Total cholesterol and low-density lipoprotein alterations in children and adolescents from Brazil: a prevalence meta-analysis

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ABSTRACT

Objective: The aim of the present study was to evaluate the prevalence of total cholesterol (TC) and low-density lipoprotein (LDL) alterations in children and adolescents in Brazil. **Materials and methods:** A systematic review and meta-analysis of prevalence. The search for articles was carried out in the databases: Medline (PubMed), Embase, Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (Lilacs). The meta-analysis was performed using the random effects model. The l² test was used to identify heterogeneity. **Results:** The present metanalysis revealed a significant prevalence of altered lipid profile in children and adolescents in Brazil. Regarding lipoprotein fractions, the prevalence of altered TC level was 27.47% (95% Cl 24.36-30.82), and a smaller prevalence was observed for LDL cholesterol (19.29% – 95% Cl 15.21-24.16). The models revealed high heterogeneity (l² = 99%; p < 0.01), however the precise source of it was not identified; although type of school, age group, year and the region of Brazil appeared to influence the estimations of altered lipid profiles. **Conclusion:** An important prevalence of lipid alterations was observed among Brazilian children and adolescents to perform early interventions for this public. Arch Endocrinol Metab. 2023;67(1):19-44

Keywords

Adolescent; child; dyslipidemia; cholesterol; prevalence

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INTRODUCTION

Lipid profile alterations are characterized by quantitative alteration of a component of the serum lipids (increase in total cholesterol [TC], low-density lipoprotein [LDL] or triglycerides and decrease in high-density lipoprotein [HDL]) (1). International cutoff like the National Heart, Lung and Blood Institute (NHLBI) consider elevated TC, a cholesterol value > 200 mg/dL and a borderline value between 170 and 199 mg/dL; while the LDL value is pathological if it is > 130 mg/dL and borderline if > 110 mg/dL (2). However, in most Brazilian studies,



the definition adopted is based on The Brazilian Society of Cardiology (BSC). The BSC classifies lipid profile for ages 2 to 19 years as follow: TC borderline 150-169 mg/dL; elevated \geq 170 mg/dL and LDL borderline 100-129 mg/dL; elevated \geq 130 mg/dL) (3-5).

Increases in LDL levels are the main predictor of CVD and LDL is the main component of TC (1). Therefore, both, TC and LD, are the focus of this study. In children and adolescents, lipid alterations can be risk factors to CVD; however, it usually occurs due to obesity (6). The association between lipid disorders and comorbidities, such as hypertension, obesity, and

diabetes, are the main risk factors influencing the development of CVD (7). The Bogalusa Heart Study from the United States reported that atheromatous lesions in the aorta begin in childhood and it increases from 10 years of age until adulthood (8). The Bogalusa Heart Study revealed the presence of fatty streaks, which are precursors of atherosclerotic plaques, in the aorta and in the coronary bed of children and adolescents; those aortic injuries were correlated with elevated serum LDL levels (8,9).

Obesity, family medical history, physical inactivity, inadequate dietary patterns/habits are risk factors for lipid profile alterations in children and adolescents (10,11). Dietary habits and physical exercise are modifiable risk factors and, as such, can be subjected to intervention (12,13). However, to perform a better public health intervention it is important to understand the prevalence of lipid alteration in children and adolescents, as well as its geographical distribution, and other risk factors that may be related to the increase of the serum lipids.

Aiming to understand the impact of risk factors for CVD, the "*Estudo de Riscos Cardiovasculares em Adolescentes*" (ERICA) study (14) evaluated adolescents in public and private schools of Brazilian cities with populations >100,000. Results from that study, however, did not include children, and were limited to cities with large populations.

Several studies have reported the prevalence of TC and LDL alterations among children and adolescents in Brazil (15-18). However, the diversity of cutoff points adopted for the classification of altered TC and LDL among Brazilian studies makes it difficult to compare results internationally. Moreover, the prevalence of TC and LDL alterations and in children and adolescents from Brazil remains unclear. The aim of the present study was to evaluate the prevalence of TC and LDL alterations in children and adolescents in Brazil through meta-analysis and identify aspects that influence these rates.

MATERIALS AND METHODS

The International Prospective Register of Systematic Reviews approved the research protocol (CRD42018103796). This systematic review followed the procedure suggested by the guidelines Preferred Reporting Items for Systematic Reviews and Metaanalysis (PRISMA) (19).

Eligibility criteria

Eligibility criteria included cross-sectional and baseline of cohort studies investigating prevalence rates of altered lipid profile among children and adolescents in Brazil.

To be included, studies were required to describe the prevalence of TC and/or altered LDL levels of children (2-10 years old) or adolescents (>10-19 years old), and report information collected in a community or in schools of Brazil. The studies must have used the international cutoff criteria for diagnosis (NHLBI) or the latest cutoff proposed by the BSC (3-5). There were no restrictions towards publication date, language, or publication status. Studies that evaluated children or adolescents with specific health conditions (e.g., diabetes, psychological and/or genetic diseases, populations with specific congenital problems, genetic syndromes, endocrine or immunological dysfunction, or primary hypertension), were excluded. Interventional studies were also excluded due to its inclusion criteria and sample size estimations that usually do not allow to estimate prevalence adequately.

Research strategy

Literature searches were performed in the Medline (PubMed), Embase, Scientific Electronic Library Online (SciELO), and Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs) databases using Medical Subject Headings (MeSH) terms and entries for PubMed and Embase, and DeCS (Health Sciences Descriptors) for the SciELO and Lilacs databases up to March 2022. Full-text versions of all potentially eligible articles were downloaded from the electronic databases or requested directly to the authors via e-mail. All searches were performed independently by two reviewers (VMJB and TPRS). Search strategies were tested using MESH and the related indexing terms for each database (Table S1) with the keywords "dyslipidemia", "total cholesterol", "low-density lipoprotein", "prevalence", "children", "adolescents" and "Brazil". No data and language restrictions were applied. An independent manual search of the reference lists of the retrieved articles was also performed.

Study selection and data extraction

According to the eligibility criteria, two reviewers independently screened titles and abstracts and, later, read the full text articles. Disagreements were resolved by a third author. When studies with a sample already

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included in the review were identified, the study with the most complete data was considered. However, if the studies were identified from the same sample and, for example, one has a prevalence of TC and the other has a prevalence of LDL, both were included in the review. Observational studies were included if they provided cross-sectional data from baseline.

For data extraction, an electronic spreadsheet was created in which the following information was recorded: study name; authors; year of data collection; city; state; objective; age group; type and size of the sample; TC and LDL levels. TC and LDL levels were considered elevated according to the cutoff values determined by the authors in each study.

Risk of bias within studies

Quality assessment of the studies was performed using the Newcastle-Ottawa Scale, with an adapted version of the scale for cross-sectional studies (20), with a maximum of 10 points for the least risk of bias study. Two authors (CKD and TPRS) evaluated the risk of bias. Although differences in quality assessment scores between investigators were unusual, they were resolved by consensus. The risk of publication bias across studies was explored with funnel plot asymmetry and Egger's Test. Trim-to-fill correction was used in the presence of publication bias.

Data analysis

The primary endpoints were the prevalence of altered TC and LDL cholesterol levels with the corresponding 95% confidence interval (CI). Summary measures were estimated for the total population and for subgroups defined according to age group, type of school, year of publication, and region of the country (i.e., Brazil). Brazil is geopolitically divided into five regions with at least three states on each region. Heterogeneity was assessed using the chi-squared test with statistical significance set at p < 0.10, and its magnitude was determined using the I² statistic. Meta-analysis was performed using a random effect model and weighted according to the inverse of variance. The meta-analyses were performed with articles using the same cutoff for diagnosis (NHLBI or BSC). Therefore, the same outcome has two forest plots: one with studies using BSC criteria and other for studies using the NHLBI criteria. Analyses were performed using the command "Metaprop" in RStudio version 3.4.4, adopting statistical significance at p < 0.05.

In March 2022, the literature search identified 831 studies in the databases. After screening of titles and abstracts and, subsequently, full-text reading of the articles, 47 (14,21-66) studies were included in the present systematic review (Figure 1). The characteristics of these studies are summarized in Table 1. Sample sizes ranged from 95 to 38,069 across the studies. All regions of Brazil were represented; however, few studies from the Northern and Midwest states were found. Most studies were conducted in cities in the Southeast region, with emphasis on the states of São Paulo and Minas Gerais (Table 1).

Seven studies (21-27) exclusively evaluated lipid profile in 2,591 children, most of whom were from the Southeast region (Table 1), ranging in age from 6 to 10 years. Twenty-two studies (14,28-48) examined exclusively adolescents (10 to 19 years old), covering 45,331 individuals, and were performed predominantly in the Northeast and Southeast regions of Brazil (Table 1). In addition, 18 studies (49-66) evaluated simultaneously children and adolescents, totaling 24,400 individuals 2 to 19 years of age (Table 1).

Some studies (14, 21 - 23, 26 - 51, 53, 54, 56 - 66)evaluated children and adolescents from schools, and both public and private schools were included. Most studies followed the BSC criteria for diagnosing lipid profile alterations. Fewer studies (25 -26,38,39,51,52,62,66) used the NHLBI diagnosis criteria for elevated TC and LDL. Some studies (21-24,26-29,32-37,40-42,44,45,48,57,59-61,63) used criteria from BSC but with the same cutoff for LDL values indicated by NHLBI ($\geq 130 \text{ mg/dL}$).

Regarding the studies methodological quality evaluation, 44 studies were graded \geq 7 of 10 stars. The articles were mostly downgraded due to lack of assessment of non-respondents (Table 1).

A subgroup meta-analysis according to the cutoff criteria used to diagnose altered TC was performed. Pooled analysis for TC prevalence according to the NHLBI criteria indicated a tendency to a lower prevalence estimate (17.22% [95% CI 9.52-29.15]; I² = 99%) than the BSC criteria (27.47% [95% CI 24.36-30.82]; I² = 98%) (p-value between groups = 0.094) (Table 2 and Figure S1A). Therefore, the following analysis were performed for each diagnostic criterion, BSC and NHLBI.

	Table 1. Characteristics	of the	studies	included i	n the	prevalence	meta-	analysis
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Study	Year	Sample	Age	Region	City	State	Population origin	Cri	teria	Quality assessment
								CT	LDL	
CHILDREN								·	-	
Almeida (21)	2016	511	6 to 9 y	Southeast	Vitória	Espírito Santo	Public School	≥170	≥130	7
Barbalho (22)	2017	150	6 to 10 y	Southeast	Lins	São Paulo	Public School	≥170	≥130	7
Filgueiras (23)	2018	378	8 to 9 y	Southeast	Viçosa	Minas Gerais	Public and Private Schools	≥170	≥100	8
Nobre (24)	2013	227	5 y	Southeast	Diamantina	Minas Gerais	-	≥170	≥130	8
Rinaldi (25)	2012	147	7,4 ± 1,4 y*	Southeast	Botucatu	São Paulo	not informed	≥200	≥130	7
Silva (26)	2013	677	6 to 10 y	Southeast	Santo André	São Paulo	Public School	≥200	≥130	6
Teixeira (27)	2020	501	6 to 10 y	Southeast	Macaé	Rio de Janeiro	Public School	≥170	≥130	8
ADOLESCENTS										
Arruda-Neta (28)	2017	774	10 to 14 y	Northeast	João Pessoa	Paraíba	Public School	≥170	≥130	7
Bauman (29)	2020	635	10 and 16 y	Southeast	Montes Claros	Minas Gerais	Public School	≥170	≥130	9
Beck (30)	2011	660	14 to 19 y	South	Três de Maio	Santa Catarina	Public and Private Schools	≥170		8
Carvalho (31)	2007	180	14 to 17 y	Northeast	Campina Grande	Paraíba	Public and Private Schools	≥170	≥110	8
Chaves (32)	2012	120	10 to 13 y	Southeast	Viçosa	Minas Gerais	Public School	≥170	≥130	9
Enes (33)	2018	525	10 to 19 y	Southeast	Piracicaba	São Paulo	Public School	≥170	≥130	5
Faria (34)	2014	100	14 to 17 y	Southeast	Viçosa	Minas Gerais	Public School	≥170	≥130	8
Faria-Neto (14)	2016	38,069	13 to 17 y	Brazil†			Public and Private Schools	≥170	≥130	9
Gadelha [‡] (35)	2019	236	15.1 ± 1.4*	Northeast	Recife	Pernambuco	Cohort study of the public school	≥170	≥130	7
Gonçalves (36)	2012	95	10 to 13 y	Southeast	Viçosa	Minas Gerais	Public School	≥170	≥130	10
Guimarães (37)	2019	997	12 to 18 y	South	Curitiba	Paraná	Public School	≥170	≥130	8
Lunardi (38)	2008	374	11.25 ± 0,28y*	South	Santa Maria	Rio Grande do Sul	Public and Private Schools	≥200	≥130	9
Lunardi (39)	2010	358	16 y	South	Santa Maria	Rio Grande do Sul	Public and Private Schools	≥200		9
Mastroeni (40)	2016	222	15 to 17 y	South	Joinville	Santa Catarina	not informed	≥170	≥130	8
Melo (41)	2016	196	11 to 19 y	Northeast	Natal	Rio Grande do Norte	Public School	≥170	≥130	9
Pereira (42)	2010	470	10 to 14 y	Northeast	Recife	Pernambuco	Public School	≥170	≥130	9
Pinto (43)	2011	117	14 to 17 y	Midwest	Brasília	Distrito- Federal	Public School	≥150	≥110	8
Queiroz (44)	2019	220	15 to 19 y	Northeast	João Pessoa	Paraíba	Public School	≥170	≥130	9

Study	Year	Sample	Age	Region	City	State	Population origin	Criteria		Quality assessment
Romero (45)	2014	199	10 to 14 y	Southeast	Piracicaba	São Paulo	Public School	≥170	≥130	9
Scheer (46)	2019	394§	13.3 ± 1,5y*	Southeast	Rio de Janeiro	Rio de Janeiro	Public School	≥170		7
Sousa (47)	2013	250	11 to 18 y	Northeast	Salvador	Bahia	Public and Private Schools	>170	>110	8
Vasconcelos(48)	2008	140	12 to 16 y	South	São Mateus do Sul	Paraná	Public School	≥170	≥130	9
CHILDREN AND AD	OLESCE	NTS								
Alcântara-Neto (49)	2012	937	7 to 14 y	Northeast	Salvador	Bahia	Public School	≥170		9
Bergmann (50)	2011	1,294	7 to 12 y	South	Caxias do Sul	Rio Grande do Sul	Public and Private Schools	≥170		9
Burgos (51)	2019	1,743	7 to 17 y	South	Santa Cruz do Sul	Rio Grande do Sul	Public and Private Schools	≥200	≥130	9
Burgos (52)	2015	1,254	7 to 17 y	South	Santa Cruz do Sul	Rio Grande do Sul	not informed	≥200	≥130	8
Guimarães (53)	2005	366	6 to 12 y	Northeast		Bahia	Public and Private Schools	≥170		6
Giuliano (54)	2005	1,053	7 to 18 y	South	Florianópolis	Santa Catarina	Public and Private Schools	≥170		8
Gomes (55)	2020	61,870	2 to 19y	Southeast	Campinas	São Paulo	Basic health unit	≥170	≥110	8
Moura (56)	2000	1,600	7 to 14 y	Southeast	Campinas	São Paulo	Public School	≥170		10
Cunha (57)	2014	399	6 to 15 y	South	Botuverá	Santa Catarina	Public School	≥170	≥130	9
Pereira(58)	2009	494	2 to 19 y	Southeast	Itapetininga	São Paulo	Public School	≥170	≥110	9
Quadros (59)	2016	1,139	6 to 18 y	Northeast	Armagosa	Bahia	Public and Private Schools	≥170	≥130	9
Quadros (60)	2015	1,139	6 to 18 y	Northeast	Armagosa	Bahia	Public and Private Schools	≥170	≥130	9
Reuter (61)	2013	564	8 to 17 y	South	Santa Cruz do Sul	Rio Grande do Sul	Public and Private Schools	≥170	≥130	10
Reuter (62)	2016	1,243	7 to 17 y	South	Santa Cruz do Sul	Rio Grande do Sul	Public School	≥200	≥130	6
Ribas (63)	2012	874	6 to 19 y	North	Belém	Pará	Public and Private Schools	≥170	≥130	9
Ribas (64)	2014	571	6 to 19 y	North	Belém	Pará	Public and Private Schools	≥170	≥110	9
Ribas (65)	2009	437	6 to 19 y	North	Belém	Pará	Private School	≥170	≥110	8
Ribeiro (66)	2010	3,106	6 to 18 y	South and Southeast	Belo Horizonte Florianópolis Blumenau	Minas Gerais e Santa Catarina	Public and Private Schools	≥200	≥130	9



Figure 1. Systematic review and meta-analysis Flowchart.

fable 2. Summary of the prevalence rates accordi	ing to the cutoff value used fo	r total cholesterol and LDL cholesterol
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Diagnostic criteria for the definition of the lipid alterations	Quoted studies	Number of subjects	Summary prevalence estimate	95% confidence interval	Forest plot	p-value
Total cholesterol						0.094
>170 mg/dL, BSC	35	117,159	27.47%	24.36-30.82	Figure S1A	
>200 mg/dL, NHLB	7	7,546	17.22%	9.52-29.15	Figure S1A	
Low-density lipoprotein						0.040
>110 mg/dL, BSC	7	64,139	19.29%	15.21-24.16	Figure S1B	
>130 mg/dL, NHLB	29	53,619	11.63%	7.45-17.71	Figure S1B	

Note: NHLBI: National Heart, Lung and Blood Institute; BSC: Brazilian Society of Cardiology.

A subgroup meta-analysis according to the region of Brazil revealed that the Southeast region had the highest prevalence (35.06% [95% CI 31.06-39.28]; I² = 99%) of elevated TC levels compared with the Northeast region (17.37% [95% CI 12.57-23.52]; I² = 95%) (p < 0.01) with the BSC criteria, with no differences when using NHLBI criteria (Figures S2A and S2B). A second subgroup meta-analysis examining the prevalence of elevated TC levels was performed according to the age group (Figures 2 A e B). Children exhibited a higher prevalence of altered TC levels (11.56% [95% CI 7.31-17.82]) than adolescents (4.78% [95% CI 3.45-6.59]) (p = 0.002) with the NHLBI criteria (Figure 2A), with no difference when using the BSC criteria (Figure 2B). A third subgroup analysis for altered TC was performed with the studies in which the samples came from school. The analysis were divided by type of school: private or public schools (Figure 2C). Children and adolescents in public schools presented a higher prevalence of altered TC levels (26.99% [95% CI 22.64-31.84]; $I^2 = 96\%$) than those in private schools (18.15% [95% CI 12.78-25.11]; $I^2 = 72\%$) (p = 0.034) (Figure 2C) with the BSC criteria, and no differences was observed when using NHLBI criteria. A fourth subgroup meta-analysis examining the year when studies were published revealed no difference (p = 0.391) in the prevalence of altered TC levels with the BSC criteria nor the NHLBI criteria (Figures S2A and S2B).

To conclude the TC analysis, a subgroup metanalysis was performed by gender. No difference in the prevalence of altered TC level between girls and boys (p = 0.3439) was observed.

Similar to TC, a subgroup meta-analysis according to the criteria adopted for altered LDL was performed. The estimated prevalence of elevated LDL levels in children and adolescents classified according to

Study	Events	Total	Ever	nts per 1 servation	00 s	Events	95%-CI	Weight
Group = Adolescente Lunardi Lunardi Random effects model Heterogeneity: $I^2 = 0\%$, τ^2	18 17 = 0, p = 0	374 358 732).97				4.81 4.75 4.78	[2.88; 7.50] [2.79; 7.49] [3.45; 6.59]	33.8% 33.4% 67.2%
Group = Criança Rinaldi Random effects model Heterogeneity: not applicab	17	147 147	_			— 11.56 — 11.56	[6.88; 17.87] [7.31; 17.82]	32.8% 32.8%
Random effects model Heterogeneity: $I^2 = 79\%$, τ^2 Residual heterogeneity: I^2	= 0.232 = 0%, p =	879 7, p < 0. = 0.97	01 · · · · · · · · · · · · · · · · · · ·	10 12	14 16	6.43	[3.59; 11.28]	100.0%

Figure 2A. Prevalence of high total cholesterol for age group according NHLBI criteria. Note: p-value = 0.021.

			Events per 100			
Study	Events	Total	observations	Events	95%-CI	Weight
Group = Adolescents			:			
Arruda-Neto	251	774		32 43	[29 14: 35 85]	4 1%
Bauman	170	635		26 77	[23, 36, 30, 40]	4.1%
Beck	134	660		20.30	[17 30: 23 58]	4 0%
Carvalho	6	180 -	—	3.33	[1.23: 7.11]	2.4%
Chaves	65	120		54.17	[44.83: 63.29]	3.7%
Enes	136	525	-	25.90	[22.21; 29.88]	4.0%
Faria	57	100		57.00	[46.71; 66.86]	3.6%
Faria-Neto	7652	38069		20.10	[19.70; 20.51]	4.2%
Gadelha	58	236		24.58	[19.22; 30.58]	3.8%
Gomes_b	10547	36369		29.00	[28.53; 29.47]	4.2%
Gonçalves	51	95		53.68	[43.15; 63.98]	3.5%
Guimarães	256	997		25.68	[22.99; 28.51]	4.1%
Mastroeni	127	222		57.21	[50.41; 63.81]	3.9%
Pereira	54	470	-	11.49	[8.75; 14.72]	3.8%
Pinto	65	117		55.56	[46.08; 64.74]	3.6%
Queiroz	57	220		25.91	[20.25; 32.23]	3.8%
Romero	55	199		27.64	[21.55; 34.41]	3.8%
Scheer	152	394		38.58	[33.75; 43.58]	4.0%
Sousa	96	470		20.43	[16.87; 24.36]	4.0%
Vasconcelos	35	140		25.00	[18.07; 33.02]	3.6%
Random effects model	2	80992		29.79	[26.21; 33.63]	76.2%
Heterogeneity: $I^2 = 98\%$, τ	= 0.1418	, p < 0.01				
Group = Children						
Almeida	177	511		34.64	[30.51; 38.94]	4.1%
Barbalho	55	150		36.67	[28.96; 44.92]	3.7%
Figueiras	87	378		23.02	[18.87; 27.59]	3.9%
Gomes_a	10200	25501	+	40.00	[39.40; 40.60]	4.2%
Nobre	73	227		32.16	[26.13; 38.66]	3.9%
Teixeira	84	501		16.77	[13.60; 20.33]	4.0%
Random effects model		27268	\sim	29.84	[22.37; 38.58]	23.8%
Heterogeneity: $I^2 = 97\%$, τ	$r^2 = 0.2229$, <i>p</i> < 0.01				
Random effects model		108260	•	29.74	[25.96: 33.81]	100.0%
Heterogeneity: $l^2 = 99\%$.	$^{2} = 0.2190$	p = 0		•		
Residual heterogeneity: 12	= 98%, p	< 0.01	10 20 30 40 50 60			

Figure 2B. Prevalence of high total cholesterol for age group according BSC criteria Note: p-value = 0.990.

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			Events per 100			
Study	Events	Total	observations	Events	95%-CI	Weight
Origin = Public						
Gadelha	58	236		24.58	[19.22; 30.58]	4.4%
Bauman	170	635	-	26.77	[23.36; 30.40]	4.6%
Teixeira	84	501		16.77	[13.60; 20.33]	4.5%
Giuliano	105	1053	+	9.97	[8.23; 11.94]	4.6%
Guimarães	2	157 🎟		1.27	[0.15; 4.53]	1.7%
Moura	560	1600		35.00	[32.66; 37.39]	4.7%
Pereira	54	470	-	11.49	[8.75; 14.72]	4.4%
Vasconcelos	35	140		25.00	[18.07; 33.02]	4.2%
Chaves	65	120		54.17	[44.83; 63.29]	4.3%
Faria	57	100		57.00	[46.71; 66.86]	4.2%
Gonçalves	51	95		53.68	[43.15; 63.98]	4.1%
Ribas	73	437		16.70	[13.33; 20.54]	4.5%
Romero	55	199		27.64	[21.55; 34.41]	4.4%
Almeida	177	511		34.64	[30.51; 38.94]	4.6%
Arruda-Neto	251	774		32.43	[29.14; 35.85]	4.7%
Enes	136	525		25.90	[22.21; 29.88]	4.6%
Guimarães	256	997		25.68	[22.99; 28.51]	4.7%
Quadros	263	1139		23.09	[20.67; 25.65]	4.7%
Queiroz	57	220	<u> </u>	25.91	[20.25; 32.23]	4.4%
Barbalho	55	150		36.67	[28.96; 44.92]	4.3%
Scheer	152	394		38.58	[33.75; 43.58]	4.6%
Random effects model	2	10453	\diamond	26.99	[22.64; 31.84]	91.3%
Heterogeneity: $I^2 = 96\%$, τ	2 = 0.2721	, <i>p</i> < 0.01				
Origin = Private						
Guimarães	31	209		14.83	[10.31; 20.39]	4.2%
Ribas	92	437		21.05	[17.32; 25.18]	4.5%
Random effects model		646	\diamond	18.15	[12.78; 25.11]	8.7%
Heterogeneity: $I^2 = 72\%$, τ^2	2 = 0.0649	, <i>p</i> = 0.06				
Random effects model		11099	~	26.09	[22.04; 30.60]	100.0%
Heterogeneity: $I^2 = 96\%$, τ^2	² = 0.2689	, <i>p</i> < 0.01				
Residual heterogeneity: l^2	= 96%, p	< 0.01	10 20 30 40 50 60			

Figure 2C. Prevalence of high total cholesterol for school administrative dependency according BSC criteria. Note: p-value = 0.034.

NHLBI (11.63% [95% CI 7.45-17.71]; I² = 99%) was different from the BSC criteria (19.29% [95% CI 15.21-24.16; $I^2 = 99\%$) (p-value between groups = 0.040) (Table 2 and Figure S1B) and the following analysis were performed for each criteria adopted. Regarding the regions of Brazil, the meta-analysis revealed that the South region had the highest prevalence of elevated LDL levels compared with the other regions (p < 0.001) using the NHLBI criteria (Figure 3A). When the regions of Brazil were analyzed with BSC criteria, the Southeast region had the highest prevalence of elevated LDL levels compared with other regions (p < 0.01) (Figure 3B). There was a tendency toward an elevated prevalence estimation of LDL in most recent studies (p < 0.05) with the NHLBI and BSC criteria (Figures 4A and 4B). There was no difference in the prevalence of altered LDL levels between girls and boys with the NHLBI criteria (p = 0.974), neither between age groups (children versus adolescents; p = 0.613) (Figures S3A and S3B).

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Subgroup analysis by gender were not performed with BSC criteria because only Ribas and Silva (63) provided data separated by gender and no difference between genders was observed in this study. Children exhibited a higher prevalence of altered LDL levels (35.00% [95% CI 34.42-35.59]) than adolescents (14.44% [95% CI 8.59-23.26]) (p < 0.002) with the BSC criteria (Figure 5). No subgroup analysis was performed according to the type of school since all studies using BSC criteria were from public schools and all using NHLBI criteria were from private schools.

The visual inspection of the funnel plot for TC and for LDL (Figures S4A and S4B) indicated publication bias. Therefore, the trim and fill correction was performed for TC and LDL (Figures S4C, S4D, S4E and S4F). The correction evidenced a very similar elevated TC prevalence estimation. On the other hand, the analysis for LDL evidenced that probably the prevalence of elevated LDL is underestimated in the previous analysis.

				Events per 100			
Study	Events	Total		observations	Events	95%-CI	Weight
Region = Southeast							
Almeida	47	511			9.20	[6.84; 12.04]	3.8%
Barbalho	71	150			47.33	[39.13: 55.64]	3.8%
Chaves	32	120			26.67	19.01: 35.511	3.7%
Enes	46	525			8.76	[6.49: 11.51]	3.8%
Faria	47	100			- 47.00	[36.94: 57.24]	3.7%
Goncalves	25	95			26.32	[17.81: 36.35]	3.7%
Nobre	45	227			19.82	[14.84: 25.61]	3.8%
Rinaldi	13	147			8.84	[4.79: 14.65]	3.6%
Romero	10	199			5.03	[2.44: 9.05]	3.5%
Silva	35	677	-+		5.17	[3.63: 7.12]	3.8%
Bauman	41	635	-+		6.46	[4.67: 8.66]	3.8%
Teixeira	16	501	-+		3.19	[1.84: 5.13]	3.6%
Random effects model		3887	_ <	>	13.32	7.64; 22.20]	44.6%
Heterogeneity: $I^2 = 97\%$, τ^2	= 1.1518	, p < 0.0	D1			. / .	
Region = Northeast							
Arruda-Neto	90	774	-+	-	11.63	[9.45: 14.10]	3.9%
Melo	3	196	æ – T		1.53	[0.32: 4.41]	2.8%
Pereira	10	470			2 13	[102:388]	3.5%
Quadros	141	1139		-	12.38	[10.52: 14.43]	3.9%
Queiroz	19	220			8.64	[5.28: 13.16]	3.7%
Gadelha	12	236			5.08	[2.65: 8.71]	3.5%
Random effects model		3035	\diamond		6.21	[3.86: 9.84]	21.3%
Heterogeneity: $I^2 = 91\%$, τ^2	= 0.3113	, p < 0.0	D1				
Region = South							
Burgos	752	1743			43.14	[40.80; 45.51]	3.9%
Burgos	286	1254			22.81	[20.51; 25.23]	3.9%
Guimarães	132	997	1	+-	13.24	[11.20; 15.50]	3.9%
Lunardi	17	374	-+		4.55	[2.67; 7.18]	3.7%
Mastroeni	39	222			17.57	[12.80; 23.22]	3.8%
Pamplona Cunha	200	399			50.13	[45.11; 55.14]	3.9%
Reuter	283	1243			22.77	[20.46; 25.20]	3.9%
Vasconcelos	7	140	+		5.00	[2.03; 10.03]	3.3%
Random effects model		6372		\sim	18.81	[11.84; 28.56]	30.2%
Heterogeneity: $I^2 = 99\%$, τ^2	= 0.5881	, p < 0.0	D1			-	
Region = North							
Ribas	150	874			17.16	[14.72; 19.83]	3.9%
Random effects model		874		\diamond	17.16	[14.80; 19.81]	3.9%
Heterogeneity: not applicat	le						
Random effects model		14168	<	>	12.59	[9.17; 17.06]	100.0%
Heterogeneity: $I^2 = 98\%$, τ^2	= 0.8413	, p < 0.0	D1 「				
Residual heterogeneity: 12:	= 98%, p	< 0.01	10	20 30 40 50			

Figure 3A. Prevalence of high LDL for region of Brazil according NHLBI criteria. Note: p-value < 0.001.

Study	Events	Total	Ev ol	ents pe bservat	r 100 ions		Events	95%-CI	Weight
Region = Northeast Carvalho Sousa Random effects mode Heterogeneity: I ² = 94%, *	3 72 ¹ ² = 2.6254	180 ≖ 470 650 ~ , <i>p</i> < 0.01	-+	-			1.67 15.32 5.60	[0.35; 4.79] [12.18; 18.90] [0.58; 37.54]	4.5% 13.6% 18.1%
Region = Southeast Gomes_a Gomes_b Pereira Random effects mode Heterogeneity: / ² = 100%,	8925 9092 200 $\tau^2 = 0.116$	25501 36369 494 62364 0, <i>p</i> < 0.01		•			35.00 25.00 40.49 33.00	[34.41; 35.59] [24.55; 25.45] [36.12; 44.96] [25.01; 42.11]	15.2% 15.2% 14.3% 44.7%
Region = Midwest Pinto Random effects mode Heterogeneity: not applica	23 I Ible	117 117	-	-	-		19.66 19.66	[12.89; 28.02] [13.43; 27.85]	11.0% 11.0%
Region = North Ribas Ribas Random effects mode Heterogeneity: / ² = 93%, /	33 88 1 2 ² = 0.2987	437 571 1008 , p < 0.01	*	-			7.55 15.41 10.99	[5.25; 10.44] [12.55; 18.64] [5.33; 21.32]	12.3% 13.9% 26.2%
Random effects mode Heterogeneity: $l^2 = 99\%$, Residual heterogeneity: l^2	l 2 ² = 0.1414 = 99%, p	64139 , <i>р</i> < 0.01 < 0.01	10	20	30	 40	19.29	[15.21; 24.16]	100.0%

Figure 3B. Prevalence of high LDL for region of Brazil according BSC criteria. Note: p-value=0.003

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				Events per 100				
Study	Events	Total		observations	E	vents	95%-CI	Weight
Period = 2016-2020								
Almeida	47	511				9.20	[6.84; 12.04]	3.5%
Arruda-Neto	90	774	-	+		11.63	[9.45; 14.10]	3.5%
Barbalho	71	150			1	47.33	[39.13; 55.64]	3.5%
Burgos	752	1743				43.14	[40.80; 45.51]	3.5%
Enes	46	525				8.76	[6.49; 11.51]	3.5%
Faria-Neto	1332	38069	+			3.50	[3.32; 3.69]	3.5%
Guimarães	132	997	ł	+-		13.24	[11.20; 15.50]	3.5%
Mastroeni	39	222				17.57	[12.80; 23.22]	3.5%
Melo	3	196	+			1.53	[0.32; 4.41]	3.0%
Quadros	141	1139		+-		12.38	[10.52; 14.43]	3.5%
Queiroz	19	220				8.64	[5.28; 13.16]	3.4%
Reuter	283	1243	_			22.77	[20.46; 25.20]	3.5%
Bauman	41	635	_			6.46	[4.67; 8.66]	3.5%
Teixeira	16	501	-			3.19	[1.84; 5.13]	3.4%
Gadelha	12	236				5.08	[2.65; 8.71]	3.4%
Random effects model	2 0.000	4/161	<			10.48	[5.29; 19.72]	51.8%
Heterogeneity: $I^{\sim} = 100\%$, r	τ= 2.098	35, p = 0						
Period = 2011-2015								
Burgos	286	1254				22.81	[20.51; 25.23]	3.5%
Chaves	32	120				26.67	[19.01; 35.51]	3.5%
Faria	47	100			1	47.00	[36.94; 57.24]	3.5%
Gonçalves	25	95				26.32	[17.81; 36.35]	3.4%
Nobre	45	227			_	19.82	[14.84; 25.61]	3.5%
Pamplona Cunha	200	399	_			50.13	[45.11; 55.14]	3.5%
Rinaldi	13	147				8.84	[4.79; 14.65]	3.4%
Romero	10	199				5.03	[2.44; 9.05]	3.3%
Silva	35	677	-	-		5.17	[3.63; 7.12]	3.5%
Ripas Developer offecto recodel	150	874				17.16	[14.72; 19.83]	3.5%
Heterogeneity: $I^2 = 97\%$, τ^2	² = 0.6901	4092 I, p < 0.0	01			19.28	[12.34; 28.80]	34.0%
Period = 2006-2010								
Lunardi	17	374				4,55	[2.67: 7.18]	3,4%
Pereira	10	470				2.13	[1.02: 3.88]	3.3%
Ribeiro	100	1382	+			7.24	[5.93: 8.73]	3.5%
Vasconcelos	7	140				5.00	[2.03; 10.03]	3.3%
Random effects model		2366	\diamond			4.51	[2.62; 7.65]	13.6%
Heterogeneity: $I^2 = 82\%, \tau^2$	2 = 0.2554	ŀ, p < 0.0	01					
Random effects model		53619	<	>		11.63	[7.45; 17.71]	100.0%
Heterogeneity: $I^2 = 99\%$, τ^2	² = 1.7780	p = 0	Г					
Residual heterogeneity: 12	= 99%, p	= 0	10	20 30 40	50			

Figure 4A. Prevalence of high LDL for period according NHLBI criteria. Note: p-value < 0.001.

	Study	Events	Total	Events per 100 observations	Events	95%-CI	Weight
	Period = 2006–2010 Carvalho Pereira Ribas Random effects model Heterogeneity: / ² = 99%, t	3 200 33 ² = 2.5807	180 - 494 437 1111 , p < 0.01	+ + +	1.67 40.49 7.55 9.51	[0.35; 4.79] [36.12; 44.96] [5.25; 10.44] [1.61; 40.28]	4.5% 14.3% 12.3% 31.2%
	Period = $2016-2020$ Gomes_a Gomes_b Random effects model Heterogeneity: $I^2 = 100\%$,	8925 9092 $\tau^2 = 0.114$	25501 36369 61870 8, <i>p</i> < 0.0	+	35.00 25.00 29.76	[34.41; 35.59] [24.55; 25.45] [20.93; 40.40]	15.2% 15.2% 30.4%
reserved.	Period = 2011–2015 Pinto Ribas Sousa Random effects model Heterogeneity: $I^2 = 0\%$, τ^2	23 88 72 = 0, p = 0	117 571 470 1158 49		19.66 15.41 15.32 15.84	[12.89; 28.02] [12.55; 18.64] [12.18; 18.90] [13.85; 18.06]	11.0% 13.9% 13.6% 38.5%
Figure 4B. Prev	Random effects model Heterogeneity: $l^2 = 99\%$, τ Residual heterogeneity: l^2 valence of high LDL for pe	² = 0.1414 = 99%, p eriod acco	64139 , <i>p</i> < 0.01 < 0.01 ording BS	10 20 30 40 GC criteria.	19.29	[15.21; 24.16]	100.0%

Note: p-value<0.001



Figure 5. Prevalence of LDL for age group according BSC criteria. Note: p-value< 0.001

DISCUSSION

The present meta-analysis revealed a significant prevalence of altered of TC and LDL alteration in children and adolescents in Brazil. Type of school, age group, year and the region of Brazil appeared to influence estimations of altered lipid profiles. In addition, the cutoff points used for the diagnosis of altered TC and LDL levels varied across the studies and influenced the prevalence estimation. We must recognize that the results on subgroup analysis were dependent of the diagnoses criteria adopted and the associations were tenuous. Although some associations were just seen when using one of the diagnoses criteria, a clinical tendency was seen on the same direction with the other criteria.

There was significant variability in the prevalence estimates for elevated TC and LDL levels among the studies. Some authors reported a very high prevalence, such as Faria and cols., who reported a rate of 57% in 100 adolescents for TC and 50% for LDL cholesterol (34), while other authors reported low values, 3.3% for altered TC and 1.7% for altered LDL in 180 adolescents (31). This discrepancies in prevalence estimation may be due to selection bias of small sample studies. However, sensitive analysis with studies with sample sizes greater than 300 subjects did not evidenced over or under estimations of lipid profile alterations prevalence (data not shown). The Brazilian Society of Pediatrics (67) recommends the use of the same cutoff values that does the BSC (3-5). However, international references (2) consider high a cholesterol value > 200 mg/dL while the LDL value is pathological if > 130 mg/dL and border line if > 110 mg/dL. Burgos and cols. (51), who analyzed 1,743 children and adolescents in the South of Brazil and adopted the borderline criteria of the NHLBI (TC > 170 mg/dL and LDL > 110 mg/dL), reported prevalence of 60.75% and 43.14%, respectively (51). Although several differences were observed on the prevalence estimates in this metaanalysis, the prevalence of altered lipids in the Brazilian pediatric population was very high, even using the most conservative limits for the diagnosis, the NHLBI parameters. Cutoff criteria is an especially important issue

and border line a value between 170 and 199 mg/dL,

because it defines treatment strategies; therefore, validity studies of diagnostic tests are needed to identify the optimal cutoff points for TC and its fractions in the child and adolescent population. In 2011, in the city of Londrina, 1000 adolescents between 11 and 16 years old were subjected to lipid profile evaluation and classified according to 3 diagnostic criteria (68). Different prevalence estimates were found according to the distinct criteria: TC (*BSC* 38.3%; National Cholesterol Education Program [NCEP] 11.2%; National Health and Nutrition Examination Survey [NHANES] 4.8%); and LDL (BSC/NCEP, 10.8% and NHANES, 5.9%). Overall, the prevalence of dyslipidemia according to each criterion was 61% (SBC), 28.6% (NCEP), and 24.2% (NHANES) (68).

Comparing the prevalence of elevated TC and LDL in public and private schools, the prevalence of altered TC and LDL in public schools were higher

than in private schools. A Brazilian study about price and availability of food products with and without trans fatty acids in food stores near elementary schools located in low- and medium-income neighborhoods observed that cheaper products containing trans fats were more readily available than products without trans fats, promoting the consumption of less nutritious food by underprivileged children and adolescents (69). Reducing trans fatty acids intake by children may result in improvements on the lipid profile (70). Although some studies have shown a predominance of obesogenic environments with high ultra-processed food intake mainly in private schools (71), this type of food is consumed by all social classes (72) and in consequence by all children, from public to private schools. Our TC estimate in private schools came from just two studies, therefore we cannot assume that it happens the same in other private schools. Furthermore, in our metaanalysis, the Southeast and South, the richest regions of Brazil, exhibited higher rates of lipid profile alterations. Through systematic search, several studies were found, contributing to a representative sample size of the population of Brazilian children and adolescents. However, despite the large number of articles, the Northern and Central-Western regions were underrepresented, which may have influenced the results according to region.

Another finding of the present study was the increase in the prevalence of elevated TC and LDL levels between 2000 and 2019. A tendency towards increase in prevalence rates was seen mainly after 2010. The pattern of food consumption in Brazilian population has been changing over the past few decades, with an increase in the consumption of ultra-processed foods (73). The early and abusive consumption of ultraprocessed foods is one of the most important factors associated with the increased prevalence of obesity and the risk for metabolic complications (3,7), such as changes in lipid profile (4,5,67,74-78).

Another important factor in childhood and adolescence is the low level of physical activity and the increase of a sedentary lifestyle over the years (79). When it is associated with changes in eating habits, this behavior may contribute to increases in obesity and metabolic changes, including dyslipidemia (12,18). Data on Brazilian adolescents from all capitals of Brazil, indicates a prevalence of leisure-time physical inactivity around 54.3% (79). The Brazilian Society of Sports Medicine recommends regular physical activity and highlights the benefit of improved lipid profiles and believes there is an association between physical inactivity, obesity and dyslipidemia, and that obese children may become obese adults prone to illnesses related to weight gain (80,81). All this changes probably had some influence on the findings, although a selection bias could be present, especially in light of the profound heterogeneity reported on the analysis.

Higher rates of TC were detected in children when compared to adolescents, but no differences between boys and girls was observed. Lipoprotein concentrations changes considerably with normal growth and maturation, and varied according to sex (82-86). During pubertal growth, cholesterol is included in growing cells, leading to decreases in serum lipid values (87) but it increases on the later adolescence, approaching adult concentrations (84). Our sample of adolescents are mainly from individuals on the late phase (mean age 14.7 years old; data not shown). Therefore, screening recommendations should consider fluctuations in serum lipid levels during growth and sexual maturation. It is recommended that every child undergo a determination of TC level at 10 years of age by means of an examination of digital pulp capillary blood (4). Because adolescence is a critical period of life for the onset or persistence of obesity and its complications (86), knowing the nutritional status of this segment of the population is important.

Strengths and limitations

Finally, it should be noted that the present metaanalysis was designed according to the standards recommended by the Cochrane Collaboration (87) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement (19) but it still presents some limitations. One of the main limitations of the present study was the high heterogeneity, the origin of which could not be explained. Although several subgroup analyses were performed to identify the source of heterogeneity, it remained elusive. Another limitation is the fact that information regarding nutritional status, dietary intake and physical activity was not reported in the articles and, consequently, was not analyzed in this study. This may also have contributed to the high heterogeneity. Most studies estimated the LDL with Friedewald's formula, but no information was provided regarding

patients with triglycerides over 400 mg/dL and if those patients were included it may have led to a biased result.

In conclusions, the present study indicates a high prevalence of altered – if not abnormal – lipid levels among children and adolescents in Brazil. These results reinforce the importance of knowing the lipid profile of children and adolescents to perform early interventions for treatment as well as to promote healthy habits that lead to prevention of lipid profile alterations and its consequences.

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Table S1. Search strategies each database

Database	Search strategy
PubMed	(((("Brazil"[Mesh] OR "Brazil"))) AND (("Child"[Mesh] OR "Child" OR "Children" OR "Adolescent" [Mesh] OR "Adolescent" OR "Adolescents" OR "Adolescence" OR "Teens" OR "Teenagers" OR "Teenager" OR "Youth" OR "Adolescent", Female" OR "Adolescent" OR "Female Adolescent" OR "Female Adolescents" OR "Adolescents, Male" OR "Adolescent, Male" OR "Male Adolescent" OR "Male Adolescents" OR "Adolescents"))) AND (("Dyslipidemias/epidemiology" [Mesh] OR "Dyslipidemias/epidemiology" OR "Dyslipidemias' or "Dyslip
SciELO	("Brazil") AND ("Child" OR "Children" OR "Adolescent" OR "Adolescents" OR "Adolescence" OR "Teens" OR "Teenagers" OR "Teenager" OR "Youth" OR "Youths") AND ("Dyslipidemias" OR "Dyslipidemia" OR "Dyslipoproteinemias" OR "Dyslipoproteinemia" OR "lipid profile" OR "Cholesterol") AND ("Prevalence" OR "Prevalences")
Lilacs	tw:((tw:(dislipidemias OR dyslipidemias OR dislipidemias OR colesterol OR cholesterol OR colesterol)) AND (tw:(brasil OR brazil OR brasil)) AND (tw:(criança OR child OR niño OR adolescente OR adolescent OR adolescente)) AND (tw:(prevalência OR prevalence OR prevalencia))) AND (instance:"regional")
Embase	('prevalence'/syn) AND('brazil'/syn OR 'brazil') AND ('child'/syn OR 'adolescent'/syn) AND ('dyslipidemia'/syn)

Study	Events	Total	Events per 100 observations	Events	95%-CI	Weight
Criteria = NHLBI Burgos	1059	17/3	-	60.76	158 42: 63 061	2.5%
Burgos	344	1254	<u>.</u>	27 43	[24 98 29 99]	2.5%
Lunardi	18	374	H	4 81	[2 88 7 50]	2.0%
Lunardi	17	358	-	4 75	[2.79: 7.49]	2.0%
Ribeiro	1118	3106		35.99	[34.30: 37.71]	2.5%
Rinaldi	17	147		11.56	[6.88; 17.87]	2.0%
Reuter	62	564	—	10.99	[8.53; 13.87]	2.3%
Random effects model		7546	\sim	17.22	[9.52; 29.15]	15.9%
Heterogeneity: $l^2 = 99\%$, τ^2	² = 0.8181	, p < 0.0	1			
Criteria = Other	244	1042		07.40	124 07: 20 041	0.5%
Almoida	177	511		21.43	[24.97, 30.01]	2.0%
America Arruda-Neto	251	774		32 13	[30.31, 36.94]	2.4%
Barbalho	201	150		36.67	[29.14, 33.00]	2.0%
Bauman	170	635	-	26 77	[23.36:30.40]	2.5%
Beck	134	660		20.77	[17 30: 23 58]	2.4%
Bergmann	345	1294		26.66	[24 27: 29 16]	2.5%
Carvalho	6	180	<u>→</u> Ī	3.33	[1.23: 7.11]	1.5%
Chaves	65	120		54.17	[44.83: 63.29]	2.2%
Enes	136	525	÷ –	25.90	[22.21: 29.88]	2.4%
Faria	57	100	· · · · ·	57.00	[46.71; 66.86]	2.2%
Faria-Neto	7652	38069	•	20.10	[19.70; 20.51]	2.5%
Figueiras	87	378		23.02	[18.87; 27.59]	2.4%
Gadelha	58	236		24.58	[19.22; 30.58]	2.3%
Giuliano	105	1053		9.97	[8.23; 11.94]	2.4%
Gomes_a	10200	25501	+	40.00	[39.40; 40.60]	2.5%
Gomes_b	10547	36369	+	29.00	[28.53; 29.47]	2.5%
Gonçalves	51	95		53.68	[43.15; 63.98]	2.2%
Guimarães	33	366	<u>≖ i</u>	9.02	[6.29; 12.43]	2.2%
Guimarães	256	997	<u> </u>	25.68	[22.99; 28.51]	2.5%
Mastroeni	127	222		57.21	[50.41; 63.81]	2.3%
Moura	560	1600	_	35.00	[32.66; 37.39]	2.5%
Nobre	/3	227		32.16	[26.13; 38.66]	2.3%
Pampiona Cunna	198	399		49.62	[44.61; 54.64]	2.4%
Pereira	04	470		11.49 51.01	[0.70, 14.72]	2.3%
Perella	202	494		55.56	[46.51, 55.50]	2.4%
Plillu	263	1120		22.00	[40.00, 04.74]	2.2%
Quadros	203	220		25.09	[20.07, 20.00]	2.3%
Rihas	165	874		18.88	[16 34: 21 63]	2.5%
Ribas	16	437	_	3.66	[2 11: 5 88]	2.4%
Romero	55	199		27 64	[21 55: 34 41]	2.3%
Scheer	152	394		38.58	[33 75 43 58]	2.4%
Sousa	96	470		20.43	[16.87: 24.36]	2.4%
Teixeira	84	501		16.77	[13.60; 20.33]	2.4%
Vasconcelos	35	140		25.00	[18.07; 33.02]	2.2%
Random effects model		117159	\diamond	27.47	[24.36; 30.82]	84.1%
Heterogeneity: $l^2 = 99\%$, τ^2	² = 0.2276	, <i>p</i> = 0				
Random effects model	0.0000	124705	¢	25.77	[22.85; 28.91]	100.0%
Heterogeneity: $I^{*} = 99\%$, τ^{*}	= 0.2608	, p = 0	10 20 20 40 50 00			
Residual neterogeneity: /-	– 99%, p	-0	10 20 30 40 50 60			

Figure S1A. Prevalence of TC according to diagnose criteria. Notes: p-value = 0.094.

				Events p	er 100			
Study	Events	Total		observa	tions	Events	95%-CI	Weight
Criteria = NHLBI	47	E11				0.00	[C 04: 40 04]	0.00/
Ameida Arruda Nata	47	511				9.20	[0.04, 12.04]	2.8%
Arruda-Neto	90	114		-		11.63	[9.45; 14.10]	2.8%
Barbaino	/1	150				47.33	[39.13; 55.64]	2.8%
Burgos	752	1743		_		43.14	[40.80; 45.51]	2.8%
Burgos	286	1254		±		22.81	[20.51; 25.23]	2.8%
Chaves	32	120	_			26.67	[19.01; 35.51]	2.7%
Enes	46	525	-+			8.76	[6.49; 11.51]	2.8%
Faria	47	100				· 47.00	[36.94; 57.24]	2.7%
Faria-Neto	1332	38069	4			3.50	[3.32; 3.69]	2.8%
Gonçalves	25	95				26.32	[17.81; 36.35]	2.7%
Guimarães	132	997		•		13.24	[11.20; 15.50]	2.8%
Lunardi	17	374	-+			4.55	[2.67; 7.18]	2.7%
Mastroeni	39	222				17.57	[12.80; 23.22]	2.7%
Melo	3	196	-+			1.53	[0.32; 4.41]	2.0%
Nobre	45	227				19.82	[14.84; 25.61]	2.8%
Pamplona Cunha	200	399		_		50,13	[45.11: 55.14]	2.8%
Pereira	10	470	-			2.13	[1.02: 3.88]	2.5%
Quadros	141	1139		:		12 38	[10 52: 14 43]	2.8%
Queiroz	19	220				8 64	[5 28: 13 16]	2.7%
Reuter	283	1243		-		22 77	[20 46: 25 20]	2.8%
Ribeiro	100	1382				7 24	[5 93 8 73]	2.0%
Pinaldi	13	1/7		_		8.84	[4 79 14 65]	2.6%
Romero	10	199				5.03	[2/1] 9.05]	2.0%
Silva	35	677				5.00	[2.44, 5.00]	2.0%
Vasconcelos	35	140				5.00	[3.03, 7.12]	2.0%
Dibao	150	140				17.10	[2.03, 10.03]	2.4%
Ribas	150	8/4				17.16	[14.72, 19.83]	2.8%
Bauman	41	635				6.46	[4.67, 8.66]	2.8%
leixeira	16	501	+			3.19	[1.84; 5.13]	2.6%
Gadelna	12	236				5.08	[2.65; 8.71]	2.6%
Random effects model	2	53619	<	\geq		11.63	[7.45; 17.71]	78.4%
Heterogeneity: I^2 = 99%, τ	- = 1.7780	, <i>p</i> = 0						
Criteria = other								
Gomes a	8925	25501				35.00	[34 41: 35 50]	2.8%
Comes h	0020	20001			100	25.00	[04.41, 00.05]	2.0%
Gonrelho	3032	100				20.00	[24.00, 20.40]	2.0%
Calvallio	200	100			121	1.07	[0.35, 4.79]	2.0%
Perella	200	494				40.49	[36.12, 44.96]	2.0%
Pinto	23	117				19.66	[12.89; 28.02]	2.7%
Ribas	33	437		_		7.55	[5.25, 10.44]	2.7%
Ribas	88	571		•		15.41	[12.55; 18.64]	2.8%
Sousa	72	470		-		15.32	[12.18; 18.90]	2.8%
Random effects model	0	64139		\diamond		19.29	[15.21; 24.16]	21.6%
Heterogeneity: $l^2 = 99\%$, τ	- = 0.1414	, p < 0.01	1					
Random effects model		117758	~	>		12 77	[9 73: 16 58]	100 0%
Heterogeneity: $l^2 = 100\%$	$\tau^2 = 0.855$	8 0 = 0	Ē		1 1	12.77	[0.70, 10.00]	//
Posidual botorogonaity: I^2	= 99% ~	- 0	10	20 20	40 50			
Residual neterogenetty. /	- 33%, p	-0	10	20 30	40 50			

Figure S1B. Prevalence of high LDL according to diagnose criteria. Notes: $\mbox{p-value}=0.040$

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			Events per 100			
Study	Events	Total	observations	Events	95%-CI	Weight
Region = South Reuter Beck Bergmann Giuliano Guimarães Mastroeni Pamplona Cunha Vasconcelos Random effects model Heterogeneity: / ² = 98%, t	341 134 345 105 256 127 198 35 25	1243 660 1294 1053 997 222 399 140 6008 , p < 0.0		27.43 20.30 26.66 9.97 25.68 57.21 49.62 25.00 28.25	[24.97; 30.01] [17.30; 23.58] [24.27; 29.16] [8.23; 11.94] [22.99; 28.51] [50.41; 63.81] [44.61; 54.64] [18.07; 33.02] [20.39; 37.71]	3.1% 3.0% 3.1% 3.0% 3.1% 2.9% 3.0% 2.6% 23.7%
Region = Southeast Almeida Barbalho Bauman Chaves Enes Faria Figueiras Gomes_a Gomes_b Gonçalves Moura Nobre Pereira Romero Scheer Teixeira Random effects model Heterogeneity: / ² = 99%, t	177 55 170 65 136 57 87 10200 10547 51 560 73 252 55 152 84 2 = 0.1205	511 150 635 120 525 100 378 25501 36369 95 1600 227 494 199 394 501 67799 , p < 0.0		34.64 36.67 26.77 54.17 25.90 23.02 40.00 29.00 53.68 35.00 32.16 51.01 27.64 38.58 16.77 35.06	[30.51; 38.94] [28.96; 44.92] [23.36; 30.40] [44.83; 63.29] [22.21; 29.88] [46.71; 66.86] [39.40; 40.60] [28.53; 29.47] [43.15; 63.98] [32.66; 37.39] [26.13; 38.66] [46.51; 55.50] [21.55; 34.41] [33.75; 43.58] [13.60; 20.33] [31.06; 39.28]	3.0% 2.7% 3.0% 2.6% 2.9% 3.2% 3.2% 3.2% 3.2% 3.2% 3.1% 2.8% 3.0% 2.8% 3.0% 2.9% 46.5%
Region = Northeast Arruda-Neto Carvalho Gadelha Guimarães Pereira Quadros Queiroz Sousa Random effects model Heterogeneity: / ² = 95%, t Region = Midwest Pinto Random effects model	251 6 58 33 54 263 57 96 ² = 0.2704 65	774 180 236 366 470 1139 220 470 3855 , p < 0.0 117 117		32.43 3.33 24.58 9.02 11.49 23.09 25.91 20.43 17.37 55.56 55.56	[29.14; 35.85] [1.23; 7.11] [19.22; 30.58] [6.29; 12.43] [8.75; 14.72] [20.67; 25.65] [20.25; 32.23] [16.87; 24.36] [12.57; 23.52] [46.08; 64.74] [46.47; 64.29]	3.1% 1.6% 2.8% 2.7% 2.8% 3.1% 2.8% 2.9% 21.8%
Heterogeneity: not applical Region = North Ribas Random effects model Heterogeneity: $l^2 = 98\%$, τ Random effects model Heterogeneity: $l^2 = 98\%$, τ	165 16 $^{2} = 1.6057$ $^{2} = 0.1757$	874 437 1311 , p < 0.0 79090 , p = 0		18.88 3.66 8.72 27.82	[16.34; 21.63] [2.11; 5.88] [1.59; 36.06] [24.98; 30.85]	3.0% 2.3% 5.4% 100.0%
Residual heterogeneity: /2	= 98%, p	< 0.01	10 20 30 40 50 60			

Figure S2A. Prevalence of TC according BSC for region of Brazil. Note: p-value < 0.001.

Study	Events	Total		Eve ob	nts p serva	er 10 tions	0 5		Events	95%-CI	Weight
Region = South											
Burgos	1059	1743							60.76	[58.42; 63.06]	17.0%
Burgos	344	1254			+				27.43	[24.98; 29.99]	17.0%
Lunardi	18	374							4.81	[2.88; 7.50]	16.4%
Lunardi	17	358	+-						4.75	[2.79; 7.49]	16.4%
Reuter	62	564	+						10.99	[8.53; 13.87]	16.8%
Random effects model		4293	\sim			-			15.38	[5.40; 36.65]	83.6%
Heterogeneity: $I^2 = 99\%$, τ^2	= 1.715	7, p < 0	.01								
Region = Southeast											
Rinaldi	17	147	- 1	_					11.56	[6.88; 17.87]	16.4%
Random effects model Heterogeneity: not applicable	ble	147		>					11.56	[7.31; 17.82]	16.4%
Random effects model Heterogeneity: $I^2 = 99\%$, τ^2	² = 1.7246	4440 6, <i>p</i> < 0	.01			1	-1-	_	14.69	[5.62; 33.24]	100.0%
Residual heterogeneity: I ²	= 99%, p	< 0.01	10	20	30	40	50	60			

Figure S2B. Prevalence of TC according NHLBI for region of Brazil. Note: p-value = 0.609.

Study	Events	Total	Events per 100 observations	Events	95%-CI	Weight
Gender = Female Almeida Arruda-Neta Burgos Faria-Neto Gonçalves Guimaraes Lunardi Pamplona Cunha Romero Vasconcelos Bauman Ribas Random effects model Heterogeneity: / ² = 99%, t	31 44 184 442 14 76 11 100 6 4 58 86	272 423 937 22822 43 568 208 208 114 132 382 452 26561 0, p < 0.0		11.40 10.40 19.64 32.56 13.38 5.29 48.08 5.26 3.03 15.18 19.03 11.52	[7.88; 15.79] [7.66; 13.71] [17.14; 22.33] [1.76; 2.12] [19.08; 48.54] [10.69; 16.46] [2.67; 9.27] [41.12; 55.09] [1.96; 11.10] [0.83; 7.58] [11.74; 19.18] [15.51; 22.95] [5.21; 23.57]	$\begin{array}{c} 4.3\% \\ 4.3\% \\ 4.4\% \\ 4.4\% \\ 4.1\% \\ 4.1\% \\ 4.3\% \\ 3.8\% \\ 3.6\% \\ 4.3\% \\ 4.4\% \\ 50.4\% \end{array}$
Gender = Male Almeida Arruda-Neta Burgos Faria-Neto Gonçalves Guimaraes Lunardi Pamplona Cunha Romero Vasconcelos Bauman Ribas Random effects model Heterogeneity: / ² = 98%, t	$ \begin{array}{r} 16\\ 46\\ 102\\ 981\\ 11\\ 56\\ 6\\ 100\\ 4\\ 3\\ 42\\ 64\\ \end{array} $	239 351 806 15247 52 429 166 191 85 108 253 422 18349 0, p < 0.0		6.69 13.11 12.66 6.43 21.15 13.05 3.61 52.36 4.71 2.78 16.60 15.17 11.35	[3.87; 10.64] [9.76; 17.09] [10.44; 15.15] [6.05; 6.84] [11.06; 34.70] [10.01; 16.61] [1.34; 7.70] [45.02; 59.62] [1.30; 11.61] [0.58; 7.90] [12.23; 21.77] [11.88; 18.95] [7.03; 17.83]	4.2% 4.3% 4.4% 4.0% 4.3% 3.9% 4.3% 3.6% 3.4% 4.3% 4.3% 4.3%
Random effects model Heterogeneity: $I^2 = 99\%$, τ Residual heterogeneity: I^2	² = 1.1920 = 99%, p	44910), <i>p</i> = 0 = 0	10 20 30 40 50	11.40	[7.58; 16.79] <i>'</i>	100.0%

Figure S3A. Prevalence of LDL for sex according NHLBI.

				Events per	100			
Study	Events	Total		observatio	ons	Events	95% -CI	Weight
Group = Adolescents								
Arruda-Neto	90	774	-	1 -		11.63	[9.45; 14.10]	4.7%
Chaves	32	120			-	26.67	[19.01; 35.51]	4.6%
Enes	46	525		-		8.76	[6.49; 11.51]	4.7%
Faria	47	100				47.00	[36.94; 57.24]	4.6%
Faria-Neto	1332	38069	+			3.50	[3.32; 3.69]	4.8%
Gonçalves	25	95			-	26.32	[17.81; 36.35]	4.6%
Guimarães	132	997	-			13.24	[11.20; 15.50]	4.7%
Lunardi	17	374	-+			4.55	[2.67; 7.18]	4.5%
Mastroeni	39	222				17.57	[12.80; 23.22]	4.7%
Melo	3	196	+			1.53	[0.32; 4.41]	3.7%
Pereira	10	470	+			2.13	[1.02; 3.88]	4.4%
Queiroz	19	220		_		8.64	[5.28; 13.16]	4.6%
Romero	10	199				5.03	[2.44; 9.05]	4.4%
Vasconcelos	7	140				5.00	[2.03; 10.03]	4.2%
Bauman	41	635	+			6.46	[4.67; 8.66]	4.7%
Gadelha****	12	236				5.08	[2.65; 8.71]	4.4%
Random effects model Heterogeneity: $I^2 = 98\%$, τ^2	² = 1.0620	43372), p < 0.()1	>		8.71	[5.36; 13.83]	72.3%
Group = Children								
Almeida	47	511		+		9.20	[6.84; 12.04]	4.7%
Barbalho	71	150				47.33	[39.13; 55.64]	4.7%
Nobre	45	227				19.82	[14.84; 25.61]	4.7%
Rinaldi	13	147	- 1			8.84	[4.79; 14.65]	4.5%
Silva	35	677	-+			5.17	[3.63; 7.12]	4.7%
Teixeira	16	501	-+			3.19	[1.84; 5.13]	4.5%
Random effects model		2213	<			11.23	[4.59; 24.96]	27.7%
Heterogeneity: $I^2 = 98\%$, τ^2	² = 1.4157	7, p < 0.0)1					
Random effects model	,	45585		>		9.34	[6.07; 14.09]	100.0%
Heterogeneity: I ² = 98%, τ ²	= 1.1792	2, p < 0.0)1	1 1	1 1			
Residual heterogeneity: I ²	= 98%, p	< 0.01	10	0 20 30	40 50			

Figure S3B. Prevalence of LDL for age groups according NHLBI. Note: p-value = 0.613.

			Events	per 1	00				
Study	Events	Total		observ	vation	IS	Events	95% - CI	Weight
Region = Southeast									
Almeida	47	511					9.20	[6.84; 12.04]	3.8%
Barbalho	71	150					47.33	[39.13; 55.64]	3.8%
Chaves	32	120		+	<u> </u>		26.67	[19.01; 35.51]	3.7%
Enes	46	525	+				8.76	[6.49; 11.51]	3.8%
Faria	47	100			-	1	- 47.00	[36.94; 57.24]	3.7%
Gonçalves	25	95			-		26.32	[17.81; 36.35]	3.7%
Nobre	45	227					19.82	[14.84; 25.61]	3.8%
Rinaldi	13	147	- +	<u>.</u>			8.84	[4.79; 14.65]	3.6%
Romero	10	199					5.03	[2.44; 9.05]	3.5%
Silva	35	677	-+				5.17	[3.63; 7.12]	3.8%
Bauman	41	635					6.46	[4.67; 8.66]	3.8%
Teixeira	16	501	-+				3.19	[1.84; 5.13]	3.6%
Random effects model		3887	<				13.32	[7.64; 22.20]	44.6%
Heterogeneity: $I^2 = 97\%$, τ^2	= 1.1518	, p < 0.0)1						
Region = Northeast									
Arruda-Neto	90	774	+	-			11.63	[9.45; 14.10]	3.9%
Melo	3	196	+				1.53	[0.32; 4.41]	2.8%
Pereira	10	470	-+				2.13	[1.02; 3.88]	3.5%
Quadros	141	1139		-			12.38	[10.52; 14.43]	3.9%
Queiroz	19	220					8.64	[5.28; 13.16]	3.7%
Gadelha	12	236					5.08	[2.65; 8.71]	3.5%
Random effects model		3035	\diamond				6.21	[3.86; 9.84]	21.3%
Heterogeneity: $I^2 = 91\%$, τ^2	= 0.3113	, p < 0.0)1						
Region = South									
Burgos	752	1743					43.14	[40.80; 45.51]	3.9%
Burgos	286	1254					22.81	[20.51; 25.23]	3.9%
Guimarães	132	997	- 1	+			13.24	[11.20; 15.50]	3.9%
Lunardi	17	374		_			4.55	[2.67; 7.18]	3.7%
Mastroeni	39	222					17.57	[12.80; 23.22]	3.8%
Pampiona Cunha	200	399					50.13	[45.11; 55.14]	3.9%
Reuter	283	1243					22.77	[20.46; 25.20]	3.9%
Vasconcelos	1	140					5.00	[2.03; 10.03]	3.3%
Heterogeneity: $I^2 = 99\%$, τ^2	= 0.5881	, p < 0.0)1		-		18.81	[11.84; 28.90]	30.2%
Region = North									
Ribas	150	874					17.16	[14.72; 19.83]	3.9%
Random effects model		874		\diamond			17.16	[14.80; 19.81]	3.9%
Heterogeneity: not applicab	le							-	
Random effects model		14168	<	>			12.59	[9.17; 17.06]	100.0%
Heterogeneity: $I^2 = 98\%$, τ^2	= 0.8413	, p < 0.0)1 「	1				_	
Residual heterogeneity: 12 :	= 98%, p	< 0.01	10	20	30 4	40 50			

Figure S3C. Prevalence of high LDL according NHLBI for region of Brazil

Study	Events	Total	I	≣vents p observa	er 100 itions		Events	95%-CI	Weight
Region = Northeast Carvalho Sousa Random effects model Heterogeneity: / ² = 94%, τ ²	3 72 = 2.6254	180 ■ 470 650 ● , <i>p</i> < 0.01		-			1.67 15.32 5.60	[0.35; 4.79] [12.18; 18.90] [0.58; 37.54]	12.7% 17.6% 30.3%
Region = Southeast Pereira Random effects model Heterogeneity: not applicat	200	494 494					40.49 40.49	[36.12; 44.96] [36.24; 44.88]	17.8% 17.8%
Region = Midwest Pinto Random effects model Heterogeneity: not applicat	23 Ile	117 117			A		19.66 19.66	[12.89; 28.02] [13.43; 27.85]	16.9% 16.9%
Region = North Ribas Ribas Random effects model Heterogeneity: / ² = 93%, τ ²	33 88 = 0.2987	437 571 1008 , <i>p</i> < 0.01	+	-			7.55 15.41 10.99	[5.25; 10.44] [12.55; 18.64] [5.33; 21.32]	17.3% 17.7% 35.0%
Random effects model Heterogeneity: $l^2 = 97\%$, τ' Residual heterogeneity: l^2	= 0.8152 = 93%, p	2269 , <i>p</i> < 0.01 < 0.01	- 10	20		40	13.47	[6.85; 24.80]	100.0%

Figure S3D. Prevalence of high LDL according BSC for region of Brazil.



Figure S4A. Funnel plot for TC.



Figure S4B. Funnel plot for LDL.

		Events per 100			
Study	TE seTE	observations	Events	95%-CI	Weight
Burgos	0.44 0.0491	+	60.76	[58.44; 63.02]	2.3%
Burgos	-0.97 0.0633	+	27.43	[25.03; 29.97]	2.2%
Lunardi	-2.98 0.2416	+	4.81	[3.05; 7.51]	1.9%
Lunardi	-3.00 0.2485	+	4.75	[2.97; 7.50]	1.9%
Reuter	-2.09 0.1346	+	10.99	[8.66; 13.85]	2.1%
Ribeiro	-0.58 0.0374		35.99	[34.32; 37.70]	2.3%
Rinaldi	-2.03 0.2579	+	11.56	[7.31; 17.82]	1.8%
Almeida	-0.63 0.0930		34.64	[30.64; 38.87]	2.2%
Arruda-Neto	-0.73 0.0768	+	32.43	[29.22; 35.81]	2.2%
Barbalho	-0.55 0.1694	-	36.67	[29.35; 44.66]	2.1%
Bauman	-1.01 0.0896	+	26.77	[23.47; 30.35]	2.2%
Beck	-1.37 0.0968	+	20.30	[17.41; 23.54]	2.2%
Bergmann	-1.01 0.0629	+	26.66	[24.32; 29.14]	2.2%
Carvalho	-3.37 0.4152	+	3.33	[1.51; 7.22]	1.4%
Chaves	0.17 0.1832	+	54.17	[45.21; 62.86]	2.0%
Enes	-1.05 0.0996	+	25.90	[22.34; 29.82]	2.2%
Faria	0.28 0.2020		57.00	[47.15; 66.32]	2.0%
Faria-Neto	-1.38 0.0128	4	20.10	[19.70; 20.51]	2.3%
Figueiras	-1.21 0.1222	+	23.02	[19.05; 27.53]	2.2%
Gadelha	-1.12 0.1512		24.58	[19.50; 30.47]	2.1%
Giuliano	-2.20 0.1029	+	9.97	[8.30; 11.93]	2.2%
Gomes a	-0.41 0.0128	+	40.00	[39.40; 40.60]	2.3%
Gomes b	-0.90 0.0116		29.00	[28.54; 29.47]	2.3%
Gonçalves	0.15 0.2058		53.68	[43.64; 63.43]	2.0%
Guimarães	-2.31 0.1825	+	9.02	[6.48; 12.41]	2.0%
Guimarães	-1.06 0.0725	+	25.68	[23.06; 28.48]	2.2%
Mastroeni	0.29 0.1356		57.21	[50.61; 63.56]	2.1%
Moura	-0.62 0.0524	+	35.00	[32.70; 37.37]	2.3%
Nobre	-0.75 0.1421	÷	32.16	[26.41; 38.51]	2.1%
Pamplona Cunha	-0.02 0.1001	+	49.62	[44.74; 54.52]	2.2%
Pereira	-2.04 0.1446	+	11.49	[8.91; 14.70]	2.1%
Pereira	0.04 0.0900	+	51.01	[46.61; 55.40]	2.2%
Pinto	0.22 0.1861		55.56	[46.47; 64.29]	2.0%
Quadros	-1.20 0.0703	+	23.09	[20.73; 25.63]	2.2%
Queiroz	-1.05 0.1539	+	25.91	[20.55; 32.10]	2.1%
Reuter	-0.97 0.0636		27.43	[25.02; 29.98]	2.2%
Ribas	-1.46 0.0864	+	18.88	[16.42; 21.61]	2.2%
Ribas	-3.27 0.2547	+	3.66	[2.25; 5.89]	1.8%
Romero	-0.96 0.1585		27.64	[21.87; 34.26]	2.1%
Scheer	-0.47 0.1035	_+-	38.58	[33.90; 43.48]	2.2%
Sousa	-1.36 0.1144	+	20.43	[17.02; 24.31]	2.2%
Teixeira	-1.60 0.1196	+	16.77	[13.74; 20.30]	2.2%
Vasconcelos	-1.10 0.1952		25.00	[18.53; 32.83]	2.0%
Filled: Guimarães	0.58 0.1825	+	64.10	[55.52; 71.85]	2.0%
Filled: Lunardi	1.25 0.2416	-	77.77	[68.55; 84.89]	1.9%
Filled: Lunardi	1.27 0.2485	-	78.02	[68.56; 85.24]	1.9%
Filled: Ribas	1.54 0.2547		82.32	[73.86; 88.46]	1.8%
Filled: Carvalho	1.64 0.4152		83.69	[69.45; 92.05]	1.4%
Random effects mo	del		29.85	[26.70; 33.21]	100.0%
Heterogeneity: $I^2 = 999$	%, $\tau^2 = 0.2770$, $p = 0$	-50 0 50			

Figure S4C. Forest plot with the trim-to-fill correction for TC.

			Event	s per 100			
Study	TE	seTE	obse	rvations	Event	s 95%-Cl	Weight
Almeida	-2.29	0.1531		+	9.2	0 [6.98: 12.03]	1.9%
Arruda-Neto	-2.03	0.1121		+	11.6	3 [9.55: 14.08]	1.9%
Barbalho	-0.11	0.1635			47.3	3 [39.48: 55.32]	1.9%
Burgos	-0.28	0.0484		+	43.1	4 [40.84: 45.48]	2.0%
Burgos	-1.22	0.0673		+	22.8	1 [20.57: 25.21]	2.0%
Chaves	-1.01	0.2064			26.6	7 [19.53: 35.27]	1.9%
Enes	-2.34	0.1544		+	8.7	6 [6.63: 11.50]	1.9%
Faria	-0.12	0.2004		-	47.0	0 [37.45: 56.77]	1.9%
Faria-Neto	-3.32	0.0279		1	3.5	0 [3.32: 3.69]	2.0%
Goncalves	-1.03	0.2330			26.3	2 [18.45: 36.06]	1.9%
Guimarães	-1.88	0.0934		+	13.2	4 [11.27: 15.49]	2.0%
Lunardi	-3.04	0.2482		+	4.5	5 [2.84; 7.19]	1.9%
Mastroeni	-1.55	0.1764		-+-	17.5	7 [13.11: 23.14]	1.9%
Melo	-4.16	0.5818		÷	1.5	3 [0.49: 4.64]	1.6%
Nobre	-1.40	0.1665		-+-	19.8	2 [15.14; 25.52]	1.9%
Pamplona Cunha	0.01	0.1001		+-	50.1	3 [45.23: 55.01]	2.0%
Pereira	-3.83	0.3196		+	2.1	3 [1.15: 3.91]	1.8%
Quadros	-1.96	0.0900		+	12.3	3 [10.59: 14.42]	2.0%
Queiroz	-2.36	0.2400		-+-	8.6	4 [5.58: 13.14]	1.9%
Reuter	-1.22	0.0676		+	22.7	7 [20.52; 25.18]	2.0%
Ribeiro	-2.55	0.1038		+	7.2	4 [5.98; 8.73]	2.0%
Rinaldi	-2.33	0.2905		-+	8.8	4 [5.20; 14.63]	1.9%
Romero	-2.94	0.3245		+	5.0	3 [2.72; 9.09]	1.8%
Silva	-2.91	0.1736		+	5.1	7 [3.73; 7.12]	1.9%
Vasconcelos	-2.94	0.3878		+	5.0	0 [2.40; 10.12]	1.8%
Ribas	-1.57	0.0897		+	17.1	5 [14.80; 19.81]	2.0%
Bauman	-2.67	0.1615		+	6.4	6 [4.79; 8.65]	1.9%
Teixeira	-3.41	0.2541		+	3.1	9 [1.97; 5.15]	1.9%
Gadelha	-2.93	0.2963		+-	5.0	8 [2.91; 8.74]	1.9%
Gomes_a	-0.62	0.0131		+	35.0	0 [34.42; 35.59]	2.0%
Gomes_b	-1.10	0.0121		4	25.0	0 [24.56; 25.45]	2.0%
Carvalho	-4.08	0.5822		+-	1.6	7 [0.54; 5.04]	1.6%
Pereira	-0.39	0.0917		-+-	40.4	9 [36.24; 44.88]	2.0%
Pinto	-1.41	0.2326		-+	19.6	6 [13.43; 27.85]	1.9%
Ribas	-2.50	0.1810		+	7.5	5 [5.42; 10.43]	1.9%
Ribas	-1.70	0.1159		+	15.4	1 [12.68; 18.61]	1.9%
Sousa	-1.71	0.1281		+	15.3	2 [12.34; 18.87]	1.9%
Filled: Rinaldi	0.53	0.2905			+ 62.9	0 [48.96; 74.97]	1.9%
Filled: Enes	0.54	0.1544		+	+ 63.1	4 [55.86; 69.86]	1.9%
Filled: Queiroz	0.55	0.2400			+ 63.5	0 [52.09; 73.58]	1.9%
Filled: Ribas	0.70	0.1810			+ 66.8	2 [58.54; 74.17]	1.9%
Filled: Ribeiro	0.75	0.1038			+ 67.8	3 [63.24; 72.10]	2.0%
Filled: Bauman	0.87	0.1615			+ 70.4	4 [63.46; 76.58]	1.9%
Filled: Silva	1.10	0.1736			+ 75.1	1 [68.22; 80.91]	1.9%
Filled: Gadelha	1.12	0.2963			75.4	3 [63.20; 84.59]	1.9%
Filled: Romero	1.13	0.3245			75.6	6 [62.20; 85.45]	1.8%
Filled: Vasconcelos	1.14	0.3878			75.7	6 [59.37; 86.98]	1.8%
Filled: Lunardi	1.24	0.2482			+ 77.5	5 [67.98; 84.89]	1.9%
Filled: Faria-Neto	1.51	0.0279			• 81.9	4 [81.11; 82.73]	2.0%
Filled: Teixeira	1.61	0.2541			+ 83.2	9 [75.19; 89.13]	1.9%
Filled: Pereira	2.02	0.3196			+ 88.3	3 [80.17; 93.40]	1.8%
Filled: Carvalho	2.27	0.5822			90.6	6 [75.61; 96.81]	1.6%
Filled: Melo	2.36	0.5818			91.3	7 [77.18; 97.07]	1.6%
						•	
Random effects model	-			<u> </u>	26.6	7 [20.71; 33.61]	100.0%
Heterogeneity: $I^2 = 100\%$,	$\tau^2 = 1.4$	526, p = 0	I	1 1			
			-50	0 50			

Figure S4D. Forest plot with the trim-to-fill correction for LDL.



Figure S4E. Funnel plot with the trim-to-fill correction for TC.



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