The effectiveness of lifestyle interventions on type 2 diabetes and gestational diabetes incidence and cardiometabolic outcomes: A systematic review and meta-analysis of evidence from low- and middle-income countries

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Summary

Background As lifestyle modification offers a unique strategy to prevent diabetes, we evaluated the effectiveness of lifestyle interventions in the prevention of type 2 diabetes and gestational diabetes in low- and middle-income countries (LMICs).

Methods We did a systematic literature review and meta-analysis. We searched MEDLINE, Embase, Web of Science, and Cochrane Library for randomised controlled trials published in English, Spanish, French, and Portuguese between 1 January 2000 and 15 June 2022, evaluating multi-target and multi-component lifestyle interventions in at-risk populations conducted in LMICs. The main outcomes were incidence of type 2 diabetes and gestational diabetes, and indicators of glycaemic control. We assessed the methodological quality of the studies using the Cochrane risk of bias tool. Inverse-variance random-effects meta-analyses estimated the overall effect sizes. Sources of heterogeneity and study bias were evaluated. The study protocol was registered in PROSPERO (CRD42021279174).

Findings From 14 330 abstracts, 48 (0·3%) studies with 50 interventions were eligible of which 56% were conducted in lower-middle-income countries, 44% in upper-middle, and none in low-income. 54% of the studies were assessed as moderate risk of bias and 14% as high risk. A median of 246 (IQR 137-511) individuals participated in the interventions with a median duration of 6 (3-12) months. Lifestyle interventions decreased the incidence risk ratio of type 2 diabetes by 25% (0·75 [95% CI 0·61 to 0·91]), and reduced the levels of HbA1c by 0·15% [−0·25 to −0·05], fasting plasma glucose by 3·44 mg/dL [−4·72 to −2·17], and 2-hr glucose tolerance by 4·18 mg/dL [−7·35 to −1·02]. No publication bias was suggested for these outcomes. High levels of heterogeneity ($I^2 \geq$ 81%) were found in most meta-analyses. Exploration using meta-regressions could not identify any explanatory variable, except for fasting glucose for which the quality score of the articles seems to be an effect modifier decreasing slightly the heterogeneity (72%) in the low risk of bias pooled estimate. The effect on gestational diabetes could not be evaluated due to the scarcity of available studies.

Interpretation Comprehensive lifestyle interventions are effective strategies to prevent type 2 diabetes among at-risk populations in LMICs. The heterogeneity identified in our results should be considered when using these interventions to address the onset of type 2 diabetes.

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Keywords: Type 2 diabetes; Gestational diabetes; Prevention; Lifestyle modification; Low - and middle-income countries; Systematic review and meta-analysis

Introduction

Diabetes represents a major public health burden worldwide.[1] In 2021, the International Diabetes Federation (IDF) estimated the global diabetes prevalence,

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Research in context

Evidence before this study

A large body of evidence from research in high-income countries (HICs) supports the effectiveness of lifestyle-based interventions for the promotion of cardiovascular health and the prevention of type 2 diabetes (T2D) and gestational diabetes (GDM). To assess whether these promising effects hold for other settings rather than HICs, we conducted preliminary searches in MEDLINE and PROSPERO databases using keywords for lifestyle interventions, prevention of T2D and GDM, and low-and-middle-income countries (LMICs). We found several intervention studies evaluating lifestyle interventions for the prevention of T2D, however, no systematic review and meta-analysis was found summarizing these interventions and providing robust estimates on health indicators related to T2D and GDM.

Added value of this study

This review and meta-analysis synthesise the findings deriving from randomised controlled trials (RCTs) carried out over the last two decades evaluating lifestyle interventions for the prevention of T2D and GDM in LMICs. Using a standardised and robust methodology, we summarised data from 48 RCTs with 50 interventions for 17 different outcomes, and estimated a significant impact on T2D prevention, as well as an overall positive effect in most other cardiometabolic-related outcomes.

Implications of all the available evidence

Our work, providing the most comprehensive and updated assessment of the available evidence, supports the use of lifestyle-based interventions as effective strategies to delay the onset of T2D and overall improve cardiometabolic health among at-risk populations in LMICs, extending the previous evidence from HICs. Our findings also identified knowledge gaps in terms of the impact of these interventions on the onset of GDM, as well as highlighted the need for more research on LMICs from the African continent.

including type 1 and 2, to be 11% among adults (20-79 years) of which 81% reside in low- and middle-income countries (LMICs).[2] Similarly, the IDF reported an overall prevalence of gestational diabetes mellitus (GDM) of 13%, also with a vast majority of cases occurring in LMICs.[2] Current projections for 2045 show a growth of 16% in the prevalence of diabetes (94% of cases in LMICs),[2] in association with the increasing trend in obesity,[3,4] driven by the epidemiological and nutritional transitions.[5]

In high-income countries (HICs), interventions aiming at improving lifestyle, widely known as diabetes prevention programmes, have become the standard for effective strategies to prevent the onset of T2D by instilling weight management and optimal dietary and physical activity habits.[6–9] Recent results evaluating lifestyle interventions in HICs have reported overall reductions of 22%[10] and 23%[11] in the risk for T2D and GDM, respectively. However, the generalisation of these promising findings to settings other than HICs remains uncertain. Besides, evidence about the impact of lifestyle interventions is often limited to a specific type of setting,[12] interventions or outcomes,[13] or includes few studies.[14] Also, frequently, the interventions are not assessed for the use of multi-target and multi-component strategies, known as the most effective approaches for lifestyle behaviour modifications,[15,16] and the prevention of T2D.[17]

We aimed to conduct a systematic review and meta-analysis to synthesise and quantify the effectiveness of multi-target and multi-component lifestyle interventions in improving T2D and GDM incidence and glycaemic indicators among at-risk populations in LMICs and explore the most influential intervention features. Secondary objectives include determining the effect of lifestyle interventions on cardiometabolic indicators, including anthropometric measurements.

Methods

Preliminary searches of reviews were performed in PubMed-MEDLINE and PROSPERO databases to explore the available literature, identify evidence gaps, and contextualise the development of the research protocol. This research was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[18] and registered in the PROSPERO database (CRD42021279174). The few deviations from the original protocol are presented in the appendix (pp 4).

Search strategy and selection criteria

The systematic searches were conducted in PubMed-MEDLINE, Embase, Web of Science, and the Cochrane Library, for studies published in English, Spanish, French, or Portuguese between 1 January 2000 and 15 June 2022. The search query (appendix pp 4-7) included synonyms and related terms for T2D, GDM, prevention, healthy lifestyle, and the list of LMICs, including low, lower-middle and upper-middle-income, according to the World Bank income classification of 2019.[19] To maximise our ability to find pertinent evidence, we carried out manual searches of citations of the retrieved systematic reviews and, also, the final results of study protocols were searched in MEDLINE. Screening of titles and abstracts and the full-text assessment of retrieved manuscripts were conducted in duplicate and independently by two investigators. Differences were solved by consensus or by consultation with a third author.

Studies were deemed eligible if they complied with the following criteria: 1) Setting: conducted in any country classified as LMICs by the World Bank income classification in 2019.[19] 2) Population: adults presenting at a minimum one risk factor for developing T2D or GDM including: overweight/obesity, central obesity, elevated blood pressure, hyperglycaemia/pre-diabetes, high risk defined by a cardiometabolic score such as Finrisk,[20] pregnant women with a pre-pregnancy body mass index (BMI) greater than 25 kg/m^2, or previous GDM. 3) Intervention: The lifestyle intervention required to have multiple (at least two) targets aiming to promote changes in modifiable risk factors for the prevention of T2D/GDM (i.e. diet, physical activity, weight control, disease awareness, and stress management, among others) and should be delivered through multiple components, for instance, individual/group education or coaching, cooking classes, community-based activities, financial incentives, etc. Only multi-target and multi-component interventions were included as evidence suggest these being the most effective approach for lifestyle modifications.[15–17] 4) Evaluation: randomised controlled trials (RCTs) with an active intervention arm compared to a comparison arm (standard care, minimal intervention or waitlist control condition). 5) Outcomes and effect measure: at least one of the following outcomes: incidence of T2D and/or GDM, glycaemic control change measured as fasting plasma glucose (FPG), 2-hr glucose tolerance, or glycated haemoglobin (HbA1c), anthropometric measurements (body weight, BMI, waist circumference, percentage of body fat or lean mass, etc), or cardiometabolic indicators (systolic and diastolic blood pressures (SBP, DBP), lipid fractions such as total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides to HDL ratio (TG/HDL), triglycerides (TG), insulin, and inflammatory markers, among others). Studies had to report a differential change between the intervention and comparison group in the outcomes of interest and a measure of uncertainty for the reported difference, or enough information to compute them. The exclusion criteria are presented in the appendix (pp 8).

Data extraction

The data extraction of the eligible studies and the quality assessment were carried out in duplicate and individually by two investigators. Data were extracted using a standardised electronic excel template developed by the authors. The information extracted included data on publication details, study design and type of analysis, population characteristics, intervention, and outcomes. More information on data extraction is presented in the appendix (pp 8).

To facilitate the identification of the most influential intervention characteristics accounting for the variability in intervention targets and components, intervention targets and components were classified into categories (appendix pp 8-9). The target categories included 1) healthy lifestyle promotion; 2) cardiometabolic risk factors; 3) prevention of T2D specifically; and 4) health during pregnancy. The component categories entailed A) individual activities; B) group activities; C) technology-based activities; D) environment-related strategies; and E) financial incentives. These categorisations of targets and components were developed to optimise the analyses and were not used for the eligibility criterium of multi-target and multi-component intervention.

The quality of the studies was assessed using the Cochrane risk-of-bias tool for randomised trials version 2 (RoB 2).[21] After the assessment, studies were given a score for each domain as well as an overall score, indicating a low risk, medium, or a high risk of bias. Authors were contacted in case of unclear or missing information, if no response, assumptions agreed upon by all investigators were made (appendix pp 10). Discrepancies in the data extraction and risk of bias assessment between the investigators, although infrequent, were discussed with a third investigator and agreed upon.

In studies assessing more than one intervention, each intervention was considered independent and included in the meta-analyses as separate estimates. When studies reported several follow-up results, the closest follow-up after the intervention was extracted to capture the immediate impact of the intervention. Estimations from the most adjusted model to ascertain the differential change in the outcome (follow-up vs baseline) between the intervention and comparison group (effect size) was extracted when available or calculated based on the information reported. Statistical variability (standard error (SE)) of effect sizes were extracted or calculated based on the provided information, or in the absence of data, assumed based on information provided in the article (appendix pp 11-13). For paired observations without covariance data, a correlation coefficient of 0·9 was used in the absence of loss to follow-up, and 0·5 if the loss to follow-up was reported.

The primary outcomes with their corresponding standardised units were the incidence of T2D or GDM (incidence risk ratio) along with changes in FPG (mg/dL), 2-hr glucose tolerance (mg/dL), and HbA1c (%). Secondary outcomes included changes in anthropometric indicators, namely body weight (kg), body weight gain during pregnancy (kg), BMI (kg/m^2), waist circumference (cm), waist-to-hip ratio, lean mass (kg), and body fat (%). Cardiometabolic outcomes were also considered, including changes in SBP and DBP (mmHg), total cholesterol (mg/dL), LDL (mg/dL), HDL (mg/dL), TG (mg/dL), TG/HDL, fasting insulin (μIU/mL), homeostatic model assessment-estimated insulin resistance (HOMA-IR), and inflammatory markers (tumour necrosis factor (pg/mL), interleukin-6 (pg/mL), c-reactive protein (mg/dL), and apolipoprotein B (mg/dL)).

Data analysis

Details of eligible studies were summarised in evidence tables. Study characteristics and baseline values of participants were quantified by measures of central tendency, mean and standard deviation (SD), or median and interquartile range (IQR). Study-specific estimates for intervention outcomes were pooled using inverse-variance random-effects meta-analyses to calculate the overall effect size with its 95% confidence interval (CI), and also visualised using forest plots. Based on visual inspection of the forest plots of primary outcomes, we carried out sensitivity analyses to evaluate the potential effect of individual study estimates dragging the overall effect size. Also, to provide further insight on a potential differential effect of the interventions on different populations' baseline risks, stratified analyses were performed for different baseline risk profiles for the outcome of FPG. The assessment of potential small study-effect or publication bias was carried out by visual inspection of funnel plots and computation of Egger's tests. When small study-effect or publication bias was suggested, the trim-and-fill method was used to calculate the adjusted pooled effect size. Between-study heterogeneity was assessed by Cochran's Q and I^2 statistics. In the presence of heterogeneity in the pooled effect sizes, univariate and multivariate meta-regressions were conducted to explore pre-specified sources of heterogeneity to further carry out sensitivity analyses. The meta-regressions consisted of the variables age, gender, country income level, continent, the median number of participants, the median duration of intervention, risk of bias, and intervention targets and components. Meta-analyses were conducted for the outcomes with a minimum of four study-specific estimates and meta-regressions only for those pooled effect sizes with substantial levels of heterogeneity (>75%) and with a minimum of nine study-specific estimates. For all analyses, a $p<0.05$ was considered as evidence against the null hypothesis, except for the multivariate meta-regressions where a Bonferroni-adjusted $p<0.001$ was considered to account for multiple comparisons. Statistical analyses were conducted in Stata (release 16/SE), and forest and funnel plots in R 4·1·2 (package *meta*[22]).

Role of funding

This research was supported by internal funds of the Unit of Non-communicable diseases, Department of Public Health, Institute of Tropical Medicine Antwerp.

Results

A total of 14 330 abstracts were identified by our systematic search from which 43 studies met our eligibility criteria. Five additional papers were identified through manual searching of citations from eligible articles, thus 48 studies were included in this meta-analysis (Figure 1). During extraction, two studies were identified reporting the evaluation of more than one eligible intervention,[23,24] resulting in a total of 50 interventions available for analysis. Study characteristics and descriptions of the interventions and main findings of eligible studies are summarised quantitatively in Table 1, and qualitatively reviewed in the appendix (pp 14-23). The majority of the eligible studies were published in the last decade, 2012-2022, (90%), and conducted in lower-middle (56%)[24–50] or upper-middle-income (44%)[23,51–70] countries. No eligible study was found in low-income countries. By continent, the vast majority of studies (84%) were performed in Asia (15 in India,[25,27–29,32,33,35,36,41,42,44,46–48,50] 12 in China,[53–58,60,61,63,66–68] five in Iran,[31,37,40,43,45] two in Thailand,[51,65] Vietnam,[30,49] Bangladesh,[24,32] and Sri Lanka,[26,32] and one in Jordan,[69] Pakistan,[39] and Mongolia[38]), followed (14%) by America (three in Brasil,[52,64,70] two in Colombia,[23,62] and one in Cuba[59]), and only one study (2%) in Africa (Egypt[34]). To define at-risk populations, most studies selected participants with impaired glucose/prediabetes (52%) or presenting a combination of cardiometabolic risks (34%). High BMI (18%), risk of T2D indicated by a risk score, high blood pressure, or previous diagnosis of GDM (12%, 6%, 4%; respectively) were also considered when selecting intervention participants. Interventions had a median number of participants of 246 (IQR 137-511) from which 66·6% (SD 27·7) were female, 33·8 % (SD 27·7) male, with a mean age of 46·3 years (SD 9·7). At baseline, most of the participants were overweight but presented normal glycaemic levels, with an average BMI of 27·3 kg/m^2 (SD 2·7) and an FPG of 99·8 mg/dL (SD 12·3). The characteristics of the participants per group (intervention vs comparator) were comparable in terms of the number of participants, age, gender distribution, BMI, and FPG. The interventions had a median duration of six months (IQR 3-12), and almost all of them include a healthy lifestyle as a target (98%), while prevention of T2D specifically or cardiometabolic risk factors were less frequently reported as a target (24%, and 16%, respectively). Only 4 (8%) interventions explicitly targeted health during pregnancy. Most interventions included individual (94%) and group activities (70%), some added technology-based components (34%), and a few entailed environment-related components (6%). No intervention components related to financial incentives were identified. As per eligibility criteria, all interventions were evaluated using an RCT design with 74% of studies using individually randomisation[23,26–29,32–44,47,50,52–56,59,61–70] and 26% clustered randomisation.[24,25,30,31,45,46,48,49,51,57,58,60] When appraising the risk of bias using RCT-specific tools, 54% of studies were ranked as having medium risk,[23,26,28,29,33,35–37,39,42,43,45–50,53–55,58,60–64] 32% low risk,[24,25,32,38,40,41,44,51,52,56,57,65,67,69,70] and 14% high risk[27,30,31,34,59,66,68] (appendix pp 24). Almost one-third (33%) of studies reported results as intention-to-treat while the rest opted

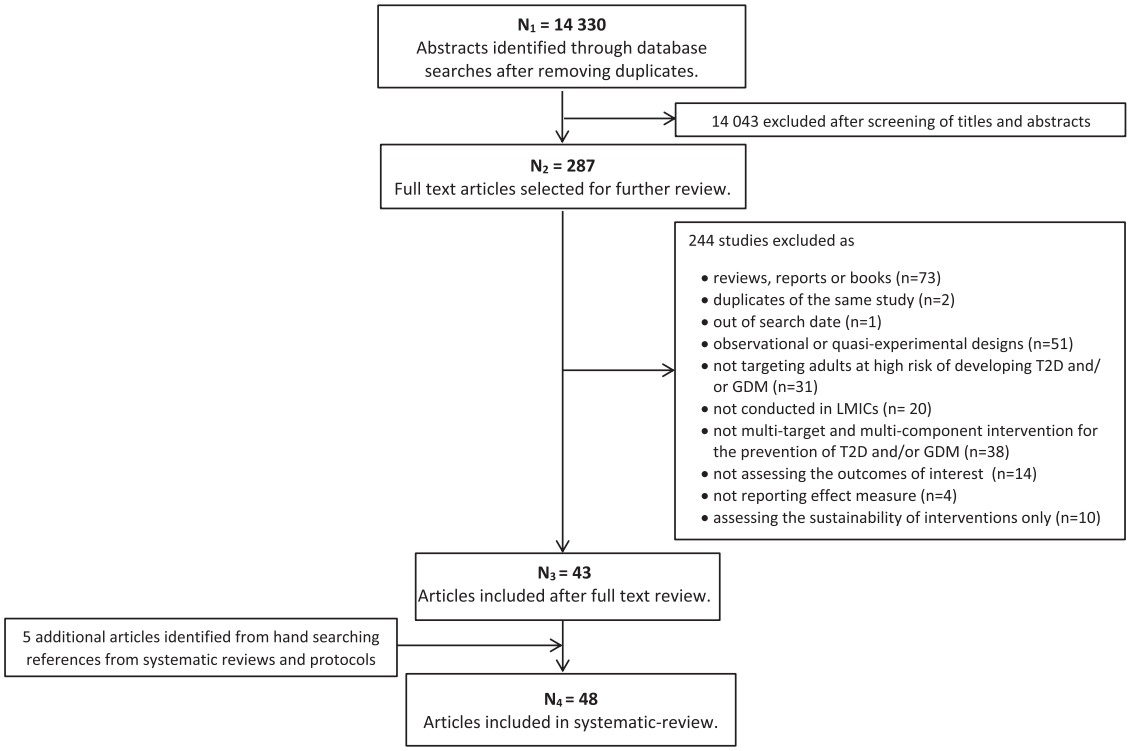

Figure 1. Results of the systematic search strategy and study selection process.

for per-protocol analysis. The interventions had a median loss to follow-up of 15·2% (IQR 8·0-23·7) and no large differences were seen between the intervention and comparison groups (intervention: median 16·2%, IQR 8·8-22·7 vs comparison: median 14·7%, IQR 8·0-25).

The pooled effect sizes for the primary outcomes are presented in Table 2. The median number of participants for these outcomes ranged from 200 participants for FPG to 556 for the incidence of T2D and the duration varied between a median of 6-18 months. All primary outcomes shared the target of a healthy lifestyle and component of individual activities as the most frequent. The meta-analysis of results from 17 interventions, involving a median of 556 participants and 18 months of duration, resulted in a pooled estimated of a 25% decrease in the incidence of T2D (risk ratio (RR): 0·75 [95% CI 0·61 to 0·91]) (Figure 2). A small but statistically significant decrease was also observed for the levels of HbA1c by 0·15% [−0·25 to −0·05] (appendix pp 25) using data from 11 interventions, including a median of 320 participants and six months of duration. Results from 39 interventions over a median of six months and 200 participants revealed a pooled estimate of 3·44 mg/dL [−4·72 to −2·17]) decrease in FPG (Figure 3); similar to the effect found for 2-hr glucose tolerance of 4·18 mg/dL [−7·35 to −1·02] decrease using results from 13 interventions over 12 months of duration, and 434 participants (appendix pp 25). No meaningful changes were observed after exclusion of individual study effects; incidence of T2D (RR: 0·76 [0·62 to 0·93]) excluding the study-specific estimate from Iqbal Hydrie,[39] HbA1c (−0·10 % [−0·19 to −0·01]) excluding Hu,[63] FPG (−3·42 mg/dL [−4·70 to −2·14]) excluding McDermont[42] and Nguyen,[30] and 2-hr glucose tolerance (−3·73 mg/dL [−6·98 to −0·48]) excluding Xu,[61] Snehalatha,[47] and Luo.[55] Stratified analyses according to population's baseline risk profiles showed a larger reduction in FPG (−5·11 mg/dL [−7·85 to −2·36]) after pooling 13 estimates when FPG was altered (≥ 100 mg/dL) at baseline than when FPG was normal (< 100 mg/dL) (−2·76 mg/dL [−4·10 to −1·42]) based on 18 estimates. Moreover, when analysing 15 estimates reporting overweight/obesity (BMI ≥25 kg/m^2) and normal FPG at baseline, a modest reduction in FPG was observed (−2·38 mg/dL [−3·74 to −1·02]).

No evidence of small study-effect or publication bias was suggested by the funnel plots (appendix pp 26-27) and Egger's test for the primary outcomes; incidence of T2D (p = 0·44), HbA1c (p = 0·89), FPG (p = 0·059), and 2-hr glucose tolerance (p = 0·41). For all primary outcomes, substantial levels of heterogeneity were observed ranging between 81% and 99% (p < 0·05). The exploration of potential sources of heterogeneity was conducted for all these outcomes. The meta-regressions corrected for multiple comparisons could not identify a potential source of heterogeneity among the

		All studies (n= 48 RCTs; 50 intervention)
Publication date, n (%)		
	2000−2011	5 (10)
	2012−2022	45 (90)
Setting		
Country income, n (%)		
	Low-income	0 (0)
	Lower-middle-income[a]	28 (56)
	Upper-middle-income[a]	22 (44)
Continent, n (%)		
	America	7 (14)
	Asia	42 (84)
	Africa	1 (2)
Overall participants characteristics		
Type of risk, n (%)[b]		
	Cardiometabolic risk[c]	17 (34)
	Impaired glucose/pre-diabetes	26 (52)
	High BMI	9 (18)
	High score by risk score	6 (12)
	High blood pressure	3 (6)
	High pre-pregnancy BMI	0 (0)
	Previous GDM	2 (4)
Total no. of participants		
Mean (SD)		522 (797)
Median (IQR)		246 (137-511)
Gender, mean (SD)[d]		
	% Female	66·2 (27·7)
	% Male	33·8 (27·7)
Age, years[d]		
Mean (SD)		46·3 (9·7)
Median (IQR)		45·9 (37·8-53·0)
BMI, kg/m^2 [d]		
Mean (SD)		27·3 (2·7)
Median (IQR)		26·6 (25·7-28·7)
FPG, mg/dL[d]		
Mean (SD)		99·8 (12·3)
Median (IQR)		99·2 (93·0-108·2)
Per group participants characteristics		
No. of participants, median (IQR)		
	Intervention group	126 (70-265)
	Comparison group	118 (67-246)
Age, years, median (IQR)		
	Intervention group	46·0 (37·7-52·2)
	Comparison group	46·1 (37·8-53·8)
% Female, mean (SD)		
	Intervention group	67·1 (28·4)
	Comparison group	66·6 (27·9)
% Male, mean (SD)		
	Intervention group	32·9 (28·4)
	Comparison group	33·4 (27·9)
BMI, kg/m^2, mean (SD)		
	Intervention group	27·4 (2·7)
	Comparison group	27·2 (2·6)

Table 1 *(Continued)*

		All studies (n= 48 RCTs; 50 intervention)
FPG, mg/dL, mean (SD)		
	Intervention group	99·5 (12·4)
	Comparison group	100·0 (12·2)
Intervention characteristics		
Duration in months		
Mean (SD)		10·0 (9·5)
Median (IQR)		6 (3.0-12.0)
Targets, n (%)[e]		
	Healthy lifestyle	49 (98)
	Cardiometabolic risk factors	8 (16)
	Prevention T2D specifically	12 (24)
	Health during pregnancy	4 (8)
Components, n (%)[f]		
	Individual activities	47 (94)
	Group activities	35 (70)
	Technology-based	17 (34)
	Environmental	3 (6)
	Financial incentives	0 (0)
Evaluation of interventions		
Unit of randomisation, n(%)		
	Individual	37 (74)
	Cluster	13 (26)
Risk of bias, n (%)[g]		
	Low risk	16 (32)
	Medium	27 (54)
	High risk	7 (14)
Type of analysis, n (%)[h]		
	Intention-to-treat	15 (33)
	Per protocol	31 (67)
Overall lost to follow-up %[h]		
Mean (SD)		17·3 (11·9)
Median (IQR)		15·2 (8·0-23·7)
Per group loss to follow-up %		
median (IQR)	Intervention group	16·2 (8·8-22·7)
	Comparison group	14·7 (8·0-25)

***Table 1*: Demographics and baseline values of the eligible studies.**

Table based on the number of interventions (50). Abbreviations: Body mass index (BMI), fasting plasma glucose (FPG), interquartile range (IQR).

[a] Lower-middle income countries include Bangladesh, Egypt, India, Iran, Mongolia, Pakistan, Sri Lanka, and Vietnam; Upper-middle income countries include Brasil, China, Colombia, Cuba, Jordan, and Thailand.

[b] Type of high risk was classified by the authors and intervention could have more than one type of risk.

[c] Cardiometabolic risks category was chosen if more than one of the following risks: high BMI, hypertension, pre-diabetes and/or central obesity.

[d] Denominator for age (45), gender (43), BMI (41), and FPG (34).

[e] Targets were classified by the authors into categories including, but not limited to, healthy lifestyle promotion (diet and/or physical activity and/or weight control, and/or alcohol and/or smoking); cardiometabolic risk factors (high blood pressure and/or pre-diabetes and/or high BMI, CVD risk factors, smoking, stress, etc); prevention of T2D specifically; health during pregnancy (GDM, healthy weight gain during pregnancy).

[f] Components were classified by the authors into four categories including, but not limited to, the following: individual activities (individual education, individual screening, personalised feedback, use of pedometer, goal-setting, diet self-monitoring); Group activities (group education, focus group, collective physical activity classes, etc); Technology-based activities (SMS, phone calls, newsletter, websites, any web-component); Environment activities (vending machines, cafeteria menus/changes, free snacks, nutrition promotion/signage); Financial incentive activities (economic incentives, economic subsidies, etc).

[g] The risk of bias was determined by the Cochrane risk-of-bias tool for randomised trials version 2 (RoB-2).

[h] Denominator for the overall lost to follow-up is 43 and for type of analysis is 46.

pre-specified covariates for the outcomes incidence of T2D, HbA1c, and 2-hr glucose tolerance (appendix pp 28-29). For FPG, the quality score of the study seems to be a significant effect modifier (p = 0·001). Therefore, a stratified analysis was conducted by categories of the quality score. This analysis showed that the pooled estimate of FPG for those studies with a low risk of bias was smaller (−2·16 mg/dL [−3·87 to −0·44]) and heterogeneity was also lower (72%), while those with medium (−2·80 mg/dL [−3·96 to −1·64]) and high risk

	No· studies (no· interventions)~	No· of participants, median (IQR)	Duration months, median (IQR)	Target, %[a]	Component, %[a]	Pooled effect size (95% CI)[b] **	I^2, %	p asymmetry (Egger's test)
Primary outcomes								
T2D incidence, incidence rate ratio	15 (17)	556 (443 - 1601)	18 (12 - 24)	100[1]	88[a]	0·75 [0·61 to 0·91]	81[c]	0·44
HbA1c, %	11 (11)	320 (120 - 970)	6 (3 - 12)	100[1]	100[a]	-0·15 [-0·25 to -0·05]	94[c]	0·89
Fasting glucose, mg/dL	38 (39)	200 (120 - 443)	6 (3 - 12)	97[1]	97[a]	-3·44 [-4·72 to -2·17]	96[c]	0·059
2-hr glucose tolerance, mg/dL	12 (13)	434 (177 - 576)	12 (9 - 24)	100[1]	100[a]	-4·18 [-7·35 to -1·02]	99[c]	0·41
Secondary outcomes								
Anthropometrics measurements								
Weight, kg	26 (26)	200 (104 - 434)	6 (3 - 11)	100[1]	96[a]	-1·54 [-2·11 to -0·96]	75[c]	0·001
Body mass index, kg/m^2	27 (27)	184 (104 - 272)	6 (3 - 11)	100[1]	96[a]	-0·71 [-0·98 to -0·45]	80[c]	0·11
Body fat, %	6 (6)	105 (58 - 561)	4 (3 - 9)	100[1]	100[ab]	-1·24 [-2·37 to -0·11]	84[c]	0·085
Waist circumference, cm	30 (30)	192 (120 - 443)	6 (4 - 12)	100[1]	93[a]	-1·81 [-2·58 to -1·04]	87[c]	0·81
Waist-to-hip ratio	6 (6)	194 (93 - 337)	6 (4 - 6)	100[1]	100[a]	-0·01 [-0·02 to -0·01]	0	0·80
Cardiometabolic indicators								
Systolic blood pressure, mmHg	29 (29)	225 (122 - 443)	6 (4 — 12)	100[1]	93[a]	-2·55 [-3·75 to -1·35]	86[c]	0·50
Diastolic blood pressure, mmHg	27 (27)	225 (122 - 443)	6 (4 - 12)	100[1]	93[a]	-2·40 [-3·33 to -1·48]	89[c]	0·27
Total cholesterol, mg/dL	23 (23)	200 (120 - 443)	6 (3 - 12)	100[1]	90[a]	-2·57 [-6·86 to 1·71]	90[c]	0·65
LDL, mg/dL	18 (18)	205 (120 - 443)	6 (4 - 12)	100[1]	94[a]	-5·42 [-9·36 to -1·47]	84[c]	0·19
HDL, mg/dL	23 (23)	180 (120 - 337)	6 (3 - 11)	100[1]	91[a]	2·42 [1·01 to 3·83]	92[c]	0·82
Triglycerides, mg/dL	27 (27)	180 (104 - 434)	6 (3 - 11)	100[1]	93[a]	-8·52 [-17·36 to 0·33]	96[c]	<0·001
HOMA-IR	6 (6)	146 (58 - 180)	3·5 (3 - 4)	83[1]	100[ab]	-0·29 [-0·72 to 0·14]	85[c]	0·47
Fasting insulin, μIU/mL	5 (5)	142 (58 - 180)	4 (3 - 9)	80[1]	100[ab]	-0·95 [-1·79 to -0·11]	27	0·70

***Table 2*: Pooled estimates of the effect of lifestyle intervention on the prevention of T2D and GDM.**

Abbreviations: glycated haemoglobin A1c (HbA1c); Low-density lipoprotein cholesterol (LDL); High-density lipoprotein cholesterol (HDL), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Some studies included more than two interventions, which were analysed separately.

[a] Target and component indicate the more frequent category of continent, income, target and component identified by the authors. Target: 1 healthy lifestyle promotion, 2 cardiometabolic risk factors, 3 T2D prevention specifically, 4 health during pregnancy. Component: A Individual activities, B group activities, C technology, D environment, E incentives.

[b] Pooled effect sizes were calculated using inverse-variance random-effects meta-analysis. The p-values of the random effect meta-analysis per outcome are the following: TD2 incidence p=0·004; HbA1c p=0·003; fasting glucose p<0·001; 2-hr glucose tolerance p=0·009; weight p<0·001; body mass index p<0·001; body fat p=0·032; waist circumference p<0·001; waist-to-hip ratio p<0·001; SBP p<0·001; DBP p<0·001; total cholesterol p=0·239; LDL p=0·007; HDL p=0·001; TG p=0·059; HOMA-IR p=0·181; Fasting insulin p=0·027.

[c] p<0·05 for I^2 heterogeneity.

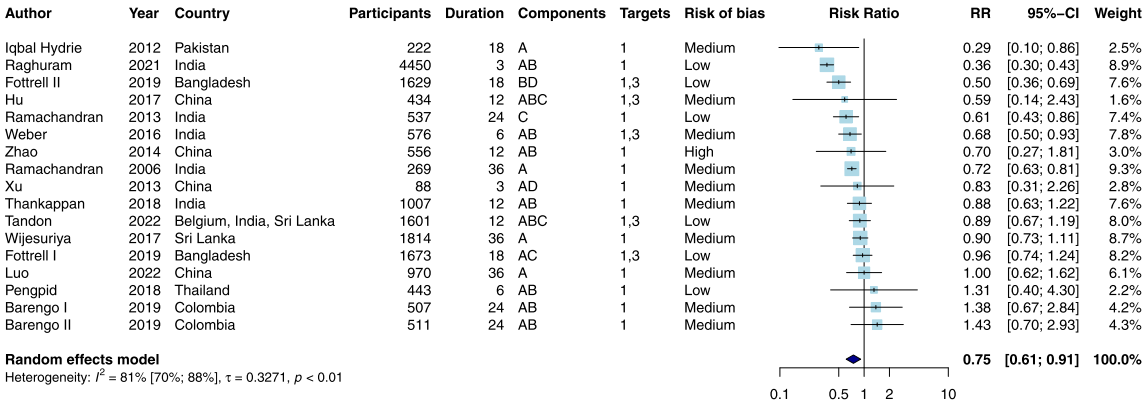

Figure 2. Forest plot of the incidence of T2D (incidence risk ratio).

The duration is provided in months. Fottrell I and II, and Barengo I and II, indicate two different interventions of the same study. Targets: 1 healthy lifestyle promotion, 2 cardiometabolic risk factors, 3 T2D prevention specifically, 4 health during pregnancy. Components: A Individual activities, B group activities, C technology-based, D environmental. An intervention could include multiple targets or components from one specific category and still be considered a multi-target/multi-component intervention, for example, an intervention including only targets of the healthy lifestyle category (diet and physical activity) and only components of the individual activities category (individual education and screening).

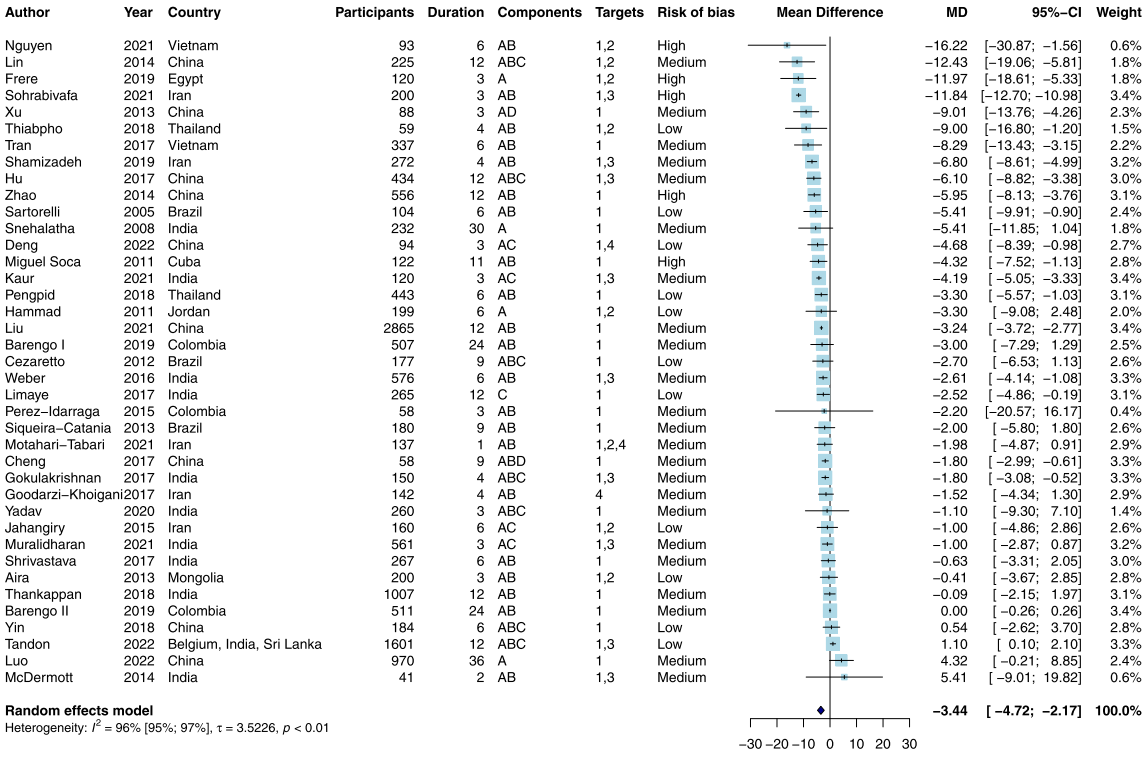

Figure 3. Forest plot for fasting plasma glucose (mg/dL).

The duration is provided in months. Barengo I and II indicate two different interventions of the same study. Targets: 1 healthy lifestyle promotion, 2 cardiometabolic risk factors, 3 T2D prevention specifically, 4 health during pregnancy. Components: A Individual activities, B group activities, C technology-based, D environmental. An intervention could include multiple targets or components from one specific category and still be considered a multi-target/multi-component intervention, for example, an intervention including only targets of the healthy lifestyle category (diet and physical activity) and only components of the individual activities category (individual education and screening).

(−8·82 mg/dL [−13·06 to −4·59]) maintained higher levels of heterogeneity, 93% and 90%, respectively (appendix pp 30).

There were only three interventions that reported the incidence of GDM as a study outcome. A study conducted by Wang and co-workers in China delivered a lifestyle individual education and enforcement based on maternal anthropometrics to 138 pregnant women at high risk for GDM and observed a lower rate of GDM for the intervention group (23/134) than for the control group (33/138), although not statistically significant (p = 0·17).[60] Another RCT from China led by Deng and co-workers. delivered a diet and exercise intervention during the 14 and 24-28 gestational weeks to 47 pregnant women at risk of GDM compared to 47 pregnant women receiving usual care showing a significant reduction in the incidence of GDM (11/46 in the intervention group vs 24/47 in the comparison group; p = 0·007).[56] Similarly, an Iranian study conducted by Motahari-Tabari and co-workers showed a lower incidence of GDM (7/70 for the intervention group and 20/67 for the control group; p = 0·004) after delivering a counselling lifestyle intervention based on the Information-Motivation and Behavioral skills model for the prevention of GDM compared to women receiving usual antenatal care, in women with an elevated BMI (>25 kg/m²).[43]

The pooled effect sizes were significant for all anthropometric indicators including body weight (−1·54 kg [−2·11 to −0·96]), BMI (−0·71 kg/m² [−0·98 to −0·45]), body fat (−1·24 % [−2·37 to −0·11]), waist circumference (−1·81 cm [−2·58 to −1·04]), and waist-to-hip ratio (−0·01 [−0·02 to −0·01]). For other cardiometabolic indicators, significant improvements were observed for SBP (−2·55 mmHg [−3·75 to −1·35]), DBP (−2·40 mmHg [−3·33 to −1·48]), LDL (−5·42 mg/dL [−9·36 to −1·47]), HDL (2·42 mg/dL [1·01 to 3·83), and fasting insulin (−0·95 μIU/mL [−1·79 to −0·11), but not for total cholesterol (−2·57 mg/dL [−6·86 to 1·71]), TG (−8·52 mg/dL [−17·36 to 0·33]), or HOMA-IR (-0·29 [−0·72 to 0·14). Forest plots for all secondary outcomes are presented in the appendix (pp 31-37). Funnel plots for secondary outcomes are presented in the appendix (pp 37-41). Asymmetric funnel plots and Egger's tests suggested potential publication bias or small-study effects for the outcomes of body weight (p = 0·001), and TG (p < 0·001). After fill-and-trim imputations of 12 and 14 estimates for the corresponding outcomes, the adjusted pooled effect sizes showed no effect for body weight (−0·41 kg [−1·02 to 0·20]) while for TG an increase was seen (13·27 mg/dL [5·51 to 21·03]). Significant levels of heterogeneity were observed for most pooled estimates of the secondary outcomes (>75%), except for fasting insulin with moderate levels (27%, p = 0·24) and waist-to-hip ratio for which no heterogeneity was observed, although based on only four estimates. No sensitivity analyses for secondary outcomes were considered needed as the univariate and multivariate meta-regressions of pre-specified potential sources of heterogeneity revealed no significant explanatory variables (appendix pp 42-47).

Due to the limited information identified for the outcomes of weight gain during pregnancy, lean mass, TG/HDL, and inflammatory markers, meta-analyses could not be conducted. Hence, these outcomes were limited to the qualitative assessment of the evidence (appendix pp 14-23).

Discussion

This systematic review and meta-analysis summarised and quantified the evidence published over the last two decades regarding the effectiveness of lifestyle interventions for the prevention of T2D and GDM among at-risk populations in LMICs. Our analyses showed that comprehensive, multi-target and multi-component, lifestyle interventions with a median duration of 18 months, exert an important effect in reducing the risk of T2D incidence by 25%, on average. In conjunction with this finding, improvements in glycaemic levels, and cardiometabolic indicators, including weight and body composition, were also favourably impacted by lifestyle interventions. Contrastingly, a combined effect could not be assessed for GDM due to insufficient studies but the few available evidence also point out a promising impact. However, although combined analyses consistently showed advantageous effects of lifestyle interventions, individual estimates were highly heterogeneous, and no specific explanatory variable or driver of the interventions' effectiveness could be singled out.

To our knowledge, this is the first study that has comprehensively mapped out lifestyle interventions for the prevention of T2D, GDM, and other metabolic health outcomes in LMICs. Reflected by the substantial number of eligible studies, 48 RCTs, the research on preventive strategies, particularly interventions focused on addressing modifiable risk factors, is increasing in LMICs with about 90% of studies published in the last 10 years, mostly from 2017 and 2022. These studies are confirming previous observations from HICs on the effectiveness of lifestyle interventions used as preventive strategies for lifestyle-related diseases. By broadly assessing a wide range of potential outcomes and actionable intervention components, this review contributes to reducing the research gap regarding the availability of evidence coming from settings with constrained resources as well as informing regarding their effectiveness.

Previous reviews summarizing evidence from LMICs are scarce or include few studies. A recent systematic review described positive health effects related to T2D of five non-pharmacological interventions evaluated through RCTs conducted in LMICs, however, was unable to provide pooled estimates due to few eligible

studies.[71] In 2019, Shirinzadeh and co-workers conducted a systematic review and meta-analysis of six RCTs evaluating community-based interventions addressing diet, physical activity, or health behaviour in LMICs showing a reduction in the incidence of diabetes (RR: 0·57 [0·30 to 1·06]) after pooling only three study-specific estimates.[14] Evidence synthesis of lifestyle interventions/T2D prevention programmes in at-risk populations conducted in HICs is in line with our findings. A meta-analysis pooling global evidence, 90% from HICs, on the impact of lifestyle modification for diabetes prevention reported a reduction of 29% (RR: 0·71 [0·58 to 0·88]) after pooling nine RCTs estimates.[72] Similarly, pooled estimates varying in between nine and 13 estimates of controlled trials have suggested reductions in the incidence of T2D of 26% (RR: 0·74 [0·58 to 0·93]),[73] and 47% (RR: 0·53 [0·41 to 0·67]).[74] Other meta-analyses including between ten and 47 RCTs, also carried out in HICs, reported reductions in the incidence of GDM fluctuating between 18-28% after receiving lifestyle interventions.[11,75,76] Aligned with this evidence, our findings extend the body of literature on the benefit of lifestyle interventions in reducing the incidence of T2D in LMICs and highlight the need for further research to evaluate if a similar effect holds for the onset of GDM.

Our findings showed modest improvements for indicators of glycaemic control after a lifestyle intervention of 6-12 months. Also, cardiometabolic indicators such as BMI, waist circumference, blood pressure, LDL and HDL cholesterols, among others, seem to benefit only modestly from lifestyle interventions. In 2021, a systematic review and meta-analysis including 51 RCTs and quasi-experimental studies including populations within LMICs in the Southeast Asian region on the overall prevention of non-communicable diseases reported significant improvements for HbA1c and DBP, however, no effects were seen for FPG, SBP, BMI, body weight, waist circumference, and lipid fractions.[12] Similarly, another systematic review and meta-analysis conducted in 2020, showed significant reductions in FPG, 2-hr glucose tolerance, and HbA1c after pooling nine RCTs investigating the effects of traditional Chinese exercises in patients with prediabetes.[13] Our findings are in accordance with the published evidence and incorporate a synthesis of 48 RCTs conducted in LMICs evaluating lifestyle interventions on cardiometabolic health, hence affording more robust results, and generalising findings to other settings.

This study identified the target of a healthy lifestyle (i.e. diet, physical activity) and components of individual (i.e. personalised feedback) and group activities (i.e. collective physical activity classes) as the most frequently used for the prevention of T2D or GDM. Our heterogeneity exploration did not identify intervention targets or components as potential sources of effect modification, thus the most influential intervention features could not be determined. As an alternative approach, we reviewed the characteristics of the interventions reporting the outcome of T2D incidence that were ranked as low risk of bias and had the greatest weights in the meta-analysis. This approach revealed that an 3-month yoga-based lifestyle intervention reduced the incidence of T2D by 64%[25] while a 12-month lifestyle intervention focused on preventing weight gain after GDM[32] and an 18-month mHealth intervention, encouraging a healthy lifestyle and awareness of T2D,[24] did not have an effect on reducing the onset of T2D. This qualitative analysis exemplifies the heterogeneity in the design of effective interventions and points to the need for contextualised intervention components and overall strategies. More research and development of standardised methods are encouraged, for instance, on the intensity (i.e. hours a week/months of intervention) and participant's adherence to the intervention, to continue identifying the most impactful interventions and facilitate implementation by health policy planners.

As our interest was to investigate the effect of lifestyle interventions on health outcomes related to the prevention of T2D and GDM, we have extracted the outcome data that was assessed immediately after the intervention or with the shortest follow-up time available. Yet, a few follow-up studies addressing the sustainability of long(er)-term effects of lifestyle interventions among the eligible RCTs were identified. Nanditha and co-workers conducted a 3-year follow-up assessment of a 2-year lifestyle intervention conducted in India[44] showing a sustained effect on the incidence of T2D between the two groups, although a common increase in BMI, waist circumference, and blood pressure.[77] Another study assessing the sustainability of a 6-month lifestyle intervention conducted in Thailand[51] revealed no significant difference in the incidence of T2D between the two groups, significant time-group improvements for HDL and LDL, but not for FPG, DBP, SBP and total cholesterol after 1·5-year follow-up assessment.[78] Furthermore, a 30-year follow-up analysis of the landmark Da Qing Diabetes prevention study, a 6-year Chinese RCT conducted in 1986,[79] has reported a significant median delay in the onset of T2D as well as a lower cumulative incidence of T2D in the intervention group compared to the control group.[80] This evidence provides limited insight into the debatable sustainability of the effect of lifestyle interventions. We recommend improving the continuity of lifestyle interventions for the prevention of T2D. Also, we raise the need for these interventions to be integrated as part of usual care, as their effect seems to fade with time,[81] as well as to prioritise the identification of differential effects of these interventions depending on the population's baseline risk factors.

This systematic review and meta-analysis is the largest study to date to estimate the incidence reduction of T2D as a result of lifestyle interventions in LMICs by

combining data from the last two decades. The selection of multi-target and multi-component interventions evidenced as the most effective approach for promoting changes in health behaviour,[15–17] and those evaluated through RCT designs allowed for the evaluation of the most evidence-based, strong designs increasing the robustness of our estimates. We conducted extensive analyses to determine potential sources of heterogeneity and adjusted our estimates for suggested publication bias or small-study effects. However, despite this comprehensive assessment, heterogeneity could not be explained by the pre-determined sources investigated in this research. Defining our own primary and secondary outcomes, we combined study-specific primary and secondary estimates, hence potentially including some underpowered individual estimates. This, however, was considered in the appraisal of the study quality which indeed identified studies where bias was of concern. Nevertheless, the bias score was not identified as an explanatory variable for the heterogeneity of our estimates, except for the outcome of FPG. No eligible study was conducted in low-income countries and also most of the studies were carried out in the Asian continent, hence the generalisation of these findings to any setting classified as LMICs remains questionable. This study did not include process evaluations of the eligible RCTs. These limitations should be taken into account when interpreting the pooled effect sizes.

In conclusion, this systematic review and meta-analysis support lifestyle interventions as effective strategies to reduce the risk of T2D and improve cardiometabolic health among at-risk populations in LMICs. Information on GDM is not yet sufficient to draw a combined estimate. This study encourages further investigation for more robust estimates and the continuation of identification of individual intervention characteristics, to influence their use at larger scales and inform policymakers regarding their effectiveness on lifestyle-related diseases.

Contributors

DS, JP conceptualised and developed the research protocol and methodology; DS, IS, EM developed standardised data extraction tools and underlying calculation algorithms for standardised estimates; DS, IS, EM, JC, CC, JP reviewed literature, selected eligible studies and performed data extraction. DS, IS, JP carried out statistical analysis; DS, IS, EM, JC, JP interpreted results, drafted, reviewed and edited the manuscript; DS, JP supervised the study. DS, IS, JP accessed and verified the data. DS, IS, EM, JC, JP authors have access to the underlying data. DS, JP were responsible for the decision to submit the manuscript for publication. All authors reviewed and approved the final manuscript.

DS, as guarantor of this manuscript, affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained and registered.

Data sharing statement

The data used in this study may be accessible under request by contacting the corresponding author: Diana Sagastume (dsagastume@itg.be).

Declaration of interests

We declare no competing risks.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101650.

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