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Protocol manuscript

The effects of physical activity interventions on the body mass index of children and adolescents in Latin America: a protocol for a systematic review and meta-analysis.

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ABSTRACT.

Introduction: In Latin America, childhood and adolescent overweight and obesity have become a public health problem; for this reason, intervention programs have been implemented, such as physical activity and food education interventions aimed at preventing and treating these weight issues, using the BMI as a mean to know the impact such interventions have made. Nevertheless, no evidence has been found about the effects of these interventions on the BMI; therefore, this study protocol provides a standardised study methodology with a view to determining the effects of physical activity interventions on the BMI of children and adolescents of Latin America.

Methods and analysis: This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). The literature search will be conducted in MEDLINE, EMBASE, Cochrane Library, Web of Science and Scielo. Randomised controlled trials, non-randomised experimental studies and controlled pre–post studies will be included. The Cochrane Collaboration's tool and the Quality Assessment Tool for Quantitative Studies will be used to assess the risk of bias for studies included in the systematic review. Standardised pre-intervention mean differences will be calculated as the primary outcome. Subgroup analyses will be performed based on the characteristics of the interventions and population included in the studies.

Ethics and dissemination: This systematic review will provide updated evidence about the effects of physical activity interventions on Latin American population; such evidence may be useful for the institutions responsible for the development of public health policies and for those in charge of the implementation of this type of interventions among children and adolescents in Latin America.

Results will be disseminated by publication in a peer-reviewed journal. Since data used for this systematic review will be extracted exclusively from published studies, the approval from an ethical committee will not be required.

Prospero registration number: CRD42019077702.

Keywords: physical activity, BMI, Latin America, children and adolescents.

STRENGHTS AND LIMITATIONS OF THIS STUDY.

- This study provides a comprehensive methodology to analyse the effect of physical activity interventions on the BMI.
- Two researchers will independently carry out the study selection, data extraction and quality assessment of the studies found.
- This research might be the first evidence of meta-analysis in Latin America providing scientific information about the effect of physical activity interventions on the BMI.
- Differences among the studies design, sample characteristics, type of physical activity interventions and poor methodological quality may restrict the comparison of the selected studies and negatively affect the quality of the evidence of this systematic review and meta-analysis.

INTRODUCTION

Latin America is a developing region and needs assistance in all aspects; one of the actions to assist development is to promote activities that contribute to address one of the greatest problems affecting the region, such as overweight and obesity, which have significantly increased among children and adolescents in the last decades, becoming a major public health concern. It is estimated that between 20% and 25% of the total Latin American population of children and adolescents are overweight or obese[1]. This situation is worrying, since it has been noted that this condition is maintained during adulthood[2,3], increasing risk factors for cardiovascular disease, increased blood pressure and some types of cancer[4,5] and increasing the possibility of premature death in all causes[6]. Therefore, this is a serious situation that must be worked on in order to prevent the future generations of Latin American society to be affected.

Body Mass Index (BMI) is a method that allows us to quickly know if a person is overweight or obese and it is a good measure to evaluate general adiposity. A high BMI during childhood and adolescence predispose subjects to develop the aforementioned diseases (high blood pressure, high cholesterol levels and type 2 diabetes) and also has become a quite reliable predictor of mortality[7] to such a degree that in 2015 more than 4.5 million deaths worldwide were associated with high values of BMI[8].

Several interventions, including physical activity interventions, nutritional interventions or a combination of both[9,10], have been suggested to mitigate the levels of overweight and obesity. Out of these interventions, physical activity appears to play an important role, contributing to reduce BMI, decrease cardiovascular risk factors and improve cardiorespiratory endurance; all this leading to a reduction of health risk factors[10–13].

Since in Latin America overweight and obesity have become a public health problem, physical activity intervention programs aimed at preventing and treating these negative situations have been implemented. In addition, these interventions have been supplemented by food education, using the BMI as a mean to know the impact these measures have made. Nevertheless, no evidence of meta-analysis addressing this subject in Latin America has been found. However, there are systematic reviews[1,14,15] which do not address the relation of physical activity interventions and their effects on BMI; therefore, it is necessary to pay closer attention to this matter. Consequently, the objective of this methodological study

protocol is to provide Latin America with a procedure which allows us to conduct a systematic review of the effects of physical activity interventions on the BMI, and, at the same time, to collaborate with public health programs related to overweight and obesity.

OBJECTIVE

The purpose of this study protocol is to provide information about a standardised methodology to perform a systematic review and a meta-analysis, with the objective of assessing the effects that physical activity interventions performed in Latin America have on the BMI.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[16] and the Cochrane Collaboration Handbook[17]. This protocol has been previously registered in PROSPERO (registration number: CRD42019077702).

Inclusion/exclusion criteria for study selection

In order to be included in the systematic review, studies must report physical activity interventions which meet the following criteria: 1) studies involving population of a Latin American country; 2) studies including participants aged 4-18 years; 3) studies reporting only a type of physical activity or combined health interventions including nutritional or psychological interventions; 4) randomised controlled trials, non-randomised experimental studies and controlled pre-post studies; 5) studies reporting any type of physical activity (physical endurance, sports or alternative exercise (games, dancing, optimised physical education classes)); 6) studies reporting BMI before and after the intervention; 7) studies written in Spanish, English or Portuguese.

Studies will be excluded when: 1) include participants younger than 4 and older than 18 years old; 2) provide self-reported data; 3) do not report BMI before and/or after the intervention.

Search strategy

The literature search will be conducted in MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science and Scielo databases from their inception. Study records will be managed using the Mendeley reference manager. The search strategy will combine boolean operators from the following relevant concepts: physical activity, physical exercise, fitness,

physical performance, exercise programs, training programs, prevention programs, intervention programs, promotion, strategy, childhood obesity, obese children, obesity, obesity review, obesity prevention (table1). Previous reviews and meta-analyses will be scanned for additional references. Also, relevant references included in the selected studies will be screened as supplemental sources.

Table 1. Search strategy for the MEDILINE database.

"physical activity"	"training programs"	"childhood obesity"
OR	OR	OR
"physical exercise"	"prevention programs"	"obese children"
OR	OR	OR
fitness	"intervention programs"	obesity
OR	OR	OR
"physical performance"	promotion	"obesity review"
OR	OR	OR
"exercise programs"	strategy	"obesity prevention"

Selection of studies and data extraction

All the titles and abstracts of the retrieved articles will be evaluated independently by two researchers, in order to identify eligible studies for this systematic review, that is, that meet the inclusion criteria. Studies will be excluded when they do not meet eligibility criteria. Abstracts not providing enough information related to inclusion/exclusion criteria will be selected to be evaluated through full-text reading. Two reviewers will examine the included and excluded studies to verify the reason for each decision. Inconsistencies in data collection will be resolved by consensus. A third researcher will be asked when consensus is not reached. The process of identification, selection and inclusion/exclusion of articles will be shown using the PRISMA[16] flow chart (Figure 1). In addition, full text of the identified studies will be examined in order to extract the following data: (1) name of the first author; (2) year of publication; (3) country; (4) study design; (5) age of the participants; (6) number of participants; (7) characteristics of the population (normal weight, overweight, obesity); and (8) characteristics of the physical activity interventions. Any disagreement during data extraction will be solved by discussion to reach a consensus.

When necessary, the authors of the potentially eligible studies will be contacted to obtain any missing data.

Assessment of risk of bias in the included studies

Two researchers will independently conduct a quality assessment according to the Cochrane Collaboration Handbook recomendations[17]. Any disagreements will be resolved by discussion and a third reviewer will solve disagreements if consensus is not reached.

The methodological quality of the RCTs will be assessed using the Cochrane Collaboration's tool for assessing risk of bias[18]. This tool evaluates the risk of bias according to six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias.

The Quality Assessment Tool for Quantitative Studies[19] assesses the quality of pre–post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data collection method, withdrawals and drop-outs.

In both quality assessment tools, each domain will be considered as strong, moderate or weak, and studies will be classified as low risk of bias (with no weak ratings), moderate risk of bias (with one weak rating) and high risk of bias (with two or more weak ratings). The agreement rate between reviewers will be reported by calculating kappa statistics.

Statistical analysis

Researchers will summarise the main characteristics of the selected studies, including the general profile of the study, methods, characteristics of the participants of the study and the results on Table 2. Reviewers will decide whether a meta-analysis is possible after data extraction. A minimum of five observations addressing the same specific outcome will be required in order to perform a meta-analysis; when meta-analysis is not feasible, researchers will conduct a narrative synthesis. Studies providing insufficient data to carry out the analyses will be omitted from data synthesis.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

			Population characteristics			Intervention characteristics	
Reference	**Country**	**Study Design**	**Age distribution**	**Sample size**	**Type of population**	**Physical activity intervention**	**Physical activity characteristics**
Author information and year of publication	Country	Design of the study	Age (years) of the participants range or means±SD	Number of participants	Population characteristics (low weight, normo weight, overweight, obesity)	Type of physical activity intervention (leisure-time physical activity, physical activity programme or physical activity counseling)	Definition of physical activity intervention (duration of intervention, number of sessions and duration of each session)

If a meta-analysis is possible, STATA V.14 software will be used to combine the pooled mean differences with 95% confidence intervals (CIs). A fixed-effects model will be used if there is no evidence of heterogeneity; otherwise, a random-effects model will be used. Study heterogeneity will be assessed with the I^2 statistic. I^2 values will be considered as: might not be important (0–40%); may represent moderate heterogeneity (30-60%); may represent substantial heterogeneity (50–90%) and considerable heterogeneity (75–100%), the corresponding p values will also be taken into account[17].

Data from intention-to-treat analyses will be considered whenever available in RCTs. The BMI pre–post intervention mean difference will be the primary indicator of the intervention outcome. Standardised mean differences will be calculated for BMI levels. Additionally, publication bias will be assessed using a funnel plot, according to the method proposed by Egger[20].

Subgroup analysis and meta-regression

Subgroup analyses and meta-regression will be performed considering the main factors which may cause heterogeneity, such as: gender; age (children aged 4-12 years and adolescents aged 12-18 years); country; type of study design; participant population (underweight, normal weight, overweight, obesity); type of intervention (only physical activity or combined with nutritional or psychological interventions); type of physical activity (endurance, sports, games, dancing); length of the intervention (above or below 12

weeks); time of physical activity per week (above or below 150 minutes). Moreover, methodological quality of the selected studies will be considered for additional subgroup analyses.

Sensitivity analysis

Sensitivity analyses will be carry out, removing the included studies one by one from the pooled analyses, to assess the robustness of summary estimates and to detect if any singular study accounts for a large proportion of heterogeneity.

ETHICS AND DISSEMINATION

Given that researchers will not collect primary data for this review, ethical approval will not be required. However, once the outcomes of this systematic review and meta-analysis are disseminated in scientific publications, they will be shared through social networks and will be presented in scientific conferences related to the subject, so that our conclusions contribute to improve the health of Latin American population.

DISCUSSION.

Studies carried out among European and United States population have shown that physical activity interventions are associated with reductions of the BMI and are also an effective way of decreasing the percentage of adipose tissue[10,13]. However, there is no information about the effects of these interventions conducted in Latin America, which geographical, socio-economic and cultural characteristics are inherent to a developing region. Thus, the development of a systematic review and, if possible, a meta-analysis, will enable us to have an overview of the current literature in Latin America about the subject of study, and, at the same time, to contribute to an efficient development of discussions regarding the benefits of physical activity interventions in the region. To this end, the protocol of this systematic review provides a structure for the extraction and synthesis of relevant information.

Another situation that is necessary to bear in mind when performing systematic review is to know if physical activity interventions supplemented by other health interventions, such as nutritional or psychological interventions, lead to a greater reduction of BMI, and to appreciate the prominence of physical activity interventions in the prevention and treatment of overweight and obesity among Latin American children and adolescents.

Among the potential limitations inherent to systematic reviews and meta-analysis we may find: publication bias, information bias, poor statistical analyses, low methodological

quality and inappropriate reporting of methods and findings of the included studies. It is important to keep in mind that these sources of bias will be greater in some countries, due to economic inequalities in the region, which result in an uneven advancement of scientific development in the different countries. Therefore, it is important to properly synthesise the information available in the manuscripts included, so this protocol becomes a necessary text that consolidates methodological structure needed to carry out a systematic review and meta-analysis based on evidence, regarding the effects of physical activity interventions on the BMI of children and adolescents.

In summary, this study will provide updated information which may be useful for public health policy makers and for those responsible for the implementation of this type of interventions among Latin American children and adolescents.

Contributors:

AG-C and IC-R designed the study: AG-C was the principal investigator. AG-C and IC-R were the coordinators of the study. AG-C and AD-G conducted the study. AG-C and IC-R gave statistical and epidemiological support. AG-C wrote the article with the support of IC-R and AD-G. All authors reviewed and approved the final version of the manuscript.

Competing interests:

None declared.

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TABLES LEGENDS.

Table 1. Search strategy for the MEDILINE database.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

FIGURE LEGENDS.

FIGURE 1. PRISMA flow diagram of identification, screening, eligibility and inclusion of studies.

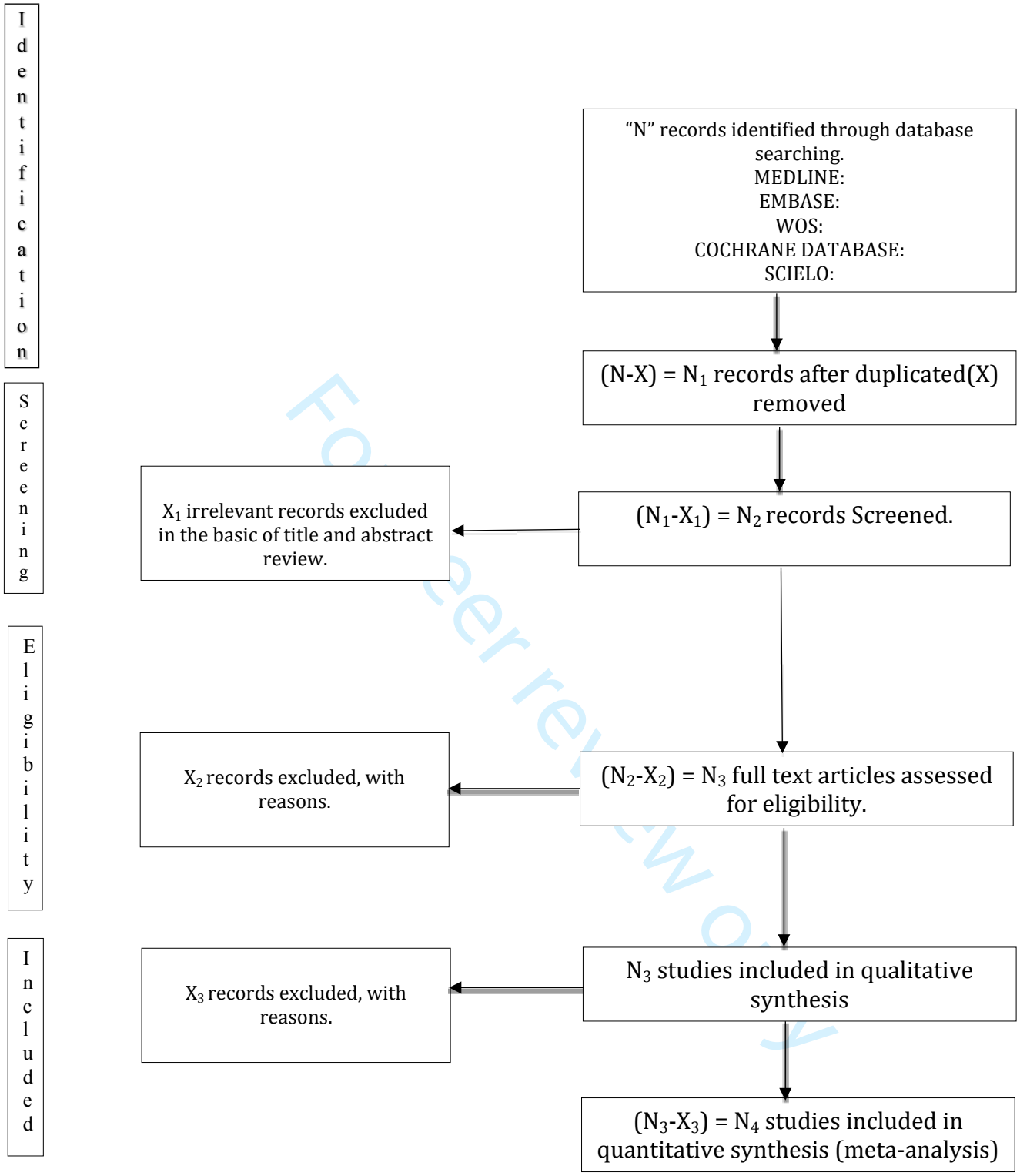

Figure 1. PRISMA flow diagram of identification, screening, eligibility and inclusion of studies.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA.	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact: pp. 1, 10	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p.10	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources: p. 10	5a	Indicate sources of financial or other support for the review
Sponsor: p. 10	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder: p.10	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: p. 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives: p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: p. 5	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources p. 5	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 5, 6	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management: pp. 6, 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process: pp. 6, 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: pp.6,7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: p. 7	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: p. 7	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p.7	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp. 7, 8, 9	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Sports and exercise medicine
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Protocol manuscript

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ABSTRACT.

Introduction: In Latin America, childhood and adolescent overweight and obesity have become a public health problem; for this reason, intervention programs have been implemented, such as physical activity and nutritional interventions aimed at preventing and treating these weight issues, using the BMI as a mean to know the impact such interventions have made. Although in Latin America some systematic reviews have been performed, any of them have meta-analysed the results of the effect of physical activity interventions on BMI. The objective of this protocol is to present a procedure to carry out a systematic review and a meta-analysis of studies on the effect of physical activity interventions on BMI in Latin American children and adolescents aged 4 to 18 years.

Methods and analysis: This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). The literature search will be conducted in MEDLINE, EMBASE, Cochrane Library, Web of Science and Scielo from their inception until December 2018. Randomised controlled trials (RCTs), non-randomised experimental studies and single-arm pre-post studies will be included. The Cochrane Collaboration's tool for RCTs studies and the Quality Assessment Tool for Quantitative Studies for non-randomised experimental studies and single-arm pre-post studies will be used to assess the risk of bias for studies included in the systematic review. Standardised pre-intervention mean differences will be calculated as the primary outcome. Subgroup analyses will be performed based on the characteristics of the interventions and population included in the studies.

Ethics and dissemination: This systematic review will provide updated evidence about the effects of physical activity interventions on Latin American population; such evidence may be useful for the institutions responsible for the development of public health policies and for those in charge of the implementation of this type of interventions among children and adolescents in Latin America.

Results will be disseminated by publication in a peer-reviewed journal. Since data used for this systematic review will be extracted exclusively from published studies, the approval from an ethical committee will not be required.

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STRENGHTS AND LIMITATIONS OF THIS STUDY.

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- Two researchers will independently carry out the study selection, data extraction and quality assessment of the studies found.
- This research might be the first evidence of meta-analysis in Latin America providing scientific information about the effect of physical activity interventions on the BMI.
- Differences among the studies design, sample characteristics, type of physical activity interventions and poor methodological quality may restrict the comparison of the selected studies and negatively affect the quality of the evidence of this systematic review and meta-analysis.

INTRODUCTION

Latin America is a developing region and needs assistance in all aspects; one of the actions to assist development is to promote activities that contribute to address one of the greatest problems affecting the region, such as overweight and obesity, which have significantly increased among children and adolescents in the last decades, becoming a major public health concern. It is estimated that between 20% and 25% of the total Latin American population of children and adolescents are overweight or obese[1]. This situation is worrying, since it has been noted that this condition is maintained during adulthood[2,3], increasing risk factors for cardiovascular disease, increased blood pressure and some types of cancer[4,5] and increasing the possibility of premature all cause mortality[6]. Therefore, this is a serious situation that must be worked on in order to prevent the future generations of Latin American society to be affected.

Body Mass Index (BMI) is a method that allows us to quickly know if a person is overweight or obese and it is a measure to evaluate general adiposity[7-9]. There is evidence that reflects that in low-income countries (most of in Latin America countries) in the last 3 decades there has been an increase in BMI values in children and adults, a situation that mainly affects women[10]. A high BMI during childhood and adolescence predispose subjects to develop the aforementioned diseases (high blood pressure, high cholesterol levels and type 2 diabetes) and also has become a quite reliable predictor of mortality[11] to such a degree that in 2015 more than 4.5 million deaths worldwide were associated with high values of BMI[12].

Several interventions, including physical activity interventions, nutritional interventions or a combination of both[13,14], have been suggested to mitigate the levels of overweight and obesity. Out of these interventions, physical activity appears to play an important role, contributing to reduce BMI, decrease cardiovascular risk factors and improve cardiorespiratory endurance; all this leading to a reduction of health risk factors[14-17].

Since in Latin America overweight and obesity have become a public health problem, physical activity intervention programs aimed at preventing and treating these negative situations have been implemented. In addition, these interventions have been supplemented by nutritional interventions, using the BMI as a mean to know the impact these measures have made. Although in Latin America some systematic reviews have been performed[1,18,19],

any of them have meta-analyzed the results of the effect of physical activity interventions on BMI. Therefore, the purpose of this protocol is to provide the methodology for a meta-analysis in order to synthetize the effect of physical activity interventions on BMI in Latin American children and adolescents.

Therefore, it is necessary to pay closer attention to this matter. Consequently, this study protocol can be collaborate with public health programs related to overweight and obesity.

OBJECTIVE

The objective of this protocol is to present a procedure to carry out a systematic review and a meta-analysis of studies on the effect of physical activity interventions on BMI in Latin American children and adolescents aged 4 to 18 years.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[20] and the Cochrane Collaboration Handbook[21]. This protocol has been previously registered in PROSPERO (registration number: CRD42019077702).

Patient and Public Involvement

No patient involved.

Search strategy

The literature search will be conducted in MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science and Scielo databases from their inception until December 2018.

Searches for unpublished studies will be conducted at: OPEN GRAY, ProQuest dissertations & Thesis Global, Theseo, Networked digital library of theses and dissertations (NDLTD), and Google Scholar. A search of ClinicalTrials.gov and EudraCT clinical trial records will also be conducted. The literature search will be complemented by screening references included in the articles considered eligible for the systematic review. Study records will be managed using the Mendeley reference manager. The search strategy will include the following free text terms combining Boolean operators from the following

relevant concepts (Table 1): physical activity, physical exercise, fitness, physical performance, exercise program, exercise programme, exercise, training program, training programme, prevention program, prevention programme, intervention program, intervention programme, promotion, strategy, childhood obesity, obese children, obesity, obesity review, obesity prevention, BMI, underweight, normal weight, overweight, obesity, studies, randomised controlled trials, RCT, non-randomised experimental, single-arm pre-post (Table1). Previous reviews and meta-analyses will be scanned for additional references. Also, relevant references included in the selected studies will be screened as supplemental sources.

Table 1. Search strategy for the MEDILINE database.

"physical activity"		"training program"		"chilhood obesity"		BMI		studies
OR		OR		OR		OR		OR
"physical exercise"		"training programme"		"obese children"		underweight		"randomised controlled trials"
OR		OR		OR		OR		OR
fitness		"prevention program"		obesity		"normal weight"		RCT
OR		OR		OR		OR		OR
"physical performance"	AND	"prevention programme"	AND	"obesity review"	AND	overweight	AND	"non-randomised experimental"
OR		OR		OR		OR		OR
"exercise programs"		"intervention program"		"obesity prevention"		obesity		"single-arm pre-post"
OR		OR						
exercise		"intervention programme"						
		OR						
		promotion						
		OR						
		strategy						

Inclusion/exclusion criteria for study selection

In order to be included in the systematic review, studies must report physical activity interventions which meet the following criteria: 1) studies involving population of a Latin American country; 2) studies including participants aged 4-18 years; 3) studies reporting only one type of physical activity (physical endurance, sports or alternative exercise (games, dancing, optimised physical education classes), which may or may not have included nutritional health interventions; 4) randomised controlled trials (RCTs), non-randomised experimental studies and single-arm pre-post studies; 5) studies reporting BMI before and after the intervention; 6) studies written in Spanish, English or Portuguese.

Studies will be excluded when: 1) include participants younger than 4 and older than 18 years old; 2) provide self-reported data; 3) do not report BMI before and/or after the intervention.

In case of finding studies with another age range, but in which population data between 4 and 18 years are available, they will be included in the analysis.

Selection of studies

All the titles and abstracts of the retrieved articles will be evaluated independently by two researchers, in order to identify eligible studies for this systematic review, that is, that meet the inclusion criteria. Also, this first review will be done to identify and exclude duplicate documents. Abstracts not providing enough information related to inclusion/exclusion criteria will be selected to be evaluated through full-text reading. Each author will extract the data of the same five studies, and then they will compare the extraction and will agree which data they will include in the Table of Characteristics of studies included**.** Two reviewers will examine the included and excluded studies to verify the reason for each decision. The inconsistencies in the selection will be resolved with a third researcher.

Data extraction

The process of identification, selection and inclusion/exclusion of articles will be shown using the PRISMA[20] flow chart (Figure 1). In addition, full text of the identified studies

will be examined in order to extract the following data: (1) name of the first author; (2) year of publication; (3) country; (4) study design; (5) age of the participants; (6) number of participants; (7) characteristics of the population (normal weight, overweight, obesity); (8) Type of physical activity intervention (leisure-time physical activity, physical activity programs or physical activity counseling); (9) characteristics of the physical activity (length of intervention, number of sessions, duration of each session, type of physical measurement [ie. Physical activity scale, accelerometer or pedometer]); (10) type of nutritional intervention (food education, nutritional counseling, diet intervention); and (11) Nutritional intervention characteristics (length of intervention). When necessary, the authors of the potentially eligible studies will be contacted to obtain any missing data.

Assessment of risk of bias in the included studies

Two researchers will independently conduct a quality assessment according to the Cochrane Collaboration Handbook recomendations[21]. Any disagreements will be resolved by discussion and a third reviewer will solve disagreements if consensus is not reached.

The methodological quality of the RCTs will be assessed using the Cochrane Collaboration's tool for assessing risk of bias[22]. This tool evaluates the risk of bias according to six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias.

The Quality Assessment Tool for Quantitative Studies[23] assesses the quality of pre–post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data collection method, withdrawals and drop-outs.

In both quality assessment tools, each domain will be considered as strong, moderate or weak, and studies will be classified as low risk of bias (with no weak ratings), moderate risk of bias (with one weak rating) and high risk of bias (with two or more weak ratings). The agreement rate between reviewers will be reported by calculating kappa statistics.

Statistical analysis

Researchers will summarise the main characteristics of the selected studies, including the general profile of the study, methods, characteristics of the participants of the study and the results on Table 2. A narrative synthesis of the data extracted in Table of characteristics of

the studies included will be conducted, then a meta-analysis will be performed based on studies that show BMI pre-post intervention. Separating studies that included physical activity interventions from those in which physical activity and nutritional health are combined. Studies providing insufficient data to carry out the analyses will be included in the systematic review but omitted from meta-analysis.

If a meta-analysis is possible, STATA V.14 software will be used to combine the pooled mean differences with 95% confidence intervals (CIs). A fixed-effects model will be used if there is no evidence of heterogeneity; otherwise, a random-effects model will be used. Study heterogeneity will be assessed with the I^2 statistic. I^2 values will be considered as: might not be important (0–40%); may represent moderate heterogeneity (30-60%); may represent substantial heterogeneity (50–90%) and considerable heterogeneity (75–100%), the corresponding *p*-values will also be taken into account[21].

Data from intention-to-treat analyses will be considered whenever available in RCTs. Two analysis will be performed: 1) BMI mean difference pre–post intervention from Physical activity intervention versus control, and 2) BMI mean difference pre-post Physical activity intervention. Standardised mean differences will be calculated for BMI levels. Additionally, publication bias will be assessed using a funnel plot, according to the method proposed by Egger[24].

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

Population characteristics						Intervention characteristics			
Reference	**Country**	**Study Design**	**Age distribution**	**Sample size**	**Type of population**	**Physical activity intervention**	**Physical activity characteristics**	**Nutritional intervention**	**Nutritional characteristics**
Author information and year of publication	Country	Design of the study	Age (years) of the participants range or means±SD	Number of participants	Population characteristics (low weight, normal weight, overweight, obesity)	Type of physical activity intervention (leisure-time physical activity, physical activity programs or physical activity counseling)	Definition of physical activity intervention (length of intervention, number of sessions, duration of each session, type of physical measurement [ie. Physical activity scale,	Type of nutritional intervention (food education, nutritional counseling, diet intervention)	Definition of nutritional intervention (length of intervention).

accelerometer
or pedometer])

Subgroup analysis and meta-regression

Subgroup analyses and meta-regression will be performed considering the main factors which may cause heterogeneity, such as: gender; age (children aged 4-12 years and adolescents aged 12-18 years); type of population (general population or native population); country; type of study design; participant population (underweight, normal weight, overweight, obesity); type of intervention (only physical activity or combined with nutritional interventions); type of physical activity (endurance, sports, games, dancing, lifestyle physical activity interventions); length of the intervention (above or below 12 weeks); duration of physical activity per week (above or below 150 minutes). Moreover, methodological quality of the selected studies will be considered for additional subgroup analyses.

Sensitivity analysis

Sensitivity analyses will be carry out, removing the included studies one by one from the pooled analyses, to assess the robustness of summary estimates and to detect if any singular study accounts for a large proportion of heterogeneity.

ETHICS AND DISSEMINATION

Given that researchers will not collect primary data for this review, ethical approval will not be required. However, once the outcomes of this systematic review and meta-analysis are disseminated in scientific publications, they will be shared through social networks and will be presented in scientific conferences related to the subject, so that our conclusions contribute to improve the health of Latin American population.

DISCUSSION.

Studies carried out among European and United States population have shown that physical activity interventions are associated with reductions of the BMI and are also an effective way of decreasing the percentage of adipose tissue[14,17]. However, there is no information about the effects of these interventions conducted in Latin America, which geographical,

socio-economic and cultural characteristics are inherent to a developing region. Thus, the development of a systematic review and, if possible, a meta-analysis, will enable us to have an overview of the current literature in Latin America about the subject of study, and, at the same time, to contribute to an efficient development of discussions regarding the benefits of physical activity interventions in the region. To this end, the protocol of this systematic review provides a structure for the extraction and synthesis of relevant information. This could allow knowing which type of interventions bring the best benefits to reduce the values of BMI, considering the setting (schools, health care centres or others), type of population (according to their nutritional status), intensity, duration and number of sessions.

Other issues that should be highlighted when performing this systematic review are whether the study design (RCTs, non-randomised experimental studies and single-arm pre-post studies) could affect the results as it has been reported in previous studies[25,26] as well as physical activity interventions supplemented by other health interventions, such as nutritional interventions, lead to a greater reduction of BMI. These considerations will allow us to check the prominence of physical activity interventions in the prevention and treatment of overweight and obesity among Latin American children and adolescents.

Among the potential limitations inherent to systematic reviews and meta-analysis we may find: publication bias, information bias, poor statistical analyses, low methodological quality and inappropriate reporting of methods and findings of the included studies. It is important to keep in mind that these sources of bias will be greater in some countries, due to economic inequalities in the region, which result in an uneven advancement of scientific development in the different countries. Therefore, it is important to properly synthesise the information available in the manuscripts included, so this protocol becomes a necessary text that consolidates methodological structure needed to carry out a systematic review and meta-analysis based on evidence, regarding the effects of physical activity interventions on the BMI of children and adolescents.

As a conclusion, this study will provide updated information which may be useful for public health policy makers and for those responsible for the implementation of this type of interventions among Latin American children and adolescents.

Contributors:

AG-C and IC-R designed the study: AG-C was the principal investigator. AG-C and IC-R were the coordinators of the study. AG-C and AD-G conducted the study. AG-C, CA-B, VM-V and IC-R gave statistical and epidemiological support. AG-C wrote the article with the support of IC-R, CA-B, VM-V and AD-G. All authors reviewed and approved the final version of the manuscript.

Competing interests:

None declared.

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TABLES LEGENDS.

Table 1. Search strategy for the MEDILINE database.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

FIGURE LEGENDS.

FIGURE 1. PRISMA flow diagram of identification, screening, eligibility and inclusion of studies.

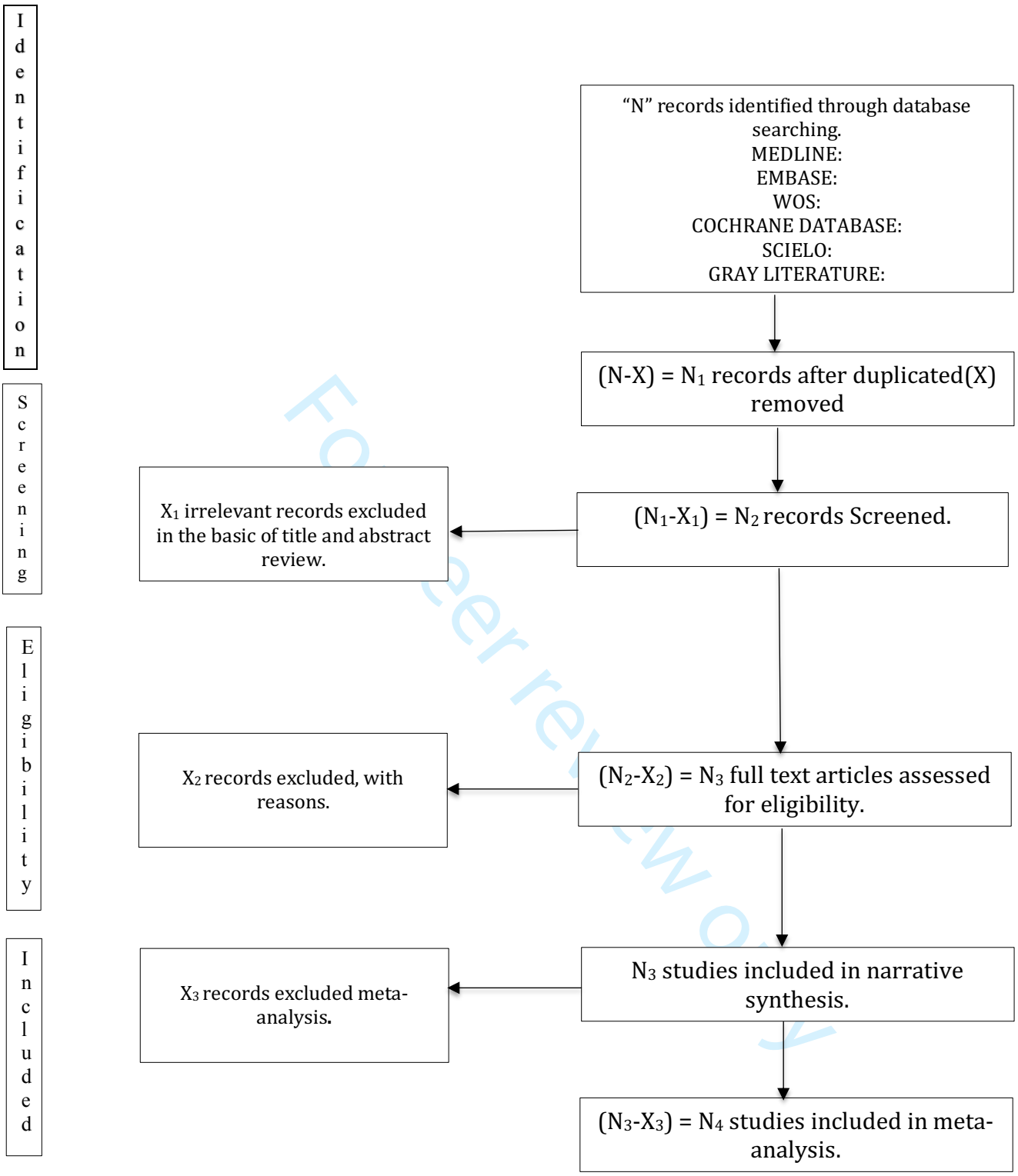

Figure 1. PRISMA flow diagram of identification, screening, eligibility and inclusion of studies.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA.	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact: pp. 1, 10	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p.10	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources: p. 10	5a	Indicate sources of financial or other support for the review
Sponsor: p. 10	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder: p.10	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: p. 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives: p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: p. 5	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources p. 5	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 5, 6	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management: pp. 6, 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process: pp. 6, 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: pp.6,7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: p. 7	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: p. 7	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p.7	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp. 7, 8, 9	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for systematic reviews and meta-analyses

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Secondary Subject Heading:	Sports and exercise medicine
Keywords:	BMI, Latin America, Children, Adolescents, Physical activity

Protocol manuscript

Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for systematic reviews and meta-analyses

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ABSTRACT.

Introduction: In Latin America, the number of children and adolescents who are overweight or obese has significantly increased in recent decades, and this situation has become a major public-health concern. To address this problem, several intervention programmes, based on factors such as physical activity and nutrition, have been implemented, and body mass index (BMI) has been widely used as a means of measuring the impact of such interventions**.** Although some Latin-America-based systematic reviews have been performed, there have been no previous meta-analyses of findings regarding the effect of physical-activity interventions on BMI. Considering this, the objective of this study protocol is to provide a standardised and transparent methodology for performing systematic reviews and meta-analyses of study findings regarding the effect physical-activity interventions have on BMI of Latin American children and adolescents aged four to 18 years.

Methods and analysis: This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement. The literature search will involve MEDLINE, EMBASE, Cochrane Library, Web of Science and Scielo for articles published up to July 2019. This search will include randomised controlled trials (RCTs), non-randomised experimental studies, and single-arm pre-post studies. Further, the Cochrane Collaboration's tool for RCT studies and the Quality Assessment Tool for Quantitative Studies for non-randomised experimental and single-arm pre-post studies will be used to assess the risk of bias among the studies included in the systematic review. For the meta-analysis, the statistical program STATA V.14 will be used, and standardised mean differences are calculated as the primary outcomes. Subgroup analyses will then be performed based on the characteristics of the interventions and populations included in the studies examined.

Ethics and dissemination: This systematic review protocol is designed to provide updated evidence regarding the effects of physical-activity interventions on the Latin American population; such evidence may be useful for institutions responsible for the development of public-health policies and for those tasked with implementing such interventions among children and adolescents in Latin America.

The results should be disseminated through publication in a peer-reviewed journal. Since the data used in systematic reviews of this type will be extracted exclusively from published studies, approval from an ethics committee will not be required.

Prospero registration number: CRD42019077702.

Keywords: physical activity, BMI, Latin America, children and adolescents.

STRENGTHS AND LIMITATIONS OF THIS STUDY.

- This study provides a comprehensive methodology for analysing the effect of physical-activity interventions on BMI.
- In the protocol, two researchers will independently perform the study selection, data extraction, and quality assessments.
- This research may produce the first Latin-America-based meta-analysis that provides scientific information regarding the effect of physical-activity interventions on BMI.
- Differences among the study designs, sample characteristics, types of physical-activity interventions, and poor methodological quality may restrict comparison of the selected studies and negatively affect the quality of the evidence obtained through associated systematic reviews and meta-analyses.

INTRODUCTION

In Latin America, levels of overweight and obesity among children and adolescents have significantly increased in recent decades, and this issue has now become a major public-health concern[1,2]. A tool that facilitates a quick assessment of whether a person is overweight or obese, as well as their level of general adiposity, is body mass index (BMI)[3-5]. As a result of BMI-based assessments, it is now estimated that between 20% and 25% of the total Latin-American population of children and adolescents are overweight or obese[5]. This is a worrying situation, as studies have suggested that these conditions are maintained into and during adulthood[6,7], and that they increase risk factors for cardiovascular disease, high blood pressure, some types of cancer[8,9], and all causes of premature mortality[10]. In fact, BMI has become such a reliable predictor of mortality[11] that in 2015 over 4.5 million deaths worldwide were associated with high BMI values[12].

However, in children and adolescents BMI values should be used and interpreted cautiously, as there is evidence that, although such values are useful for classifying adiposity[13], they can be a poor measure of changes in adiposity[14]. Moreover, childhood weight gain can generally be attributed to fat-free mass rather than fat mass, and this means that BMI is unable to precisely reflect changes that occur over time[15], particularly in adolescent males and children with low BMI[16].

Physical activity plays an important role in reducing BMI, along with lowering risk factors for cardiovascular disease and improving cardiorespiratory fitness; this, in turn, leads to a reduction in risk factors for overall health[17-20]. As a result of these benefits, researchers have implemented physical-activity-focussed interventions, nutritional-focussed interventions, or a combination of both[20,21], and have used BMI to measure their effect. Underlining this approach, previous systematic reviews performed in Latin America have shown that, while few studies have implemented physical-activity interventions to treat overweight and obesity, the implementation of physical-education policies and programmes is necessary to promote children's and adolescents' health, because these interventions can effectively create positive changes among this population[1,22,23]. However, there have been no previous Latin-America-based meta-analyses of the effects physical-activity interventions have on BMI. Considering this, the present study aims to attract more

attention to the necessity of such interventions, and to generate evidence that can encourage changes in public policy that can contribute to addressing this public-health crisis.

OBJECTIVE

This study protocol seeks to provide a standardised and transparent methodology for performing systematic reviews and meta-analyses of findings concerning the effect physical-activity interventions have on BMI of Latin American children and adolescents aged four to 18 years.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement[24] and the Cochrane Collaboration Handbook[25]. This protocol has previously been registered in PROSPERO (registration number: CRD42019077702).

Inclusion/exclusion criteria for study selection

For this protocol, in order to be included in associated systematic reviews studies must have reported physical-activity interventions that meet the following criteria: 1) involving the population of a Latin American country; 2) including participants aged 4–18 years; 3) reporting any type of physical activity (physical endurance, sports, or alternative exercise [e.g. games, dancing, optimised physical education classes], which may or may not have included nutritional interventions); 4) being a randomised controlled trial (RCT), non-randomised experimental study, or single-arm pre-post study; 5) reporting BMI both before and after the intervention; 6) written in Spanish, English, or Portuguese; and 7) published before July 2019.

Meanwhile, the following exclusion criteria will be set: 1) only including participants younger than four or older than 18 years old; 2) providing self-reported data for BMI.

Studies that feature different age ranges, but that nevertheless include population data for the ages of four to 18 years, will be included in the analysis.

Search strategy

Literature searches will be conducted through the MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science, and Scielo databases.

Meanwhile, searches for unpublished studies will be conducted using OPEN GRAY, ProQuest Dissertations & Thesis Global, Theseo, Networked Digital Library of Theses and Dissertations, and Google Scholar. Further, a search of ClinicalTrials.gov and EudraCT clinical trial records will also be conducted. The literature search will be complemented by screening references included in articles that are considered eligible for systematic review. Study records will then be managed using the Mendeley reference manager. The search strategy will include free text terms, combining Boolean operators from the relevant concepts presented in Table 1. Previous reviews and meta-analyses will also be scanned for additional references. Finally, relevant references included in the selected studies will be screened as supplemental sources.

Table 1. Search strategy for the MEDILINE database.

physical activity [tw]		training program* [tiab]		chilhood obesity [tiab]		underweight [tw]		studies [tiab]
OR		OR		OR		OR		OR
physical exercise [tw]		prevention program* [tiab]		obese children [tiab]		normal weight [tw]		randomised controlled trials [tiab]
OR		OR		OR		OR		OR
physical performance [tw]		intervention program* [tiab]		obesity prevention [tiab]		overweight [tw]		RCT [tiab]
OR		OR		OR		OR		OR
exercise program* [tiab]	AND	promotion [tw]	AND	obesity review [tiab]	AND	BMI [tiab]	AND	non-randomised experimental [tiab]
OR		OR		OR		OR		OR
physical fitness [mh]		strategy [tw]		paediatric obesity [mh]		obesity [tiab]		single-arm pre-post [tiab]
OR						OR		
exercise [mh]						body mass index [mh]		

mh: MeSH terms; tiab: title/abstract; tw: text word. * is used to search for or all terms that begin with a word (e.g. 'training program*' would return results such as 'training programs' and 'training programme'

Study selection

After excluding duplicated records, two researchers will independently evaluate the titles and abstracts of the retrieved articles in order to identify eligible studies for the systematic review. Abstracts that do not provide sufficient information regarding inclusion/exclusion criteria will then be evaluated through a full-text reading. Then, two researchers will examine the included and excluded studies to verify the reason for each decision. Inconsistencies between these two researchers regarding selection will be resolved by a third researcher, who will make the final decision, always based on the inclusion/exclusion criteria.

Data extraction

The process of identification, selection, and the inclusion/exclusion of articles will follow the PRISMA[24] flow chart (shown in Figure 1). For the first five studies, the extraction tool will be operated by all researchers; this is performed to ensure that the data extraction is consistent and to create a 'Table of Characteristics' (Table 2). In addition, the full texts of the identified studies will be examined to extract the following data: (1) name of the first author; (2) year of publication; (3) country; (4) study design; (5) participants' ages; (6) number of participants; (7) population characteristics (normal weight, overweight, obesity); (8) type of physical-activity intervention (leisure-time physical activity, lifestyle physical activity, physical-activity programme, or physical activity counselling); (9) characteristics of the physical activity in question (length of intervention, intervention setting, number of sessions, duration of each session, type of physical measurement applied [i.e. physical-activity scale, accelerometer, or pedometer]); (10) type of nutritional intervention (food education, nutritional counselling, diet intervention); and (11) characteristics of this nutritional intervention (length of intervention). When necessary, the authors of potentially eligible studies will be contacted to obtain any missing data.

Assessment of risk of bias in the included studies

Two researchers will independently conduct a quality assessment, following the Cochrane Collaboration Handbook recommendations[25]. Any disagreements will be resolved through discussion and, if a consensus cannot be reached, a third reviewer will intervene to resolve the disagreement.

The methodological quality of the RCTs will be assessed using the Cochrane Collaboration's tool for assessing risk of bias[26]. This tool evaluates risk of bias in terms of six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.

Meanwhile, the Quality Assessment Tool for Quantitative Studies[27] will be used to assess the quality of pre-post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data-collection method, withdrawals, and drop-outs.

In both quality-assessment tools, each domain is considered 'strong', 'moderate', or 'weak' and, based on this, studies will be classified as having a low risk of bias (with no weak ratings), a moderate risk of bias (with one weak rating), or a high risk of bias (with two or more weak ratings). The agreement rate between reviewers will be reported by calculating kappa statistics.

Statistical analysis

Researchers will summarise the main characteristics of each selected study, including the general profile of the study, the methods, the characteristics of the study participants, and the results (as shown in Table 2). A narrative synthesis of the data extracted in the Table of Characteristics for the included studies will be conducted, and then a meta-analysis will be performed on studies that featured BMI pre-post interventions (separating studies that included physical-activity interventions from those in which physical activity and nutritional health were combined). Studies providing insufficient data to perform such analyses will be included in the systematic review, but will be omitted from the meta-analysis.

For studies for which a meta-analysis is appropriate, STATA V.14 software will be used to combine the pooled mean differences with 95% confidence intervals. If there is no evidence of heterogeneity, a fixed-effects model will be used; otherwise, a random-effects model will be used. Study heterogeneity will be assessed using the I^2 statistic. Specifically, I^2 values will be stratified as follows: 'might not be important' (0–40%); 'may represent moderate heterogeneity' (30–60%); 'may represent substantial heterogeneity' (50–90%) and 'considerable heterogeneity' (75–100%); the corresponding *p*-values will also be taken into account[24].

For RCTs, data from intention-to-treat analyses will be considered, whenever available. Specifically, two analysis will be performed: 1) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention) versus a control group, and 2) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention), without a control group. Standardised mean differences will be calculated for BMI levels. Additionally, publication bias will be assessed using a funnel plot, following the method proposed by Egger[28].

Subgroup analysis and meta-regression

Next, subgroup analyses and meta-regression will be performed, considering the main factors that may cause heterogeneity, such as gender; age (children aged 4–12 years and/or adolescents aged 12–18 years); type of population (general population, indigenous population, or a mix of both); country; type of study design; participant population (underweight, normal weight, overweight, and/or obese); type of intervention (only physical activity or combined with nutritional intervention); type of physical activity (endurance, sports, games, dancing, and/or lifestyle physical-activity intervention); length of the intervention (above or below 12 weeks); the setting in which the intervention occurs; and duration of physical activity per week (above or below 150 minutes). Moreover, the methodological quality of the selected studies will be considered for additional subgroup analyses.

Sensitivity analysis

Finally, to assess the robustness of summary estimates and to detect whether any singular study accounts for a large proportion of heterogeneity, sensitivity analyses will be performed, removing the included studies one-by-one from the pooled analyses.

ETHICS AND DISSEMINATION

Given that, in this protocol, researchers will not collect primary data for their reviews, ethical approval will not be required. Once the outcomes of the associated systematic reviews and meta-analyses are disseminated in scientific publications, they may be shared through social networks and presented in scientific conferences related to the subject; thus, the conclusions may contribute to improving the health of the Latin American population.

1

Table 2. Characteristics of studies included in the systematic review and/or meta-analyses.

Population characteristics						Intervention characteristics			
Reference	**Country**	**Study Design**	**Age distribution**	**Sample size**	**Type of population**	**Physical-activity intervention**	**Physical activity characteristics**	**Nutritional intervention**	**Nutritional characteristics**
Author information and year of publication	Country	Design of the study	Age (years) of the participants range or means ± SD	Number of participants	Population characteristics (low weight, normal weight, overweight, obese)	Type of physical-activity intervention (leisure-time physical activity, physical activity programme, and/or physical activity counselling)	Definition of physical-activity intervention (length of intervention, number of sessions, duration of each session, type of physical measurement [i.e. Physical activity scale, accelerometer or pedometer])	Type of nutritional intervention (food education, nutritional counselling, diet intervention)	Definition of nutritional intervention (length of intervention).

DISCUSSION

Studies conducted among populations in Europe and the United States have shown that physical-activity interventions are associated with reductions of BMI, and are also an effective method of decreasing the percentage of adipose tissue[17,20]. However, there have been no previous meta-analyses of the effects of these interventions in the context of Latin America, which has geographical, socio-economic, and cultural characteristics that are inherent to a developing region. Thus, a suitable systematic review and, if appropriate, a meta-analysis, will enable us to gain an overview of the current Latin-America-based literature regarding the study subject and, concurrently, could contribute to the efficient development of discussions regarding the benefits of physical-activity interventions in the region. To this end, the systematic review protocol provides a structure for the extraction and synthesis of relevant information. This could provide us with evidence regarding the types of interventions that are most beneficial for reducing BMI values, particularly in regard to setting (school, health-care centre, or other), population type (as nutritional effects can vary between population types), intensity, duration, and number of sessions.

Other issues that should be highlighted when performing systematic reviews based on this protocol are whether the study design (RCTs, non-randomised experimental studies, and single-arm pre-post studies) could affect the results (as has been reported in previous studies[29,30]), as well as whether physical-activity interventions supplemented by other health interventions, such as nutritional interventions, can lead to a greater reduction in BMI. Such considerations would allow us to measure the effect of physical-activity interventions in regard to the prevention and treatment of overweight and obesity among Latin American children and adolescents.

Among the potential limitations inherent to systematic reviews and meta-analyses, the following (as elements of the studies examined) are particularly notable: publication bias, information bias, poor statistical analyses, low methodological quality, and inappropriate reporting of methods and findings. It is important to remember that, as a result of economic inequalities, these biases may be greater in some countries, which can result in an uneven advancement of scientific development across the region as a whole. Therefore, it is important to properly synthesise the information available in examined manuscripts; thus, this protocol represents a necessary text that consolidates the methodological structure

needed to perform appropriate, evidence-based systematic reviews and meta-analyses regarding the effects of physical-activity interventions on BMI of children and adolescents. In conclusion, application of this study protocol can provide updated information regarding the effects of physical-activity interventions on BMI of Latin American children and adolescents. Such information may assist the roles of public-health policy makers and those responsible for the implementation of such interventions.

Patient and Public Involvement

No patients or members of the public were involved in the design of this protocol.

Contributors:

AG-C and IC-R designed the study: AG-C was the principal investigator. AG-C and IC-R coordinated the study. AG-C and AD conducted the study. AG-C, CA-B, VM-V, and IC-R provided statistical and epidemiological support. AG-C wrote the article with the support of IC-R, CA-B, VM-V, and AD. All authors reviewed and approved the final version of the manuscript.

Competing interests:

None declared.

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TABLE LEGENDS.

Table 1. Search strategy for the MEDLINE database.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

FIGURE LEGENDS.

FIGURE 1. PRISMA flow diagram for identifying, screening, and determining the eligibility of and whether to include studies.

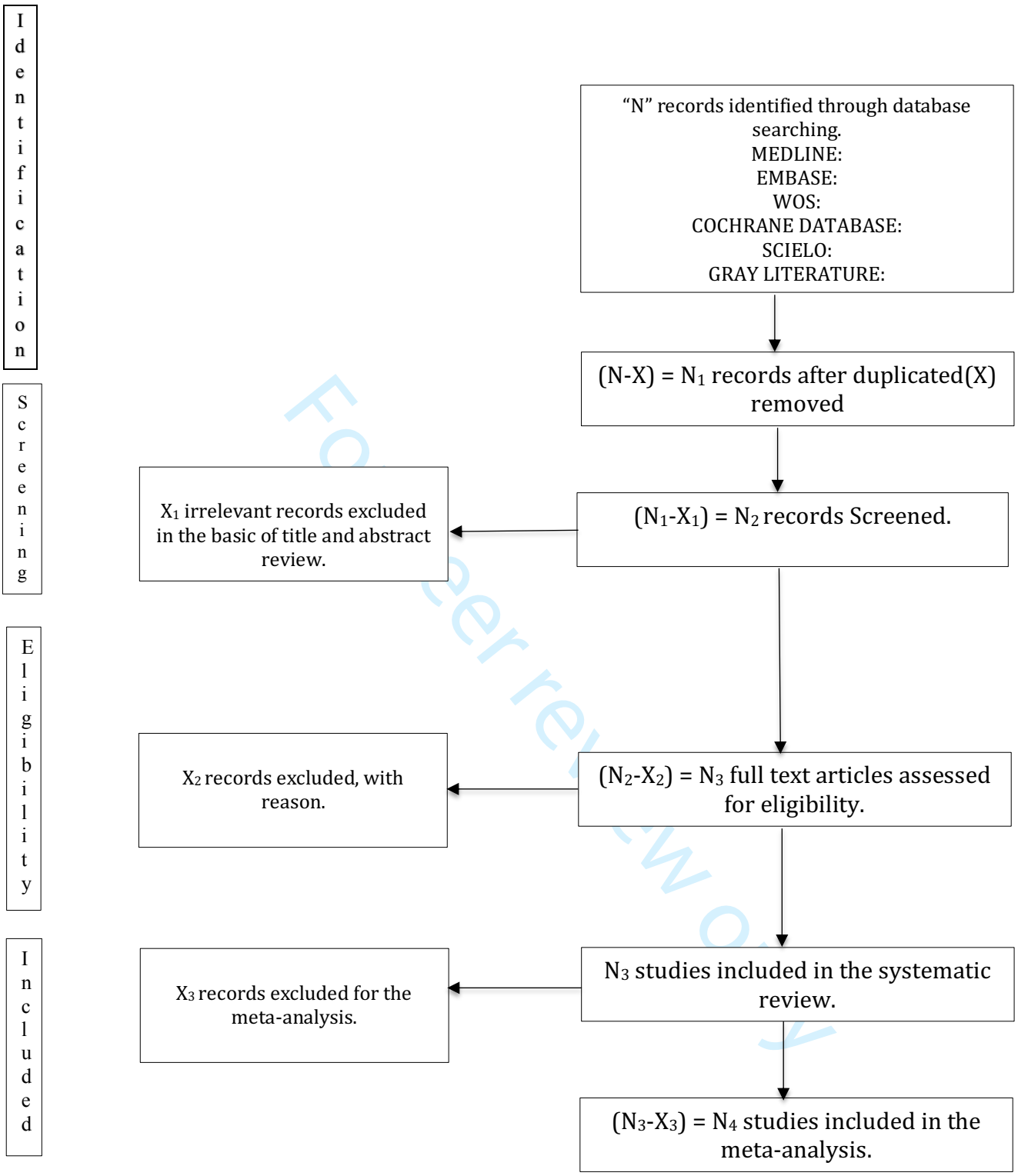

Figure 1. PRISMA flow diagram of identification, screening, eligibility and inclusion of studies.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA.	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact: pp. 1, 10	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p.10	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources: p. 10	5a	Indicate sources of financial or other support for the review
Sponsor: p. 10	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder: p.10	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: p. 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives: p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: p. 5	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources p. 5	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 5, 6	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management: pp. 6, 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process: pp. 6, 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: pp.6,7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: p. 7	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: p. 7	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p.7	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp. 7, 8, 9	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for a systematic review and meta-analysis

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Secondary Subject Heading:	Sports and exercise medicine
Keywords:	BMI, Latin America, Children, Adolescents, Physical activity

Protocol manuscript

Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for a systematic review and meta-analysis

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ABSTRACT.

Introduction: In Latin America, the number of children and adolescents who are overweight or obese has significantly increased in recent decades, and this situation has become a major public-health concern. To address this problem, several intervention programmes, based on factors such as physical activity and nutrition, have been implemented, and body mass index (BMI) has been widely used as a means of measuring the impact of such interventions**.** Although some Latin-America-based systematic reviews have been performed, there have been no previous meta-analyses of findings regarding the effect of physical-activity interventions on BMI. Thus, the objective of the systematic review and meta-analysis will be to provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years.

Methods and analysis: This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement. The literature search will involve MEDLINE, EMBASE, Cochrane Library, Web of Science and Scielo for articles published up to July 2019. This search will include randomised controlled trials (RCTs), non-randomised experimental studies, and single-arm pre-post studies. Further, the Cochrane Collaboration's tool for RCT studies and the Quality Assessment Tool for Quantitative Studies for non-randomised experimental and single-arm pre-post studies will be used to assess the risk of bias among the studies included in the systematic review. For the meta-analysis, the statistical program STATA V.14 will be used, and standardised mean differences are calculated as the primary outcomes. Subgroup analyses will then be performed based on the characteristics of the interventions and populations included in the studies examined.

Ethics and dissemination: This systematic review protocol is designed to provide updated evidence regarding the effects of physical-activity interventions on the Latin American population; such evidence may be useful for institutions responsible for the development of public-health policies and for those tasked with implementing such interventions among children and adolescents in Latin America.

The results should be disseminated through publication in a peer-reviewed journal. Since the data used in systematic reviews of this type will be extracted exclusively from published studies, approval from an ethics committee will not be required.

Prospero registration number: CRD42019077702.

Keywords: physical activity, BMI, Latin America, children and adolescents.

STRENGTHS AND LIMITATIONS OF THIS STUDY.

- In the protocol, two reviewers will independently perform the study selection, data extraction, and quality assessments.
- This review may produce the first Latin-America-based meta-analysis that provides scientific information regarding the effect of physical-activity interventions on BMI.
- Differences among the study designs, sample characteristics, types of physical-activity interventions, and poor methodological quality may restrict comparison of the selected studies and negatively affect the quality of the evidence obtained through associated systematic reviews and meta-analyses.

INTRODUCTION

In Latin America, levels of overweight and obesity among children and adolescents have significantly increased in recent decades, and this issue has now become a major public-health concern[1,2]. A tool that facilitates a quick assessment of whether a person is overweight or obese, as well as their level of general adiposity, is body mass index (BMI)[3-5]. As a result of BMI-based assessments, it is now estimated that between 20% and 25% of the total Latin-American population of children and adolescents are overweight or obese[5]. This is a worrying situation, as studies have suggested that these conditions are maintained into and during adulthood[6,7], and that they increase risk factors for cardiovascular disease, high blood pressure, some types of cancer[8,9], and all causes of premature mortality[10]. In fact, BMI has become such a reliable predictor of mortality[11] that in 2015 over 4.5 million deaths worldwide were associated with high BMI values[12].

However, in children and adolescents BMI values should be used and interpreted cautiously, as there is evidence that, although such values are useful for classifying adiposity[13], they can be a poor measure of changes in adiposity[14]. Moreover, childhood weight gain can generally be attributed to fat-free mass rather than fat mass, and this means that BMI is unable to precisely reflect changes that occur over time[15], particularly in adolescent males and children with low BMI[16]. Despite these problems, BMI will be used because it is one of the most practical methods to evaluate the changes in adiposity in children and adolescents[14]. Furthermore, it is widely used to measure the prevalence of overweight, obesity, and underweight in childhood[17].

Physical activity plays an important role in reducing BMI, along with lowering risk factors for cardiovascular disease and improving cardiorespiratory fitness; this, in turn, leads to a reduction in risk factors for overall health[18-21]. As a result of these benefits, researchers have implemented physical-activity-focused interventions, nutritional-focussed interventions, or a combination of both[21,22], and have used BMI to measure their effect. Underlining this approach, previous systematic reviews performed in Latin America have shown that, while few studies have implemented physical-activity interventions to treat overweight and obesity, the implementation of physical-education policies and programmes is necessary to promote children's and adolescents' health, because these interventions can effectively create positive changes among this population[1,23,24], such as having a significant positive effect on BMI, as

well as some anthropometric variables in children and youth with overweight and obesity, all through the promotion of physical activity and healthy diet. However, there have been no previous Latin-America-based meta-analyses of the effects physical-activity interventions have on BMI. Considering this, the present study aims to attract more attention to the necessity of such interventions, and to generate evidence that can encourage changes in public policy that can contribute to addressing this public-health crisis.

OBJECTIVE

The systematic review and meta-analysis will provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement[25] and the Cochrane Collaboration Handbook[26]. This protocol has previously been registered in PROSPERO (registration number: CRD42019077702).

Inclusion/exclusion criteria for study selection

For this protocol, in order to be included in associated systematic reviews studies must have reported physical-activity interventions that meet the following criteria: 1) involving the population of a Latin American country; 2) including participants aged 4–18 years; 3) reporting any type of physical activity (physical endurance, sports, or alternative exercise [e.g. games, dancing, optimised physical education classes], which may or may not have included nutritional interventions); 4) being a randomised controlled trial (RCT), non-randomised experimental study, or single-arm pre-post study; 5) reporting BMI both before and after the intervention; 6) written in Spanish, English, or Portuguese; and 7) published before October 2019.

Meanwhile, the following exclusion criteria will be set: 1) only including participants younger than four or older than 18 years old; 2) providing self-reported data for BMI.

Studies that feature different age ranges, but that nevertheless include population data for the ages of four to 18 years, will be included in the analysis.

Search strategy

Literature searches will be conducted through the MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science, and Scielo databases.

Meanwhile, searches for unpublished studies will be conducted using OPEN GRAY, ProQuest Dissertations & Thesis Global, Theseo, Networked Digital Library of Theses and Dissertations, and Google Scholar. Further, a search of ClinicalTrials.gov and EudraCT clinical trial records will also be conducted. The literature search will be complemented by screening references included in articles that are considered eligible for systematic review. Study records will then be managed using the Mendeley reference manager. The search strategy will include free text terms, combining Boolean operators from the relevant concepts presented in Table 1. Previous reviews and meta-analyses will also be scanned for additional references. Finally, reference lists of included papers will be hand-searched.

Table 1. Search strategy for the MEDILINE database.

Search set	Medline	Search set	Medline
#1	physical activity [tw]	#18	paediatric obesity [mh]
#2	physical exercise [tw]	#19	14 OR 15 OR 16 OR 17 OR 18
#3	physical performance [tw]	#20	underweight [tw]
#4	exercise program* [tiab]	#21	normal weight [tw]
#5	physical fitness [mh]	#22	overweight [tw]
#6	exercise [mh]	#23	BMI [tiab]
#7	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR	#24	obesity [tiab]
#8	training program* [tiab]	#25	body mass index [mh]
#9	prevention program* [tiab]	#26	20 OR 21 OR 22 OR 23 OR 24 OR 25
#10	intervention program* [tiab]	#27	studies [tiab]
#11	promotion [tw]	#28	randomised controlled trials [tiab]
#12	strategy [tw]	#29	RCT [tiab]
#13	8 OR 9 OR 10 OR 11 OR 12	#30	non-randomised experimental [tiab]
#14	chilhood obesity [tiab]	#31	single-arm pre-post [tiab]
#15	obese children [tiab]	#32	27 OR 28 OR 29 OR 30 OR 31
#16	obesity prevention [tiab]	#33	7 AND 13 AND 19 AND 26 AND 32
#17	obesity review [tiab]		

mh: MeSH terms; tiab: title/abstract; tw: text word. * is used to search for or all terms that begin with a word (e.g. 'training program*' would return results such as 'training programs' and 'training programme')

Study selection

After excluding duplicated records, two researchers will independently evaluate the titles and abstracts of the retrieved articles in order to identify eligible studies for the systematic review. Abstracts that do not provide sufficient information regarding inclusion/exclusion criteria will then be evaluated through a full-text reading. Then, two researchers will examine the included and excluded studies to verify the reason for each decision. Inconsistencies between these two researchers regarding selection will be resolved by a third researcher, who will make the final decision, always based on the inclusion/exclusion criteria.

Data extraction

The process of identification, selection, and the inclusion/exclusion of articles will follow the PRISMA[25] flow chart (shown in Figure 1). Once the included studies will be identified, the information will be summarized in the 'Table of Characteristics' (Table 2), being the data independently extracted by two reviewers. For the first five studies, the extraction process will be performed by these two reviewers; this is performed to ensure that the data extraction is consistent. In addition, the full texts of the identified studies will be examined to extract the following data: (1) name of the first author; (2) year of publication; (3) country; (4) study design; (5) participants' ages; (6) number of participants; (7) population characteristics (normal weight, overweight, obesity); (8) type of physical-activity intervention (leisure-time physical activity, lifestyle physical activity, physical-activity programme, or physical activity counselling); (9) characteristics of the physical activity in question (length of intervention, intervention setting, number of sessions, duration of each session, type of physical measurement applied [i.e. physical-activity scale, accelerometer, or pedometer]); (10) type of nutritional intervention (food education, nutritional counselling, diet intervention); and (11) characteristics of this nutritional intervention (length of intervention). When necessary, the authors of potentially eligible studies will be contacted to obtain any missing data.

Assessment of risk of bias in the included studies

Two researchers will independently conduct a quality assessment, following the Cochrane Collaboration Handbook recommendations[26]. Any disagreements will be resolved through discussion and, if a consensus cannot be reached, a third reviewer will intervene to resolve the disagreement.

The methodological quality of the RCTs will be assessed using the Cochrane Collaboration's tool for assessing risk of bias[27]. This tool evaluates risk of bias in terms of six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Meanwhile, the Quality Assessment Tool for Quantitative Studies[28] will be used to assess the quality of pre-post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data-collection method, withdrawals, and drop-outs.

In both quality-assessment tools, each domain is considered 'strong', 'moderate', or 'weak' and, based on this, studies will be classified as having a low risk of bias (with no weak

ratings), a moderate risk of bias (with one weak rating), or a high risk of bias (with two or more weak ratings). The agreement rate between reviewers will be reported by calculating kappa statistics.

Statistical analysis

Researchers will summarize the main characteristics of each included study, including the general profile of the study, the methods, the characteristics of the study participants, and the results (as shown in Table 2). A meta-analysis will be performed on studies that showed BMI pre-post interventions (separating studies that included physical-activity interventions from those in which physical activity and nutritional health were combined). Studies providing insufficient data to perform such analyses will be included in the systematic review but will be omitted from the meta-analysis.

For studies for which a meta-analysis is appropriate, STATA V.14 software will be used to combine the pooled mean differences with 95% confidence intervals. If there is no evidence of heterogeneity, a fixed-effects model will be used; otherwise, a random-effects model will be used. Study heterogeneity will be assessed using the I^2 statistic. Specifically, I^2 values will be stratified as follows: 'might not be important' (0–40%); 'may represent moderate heterogeneity' (30–60%); 'may represent substantial heterogeneity' (50–90%) and 'considerable heterogeneity' (75–100%); the corresponding *p*-values will also be taken into account[25].

For RCTs, data from intention-to-treat analyses will be considered, whenever available. Specifically, two analyses will be performed: 1) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention) versus a control group, and 2) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention), without a control group. Standardised mean differences will be calculated for BMI levels. Additionally, publication bias will be assessed using a funnel plot, following the method proposed by Egger[29].

Subgroup analysis and meta-regression

Next, subgroup analyses and meta-regression will be performed, considering the main factors that may cause heterogeneity, such as gender; age (children aged 4–12 years and/or adolescents aged 12–18 years); type of population (general population, indigenous

population, or a mix of both); country; type of study design; participant population (underweight, normal weight, overweight, and/or obese); type of intervention (only physical activity or combined with nutritional intervention); type of physical activity (endurance, sports, games, dancing, and/or lifestyle physical-activity intervention); length of the intervention (above or below 12 weeks); the setting in which the intervention occurs; and duration of physical activity per week (above or below 150 minutes). Moreover, the methodological quality of the selected studies will be considered for additional subgroup analyses.

Sensitivity analysis

Finally, to assess the robustness of summary estimates and to detect whether any singular study accounts for a large proportion of heterogeneity, sensitivity analyses will be performed, removing the included studies one-by-one from the pooled analyses.

ETHICS AND DISSEMINATION

Given that, in this protocol, researchers will not collect primary data for their reviews, ethical approval will not be required. Once the outcomes of the associated systematic reviews and meta-analyses are disseminated in scientific publications, they may be shared through social networks and presented in scientific conferences related to the subject; thus, the conclusions may contribute to improving the health of the Latin American population.

1

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

Population characteristics						Intervention characteristics			
Reference	**Country**	**Study Design**	**Age distribution**	**Sample size**	**Type of population**	**Physical-activity intervention**	**Physical activity characteristics**	**Nutritional intervention**	**Nutritional characteristics**
Author information and year of publication	Country	Design of the study	Age (years) of the participants range or means ± SD	Number of participants	Population characteristics (low weight, normal weight, overweight, obese)	Type of physical-activity intervention (leisure-time physical activity, physical activity programme, and/or physical activity counselling)	Definition of physical-activity intervention (length of intervention, number of sessions, duration of each session, type of physical measurement [i.e. Physical activity scale, accelerometer or pedometer])	Type of nutritional intervention (food education, nutritional counselling, diet intervention)	Definition of nutritional intervention (length of intervention).

DISCUSSION

Studies conducted among populations in Europe and the United States have shown that physical-activity interventions are associated with reductions of BMI, and are also an effective method of decreasing the percentage of adipose tissue[18,21]. However, there have been no previous meta-analyses of the effects of these interventions in the context of Latin America, which has geographical, socio-economic, and cultural characteristics that are inherent to a developing region. Thus, a suitable systematic review and, if appropriate, a meta-analysis, will enable us to gain an overview of the current Latin-America-based literature regarding the study subject and, concurrently, could contribute to the efficient development of discussions regarding the benefits of physical-activity interventions in the region. To this end, the systematic review protocol provides a structure for the extraction and synthesis of relevant information. This could provide us with evidence regarding the types of interventions that are most beneficial for reducing BMI values, particularly in regard to setting (school, health-care centre, or other), population type (as nutritional effects can vary between population types), intensity, duration, and number of sessions.

Other issues that should be highlighted when performing systematic reviews based on this protocol are whether the study design (RCTs, non-randomised experimental studies, and single-arm pre-post studies) could affect the results (as has been reported in previous studies[30,31]), as well as whether physical-activity interventions supplemented by other health interventions, such as nutritional interventions, can lead to a greater reduction in BMI. Such considerations would allow us to measure the effect of physical-activity interventions in regard to the prevention and treatment of overweight and obesity among Latin American children and adolescents.

Among the potential limitations inherent to systematic reviews and meta-analyses, the following (as elements of the studies examined) are particularly notable: publication bias, information bias, poor statistical analyses, low methodological quality, and inappropriate reporting of methods and findings. It is important to remember that, as a result of economic inequalities, these biases may be greater in some countries, which can result in an uneven advancement of scientific development across the region as a whole. Therefore, it is important to properly synthesise the information available in examined manuscripts; thus, this protocol represents a necessary text that consolidates the methodological structure

needed to perform appropriate, evidence-based systematic reviews and meta-analyses regarding the effects of physical-activity interventions on BMI of children and adolescents. In conclusion, the systematic review and meta-analysis will provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years. Such information may assist the roles of public-health policy makers and those responsible for the implementation of such interventions.

Patient and Public Involvement

No patients or members of the public were involved in the design of this protocol.

Contributors:

AG-C and IC-R designed the study: AG-C was the principal investigator. AG-C and IC-R coordinated the study. AG-C and AD conducted the study. AG-C, CA-B, VM-V, and IC-R provided statistical and epidemiological support. AG-C wrote the article with the support of IC-R, CA-B, VM-V, and AD. All authors reviewed and approved the final version of the manuscript.

Competing interests:

None declared.

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TABLE LEGENDS.

Table 1. Search strategy for the MEDLINE database.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

FIGURE LEGENDS.

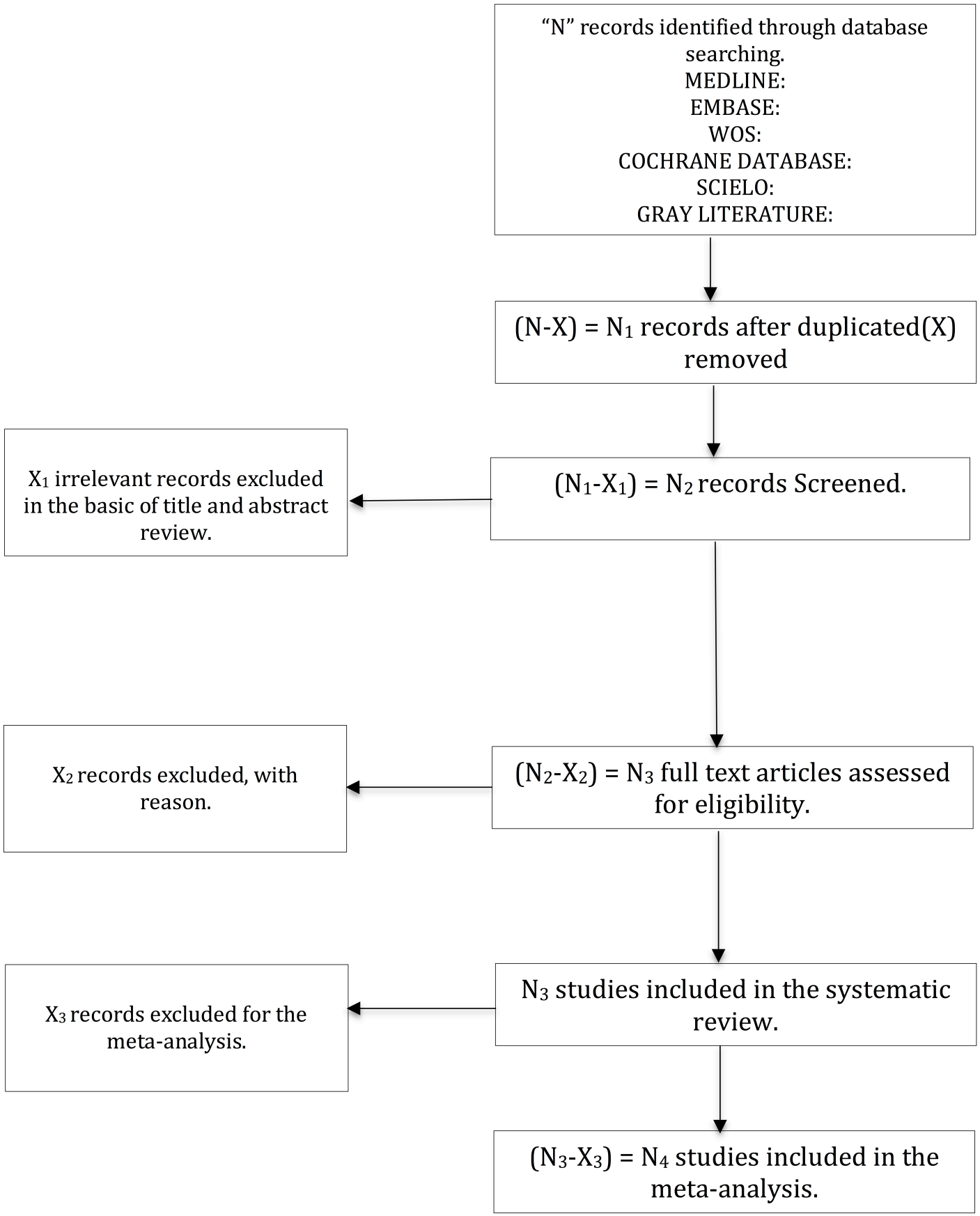
FIGURE 1. PRISMA flow diagram for identifying, screening, and determining the eligibility of and whether to include studies.

IDENTIFICATION

SCREENING

ELIGIBILITY

INCLUDED



PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA.	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact: pp. 1, 10	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p.10	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources: p. 10	5a	Indicate sources of financial or other support for the review
Sponsor: p. 10	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder: p.10	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: p. 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives: p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: p. 5	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources p. 5	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 5, 6	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management: pp. 6, 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process: pp. 6, 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: pp.6,7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: p. 7	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: p. 7	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p.7	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp. 7, 8, 9	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for a systematic review and meta-analysis

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Secondary Subject Heading:	Sports and exercise medicine
Keywords:	BMI, Latin America, Children, Adolescents, Physical activity

Protocol manuscript

Effects of physical-activity interventions on the body mass index of children and adolescents in Latin America: A protocol for a systematic review and meta-analysis

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ABSTRACT.

Introduction: In Latin America, the number of children and adolescents who are overweight or obese has significantly increased in recent decades, and this situation has become a major public-health concern. To address this problem, several intervention programmes, based on factors such as physical activity and nutrition, have been implemented, and body mass index (BMI) has been widely used as a means of measuring the impact of such interventions**.** Although some Latin-America-based systematic reviews have been performed, there have been no previous meta-analyses of findings regarding the effect of physical-activity interventions on BMI. Thus, the objective of the systematic review and meta-analysis will be to provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years.

Methods and analysis: This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement. The literature search will involve MEDLINE, EMBASE, Cochrane Library, Web of Science and Scielo for articles published up to July 2019. This search will include randomised controlled trials (RCTs), non-randomised experimental studies, and single-arm pre-post studies. Further, the Cochrane Collaboration's tool for RCT studies and the Quality Assessment Tool for Quantitative Studies for non-randomised experimental and single-arm pre-post studies will be used to assess the risk of bias among the studies included in the systematic review. For the meta-analysis, the statistical program STATA V.14 will be used, and standardised mean differences are calculated as the primary outcomes. Subgroup analyses will then be performed based on the characteristics of the interventions and populations included in the studies examined.

Ethics and dissemination: This systematic review protocol is designed to provide updated evidence regarding the effects of physical-activity interventions on the Latin American population; such evidence may be useful for institutions responsible for the development of public-health policies and for those tasked with implementing such interventions among children and adolescents in Latin America.

The results should be disseminated through publication in a peer-reviewed journal. Since the data used in systematic reviews of this type will be extracted exclusively from published studies, approval from an ethics committee will not be required.

Prospero registration number: CRD42019077702.

Keywords: physical activity, BMI, Latin America, children and adolescents.

STRENGTHS AND LIMITATIONS OF THIS STUDY.

- In the protocol, two reviewers will independently perform the study selection, data extraction, and quality assessments.
- This review may produce the first Latin-America-based meta-analysis that provides scientific information regarding the effect of physical-activity interventions on BMI.
- Differences among the study designs, sample characteristics, types of physical-activity interventions, and poor methodological quality may restrict comparison of the selected studies and negatively affect the quality of the evidence obtained through associated systematic reviews and meta-analyses.

INTRODUCTION

In Latin America, levels of overweight and obesity among children and adolescents have significantly increased in recent decades, and this issue has now become a major public-health concern[1,2]. A tool that facilitates a quick assessment of whether a person is overweight or obese, as well as their level of general adiposity, is body mass index (BMI)[3-5]. As a result of BMI-based assessments, it is now estimated that between 20% and 25% of the total Latin-American population of children and adolescents are overweight or obese[5]. This is a worrying situation, as studies have suggested that these conditions are maintained into and during adulthood[6,7], and that they increase risk factors for cardiovascular disease, high blood pressure, some types of cancer[8,9], and all causes of premature mortality[10]. In fact, BMI has become such a reliable predictor of mortality[11] that in 2015 over 4.5 million deaths worldwide were associated with high BMI values[12].

However, in children and adolescents BMI values should be used and interpreted cautiously, as there is evidence that, although such values are useful for classifying adiposity[13], they can be a poor measure of changes in adiposity[14]. Moreover, childhood weight gain can generally be attributed to fat-free mass rather than fat mass, and this means that BMI is unable to precisely reflect changes that occur over time[15], particularly in adolescent males and children with low BMI[16]. Despite these problems, BMI will be used because it is one of the most practical methods to evaluate the changes in adiposity in children and adolescents[14]. Furthermore, it is widely used to measure the prevalence of overweight, obesity, and underweight in childhood[17].

Physical activity plays an important role in reducing BMI, along with lowering risk factors for cardiovascular disease and improving cardiorespiratory fitness; this, in turn, leads to a reduction in risk factors for overall health[18-21]. As a result of these benefits, researchers have implemented physical-activity-focused interventions, nutritional-focussed interventions, or a combination of both[21,22], and have used BMI to measure their effect. Underlining this approach, previous systematic reviews performed in Latin America have shown that, while few studies have implemented physical-activity interventions to treat overweight and obesity, the implementation of physical-education policies and programmes is necessary to promote children's and adolescents' health, because these interventions can effectively create positive changes among this population[1,23,24], such as having a significant positive effect on BMI, as

well as some anthropometric variables in children and youth with overweight and obesity, all through the promotion of physical activity and healthy diet. However, there have been no previous Latin-America-based meta-analyses of the effects physical-activity interventions have on BMI. Considering this, the present study aims to attract more attention to the necessity of such interventions, and to generate evidence that can encourage changes in public policy that can contribute to addressing this public-health crisis.

OBJECTIVE

The systematic review and meta-analysis will provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement[25] and the Cochrane Collaboration Handbook[26]. This protocol has previously been registered in PROSPERO (registration number: CRD42019077702).

Inclusion/exclusion criteria for study selection

For this protocol, in order to be included in associated systematic reviews studies must have reported physical-activity interventions that meet the following criteria: 1) involving the population of a Latin American country; 2) including participants aged 4–18 years; 3) reporting any type of physical activity (physical endurance, sports, or alternative exercise [e.g. games, dancing, optimised physical education classes], which may or may not have included nutritional interventions); 4) being a randomised controlled trial (RCT), non-randomised experimental study, or single-arm pre-post study; 5) reporting BMI both before and after the intervention; 6) written in Spanish, English, or Portuguese; and 7) published before October 2019.

Meanwhile, the following exclusion criteria will be set: 1) only including participants younger than four or older than 18 years old; 2) providing self-reported data for BMI.

Studies that feature different age ranges, but that nevertheless include population data for the ages of four to 18 years, will be included in the analysis.

Search strategy

Literature searches will be conducted through the MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science, and Scielo databases.

Meanwhile, searches for unpublished studies will be conducted using OPEN GRAY, ProQuest Dissertations & Thesis Global, Theseo, Networked Digital Library of Theses and Dissertations, and Google Scholar. Further, a search of ClinicalTrials.gov and EudraCT clinical trial records will also be conducted. The literature search will be complemented by screening references included in articles that are considered eligible for systematic review. Study records will then be managed using the Mendeley reference manager. The search strategy will include free text terms, combining Boolean operators from the relevant concepts presented in Table 1. Previous reviews and meta-analyses will also be scanned for additional references. Finally, reference lists of included papers will be hand-searched.

Table 1. Search strategy for the MEDILINE database.

Search set	Medline	Search set	Medline
#1	physical activity [tw]	#18	paediatric obesity [mh]
#2	physical exercise [tw]	#19	14 OR 15 OR 16 OR 17 OR 18
#3	physical performance [tw]	#20	underweight [tw]
#4	exercise program* [tiab]	#21	normal weight [tw]
#5	physical fitness [mh]	#22	overweight [tw]
#6	exercise [mh]	#23	BMI [tiab]
#7	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR	#24	obesity [tiab]
#8	training program* [tiab]	#25	body mass index [mh]
#9	prevention program* [tiab]	#26	20 OR 21 OR 22 OR 23 OR 24 OR 25
#10	intervention program* [tiab]	#27	studies [tiab]
#11	promotion [tw]	#28	randomised controlled trials [tiab]
#12	strategy [tw]	#29	RCT [tiab]
#13	8 OR 9 OR 10 OR 11 OR 12	#30	non-randomised experimental [tiab]
#14	chilhood obesity [tiab]	#31	single-arm pre-post [tiab]
#15	obese children [tiab]	#32	27 OR 28 OR 29 OR 30 OR 31
#16	obesity prevention [tiab]	#33	7 AND 13 AND 19 AND 26 AND 32
#17	obesity review [tiab]		

mh: MeSH terms; tiab: title/abstract; tw: text word. * is used to search for or all terms that begin with a word (e.g. 'training program*' would return results such as 'training programs' and 'training programme')

Study selection

After excluding duplicated records, two researchers will independently evaluate the titles and abstracts of the retrieved articles in order to identify eligible studies for the systematic review. Abstracts that meet inclusion criteria or that do not provide sufficient information regarding the inclusion/exclusion criteria will then be evaluated through a full-text reading. Then, two researchers will examine the included and excluded studies to verify the reason for each decision. Inconsistencies between these two researchers regarding selection will be resolved by a third researcher, who will make the final decision, always based on the inclusion/exclusion criteria.

Data extraction

The process of identification, selection, and the inclusion/exclusion of articles will follow the PRISMA[25] flow chart (shown in Figure 1). The full texts of the identified studies will be examined to extract the following data: (1) name of the first author; (2) year of publication; (3) country; (4) study design; (5) participants' ages; (6) number of participants; (7) population characteristics (normal weight, overweight, obesity); (8) type of physical-activity intervention (leisure-time physical activity, lifestyle physical activity, physical-activity programme, or physical activity counselling); (9) characteristics of the physical activity in question (length of intervention, intervention setting, number of sessions, duration of each session, type of physical measurement applied [i.e. physical-activity scale, accelerometer, or pedometer]); (10) type of nutritional intervention (food education, nutritional counselling, diet intervention); and (11) characteristics of this nutritional intervention (length of intervention). When necessary, the authors of potentially eligible studies will be contacted to obtain any missing data. The information will be summarized in the 'Table of Characteristics' (Table 2), being the data independently extracted by two reviewers. For the first five studies, the extraction process will be performed by these two reviewers; this is performed to ensure that the data extraction is consistent.

Assessment of risk of bias in the included studies

Two researchers will independently conduct a quality assessment, following the Cochrane Collaboration Handbook recommendations[26]. Any disagreements will be resolved through discussion and, if a consensus cannot be reached, a third reviewer will intervene to resolve the disagreement.

The methodological quality of the RCTs will be assessed using the Cochrane Collaboration's tool for assessing risk of bias[27]. This tool evaluates risk of bias in terms of six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Meanwhile, the Quality Assessment Tool for Quantitative Studies[28] will be used to assess the quality of pre-post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data-collection method, withdrawals, and drop-outs.

In both quality-assessment tools, each domain is considered 'strong', 'moderate', or 'weak' and, based on this, studies will be classified as having a low risk of bias (with no weak

ratings), a moderate risk of bias (with one weak rating), or a high risk of bias (with two or more weak ratings). The agreement rate between reviewers will be reported by calculating kappa statistics.

Statistical analysis

Researchers will summarize the main characteristics of each included study, including the general profile of the study, the methods, the characteristics of the study participants, and the results (as shown in Table 2). A meta-analysis will be performed on studies that showed BMI pre-post interventions (separating studies that included physical-activity interventions from those in which physical activity and nutritional health were combined). Studies providing insufficient data to perform such analyses will be included in the systematic review but will be omitted from the meta-analysis.

For studies for which a meta-analysis is appropriate, STATA V.14 software will be used to combine the pooled mean differences with 95% confidence intervals. If there is no evidence of heterogeneity, a fixed-effects model will be used; otherwise, a random-effects model will be used. Study heterogeneity will be assessed using the I^2 statistic. Specifically, I^2 values will be stratified as follows: 'might not be important' (0–40%); 'may represent moderate heterogeneity' (30–60%); 'may represent substantial heterogeneity' (50–90%) and 'considerable heterogeneity' (75–100%); the corresponding *p*-values will also be taken into account[25].

For RCTs, data from intention-to-treat analyses will be considered, whenever available. Specifically, two analyses will be performed: 1) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention) versus a control group, and 2) mean difference in BMI pre-post physical-activity-based intervention (with or without nutritional intervention), without a control group. Standardised mean differences will be calculated for BMI levels. Additionally, publication bias will be assessed using a funnel plot, following the method proposed by Egger[29].

Subgroup analysis and meta-regression

Next, subgroup analyses and meta-regression will be performed, considering the main factors that may cause heterogeneity, such as gender; age (children aged 4–12 years and/or adolescents aged 12–18 years); type of population (general population, indigenous

population, or a mix of both); country; type of study design; participant population (underweight, normal weight, overweight, and/or obese); type of intervention (only physical activity or combined with nutritional intervention); type of physical activity (endurance, sports, games, dancing, and/or lifestyle physical-activity intervention); length of the intervention (above or below 12 weeks); the setting in which the intervention occurs; and duration of physical activity per week (above or below 150 minutes). Moreover, the methodological quality of the selected studies will be considered for additional subgroup analyses.

Sensitivity analysis

Finally, to assess the robustness of summary estimates and to detect whether any singular study accounts for a large proportion of heterogeneity, sensitivity analyses will be performed, removing the included studies one-by-one from the pooled analyses.

ETHICS AND DISSEMINATION

Given that, in this protocol, researchers will not collect primary data for their reviews, ethical approval will not be required. Once the outcomes of the associated systematic reviews and meta-analyses are disseminated in scientific publications, they may be shared through social networks and presented in scientific conferences related to the subject; thus, the conclusions may contribute to improving the health of the Latin American population.

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Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

Population characteristics						Intervention characteristics			
Reference	**Country**	**Study Design**	**Age distribution**	**Sample size**	**Type of population**	**Physical-activity intervention**	**Physical activity characteristics**	**Nutritional intervention**	**Nutritional characteristics**
Author information and year of publication	Country	Design of the study	Age (years) of the participants range or means ± SD	Number of participants	Population characteristics (low weight, normal weight, overweight, obese)	Type of physical-activity intervention (leisure-time physical activity, physical activity programme, and/or physical activity counselling)	Definition of physical-activity intervention (length of intervention, number of sessions, duration of each session, type of physical measurement [i.e. Physical activity scale, accelerometer or pedometer])	Type of nutritional intervention (food education, nutritional counselling, diet intervention)	Definition of nutritional intervention (length of intervention).

DISCUSSION

Studies conducted among populations in Europe and the United States have shown that physical-activity interventions are associated with reductions of BMI, and are also an effective method of decreasing the percentage of adipose tissue[18,21]. However, there have been no previous meta-analyses of the effects of these interventions in the context of Latin America, which has geographical, socio-economic, and cultural characteristics that are inherent to a developing region. Thus, a suitable systematic review and, if appropriate, a meta-analysis, will enable us to gain an overview of the current Latin-America-based literature regarding the study subject and, concurrently, could contribute to the efficient development of discussions regarding the benefits of physical-activity interventions in the region. To this end, the systematic review protocol provides a structure for the extraction and synthesis of relevant information. This could provide us with evidence regarding the types of interventions that are most beneficial for reducing BMI values, particularly in regard to setting (school, health-care centre, or other), population type (as nutritional effects can vary between population types), intensity, duration, and number of sessions.

Other issues that should be highlighted when performing systematic reviews based on this protocol are whether the study design (RCTs, non-randomised experimental studies, and single-arm pre-post studies) could affect the results (as has been reported in previous studies[30,31]), as well as whether physical-activity interventions supplemented by other health interventions, such as nutritional interventions, can lead to a greater reduction in BMI. Such considerations would allow us to measure the effect of physical-activity interventions in regard to the prevention and treatment of overweight and obesity among Latin American children and adolescents.

Among the potential limitations inherent to systematic reviews and meta-analyses, the following (as elements of the studies examined) are particularly notable: publication bias, information bias, poor statistical analyses, low methodological quality, and inappropriate reporting of methods and findings. It is important to remember that, as a result of economic inequalities, these biases may be greater in some countries, which can result in an uneven advancement of scientific development across the region as a whole. Therefore, it is important to properly synthesise the information available in examined manuscripts; thus, this protocol represents a necessary text that consolidates the methodological structure

needed to perform appropriate, evidence-based systematic reviews and meta-analyses regarding the effects of physical-activity interventions on BMI of children and adolescents. In conclusion, the systematic review and meta-analysis will provide an up-to-date synthesis of the effects of physical-activity interventions on BMI of Latin American children and adolescents aged four to 18 years. Such information may assist the roles of public-health policy makers and those responsible for the implementation of such interventions.

Patient and Public Involvement

No patients or members of the public were involved in the design of this protocol.

Contributors:

AG-C and IC-R designed the study: AG-C was the principal investigator. AG-C and IC-R coordinated the study. AG-C and AD conducted the study. AG-C, CA-B, VM-V, and IC-R provided statistical and epidemiological support. AG-C wrote the article with the support of IC-R, CA-B, VM-V, and AD. All authors reviewed and approved the final version of the manuscript.

Competing interests:

None declared.

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TABLE LEGENDS.

Table 1. Search strategy for the MEDLINE database.

Table 2. Characteristics of studies included in the systematic review and/or meta-analysis.

FIGURE LEGENDS.

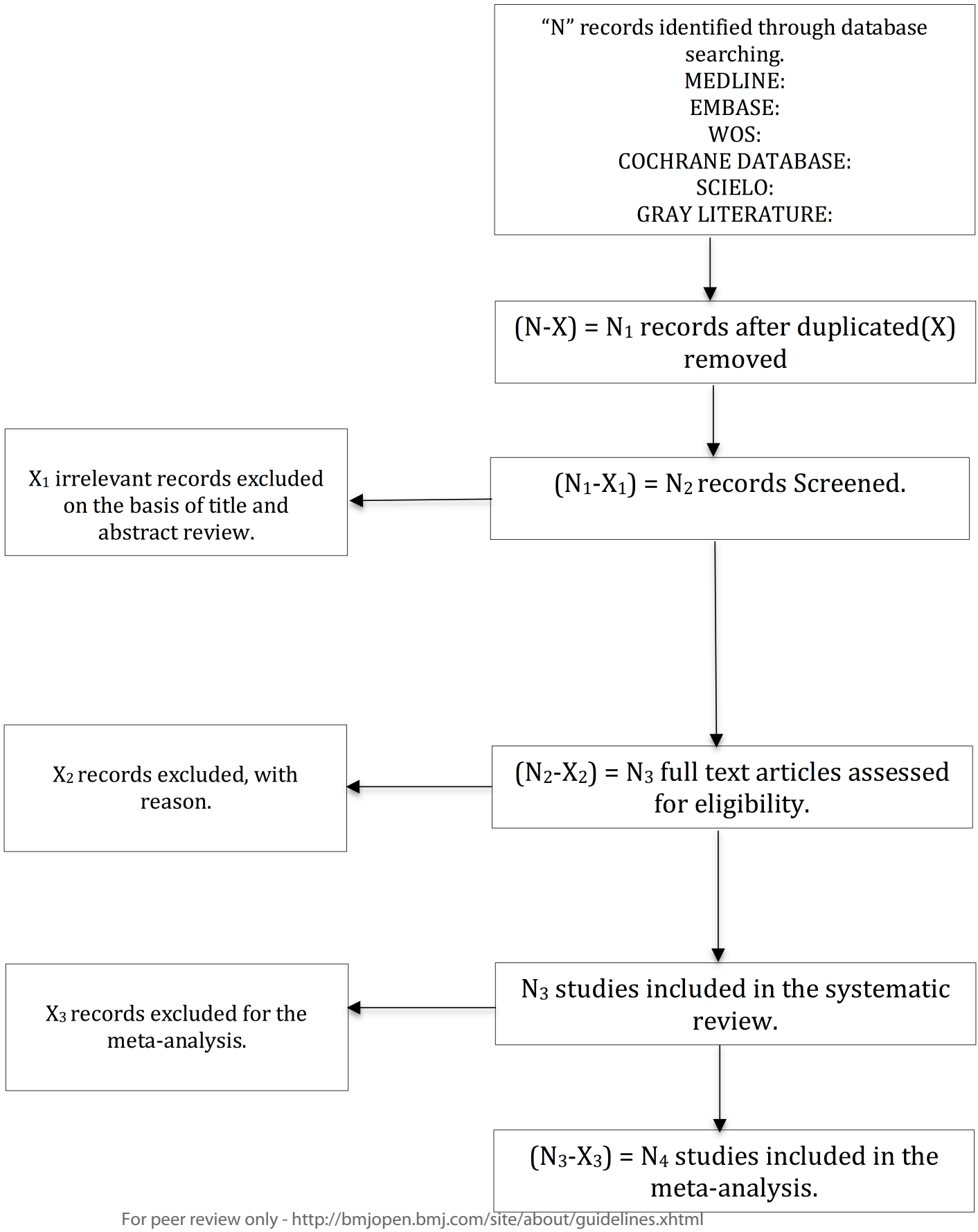
FIGURE 1. PRISMA flow diagram for identifying, screening, and determining the eligibility of and whether to include studies.

IDENTIFICATION

SCREENING

ELIGIBILITY

INCLUDED



PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA.	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact: pp. 1, 10	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p.10	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources: p. 10	5a	Indicate sources of financial or other support for the review
Sponsor: p. 10	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder: p.10	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: p. 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives: p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: p. 5	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources p. 5	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 5, 6	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management: pp. 6, 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process: pp. 6, 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: pp.6,7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: p. 7	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: p. 7	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p.7	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp. 7, 8, 9	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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