



Which Physical Exercise Interventions Increase HDL-Cholesterol Levels? A Systematic Review of Meta-analyses of Randomized Controlled Trials

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Abstract

Background Meta-analyses of randomized controlled trials (RCTs) have shown the beneficial effect of exercise on HDL-cholesterol (HDL-C) levels. However, systematic reviews are not free of bias, and this could call into question their results.

Objectives The aim of this work was to conduct a critical assessment of meta-analyses of RCTs that analyze the association between exercise and HDL-C levels, evaluating their results and the risk of bias (RoB).

Methods This systematic review of MEDLINE and EMBASE included meta-analyses of RCTs that studied the effects of exercise on HDL-C levels in healthy adults or patients at cardiovascular risk. The RoB was determined using AMSTAR-2, and information was obtained on exercise and the variation in HDL-C levels.

Results Twenty-three meta-analyses were included. Great variability was found in exercise (different types, frequencies or intensities in the studied interventions). All the analyses found an improvement in HDL-C levels, ranging from 0.27 to 5.41 mg/dl, in comparison with the control group (no exercise). The RoB was very high, with 18 reviews obtaining a critically low confidence level and the remaining works obtaining the highest confidence level.

Conclusions Only one meta-analysis showed good quality, in which HDL-C levels increased by 3.09 mg/dl in healthy adults and patients at high cardiovascular risk who practiced yoga. The rest had high RoB. Therefore, new systematic reviews with low RoB are needed to apply the results to clinical practice.

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Key Points

Meta-analyses have shown that exercise can increase HDL-C levels.

Systematic reviews should have a low risk of bias for conclusions to be applicable to clinical practice.

A systematic review was performed evaluating these meta-analyses, finding that only one work meets the accepted standards for this purpose (yoga).

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1 Introduction

Cardiovascular diseases (CVD) are a major cause of morbidity and the leading cause of premature death, with coronary heart disease and stroke being the types of events that produce the highest number of deaths [1, 2]. Traditionally, CVD has been considered to have a higher prevalence and incidence in men, although it is currently prevalent in women [3]. In addition, differences between the sexes can be seen in the various cardiovascular risk factors, such as high blood pressure, total cholesterol (TC), high- and low-density lipoprotein cholesterol (HDL-C and LDL-C), diabetes mellitus (DM), smoking, sedentary lifestyle, alcohol use and stress. Most of these are largely modifiable when identified early and addressed [3].

Coronary events are associated with blood levels of lipid parameters [TC, HDL-C, LDL-C, and triglycerides (TG)]. Increased LDL-C, TC and TG levels above recommended values together with decreased HDL-C levels lead to cholesterol accumulating, contributing to atheroma and atherosclerotic plaques, increasing the risk and development of CVD. These parameters therefore need to be addressed, generally, with pharmacological interventions [4].

Focusing only on HDL-C levels, these can be modified with non-pharmacological therapy, especially nutrition. For example, the Mediterranean diet has numerous benefits with regard to chronic diseases, but it has also been shown to be effective at increasing HDL-C levels, especially with the addition of olive oil [5]. Similarly, various chemical compounds produced by living organisms have shown benefit in raising HDL-C levels [6–8]. Another important element in raising HDL-C levels is exercise, as numerous meta-analyses associate physical exercise with this increase [9–13].

According to the Centre for Evidence-Based Medicine, when assessing the effectiveness of an intervention, the meta-analysis of randomized controlled trials (RCTs) is the type of study with the best scientific evidence [14], making it an essential tool for clinical decision-making. However, the fact that certain authors have published a meta-analysis in a scientific journal does not mean that the study is free of bias. In other words, it is possible that errors were made in the design or execution of the systematic search, as well as in obtaining and interpreting results. For this reason, tools have been developed to assess the methodological quality of these reviews, one of the most widely used being AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews) [15]. This is an instrument consisting of 16 questions that enable the assessment of the quality of systematic reviews of RCTs and non-randomized clinical trials. The analysis results in four levels

of confidence: high, moderate, low and critically low [15]. Concerning the degree of quality of published meta-analyses, reviews that have used this tool have found an inadequate methodological level, finding that most meta-analyses have a low level of confidence [16, 17].

Taking into account the importance of raising HDL-C levels to prevent the onset of CVD and the role of physical exercise in this aspect [4, 9–13], a document is needed that analyzes the results found in meta-analyses of RCTs on this subject, specifying the type, duration and intensity of the exercise. Furthermore, given the precedents found with other diseases (diabetes mellitus and fibromyalgia) [16, 17], it is of interest to evaluate whether these meta-analyses have been performed correctly in terms of their methodology, since they could present a risk of bias and therefore cast doubt on the results obtained (AMSTAR-2) [15].

2 Methods

2.1 Protocol and PROSPERO Registration

This systematic review protocol has been recorded in the PROSPERO database (CRD42020158471) and follows the guidelines of both the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the AMSTAR-2 statements [15, 18].

2.2 Selection Criteria

The scientific articles selected were those that had performed a meta-analysis of RCTs and that assessed the following PICO(T) question (population, intervention, comparator, and objective [with or without time]):

1. Population: healthy adults or those with a condition that increased their cardiovascular risk, such as having high blood pressure, diabetes, dyslipemia, obesity or metabolic syndrome. They could regularly engage in some form of physical training or be sedentary. Reviews that included only men, only women or both sexes were considered.
2. Intervention: any type of physical exercise, whether aerobic, endurance, strength or combined, as long as its influence on HDL-C levels was studied.
3. Comparator: not engaging in any type of physical exercise or having another condition that could alter HDL-C levels, such as following a certain type of diet [5].
4. Objective: the main variable was HDL-C levels, and secondarily, possible improvements in other lipid parameters (TC, LDL-C and TG).
5. Time: no time frame was established to find benefits from the intervention to be evaluated.

Only meta-analyses of RCTs were selected, as this is the design with the best scientific evidence when assessing the benefit of an intervention [14].

2.3 Information Sources and Search

A systematic search was conducted in the MEDLINE (through the PubMed portal) and EMBASE databases, from their inception (MEDLINE, 1966; EMBASE, 1947) until October 30, 2019, using the following keywords, which were searched as MESH (for MEDLINE only) or Emtree terms (for EMBASE only) in the title and abstract: HDL, trial, clinical trial, randomized controlled trial, exercise, physical activity, sports, activity, 'physical activity, capacity and performance', and training. No publication date-based exclusion criteria were applied, and no systematic reviews were excluded based upon the number of studies included in the meta-analysis.

The following database filters were established: (1) meta-analysis: this requirement was set as only studies with this type of design were of interest; (2) humans: as we were not interested in studies involving cells or animals; (3) with an abstract: a necessary criterion to assess whether a paper could meet the selection criteria of our research question; (4) English or Spanish language: as these were the only two languages we were able to read and understand adequately, given that full texts had to be analyzed as this was a systematic review.

In addition to analyzing MEDLINE and EMBASE, we examined the reference lists of the selected articles. We also hand searched the PROSPERO database, which is a registry of systematic reviews, either ongoing or completed. In PROSPERO, the protocols of the systematic reviews are registered before the reviews are undertaken. Protocols are updated regularly to include their status. Consequently, PROSPERO is a source for obtaining systematic reviews that have been published on the subject. It is important to note that the authors are experts in cardiovascular risk and/or meta-analysis. No grey literature was analyzed as we were focused solely on meta-analyses, which, as far as we know, are generally published in scientific journals. More information about the search strategy is available in Electronic Supplementary Material Appendix S1 and in the PRISMA checklist (Electronic Supplementary Material Appendix S2).

2.4 Selection of Reviews

Following the current gold standard in meta-analytic technique, two people (AP and DH) independently and in duplicate analyzed all titles and abstracts obtained from the above search equations. In the event of discrepancies, a meeting was held to reach consensus, and if no consensus was reached, a third reviewer resolved the disagreement (VFG).

After selecting the valid titles and abstracts, the same procedure was followed with the full texts, as well as with the analysis of their references and of PROSPERO. Finally, if we had articles that assessed the same type of intervention in the same type of patients, we retained only the most recent review, that is, the one that covered a longer time period for reviewing scientific studies. In other words, we removed reviews when they had overlap in the population and intervention of focus, retaining the most updated papers.

2.5 Data Extraction

The same two reviewers (AP and DH) independently extracted the following information: (1) population; (2) intervention (which forms of physical exercise were assessed?); (3) sessions/week; (4) minutes/session; (5) duration (weeks); and (6) modification in HDL-C (mg/dl) obtained in the meta-analysis. If this figure was in mmol/l, the units were converted. If any data were missing, the authors of the original systematic review were contacted through the corresponding author, although none of the information provided was used in our review.

2.6 Risk of Bias

We applied the AMSTAR-2 checklist to assess the methodological quality of the articles finally included. This tool has a total of 16 items [15]. Generally, the items consider aspects of the review protocol, the way in which the systematic review or meta-analysis was conducted, as well as the interpretation of its results. The checklist objectively indicates how to assess each of the items, indicating whether each associated aspect has been carried out in a completely correct manner (yes), partially (probably yes) or inadequately (no). After quantifying the 16 items, a confidence level for the review is determined and is classified into four levels: high, moderate, low and critically low. This confidence level is based on the response to the items, with seven of them considered as critical domains (or weaknesses): protocol registration before commencement of the review (#2), adequate literature search (#4), justification for the excluded studies (#7), risk of bias from individual studies (#9), appropriate statistical methods (#11), consideration of risk of bias in the interpretation of results (#13) and analysis of publication bias (#15). The remaining nine are considered non-critical weaknesses. The AMSTAR statement provides the following guidelines for rating confidence [15]:

1. Critically low: more than one critical weakness.
2. Low: at most one critical weakness.
3. Moderate: no critical weakness and more than one non-critical weakness.

4. High: no critical weakness and at most one non-critical weakness.
5. To assess the items concerning the statistical methods of the systematic review (meta-analysis), the recommendations of the Cochrane Library were followed [19].

2.7 Statistical Analysis

As this is a systematic review with no meta-analysis, a descriptive analysis of the information extracted and of the confidence obtained through the AMSTAR-2 was carried out [15].

3 Results

Figure 1 shows the outline of our systematic review, in which we started with a total of 268 scientific articles, 62 in MEDLINE and 206 in EMBASE. After eliminating duplicates and screening the abstracts, we analyzed a total of 34 articles [9–13, 20–48]. Of these, 7 were eliminated [20, 22–24, 28, 29, 46] because there was one group which could included diet or another kind of intervention (exercise or medication), 3 due to the availability of a more updated review on the same type of physical exercise [25–27], and one for not restricting the review to just RCTs [45]. Consequently, 23 articles were finally included in the systematic review (Table 1). These were published between 1999 and 2019

(mean 2013) and all of them showed an increase in HDL-C levels after the intervention [9–13, 21, 30–44, 47, 48].

Table 1 shows the main features of the meta-analyses of RCTs included in this systematic review. First, we would like to highlight that no great variability (generally all subjects were adults with a particular disease or no mention of this) was seen in the populations, with the majority being patients with cardiovascular risk factors (including diabetes and high blood pressure) [11–13, 21, 33, 36, 37, 40, 43, 48], or presumably healthy people [9, 10, 30–32, 34–36, 38–42, 44, 47], and either distinguishing by sex [32, 39, 42] or grouping together men and women [9–13, 21, 30, 31, 33–38, 40, 41, 43, 44, 47, 48]. With regard to the type of physical exercise assessed, it was generally observed that nearly all the meta-analyses included groupings of different types. For example, many assessed aerobic exercise in any form [11, 12, 21, 30, 32, 33, 35, 37–43, 47, 48], and these are detailed in Table 1. However, other systematic reviews focused on a single type of physical exercise, such as yoga [13, 36], Wuqinxi Qigong [9], running [34], walking [44], or exercises focused on strength performance as opposed to resistance [31]. None of the control groups performed any special physical exercise, as this was a criterion for exclusion from our review.

With regard to the frequency and time spent practicing the exercise, there was great variability in the reviews included (Table 1). First, the frequency varied from every day to only once per week, with ranges always provided,

Fig. 1 Flow chart of the systematic review following the PRISMA statement. HDL-C, high-density lipoprotein cholesterol; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses

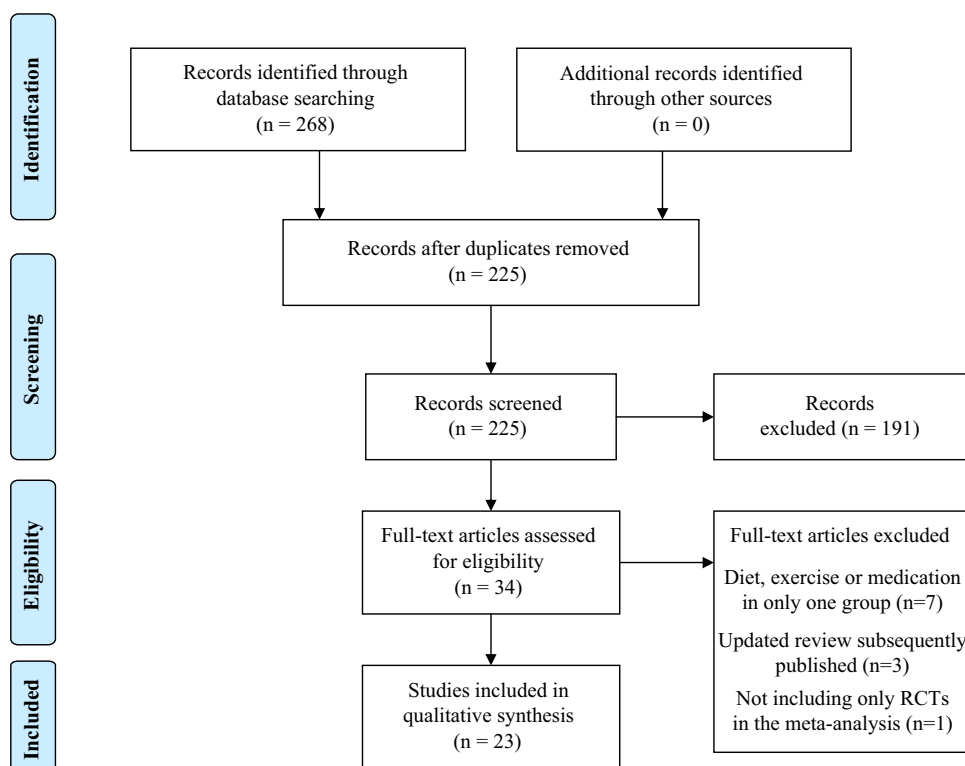


Table 1 Main characteristics of the included meta-analyses that analyzed HDL-C levels after an intervention based on the practice of physical exercise

Reference	Population	Intervention	Frequency (sessions per week)	Session duration (min)	Duration (weeks)	HDL-C improvement (mg/dl)	Other lipid parameters
Zou et al. 2019 [9]	35–75 years	Wuqinxi Qigong	3–7	30–60	8–48	0.27	↓TC, ↓LDL-C, ↓TG
Igarashi et al. 2019 [30]	East Asian adults with an average age ≥40	Stationary bicycle, jogging, walking and step	2–6	15–60	4–24	2.2	↓TC, ↓TG
Igarashi et al. 2019 [10]	Healthy adults with an average age ≥20	Water-gym ^a and moderate-vigorous intensity swimming	1–4	15–50	6–15	4.6	↓TC, ↓LDL-C
Costa et al. 2019 [31]	Adults	Series of 4–25 repetitions against an opposing force at high intensity	2–5	12–90	8–52	2.81	↓TC, ↓TG, ↓LDL-C
Wewege et al. 2018 [11]	Adults with metabolic syndrome without type 2 diabetes	Aerobics, circuit training, walking, fast jogging, running, treadmill, cycle ergometer, arm ergometer and cycling	3–5	30–60	12–52	1.93	↓TG
Zhang et al. 2018 [32]	Adult women who do not exercise regularly	Aerobic exercise, football, running, walking, cycling, swimming	2–3	60	8–52	3.48	↓TC, ↓LDL-C
Lemes et al. 2018 [21]	Adults with metabolic syndrome	Aerobic training	2–5	19–70	1.5–12	3.15	↓TC
Ostman et al. 2017 [12]	Adults with metabolic syndrome	Aerobic exercise combined with endurance	3	40–60	12–52	5.41	
Cui et al. 2017 [13]	Adults with type 2 diabetes	Yoga	1–7	25–120	2–36	4.30	↓TC, ↓LDL-C
Zou et al. 2016 [33]	Adults with obesity and type 2 diabetes	Aerobic exercise, aerobic plus endurance exercise	2–4	45–60	52	3.57	↓TG
Hespanhol Junior et al. 2015 [34]	Physically inactive adults but without disease	Running	2–7	25–60	52–69	3.3	↓TG
Lin et al. 2015 [35]	Adults	Exercise of any kind	Not indicated	Not indicated	2–104	2.32	↓TG
Murtagh et al. 2015 [44]	Sedentary adults	Walking	2–7	20–45	8–24	0.39	
Hartley et al. 2014 [36]	Healthy adults or those at high cardiovascular risk	Yoga	2–7	60	12–20	3.09	↓TG
Hayashino et al. 2012 [37]	Adults with type 2 diabetes	Aerobic and endurance exercise	2–4	30–75	12–108	3.09	
Kelley et al. 2009 [47]	Adults	Progressive resistance training	2–3	24–60	8–78	0.7	↓TC, ↓TG, ↓LDL-C
Kodama et al. 2007 [38]	Adults	Walking, cycling, jogging, swimming, skiing or elliptical	2–6	23–60	12–52	2.53	

Table 1 (continued)

Reference	Population	Intervention	Frequency (sessions per week)	Session duration (min)	Duration (weeks)	HDL-C improvement (mg/dl)	Other lipid parameters
Kelley et al. 2006 [39]	Adult men	Walking, jogging, cycling, swimming, gymnastics, stair climbing and calisthenics	2-5	8-60	8-156	1.3	↓TC, ↓TG, ↓LDL-C
Cornelissen et al. 2005 [40]	Healthy, sedentary adults and hypertensive patients	Running, swimming, cycling (endurance)	1-7	15-63.3	4-52	1.24	
Kelley et al. 2005 [41]	Adults > 50 years	Walking, jogging, running, cycling, swimming, aerobic exercise, arm ergometer, treadmill, water-gym ^a , rowing and hand pedaling	2-6	17-90	8-104	2.5	↓TC, ↓LDL-C
Kelley et al. 2005 [48]	Adults with obesity or overweight	Walking, jogging, aerobic dance, stationary cycling, stair climbing and swimming	3-5	17-75	10-52	1.6	↓TC, ↓TG
Kelley et al. 2004 [42]	Adult women	Walking, jogging, running, dancing, cycling, aerobic exercise, trampoline jumping, step, aerobics, elliptical, stationary bicycle and treadmill	1-7	15-90	8-104	1.8	↓TC, ↓TG, ↓LDL-C
Halbert et al. 1999 [43]	Adults with dyslipidemia and normolipidemia who are sedentary	Walking, jogging, running, stair climbing, treadmill and stationary bicycle	2.5-7	15-60	9-52	1.93	↓TC, ↓TG, ↓LDL-C

All the studies found an improvement in HDL-C levels after the intervention

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides

^aWater-gym is any physical activity performed in the water other than swimming, such as walking, dancing, Tai Chi, aerobics or running

since the RCTs included in these reviews did not always use the same duration. Second, the length of each session had a fairly wide range, lasting from 12 min to 2 h, depending on the type of physical exercise. In addition, the period used to assess a change in HDL-C levels ranged from 2 to 108 weeks, that is, 2 years. Finally, HDL-C levels increased between 0.27 and 5.41 mg/dl, with positive changes also found in TC, LDL-C and TG.

Table 2 and Fig. 2 summarize the AMSTAR-2 items for the meta-analyses included in this systematic review. Table 2 gives detailed assessments of all the items for each work and Fig. 2 provides a graphical analysis of the situation at the group level. It is also important to note that only one systematic review reached the highest level of confidence, [36] while the rest were rated as critically low. This work was a Cochrane review, which determined the effectiveness of yoga in healthy adults or those at high cardiovascular risk [36].

The analysis of Fig. 2 highlights positively that all systematic reviews defined the PICO(T) question correctly, as well as the description of the included studies, giving information on time and form of practice of the physical exercise assessed. We would also like to point out that 82.6% of the reviews analyzed took into account the heterogeneity of the results when interpreting them. By contrast, several negative aspects were observed, notably that no review justified why it was restricted to RCTs alone and that 95.7% did not explain why they chose to pool the results of the RCTs through a meta-analysis. Finally, the absence of a protocol or the lack of information within it for review is striking, with this error being present in 91.3% of the cases. Furthermore, in 91.3% of the systematic reviews, the list of excluded studies was not given, and very few meta-analyses indicated which studies specifically (with references) were excluded and the reason for this.

4 Discussion

4.1 Summary

Twenty-three meta-analyses of RCTs were studied that assessed the application of a physical exercise protocol in a general population or in patients at risk of cardiovascular disease, in which a change in HDL-C levels was observed after the intervention. There was great variability in their characteristics (different types, frequencies or intensities in the studied interventions), and with the exception of one systematic review [36] they all presented a low level of confidence.

4.2 Strengths and Limitations

The main strength of this review is the research question developed, since it is clinically relevant to know which therapeutic options based on physical exercise increase HDL-C levels, to advise patients who have below-normal values. In other words, according to the initial HDL-C level, preferences, time available and possible physical limitations, a patient with these characteristics can be given physical exercise options: type, frequency and intensity. Another strength is the study design, since a systematic review of meta-analyses based on RCTs has a high level of evidence, provided that it has been properly conducted [15]. To achieve this, we applied the recommendations of the Cochrane Library and AMSTAR-2 [15, 19]. Finally, it is important not to assume that a published meta-analysis presents the highest level of evidence, since it may contain errors that reduce the confidence level, as assessed through the application of AMSTAR-2 [15].

The limitations of this review are mainly defined by the study design as we may have excluded systematic reviews indexed in MEDLINE or EMBASE. However, by performing our search independently and in duplicate, this type of bias is minimized. It is also possible that other articles met our inclusion criteria but were not in the two databases mentioned above. Nonetheless, we analyzed the references of the included publications, as well as the PROSPERO registry, which minimized the likelihood of this happening. Finally, reviews in which participants followed some type of diet could have been included [28, 29], and would have increased the number of publications analyzed, but as we wanted to isolate the effect of physical exercise, these were directly excluded.

4.3 Comparison with the Existing Literature

The increase in HDL-C levels found in the meta-analyses consulted ranged from 0.27 to 5.41 mg/dl, depending on the type of patient, type of physical exercise, frequency and intensity. Comparing these figures with studies that have analyzed components of the Mediterranean diet, such as olive oil or oily fish, a greater improvement was observed, [49, 50] as these increased levels by 2.37 and 2.32 mg/dl, respectively. However, when a diet that uses this type of unsaturated fat is combined with physical exercise at a general level, the increase in HDL-C levels rises to almost 4 mg/dl [51]. Consequently, physical exercise potentiates the increase. Therefore, if we choose the most appropriate type of activity for the patient based on that described above, the ranges indicated could be increased. However, we must take into account that for HDL-C levels to be beneficial, the patient must have a high level of adherence to the chosen exercise to improve the antioxidative and anti-inflammatory

Table 2 Assessment of the AMSTAR-2 items of the included meta-analyses that analyzed HDL-c levels after an intervention based on the practice of physical exercise

Reference	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Overall confidence
Zou et al. 2019 [9]	Y	N	N	PY	Y	Y	N	Y	PY	Y	N	N	N	N	Y	Y	Critically low
Igarashi et al. 2019 [30]	Y	N	N	PY	Y	N	N	Y	Y	Y	N	Y	N	Y	Y	Y	Critically low
Igarashi et al. 2019 [10]	Y	N	N	PY	Y	Y	N	Y	PY	Y	N	N	N	Y	Y	Y	Critically low
Costa et al. 2019 [31]	Y	N	N	N	Y	Y	N	Y	Y	Y	N	N	N	Y	Y	N	Critically low
Wewege et al. 2018 [11]	Y	N	N	PY	Y	N	N	Y	PY	Y	N	N	N	Y	Y	Y	Critically low
Zhang et al. 2018 [32]	Y	Y	N	N	Y	Y	N	Y	Y	Y	N	N	Y	Y	N	Y	Critically low
Lemes et al. 2018 [21]	Y	N	N	N	Y	N	N	Y	PY	Y	N	N	N	Y	N	Y	Critically low
Ostman et al. 2017 [12]	Y	N	N	N	Y	N	N	Y	N	Y	N	N	N	N	Y	Y	Critically low
Cui et al. 2017 [13]	Y	N	N	N	N	Y	N	Y	Y	N	N	N	Y	Y	N	Y	Critically low
Zou et al. 2016 [33]	Y	N	N	N	Y	Y	N	Y	Y	Y	N	N	N	Y	N	Y	Critically low
Hespanhol Junior et al. 2015 [34]	Y	N	N	PY	Y	Y	N	Y	Y	Y	N	N	Y	Y	N	Y	Critically low
Lin et al. 2015 [35]	Y	N	N	PY	Y	Y	N	Y	Y	Y	N	N	Y	Y	Y	Y	Critically low
Murtagh et al. 2015 [44]	Y	N	N	N	N	Y	N	Y	Y	Y	N	N	Y	N	Y	Y	Critically low
Hartley et al. 2014 [36]	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Hayashino et al. 2012 [37]	Y	N	N	N	N	Y	N	Y	PY	Y	N	Y	Y	Y	Y	Y	Critically low
Kelley et al. 2009 [47]	Y	N	N	PY	N	Y	N	Y	PY	Y	N	Y	N	Y	Y	Y	Critically low
Kodama et al. 2007 [38]	Y	N	N	N	Y	Y	Y	Y	PY	Y	N	N	N	Y	Y	Y	Critically low
Kelley et al. 2006 [39]	Y	N	N	N	N	Y	N	Y	PY	Y	N	Y	Y	Y	Y	Y	Critically low
Cornelissen et al. 2005 [40]	Y	N	N	N	N	Y	N	Y	N	Y	N	N	N	Y	N	N	Critically low
Kelley et al. 2005 [41]	Y	N	N	PY	N	Y	N	Y	PY	Y	N	N	N	Y	Y	N	Critically low
Kelley et al. 2005 [48]	Y	N	N	N	Y	Y	N	Y	PY	Y	N	N	N	N	Y	N	Critically low
Kelley et al. 2004 [42]	Y	N	N	PY	N	Y	N	Y	PY	N	N	N	Y	Y	Y	N	Critically low
Halbert et al. 1999 [43]	Y	N	N	PY	N	N	N	Y	Y	N	N	N	Y	Y	Y	N	Critically low

AMSTAR, A MeaSurement Tool to Assess systematic Reviews; HDL-c, high-density lipoprotein cholesterol; N, no; PY, partial yes; Q, question; Y, yes

Q1: Did the research questions and inclusion criteria for the review include the components of PICO/PICOT?

Q2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

Q3: Did the review authors explain their selection of the study designs for inclusion in the review?

Q4: Did the review authors use a comprehensive literature search strategy?

Q5: Did the review authors perform study selection in duplicate?

Q6: Did the review authors perform data extraction in duplicate?

Q7: Did the review authors provide a list of excluded studies and justify the exclusions?

Q8: Did the review authors describe the included studies in adequate detail?

Q9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

Q10: Did the review authors report on the sources of funding for the studies included in the review?

Q11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

Q12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

Q13: Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?

Q14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

Q15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

Q16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?



Fig. 2 Analysis of the AMSTAR-2 items of the included meta-analyses that studied HDL-C levels after an intervention based on the practice of physical exercise. AMSTAR, A Measurement Tool to Assess systematic Reviews; HDL-C, high-density lipoprotein cholesterol. Q=question; Red=no, yellow=partial yes, green=yes. Q1: Did the research questions and inclusion criteria for the review include the components of PICO(T)? Q2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? Q3: Did the review authors explain their selection of the study designs for inclusion in the review? Q4: Did the review authors use a comprehensive literature search strategy? Q5: Did the review authors perform study selection in duplicate? Q6: Did the review authors perform data extraction in duplicate? Q7: Did the review authors provide a list of excluded studies and justify the exclusions? Q8: Did the review authors describe the included studies in adequate detail? Q9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? Q10: Did the review authors report on the sources of funding for the studies included in the review? Q11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? Q12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? Q13: Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review? Q14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? Q15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? Q16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

properties of HDL-C [52]. Finally, with respect to quality by applying the AMSTAR-2 scale [15], results similar to ours have been found in other diseases, i.e. low quality in the systematic reviews analyzed [16, 17].

4.4 Implications for Research and Clinical Practice

Regarding clinical practice and considering the results together with the quality of the reviews, we see that for a patient with or without high cardiovascular risk who also has low HDL-C levels, there is strong scientific evidence to recommend yoga. This activity can be practiced by individuals of all ages and improves HDL-C by an average of 4.30 mg/dl over a period of 2–36 weeks [36]. Yoga can be performed outdoors or in a group, thereby increasing adherence. Since the remaining reviews were found to have a critically low level of confidence, they should be updated according to the principles of AMSTAR-2 [15] to obtain a high level of confidence, which would allow the recommendation of their results for use in routine clinical practice. Although no statistical pooling or similar statistical analysis was performed, the critically low quality of the meta-analyses included suggests that statistical analysis was likely unwarranted. Accordingly, the reviews should be updated or the process of reviewing meta-analyses should be strengthened, improving the peer-review process, which is a key point for the scientific validity of a work [53]. In addition, the process should be critical of papers that have already been published, applying tools like AMSTAR-2 [15].

5 Conclusions

This systematic review analyzed the MEDLINE and EMBASE databases, assessing meta-analyses of RCTs that determined the relationship between engaging in physical exercise and a modification in HDL-C levels in the general population or in patients with cardiovascular risk factors. A total of 23 publications were studied. These meta-analyses showed great variability in the types of physical exercise, duration and intensity, as well as the type of populations examined. These publications showed an increase in HDL-C levels ranging from 0.27 to 5.41 mg/dl. However, their confidence level was critically low, except for one systematic review (yoga), which had the highest confidence level [36]. This lack of confidence was mainly due to the absence of a protocol for the review or lack of information contained therein, as well as the failure to detail precisely which studies were consulted in full text and excluded from the review, indicating the reason.

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Compliance with Ethical Standards

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