Dyslipidaemia, and Mean Blood Cholesterol and Triglycerides Levels in the Portuguese Population: a Systematic Review

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ABSTRACT

Introduction: Dyslipidaemia is a major risk factor for cardiovascular disease, the leading cause of death in Portugal. We aimed to critically summarize the evidence from studies that quantified the distribution of total cholesterol, cholesterol fractions and triglycerides, in order to estimate time trends in the Portuguese adult population.

Methods: A systematic review was performed through Pubmed search up to January 2011. References' screening and data extraction were performed independently by two researchers and 28 eligible studies identified. Ecologic estimates of mean total cholesterol, LDL, HDL, and triglycerides were computed by linear regression, adjusting for participants' mean age, year of data collection and geographical coverage.

Results: In 2005, the mean total cholesterol at 50 years of age was 215 mg/dL [95% confidence interval (95%CI): 210 to 219] among women and 219 mg/dL (95%CI: 206 to 232) among men. Between 1985 and 2005, the mean adjusted variation in total cholesterol per calendar year was 0.4 mg/dL (95%CI: -0.3 to 1.2) among women and -0.1 mg/dL (95%CI: -0.6 to 0.4) among men. Data on LDL, HDL and triglycerides covered a much narrower period, precluding analysis of time trends. In 2001 the adjusted mean levels of LDL, HDL and triglycerides were 132 mg/dL, 59 mg/dL and 111 mg/dL, respectively, among women, and 132 mg/dL, 49 mg/dL and 150 mg/dL, respectively, among men.

Conclusions: Estimated mean cholesterol, respective fractions, and prevalence of dyslipidaemia suggest a high proportion of high-risk subjects in the Portuguese population. Between 1985 and 2005, mean total cholesterol did not vary significantly.

KEY-WORDS: CHOLESTEROL; CHOLESTEROL, LDL; CHOLESTEROL, HDL; DYSLIPIDAEMIA; PREVALENCE; TRIGLYCERIDES

DISLIPIDEMIA, E NÍVEIS MÉDIOS DE COLESTEROL E TRIGLICERÍDEOS NA POPULAÇÃO PORTUGUESA: REVISÃO SISTEMÁTICA DA LITERATURA

RESUMO

Introdução: A dislipidemia é um importante factor de risco para as doenças cardiovasculares, a principal causa de morte em Portugal. O objectivo deste estudo foi descrever tendências temporais de colesterol total, LDL, HDL e triglicerídeos na população adulta Portuguesa.

Métodos: Efectuou-se uma revisão sistemática da literatura, utilizando a base de dados Pubmed, até Janeiro de 2011. A selecção dos estudos e a extracção dos dados foram realizadas de forma independente por dois investigadores, identificando-se 28 estudos elegíveis. Obtiveram-se estimativas ecológicas de colesterol total, LDL, HDL, e triglicerídeos, ajustadas para a idade, ano de recolha de dados e cobertura geográfica, através de modelos de regressão linear.

Resultados: Em 2005, o colesterol total médio aos 50 anos de idade foi 215 mg/dL [intervalo de confiança a 95% (IC95%): 210 a 219] nas mulheres e 219 mg/dL (IC95%: 206 a 232) nos homens. Entre 1985 e 2005, o colesterol total médio nos homens variou 0,4 mg/dL (IC95%: -0,3 a 1,2) por cada ano, e nas mulheres -0,1 mg/dL por ano (IC95%: -0,6 a 0,4). Os dados de colesterol LDL, HDL, e triglicerídeos cobriram um curto período, impossibilitando a análise de tendências temporais. Em 2001, o colesterol LDL, HDL, e triglicerídeos médios foram 132 mg/dL, 59 mg/dL, e 111 mg/dL, respectivamente, nas mulheres, e 132 mg/dL, 49 mg/dL e 150 mg/dL, respectivamente, nos homens.

Conclusões: Os níveis de colesterol e de prevalência de dislipidemia sugerem uma elevada proporção de indivíduos em alto risco na população Portuguesa. Entre 1985 e 2005, o colesterol total não variou significativamente.

PALAVRAS-CHAVE: COLESTEROL; COLESTEROL HDL; COLESTEROL LDL; DISLIPIDEMIA; PREVALÊNCIA; TRIGLICERÍDEOS

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INTRODUCTION

Due to its close relation with atherosclerosis, dyslipidaemia increases the risk of ischemic heart disease,[1] ischemic stroke and other vascular diseases.[2] It is estimated to be responsible for 56% of global ischemic heart disease,[2] 4.4 million deaths overall (7.9% of the total) and 40.4 million of disability-adjusted life years (2.8% of the total).[2]

In Portugal, cardiovascular diseases are the leading cause of death[3] but mortality by both cerebrovascular and coronary heart disease decreased markedly since the 1980s.[4] The declining trends in coronary heart disease mortality in many developed countries have been associated with changes in risk factors prevalence and pharmacological and surgical treatments.[5,6] In the last decades, blood total cholesterol levels decreased in many high-income countries,[7] contributing to an estimated fraction of the decline in coronary heart disease mortality ranging from 10% to 37%.[5,8] However, there are no reliable data on time trends of blood cholesterol or its fractions in Portugal.

An accurate understanding of the burden of dyslipidaemia in Portugal requires the use of reliable and robust data on blood total cholesterol, triglycerides and other lipid fractions, including both central tendency measures in the general population and the prevalence of high-risk levels. Recently, two national surveys that assessed the distribution of cardiovascular risk factors reported data on dyslipidaemia in the Portuguese population,[9,10] based on self-reported information[9] or on data from clinical records of attendants to primary health care centers.[10] There is a single national survey of the Portuguese general population based on biochemical measurements of fasting blood lipids, conducted in 2001.[11] The absence of large national studies justifies the utilization of smaller studies reporting data on blood lipids fractions across Portuguese populations, in specific age-groups and different years of data collection. A systematic review may allow their identification and description in a standardized format, considering the methodological

aspects from each study that may compromise their internal and external validity.

Therefore, we conducted a comprehensive systematic review to critically summarize the evidence from studies that quantified the distribution of blood lipids and its fractions, as well as triglycerides. We aimed to estimate the sex-specific mean levels of blood lipids and prevalence of dyslipidaemia, and their time trends in the Portuguese adult population.

METHODS

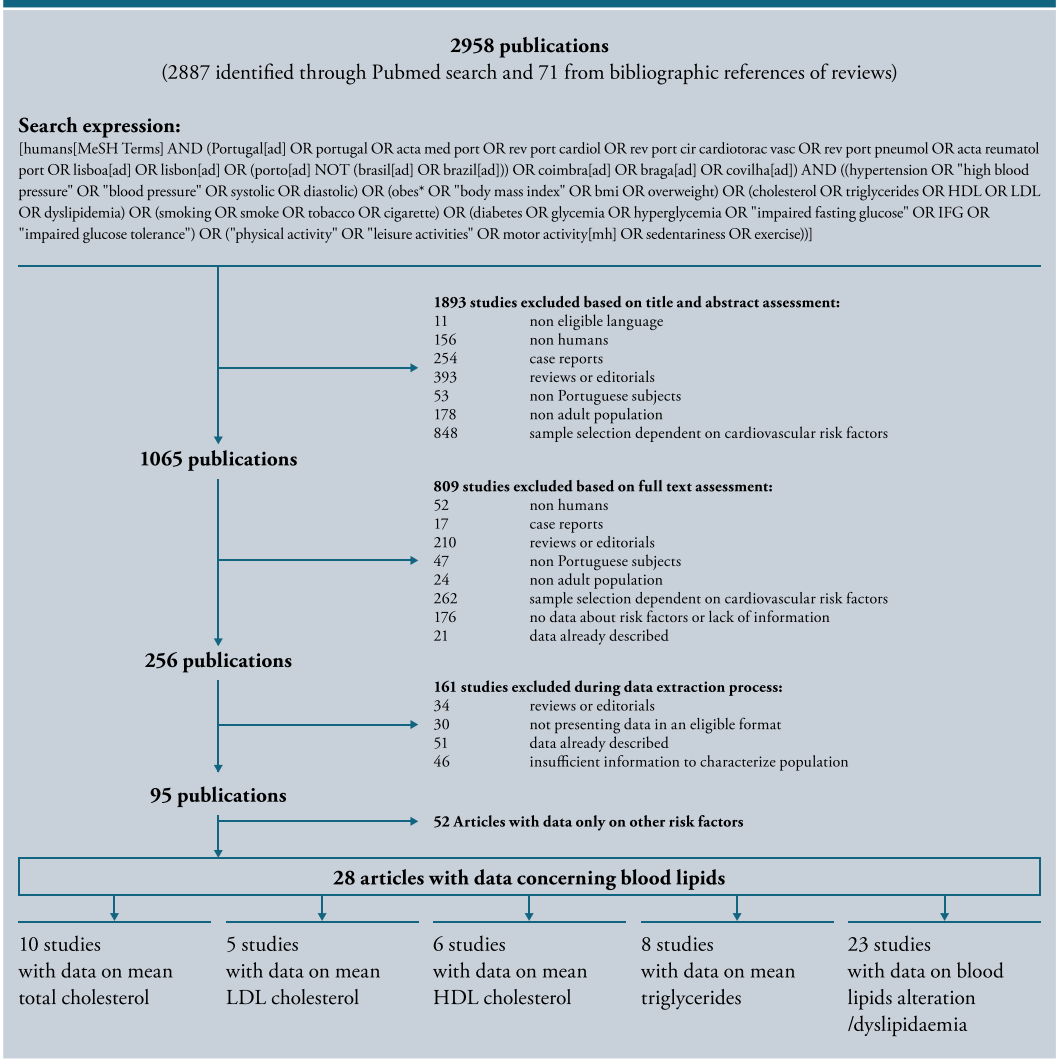
SYSTEMATIC REVIEW AND SEARCH STRATEGY

The present systematic review was conducted as part of a more comprehensive review that addressed the distribution of six major cardiovascular risk factors (hypertension,[12] obesity,[13] dyslipidaemia, smoking, diabetes mellitus, and physical inactivity) in Portuguese adults. A Pubmed search was conducted in January 2011 (the search expression is provided in **Figure 1**). The reference lists of review articles addressing the distribution of cardiovascular risk factors were screened to identify potentially eligible original reports. The current analysis only considers studies with data on mean blood lipids, dyslipidaemia and/or alterations of serum lipid fractions.

ELIGIBILITY CRITERIA AND SCREENING OF REFERENCE LISTS

Two reviewers independently evaluated the studies in three consecutive steps, following predefined criteria, to determine the eligibility of each report. The first two steps relied on the same criteria. In step 1 the exclusion of irrelevant studies was decided by considering only the title and abstract; when the abstract of a particular article was not available, the article was selected for evaluation in step 2, except when the title unequivocally presented information for exclusion (*e.g.* case report, studies of risk factors in a specified population). The full texts of studies selected for step 2 were then evaluated to decide on their eligibility and availability of relevant data. The studies selected

FIGURE 1 - Systematic review flowchart.



for step 3 were re-evaluated to determine their adequacy for data extraction of relevant data.

The criteria for exclusion of studies were the following: reports not written in Portuguese, English, Spanish, French or Italian; studies not involving humans (*e.g. in vitro* or animal research); editorials, reviews or comments; reports not providing data specifically for Portuguese subjects; studies not evaluating adult populations; studies evaluating samples of participants not expected to represent the general population regarding the frequency of the cardiovascular risk factors under study (*e.g.* subjects with diabetes, athletes, sedentary elderly); not presenting data on blood cholesterol, triglycerides or dyslipidaemia; insufficient characterization of the methods (*e.g.* not specifying the region where the sample was assembled, not describing the data collection procedures).

The decisions taken independently by the two reviewers in all steps were compared and the disagreements were resolved by consensus or after discussion with a third researcher. The agreement between the reviewers was 73.0%, 81.7% and 82.0%, in step 1, step 2 and step 3, respectively.

DATA EXTRACTION

Two investigators independently evaluated the selected studies to extract the following data for sample characterization: sample characteristics (sex, age, sample size); type of population (general population, university students, volunteers, occupational groups and primary health care users); sampling strategy (probability or non probability sampling); and geographical coverage (national or regional).

Quantitative data on the distribution of mean total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and prevalence of blood fractions alterations or dyslipidaemia (with the respective criteria), and the methods used for data collection (*e.g.* biochemical measurements, self-report or clinical records) were also extracted. Age- and sex-specific estimates were extracted whenever available. When a study did not present the mean age of the participants in each age group we assumed the mid-point of the age interval. When an age group also included subjects aged below 18 years old (*e.g.* age group 17-20 years), we computed the mid-point and excluded the data if the mid-point was lower than 17.5 years. For surveys that reported data by age groups but provided open age intervals at the extremes, we considered the upper/lower limit by assuming the same width for extreme classes as that of the adjacent class (*e.g.* for surveys reporting data in participants aged <30, 30–39, 40–49, and ≥50 years, we considered the overall range as 20–59 years).

Differences in the data extracted by the two investigators were discussed until consensus, and involving a third investigator when necessary.

DATA ANALYSIS

Data referring to mean levels of total cholesterol, LDL and HDL cholesterol, and triglycerides are summarized in figures depicting the age- and sex-specific estimates. Each figure includes the sex-specific prediction for each outcome based on linear regression models including the mean participants' age and, when appropriate, a quadratic term of the participants' age as independent variables.

We fitted sex-specific multiple linear regression models of the mean levels of total cholesterol, LDL and HDL cholesterol and triglycerides, on the following independent variables: year of data collection, geographical coverage and participants' mean age. For mean total cholesterol and triglycerides in men, and LDL cholesterol in men and women we also included a quadratic term of age to account for the non linear relation. Studies that did not present data stratified by gender were excluded from this analysis. Only studies in which total cholesterol was reported to be measured in fasting conditions were included in the analysis. Only one study provided information with no mention to the fasting conditions of the participants, and it was not included in the analysis also because it did not provide information stratified by gender.[14] We used the linear regression equations to predict the mean levels of the outcomes for each sex at the age of 50 years for specific calendar years. For total cholesterol, time trends were quantified by the regression coefficient of calendar year. Data on mean LDL, HDL and triglycerides covered a much narrower period, precluding analysis of time trends, and predictions were made for only one survey year (2001).

Estimation of time trends in prevalence of dyslipidaemia or single blood lipids fractions alterations, was not performed due to the diversity of cut-off points used to define the outcome.

As one or more estimates of the outcomes were extracted from each study, corresponding to different age strata, the confidence intervals were calculated using robust estimates of the standard errors, to account for the lack of independence of the observations from the same study.

RESULTS

We identified 28 studies eligible for data extraction in this systematic review.[9-11, 14-38] Ten presented data on mean total cholesterol[11, 14-16, 26, 30, 32, 34, 36, 37], 5 on

mean LDL cholesterol[11, 26, 30, 36, 37], 6 on mean HDL cholesterol[11, 30, 32, 34, 36, 37], 8 on mean triglycerides[11, 14-16, 30, 34, 36, 37], and 23 presented data on the prevalence of blood lipid disorders, either based on alteration of single lipid fractions[10, 11, 15-28, 30, 35, 39] or on the prevalence of dyslipidaemia (self-reported or composite outcome)[9, 16, 18, 29-31] (**Figure 1**).

The main characteristics of the studies providing data on alterations of single blood lipids fractions and on the prevalence of dyslipidaemia, as well as the respective age- and sex-specific estimates, are presented in **Tables 1 and 2**. Only 8 studies relied on probability samples of the general population, and eleven were based on samples of users of specified health care facilities. Four different criteria were used for classification of blood lipids alterations. The proportion of elevated LDL cholesterol ranged from 4.8%, when defined as LDL cholesterol ≥130 mg/dL, among young women, in 2005[26] to 73.8%, when defined as LDL cholesterol ≥115 mg/dL, among men aged 30-80 years, in 2007.[25] Low HDL cholesterol ranged from 15% among women to 55% among men age 20-29 years when defined as ≤45 mg/dL, in 2007.[25] In general, the proportion of subjects with blood lipids alterations increased with age and was higher among men, regardless of the criteria used to define the outcome.

Figure 2 depicts the variation of sex-specific estimates of mean total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides with age. Total cholesterol, LDL cholesterol and triglycerides increased progressively with age among women, despite an attenuation of the slope for LDL in the very elderly, while among men an increase up to approximately 60 years was followed by a decrease in these three lipid fractions. HDL hardly varied with age in both sexes. Despite the small sex differences observed under the age of 30, men had higher levels of total cholesterol, LDL cholesterol and triglycerides until the age of 60, while after 60 years the mean levels of these lipid fractions were higher among women. Women had higher levels of HDL cholesterol at all ages. Detailed information on mean blood lipids is provided in **Table 3**.

In 2005, the mean total cholesterol at 50 years of age, predicted by a model adjusting for geographical coverage, was 215 mg/dL (95%CI: 210 to 219) among women and 219 mg/dL (95%CI: 206

FIGURE 2 - Mean total, LDL and HDL cholesterol, and triglycerides levels, according to age, in women and men. Only estimates from studies in which fasting blood samples were collected are presented.

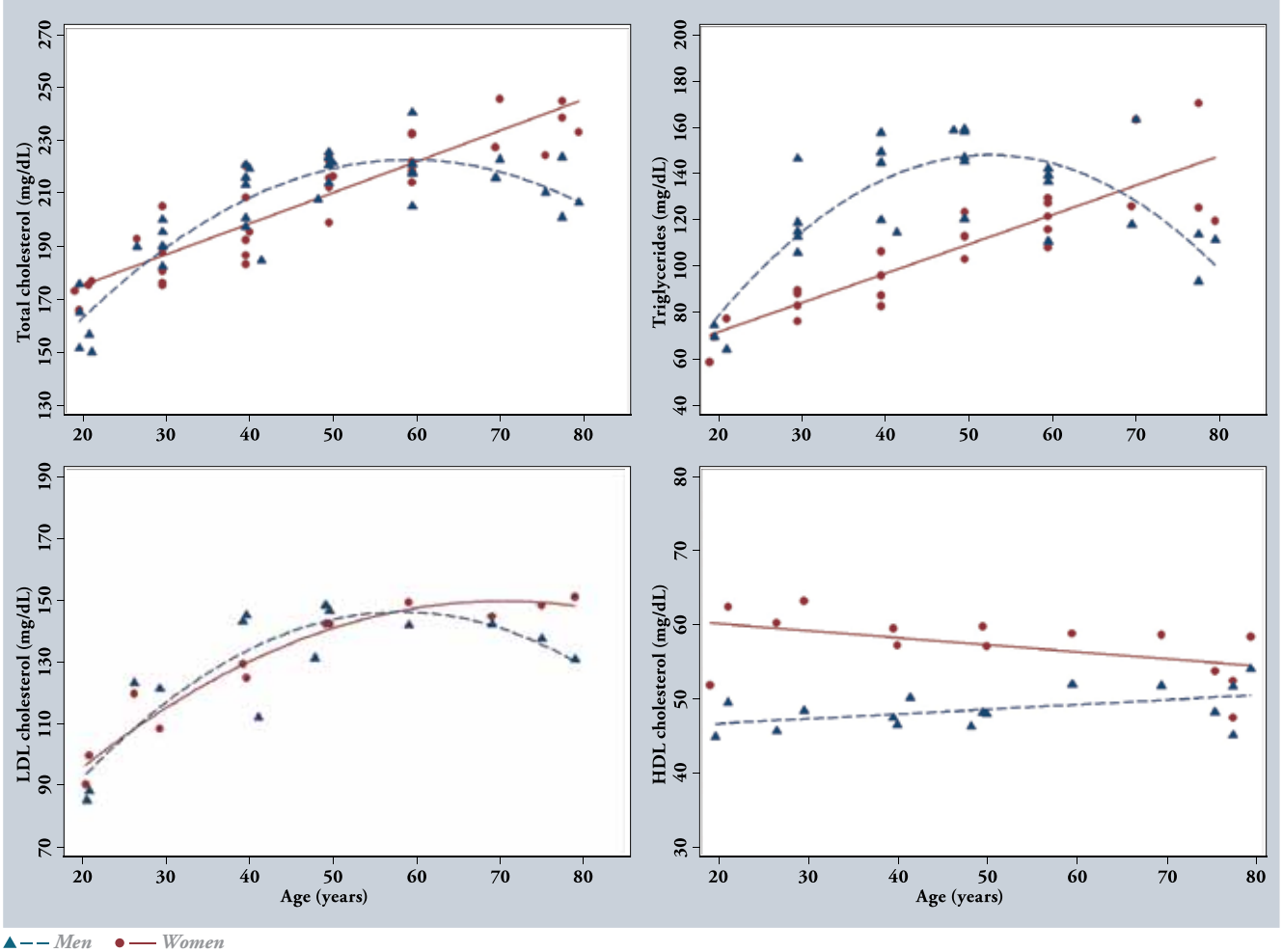


TABLE 1 - Main characteristics and results of studies with data on dyslipidaemia defined with base on alterations of a single blood lipids fraction.

1st Author, year of publication	Year/period of data collection	Population type	Sampling process	Recruitment place	Lipids fasting	Sex	Age range	Sample size
Pereira-Miguel, 1983[15]	1981	General population	Probability	Urban sample: Santarém, Leiria, Castelo Branco, Guarda, Lisboa	Yes	F	25-34 35-44 45-54 55-64	103 115 107 101
						M	25-34 35-44 45-54 55-64	92 123 112 105
				Rural sample: Outeiro da Cortiçada, Aljubarrota, Alcongosta, Celorico da Beira, Alcáçovas, Romeu	Yes	F	25-34 35-44 45-54 55-64	87 132 131 147
						M	25-34 35-44 45-54 55-64	104 158 146 128
Martins, 1993[16]	1987	General population	Probability	Sesimbra, Palmela, Barreiro, Setúbal	Yes	F	15-64	866
						M	15-64	734
	1993	General population	Probability	Sesimbra, Palmela, Barreiro, Setúbal	Yes	F	15-64	519
						M	15-64	483
Schneider, 1995[35]	1994 *	General population	Probability	Açores	ND	MF	20-40 40-60 20-60	521 568 1089
Nunes, 1997[17]	1995	Volunteers	Non probability	Viseu	ND	F	20-29 30-39 40-49 50-59 60-69 70-79 80-89†	1173
						M	20-29 30-39 40-49 50-59 60-69 70-79 80-89†	679
Ribas, 1997[18]	1996 *	Primary health care users	Probability	Porto	Yes §	M	40-89†	164
Reis, 1997[19]	1996 *	Volunteers	Non probability	Linha do Estoril	ND	MF	ND	5083
Ferreira, 1998[20]	1997 *	Primary health care users	Non probability	Mata Mourisca	ND	F	20-79	826
						M	20-79	826
Canhão, 1999[58]	1993 *	Primary health care users	Probability	Lisboa	Yes	F	20†-80†	ND
						M	20†-80†	ND
Simões, 2000[21]	1998-1999	General population	Probability	Góis	Yes	F	25-29 30-34 35-39 40-44	49 42 53 30
						M	25-29 30-34 35-39 40-44	44 44 48 30
Cardoso, 2001[22]	1999	Occupational group	Non probability	Coimbra	Yes	MF	20-69	283
Instituto de Alimentação Becel, 2001[11]	2001	General population	Probability	Portugal	Yes	F	18-35 35-44 45-54 55-96	1428
						M	18-35 35-44 45-54 55-96	

Total cholesterol		LDL - cholesterol		HDL - cholesterol		Triglycerides	
% Hyperchol	Hyperchol criteria	% High LDL	LDL criteria	% Low HDL	HDL criteria	% Hypertrig	Hypertrig criteria
2.0 6.1 19.5 22.8	≥ 250mg/100mL	ND	ND	ND	ND	2.0 2.7 9.6 12.3	≥ 175mg/100mL
8.7 21.1 22.3 22.9	≥ 250mg/100mL	ND	ND	ND	ND	8.8 21.0 17.3 17.9	≥ 175mg/100mL
2.0 6.3 13.7 22.7	≥ 250mg/100mL	ND	ND	ND	ND	6.6 4.9 7.0 9.9	≥ 175mg/100mL
10.1 12.9 17.6 17.1	≥ 250mg/100mL	ND	ND	ND	ND	7.2 14.7 12.2 8.6	≥ 175mg/100mL
55.1	≥ 200mg/dL	ND	ND	ND	ND	4.7	> 200mg/dL
57.3	≥ 200mg/dL	ND	ND	ND	ND	14.0	> 200mg/dL
51.2	≥ 200mg/dL	46	> 135mg/dL	3.7	< 40mg/dL	16.1	> 200mg/dL
52.6	≥ 200mg/dL	44	> 135mg/dL	18.8	< 35mg/dL	5.7	> 200mg/dL
34.8 58.1 47.3	> 200mg/dL	ND	ND	ND ND 17.4	ND ND < 35mg/dL	20.2 40.0 30.9	> 180mg/dL
11.1 13.3 27.2 38.2 48.6 53.2 66.7	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
5‡ 30‡ 35‡ 41‡ 39‡ 39‡ 82‡	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
57‡	> 200mg/dL	36‡	> 135mg/dL	15‡	< 35mg/dL	26‡	> 150mg/dL
26	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
11.2	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
14.0	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
37.1	> 240mg/dL	ND	ND	ND	ND	8.6	> 200mg/dL
37.3	> 240mg/dL	ND	ND	ND	ND	12.0	> 200mg/dL
10.2 16.6 30.2 26.6	≥ 200mg/dL and/or treated	ND	ND	ND	ND	ND	ND
38.6 45.5 47.9 43.3	≥ 200mg/dL and/or treated	ND	ND	ND	ND	ND	ND
41.0	> 190mg/dL	ND	ND	ND	ND	33.9	> 200mg/dL
10.2 10.5 20.8 38.6	≥ 240mg/dL	ND	ND	ND	ND	ND	ND
9.7 32.2 34.0 22.7	≥ 240mg/dL	ND	ND	ND	ND	ND	ND

Hyperchol – hypercholesterolaemia;

Hypertrig – hypertriglyceridaemia;

F – Female;

M – Male;

MF – Male and female;

ND – no data;

† For surveys that reported data by age groups but provided open age intervals at the extremes, we considered the upper/lower limit by assuming the same width for extreme classes as that of the adjacent class (e.g. for surveys reporting data in participants aged <30, 30–39, 40–49, and ≥50 years, we considered the overall range as 20–59 years);

‡ Data estimated from the graphs presented in the original report;

§ Data assumed to be obtained in fasting conditions as it was abstracted from the clinical records;

|| Data referring only to the 2839 evaluated subjects;

¶ Mean age of the participants reported in the original studies, as the total age range of the participants was not reported;

*** To convert the values of total cholesterol in mmol/L to mg/dL divide by 0.02586, and to convert triglycerides in mmol/L to mg/dL divide by 0.0113.*

TABLE 1 (cont.) - Main characteristics and results of studies with data on dyslipidaemia defined with base on alterations of a single blood lipids fraction.

1st Author, year of publication	Year/period of data collection	Population type	Sampling process	Recruitment place	Lipids fasting	Sex	Age range	Sample size
Rocha, 2003[23]	1999-2000	Primary health care users	Non probability	Lisboa	Yes §	MF	†30-89†	3228
Santiago, 2003[24]	2002	Volunteers	Non probability	Districts of Aveiro, Coimbra, Viseu, Guarda and Leiria	ND	F	48.7 (12.6) ¶	532
						M	47.0 (11.7) ¶	461
Fiuza, 2008[10]	2006-2007	Primary health care users	Non probability	Portugal	Yes	F	18-29 30-39 40-49 50-59 60-69 70-79 80-89†	10386
						M	18-29 30-39 40-49 50-59 60-69 70-79 80- 89†	6469
Carmo Martins, 2008[25]	2007	Health care users	Non probability	Lisboa	Yes	F	20-29 30-80	67 341
						M	20-29 30-80	47 217
Brandão, 2008[26]	2005	University students	Probability	Aveiro	Yes	F	20.6 (ND) ¶	254
						M	20.7 (ND) ¶	124
Cavaco, 2010[27]	2009	Health care users	Non probability	Lisboa	No	MF	18-76	32
Lobão, 2010[28]	2007	Primary health care users	Non probability	Vila Nova de Gaia	ND	MF	18-84	502

to 232) among men. Between 1985 and 2005 the mean total cholesterol varied 0.4 mg/dL per calendar year (95% confidence interval (95%CI): -0.3 to 1.2) among women, adjusting for the age of participants, year of data collection and geographical coverage of the study. Among men, mean total cholesterol varied -0.1 mg/dL per year (95%CI: -0.6 to 0.4) in the same calendar period.

In 2001, the adjusted mean levels of HDL cholesterol, LDL cholesterol and triglycerides in women at 50 years of age were 59 mg/dL, 140 mg/dL and 111 mg/dL, respectively. In men, at 50 years, the adjusted mean levels of HDL cholesterol, LDL cholesterol and triglycerides were 49 mg/dL, 146 mg/dL and 150 mg/dL, respectively.

DISCUSSION

The mean levels of total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides observed in the Portuguese population suggest a profile of high risk, and a small and non significant variation of the mean blood total cholesterol levels was observed between 1985 and 2005. The scarcity of data using standardized methodology and homogeneous criteria across a wide time span precludes the analysis of time trends for cholesterol subfractions and triglycerides as well as for prevalence of lipid alterations. This study provides a summary of the best available evidence on blood lipid profile in Portuguese adults. However, the present study is limited by the use of ecological summary estimates and the diversity of methodological options adopted in the original reports. The primary sources of information are heterogeneous regarding the methods used to determine the blood lipids, the time of data collection, the age range of groups, and the quality of reporting of data. These limitations were partially overcome through stratified analyses by sex and multivariate modeling of the data. The heterogeneity of the criteria used to define blood lipids alterations impaired the assessment of its trends, but attending to the extensive literature search this is inevitable, since cut-off points changed over time and at a certain time point are not consensual among recommendations from different entities.

Most studies used to assess time trends in mean total cholesterol involved samples of the general population. Since blood total cholesterol is associated with education[40] and two studies included in our analysis evaluated samples of university students,[26, 32] we reanalyzed the data excluding these reports and the conclusions were unchanged.

Total cholesterol		LDL - cholesterol		HDL - cholesterol		Triglycerides	
% Hyperchol	Hyperchol criteria	% High LDL	LDL criteria	% Low HDL	HDL criteria	% Hypertrig	Hypertrig criteria
30.4 ‖	≥ 220mg/dL	ND	ND	ND	ND	ND	ND
37.7	≥ 190mg/dL	ND	ND	ND	ND	ND	ND
57.5	≥ 190mg/dL	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	23.4 28.8 35.2 34.9 36.5 34.2 34.9	< 40mg/dL	14.1 22.1 25.4 30.9 33.6 34.5 28.3	≥ 150mg/dL
ND	ND	ND	ND	37.1 49.3 54.4 52.8 48.0 41.6 38.0	< 40mg/dL	25.8 40.0 43.2 44.6 40.8 32.5 27.6	≥ 150mg/dL
31.3 63.3	≥ 4.9mmol/L **	28.4 64.8	≥ 2.97mmol/L **	14.9 23.8	≤ 1.16mmol/L **	4.5 10.9	≥ 2.05mmol/L **
25.5 66.4	≥ 4.9mmol/L **	45.7 73.8	≥ 2.97mmol/L **	55.3 53.0	≤ 1.16mmol/L **	10.6 22.1	≥ 2.05mmol/L **
23.2	≥ 200mg/dL	8.7	≥ 130mg/dL	ND	ND	ND	ND
6.4	≥ 200mg/dL	4.8	≥130mg/dL	ND	ND	ND	ND
50.0	≥ 200mg/dL	ND	ND	ND	ND	ND	ND
29.1	≥ 200mg/dL	ND	ND	ND	ND	ND	ND

Hyperchol – hypercholesterolaemia;

Hypertrig – hypertriglyceridaemia;

F – Female;

M – Male;

MF – Male and female;

ND – no data;

† For surveys that reported data by age groups but provided open age intervals at the extremes, we considered the upper/lower limit by assuming the same width for extreme classes as that of the adjacent class (e.g. for surveys reporting data in participants aged <30, 30–39, 40–49, and ≥50 years, we considered the overall range as 20–59 years);

‡ Data estimated from the graphs presented in the original report;

§ Data assumed to be obtained in fasting conditions as it was abstracted from the clinical records;

‖ Data referring only to the 2839 evaluated subjects;

¶ Mean age of the participants reported in the original studies, as the total age range of the participants was not reported;

*** To convert the values of total cholesterol in mmol/L to mg/dL divide by 0.02586, and to convert triglycerides in mmol/L to mg/dL divide by 0.0113.*

At the individual level, total and LDL cholesterol are known to increase with obesity,[41, 42] smoking[43] and high intake of saturated and trans fatty acids and dietary cholesterol.[44, 45] The efficacy of lipid lowering drugs has also been demonstrated by several high quality clinical trials.[46, 47] The time trends in cholesterol observed in our review are likely to be driven by the variation in the exposure to these factors. In Portugal, between 1995 and 2005, the prevalence of overweight increased 3% and 4%, and the prevalence of obesity increased 7% and 1% among women and men, respectively.[13] Data from the 1998-1999 and 2005-2006 National Health Surveys indicate that during this period the consumption of fish and soup declined, but the consumption of fat-containing foods such as meat and milk increased.[48] Data on physical activity trends in Portugal are not available. However, the National Health Survey conducted in 1998-1999 showed that overall 71% of Portuguese subjects aged over 15 years were sedentary.[49] Smoking in Portugal has decreased among men, but increased among women.[50] These trends could account for a deleterious effect on blood lipids over time. However, our results contradict this expectation and the non-significant change in the total cholesterol over time seems to be explained by other determinants, including the use of cholesterol lowering medication. Statins are able to reduce as much as 20% of total cholesterol levels after a mean follow-up period of 5 years, compared with those who do not use cholesterol lowering medication.[51] In 1985, statins were hardly ever used and data from the lipid-lowering drugs prescribed and sold to outpatients in mainland Portugal showed an increase from 10.21 defined daily doses (DDD) per 1000 inhabitants per day in 1995 to 67.93 in 2004, mainly due to an average annual growth of 34.5% in the use of statins (from 4.43 DDD per 1000 inhabitants per day in 1995 to 60.73 in 2004).[52]

Current guidelines for the evaluation and treatment of dyslipidaemia identify concentrations of LDL cholesterol rather than total cholesterol as the primary target of treatment[53, 54] and highlight the importance of risk reduction by targeting triglycerides and HDL cholesterol.[55] Our results highlight a large proportion of subjects with alterations of blood lipids, despite not being possible to quantify time trends for LDL cholesterol nor HDL cholesterol. We have previously estimated that, in 2005, the prevalence of overweight at 50 years of age exceeded 40% among women and 50% among men, while the prevalence of obesity was nearly 20% in both sexes,[13] certainly contributing for the observed prevalence of high-risk lipid levels.

TABLE 2 - Main characteristics and results of the studies providing data on prevalence of dyslipidaemia, considered as self-reported or based on alterations of multiple blood lipids fractions.

1st Author, year of publication	Year/period of data collection	Population type	Sampling process	Recruitment place	Lipids fasting	Sex	Age range	Sample size	Dyslipidaemia prevalence (%)	Criteria
Teles, 2008[29]	2004-2005	Primary health care users	Non probability	Portugal	NA	M	40-69	3067	31.0	Self-reported
Bonhorst, 2010[9]	2009	General population	Probability	Portugal	NA	MF	40-101	10447	36.8	Self-reported
Alves, 2008[30] *	1999-2003	General population	Probability	Porto	NA	F	18-24	81	9.9	Self-reported
							25-34	141	11.3	
							35-44	275	21.8	
							45-54	366	32.8	
							55-64	316	49.7	
							65-74	269	52.4	
							75-84	83	57.8	
							85-94	8	50.0	
						M	18-24	50	2.0	
							25-34	84	15.5	
							35-44	164	31.7	
							45-54	213	37.1	
							55-64	195	44.1	
							65-74	169	39.1	
							75-84	64	21.9	
							85-94	7	28.6	
					Yes	F	40-44	135	76.3	If low risk †: Total cholesterol ≥5mmol/L ‡ or LDL-C ≥3mmol/L ‡ If high risk †: total cholesterol ≥4.5mmol/L ‡ or LDL-C ≥2.5mmol/L ‡
							45-49	158	84.8	
							50-54	166	84.3	
							55-59	159	89.3	
							60-65	146	90.4	
						M	40-44	80	83.8	
							45-49	92	84.8	
							50-54	101	85.2	
							55-59	72	79.2	
							60-65	106	86.8	
dos Reis, 1990[31]	1989 §	Primary health care users	Probability	Algés	Yes ‖	F	21-40	136	1	Total cholesterol ≥ 250 mg/dL or (total cholesterol – HDL) ≥ 200 mg/dL
							41-60	178	10	
							60-79 ¶	317	19	
						M	21-40	87	8	
							41-60	133	16	
							60-79 ¶	136	27	
Martins, 1993[16]	1993	General population	Probability	Sesimbra, Palmela, Barreiro, Setúbal	Yes	F	15-64	519	3.3	Trig >200mg/dL, HDL <35 mg/dL for men or <40mg/dL for women
						M	15-64	481	2.7	
Ribas, 1997[18]	1996 §	Primary health care users	Probability	Porto	Yes §	M	40-89†	164	60 **	Total cholesterol >200mg/dL, HDL <35, LDL>135

F – Female; M – Male; MF – Male and female; NA – not applicable; Trig – Triglycerides; HDL – HDL cholesterol; LDL – LDL cholesterol;

** Age- and sex- estimates obtained directly from the authors;*

† Subjects were considered low risk or high risk as indicated in the European guidelines;

‡ To convert the values of total cholesterol in mmol/L to mg/dL divide by 0.02586;

§ When the period of data collection was not reported we assumed the publication year minus the median difference between the publication year and date of data collection in the articles for which that information was available (1.0 years);

‖ *Data assumed to be obtained in fasting conditions as it was abstracted from the clinical records;*

¶ For surveys that reported data by age groups but provided open age intervals at the extremes, we considered the upper/lower limit by assuming the same width for extreme classes as that of the closest class (e.g. for surveys reporting data in participants aged <30, 30–39, 40–49, and ≥50 years, we considered the overall range as 20–59 years);

*** Data estimated from the graphics presented in the original report.*

In several other high income countries blood cholesterol levels have declined during the last decades.[56] Recently a decrease of 0.19 mmol/L and 0.21 mmol/L per decade for men and women in Australasia, North America and Western Europe between 1980 and 2008 was reported.[7] It is not clear what drives this difference, but changes in the pattern of blood lipids determinants are likely to be the cause.[7]

Recent European guidelines recommend levels of total cholesterol in the general population below 5 mmol/L.[54] The estimated levels of mean total cholesterol at 50 years are far above this goal. Longitudinal studies have shown that a plasma total cholesterol reduction of 1% results in a decrease of coronary heart disease mortality of 2-3%.[57] Therefore the benefits of blood lipids reduction could not

TABLE 3 - Main characteristics and results of studies presenting data on mean blood lipids levels.

1st Author, year of publication	Year/period of data collection	Population type	Sampling process	Recruitment place	Lipids fasting	Sex	Age range	Sample size	Cholesterol			Triglycerides (mg/dL*)
									Total (mg/dL*)	LDL (mg/dL*)	HDL (mg/dL*)	
Pereira-Miguel, 1974[14]	1974	Volunteers	Non probability	Alcáçovas	ND	MF	† 15-24	4	138.7	ND	ND	118.2
							25-34	5	170.0			112.8
							35-44	10	177.0			206.3
							45-54	17	215.7			186.3
							55-64	16	189.6			170.0
							65-74	18	199.1			170.9
							75-84 †	6	205.8			171.0
				Alfeizerão	ND	MF	† 15-24	7	151.1	ND	ND	163.1
							25-34	14	147.7			157.6
							35-44	16	158.7			179.3
							45-54	29	163.6			193.6
							55-64	30	175.6			196.2
							65-74	22	175.1			198.1
							75-84 †	3	170.0			233.6
Pereira-Miguel, 1983[15]	1982 ‡	General population	Probability	Urban (Santarém, Leiria, Castelo Branco, Guarda, MSD Lisboa)	Yes	F	25-34	103	177.1	ND	ND	88.6
							35-44	115	187.6			87.9
							45-54	107	216.9			113.8
							55-64	101	219.7			108.6
						M	25-34	92	201.2	ND	ND	119.4
							35-44	123	214.3			145.4
							45-54	112	221.7			145.8
							55-64	105	219.0			137.2
				Rural (Alcáçovas and Romeu)	Yes	F	25-34	87	176.3	ND	ND	90.2
							35-44	132	184.1			96.4
							45-54	131	199.9			103.5
							55-64	147	215.2			116.5
						M	25-34	104	196.5	ND	ND	115.6
							35-44	158	201.7			120.5
							45-54	146	215.0			121.1
							55-64	128	206.1			111.3
Kafatos, 1991[34]	1990 ‡	General population	Probability	Vila Franca de Xira	Yes	F	75-80	103	6.4 mmol/L	ND	1.23 mmol/L	1.42 mmol/L
						M	75-80	104	5.8 mmol/L	ND	1.17 mmol/L	1.29 mmol/L
				Coimbra	Yes	F	75-80	17	6.20 mmol/L	ND	1.36 mmol/L	1.93 mmol/L
						M	75-80	17	5.22 mmol/L	ND	1.34 mmol/L	1.06 mmol/L
Martins, 1993[16]	1987	General population	Probability	Sesimbra, Palmela, Barreiro, Setúbal	Yes	F	15-24	156	176.7	ND	ND	70 §
							25-34	123	183.3			77 §
							35-44	174	198.3			83 §
							45-54	206	226.6			113 §
							55-64	207	241.6			122 §
						M	15-24	136	166.2	ND	ND	75 §
							25-34	122	206.1			113 §
							35-44	143	221.5			150 §
							45-54	163	223.0			159 §
							55-64	170	223.0			140 §
	1993	General population	Probability	Sesimbra, Palmela, Barreiro, Setúbal	Yes	F	15-24	83	166.7	ND	ND	70 §
							25-34	66	181.6			90 §
							35-44	89	193.3			107 §
							45-54	124	213.3			113 §
							55-64	145	233.3			130 §
							64-74 *	12	246.7			164 §
						M	15-24	75	152.3	ND	ND	75 §
							25-34	71	190.8			147 §
							35-44	96	217.0			158 §
							45-54	106	224.5			160 §
							55-64	122	218.5			140 §
							64-74 *	13	223.9			164 §
Torres, 2000[33]	1999	General population	Probability	Madeira	Yes	M	25-65	50	4.8 mmol/L	2.9 mmol/L	1.3 mmol/L	1.3 mmol/L
						M	25-65	37	5.4 mmol/L	3.4 mmol/L	1.2 mmol/L	1.8 mmol/L
Marques-Vidal, 2001[32]	1994-1995	University students	Probability	Monte da Caparica	Yes	F	19.0 (3.0)¶	585	174	ND	52	59
						M	19.6 (3.6)¶	416	166	ND	45	70

TABLE 3 (cont.) - Main characteristics and results of studies presenting data on mean blood lipids levels.

1st Author, year of publication	Year/period of data collection	Population type	Sampling process	Recruitment place	Lipids fasting	Sex	Age range	Sample size	Cholesterol			Triglycerides (mg/dL*)
									Total (mg/dL*)	LDL (mg/dL*)	HDL (mg/dL*)	
Instituto de Alimentação Becel, 2001[11] ‖	2001	General population	Probability	Portugal	Yes	F	18-35	1428	193.8	119.8	60.4	ND
							35-44		196.4	125.0	57.4	
							45-54		217.4	142.6	57.3	
							55-96		225.4	148.6	53.9	
						M	18-35		190.8	123.4	45.8	ND
							35-44		220.5	145.6	46.6	
							45-54		222.6	146.9	48.1	
							55-96		211.4	137.8	48.3	
						MF	18-25	58	169.4	106.6	50.6	93.8
							25-34	233	197.4	125.3	52.8	134.4
							35-44	340	205.8	133.1	53.2	126.7
							45-54	327	220.0	144.8	52.8	138.1
							55-64	169	228.0	148.0	55.3	142.3
							65-74	106	228.0	153.6	50.7	146.1
							75-96	195	209.9	137.2	49.8	127.5
Brandão, 2008[26]	2005	University students	Probability	Aveiro	Yes	F	20.6 (2.5)¶	254	176.3	90.4	ND	ND
						M	20.7 (3.0)¶	124	157.5	85.2	ND	ND
Freitas, 2008[37]	2001	General population	Probability	Madeira	Yes	MF	46.1 (11)¶	510	217.7	114.7	57.1	130.7
Alves, 2008[30] ‖	1999-2003	General population	Probability	Porto	Yes	F	18-24	81	178	100	63	78
							25-34	141	188	108	63	83
							35-44	275	209	130	60	96
							45-54	366	225	143	60	110
							55-64	316	234	150	59	125
							65-74	269	228	145	59	123
							75-84	83	231	149	59	117
							85-93	8	269	190	54	144
						M	18-24	50	151	88	50	65
							25-34	84	191	122	49	107
							35-44	164	222	144	48	158
							45-54	213	225	149	48	143
							55-64	195	222	142	52	138
							65-74	169	217	143	52	119
							75-84	64	207	130	53	115
							85-93	7	217	141	69	70

F – Female; M – Male; MF – Male and female; ND – not defined in the original report;

** Mean cholesterol and triglycerides values are presented in mg/dL, with the exception of the mean values indicated with other units. To convert the values of total cholesterol in mmol/L to mg/dL divide by 0.02586, and to convert triglycerides in mmol/L to mg/dL divide by 0.0113;*

† For surveys that reported data by age groups but provided open age intervals at the extremes, we considered the upper/lower limit by assuming the same width for extreme classes as that of the closest class (e.g. for surveys reporting data in participants aged <30, 30–39, 40–49, and ≥50 years, we considered the overall range as 20–59 years);

‡ When the period of data collection was not reported we assumed the publication year minus the median difference between the publication year and date of data collection in the articles for which that information was available (1.0 years);

§ Data estimated from the graphs presented in the original report;

|| Age- and sex-specific estimates obtained directly from the authors;

¶ Mean age and standard deviation of the participants reported in the original studies, as the total age range of the participants was not reported.

be overemphasized. However, a strict interpretation of international guidelines may lead to individuals with optimal lipid profiles being the exception, rising issues related to medicalization and risk labeling of asymptomatic subjects.[30] The physicians' role in aggressively promoting the need for behavioral changes in all patients and using drug therapies with appropriate targeting has become of paramount importance. Strategies to improve blood lipids profile of the population may include measures not only at an individual level but also a national level. These should include concerted efforts for the adoption of healthy lifestyles, through smoking cessation, healthy diet and increased physical activity.

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