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CLINICAL RESEARCH
Dyslipidaemias

Lipid distributions in the Global Diagnostics Network across five continents

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See the editorial comment for this article 'The global diagnostic network: what can we learn from half a billion lipid measurements between 2018 and 2020?', by F. Barkas and K.K. Ray, https://doi.org/10.1093/eurheartj/ehad308.

Abstract

Aims Lipids are central in the development of cardiovascular disease, and the present study aimed to characterize variation in lipid profiles across different countries to improve understanding of cardiovascular risk and opportunities for risk-reducing interventions.

Methods and results This first collaborative report of the Global Diagnostics Network (GDN) evaluated lipid distributions from nine laboratory organizations providing clinical laboratory testing in 17 countries on five continents. This cross-sectional study assessed aggregated lipid results from patients aged 20–89 years, tested at GDN laboratories, from 2018 through 2020. In addition to mean levels, the World Health Organization total cholesterol risk target (<5.00 mmol/L, <193 mg/dL) and proportions in guideline-based low-density lipoprotein cholesterol (LDL-C) categories were assessed. This study of 461 888 753 lipid results found wide variation by country/region, sex, and age. In most countries, total cholesterol and LDL-C peaked at 50–59 years in females and 40–49 years in males. Sex- and age-group adjusted mean total cholesterol levels ranged from 4.58 mmol/L (177.1 mg/dL) in the Republic of Korea to 5.40 mmol/L (208.8 mg/dL) in Austria. Mean total cholesterol levels exceeded the World Health Organization target in Japan, Australia, North Macedonia, Switzerland, Germany, Slovakia, and Austria. Considering LDL-C categories, North Macedonia had the highest proportions of LDL-C results >4.91 mmol/L (>190 mg/dL) for both females (9.9%) and males (8.7%). LDL-C levels <1.55 mmol/L (<60 mg/dL) were most common among females in Canada (10.7%) and males in the UK (17.3%).

Conclusion With nearly a half billion lipid results, this study sheds light on the worldwide variability in lipid levels, which may reflect inter-country differences in genetics, lipid testing, lifestyle habits, and pharmacologic treatment. Despite variability, elevated atherogenic lipid levels are a common global problem, and these results can help inform national policies and health system approaches to mitigate lipid-mediated risk of cardiovascular disease.

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Structured Graphical Abstract

Key Question

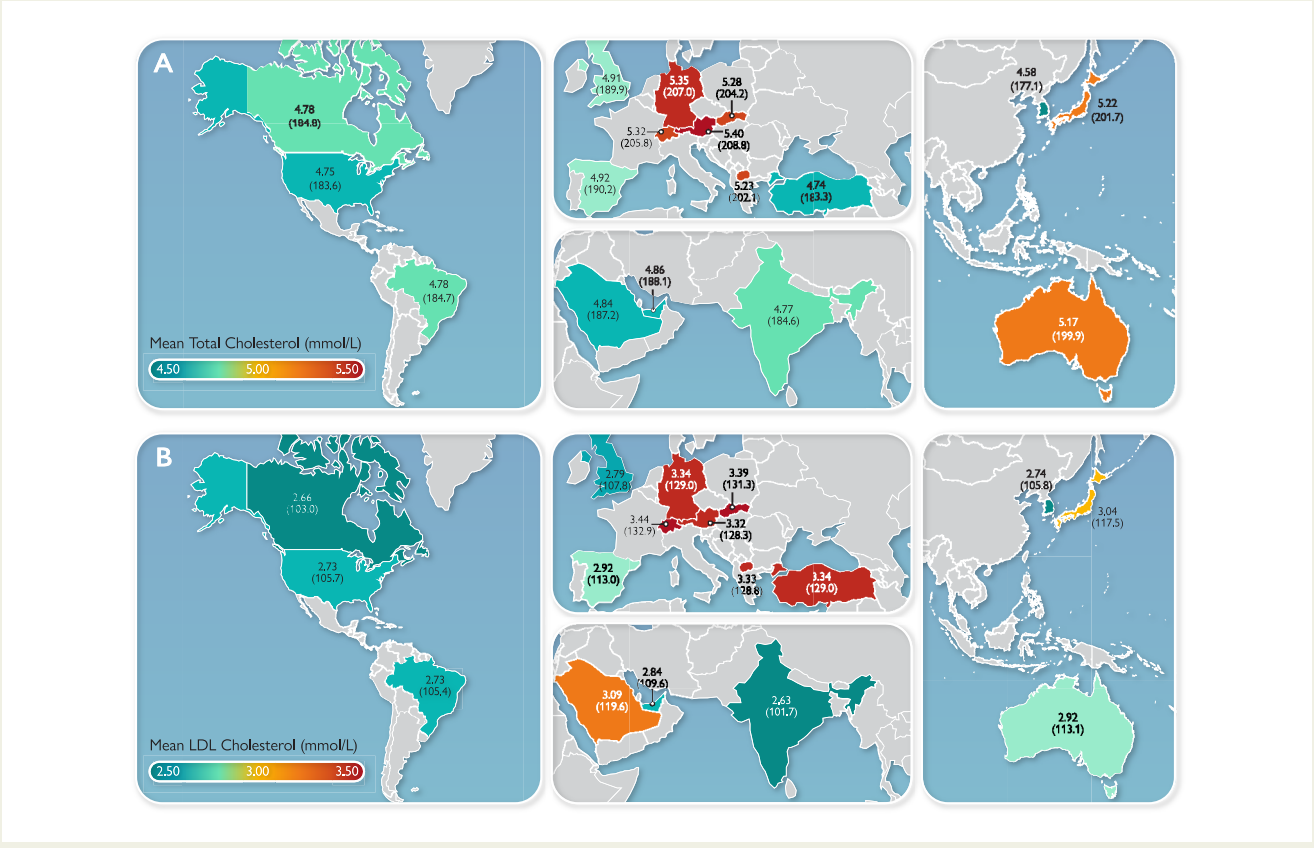
How do lipid profiles compare across countries? Do elevated atherogenic lipid levels remain a common global problem?

Key Finding

This first report of the Global Diagnostics Network evaluated lipid results across 17 countries and 5 continents. Analysis of 461 888 753 lipid results showed variation by country and region, which persisted after age/sex adjustment. Mean adjusted total cholesterol levels exceeded the World Health Organization risk threshold (>5.00 mmol/L) in 7 countries. LDL cholesterol levels showed generally similar variations.

Take Home Message

This study sheds light on the worldwide variability in lipid levels. Elevated atherogenic lipid levels are a common global problem. These results can help to improve national policies and health system approaches in the effort to mitigate lipid-mediated risk of cardiovascular disease.



Key question, findings, and take-home messages: The world map displays age- and sex-adjusted mean total cholesterol levels (*A*) and low-density lipoprotein cholesterol levels (*B*) by country across World Health Organization regions. Levels are presented first in mmol/L, and in parentheses, mg/dL units are also provided. There is a continuous green/yellow/orange/red shading scale ranging from 4.50 to 5.50 mmol/L (174–213 mg/dL) for total cholesterol and from 2.5 to 3.5 mmol/L (97–135 mg/dL) for low-density lipoprotein cholesterol levels. Country codes are as follows: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA). LDL, low-density lipoprotein.

Keywords Cholesterol • Lipids • Hyperlipidemia • Cardiovascular disease • Global health

Introduction

Atherogenic lipids play a centrally important role in promoting cardiovascular disease, which in turn is the leading cause of morbidity and mortality worldwide.[1,2] The World Health Organization (WHO) reports an estimated 18 million people die annually of cardiovascular disease.[2] Long-term cumulative exposure to elevations in atherogenic lipids, in combination with other risk factors, leads to atherosclerotic

plaque in the vascular walls.[3] This is the substrate for atherosclerotic cardiovascular disease (ASCVD) events, including ischemic heart disease and stroke, which are a leading cause of cardiovascular death.

The comprehensive global monitoring framework of the WHO recognizes elevated total cholesterol levels as a biological risk target for prevention and control of non-communicable diseases.[2] Furthermore, global clinical practice guidelines recognize the central role of lipids for the primary and secondary prevention of ASCVD.[3–6] Low-density lipoprotein cholesterol (LDL-C) is a therapeutic target of statins (HMG-CoA reductase inhibitors) and an increasing number of non-statin therapies to reduce ASCVD risk.[3–8] Low concentrations of high-density lipoprotein cholesterol (HDL-C) are widely recognized as a risk factor for ASCVD, and HDL-C levels are used in risk estimation equations to guide prevention measures.[3–6] Additionally, levels of triglycerides are associated with obesity, insulin resistance, and diabetes and circulate on remnant lipoproteins that are an emerging risk factor and target of preventive interventions.[9]

There is insufficient knowledge of lipid levels across different countries. Prior studies have been focused on lipid levels in the secondary prevention setting in Europe but not in broader populations across countries. Addressing this knowledge gap can illuminate opportunities to better implement strategies for lipid management to improve cardiovascular health globally. Such strategies to manage cholesterol and ASCVD throughout the human life course are provided in the 2022 World Heart Federation Cholesterol Roadmap.[10] Aiming to guide and catalyze implementation of these strategies, the present study provides contemporary data spanning 2018–20 on lipid distributions from nine laboratory organizations providing clinical testing in 17 countries across five continents and WHO regions.

Methods

Study design and population

This cross-sectional study analyzed lipid results from nine clinical laboratories, representing 17 countries across five continents, in the Global Diagnostics Network (GDN).[11] It is the first report of the GDN, established in 2018, as a strategic working group of diagnostic laboratories, each committed to unleashing and sharing local innovation to increase global access to diagnostic science and services—aimed at generating diagnostic insights and enhancing global healthcare. The GDN has a presence in countries representing two-thirds of the world's population, with plans for further expansion.

Lipid tests were performed in Australia (Healius), Brazil (DASA), Canada (Life Labs), India (Strand Life Sciences), Japan (LSI Medience), Republic of Korea (GC Labs), Saudi Arabia (Al Borg Diagnostics), and the USA (Quest Diagnostics). Additionally, SYNLAB performed tests in Austria, Germany, North Macedonia, Slovakia, Spain, Switzerland, Turkey, United Arab Emirates, and the United Kingdom. All countries included results from 2018 and 2019. Australia, Austria, Brazil, North Macedonia, Republic of Korea, Slovakia, Spain, Switzerland, Turkey, and the USA also included results from 2020. Country income statuses according to the World Bank groupings are provided in Supplementary data online, *Table S1*.

Lipid testing was generally community-based without restrictions based on age, sex, CVD, CVD risk factors, or treatment. Therefore, similar to other large laboratory studies, the data are likely representative of specific countries. Further information on the populations tested by country is provided in Supplementary data online, *Table S2*. There was no requirement for fasting, and fasting status was not collected. Additionally, there was no restriction on the number of lipid results an individual could contribute in this analysis.

In the tables and figures, country names are abbreviated using International Organization for Standardization (ISO) 3-letter country codes. Results for all years were pooled by country for analysis and examined by WHO regions (Americas, South-East Asian, European, Eastern Mediterranean, and Western Pacific); data were unavailable from the African region.[12] Data were collected in aggregate from each participating laboratory without any personal identifiable information. These analyses were determined to be exempt from human subjects review because all data were collected and analyzed in aggregate.

Lipid measurements

Each country's laboratory instruments, reagents, proficiency program participation, and population served for lipid measurements are detailed in Supplementary data online, *Table S2*. In the USA and Brazil, the Martin-Hopkins equation was used for determination of LDL-C.[13] Direct chemical-based LDL-C assays were used for determination of LDL-C in Australia, India, Japan, Republic of Korea, Turkey, Slovakia, Germany, and Switzerland. The remaining countries used the Friedewald equation to estimate LDL-C.[14] All laboratories participated in one or more proficiency programs to ensure accuracy of all lipid measurements.

Statistical analysis

Results from all patients 20–89 years of age were extracted from each laboratory's clinical database and shared with the GDN writing group in aggregate by individual lipid components (total cholesterol, LDL-C, HDL-C, and triglycerides). The mean and standard deviation for each lipid component were assessed by sex and by sex-stratified age groups. Calculated and directly assessed LDL-C measurements were combined for analysis. Lipid levels were examined in mmol/L and mg/dL units; mg/dL units were converted to standard international (SI) units (mmol/L) for cholesterol by multiplying by 0.02586 and for triglycerides by multiplying by 0.01129. Given the focus of lipid treatment guidelines on LDL-C, proportions of results in the following guideline based[3–6] LDL-C categories were also assessed for each country's total population and by sex: <1.55 mmol/L (<60 mg/dL), 1.55–2.58 mmol/L (60–99 mg/dL), 2.59–3.35 mmol/L (100–129 mg/dL), 3.36–4.12 mmol/L (130–159 mg/dL), 4.13–4.90 mmol/L (160–189 mg/dL), and ≥4.91 mmol/L (≥190 mg/dL). These categories were selected based on common guideline cut-points or in the case of 60 mg/dL, as a blend of the secondary prevention guideline cut-points of ~50 and 70 mg/dL.

Countries with mean total cholesterol levels exceeding the WHO risk threshold of ≥5.00 mmol/L (193 mg/dL) were identified. Statistical comparisons between mean aggregate measurements (for age groups, sexes, or countries) were assessed using the *t*-test. Comparisons of proportions were assessed with the chi-square test. Country-specific age-adjusted means by sex were calculated by multiplying the proportion of the entire sex-specific study population in each age group by the mean cholesterol value in the corresponding age group and then summing the components. For example, LDL-C testing from females aged 50–59 years made up 11.44% of all LDL-C testing included in the study. When age-adjusted means were calculated, the mean LDL-C for females aged 50–59 years for each country was multiplied by 0.1144. The same methodology was applied for each sex-stratified age group, and the sums were combined to form the weighted average. We provide 95% confidence interval where they add information; when not presented, they were indistinguishable from the point estimates. Analyses were performed using SAS Studio 3.6 on SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Map figures were made using Tableau 2021.4.13 (Salesforce Inc., San Francisco, CA, USA).

Results

Overall characteristics

This study included 461 888 753 lipid results (115 419 439, total cholesterol; 114 550 486, HDL-C; 114 192 290, LDL-C; and 117 726 538,

Table 1 Characteristics of the study population

	2018		2019		2020		Total	
	n	%	*n*	%	*n*	%	*N*	%
All results	**154 804 067**		**170 356 802**		**136 727 884**		**461 888 753**	
Total cholesterol	38 786 360		41 953 785		34 679 294		115 419 439	
LDL-C	38 347 914		42 253 075		33 591 301		114 192 290	
HDL-C	38 231 326		42 397 937		33 921 223		114 550 486	
Triglycerides	39 438 467		43 752 005		34 536 066		117 726 538	
Sex								
Male	**71 977 131**	46.50	79 605 731	46.73	61 850 129	45.24	213 432 991	46.21
Female	**82 670 301**	53.40	90 560 504	53.16	74 796 479	54.70	248 027 284	53.70
Unspecified	**156 460**	0.10	190 564	0.11	81 276	0.06	428 300	0.09
Age group (years)								
20–29	**10 428 185**	6.74	11 882 142	6.97	9 053 847	6.62	31 364 174	6.79
30–39	**16 837 993**	10.88	18 869 493	11.08	14 661 797	10.72	50 369 283	10.91
40–49	**24 558 133**	15.86	27 054 183	15.88	21 170 985	15.48	72 783 301	15.76
50–59	**34 324 064**	22.17	37 129 980	21.80	29 904 946	21.87	101 358 990	21.94
60–69	**35 301 059**	22.80	38 435 792	22.56	32 354 027	23.66	106 090 878	22.97
70–79	**23 901 947**	15.44	26 450 732	15.53	21 684 912	15.86	72 037 591	15.60
80–89	**9 451 654**	6.11	10 533 359	6.18	7 897 370	5.78	27 882 383	6.04
Country								
Australia (AUS)	**3 243 117**	2.09	3 346 362	1.96	3 281 195	2.40	9 870 674	2.14
Austria (AUT)	**1 212 952**	0.78	1 291 908	0.76	1 183 711	0.87	3 688 571	0.80
Brazil (BRA)	**7 851 412**	5.07	10 764 372	6.32	11 622 260	8.50	30 238 044	6.55
Canada (CAN)	**2 455 092**	1.59	2 402 515	1.41			4 857 607	1.05
Germany (DEU)	**3 497 936**	2.26	3 614 700	2.12			7 112 636	1.54
India (IND)	**121 570**	0.08	38 140	0.02			159 710	0.03
Japan (JPN)	**9 240 566**	5.97	15 543 220	9.12			24 783 786	5.37
North Macedonia (MKD)	**230 846**	0.15	251 299	0.15	209 326	0.15	691 471	0.15
Republic of Korea (KOR)	**1 510 393**	0.98	2 010 766	1.18	2 497 279	1.83	6 018 438	1.30
Saudi Arabia (SAU)	**50 704**	0.03	50 596	0.03			101 300	0.02
Slovakia (SVK)	**635 969**	0.41	730 225	0.43	643 275	0.47	2 009 469	0.44
Spain (ESP)	**2 359 205**	1.52	2 079 686	1.22	1 676 299	1.23	6 115 190	1.32
Switzerland (CHE)	**180 172**	0.12	169 791	0.10	137 819	0.10	487 782	0.11
Turkey (TUR)	**114 873**	0.07	123 250	0.07	173 192	0.13	411 315	0.09
United Arab Emirates (ARE)	**23 195**	0.01	23 618	0.01			46 813	0.01
United Kingdom (GBR)	**421 420**	0.27	450 097	0.26			871 517	0.19
United States of America (USA)	**121 654 645**	78.59	127 466 257	74.82	115 303 528	84.33	364 424 430	78.90

Demographic data were missing for a small number of records (for sex, $n = 178$; and for age group, $n = 2153$).

triglycerides), with a higher proportion of results from females than males (53.7% vs. 46.2%). The number of results increased from 2018 (154 804 067) to 2019 (170 356 802) but declined in 2020 (136 727 884). Given the large size of the data set, all comparisons noted in the results below were highly statistically significant to a *P*-value of <0.001. Age-group and country descriptions are provided in *Table 1*.

Total cholesterol

The highest mean total cholesterol levels adjusted for sex and age-group were in Austria (5.40 mmol/L, 208.8 mg/dL) and Germany (5.35 mmol/L, 207.0 mg/dL); the lowest mean adjusted levels were in the Republic of Korea (4.58 mmol/L, 177.1 mg/dL) and Turkey (4.74 mmol/L, 183.3 mg/dL) (*Figure 1*). Japan, Australia, North Macedonia, Switzerland, Germany, Slovakia, and Austria all had sex- and age-adjusted mean total cholesterol levels above the WHO risk threshold of 5.00 mmol/L (193 mg/dL). The highest age-adjusted mean levels of total cholesterol among females were in Austria (5.59 mmol/L, 216.0 mg/dL) and Germany (5.53 mmol/L, 213.9 mg/dL), and the lowest levels were in Republic of Korea (4.68 mmol/L, 181.1 mg/dL) and India (4.79 mmol/L, 185.2 mg/dL) (*Figure 2*). The highest age-adjusted mean total cholesterol levels among males were in Austria (5.18 mmol/L, 200.3 mg/dL) and Germany (5.15 mmol/L, 199.0 mg/dL), and the lowest levels were in the Republic of Korea (4.46 mmol/L, 172.6 mg/dL) and Turkey (4.49 mmol/L, 173.5 mg/dL) (*Figure 3*). Unadjusted mean total cholesterol levels demonstrated similar findings to age-adjusted levels for both females and males.

In every country except India, total cholesterol levels among females were highest in the 50-59-year age group (*Figure 4*). Age group-based patterns of total cholesterol in females and males were remarkably similar among the three countries in the Region of the Americas (Brazil, Canada, and the USA) (*Figures 4A* and *5A*). The peak levels of total cholesterol in females were highest in Austria (5.94 mmol/L, 229.7 mg/dL; *Figure 4C*) and lowest in the Republic of Korea (4.95 mmol/L, 191.2 mg/dL; *Figure 4E*). Total cholesterol levels peaked a decade earlier in males (ages 40–49 years) than in females (*Figure 5*) in every country except the Republic of Korea and Turkey (peaking in the 30–39 year age group) and Spain (peaking in the 50–59 year age group). Peak levels of total cholesterol among males were highest in Austria (5.60 mmol/L, 216.4 mg/dL), though Switzerland, Germany, North Macedonia, and Slovakia all had similar age-based patterns to Austria, and peak levels were lowest in Turkey (4.87 mmol/L, 188.2 mg/dL) (*Figure 5C*).

Low-density lipoprotein cholesterol

For females, the highest mean age-adjusted LDL-C levels were in Switzerland (3.49 mmol/L, 135.1 mg/dL) and Turkey (3.46 mmol/L, 133.9 mg/dL), and the lowest levels were in India (2.66 mmol/L, 102.8 mg/dL) and Canada (2.72 mmol/L, 105.1 mg/dL) (*Figure 2*). For males, the highest mean age-adjusted LDL-C levels were in Switzerland (3.37 mmol/L, 130.4 mg/dL) and Slovakia (3.34 mmol/L, 129.0 mg/dL), and the lowest levels were in India (2.60 mmol/L, 100.4 mg/dL) and Canada (2.60 mmol/L, 100.5 mg/dL) (*Figure 3*). Age-adjusted mean LDL-C values were notably higher among females and males among six countries from the European Region (Switzerland, Turkey, Slovakia, Germany, North Macedonia, and Austria) compared with other countries (*Figures 2B* and *3B*). This same group of countries demonstrated the highest peak mean LDL-C levels among males in the age group of 40–49 years (*Table 2*). Similar to total cholesterol, mean LDL-C peaked in females in the 50–59 age group and in males in the 40–49 age group in nearly all countries (*Table 2*). Spain and the UK demonstrated significantly lower mean LDL-C for all female age groups compared with other European countries.

The proportions of individuals in LDL-C categories, stratified by sex and country, are presented in Supplementary data online, *Table S3*. Consistent with the results for total cholesterol, the distributions of results across LDL-C groups were similar among the three countries from the Region of the Americas for both females and males. India had the lowest proportion of LDL-C results ≥4.91 mmol/L (≥190 mg/dL) LDL-C levels among both females (0.3%) and males (0.7%). In the European Region, the proportion of LDL-C results ≥4.91 mmol/L was lowest in Spain among females (0.9%) and lowest in the UK among males (1.4%). North Macedonia had the highest proportions of results ≥4.91 mmol/L (≥190 mg/dL) for both females (9.9%) and males (8.7%). Considering LDL-C levels <1.55 mmol/L (<60 mg/dL), the highest proportion was in Canada for females (10.7%) and the UK for males (17.3%). Slovakia had the lowest proportions of results <1.55 mmol/L (<60 mg/dL) for both females (0.9%) and males (1.8%).

High-density lipoprotein cholesterol

For females, the highest mean age-adjusted HDL-C levels were in Japan (1.75 mmol/L, 67.7 mg/dL) and Spain (1.65 mmol/L, 63.7 mg/dL), and the lowest levels were in India (1.26 mmol/L, 48.7 mg/dL) and Saudi Arabia (1.39 mmol/L, 53.7 mg/dL) (*Figure 2*). For males, the highest mean age-adjusted HDL-C levels were in Japan (1.46 mmol/L, 56.3 mg/dL) and Spain (1.30 mmol/L, 50.4 mg/dL), and the lowest levels were in India (1.05 mmol/L, 40.6 mg/dL) and Turkey (1.13 mmol/L, 43.6 mg/dL) (*Figure 3*). Unadjusted mean HDL-C had similar patterns. Generally, age-based patterns of mean HDL-C were less consistent than observed for total cholesterol. Among females, some countries (e.g. UK) had increasing mean HDL-C across progressive age groups, while others, including the Republic of Korea, had decreasing mean HDL-C across progressive age groups. The similarity of mean HDL-C patterns across male age groups in the Americas and European countries was also notable (see Supplementary data online, *Table S4*).

Triglycerides

For females, the highest mean age-adjusted triglyceride levels were in the UK (1.71 mmol/L, 151.2 mg/dL) and North Macedonia (1.57 mmol/L, 139.1 mg/dL), and the lowest levels were in Spain (1.07 mmol/L, 95.1 mg/dL) and Japan (1.23 mmol/L, 108.8 mg/dL) (*Figure 2*). For males, the highest mean age-adjusted triglyceride levels were in the UK (2.09 mmol/L, 185.2 mg/dL) and the Republic of Korea (1.97 mmol/L, 174.7 mg/dL), while the lowest levels were in Spain (1.32 mmol/L, 116.7 mg/dL) and Saudi Arabia (1.52 mmol/L, 134.7 mg/dL) (*Figure 3*). Among females 50–59 years of age, the mean triglyceride level was 0.78 mmol/L (69 mg/dL) lower in Spain than that in the UK (1.06 mmol/L, 93.9 mg/dL vs. 1.84 mmol/L, 163.0 mg/dL). Among males 40–49 years of age, the mean triglyceride level was 0.98 mmol/L (86.8 mg/dL) lower in Spain than in the UK (1.37 mmol/L, 121.3 mg/dL vs. 2.58 mmol/L, 228.5 mg/dL mg/dL. Age group–based triglyceride patterns for all countries in the study are included in Supplementary data online, *Table S4*.

Discussion

With nearly half a billion lipid results, this analysis included a huge scale of recent data that was examined across the globe to inform public health. We observed significant lipid variations across countries and WHO regions, even after accounting for age and sex differences. These worldwide lipid variations may reflect a combination of factors of genetic and environmental heterogeneity. Despite these variations, lipid levels around the world generally remain suboptimal (*Structured Graphical Abstract*). Thus, there is a critical need for national policies

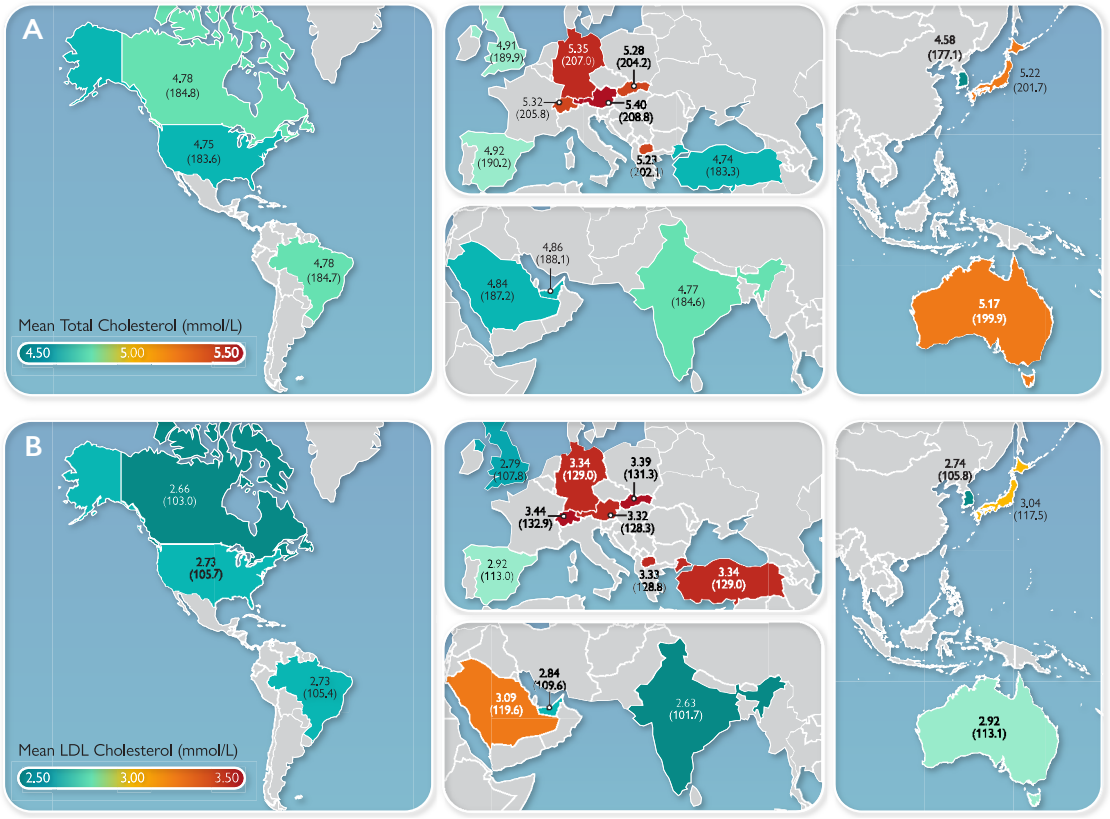


Figure 1 World map of age- and sex-adjusted mean total cholesterol and low-density lipoprotein cholesterol levels by country across World Health Organization regions. The world map displays age- and sex-adjusted mean total cholesterol levels (*A*) and low-density lipoprotein cholesterol levels (*B*) by country across World Health Organization regions. Levels are presented first in mmol/L, and in parentheses, mg/dL units are also provided. Country codes are as follows: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA).

and health systems approaches to improve implementation of hyperlipidemia management as detailed in the World Heart Federation Cholesterol Roadmap.[10] This GDN report represents the beginning of strategic collaboration among diagnostic laboratories to understand the global lipid landscape and will shape future iterations of the GDN as it evolves to best serve global efforts to improve health.

Our study builds on prior surveys of lipids by providing both updated results and a scale that is orders of magnitude beyond prior studies. Nine countries in Europe (Czech Republic, Finland, France, Germany, Hungary, Italy, the Netherlands, Slovenia, and Spain) participated in the first European Action on Secondary Prevention by Intervention to Reduce Events (EUROASPIRE) survey in 1995–96 among 3569 patients with established coronary heart disease.[15] A second survey of 3379 patients was conducted in the same countries in 1999–2000. The prevalence of high total cholesterol concentrations of ≥5.00 mmol/L (193 mg/dL) decreased from 86% to 59%. Subsequent EUROASPIRE surveys expanded to 78 centers across 24 European countries and examined 7998 patients after a coronary artery disease event and documented suboptimal LDL-C control.[16] The upcoming INTERASPIRE study will provide an updated international survey of secondary prevention of coronary heart disease with countries from each of the six WHO regions.[17]

The focus in this report on total cholesterol levels is aligned with the comprehensive global monitoring framework of the WHO.[2] That framework identifies total cholesterol levels of ≥5.00 mmol/L (193 mg/dL) as a risk target. These GDN data show that seven of 17 of countries evaluated have mean total cholesterol levels above this total cholesterol level, with disparities across countries remaining after sex and age adjustments. These differences may reflect genetic heterogeneity; for example, the prevalence of familial hypercholesterolemia varies throughout the globe, and indeed in our analysis, we see wide variation in the prevalence of severely elevated LDL-C. Additionally, environmental factors are of major relevance as variation in cultural dietary, and physical activity patterns across countries, as well as economic conditions and, relatedly, access to lipid testing and treatment, may contribute to differences between countries. Increased cross talk and learning between countries may enable countries with higher total cholesterol and LDL-C levels to better plan interventions related to testing, lifestyle, and pharmaceutical strategies to increase the population and individuals within each country achieving the risk target of <5.00 mmol/L (<193 mg/dL). These data can help in planning initiatives to address dyslipidemia and ASCVD that are tailored to the local needs while drawing upon global best practices.

Furthermore, global clinical practice guidelines recognize the central role of lipids for the primary and secondary prevention of ASCVD.[3–6]

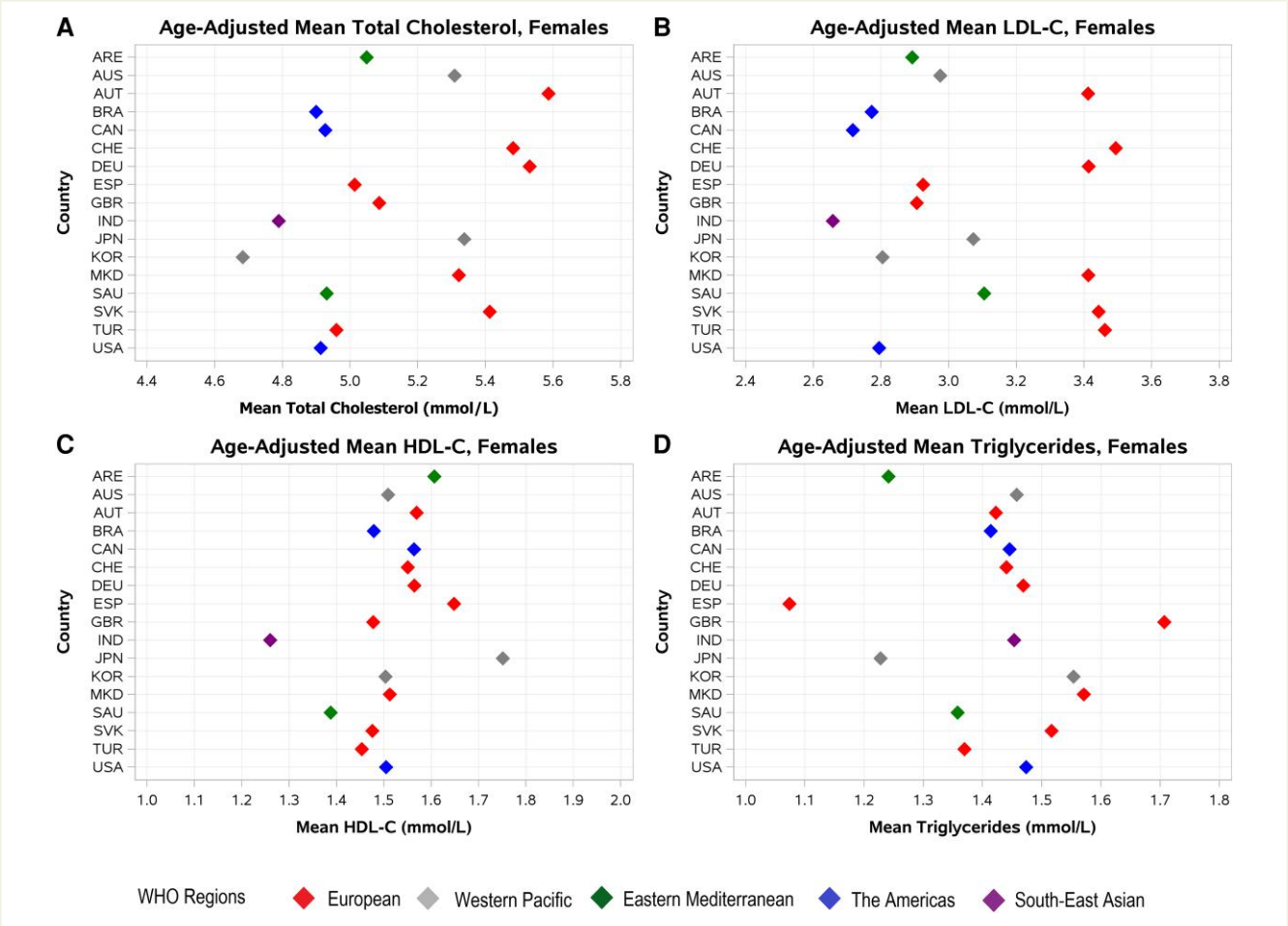


Figure 2 Age-adjusted mean lipid levels in females, by country and World Health Organization region. Total cholesterol is shown in *A*, low-density lipoprotein cholesterol in *B*, high-density lipoprotein cholesterol in *C*, and triglycerides in *D*. Note that 95% confidence intervals are indistinguishable from point estimates due to the size of the data set. Country codes: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA). Unadjusted mean total cholesterol (mmol/L)—ARE 4.96, AUS 5.33, AUT 5.54, BRA 4.85, CAN 4.95, CHE 5.46, DEU 5.54, ESP 4.86, GBR 5.07, IND 4.67, JPN 5.27, KOR 4.70, MKD 5.28, SAU 4.96, SVK 5.39, TUR 4.90, and USA 4.92. Unadjusted mean low-density lipoprotein cholesterol (mmol/L)—ARE 2.86, AUS 2.98, AUT 3.38, BRA 2.75, CAN 2.73, CHE 3.49, DEU 3.42, ESP 2.87, GBR 2.86, IND 2.42, JPN 3.02, KOR 2.81, MKD 3.46, SAU 3.14, SVK 3.44, TUR 3.39, and USA 2.80. Unadjusted mean high-density lipoprotein cholesterol (mmol/L)—ARE 1.60, AUS 1.51, AUT 1.57, BRA 1.49, CAN 1.57, CHE 1.55, DEU 1.57, ESP 1.65, GBR 1.51, IND 1.24, JPN 1.74, KOR 1.50, MKD 1.51, SAU 1.40, SVK 1.46, TUR 1.48, and USA 1.51. Unadjusted mean triglycerides (mmol/L)—ARE 1.13, AUS 1.47, AUT 1.40, BRA 1.34, CAN 1.46, CHE 1.44, DEU 1.49, ESP 0.99, GBR 1.71, IND 1.23, JPN 1.22, KOR 1.57, MKD 1.50, SAU 1.30, SVK 1.55, TUR 1.26, and USA 1.48. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Low-density lipoprotein cholesterol is a therapeutic target of statins and an increasing number of non-statin therapies to prevent ASCVD.[3–8] Given that LDL-C is not currently a WHO metric, and considering the variations in methods to assess LDL-C around the globe, we chose to focus on LDL-C secondarily to total cholesterol levels. We observed striking differences among countries, both at the high and low ends of LDL-C distributions. An LDL-C of ≥4.91 mmol/L (≥190 mg/dL), universally accepted as severely elevated, is commonly flagged by clinical laboratories and raises concern for familial hypercholesterolemia. We found that the prevalence of LDL-C ≥ 4.91 mmol/L (≥190 mg/dL) ranged from <1% in some countries to ~10% in females from North Macedonia. Considering LDL-C levels of <1.55 mmol/L (<60 mg/dL), a category that was selected as a balance of guideline recommended LDL-C cut-points, these were most common among males in the UK (17%) but varied widely. For example, only 0.9% of females in Slovakia had these low levels. Greater proportions of individuals with low LDL-C levels could reflect testing and treatment patterns, including adoption of non-statin therapies. Other important atherogenic lipid risk measures beyond LDL-C, namely apolipoprotein B and lipoprotein(a), were notably absent in this first iteration of the GDN and also may benefit from international collaboration to track and intervene upon elevated levels.

The 2022 update to the World Heart Federation Cholesterol Roadmap offers a path forward in addressing overall gaps in cholesterol management around the globe and disparities across countries and regions.[10] It highlights the importance of cumulative exposure to LDL-C and apolipoprotein B

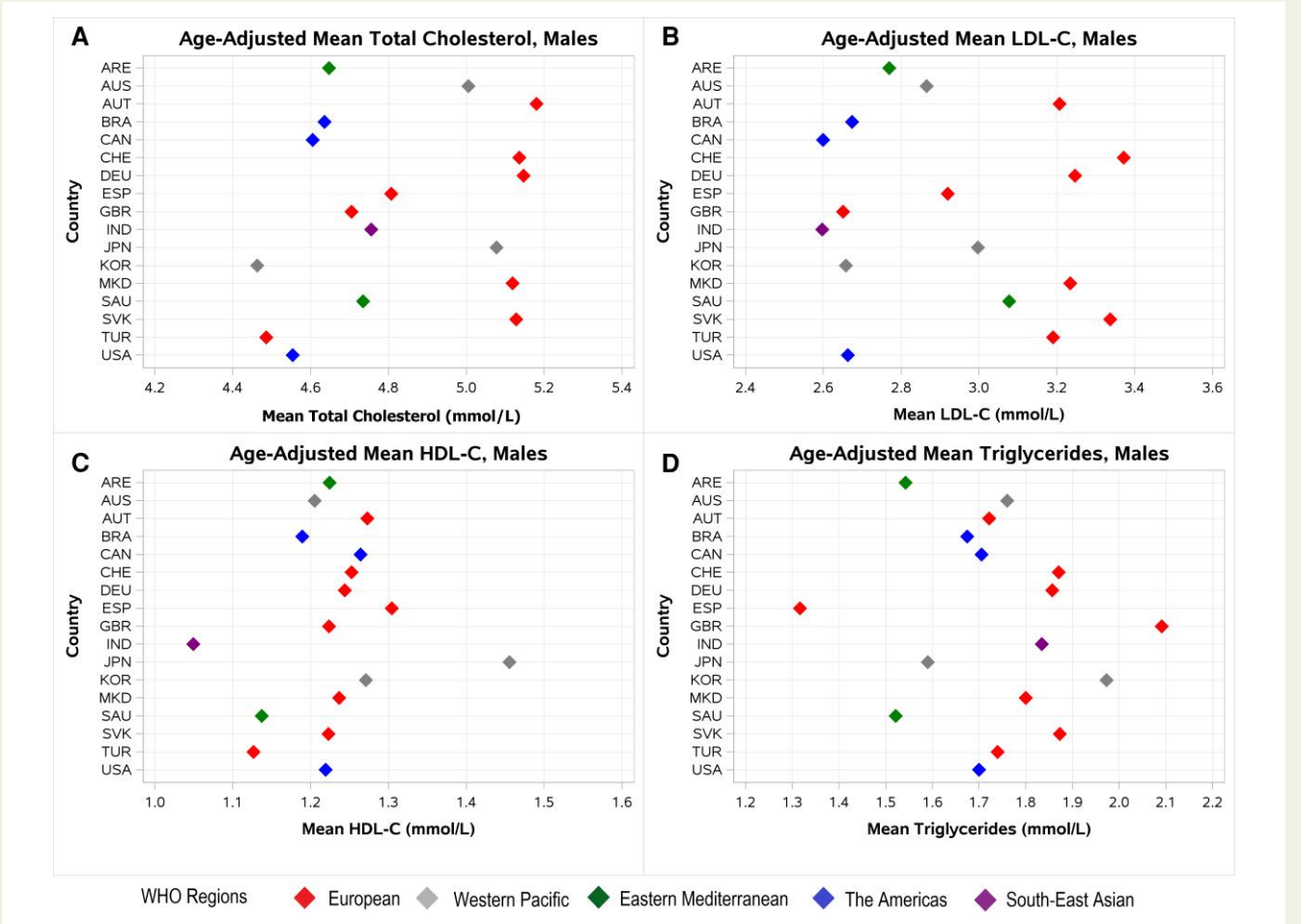


Figure 3 Age-adjusted mean lipid levels in males, by country and World Health Organization region. Total cholesterol is shown in *A*, low-density lipoprotein cholesterol in *B*, high-density lipoprotein cholesterol in *C*, and triglycerides in *D*. Note that 95% confidence intervals are indistinguishable from point estimates due to the size of the data set. Country codes: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA). Unadjusted mean total cholesterol (mmol/L)—ARE 4.87, AUS 4.98, AUT 5.16, BRA 4.68, CAN 4.57, CHE 5.10, DEU 5.10, ESP 4.88, GBR 4.53, IND 5.09, JPN 5.09, KOR 4.51, MKD 5.17, SAU 4.88, SVK 5.10, TUR 4.49, and USA 4.54. Unadjusted mean low-density lipoprotein cholesterol (mmol/L)—ARE 3.01, AUS 2.84, AUT 3.19, BRA 2.74, CAN 2.57, CHE 3.35, DEU 3.19, ESP 3.02, GBR 2.52, IND 2.71, JPN 3.00, KOR 2.69, MKD 3.37, SAU 3.21, SVK 3.31, TUR 3.17, and USA 2.65. Unadjusted mean high-density lipoprotein cholesterol (mmol/L)—ARE 1.19, AUS 1.21, AUT 1.27, BRA 1.19, CAN 1.27, CHE 1.26, DEU 1.25, ESP 1.31, GBR 1.23, IND 1.04, JPN 1.45, KOR 1.27, MKD 1.23, SAU 1.14, SVK 1.22, TUR 1.19, and USA 1.22. Unadjusted mean triglycerides (mmol/L)—ARE 1.57, AUS 1.76, AUT 1.70, BRA 1.66, CAN 1.69, CHE 1.85, DEU 1.83, ESP 1.31, GBR 1.96, IND 1.79, JPN 1.56, KOR 2.03, MKD 1.82, SAU 1.53, SVK 1.86, TUR 1.70, and USA 1.70. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

containing lipoproteins in development of ASCVD and provides a framework to overcome roadblocks to cholesterol management and ASCVD prevention at different stages throughout the human life course. The Roadmap advocates for a shift toward early preventive strategies to preserve cardiovascular health, as opposed to a later reactionary approach managing the consequences of ASCVD. As the push for earlier initiation of lipid-lowering therapy is further debated and pursued in practice and indications for novel therapies are further defined, the data in the present report on lipid levels across age groups may be of interest. Overall, the Roadmap recommends that five focus areas guide implementation of actionable solutions for cholesterol control to reduce ASCVD: (i) improve awareness; (ii) roll out population-based approaches to prevent ASCVD and reduce cumulative lipid exposure; (iii) reinforce risk assessment and population screening to identify genetic dyslipidemias; (iv) implement system-level approaches targeting high-risk groups; and (v) establish national/regional surveillance for cholesterol/ASCVD.

In practice, lipid levels are used in the context of the interpretative ranges and alert values that are implemented by clinical laboratories. These inform the conversation that patients and clinicians have when selecting therapy. The distributions observed in our study might be useful to laboratories in refining interpretative ranges and alert values. In surveying the GDN laboratories, we found heterogeneity in the guidelines followed for determining reference ranges and alert values. Many country- and region-specific cholesterol guidelines have been introduced over the preceding decades. The European guidelines have a framework that can be adapted to reflect different political, economic,

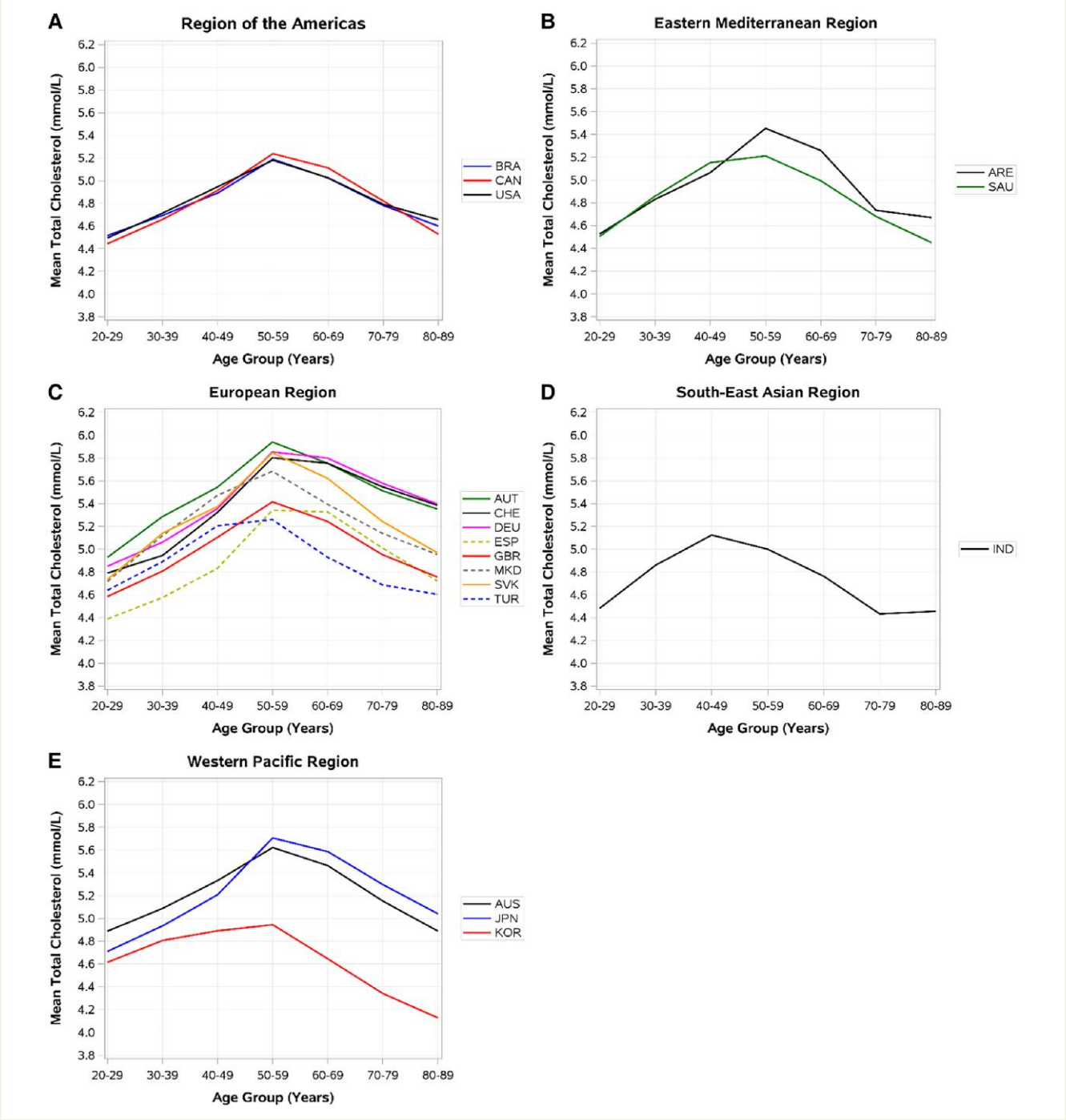


Figure 4 Mean total cholesterol levels in females, by age group, country, and World Health Organization region. Country codes: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA).

social, and medical circumstances in the different countries of Europe.[6,18–22] Lipid levels in people ≥40 years of age are particularly relevant when estimating cardiovascular risk using SCORE2[20] and SCORE2-OP[19] in Europe or using other country-specific risk estimators elsewhere in the world. Australia has developed guidelines for general practice that include recommendations for assessing and managing lipids,[23] and the Republic of Korea has also developed guidelines for lipid management.[24] The Indian Heart Association and Indian Stroke Association follow the general approach of USA guidelines but suggest that the optimal levels of total cholesterol and LDL-C are lower in South Asian individuals.[4] In the USA, clinical practice guidelines have evolved from the National Cholesterol Education Program (Adult Treatment Panel III)[25] published in 2002 to the 2013 American College of Cardiology and American Heart Association (ACC/AHA)

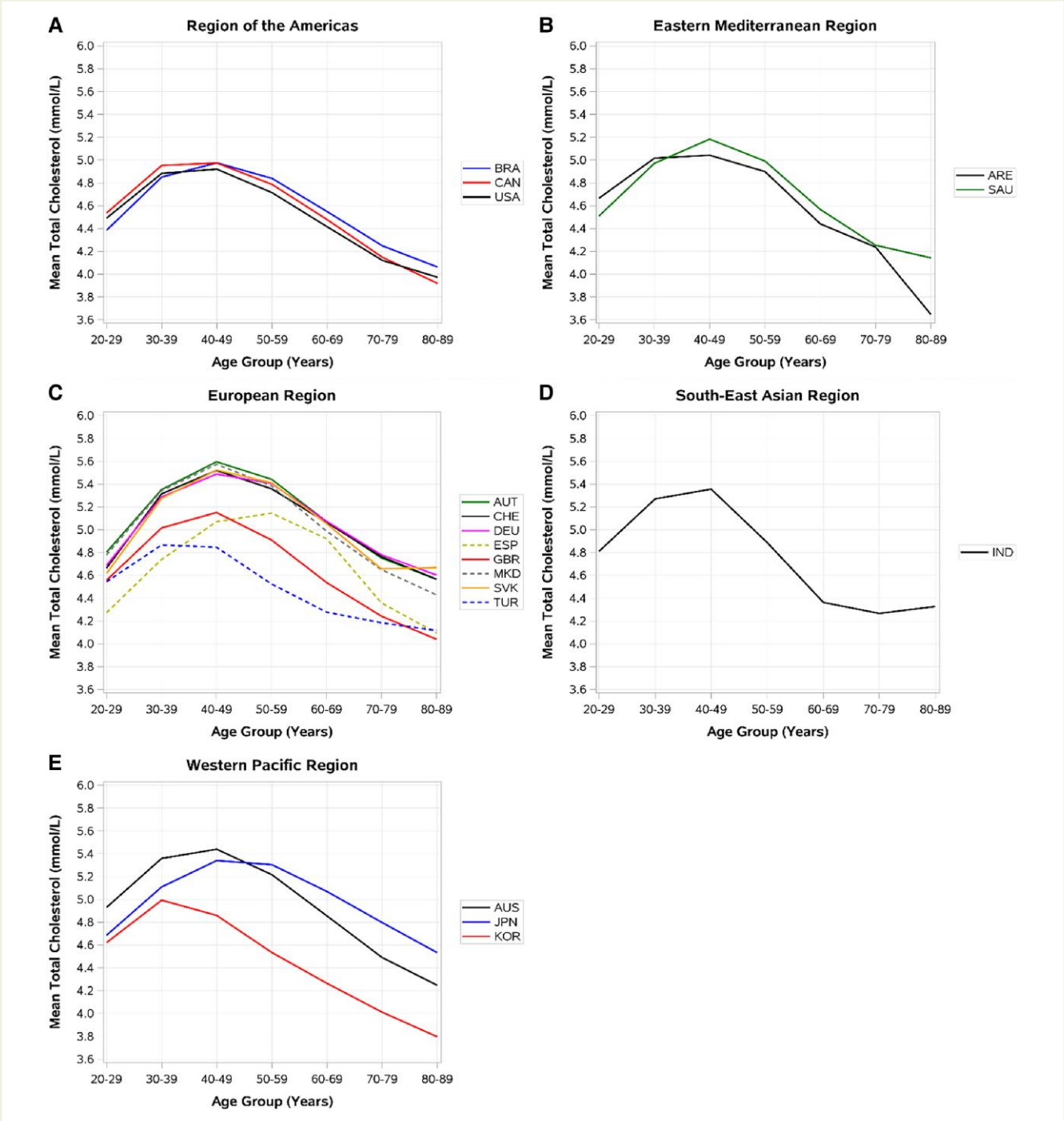


Figure 5 Mean total cholesterol levels in males, by age group, country, and World Health Organization region. Country codes: Australia (AUS); Austria (AUT); Brazil (BRA); Canada (CAN); Germany (DEU); India (IND); Japan (JPN); North Macedonia (MKD); Republic of Korea (KOR); Saudi Arabia (SAU); Slovakia (SVK); Spain (ESP); Switzerland (CHE); Turkey (TUR); United Arab Emirates (ARE); United Kingdom (GBR); United States of America (USA).

guidelines[3] and then the 2018 AHA/ACC cholesterol management guidelines.[5] Although clinical management in the USA has shifted to following the 2018 AHA/ACC guidelines, which target LDL-C primarily, as well as a 2019 primary prevention guideline,[26] laboratory reporting tends to follow Adult Treatment Panel III, which has convenient categories for laboratory reporting for each component of the traditional lipid panel.

Therefore, clinical laboratories around the world use different professional society guidelines to determine interpretative values and alert flagging on laboratory reports, and the guidelines used may differ from those being referred to by clinicians and patients to make decisions. The lack of international standards makes comparison with any one standard open for re-interpretation based on local guidelines. This suggests an opportunity to carve a path toward greater global

Table 2 Mean (95% confidence interval) levels of total cholesterol and LDL-C in males and females by country across age groups

		Male age groups (years)							Female age groups (years)						
	Country	20–29	30–39	40–49	50–59	60–69	70–79	80–89	20–29	30–39	40–49	50–59	60–69	70–79	80–89
Total cholesterol (mmol/L)	Australia (AUS)	4.93 (4.92–4.94)	5.36 (5.35–5.37)	5.44 (5.43–5.44)	5.22 (5.21–5.22)	4.86 (4.85–4.86)	4.49 (4.49–4.50)	4.25 (4.24–4.26)	4.89 (4.88–4.90)	5.09 (5.08–5.10)	5.33 (5.33–5.34)	5.62 (5.62–5.63)	5.46 (5.46–5.47)	5.15 (5.15–5.16)	4.89 (4.88–4.90)
	Austria (AUT)	4.80 (4.79–4.81)	5.35 (5.34–5.36)	5.60 (5.59–5.61)	5.44 (5.43–5.45)	5.07 (5.06–5.08)	4.75 (4.74–4.76)	4.57 (4.55–4.58)	4.93 (4.92–4.94)	5.29 (5.28–5.30)	5.54 (5.54–5.55)	5.94 (5.93–5.95)	5.75 (5.75–5.76)	5.51 (5.50–5.52)	5.35 (5.34–5.37)
	Brazil (BRA)	4.38 (4.38–4.39)	4.85 (4.85–4.85)	4.98 (4.97–4.98)	4.84 (4.84–4.84)	4.55 (4.54–4.55)	4.25 (4.24–4.25)	4.06 (4.06–4.07)	4.52 (4.51–4.52)	4.69 (4.69–4.70)	4.89 (4.89–4.89)	5.19 (5.19–5.19)	5.02 (5.02–5.03)	4.78 (4.78–4.78)	4.60 (4.59–4.60)
	Canada (CAN)	4.54 (4.52–4.55)	4.95 (4.94–4.96)	4.97 (4.97–4.98)	4.79 (4.78–4.79)	4.48 (4.47–4.48)	4.15 (4.14–4.15)	3.92 (3.91–3.93)	4.44 (4.43–4.45)	4.66 (4.65–4.67)	4.91 (4.91–4.92)	5.24 (5.23–5.24)	5.11 (5.11–5.12)	4.82 (4.81–4.83)	4.53 (4.52–4.54)
	Germany (DEU)	4.69 (4.68–4.70)	5.29 (5.28–5.30)	5.49 (5.48–5.49)	5.41 (5.40–5.41)	5.07 (5.07–5.08)	4.78 (4.78–4.79)	4.60 (4.60–4.61)	4.85 (4.84–4.86)	5.06 (5.06–5.07)	5.36 (5.35–5.36)	5.85 (5.85–5.86)	5.80 (5.80–5.81)	5.58 (5.57–5.58)	5.40 (5.39–5.40)
	India (IND)	4.81 (4.79–4.83)	5.27 (5.26–5.29)	5.36 (5.31–5.40)	4.89 (4.79–4.99)	4.36 (4.20–4.52)	4.27 (3.94–4.59)	4.33 (3.77–4.88)	4.48 (4.46–4.50)	4.86 (4.84–4.89)	5.12 (5.05–5.20)	5.00 (4.88–5.12)	4.76 (4.57–4.96)	4.43 (3.99–4.88)	4.46 (4.19–4.72)
	Japan (JPN)	4.69 (4.68–4.69)	5.11 (5.11–5.11)	5.34 (5.34–5.34)	5.30 (5.30–5.31)	5.07 (5.07–5.07)	4.80 (4.79–4.80)	4.53 (4.53–4.54)	4.71 (4.71–4.71)	4.94 (4.93–4.94)	5.21 (5.21–5.21)	5.71 (5.70–5.71)	5.59 (5.58–5.59)	5.30 (5.29–5.30)	5.04 (5.04–5.05)
	North Macedonia (MKD)	4.78 (4.76–4.80)	5.34 (5.33–5.36)	5.57 (5.56–5.59)	5.39 (5.37–5.40)	4.99 (4.97–5.01)	4.65 (4.63–4.67)	4.43 (4.39–4.46)	4.72 (4.70–4.73)	5.12 (5.11–5.13)	5.47 (5.46–5.48)	5.68 (5.67–5.70)	5.40 (5.38–5.41)	5.14 (5.12–5.16)	4.95 (4.92–4.98)
	Republic of Korea (KOR)	4.62 (4.61–4.63)	4.99 (4.99–5.00)	4.86 (4.85–4.86)	4.53 (4.53–4.54)	4.26 (4.26–4.27)	4.01 (4.01–4.02)	3.80 (3.79–3.81)	4.62 (4.61–4.62)	4.81 (4.80–4.81)	4.89 (4.89–4.90)	4.95 (4.94–4.95)	4.65 (4.64–4.65)	4.34 (4.34–4.35)	4.13 (4.12–4.14)
	Saudi Arabia (SAU)	4.51 (4.44–4.58)	4.97 (4.94–5.01)	5.18 (5.15–5.22)	4.99 (4.95–5.03)	4.57 (4.52–4.61)	4.25 (4.19–4.32)	4.14 (4.04–4.25)	4.50 (4.45–4.56)	4.86 (4.81–4.90)	5.15 (5.11–5.19)	5.21 (5.17–5.25)	4.99 (4.94–5.04)	4.68 (4.61–4.75)	4.45 (4.34–4.56)
	Slovakia (SVK)	4.62 (4.60–4.63)	5.27 (5.26–5.29)	5.52 (5.51–5.54)	5.41 (5.40–5.42)	5.05 (5.04–5.06)	4.66 (4.65–4.67)	4.67 (4.65–4.69)	4.74 (4.72–4.75)	5.14 (5.13–5.16)	5.37 (5.36–5.38)	5.85 (5.84–5.86)	5.62 (5.61–5.63)	5.24 (5.24–5.25)	4.97 (4.96–4.98)
	Spain (ESP)	4.27 (4.27–4.28)	4.74 (4.74–4.74)	5.07 (5.07–5.07)	5.15 (5.14–5.15)	4.92 (4.92–4.93)	4.36 (4.35–4.37)	4.10 (4.08–4.11)	4.39 (4.38–4.39)	4.58 (4.57–4.58)	4.83 (4.83–4.83)	5.34 (5.34–5.35)	5.33 (5.32–5.33)	5.01 (5.00–5.02)	4.72 (4.71–4.74)
	Switzerland (CHE)	4.66 (4.63–4.70)	5.31 (5.28–5.35)	5.52 (5.49–5.55)	5.36 (5.34–5.38)	5.06 (5.04–5.09)	4.76 (4.74–4.79)	4.57 (4.53–4.60)	4.79 (4.77–4.81)	4.95 (4.92–4.97)	5.32 (5.30–5.34)	5.80 (5.78–5.82)	5.76 (5.73–5.78)	5.55 (5.53–5.57)	5.39 (5.35–5.42)
	Turkey (TUR)	4.54 (4.51–4.58)	4.87 (4.84–4.89)	4.85 (4.82–4.87)	4.52 (4.50–4.55)	4.28 (4.26–4.30)	4.18 (4.16–4.21)	4.12 (4.08–4.15)	4.64 (4.61–4.67)	4.89 (4.87–4.92)	5.21 (5.18–5.23)	5.26 (5.23–5.29)	4.93 (4.91–4.95)	4.69 (4.66–4.71)	4.60 (4.56–4.64)
	United Arab Emirates (ARE)	4.67 (4.59–4.75)	5.02 (4.97–5.06)	5.04 (5.00–5.09)	4.90 (4.84–4.96)	4.44 (4.34–4.54)	4.24 (4.08–4.40)	3.65 (3.32–3.98)	4.53 (4.45–4.60)	4.83 (4.77–4.88)	5.06 (5.00–5.13)	5.45 (5.36–5.54)	5.26 (5.12–5.40)	4.73 (4.52–4.94)	4.67 (4.24–5.10)
	United Kingdom (GBR)	4.56 (4.52–4.59)	5.02 (4.98–5.05)	5.15 (5.13–5.17)	4.91 (4.90–4.92)	4.54 (4.53–4.55)	4.24 (4.23–4.25)	4.04 (4.03–4.05)	4.59 (4.55–4.62)	4.81 (4.78–4.84)	5.10 (5.08–5.12)	5.42 (5.40–5.43)	5.24 (5.23–5.26)	4.95 (4.94–4.97)	4.76 (4.74–4.77)
	United States of America (USA)	4.49 (4.49–4.49)	4.88 (4.88–4.88)	4.92 (4.92–4.92)	4.71 (4.71–4.71)	4.41 (4.41–4.42)	4.12 (4.12–4.12)	3.97 (3.97–3.97)	4.49 (4.49–4.50)	4.71 (4.71–4.71)	4.95 (4.95–4.95)	5.18 (5.18–5.18)	5.03 (5.02–5.03)	4.79 (4.79–4.79)	4.66 (4.65–4.66)
LDL-C (mmol/L)	Australia (AUS)	2.94 (2.93–2.95)	3.25 (3.25–3.26)	3.27 (3.26–3.27)	3.05 (3.05–3.06)	2.72 (2.71–2.72)	2.37 (2.37–2.38)	2.14 (2.13–2.14)	2.79 (2.78–2.80)	2.95 (2.94–2.95)	3.11 (3.10–3.11)	3.24 (3.24–3.24)	3.04 (3.04–3.05)	2.72 (2.71–2.72)	2.44 (2.44–2.45)
	Austria (AUT)	2.99 (2.99–3.00)	3.42 (3.41–3.43)	3.58 (3.57–3.58)	3.41 (3.41–3.42)	3.08 (3.07–3.09)	2.83 (2.83–2.84)	2.72 (2.71–2.73)	2.92 (2.91–2.93)	3.22 (3.21–3.22)	3.44 (3.44–3.45)	3.70 (3.70–3.71)	3.51 (3.50–3.52)	3.29 (3.28–3.30)	3.21 (3.20–3.22)
	Brazil (BRA)	2.62 (2.62–2.62)	2.95 (2.95–2.95)	2.98 (2.97–2.98)	2.82 (2.81–2.82)	2.56 (2.56–2.57)	2.33 (2.33–2.33)	2.20 (2.20–2.21)	2.47 (2.47–2.47)	2.64 (2.64–2.65)	2.82 (2.82–2.82)	3.03 (3.03–3.03)	2.85 (2.85–2.85)	2.62 (2.61–2.62)	2.47 (2.47–2.48)
	Canada (CAN)	2.62 (2.61–2.63)	2.94 (2.93–2.94)	2.93 (2.93–2.94)	2.76 (2.75–2.76)	2.48 (2.47–2.48)	2.19 (2.19–2.20)	1.99 (1.98–2.00)	2.42 (2.41–2.43)	2.61 (2.60–2.61)	2.79 (2.78–2.79)	2.97 (2.97–2.98)	2.83 (2.82–2.83)	2.54 (2.53–2.55)	2.28 (2.27–2.29)
	Germany (DEU)	3.02 (3.01–3.03)	3.45 (3.44–3.46)	3.57 (3.56–3.57)	3.44 (3.44–3.44)	3.15 (3.15–3.15)	2.91 (2.90–2.91)	2.77 (2.76–2.78)	2.92 (2.91–2.93)	3.13 (3.12–3.13)	3.36 (3.35–3.37)	3.67 (3.66–3.67)	3.58 (3.58–3.59)	3.38 (3.37–3.38)	3.23 (3.23–3.24)
	India (IND)	2.58 (2.57–2.59)	2.79 (2.78–2.80)	2.79 (2.76–2.82)	2.70 (2.62–2.78)	2.50 (2.37–2.64)	2.37 (2.12–2.62)	2.32 (1.96–2.67)	2.30 (2.29–2.32)	2.50 (2.48–2.52)	2.66 (2.61–2.72)	2.92 (2.82–3.03)	2.81 (2.64–2.98)	2.40 (1.97–2.84)	2.51 (2.17–2.85)
	Japan (JPN)	2.73 (2.72–2.73)	3.06 (3.06–3.06)	3.21 (3.21–3.21)	3.14 (3.14–3.14)	2.97 (2.96–2.97)	2.80 (2.80–2.81)	2.66 (2.65–2.66)	2.56 (2.56–2.56)	2.74 (2.73–2.74)	2.98 (2.97–2.98)	3.34 (3.33–3.34)	3.26 (3.26–3.26)	3.07 (3.07–3.08)	2.92 (2.92–2.92)
	North Macedonia (MKD)	3.27 (3.27–3.27)	3.66 (3.66–3.66)	3.71 (3.71–3.71)	3.43 (3.43–3.43)	3.01 (3.01–3.01)	2.70 (2.70–2.70)	2.66 (2.66–2.66)	3.11 (3.11–3.11)	3.37 (3.37–3.37)	3.70 (3.70–3.70)	3.75 (3.75–3.75)	3.38 (3.38–3.38)	3.10 (3.10–3.10)	2.92 (2.92–2.92)
	Republic of Korea (KOR)	2.96 (2.95–2.98)	3.13 (3.12–3.14)	2.91 (2.90–2.92)	2.67 (2.67–2.68)	2.48 (2.48–2.49)	2.34 (2.34–2.35)	2.25 (2.23–2.26)	2.77 (2.76–2.78)	2.93 (2.92–2.94)	2.99 (2.99–3.00)	3.01 (3.01–3.02)	2.74 (2.74–2.75)	2.52 (2.51–2.52)	2.43 (2.42–2.44)
	Saudi Arabia (SAU)	2.95 (2.89–3.01)	3.34 (3.31–3.37)	3.50 (3.46–3.53)	3.30 (3.27–3.34)	2.90 (2.87–2.94)	2.65 (2.59–2.71)	2.55 (2.45–2.64)	2.76 (2.72–2.81)	3.06 (3.02–3.10)	3.34 (3.30–3.38)	3.34 (3.30–3.38)	3.15 (3.10–3.19)	2.87 (2.80–2.93)	2.68 (2.58–2.78)
	Slovakia (SVK)	3.08 (3.06–3.10)	3.50 (3.49–3.51)	3.66 (3.65–3.67)	3.54 (3.53–3.55)	3.28 (3.27–3.29)	2.98 (2.98–2.99)	2.78 (2.77–2.80)	2.95 (2.93–2.96)	3.20 (3.18–3.21)	3.43 (3.42–3.44)	3.78 (3.77–3.79)	3.60 (3.59–3.61)	3.31 (3.31–3.32)	3.11 (3.10–3.12)
	Spain (ESP)	2.56 (2.55–2.56)	2.97 (2.96–2.97)	3.20 (3.20–3.21)	3.19 (3.19–3.20)	2.94 (2.93–2.95)	2.53 (2.52–2.54)	2.31 (2.29–2.32)	2.41 (2.41–2.42)	2.61 (2.61–2.62)	2.84 (2.84–2.84)	3.20 (3.20–3.21)	3.14 (3.14–3.15)	2.88 (2.87–2.89)	2.65 (2.63–2.66)
	Switzerland (CHE)	3.07 (3.04–3.10)	3.55 (3.52–3.57)	3.68 (3.66–3.70)	3.55 (3.53–3.56)	3.30 (3.29–3.32)	3.07 (3.05–3.09)	2.91 (2.89–2.94)	2.97 (2.95–2.98)	3.12 (3.10–3.14)	3.41 (3.40–3.43)	3.73 (3.71–3.74)	3.67 (3.66–3.69)	3.52 (3.51–3.54)	3.43 (3.40–3.45)

Continued

Table 2 *Continued*

Country	Male age groups (years)								Female age groups (years)							
	20–29	30–39	40–49	50–59	60–69	70–79	80–89		20–29	30–39	40–49	50–59	60–69	70–79	80–89	
Turkey (TUR)	3.14 (3.10–3.18)	3.46 (3.43–3.49)	3.46 (3.44–3.49)	3.27 (3.25–3.30)	3.05 (3.02–3.07)	2.95 (2.92–2.98)	2.89 (2.84–2.94)		3.05 (3.02–3.09)	3.27 (3.24–3.29)	3.56 (3.53–3.58)	3.75 (3.72–3.78)	3.53 (3.50–3.56)	3.31 (3.28–3.34)	3.22 (3.16–3.27)	
United Arab Emirates (ARE)	2.88 (2.88–2.88)	3.13 (3.13–3.13)	3.17 (3.17–3.17)	2.97 (2.97–2.97)	2.54 (2.54–2.54)	2.47 (2.47–2.47)	1.79 (1.79–1.79)		2.58 (2.58–2.58)	2.77 (2.77–2.77)	2.98 (2.98–2.98)	3.21 (3.21–3.21)	3.04 (3.04–3.04)	2.55 (2.55–2.55)	2.53 (2.53–2.53)	
United Kingdom (GBR)	2.64 (2.60–2.67)	2.93 (2.89–2.96)	3.00 (2.98–3.02)	2.81 (2.80–2.83)	2.52 (2.50–2.53)	2.26 (2.25–2.27)	2.13 (2.12–2.15)		2.66 (2.63–2.70)	2.76 (2.73–2.79)	2.98 (2.96–3.00)	3.18 (3.16–3.19)	2.99 (2.97–3.00)	2.71 (2.70–2.72)	2.54 (2.52–2.56)	
United States of America (USA)	2.66 (2.66–2.67)	2.98 (2.97–2.98)	2.99 (2.99–2.99)	2.80 (2.80–2.80)	2.54 (2.54–2.54)	2.29 (2.29–2.29)	2.17 (2.16–2.17)		2.52 (2.52–2.52)	2.71 (2.71–2.71)	2.88 (2.88–2.88)	3.01 (3.01–3.01)	2.86 (2.85–2.86)	2.64 (2.64–2.64)	2.52 (2.52–2.52)	

coordination in the approach to interpretation and management of lipids. Additionally, the disconnection between guidelines that laboratories use in association with creating laboratory reports and the guidelines and clinicians are using together with patients in practice (e.g. 2002 Adult Treatment Panel III vs. 2018 AHA/ACC guidelines) suggests an opportunity to better harmonize laboratory practice and clinical practice. As a positive example of this, the Canadian Society of Clinical Chemists issued harmonized clinical laboratory lipid reporting recommendations based on the 2021 Canadian Cardiovascular Society Lipid Guidelines.[27] The GDN may evolve to serve in a leadership capacity in such harmonization efforts, while helping to monitor progress in lipid control on a global scale.

This study has limitations warranting consideration. The cross-sectional study design does not account for possible repeated measurements, laboratory sampling error margin, and percent and type of lipid-lowering therapies. As real-world evidence from routine lipid testing in day-to-day practice, these data were collected in a manner similar to the Very Large Database of Lipids, which showed that the lipid distributions were similar to a nationally representative USA survey.[12,28] Furthermore, the patterns in lipid levels that we observed across age groups are consistent with prior studies.[29–32] However, the extent to which the data from each country are nationally representative is uncertain. Individuals lacking access to healthcare services, including lipid testing and treatment, were not reflected in the study and may have even more unfavorable lipid profiles than appreciated in this analysis. Notably, most data (79%) were from the USA, and data were lacking for certain countries and the African WHO region. A future goal of GDN is to expand to additional countries, including more low- or middle-income countries, and to add representation from Africa.

As this was a large-scale laboratory study, we did not have access to data on medical conditions or lipid treatments. Additionally, fasting status was unknown and may have impacted triglyceride levels and LDL-C calculation. Collecting data on fasting status will be considered for future iterations of the GDN analyses. The LDL-C categories that were used for data collection and analysis are also a potential limitation, as the lower cut-point of 60 mg/dL reflected a balance of the guideline cut-points of ~50 and 70 mg/dL. Future iterations of the GDN analyses can evolve to reflect additional clinically relevant cut-points. They may also incorporate data on other important lipid measures that were unavailable for the present analysis, particularly apolipoprotein B and lipoprotein(a). Lastly, information on the repetitive measurements on individuals was unknown, and from a clinical perspective, extreme values are more likely to be repeated.

In conclusion, this collaborative study of 462 million lipid test results from 17 countries and five WHO regions represents an innovative approach to provide timely public health insights by combining observations from leading clinical laboratories from across the world in the GDN. This specific study underscores the huge scale of data that can be evaluated from diverse countries. The results from this study highlight the need for coordinated efforts to implement strategies described in the WHF Cholesterol Roadmap[10] to reduce the global burden of ASCVD morbidity and mortality. Importantly, the data presented in this study can help in establishing targets and initiatives to address dyslipidemia and ASCVD that are tailored to the local needs while drawing upon global best practices. Future observational studies from the GDN have the potential to not only provide follow-up on progress in addressing hyperlipidemia globally but also to serve as sentries for acute infectious diseases and other chronic medical conditions involving clinical laboratory testing.

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

Outside of this work, S.S.M. reports consulting fees from Amgen, AstraZeneca, iHealth, NewAmsterdam, Novartis, Novo Nordisk, and Sanofi. S.S.M. is a co-inventor on a patent application filed by Johns Hopkins University for the Martin/Hopkins method of low-density lipoprotein cholesterol and that patent application has since been abandoned to enable use without intellectual property restrictions. H.K. was an employee of Quest Diagnostics during the conduct of this study and has since joined HK Healthcare Consultant, LLC. H.W.K. and J.K.N. are current employees of Quest Diagnostics. H.K. and H.W.K. own stock in Quest Diagnostics. The other authors are current or past employees of the commercial laboratories noted in the affiliations above.

Data Availability

To request the data underlying this article, please contact the corresponding author.

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Ethical Approval

Ethical Approval was not required.

Pre-Registered Clinical Trial Number

None supplied.

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