Yes/ No
The study concerns Turmeric extracts..... Yes/ No
The study concerns pain or physical function measurements..... Yes/ No
The study is a human study, not animal/laboratory experiment…… Yes/ No

Please Tick Only One Box Below

Included	Excluded	Pending*

*** Issue relates to selective reporting – when authors may have taken pain or physical function measurements, but not reported these within the paper. Reviewers should contact correspondent author for information on possible non-reported pain or physical function & reasons for exclusion from publication. Study should be listed in 'Pending' until clarified. If no clarification is received after three attempts, study should then be excluded.**

References to Other Trials

Did this report include any references to **published reports** of potentially eligible trials not already identified for this review?		
First author	Journal / Conference	Year of publication

Did this report include any references to **unpublished data** from potentially eligible trials not already identified for this review? If yes, give list contact name and details

Risk-of-Bias Form

Risk of bias	Author's judgement	Support for judgement
Random sequence generation (selection bias) Was the allocation sequence adequately generated?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Describe selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
Allocation concealment (selection bias) Was allocation adequately concealed?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Describe selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
Blinding (performance bias and detection bias) Was knowledge of the allocated interventions adequately prevented during the study?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Performance bias or detection bias due to knowledge of the allocated interventions after assignment
Incomplete outcome data (attrition bias) Were incomplete outcome data adequately addressed?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Evaluate attrition bias due to amount, nature or handling of incomplete outcome data
Selective reporting (reporting bias) Are reports of the study free of suggestion of selective outcome reporting?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Evaluate reporting bias due to selective outcome reporting
Other bias Was the study apparently free of other problems that could put it at a high risk of bias?	☐ Low risk of bias ☐ Unclear risk of bias ☐ High risk of bias	Bias due to problems not covered elsewhere in the table

Data Extraction Form

Study and Participants characteristics

Study characteristics	
	Further details
Country / Countries	
Study registration	
Funding	
How was participant eligibility defined? (e.g. How osteoarthritis was defined?)	
Details and dosage for Turmeric or control medication?	
How pain was measured?	
How physical function was measured?	
How many people were recruited?	
Duration of study (randomised clinical trial)	
Adverse events reported?	
Other	
Participant characteristics	
	Further details
Number of participants (cases versus controls)	
Age (mean, median, range, etc)	
BMI (mean, median, range, etc)	
Female of OA participants (numbers / %, etc)	Female of OA participants (numbers / %, etc)
Type of OA (hand, knee, hip, etc)	
Other	

Measures relevant to the review	
Pain	VAS / WOMAC/ KOOS
Physical Function	WOMAC/ KOOS
Adverse events	YES/ NO
Biochemical measurements	YES/ NO
Others	

For dichotomous data

OR/ RR (95% CI, p value)	Treatment group (n) n = number of participants, not number of events	Control group (n) n = number of participants, not number of events

Other Information (eg. adjustment, cut-off, etc):

For continuous data

Unit	Treatment group		Control group		Details
	n	Mean (SD)	n	Mean (SD)	

Other relevant data