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GLOBAL, REGIONAL, AND NATIONAL TRENDS IN STATIN UTILIZATION IN HIGH INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES, 2015-2020

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Abstract

Background

Prior studies have reported inequitable global access to essential medicines for cardiovascular disease (CVD) prevention, especially statins. We examine recent trends and disparities in statin utilization at the income group, regional, and country levels.

Methods

Pharmaceutical sales data was used to examine statin utilization in 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs) from 2015 to 2020. Utilization was measured using defined daily doses (DDD) per 1000 population ≥40 years per day (TPD). Fixed-effects panel regression analysis was used to examine associations between statin utilization and country-level factors.

Findings

Globally, statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68.3 DDD/TPD in 2020. However, regional and income group disparities persisted during this period. In 2020, statin utilization was more than six-times higher in HICs than LMIC (192·4 vs. 28·4 DDD/TDP, $p<0·01$). Substantial disparities were also observed between LMICs, ranging from 3·1 DDDs/TDPs in West African nations to 225.0 DDD/TDP in Lebanon in 2020. While statin utilization increased in most LMIC between 2015 to 2020, several experienced declines in utilization, most notably Venezuela (-85·1%, from 92·3 to 14·0 DDD/TPD). In LMICs, every $100 increase in per capita health spending was associated with a 17% increase in statin utilization, while every 10% increase in out-of-pocket health spending was associated with a 11% decline (both $p<0·05$).

Interpretation

Despite global increases in statin utilization, there are substantial regional and country-level disparities between HIC and LMICs. To address global CVD disparities, policymakers should promote increased and equitable access to statins in LMICs.

Strengths and Limitations

Strength: Pharmaceutical sales data was used to examine statin utilization in 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs). These countries represent approximately 90% of the global population older than 40 years of age.

Limitations:

- Comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries.
- IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs.
- Relationships between changes in statin utilization and country-level characteristics are not casual.

INTRODUCTION

Cardiovascular disease (CVD)—primarily ischemic heart disease (IHD)—causes approximately one-third of deaths worldwide.[1] While age-standardized CVD mortality rates have declined globally, the number of deaths due to CVD has increased from 12.1 million in 1990 to 18.6 million in 2019[1] and substantial regional, income group, and country level disparities exist.[2,3] For example, age-standardized CVD mortality rates were lowest in high-income countries (HICs) in Asia-Pacific, Europe, and North America and highest in low- and middle-income countries (LMICs) in Eastern Europe, Middle East and North Africa, and South Asia.[4] Moreover, the CVD burden has increased in nearly every LMIC during the past three decades.[1] Currently, LMICs account for approximately 80% of global CVD deaths.[2]

Medicines, alongside lifestyle changes such as diet, exercise, and smoking cessation, are a cornerstone of CVD prevention.[5] Statins (HMG-CoA reductase inhibitors) are particularly important because they are widely recommended for primary and secondary prevention—that is, among adults with and without known CVD.[5–7] Statins have been included in the World Health Organization (WHO) Model Essential Medicines List (EML)—used to develop national EMLs that guide public procurement—since 2007.[8] Despite statins steadily losing patent protections throughout the world since 2006,[8] only 60% of LMICs include these medicines in their EMLs as of 2017.[9] As medicines included in EMLs have higher availability in the private and public sectors,[10] these policies—as well as differences in income, health spending, and disease burden—may result in global disparities in statin utilization.

While utilization of preventative cardiovascular medicines, including statins, has increased globally in the past decade, large disparities exist.[11,12] For example, a study using pharmaceutical sales data from 65 countries found that consumption of cardiovascular medicines was approximately six-times higher in HICs than in LMICs in 2018.[11] A separate study using sales data from 83 countries found that consumption of lipid-lowering medicines was at least three-times higher in HICs than in LMICs in 2018.[12] However, these studies do not focus on the population at greatest need, adults older than 40 years,[6,7] nor do they evaluate country-level factors associated with statin utilization. Furthermore, an updated analysis of statin utilization is imperative considering the ongoing COVID-19 pandemic that has caused severe disruptions to the pharmaceutical supply chain and the provision of healthcare.[13–15]

This study used global pharmaceutical sales data to estimate statin utilization per population aged 40 years and older in 91 countries from 2015 to 2020. Disparities across and within regions and income groups were examined over time, including in the six months prior to and following the start of the COVID-19 pandemic. To inform global efforts to improve access to essential medicines, we also examined the extent to which country-level factors, such as gross domestic product (GDP), health spending, and underlying IHD burden, are associated with statin utilization.

Methods

Design and Data Sources

We conducted a cross-sectional study examining trends and disparities in statin utilization in 91 countries using pharmaceutical sales data collected by IQVIA (Multinational Integrated Data

Analysis System, MIDAS) from January 2015 to October 2020. These countries represent approximately 90% of the global population older than 40 years of age.[16] IQVIA samples pharmaceutical sales from multiple distribution channels (*e.g.,* manufacturers, wholesalers, and medical facilities) to develop nationally representative estimates of retail and non-retail pharmaceutical sales in each country.[17] If necessary, IQVIA projects its samples to represent 100% of the retail and non-retail sales in each country and reports >90% global precision in recent years.[17] However, IQVIA does not publicly disclose detailed information on data collection, projection, and validation.

Several sources were used to further characterize these countries. Countries were grouped based on their income and geographical regions per the World Bank (2020).[18] Population estimates and age-standardized IHD mortality rates were obtained from the Global Burden of Disease (GBD) (2015-2019).[16] Health expenditures (total, public, out-of-pocket) were also obtained from the World Bank (2015-2018).[19] We projected the values of these estimates through 2020 by applying the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on data availability). Finally, whether statins were included in national essential medicine lists was determined, for reference, using the Global Essential Medicines database (2017).[9]

Measuring Statin Utilization

We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating to statins (C10AA). As IQVIA does not report country-specific data for six countries in Centra America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and twelve countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined these countries in aggregate. We examined total market data, or retail and non-retail statin sales, for 52 countries (**eTable A**). In the 23 countries/groups that lack non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available (85% of all statins were dispensed through the retail sector).

To enable international comparisons over time, we converted statin sales (expressed in milligrams) into defined daily doses (DDDs) using the Anatomical Therapeutic Chemical Classification System developed by the WHO Collaborating Centre for Drug Statistics Methodology.[20] To account for differences in population size and age distribution, we report statin utilization as DDDs per 1000 population ≥40 years per day (TPD) for each country. Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating statin sale and population estimates.

Statistical Analysis

Descriptive statistics were used to examine trends and disparities in statin utilization from 2015 to 2020. Simple linear regressions were used to determine statistical significance in trends and disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-COVID-19 (April 2020 to October 2020) periods were also evaluated.

Fixed-effects panel regression analysis was used to quantify the association between economic and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin

utilization estimates were logged in these models to enable interpretation as percent change associated with each unit of the independent variables examined. The independent variables included time-varying health expenditure per capita, out-of-pocket health expenditure (as a percentage of total expenditure), and age-standardized IHD mortality rate. Errors were clustered by year and country to account for serial correlation.

All *p*-values are two-sided. STATA version 17·1 was used for all statistical analyses.

This study was considered exempt by the Institutional Review Board at the University of Southern California because this study was not considered human subjects research.

Patient and public involvement
No patient involved.

RESULTS
As shown in **Figure 1**, global statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68·3 DDD/TPD ($p<0·01$). While statin utilization increased, to varying degrees, in all regions and income groups (all $p<0·05$), disparities persisted. In 2020, statin utilization was highest in North America and Europe (279·7 and 159·9 DDD/TPD, respectively) and substantially lower in Latin America, MENA, East Asia, South Asia, and sub-Saharan Africa (66·1, 64·1, 29·3, 16·1, and 24·7 DDD/TPD, respectively). From 2015 to 2020, statin utilization increased substantially in HICs (19·3% from 161·3 to 192·4 DDD/TPD) and LMICs (57·9% from 18·0 to 28·4 DDD/TPD). However, disparities by income group remained throughout this period—by 2020, statin utilization was seven times greater in HICs than in LMICs.

Figure 2 depicts country-specific variation in statin utilization. From 2015 to 2020, statin utilization increased or remained stable in most HICs, except Singapore (125·2 to 95·0, -24·1%, $p=0·27$), the United Arab Emirates (104·4 to 83·9, -19·7%, $p=0·02$), Luxembourg (216·6 to 185·3, -14·4%, $p<0·01$, and New Zealand (295·4 to 256·0, -13·4%, $p=0·12$). HICs located in North America and Europe have substantially higher statin utilization than comparable countries located in other regions. For example, in 2020, statin utilization in HICs ranged from over 300 DDD/TPD in Denmark, Canada, and United Kingdom to less than 50 DDD/TPD in Japan, Chile, and Kuwait.

From 2015 to 2020, statin utilization increased by more than 10% in nearly all LMICs. Exceptions included India (12·9 to 14·1, 9·1%, $p=0·02$), Malaysia (57·8 to 60·0, 3·9%, $p=0·41$), Ecuador (20·2 to 20·9, 3·6%, $p=0·09$), and Jordan (28·6 to 27·1, -5·4%, $p=0·20$), where utilization remained relatively stable, and Venezuela, where utilization sharply declined (92·3 to 13·8, -85·1%, $p<0·01$). Several LMICs had higher statin utilization than the global average in 2020, including Lebanon, Algeria, Brazil, Thailand, and South Africa (224·9, 111·8, 109·3, 96·8, and 85·4 DDD/TPD, respectively). Statin utilization is lower than 34 DDD/TPD (approximately half the global average) in 35 LMICs, including some of the most populous nations, such as China, India, Indonesia, Pakistan, Bangladesh, and Mexico.

Table 1 presents factors associated with changes in statin utilization. In HICs, only health expenditure per capita was significantly and positively associated with statin utilization. In

LMICs, every $100 increase in health expenditure per capita was associated with a 17% increase in utilization, while every 10% increase in out-of-pocket health expenditure (as percentage of total health expenditure) was associated with a 11% decline in utilization (both $p<0{\cdot}05$). Greater rates of IHD mortality were also positively associated with more statin utilization in LMICs.

Compared with the pre–COVID-19 period, statin utilization declined by more than 5·0% in 41 countries, including 19 HICs and 22 LMICs (**Figure 3**). Severe disruptions in statin utilization—or ≥10% decline—were found in 13 HICs, including Australia (327·5 to 265·2 DDD/TPD, -19.0%), the United Arab Emirates (92·7 to 77·8 DDD/TPD, -16·1%), and Germany (180·6 to 160·6 DDD/TPD, -11·1%) (**eTable B**). Some of the most severe disruptions in statin utilization were observed among LMICs, including in Tunisia (76·5 to 52·7 DDD/TPD, -31·1%), Vietnam (23·3 to 17·2 DDD/TPD, -26·3%), Ukraine (32·1 to 26·1 DDD/TPD, -18·7%), and Mexico (28·4 to 23·8 DDD/TPD, -16·3%).

DISCUSSION

Using a global database, representing approximately 90% of the global population older than 40 years of age,[16] we found persistent disparities across regions, income groups, and countries in statin utilization which may contribute to worsening disparities in CVD mortality. While global statin utilization has increased 25% from 2015 to 2020, statin utilization remains higher in the "global north" (*e.g.*, North America, Europe, and Oceania) and in HICs than countries in other regions and LMICs.[4] In 2020, statin utilization was seventeen times higher in North America versus South Asia—the region with the highest age-adjusted CVD mortality rate in the world[4]—and seven times higher in HICs versus LMICs—that are experiencing a near universal increase in the number of CVD deaths.[1]

Statin utilization is also substantially lower in countries with disproportionately high age-standardized CVD mortality rates, namely LMICs in South Asia, MENA, and sub-Saharan Africa.[4] The WHO Global Non-Communicable Disease (NDC) Action Plan 2013-2020 aimed for a 25% reduction in premature deaths from NDC, especially CVD, from 2010 to 2025 by ensuring that at least half of adults at high CVD risk receive cardiovascular medicines and that 80% of public and private facilities have these essential medicines available on-site.[21] Growth in statin utilization in LMICs was concentrated among those countries with worsening IHD mortality—suggesting reactionary policies for the management of CVD morbidity and mortality versus preventative strategies for the provision of essential medicines. Together, our findings suggest that global efforts to reduce the burden of CVD need to be strengthened—statin utilization remains inequitable and suboptimal in LMICs, including those with worsening rates of CVD mortality.

Importantly, there is a substantial gap between CVD burden and statin utilization between HIC and LMICs. For example, statin utilization is very low (less than half the global average) in 70% of the LMICs examined, yet account for 68% of the global population of middle aged and older adults and 55% CVD deaths worldwide.[16] Forty-two percent of CVD deaths occur in China (25%), India (14%), and Indonesia (4%),[16] all of whom have very low statin utilization and together account for less than 11% of statins dispensed in the world. From 2015 to 2019, the IHD mortality rate has declined or remained stable in most LMICs, with notable exceptions of Bangladesh (5%), Malaysia (5%), and Venezuela (10%) that have experienced substantial

increases in recent years.[16] These countries, with worsening IHD mortality, have comparatively low statin utilization in given their regional and income group averages. However, Venezuela has also experienced substantial declines in statin utilization in this period—aggravating the IHD burden experienced by its populace.

Among LMICs, we found that every $100 increase in per capita health spending was associated with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-pocket health spending was associated with an 11% decline. These findings suggest that policy efforts to address global disparities in statin utilization, may need to increase health spending while shifting the burden of health spending from individuals to the public sector (either via the direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public investment in health (as measured by government health spending as a percentage of total expenditures) has declined in LMICs during the last two decades.[22] Only high-income and upper-middle countries have seen moderate increases in government health spending,[22] countries that consume a disproportionate share of statins. Out-of-pocket spending as a share of total health spending has remained stubbornly high in LMICs (above 40% and twice the percentage in HICs) during this period.[22] International aid—a major source of health spending in LMICs—is disproportionately directed to communicable diseases,[22] and these policies may aggravate global disparities in the use of essential medicines, including statins, and hinder efforts to reduce CVD mortality. International aid for health, which could alleviate costs of essential medicines for governments and the public, has also stagnated since 2013.[22]

Economic or political crises, which are often followed by sharp declines in total health spending, may also impact access to essential medicines. The starkest example is Venezuela, where statin utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as well as widespread and chronic shortages of essential medicines in the past decade.[19,23]

Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of medicines that impact domestic and international markets, transportation hurdles, and restrictions on movement (internationally and domestically and by providers and patients).[24] For example, early in the pandemic, active pharmaceutical ingredient production in China was severely curtailed—leading to shortages and delays in the production of medicines throughout the world, including in the United States, the European Union, and India.[25]

During the first six months of COVID-19 pandemic, statin utilization declined by more than 5% in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the pandemic.[26] However, the most severe disruptions in individual countries occurred in LMICs, which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19 disparities, including inequitable access to vaccinations,[26] may result in persistent disruptions to statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the

COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and country level CVD disparities between HIC and LMICs.

Limitations

This study had several limitations. First, comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and we account for missing non-retail sales through interpolation (using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available). Second, IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs. Finally, relationships between changes in statin utilization and country-level characteristics are not casual. However, the trends and disparities in statin utilization described in this study help evaluate the global progress in ensuring equitable access to essential medicines and inform efforts to reduce the global burden of CVD.

Conclusion

Despite a 25% increase in global statin utilization from 2015 to 2020, there are substantial and persistent regional and country-level disparities between HIC and LMICs. To address worsening CVD disparities, global, regional, and national policymakers should promote increased and equitable access to statins in LMICs.

Contributorship statements

- Guadamuz JS: Conceptualisation, data curation, formal analysis, methodology, validation, visualisation, software, writing – original draft, and writing – review & editing.
- Shooshtari A: Project administration and writing – original draft.
- Qato DM: Conceptualisation, funding acquisition, writing – original draft, and writing – review & editing

Competing interests

Dr. Guadamuz current reports employment with Flatiron Health, Inc, which is an independent subsidiary of the Roche Group. Flatiron Health, Inc., had no role in the design and conduct of the study, analysis or interpretation of the data, and preparation, or final approval of the article before publication.

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Data sharing statement

Data for this study will not be made available due to licensing agreements with IQVIA.

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Table 1. Factors Associated with Statin Utilization, 2015 to 2020

	Exponentiated Coefficient (CI) [a]	
	High-income countries	Low-and middle-income countries
No. [b]	40	33
Health expenditure per capita ($) [c]	1·01 (1·01, 1·02)*	1·17 (1·12, 1·22)*
OOP health expenditure (%) [d]	0·99 (0·91, 1·09)	0·89 (0·82, 0·96)*
IHD mortality rate [e]	1·00 (0·99, 1·02)	1·02 (1·01, 1·03)*

Notes: IHD=ischemic heart disease, OOP=out-of-pocket, No.=number.
a Statin utilization is defined as defined daily doses per 1000 population ≥ 40 y per day. Here logged statin utilization is examined. Data for 2020 is based on statin utilization from January to September 2020. **b** Countries in Central America and West Africa were excluded because IQVIA does not report country-specific information for these regions. **c** Increments of 100. **d** Increments of 10. **e** Age-standardized IHD mortality rate, increments of 10. * $p<0·05$

Figure Legends

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant ($p<0·05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

Figure 2. Statin Utilization by Country, 2015 to 2020

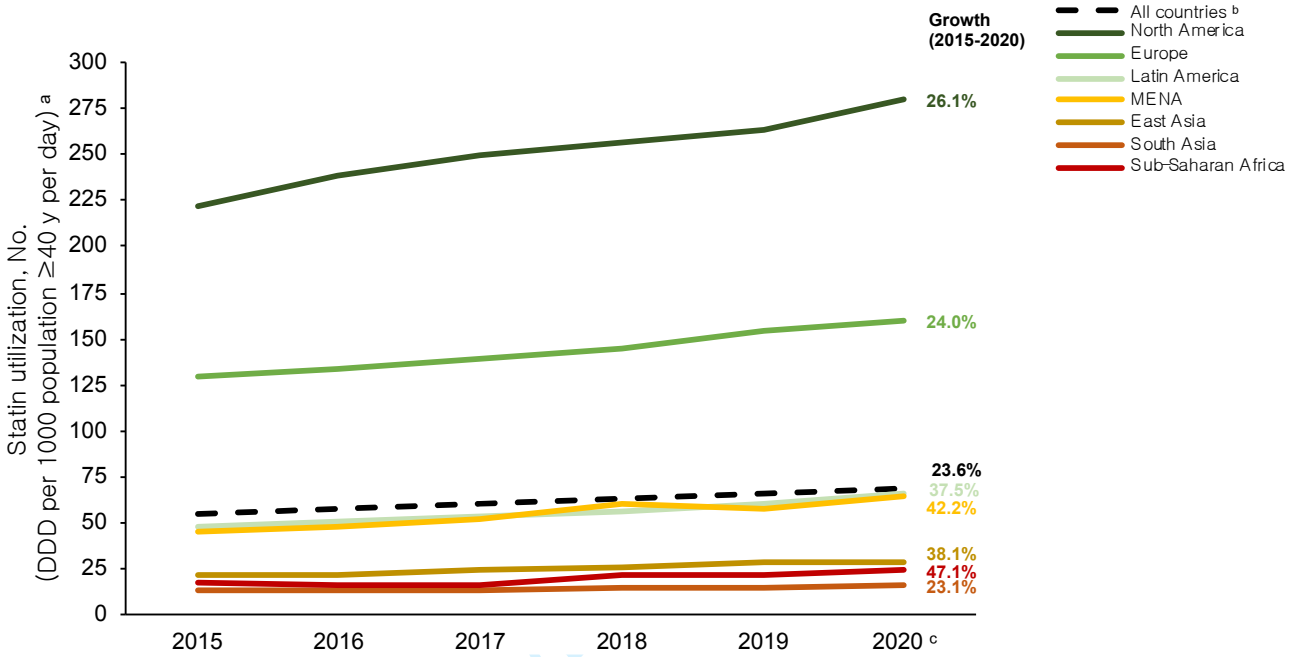
Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

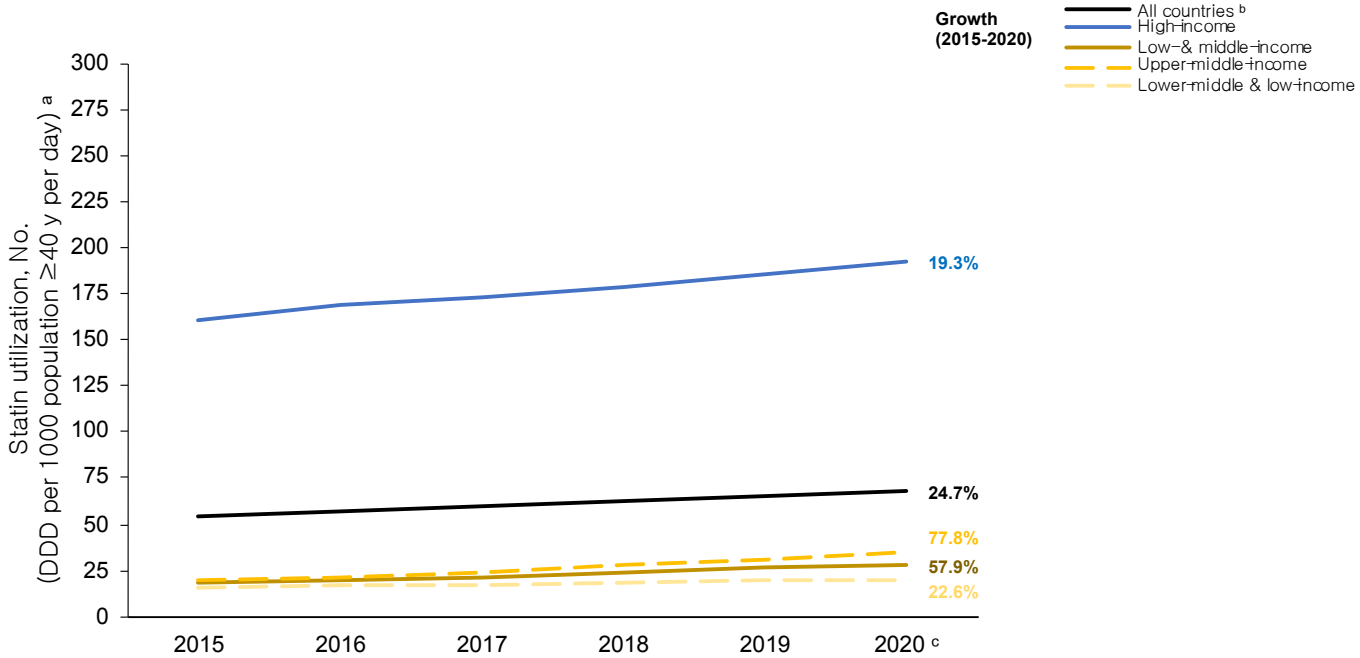
Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

a. By Region



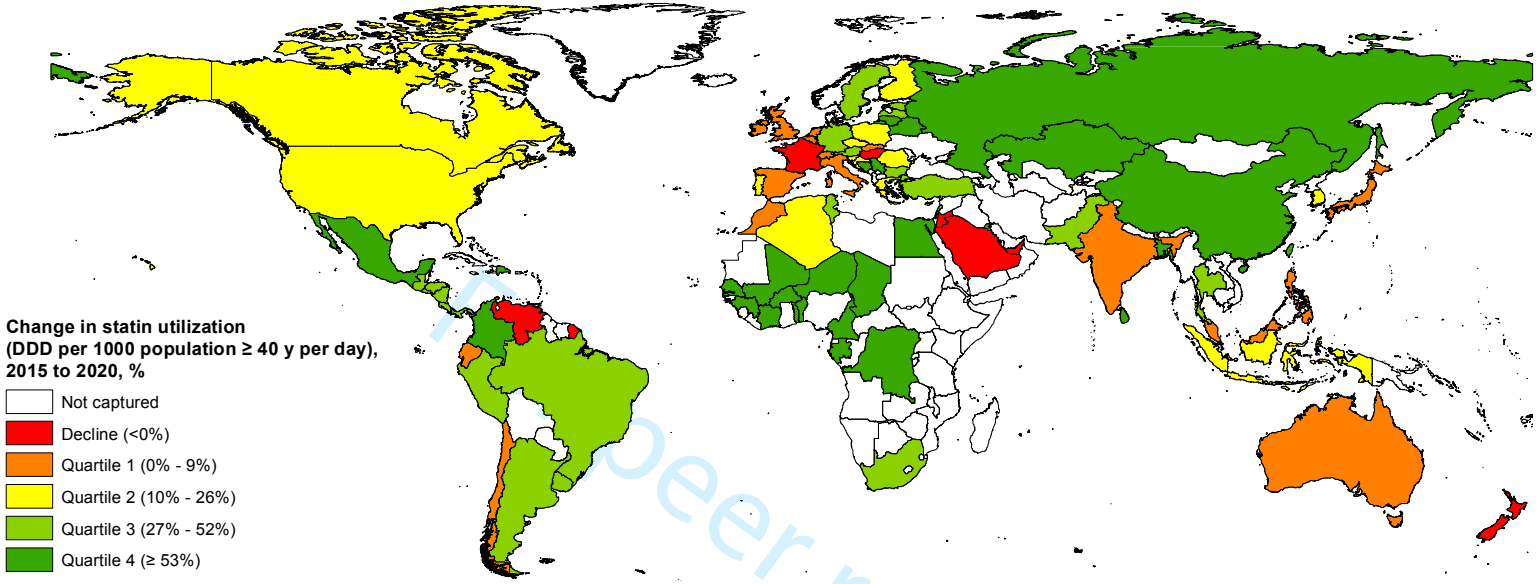
b. By Income



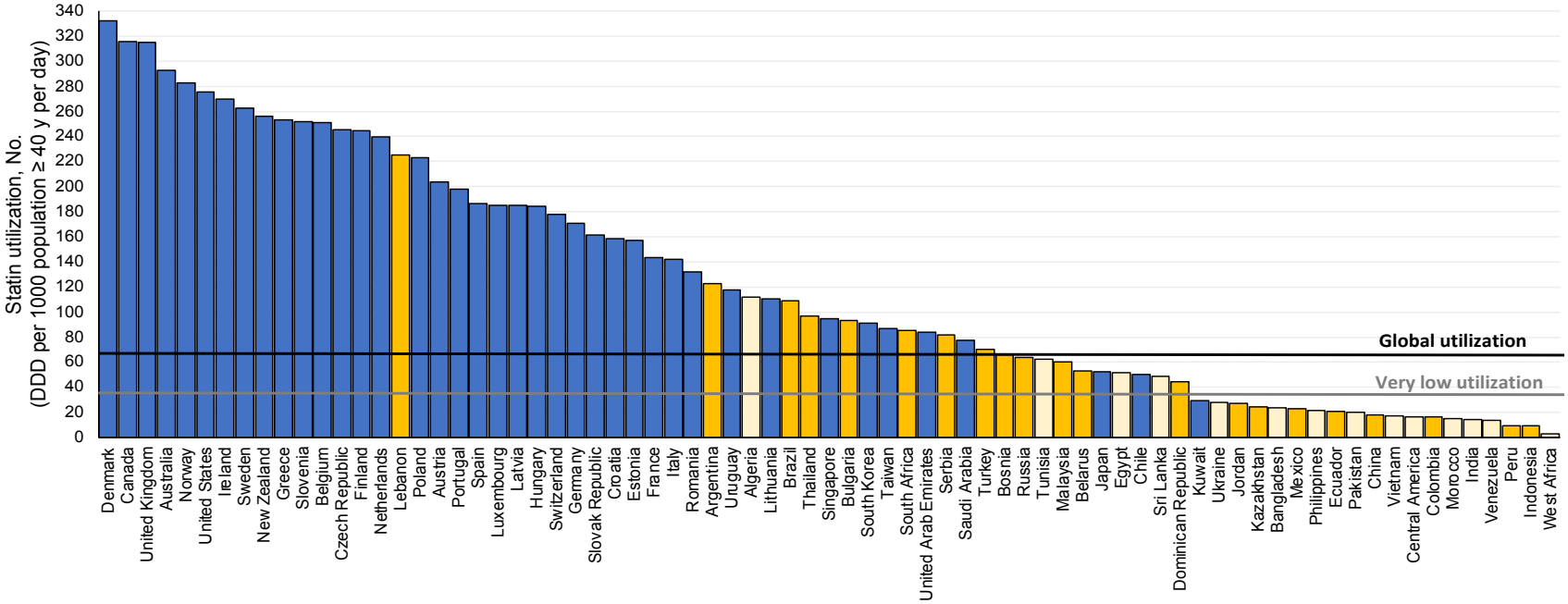
Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant (p<0·05), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by County, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

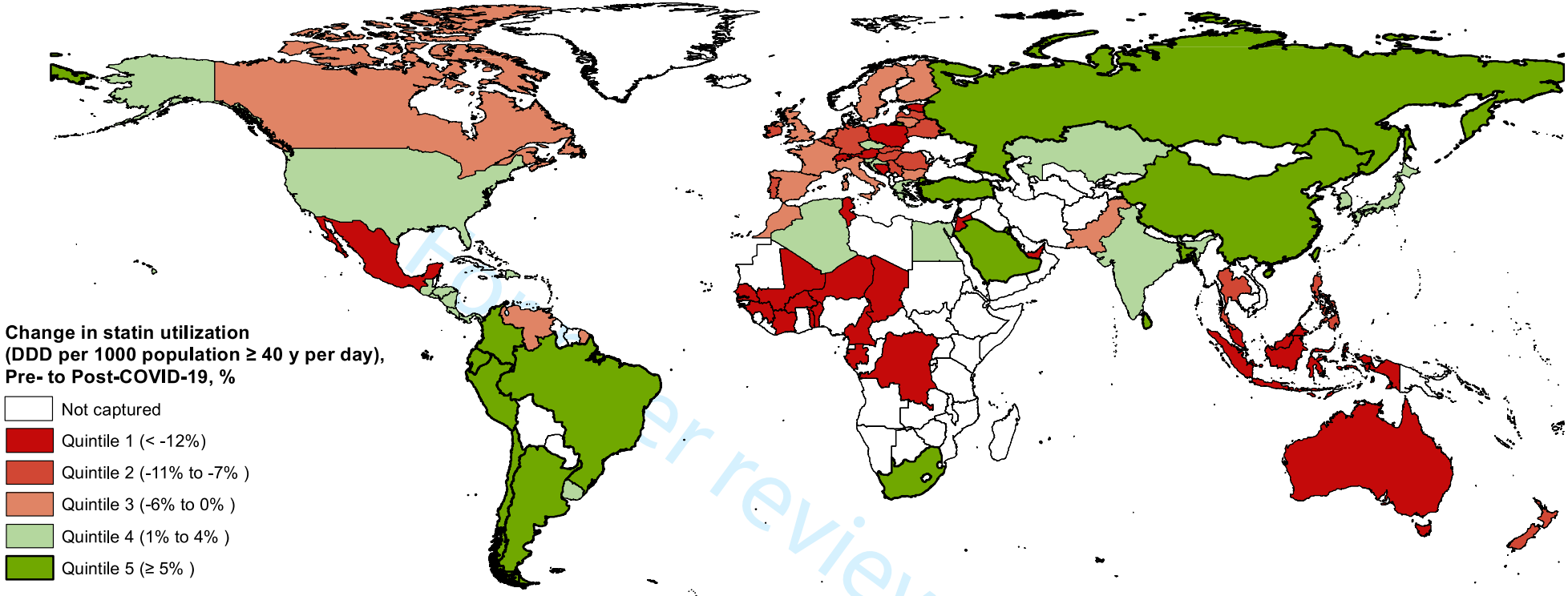


b. Statin utilization, 2020



Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization.

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020



Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

ONLINE SUPPLEMENT

eTable A. Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019) [d]
						Public	OOP		
Australia	Total market	East Asia & Pacific	High	$51,812	$5,425	69	18	-	56·1
Japan	Total market	East Asia & Pacific	High	$40,113	$4,267	84	13	-	29·9
New Zealand	Total market	East Asia & Pacific	High	$41,792	$4,037	75	13	-	75·0
Singapore	Total market	East Asia & Pacific	High	$59,798	$2,824	50	31	-	52·3
South Korea	Total market	East Asia & Pacific	High	$31,489	$2,543	58	33	-	35·0
Taiwan	Total market	East Asia & Pacific	High [e]	$28,371 [e]	$1,882 [e]			-	41·2
China	Total market	East Asia & Pacific	Upper middle	$10,500	$501	56	36	Yes	116·4
Indonesia	Total market	East Asia & Pacific	Upper middle	$3,870	$112	49	35	Yes	140·3
Malaysia	Total market	East Asia & Pacific	Upper middle	$10,402	$427	51	35	Yes	145·7
Thailand	Total market	East Asia & Pacific	Upper middle	$7,189	$276	76	11	Yes	52·6
Philippines	Total market	East Asia & Pacific	Lower middle	$3,299	$137	33	54	Yes	148·1
Vietnam	Total market	East Asia & Pacific	Lower middle	$2,786	$152	46	45	Yes	95·6
Austria	Total market	Europe	High	$48,105	$5,326	73	18	-	83·3
Belgium	Total market	Europe	High	$44,594	$4,913	76	19	-	54·8
Croatia	Total market	Europe	High	$13,828	$1,014	83	10	Yes	143·8
Czech Republic	Total market	Europe	High	$22,762	$1,766	83	14	Yes	149·0
Denmark	Total market	Europe	High	$60,909	$6,217	84	14	-	55·6
Estonia	Retail only	Europe	High	$23,312	$1,553	74	25	Yes	144·2
Finland	Total market	Europe	High	$49,041	$4,516	79	18	-	100·6
France	Total market	Europe	High	$38,625	$4,690	73	9	-	38·4
Germany	Total market	Europe	High	$45,724	$5,472	78	13	-	81·4
Greece	Retail only	Europe	High	$17,676	$1,567	52	36	-	91·9
Hungary	Total market	Europe	High	$15,899	$1,082	69	27	-	174·6
Ireland	Total market	Europe	High	$83,813	$5,489	74	12	-	74·7
Italy	Total market	Europe	High	$31,676	$2,989	74	24	-	55·3
Latvia	Total market	Europe	High	$17,620	$1,101	60	39	Yes	200·4
Lithuania	Total market	Europe	High	$19,998	$1,249	66	32	Yes	222·9
Luxembourg	Retail only	Europe	High	$115,874	$6,227	85	10	-	54·2
Netherlands	Total market	Europe	High	$52,304	$5,307	65	11	-	47·4
Norway	Total market	Europe	High	$67,294	$8,239	85	14	-	55·5
Poland	Total market	Europe	High	$15,656	$979	71	21	Yes	130·3
Portugal	Total market	Europe	High	$22,440	$2,215	61	30	Yes	45·8
Romania	Total market	Europe	High	$12,896	$687	80	19	Yes	177·1
Slovak Republic	Total market	Europe	High	$19,157	$1,300	79	19	Yes	198·9
Slovenia	Total market	Europe	High	$25,180	$2,170	72	12	Yes	59·0
Spain	Total market	Europe	High	$27,057	$2,736	70	22	-	45·0
Sweden	Total market	Europe	High	$51,926	$5,982	85	14	Yes	73·7
Switzerland	Total market	Europe	High	$86,602	$9,871	31	28	-	55·7
United Kingdom	Total market	Europe	High	$40,285	$4,315	79	17	-	66·8
Belarus	Total market	Europe	Upper middle	$6,411	$356	70	25	Yes	334·2
Bosnia & Herzegovina	Total market	Europe	Upper middle	$6,032	$540	70	29	Yes	162·9
Bulgaria	Total market	Europe	Upper middle	$9,976	$690	58	41	Yes	239·1
Russia	Total market	Europe	Upper middle	$10,127	$609	59	38	Yes	240·6
Serbia	Total market	Europe	Upper middle	$7,666	$617	59	38	Yes	204·4
Ukraine	Total market	Europe	Lower middle	$3,727	$228	48	49	Yes	424·2
Chile	Retail only	Latin America	High	$13,232	$1,456	51	33	Yes	50·4
Uruguay	Retail only	Latin America	High	$15,438	$1,590	73	17	Yes	67·0
Argentina	Retail only	Latin America	Upper middle	$8,442	$1,128	61	28	Yes	82·1
Brazil	Total market	Latin America	Upper middle	$6,797	$848	42	28	Yes	74·9
Colombia	Retail only	Latin America	Upper middle	$5,333	$513	72	15	Yes	75·3
Dominican Republic	Total market	Latin America	Upper middle	$7,268	$462	44	45	Yes	175·6
Ecuador	Retail only	Latin America	Upper middle	$5,600	$516	52	40	Yes	81·8
Mexico	Retail only	Latin America	Upper middle	$8,347	$520	50	42	Yes	100·0
Peru	Retail only	Latin America	Upper middle	$6,127	$369	63	29	Yes	48·7
Venezuela	Retail only	Latin America	Lower middle [f]	$1,739 [f]	$257	48	38	Yes	130·0
Central America [g]	Retail only								
Panama		Latin America	High	$12,269	$1,132	64	29	Yes	58·2
Costa Rica		Latin America	Upper middle	$12,077	$910	72	22	Yes	71·5
Guatemala		Latin America	Upper middle	$4,603	$260	36	58	Yes	106·3
El Salvador		Latin America	Lower middle	$3,799	$289	64	29	Yes	100·4
Honduras		Latin America	Lower middle	$2,406	$176	40	51	Yes	154·8
Nicaragua		Latin America	Lower middle	$1,905	$174	60	33	Yes	148·3

eTable A (continued). Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019)[d]
						Public	OOP		
Kuwait	Retail only	MENA	High	$32,373	$1,711	88	11	-	108·5
Saudi Arabia	Total market	MENA	High	$20,110	$1,485	62	14	-	205·6
United Arab Emirates	Retail only	MENA	High	$43,103	$1,817	52	13	-	175·4
Algeria	Retail only	MENA	Lower middle	$3,310	$256	66	33	Yes	237·3
Egypt	Retail only	MENA	Lower middle	$3,548	$126	29	62	Yes	359·3
Morocco	Retail only	MENA	Lower middle	$3,009	$175	40	47	Yes	278·5
Tunisia	Total market	MENA	Lower middle	$3,320	$252	57	39	Yes	193·5
Jordan	Retail only	MENA	Upper middle	$4,283	$330	49	31	Yes	121·9
Kazakhstan	Total market	MENA	Upper middle	$9,056	$276	61	33	-	251·4
Lebanon	Retail only	MENA	Upper middle	$4,891	$686	50	33	Yes	241·2
Turkey	Total market	MENA	Upper middle	$8,538	$390	77	17	-	121·0
Canada	Total market	North America	High	$43,242	$4,995	73	15	No	63·9
United States	Total market	North America	High	$63,544	$10,624	50	11	-	91·0
Bangladesh	Retail only	South Asia	Lower middle	$1,969	$42	17	74	No	111·2
India	Total market	South Asia	Lower middle	$1,901	$73	27	63	Yes	150·5
Pakistan	Retail only	South Asia	Lower middle	$1,194	$43	36	56	Yes	189·3
Sri Lanka	Retail only	South Asia	Lower middle	$3,682	$157	41	51	Yes	109·0
South Africa	Total market	Sub-Saharan Africa	Upper middle	$5,091	$526	54	8	Yes	81·4
West Africa [g]	Retail only								
Gabon		Sub-Saharan Africa	Upper middle	$7,006	$218	59	23	-	117·4
Benin		Sub-Saharan Africa	Lower middle	$1,291	$31	20	45	-	113·1
Cameroon		Sub-Saharan Africa	Lower middle	$1,499	$54	6	76	-	115·5
Côte d'Ivoire		Sub-Saharan Africa	Lower middle	$2,326	$72	29	39	-	122·0
Senegal		Sub-Saharan Africa	Lower middle	$1,488	$59	24	56	-	117·6
Burkina Faso		Sub-Saharan Africa	Low	$831	$40	43	36	-	130·2
Chad		Sub-Saharan Africa	Low	$614	$29	17	62	-	120·1
Democratic Republic of the Congo		Sub-Saharan Africa	Low	$557	$19	15	42	-	114·7
Guinea		Sub-Saharan Africa	Low	$1,194	$38	16	61	-	123·7
Mali		Sub-Saharan Africa	Low	$859	$35	28	34	-	116·0
Niger		Sub-Saharan Africa	Low	$565	$30	33	49	-	118·1
Togo		Sub-Saharan Africa	Low	$915	$42	17	56	-	134·9

Notes: EML=essential medicines list, IHD=ischemic heart disease, MENA=Middle East and North Africa, OOP=out-of-pocket. **a** Based on "sell-in" data or the volume purchased by retail (*e.g.*, pharmacies) or non-retail (*e.g.*, hospitals) sectors. As an exception, we used "sell-out" data, or the volume dispensed to patients, in the United Kingdom. We present data on the total market, or retail and non-retail drug sales, for 52 countries. In the 39 countries lacking non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available. In 2020, 85% of statins were dispensed via retail sectors (based on countries with data for retail and non-retail sectors). **b** World Bank. **c** World Health Organization. **d** Global Burden Disease, age-standardized IHD mortality rate. **e** Republic of China (Taiwan), Statistical Bureau. **f** Australian Department of Foreign Affairs & Trade, Venezuela Fact Sheet. **g** IQVIA does not provide country specific utilization for this region.

eTable B. Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Denmark	331·7	326·1	0·73	-1·7
Canada	322·9	314·3	0·68	-2·7
United Kingdom	324·5	308·8	0·14	-4·8
Australia	**327·5**	**265·2**	**0·26**	**-19·0**
Norway	**304·7**	**274·4**	**0·26**	**-9·9**
United States	271·6	271·2	·98	-0·1
Ireland	**280·3**	**257·8**	**0·38**	**-8·0**
Sweden	265·0	255·5	0·61	-3·6
New Zealand	**275·3**	**243·6**	**0·74**	**-11·5**
Greece	250·5	253·7	0·33	1·3
Slovenia	250·8	256·1	0·55	2·1
Belgium	**271·5**	**243·0**	**0·14**	**-10·5**
Czech Republic	241·7	248·3	0·15	2·7
Finland	253·0	243·2	0·47	-3·9
Netherlands	248·8	237·9	0·22	-4·4
Lebanon	201·9	232·4	0·17	15·1
Poland	**241·2**	**202·5**	**0·32**	**-16·0**
Austria	**223·5**	**190·8**	**0·18**	**-14·7**
Portugal	**205·4**	**184·8**	**0·43**	**-10·0**
Spain	188·6	180·1	0·51	-4·5
Luxembourg	**198·1**	**176·2**	**0·21**	**-11·0**
Latvia	**193·1**	**174·8**	**0·40**	**-9·5**
Hungary	**192·9**	**175·0**	**0·30**	**-9·3**
Switzerland	**202·8**	**170·1**	**0·15**	**-16·1**
Germany	**180·6**	**160·6**	**0·27**	**-11·1**
Slovak Republic	**175·5**	**155·2**	**0·09**	**-11·6**
Croatia	156·5	158·3	0·67	1·2
Estonia	**174·5**	**148·9**	**0·39**	**-14·7**
France	145·8	141·8	0·17	-2·7
Italy	**144·7**	**135·1**	**0·52**	**-6·6**
Romania	**141·6**	**125·4**	**0·34**	**-11·4**
Argentina	108·7	130·2	0·03	19·8
Uruguay	116·1	118·1	0·35	1·8
Algeria	108·9	111·6	0·88	2·5
Lithuania	**113·8**	**106·0**	**0·52**	**-6·8**
Brazil	107·0	112·0	0·25	4·7
Thailand	**102·6**	**92·9**	**0·34**	**-9·4**
Singapore	96·6	93·4	0·59	-3·3
Bulgaria	94·0	90·8	0·50	-3·4
South Korea	90·5	91·4	0·72	1·0
Taiwan	87·0	86·8	0·96	-0·2
South Africa	83·9	87·8	0·64	4·6
United Arab Emirates	**92·7**	**77·8**	**0·60**	**-16·1**
Serbia	**85·1**	**78·7**	**0·25**	**-7·5**
Saudi Arabia	72·1	81·1	0·26	12·4
Turkey	65·0	73·1	0·04	12·4
Bosnia	**70·5**	**61·2**	**0·37**	**-13·2**
Russia	58·6	66·2	0·08	13·0
Tunisia	**76·5**	**52·7**	**0·05**	**-31·1**
Malaysia	**65·9**	**53·7**	**0·21**	**-18·6**
Belarus	**55·0**	**51·0**	**0·25**	**-7·2**
Japan	53·2	54·1	0·82	1·7
Egypt	51·4	53·3	0·50	3·7
Chile	45·5	50·6	0·25	11·4
Sri Lanka	44·5	50·0	0·14	12·4
Dominican Republic	44·7	44·7	0·00	0·0
Kuwait	26·3	27·7	0·84	5·4
Ukraine	**32·1**	**26·1**	**0·22**	**-18·7**
Jordan	**28·7**	**24·1**	**0·50**	**-16·1**
Kazakhstan	22·8	22·9	0·97	0·8
Bangladesh	20·9	24·9	0·17	19·3

eTable B (continued). Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Mexico	**28·4**	**23·8**	**0·60**	**-16·3**
Philippines	**23·2**	**21·3**	**0·54**	**-8·1**
Ecuador	18·1	22·3	0·30	23·6
Pakistan	20·4	19·4	0·40	-4·8
China	16·2	18·3	0·17	13·3
Vietnam	**23·3**	**17·2**	**0·38**	**-26·3**
Central America [c, d]	16·1	16·7	0·75	4·0
Colombia	14·3	17·3	0·08	20·7
Morocco	**15·5**	**15·1**	**0·75**	**-3·1**
India	13·7	14·3	<0·01	4·3
Venezuela	**14·5**	**14·4**	**0·95**	**-0·9**
Peru	5·9	10·3	0·41	74·7
Indonesia	**10·9**	**8·9**	**0·32**	**-18·3**
West Africa [c, e]	**4·0**	**2·8**	**0·04**	**-30·1**

Notes: DDD=defined daily doses; No.=number.

a Statistical significance was determined using simple linear regression. Countries in bold declined ≥5%. **b** Sorted based on statin utilization in 2020, refer to **Error! Reference source not found.**. **c** IQVIA does not provide country specific utilization for this region. **d** Central American countries included Costa Rica, El Salvador, Honduras, Guatemala, Nicaragua, and Panama. **e** West African countries included Benin, Burkina Faso, Cameroon, Chad, Democratic Republic of the Congo, Gabon, Guinea, Ivory Coast, Mali, Niger, Senegal, and Togo.

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GLOBAL, REGIONAL, AND NATIONAL TRENDS IN STATIN UTILIZATION IN HIGH INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES, 2015-2020

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GLOBAL, REGIONAL, AND NATIONAL TRENDS IN STATIN UTILIZATION IN HIGH INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES, 2015-2020

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Abstract

Background

Prior studies have reported inequitable global access to essential medicines for cardiovascular disease (CVD) prevention, especially statins. We examine recent trends and disparities in statin utilization at the income group, regional, and country levels.

Methods

Pharmaceutical sales data was used to examine statin utilization in 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs) from 2015 to 2020. Utilization was measured using defined daily doses (DDD) per 1000 population ≥40 years per day (TPD). Fixed-effects panel regression analysis was used to examine associations between statin utilization and country-level factors.

Findings

Globally, statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68.3 DDD/TPD in 2020. However, regional and income group disparities persisted during this period. In 2020, statin utilization was more than six-times higher in HICs than LMIC (192·4 vs. 28·4 DDD/TDP, $p<0·01$). Substantial disparities were also observed between LMICs, ranging from 3·1 DDDs/TDPs in West African nations to 225.0 DDD/TDP in Lebanon in 2020. While statin utilization increased in most LMIC between 2015 to 2020, several experienced declines in utilization, most notably Venezuela (-85·1%, from 92·3 to 14·0 DDD/TPD). In LMICs, every $100 increase in per capita health spending was associated with a 17% increase in statin utilization, while every 10% increase in out-of-pocket health spending was associated with a 11% decline (both $p<0·05$).

Interpretation

Despite global increases in statin utilization, there are substantial regional and country-level disparities between HIC and LMICs. To address global CVD disparities, policymakers should promote increased and equitable access to statins in LMICs.

Strengths and Limitations

- Pharmaceutical sales data was used to examine statin utilization in 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs) — representing approximately 90% of the global population older than 40 years of age.
- Comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries.
- IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs.
- Relationships between changes in statin utilization and country-level characteristics are not casual.

INTRODUCTION

Cardiovascular disease (CVD)—primarily ischemic heart disease (IHD)—causes approximately one-third of deaths worldwide.[1] While age-standardized CVD mortality rates have declined globally, the number of deaths due to CVD has increased from 12.1 million in 1990 to 18.6 million in 2019[1] and substantial regional, income group, and country level disparities exist.[2,3] For example, age-standardized CVD mortality rates were lowest in high-income countries (HICs) in Asia-Pacific, Europe, and North America and highest in low- and middle-income countries (LMICs) in Eastern Europe, Middle East and North Africa, and South Asia.[4] Moreover, the CVD burden has increased in nearly every LMIC during the past three decades.[1] Currently, LMICs account for approximately 80% of global CVD deaths.[2]

Medicines, alongside lifestyle changes such as diet, exercise, and smoking cessation, are a cornerstone of CVD prevention.[5] Statins (HMG-CoA reductase inhibitors) are particularly important because they are widely recommended for primary and secondary prevention—that is, among adults with and without known CVD.[5–7] Statins have been included in the World Health Organization (WHO) Model Essential Medicines List (EML)—used to develop national EMLs that guide public procurement—since 2007.[8] Despite statins steadily losing patent protections throughout the world since 2006,[8] only 60% of LMICs include these medicines in their EMLs as of 2017.[9] As medicines included in EMLs have higher availability in the private and public sectors,[10] these policies—as well as differences in income, health spending, and disease burden—may result in global disparities in statin utilization.

While utilization of preventative cardiovascular medicines, including statins, has increased globally in the past decade, large disparities exist.[11,12] For example, a study using pharmaceutical sales data from 65 countries found that consumption of cardiovascular medicines was approximately six-times higher in HICs than in LMICs in 2018.[11] A separate study using sales data from 83 countries found that consumption of lipid-lowering medicines was at least three-times higher in HICs than in LMICs in 2018.[12] However, these studies do not focus on the population at greatest need, adults older than 40 years,[6,7] nor do they evaluate country-level factors associated with statin utilization. Furthermore, an updated analysis of statin utilization is imperative considering the ongoing COVID-19 pandemic that has caused severe disruptions to the pharmaceutical supply chain and the provision of healthcare.[13–15]

This study used global pharmaceutical sales data to estimate statin utilization per population aged 40 years and older in 91 countries from 2015 to 2020. Disparities across and within regions and income groups were examined over time, including in the six months prior to and following the start of the COVID-19 pandemic. To inform global efforts to improve access to essential medicines, we also examined the extent to which country-level factors, such as gross domestic product (GDP), health spending, and underlying IHD burden, are associated with statin utilization.

Methods

Design and Data Sources

We conducted a cross-sectional study examining trends and disparities in statin utilization in 91 countries using pharmaceutical sales data collected by IQVIA (Multinational Integrated Data

Analysis System, MIDAS) from January 2015 to October 2020. These countries represent approximately 90% of the global population older than 40 years of age.[16] IQVIA samples pharmaceutical sales from multiple distribution channels (*e.g.,* manufacturers, wholesalers, and medical facilities) to develop nationally representative estimates of retail and non-retail pharmaceutical sales in each country.[17] If necessary, IQVIA projects its samples to represent 100% of the retail and non-retail sales in each country and reports >90% global precision in recent years.[17] However, IQVIA does not publicly disclose detailed information on data collection, projection, and validation.

Several sources were used to further characterize these countries. Countries were grouped based on their income and geographical regions per the World Bank (2020).[18] Population estimates and age-standardized IHD mortality rates (GBD 2019 causes of death were mapped to International Classification of Diseases[19]were obtained from the Global Burden of Disease (GBD) (2015-2019).[16] Health expenditures (total, public, out-of-pocket) were also obtained from the World Bank (2015-2018).[20] We projected the values of these estimates through 2020 by applying the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on data availability). Finally, whether statins were included in national essential medicine lists was determined, for reference, using the Global Essential Medicines database (2017).[9]

Measuring Statin Utilization

We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating to statins (C10AA).[21] As IQVIA does not report country-specific data for six countries in Centra America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and twelve countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined these countries in aggregate. We examined total market data, or retail and non-retail statin sales, for 52 countries (**eTable A**). In the 23 countries/groups that lack non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available (85% of all statins were dispensed through the retail sector).

To enable international comparisons over time, we converted statin sales (expressed in milligrams) into defined daily doses (DDDs) using the Anatomical Therapeutic Chemical Classification System developed by the WHO Collaborating Centre for Drug Statistics Methodology.[21] To account for differences in population size and age distribution, we report statin utilization as DDDs per 1000 population ≥40 years per day (TPD) for each country. Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating statin sale and population estimates.

Statistical Analysis

Descriptive statistics were used to examine trends and disparities in statin utilization from 2015 to 2020. Simple linear regressions were used to determine statistical significance in trends and disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-COVID-19 (April 2020 to October 2020) periods were also evaluated.

Fixed-effects panel regression analysis was used to quantify the association between economic and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin utilization estimates were logged in these models to enable interpretation as percent change associated with each unit of the independent variables examined. The independent variables included time-varying health expenditure per capita, out-of-pocket health expenditure (as a percentage of total expenditure), and age-standardized IHD mortality rate. Errors were clustered by year and country to account for serial correlation.

All *p*-values are two-sided. STATA version 17·1 was used for all statistical analyses.

This study was considered exempt by the Institutional Review Board at the University of Southern California because this study was not considered human subjects research.

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

RESULTS

As shown in **Figure 1**, global statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68·3 DDD/TPD ($p<0·01$). While statin utilization increased, to varying degrees, in all regions and income groups (all $p<0·05$), disparities persisted. In 2020, statin utilization was highest in North America and Europe (279·7 and 159·9 DDD/TPD, respectively) and substantially lower in Latin America, MENA, East Asia, South Asia, and sub-Saharan Africa (66·1, 64·1, 29·3, 16·1, and 24·7 DDD/TPD, respectively). From 2015 to 2020, statin utilization increased substantially in HICs (19·3% from 161·3 to 192·4 DDD/TPD) and LMICs (57·9% from 18·0 to 28·4 DDD/TPD). However, disparities by income group remained throughout this period—by 2020, statin utilization was seven times greater in HICs than in LMICs.

Figure 2 depicts country-specific variation in statin utilization. From 2015 to 2020, statin utilization increased or remained stable in most HICs, except Singapore (125·2 to 95·0, -24·1%, $p=0·27$), the United Arab Emirates (104·4 to 83·9, -19·7%, $p=0·02$), Luxembourg (216·6 to 185·3, -14·4%, $p<0·01$, and New Zealand (295·4 to 256·0, -13·4%, $p=0·12$). HICs located in North America and Europe have substantially higher statin utilization than comparable countries located in other regions. For example, in 2020, statin utilization in HICs ranged from over 300 DDD/TPD in Denmark, Canada, and United Kingdom to less than 50 DDD/TPD in Japan, Chile, and Kuwait.

From 2015 to 2020, statin utilization increased by more than 10% in nearly all LMICs. Exceptions included India (12·9 to 14·1, 9·1%, $p=0·02$), Malaysia (57·8 to 60·0, 3·9%, $p=0·41$), Ecuador (20·2 to 20·9, 3·6%, $p=0·09$), and Jordan (28·6 to 27·1, -5·4%, $p=0·20$), where utilization remained relatively stable, and Venezuela, where utilization sharply declined (92·3 to 13·8, -85·1%, $p<0·01$). Several LMICs had higher statin utilization than the global average in 2020, including Lebanon, Algeria, Brazil, Thailand, and South Africa (224·9, 111·8, 109·3, 96·8, and 85·4 DDD/TPD, respectively). Statin utilization is lower than 34 DDD/TPD (approximately half the global average) in 35 LMICs, including some of the most populous nations, such as China, India, Indonesia, Pakistan, Bangladesh, and Mexico.

Table 1 presents factors associated with changes in statin utilization. In HICs, only health expenditure per capita was significantly and positively associated with statin utilization. In LMICs, every $100 increase in health expenditure per capita was associated with a 17% increase in utilization, while every 10% increase in out-of-pocket health expenditure (as percentage of total health expenditure) was associated with a 11% decline in utilization (both $p<0{\cdot}05$). Greater rates of IHD mortality were also positively associated with more statin utilization in LMICs.

Compared with the pre–COVID-19 period, statin utilization declined by more than 5·0% in 41 countries, including 19 HICs and 22 LMICs (**Figure 3**). Severe disruptions in statin utilization—or ≥10% decline—were found in 13 HICs, including Australia (327·5 to 265·2 DDD/TPD, -19.0%), the United Arab Emirates (92·7 to 77·8 DDD/TPD, -16·1%), and Germany (180·6 to 160·6 DDD/TPD, -11·1%) (**eTable B**). Some of the most severe disruptions in statin utilization were observed among LMICs, including in Tunisia (76·5 to 52·7 DDD/TPD, -31·1%), Vietnam (23·3 to 17·2 DDD/TPD, -26·3%), Ukraine (32·1 to 26·1 DDD/TPD, -18·7%), and Mexico (28·4 to 23·8 DDD/TPD, -16·3%).

DISCUSSION

Using a global database, representing approximately 90% of the global population older than 40 years of age,[16] we found persistent disparities across regions, income groups, and countries in statin utilization which may contribute to worsening disparities in CVD mortality. While global statin utilization has increased 25% from 2015 to 2020, statin utilization remains higher in the "global north" (*e.g.*, North America, Europe, and Oceania) and in HICs than countries in other regions and LMICs.[4] In 2020, statin utilization was seventeen times higher in North America versus South Asia—the region with the highest age-adjusted CVD mortality rate in the world[4]—and seven times higher in HICs versus LMICs—that are experiencing a near universal increase in the number of CVD deaths.[1]

Statin utilization is also substantially lower in countries with disproportionately high age-standardized CVD mortality rates, namely LMICs in South Asia, MENA, and sub-Saharan Africa.[4] The WHO Global Non-Communicable Disease (NDC) Action Plan 2013-2020 aimed for a 25% reduction in premature deaths from NDC, especially CVD, from 2010 to 2025 by ensuring that at least half of adults at high CVD risk receive cardiovascular medicines and that 80% of public and private facilities have these essential medicines available on-site.[22] Growth in statin utilization in LMICs was concentrated among those countries with worsening IHD mortality—suggesting reactionary policies for the management of CVD morbidity and mortality versus preventative strategies for the provision of essential medicines. Together, our findings suggest that global efforts to reduce the burden of CVD need to be strengthened—statin utilization remains inequitable and suboptimal in LMICs, including those with worsening rates of CVD mortality.

Importantly, there is a substantial gap between CVD burden and statin utilization between HIC and LMICs. For example, statin utilization is very low (less than half the global average) in 70% of the LMICs examined, yet account for 68% of the global population of middle aged and older adults and 55% CVD deaths worldwide.[16] Forty-two percent of CVD deaths occur in China (25%), India (14%), and Indonesia (4%),[16] all of whom have very low statin utilization and together account for less than 11% of statins dispensed in the world. From 2015 to 2019, the IHD

mortality rate has declined or remained stable in most LMICs, with notable exceptions of Bangladesh (5%), Malaysia (5%), and Venezuela (10%) that have experienced substantial increases in recent years.[16] These countries, with worsening IHD mortality, have comparatively low statin utilization in given their regional and income group averages. However, Venezuela has also experienced substantial declines in statin utilization in this period—aggravating the IHD burden experienced by its populace.

Among LMICs, we found that every $100 increase in per capita health spending was associated with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-pocket health spending was associated with an 11% decline. These findings suggest that policy efforts to address global disparities in statin utilization, may need to increase health spending while shifting the burden of health spending from individuals to the public sector (either via the direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public investment in health (as measured by government health spending as a percentage of total expenditures) has declined in LMICs during the last two decades.[23] Only high-income and upper-middle countries have seen moderate increases in government health spending,[23] countries that consume a disproportionate share of statins. Out-of-pocket spending as a share of total health spending has remained stubbornly high in LMICs (above 40% and twice the percentage in HICs) during this period.[23] International aid—a major source of health spending in LMICs—is disproportionately directed to communicable diseases,[23] and these policies may aggravate global disparities in the use of essential medicines, including statins, and hinder efforts to reduce CVD mortality. International aid for health, which could alleviate costs of essential medicines for governments and the public, has also stagnated since 2013.[23]

Economic or political crises, which are often followed by sharp declines in total health spending, may also impact access to essential medicines. The starkest example is Venezuela, where statin utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as well as widespread and chronic shortages of essential medicines in the past decade.[20,24]

Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of medicines that impact domestic and international markets, transportation hurdles, and restrictions on movement (internationally and domestically and by providers and patients).[25] For example, early in the pandemic, active pharmaceutical ingredient production in China was severely curtailed—leading to shortages and delays in the production of medicines throughout the world, including in the United States, the European Union, and India.[26]

During the first six months of COVID-19 pandemic, statin utilization declined by more than 5% in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the pandemic.[27] However, the most severe disruptions in individual countries occurred in LMICs, which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19

disparities, including inequitable access to vaccinations,[27] may result in persistent disruptions to statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and country level CVD disparities between HIC and LMICs.

Limitations

This study had several limitations. First, comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and we account for missing non-retail sales through interpolation (using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available). Second, IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs. Finally, relationships between changes in statin utilization and country-level characteristics are not casual. However, the trends and disparities in statin utilization described in this study help evaluate the global progress in ensuring equitable access to essential medicines and inform efforts to reduce the global burden of CVD.

Conclusion

Despite a 25% increase in global statin utilization from 2015 to 2020, there are substantial and persistent regional and country-level disparities between HIC and LMICs. To address worsening CVD disparities, global, regional, and national policymakers should promote increased and equitable access to statins in LMICs.

Contributorship statements

- Guadamuz JS: Conceptualisation, data curation, formal analysis, methodology, validation, visualisation, software, writing – original draft, and writing – review & editing.
- Shooshtari A: Project administration and writing – original draft.
- Qato DM: Conceptualisation, funding acquisition, writing – original draft, and writing – review & editing

Competing interests

Dr. Guadamuz current reports employment with Flatiron Health, Inc, which is an independent subsidiary of the Roche Group. Flatiron Health, Inc., had no role in the design and conduct of the study, analysis or interpretation of the data, and preparation, or final approval of the article before publication.

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Data sharing statement

Data for this study will not be made available due to licensing agreements with IQVIA.

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Table 1. Factors Associated with Statin Utilization, 2015 to 2020

	Exponentiated Coefficient (CI) [a]	
	High-income countries	Low-and middle-income countries
No. [b]	40	33
Health expenditure per capita ($) [c]	1·01 (1·01, 1·02)*	1·17 (1·12, 1·22)*
OOP health expenditure (%) [d]	0·99 (0·91, 1·09)	0·89 (0·82, 0·96)*
IHD mortality rate [e]	1·00 (0·99, 1·02)	1·02 (1·01, 1·03)*

Notes: IHD=ischemic heart disease, OOP=out-of-pocket, No.=number.
a Statin utilization is defined as defined daily doses per 1000 population ≥ 40 y per day. Here logged statin utilization is examined. Data for 2020 is based on statin utilization from January to September 2020. **b** Countries in Central America and West Africa were excluded because IQVIA does not report country-specific information for these regions. **c** Increments of 100. **d** Increments of 10. **e** Age-standardized IHD mortality rate, increments of 10. * $p<0·05$

Figure Legends

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant ($p<0·05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

Figure 2. Statin Utilization by Country, 2015 to 2020

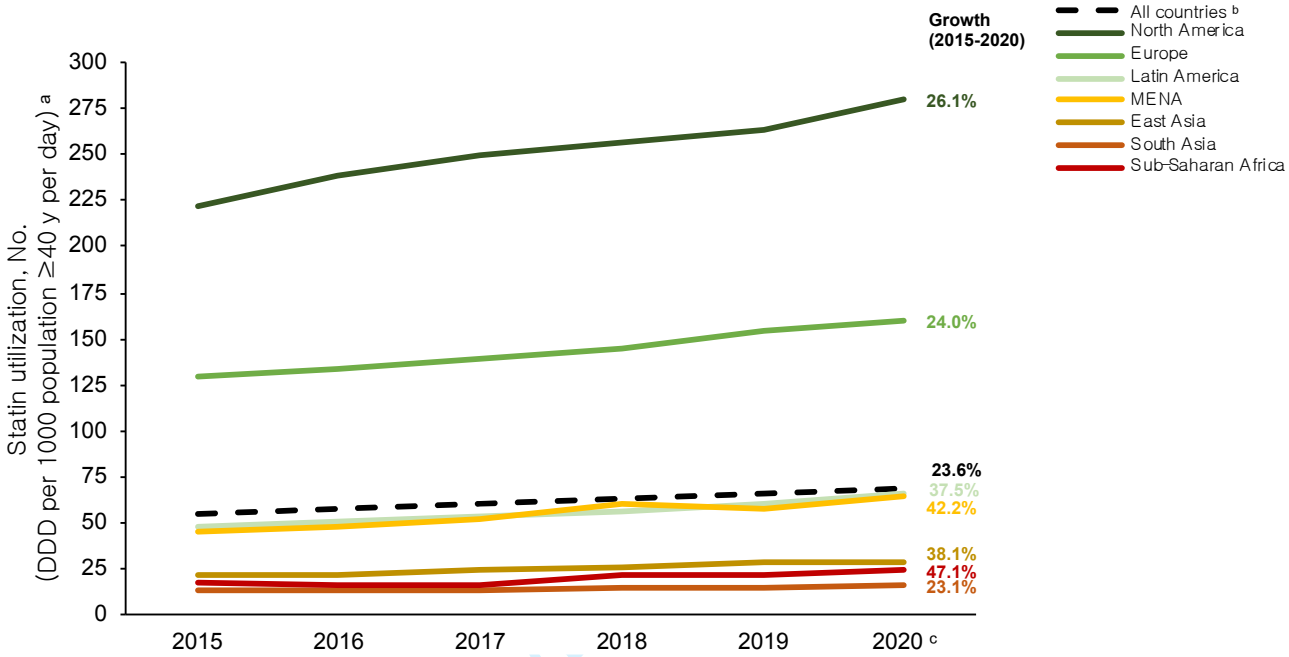
Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

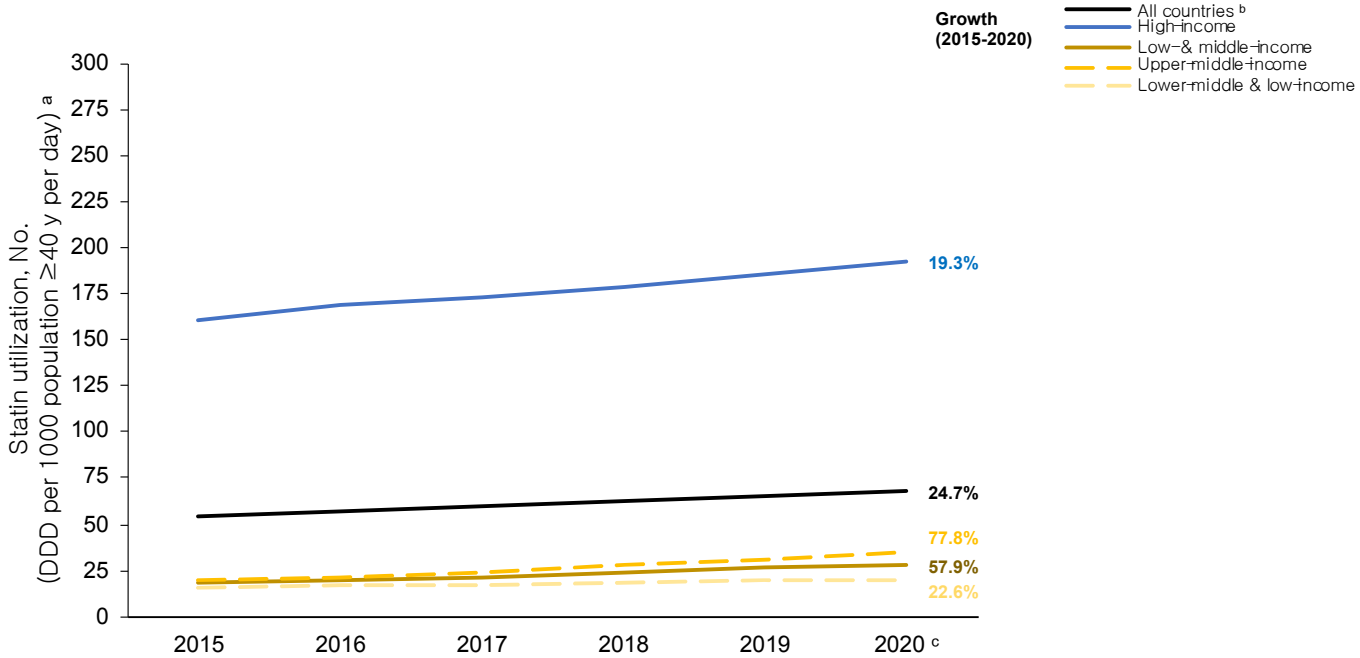
Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

a. By Region



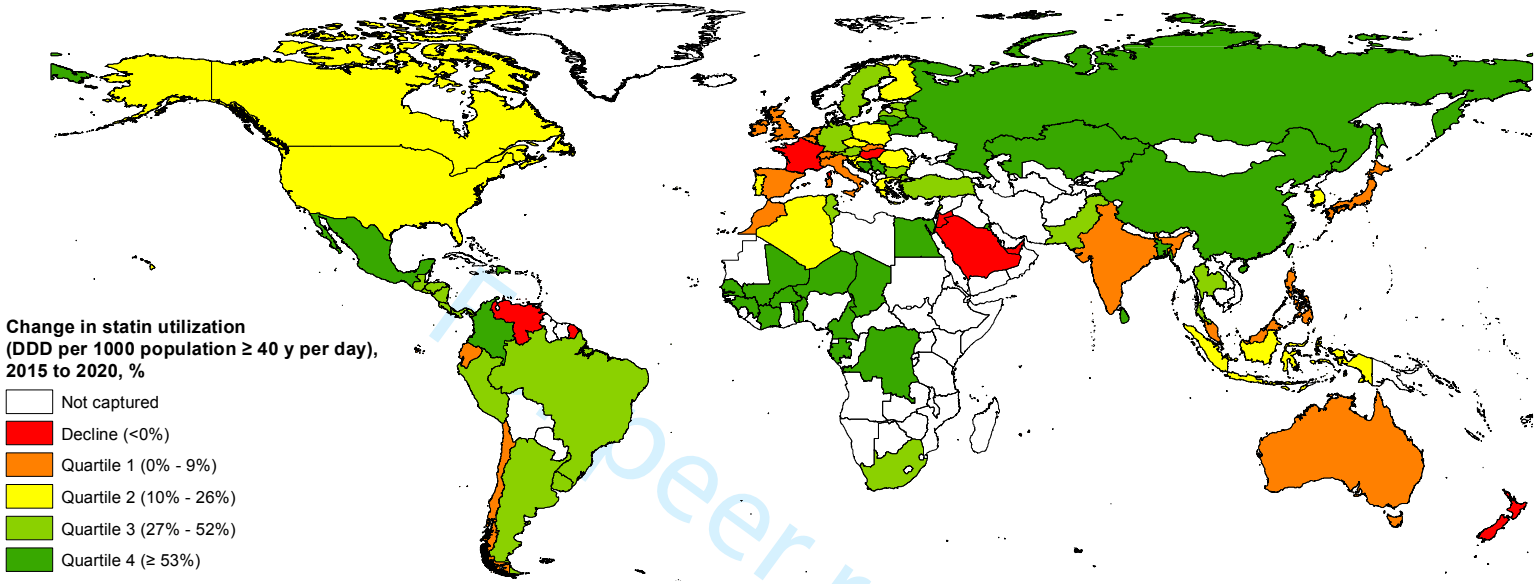
b. By Income



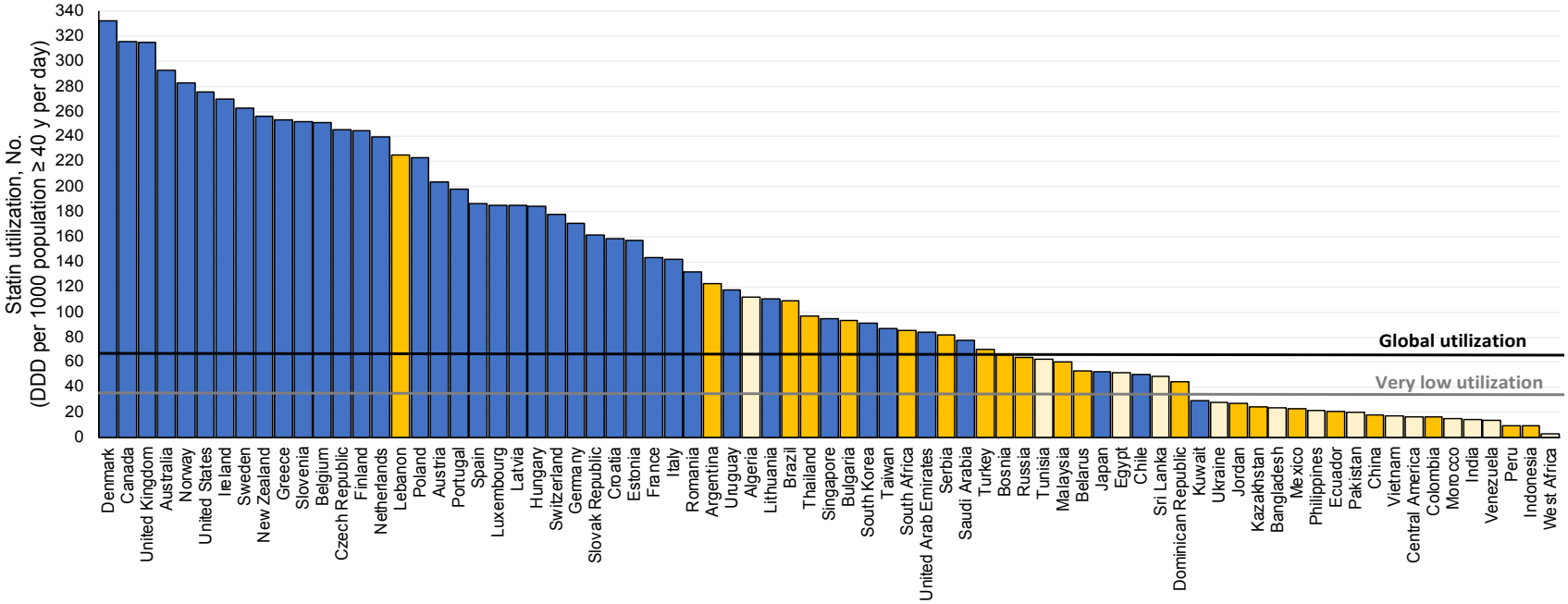
Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant (p<0·05), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by Country, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

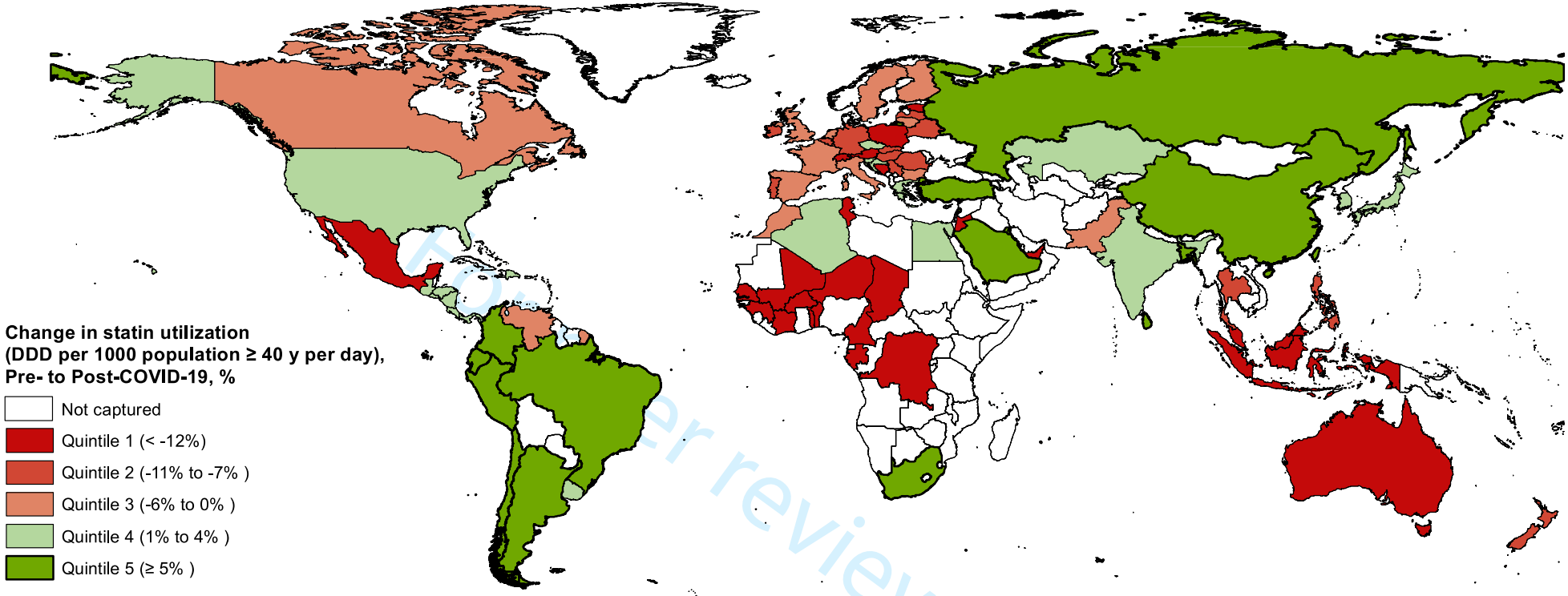


b. Statin utilization, 2020



Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization.

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020



Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

ONLINE SUPPLEMENT

eTable A. Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019) [d]
						Public	OOP		
Australia	Total market	East Asia & Pacific	High	$51,812	$5,425	69	18	-	56·1
Japan	Total market	East Asia & Pacific	High	$40,113	$4,267	84	13	-	29·9
New Zealand	Total market	East Asia & Pacific	High	$41,792	$4,037	75	13	-	75·0
Singapore	Total market	East Asia & Pacific	High	$59,798	$2,824	50	31	-	52·3
South Korea	Total market	East Asia & Pacific	High	$31,489	$2,543	58	33	-	35·0
Taiwan	Total market	East Asia & Pacific	High [e]	$28,371 [e]	$1,882 [e]			-	41·2
China	Total market	East Asia & Pacific	Upper middle	$10,500	$501	56	36	Yes	116·4
Indonesia	Total market	East Asia & Pacific	Upper middle	$3,870	$112	49	35	Yes	140·3
Malaysia	Total market	East Asia & Pacific	Upper middle	$10,402	$427	51	35	Yes	145·7
Thailand	Total market	East Asia & Pacific	Upper middle	$7,189	$276	76	11	Yes	52·6
Philippines	Total market	East Asia & Pacific	Lower middle	$3,299	$137	33	54	Yes	148·1
Vietnam	Total market	East Asia & Pacific	Lower middle	$2,786	$152	46	45	Yes	95·6
Austria	Total market	Europe	High	$48,105	$5,326	73	18	-	83·3
Belgium	Total market	Europe	High	$44,594	$4,913	76	19	-	54·8
Croatia	Total market	Europe	High	$13,828	$1,014	83	10	Yes	143·8
Czech Republic	Total market	Europe	High	$22,762	$1,766	83	14	Yes	149·0
Denmark	Total market	Europe	High	$60,909	$6,217	84	14	-	55·6
Estonia	Retail only	Europe	High	$23,312	$1,553	74	25	Yes	144·2
Finland	Total market	Europe	High	$49,041	$4,516	79	18	-	100·6
France	Total market	Europe	High	$38,625	$4,690	73	9	-	38·4
Germany	Total market	Europe	High	$45,724	$5,472	78	13	-	81·4
Greece	Retail only	Europe	High	$17,676	$1,567	52	36	-	91·9
Hungary	Total market	Europe	High	$15,899	$1,082	69	27	-	174·6
Ireland	Total market	Europe	High	$83,813	$5,489	74	12	-	74·7
Italy	Total market	Europe	High	$31,676	$2,989	74	24	-	55·3
Latvia	Total market	Europe	High	$17,620	$1,101	60	39	Yes	200·4
Lithuania	Total market	Europe	High	$19,998	$1,249	66	32	Yes	222·9
Luxembourg	Retail only	Europe	High	$115,874	$6,227	85	10	-	54·2
Netherlands	Total market	Europe	High	$52,304	$5,307	65	11	-	47·4
Norway	Total market	Europe	High	$67,294	$8,239	85	14	-	55·5
Poland	Total market	Europe	High	$15,656	$979	71	21	Yes	130·3
Portugal	Total market	Europe	High	$22,440	$2,215	61	30	Yes	45·8
Romania	Total market	Europe	High	$12,896	$687	80	19	Yes	177·1
Slovak Republic	Total market	Europe	High	$19,157	$1,300	79	19	Yes	198·9
Slovenia	Total market	Europe	High	$25,180	$2,170	72	12	Yes	59·0
Spain	Total market	Europe	High	$27,057	$2,736	70	22	-	45·0
Sweden	Total market	Europe	High	$51,926	$5,982	85	14	Yes	73·7
Switzerland	Total market	Europe	High	$86,602	$9,871	31	28	-	55·7
United Kingdom	Total market	Europe	High	$40,285	$4,315	79	17	-	66·8
Belarus	Total market	Europe	Upper middle	$6,411	$356	70	25	Yes	334·2
Bosnia & Herzegovina	Total market	Europe	Upper middle	$6,032	$540	70	29	Yes	162·9
Bulgaria	Total market	Europe	Upper middle	$9,976	$690	58	41	Yes	239·1
Russia	Total market	Europe	Upper middle	$10,127	$609	59	38	Yes	240·6
Serbia	Total market	Europe	Upper middle	$7,666	$617	59	38	Yes	204·4
Ukraine	Total market	Europe	Lower middle	$3,727	$228	48	49	Yes	424·2
Chile	Retail only	Latin America	High	$13,232	$1,456	51	33	Yes	50·4
Uruguay	Retail only	Latin America	High	$15,438	$1,590	73	17	Yes	67·0
Argentina	Retail only	Latin America	Upper middle	$8,442	$1,128	61	28	Yes	82·1
Brazil	Total market	Latin America	Upper middle	$6,797	$848	42	28	Yes	74·9
Colombia	Retail only	Latin America	Upper middle	$5,333	$513	72	15	Yes	75·3
Dominican Republic	Total market	Latin America	Upper middle	$7,268	$462	44	45	Yes	175·6
Ecuador	Retail only	Latin America	Upper middle	$5,600	$516	52	40	Yes	81·8
Mexico	Retail only	Latin America	Upper middle	$8,347	$520	50	42	Yes	100·0
Peru	Retail only	Latin America	Upper middle	$6,127	$369	63	29	Yes	48·7
Venezuela	Retail only	Latin America	Lower middle [f]	$1,739 [f]	$257	48	38	Yes	130·0
Central America [g]	Retail only								
Panama		Latin America	High	$12,269	$1,132	64	29	Yes	58·2
Costa Rica		Latin America	Upper middle	$12,077	$910	72	22	Yes	71·5
Guatemala		Latin America	Upper middle	$4,603	$260	36	58	Yes	106·3
El Salvador		Latin America	Lower middle	$3,799	$289	64	29	Yes	100·4
Honduras		Latin America	Lower middle	$2,406	$176	40	51	Yes	154·8
Nicaragua		Latin America	Lower middle	$1,905	$174	60	33	Yes	148·3

eTable A (continued). Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019)[d]
						Public	OOP		
Kuwait	Retail only	MENA	High	$32,373	$1,711	88	11	-	108·5
Saudi Arabia	Total market	MENA	High	$20,110	$1,485	62	14	-	205·6
United Arab Emirates	Retail only	MENA	High	$43,103	$1,817	52	13	-	175·4
Algeria	Retail only	MENA	Lower middle	$3,310	$256	66	33	Yes	237·3
Egypt	Retail only	MENA	Lower middle	$3,548	$126	29	62	Yes	359·3
Morocco	Retail only	MENA	Lower middle	$3,009	$175	40	47	Yes	278·5
Tunisia	Total market	MENA	Lower middle	$3,320	$252	57	39	Yes	193·5
Jordan	Retail only	MENA	Upper middle	$4,283	$330	49	31	Yes	121·9
Kazakhstan	Total market	MENA	Upper middle	$9,056	$276	61	33	-	251·4
Lebanon	Retail only	MENA	Upper middle	$4,891	$686	50	33	Yes	241·2
Turkey	Total market	MENA	Upper middle	$8,538	$390	77	17	-	121·0
Canada	Total market	North America	High	$43,242	$4,995	73	15	No	63·9
United States	Total market	North America	High	$63,544	$10,624	50	11	-	91·0
Bangladesh	Retail only	South Asia	Lower middle	$1,969	$42	17	74	No	111·2
India	Total market	South Asia	Lower middle	$1,901	$73	27	63	Yes	150·5
Pakistan	Retail only	South Asia	Lower middle	$1,194	$43	36	56	Yes	189·3
Sri Lanka	Retail only	South Asia	Lower middle	$3,682	$157	41	51	Yes	109·0
South Africa	Total market	Sub-Saharan Africa	Upper middle	$5,091	$526	54	8	Yes	81·4
West Africa [g]	Retail only								
Gabon		Sub-Saharan Africa	Upper middle	$7,006	$218	59	23	-	117·4
Benin		Sub-Saharan Africa	Lower middle	$1,291	$31	20	45	-	113·1
Cameroon		Sub-Saharan Africa	Lower middle	$1,499	$54	6	76	-	115·5
Côte d'Ivoire		Sub-Saharan Africa	Lower middle	$2,326	$72	29	39	-	122·0
Senegal		Sub-Saharan Africa	Lower middle	$1,488	$59	24	56	-	117·6
Burkina Faso		Sub-Saharan Africa	Low	$831	$40	43	36	-	130·2
Chad		Sub-Saharan Africa	Low	$614	$29	17	62	-	120·1
Democratic Republic of the Congo		Sub-Saharan Africa	Low	$557	$19	15	42	-	114·7
Guinea		Sub-Saharan Africa	Low	$1,194	$38	16	61	-	123·7
Mali		Sub-Saharan Africa	Low	$859	$35	28	34	-	116·0
Niger		Sub-Saharan Africa	Low	$565	$30	33	49	-	118·1
Togo		Sub-Saharan Africa	Low	$915	$42	17	56	-	134·9

Notes: EML=essential medicines list, IHD=ischemic heart disease, MENA=Middle East and North Africa, OOP=out-of-pocket. **a** Based on "sell-in" data or the volume purchased by retail (*e.g.*, pharmacies) or non-retail (*e.g.*, hospitals) sectors. As an exception, we used "sell-out" data, or the volume dispensed to patients, in the United Kingdom. We present data on the total market, or retail and non-retail drug sales, for 52 countries. In the 39 countries lacking non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available. In 2020, 85% of statins were dispensed via retail sectors (based on countries with data for retail and non-retail sectors). **b** World Bank. **c** World Health Organization. **d** Global Burden Disease, age-standardized IHD mortality rate. **e** Republic of China (Taiwan), Statistical Bureau. **f** Australian Department of Foreign Affairs & Trade, Venezuela Fact Sheet. **g** IQVIA does not provide country specific utilization for this region.

eTable B. Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Denmark	331·7	326·1	0·73	-1·7
Canada	322·9	314·3	0·68	-2·7
United Kingdom	324·5	308·8	0·14	-4·8
Australia	**327·5**	**265·2**	**0·26**	**-19·0**
Norway	**304·7**	**274·4**	**0·26**	**-9·9**
United States	271·6	271·2	·98	-0·1
Ireland	**280·3**	**257·8**	**0·38**	**-8·0**
Sweden	265·0	255·5	0·61	-3·6
New Zealand	**275·3**	**243·6**	**0·74**	**-11·5**
Greece	250·5	253·7	0·33	1·3
Slovenia	250·8	256·1	0·55	2·1
Belgium	**271·5**	**243·0**	**0·14**	**-10·5**
Czech Republic	241·7	248·3	0·15	2·7
Finland	253·0	243·2	0·47	-3·9
Netherlands	248·8	237·9	0·22	-4·4
Lebanon	201·9	232·4	0·17	15·1
Poland	**241·2**	**202·5**	**0·32**	**-16·0**
Austria	**223·5**	**190·8**	**0·18**	**-14·7**
Portugal	**205·4**	**184·8**	**0·43**	**-10·0**
Spain	188·6	180·1	0·51	-4·5
Luxembourg	**198·1**	**176·2**	**0·21**	**-11·0**
Latvia	**193·1**	**174·8**	**0·40**	**-9·5**
Hungary	**192·9**	**175·0**	**0·30**	**-9·3**
Switzerland	**202·8**	**170·1**	**0·15**	**-16·1**
Germany	**180·6**	**160·6**	**0·27**	**-11·1**
Slovak Republic	**175·5**	**155·2**	**0·09**	**-11·6**
Croatia	156·5	158·3	0·67	1·2
Estonia	**174·5**	**148·9**	**0·39**	**-14·7**
France	145·8	141·8	0·17	-2·7
Italy	**144·7**	**135·1**	**0·52**	**-6·6**
Romania	**141·6**	**125·4**	**0·34**	**-11·4**
Argentina	108·7	130·2	0·03	19·8
Uruguay	116·1	118·1	0·35	1·8
Algeria	108·9	111·6	0·88	2·5
Lithuania	**113·8**	**106·0**	**0·52**	**-6·8**
Brazil	107·0	112·0	0·25	4·7
Thailand	**102·6**	**92·9**	**0·34**	**-9·4**
Singapore	96·6	93·4	0·59	-3·3
Bulgaria	94·0	90·8	0·50	-3·4
South Korea	90·5	91·4	0·72	1·0
Taiwan	87·0	86·8	0·96	-0·2
South Africa	83·9	87·8	0·64	4·6
United Arab Emirates	**92·7**	**77·8**	**0·60**	**-16·1**
Serbia	**85·1**	**78·7**	**0·25**	**-7·5**
Saudi Arabia	72·1	81·1	0·26	12·4
Turkey	65·0	73·1	0·04	12·4
Bosnia	**70·5**	**61·2**	**0·37**	**-13·2**
Russia	58·6	66·2	0·08	13·0
Tunisia	**76·5**	**52·7**	**0·05**	**-31·1**
Malaysia	**65·9**	**53·7**	**0·21**	**-18·6**
Belarus	**55·0**	**51·0**	**0·25**	**-7·2**
Japan	53·2	54·1	0·82	1·7
Egypt	51·4	53·3	0·50	3·7
Chile	45·5	50·6	0·25	11·4
Sri Lanka	44·5	50·0	0·14	12·4
Dominican Republic	44·7	44·7	0·00	0·0
Kuwait	26·3	27·7	0·84	5·4
Ukraine	**32·1**	**26·1**	**0·22**	**-18·7**
Jordan	**28·7**	**24·1**	**0·50**	**-16·1**
Kazakhstan	22·8	22·9	0·97	0·8
Bangladesh	20·9	24·9	0·17	19·3

eTable B (continued). Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Mexico	**28·4**	**23·8**	**0·60**	**-16·3**
Philippines	**23·2**	**21·3**	**0·54**	**-8·1**
Ecuador	18·1	22·3	0·30	23·6
Pakistan	20·4	19·4	0·40	-4·8
China	16·2	18·3	0·17	13·3
Vietnam	**23·3**	**17·2**	**0·38**	**-26·3**
Central America [c, d]	16·1	16·7	0·75	4·0
Colombia	14·3	17·3	0·08	20·7
Morocco	**15·5**	**15·1**	**0·75**	**-3·1**
India	13·7	14·3	<0·01	4·3
Venezuela	**14·5**	**14·4**	**0·95**	**-0·9**
Peru	5·9	10·3	0·41	74·7
Indonesia	**10·9**	**8·9**	**0·32**	**-18·3**
West Africa [c, e]	**4·0**	**2·8**	**0·04**	**-30·1**

Notes: DDD=defined daily doses; No.=number.

a Statistical significance was determined using simple linear regression. Countries in bold declined ≥5%. **b** Sorted based on statin utilization in 2020, refer to **Error! Reference source not found.**. **c** IQVIA does not provide country specific utilization for this region. **d** Central American countries included Costa Rica, El Salvador, Honduras, Guatemala, Nicaragua, and Panama. **e** West African countries included Benin, Burkina Faso, Cameroon, Chad, Democratic Republic of the Congo, Gabon, Guinea, Ivory Coast, Mali, Niger, Senegal, and Togo.

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GLOBAL, REGIONAL, AND NATIONAL TRENDS IN STATIN UTILIZATION IN HIGH INCOME AND LOW- AND MIDDLE-INCOME COUNTRIES, 2015-2020

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Abstract

Objective: Prior studies have reported inequitable global access to essential medicines for cardiovascular disease (CVD) prevention, especially statins. Here we examine recent trends and disparities in statin utilization at the income group, regional, and country levels.

Design: Ecologic study. Pharmaceutical sales data was used to examine statin utilization in high-income counties (HICs) and low- and middle-income countries (LMICs) from 2015 to 2020. Population estimates were obtained from the Global Burden of Disease (GBD). Fixed-effects panel regression analysis was used to examine associations between statin utilization and country-level factors.

Setting: Global, including 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs).

Participants: Population older than 40 years of age.

Primary & secondary outcome measures: Statin utilization was measured using defined daily doses (DDD) per 1000 population ≥40 years per day (TPD).

Results: Globally, statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68.3 DDD/TPD in 2020. However, regional and income group disparities persisted during this period. In 2020, statin utilization was more than six-times higher in HICs than LMIC (192·4 vs. 28·4 DDD/TDP, $p<0·01$). Substantial disparities were also observed between LMICs, ranging from 3·1 DDDs/TDPs in West African nations to 225.0 DDD/TDP in Lebanon in 2020. While statin utilization increased in most LMIC between 2015 to 2020, several experienced declines in utilization, most notably Venezuela (-85·1%, from 92·3 to 14·0 DDD/TPD). In LMICs, every $100 increase in per capita health spending was associated with a 17% increase in statin utilization, while every 10% increase in out-of-pocket health spending was associated with a 11% decline (both $p<0·05$).

Conclusions: Despite global increases in statin utilization, there are substantial regional and country-level disparities between HIC and LMICs. To address global CVD disparities, policymakers should promote increased and equitable access to statins in LMICs.

Strengths and Limitations

- Pharmaceutical sales data was used to examine statin utilization in 41 high-income counties (HICs) and 50 low- and middle-income countries (LMICs) — representing approximately 90% of the global population older than 40 years of age.
- Comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries.
- IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs.
- Relationships between changes in statin utilization and country-level characteristics are not casual.

INTRODUCTION

Cardiovascular disease (CVD)—primarily ischemic heart disease (IHD)—causes approximately one-third of deaths worldwide.[1] While age-standardized CVD mortality rates have declined globally, the number of deaths due to CVD has increased from 12.1 million in 1990 to 18.6 million in 2019[1] and substantial regional, income group, and country level disparities exist.[2,3] For example, age-standardized CVD mortality rates were lowest in high-income countries (HICs) in Asia-Pacific, Europe, and North America and highest in low- and middle-income countries (LMICs) in Eastern Europe, Middle East and North Africa, and South Asia.[4] Moreover, the CVD burden has increased in nearly every LMIC during the past three decades.[1] Currently, LMICs account for approximately 80% of global CVD deaths.[2]

Medicines, alongside lifestyle changes such as diet, exercise, and smoking cessation, are a cornerstone of CVD prevention.[5] Statins (HMG-CoA reductase inhibitors) are particularly important because they are widely recommended for primary and secondary prevention—that is, among adults with and without known CVD.[5–7] Statins have been included in the World Health Organization (WHO) Model Essential Medicines List (EML)—used to develop national EMLs that guide public procurement—since 2007.[8] Despite statins steadily losing patent protections throughout the world since 2006,[8] only 60% of LMICs include these medicines in their EMLs as of 2017.[9] As medicines included in EMLs have higher availability in the private and public sectors,[10] these policies—as well as differences in income, health spending, and disease burden—may result in global disparities in statin utilization.

While utilization of preventative cardiovascular medicines, including statins, has increased globally in the past decade, large disparities exist.[11,12] For example, a study using pharmaceutical sales data from 65 countries found that consumption of cardiovascular medicines was approximately six-times higher in HICs than in LMICs in 2018.[11] A separate study using sales data from 83 countries found that consumption of lipid-lowering medicines was at least three-times higher in HICs than in LMICs in 2018.[12] However, these studies do not focus on the population at greatest need, adults older than 40 years,[6,7] nor do they evaluate country-level factors associated with statin utilization. Furthermore, an updated analysis of statin utilization is imperative considering the ongoing COVID-19 pandemic that has caused severe disruptions to the pharmaceutical supply chain and the provision of healthcare.[13–15]

This study used global pharmaceutical sales data to estimate statin utilization per population aged 40 years and older in 91 countries from 2015 to 2020. Disparities across and within regions and income groups were examined over time, including in the six months prior to and following the start of the COVID-19 pandemic. To inform global efforts to improve access to essential medicines, we also examined the extent to which country-level factors, such as gross domestic product (GDP), health spending, and underlying IHD burden, are associated with statin utilization.

Methods

Design and Data Sources

We conducted a cross-sectional study examining trends and disparities in statin utilization in 91 countries using pharmaceutical sales data collected by IQVIA (Multinational Integrated Data

Analysis System, MIDAS) from January 2015 to October 2020. These countries represent approximately 90% of the global population older than 40 years of age.[16] IQVIA samples pharmaceutical sales from multiple distribution channels (*e.g.,* manufacturers, wholesalers, and medical facilities) to develop nationally representative estimates of retail and non-retail pharmaceutical sales in each country.[17] If necessary, IQVIA projects its samples to represent 100% of the retail and non-retail sales in each country and reports >90% global precision in recent years.[17] However, IQVIA does not publicly disclose detailed information on data collection, projection, and validation.

Several sources were used to further characterize these countries. Countries were grouped based on their income and geographical regions per the World Bank (2020).[18] Population estimates and age-standardized IHD mortality rates (GBD 2019 causes of death were mapped to International Classification of Diseases[19]were obtained from the Global Burden of Disease (GBD) (2015-2019).[16] Health expenditures (total, public, out-of-pocket) were also obtained from the World Bank (2015-2018).[20] We projected the values of these estimates through 2020 by applying the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on data availability). Finally, whether statins were included in national essential medicine lists was determined, for reference, using the Global Essential Medicines database (2017).[9]

Measuring Statin Utilization

We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating to statins (C10AA).[21] As IQVIA does not report country-specific data for six countries in Centra America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and twelve countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined these countries in aggregate. We examined total market data, or retail and non-retail statin sales, for 52 countries (**eTable A**). In the 23 countries/groups that lack non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available (85% of all statins were dispensed through the retail sector).

To enable international comparisons over time, we converted statin sales (expressed in milligrams) into defined daily doses (DDDs) using the Anatomical Therapeutic Chemical Classification System developed by the WHO Collaborating Centre for Drug Statistics Methodology.[21] To account for differences in population size and age distribution, we report statin utilization as DDDs per 1000 population ≥40 years per day (TPD) for each country. Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating statin sale and population estimates.

Statistical Analysis

Descriptive statistics were used to examine trends and disparities in statin utilization from 2015 to 2020. Simple linear regressions were used to determine statistical significance in trends and disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-COVID-19 (April 2020 to October 2020) periods were also evaluated.

Fixed-effects panel regression analysis was used to quantify the association between economic and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin utilization estimates were logged in these models to enable interpretation as percent change associated with each unit of the independent variables examined. The independent variables included time-varying health expenditure per capita, out-of-pocket health expenditure (as a percentage of total expenditure), and age-standardized IHD mortality rate. Errors were clustered by year and country to account for serial correlation.

All *p*-values are two-sided. STATA version 17·1 was used for all statistical analyses.

This study was considered exempt by the Institutional Review Board at the University of Southern California because this study was not considered human subjects research.

Patient and Public Involvement

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

RESULTS

As shown in **Figure 1**, global statin utilization increased 24·7% from 54·7 DDD/TPD in 2015 to 68·3 DDD/TPD ($p<0·01$). While statin utilization increased, to varying degrees, in all regions and income groups (all $p<0·05$), disparities persisted. In 2020, statin utilization was highest in North America and Europe (279·7 and 159·9 DDD/TPD, respectively) and substantially lower in Latin America, MENA, East Asia, South Asia, and sub-Saharan Africa (66·1, 64·1, 29·3, 16·1, and 24·7 DDD/TPD, respectively). From 2015 to 2020, statin utilization increased substantially in HICs (19·3% from 161·3 to 192·4 DDD/TPD) and LMICs (57·9% from 18·0 to 28·4 DDD/TPD). However, disparities by income group remained throughout this period—by 2020, statin utilization was seven times greater in HICs than in LMICs.

Figure 2 depicts country-specific variation in statin utilization. From 2015 to 2020, statin utilization increased or remained stable in most HICs, except Singapore (125·2 to 95·0, -24·1%, $p=0·27$), the United Arab Emirates (104·4 to 83·9, -19·7%, $p=0·02$), Luxembourg (216·6 to 185·3, -14·4%, $p<0·01$, and New Zealand (295·4 to 256·0, -13·4%, $p=0·12$). HICs located in North America and Europe have substantially higher statin utilization than comparable countries located in other regions. For example, in 2020, statin utilization in HICs ranged from over 300 DDD/TPD in Denmark, Canada, and United Kingdom to less than 50 DDD/TPD in Japan, Chile, and Kuwait.

From 2015 to 2020, statin utilization increased by more than 10% in nearly all LMICs. Exceptions included India (12·9 to 14·1, 9·1%, $p=0·02$), Malaysia (57·8 to 60·0, 3·9%, $p=0·41$), Ecuador (20·2 to 20·9, 3·6%, $p=0·09$), and Jordan (28·6 to 27·1, -5·4%, $p=0·20$), where utilization remained relatively stable, and Venezuela, where utilization sharply declined (92·3 to 13·8, -85·1%, $p<0·01$). Several LMICs had higher statin utilization than the global average in 2020, including Lebanon, Algeria, Brazil, Thailand, and South Africa (224·9, 111·8, 109·3, 96·8, and 85·4 DDD/TPD, respectively). Statin utilization is lower than 34 DDD/TPD (approximately half the global average) in 35 LMICs, including some of the most populous nations, such as China, India, Indonesia, Pakistan, Bangladesh, and Mexico.

Table 1 presents factors associated with changes in statin utilization. In HICs, only health expenditure per capita was significantly and positively associated with statin utilization. In LMICs, every $100 increase in health expenditure per capita was associated with a 17% increase in utilization, while every 10% increase in out-of-pocket health expenditure (as percentage of total health expenditure) was associated with a 11% decline in utilization (both $p<0{\cdot}05$). Greater rates of IHD mortality were also positively associated with more statin utilization in LMICs.

Compared with the pre–COVID-19 period, statin utilization declined by more than 5·0% in 41 countries, including 19 HICs and 22 LMICs (**Figure 3**). Severe disruptions in statin utilization—or ≥10% decline—were found in 13 HICs, including Australia (327·5 to 265·2 DDD/TPD, -19.0%), the United Arab Emirates (92·7 to 77·8 DDD/TPD, -16·1%), and Germany (180·6 to 160·6 DDD/TPD, -11·1%) (**eTable B**). Some of the most severe disruptions in statin utilization were observed among LMICs, including in Tunisia (76·5 to 52·7 DDD/TPD, -31·1%), Vietnam (23·3 to 17·2 DDD/TPD, -26·3%), Ukraine (32·1 to 26·1 DDD/TPD, -18·7%), and Mexico (28·4 to 23·8 DDD/TPD, -16·3%).

DISCUSSION

Using a global database, representing approximately 90% of the global population older than 40 years of age,[16] we found persistent disparities across regions, income groups, and countries in statin utilization which may contribute to worsening disparities in CVD mortality. While global statin utilization has increased 25% from 2015 to 2020, statin utilization remains higher in the "global north" (*e.g.*, North America, Europe, and Oceania) and in HICs than countries in other regions and LMICs.[4] In 2020, statin utilization was seventeen times higher in North America versus South Asia—the region with the highest age-adjusted CVD mortality rate in the world[4]—and seven times higher in HICs versus LMICs—that are experiencing a near universal increase in the number of CVD deaths.[1]

Statin utilization is also substantially lower in countries with disproportionately high age-standardized CVD mortality rates, namely LMICs in South Asia, MENA, and sub-Saharan Africa.[4] The WHO Global Non-Communicable Disease (NDC) Action Plan 2013-2020 aimed for a 25% reduction in premature deaths from NDC, especially CVD, from 2010 to 2025 by ensuring that at least half of adults at high CVD risk receive cardiovascular medicines and that 80% of public and private facilities have these essential medicines available on-site.[22] Growth in statin utilization in LMICs was concentrated among those countries with worsening IHD mortality—suggesting reactionary policies for the management of CVD morbidity and mortality versus preventative strategies for the provision of essential medicines. Together, our findings suggest that global efforts to reduce the burden of CVD need to be strengthened—statin utilization remains inequitable and suboptimal in LMICs, including those with worsening rates of CVD mortality.

Importantly, there is a substantial gap between CVD burden and statin utilization between HIC and LMICs. For example, statin utilization is very low (less than half the global average) in 70% of the LMICs examined, yet account for 68% of the global population of middle aged and older adults and 55% CVD deaths worldwide.[16] Forty-two percent of CVD deaths occur in China (25%), India (14%), and Indonesia (4%),[16] all of whom have very low statin utilization and together account for less than 11% of statins dispensed in the world. From 2015 to 2019, the IHD

mortality rate has declined or remained stable in most LMICs, with notable exceptions of Bangladesh (5%), Malaysia (5%), and Venezuela (10%) that have experienced substantial increases in recent years.[16] These countries, with worsening IHD mortality, have comparatively low statin utilization in given their regional and income group averages. However, Venezuela has also experienced substantial declines in statin utilization in this period—aggravating the IHD burden experienced by its populace.

Among LMICs, we found that every $100 increase in per capita health spending was associated with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-pocket health spending was associated with an 11% decline. These findings suggest that policy efforts to address global disparities in statin utilization, may need to increase health spending while shifting the burden of health spending from individuals to the public sector (either via the direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public investment in health (as measured by government health spending as a percentage of total expenditures) has declined in LMICs during the last two decades.[23] Only high-income and upper-middle countries have seen moderate increases in government health spending,[23] countries that consume a disproportionate share of statins. Out-of-pocket spending as a share of total health spending has remained stubbornly high in LMICs (above 40% and twice the percentage in HICs) during this period.[23] International aid—a major source of health spending in LMICs—is disproportionately directed to communicable diseases,[23] and these policies may aggravate global disparities in the use of essential medicines, including statins, and hinder efforts to reduce CVD mortality. International aid for health, which could alleviate costs of essential medicines for governments and the public, has also stagnated since 2013.[23]

Economic or political crises, which are often followed by sharp declines in total health spending, may also impact access to essential medicines. The starkest example is Venezuela, where statin utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as well as widespread and chronic shortages of essential medicines in the past decade.[20,24]

Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of medicines that impact domestic and international markets, transportation hurdles, and restrictions on movement (internationally and domestically and by providers and patients).[25] For example, early in the pandemic, active pharmaceutical ingredient production in China was severely curtailed—leading to shortages and delays in the production of medicines throughout the world, including in the United States, the European Union, and India.[26]

During the first six months of COVID-19 pandemic, statin utilization declined by more than 5% in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the pandemic.[27] However, the most severe disruptions in individual countries occurred in LMICs, which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19

disparities, including inequitable access to vaccinations,[27] may result in persistent disruptions to statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and country level CVD disparities between HIC and LMICs.

Limitations

This study had several limitations. First, comparisons between regions, income groups, and countries should be interpreted in the context of the available data and total market coverage of the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and we account for missing non-retail sales through interpolation (using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available). Second, IQVIA does not provide sales data for most low-income countries; therefore, this study may underestimate the magnitude of statin utilization disparities between HICs and LMICs. Finally, relationships between changes in statin utilization and country-level characteristics are not casual. However, the trends and disparities in statin utilization described in this study help evaluate the global progress in ensuring equitable access to essential medicines and inform efforts to reduce the global burden of CVD.

Conclusion

Despite a 25% increase in global statin utilization from 2015 to 2020, there are substantial and persistent regional and country-level disparities between HIC and LMICs. To address worsening CVD disparities, global, regional, and national policymakers should promote increased and equitable access to statins in LMICs.

Contributorship Statement

Dr. Guadamuz developed the methodology, conducted the analyses, wrote the first draft, and received funding for the study. Mr. Shooshtari provided administrative support and supplied suggestions for the analyses, data interpretation, and article drafting. Dr. Qato provided critical revisions to the article resulting in improvements to the design, analyses, and interpretations, and received funding for the study. All authors reviewed, revised, and approved the final version of the article.

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Competing Interests Statement

Dr. Guadamuz current reports employment with Flatiron Health, Inc, which is an independent subsidiary of the Roche Group. Flatiron Health, Inc., had no role in the design and conduct of the study, analysis or interpretation of the data, and preparation, or final approval of the article before publication.

Ethical Approval Statement

This study was considered exempt by the Institutional Review Board at the University of Southern California because this study was not considered human subjects research.

Data Sharing Statement

Data for this study will not be made available due to licensing agreements with IQVIA.

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Table 1. Factors Associated with Statin Utilization, 2015 to 2020

	Exponentiated Coefficient (CI) [a]	
	High-income countries	Low-and middle-income countries
No. [b]	40	33
Health expenditure per capita ($) [c]	1·01 (1·01, 1·02)*	1·17 (1·12, 1·22)*
OOP health expenditure (%) [d]	0·99 (0·91, 1·09)	0·89 (0·82, 0·96)*
IHD mortality rate [e]	1·00 (0·99, 1·02)	1·02 (1·01, 1·03)*

Notes: IHD=ischemic heart disease, OOP=out-of-pocket, No.=number.
a Statin utilization is defined as defined daily doses per 1000 population ≥ 40 y per day. Here logged statin utilization is examined. Data for 2020 is based on statin utilization from January to September 2020. **b** Countries in Central America and West Africa were excluded because IQVIA does not report country-specific information for these regions. **c** Increments of 100. **d** Increments of 10. **e** Age-standardized IHD mortality rate, increments of 10. * $p<0·05$

Figure Legends

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant ($p<0·05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

Figure 2. Statin Utilization by Country, 2015 to 2020

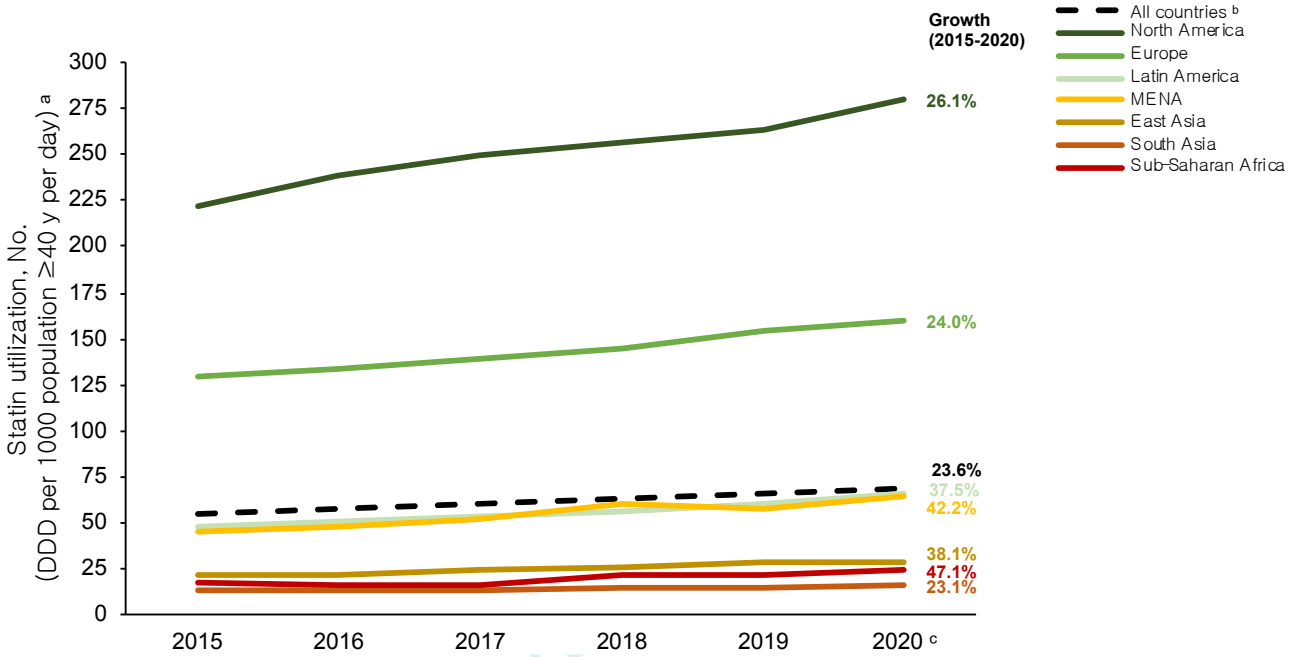
Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

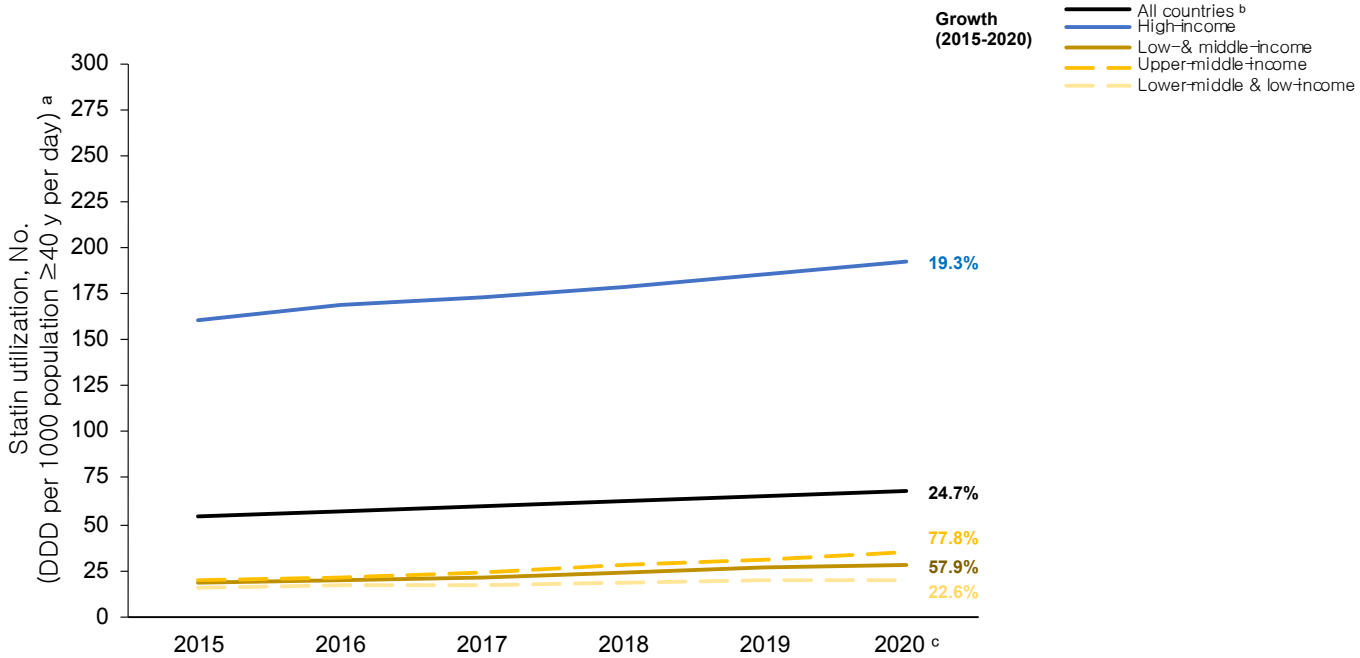
Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020

a. By Region



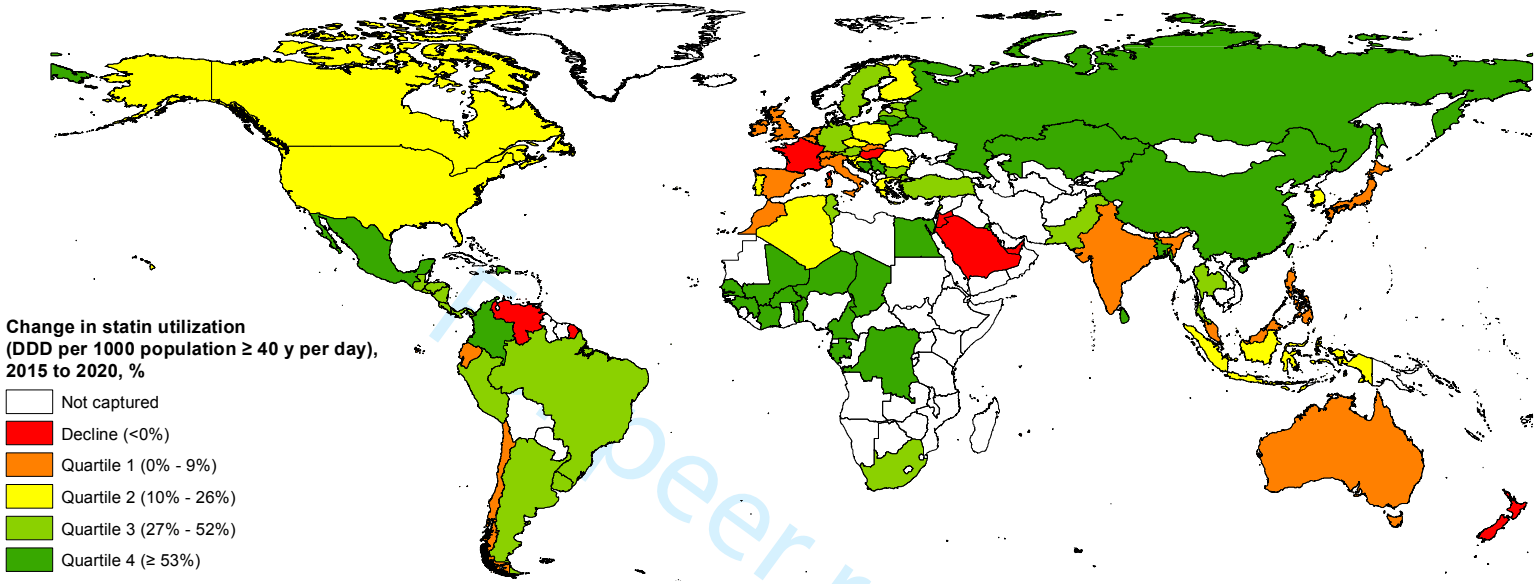
b. By Income



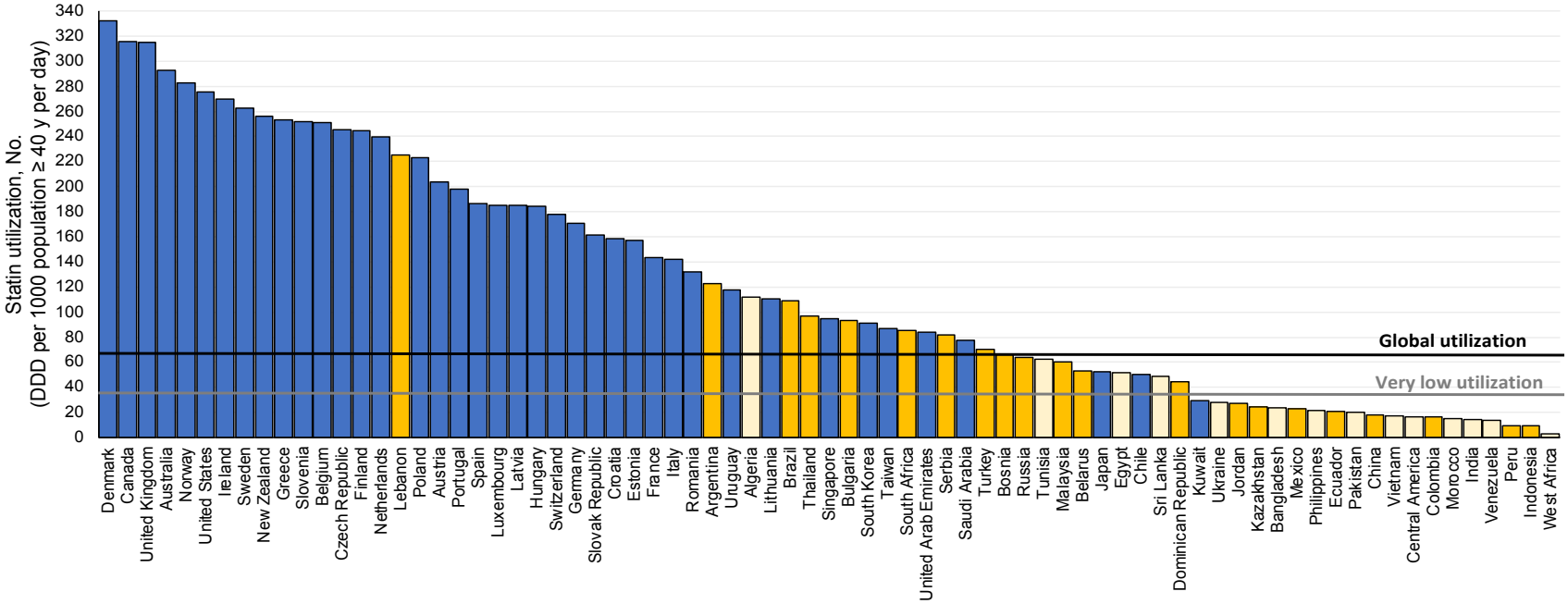
Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.
a All trends in statin utilization were statistically significant (p<0·05), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by Country, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

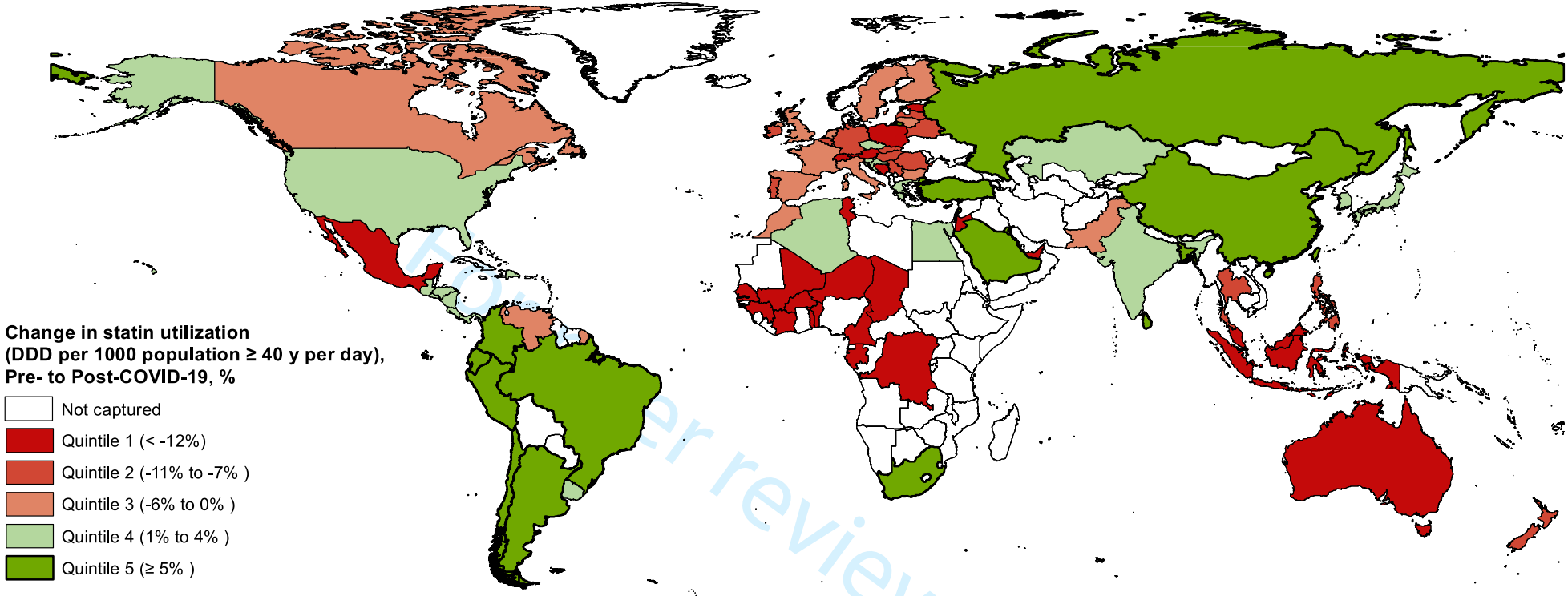


b. Statin utilization, 2020



Notes: DDD=defined daily doses; No.=number. Data for 2020 is based on statin utilization from January to September 2020. "Very low utilization" refers to utilization < ½ global statin utilization.

Figure 3. Change in Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020



Notes: DDD=defined daily doses; No.=number. Pre-COVID-19 includes the period of October 2019 to March 2020 and post-COVID-19 includes the period of April 2020 to October 2020.

ONLINE SUPPLEMENT

eTable A. Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019) [d]
						Public	OOP		
Australia	Total market	East Asia & Pacific	High	$51,812	$5,425	69	18	-	56·1
Japan	Total market	East Asia & Pacific	High	$40,113	$4,267	84	13	-	29·9
New Zealand	Total market	East Asia & Pacific	High	$41,792	$4,037	75	13	-	75·0
Singapore	Total market	East Asia & Pacific	High	$59,798	$2,824	50	31	-	52·3
South Korea	Total market	East Asia & Pacific	High	$31,489	$2,543	58	33	-	35·0
Taiwan	Total market	East Asia & Pacific	High [e]	$28,371 [e]	$1,882 [e]			-	41·2
China	Total market	East Asia & Pacific	Upper middle	$10,500	$501	56	36	Yes	116·4
Indonesia	Total market	East Asia & Pacific	Upper middle	$3,870	$112	49	35	Yes	140·3
Malaysia	Total market	East Asia & Pacific	Upper middle	$10,402	$427	51	35	Yes	145·7
Thailand	Total market	East Asia & Pacific	Upper middle	$7,189	$276	76	11	Yes	52·6
Philippines	Total market	East Asia & Pacific	Lower middle	$3,299	$137	33	54	Yes	148·1
Vietnam	Total market	East Asia & Pacific	Lower middle	$2,786	$152	46	45	Yes	95·6
Austria	Total market	Europe	High	$48,105	$5,326	73	18	-	83·3
Belgium	Total market	Europe	High	$44,594	$4,913	76	19	-	54·8
Croatia	Total market	Europe	High	$13,828	$1,014	83	10	Yes	143·8
Czech Republic	Total market	Europe	High	$22,762	$1,766	83	14	Yes	149·0
Denmark	Total market	Europe	High	$60,909	$6,217	84	14	-	55·6
Estonia	Retail only	Europe	High	$23,312	$1,553	74	25	Yes	144·2
Finland	Total market	Europe	High	$49,041	$4,516	79	18	-	100·6
France	Total market	Europe	High	$38,625	$4,690	73	9	-	38·4
Germany	Total market	Europe	High	$45,724	$5,472	78	13	-	81·4
Greece	Retail only	Europe	High	$17,676	$1,567	52	36	-	91·9
Hungary	Total market	Europe	High	$15,899	$1,082	69	27	-	174·6
Ireland	Total market	Europe	High	$83,813	$5,489	74	12	-	74·7
Italy	Total market	Europe	High	$31,676	$2,989	74	24	-	55·3
Latvia	Total market	Europe	High	$17,620	$1,101	60	39	Yes	200·4
Lithuania	Total market	Europe	High	$19,998	$1,249	66	32	Yes	222·9
Luxembourg	Retail only	Europe	High	$115,874	$6,227	85	10	-	54·2
Netherlands	Total market	Europe	High	$52,304	$5,307	65	11	-	47·4
Norway	Total market	Europe	High	$67,294	$8,239	85	14	-	55·5
Poland	Total market	Europe	High	$15,656	$979	71	21	Yes	130·3
Portugal	Total market	Europe	High	$22,440	$2,215	61	30	Yes	45·8
Romania	Total market	Europe	High	$12,896	$687	80	19	Yes	177·1
Slovak Republic	Total market	Europe	High	$19,157	$1,300	79	19	Yes	198·9
Slovenia	Total market	Europe	High	$25,180	$2,170	72	12	Yes	59·0
Spain	Total market	Europe	High	$27,057	$2,736	70	22	-	45·0
Sweden	Total market	Europe	High	$51,926	$5,982	85	14	Yes	73·7
Switzerland	Total market	Europe	High	$86,602	$9,871	31	28	-	55·7
United Kingdom	Total market	Europe	High	$40,285	$4,315	79	17	-	66·8
Belarus	Total market	Europe	Upper middle	$6,411	$356	70	25	Yes	334·2
Bosnia & Herzegovina	Total market	Europe	Upper middle	$6,032	$540	70	29	Yes	162·9
Bulgaria	Total market	Europe	Upper middle	$9,976	$690	58	41	Yes	239·1
Russia	Total market	Europe	Upper middle	$10,127	$609	59	38	Yes	240·6
Serbia	Total market	Europe	Upper middle	$7,666	$617	59	38	Yes	204·4
Ukraine	Total market	Europe	Lower middle	$3,727	$228	48	49	Yes	424·2
Chile	Retail only	Latin America	High	$13,232	$1,456	51	33	Yes	50·4
Uruguay	Retail only	Latin America	High	$15,438	$1,590	73	17	Yes	67·0
Argentina	Retail only	Latin America	Upper middle	$8,442	$1,128	61	28	Yes	82·1
Brazil	Total market	Latin America	Upper middle	$6,797	$848	42	28	Yes	74·9
Colombia	Retail only	Latin America	Upper middle	$5,333	$513	72	15	Yes	75·3
Dominican Republic	Total market	Latin America	Upper middle	$7,268	$462	44	45	Yes	175·6
Ecuador	Retail only	Latin America	Upper middle	$5,600	$516	52	40	Yes	81·8
Mexico	Retail only	Latin America	Upper middle	$8,347	$520	50	42	Yes	100·0
Peru	Retail only	Latin America	Upper middle	$6,127	$369	63	29	Yes	48·7
Venezuela	Retail only	Latin America	Lower middle [f]	$1,739 [f]	$257	48	38	Yes	130·0
Central America [g]	Retail only								
Panama		Latin America	High	$12,269	$1,132	64	29	Yes	58·2
Costa Rica		Latin America	Upper middle	$12,077	$910	72	22	Yes	71·5
Guatemala		Latin America	Upper middle	$4,603	$260	36	58	Yes	106·3
El Salvador		Latin America	Lower middle	$3,799	$289	64	29	Yes	100·4
Honduras		Latin America	Lower middle	$2,406	$176	40	51	Yes	154·8
Nicaragua		Latin America	Lower middle	$1,905	$174	60	33	Yes	148·3

eTable A (continued). Economic and Health Indicators of Countries Examined

	Drug utilization data source [a]	Region [b]	Income (2020) [b]	GDP per capita (2020) [b]	Health expenditure per capita (2018) [b]	% of health expenditure [b]		Statins included in EML (2017) [c]	IHD mortality rate (2019)[d]
						Public	OOP		
Kuwait	Retail only	MENA	High	$32,373	$1,711	88	11	-	108·5
Saudi Arabia	Total market	MENA	High	$20,110	$1,485	62	14	-	205·6
United Arab Emirates	Retail only	MENA	High	$43,103	$1,817	52	13	-	175·4
Algeria	Retail only	MENA	Lower middle	$3,310	$256	66	33	Yes	237·3
Egypt	Retail only	MENA	Lower middle	$3,548	$126	29	62	Yes	359·3
Morocco	Retail only	MENA	Lower middle	$3,009	$175	40	47	Yes	278·5
Tunisia	Total market	MENA	Lower middle	$3,320	$252	57	39	Yes	193·5
Jordan	Retail only	MENA	Upper middle	$4,283	$330	49	31	Yes	121·9
Kazakhstan	Total market	MENA	Upper middle	$9,056	$276	61	33	-	251·4
Lebanon	Retail only	MENA	Upper middle	$4,891	$686	50	33	Yes	241·2
Turkey	Total market	MENA	Upper middle	$8,538	$390	77	17	-	121·0
Canada	Total market	North America	High	$43,242	$4,995	73	15	No	63·9
United States	Total market	North America	High	$63,544	$10,624	50	11	-	91·0
Bangladesh	Retail only	South Asia	Lower middle	$1,969	$42	17	74	No	111·2
India	Total market	South Asia	Lower middle	$1,901	$73	27	63	Yes	150·5
Pakistan	Retail only	South Asia	Lower middle	$1,194	$43	36	56	Yes	189·3
Sri Lanka	Retail only	South Asia	Lower middle	$3,682	$157	41	51	Yes	109·0
South Africa	Total market	Sub-Saharan Africa	Upper middle	$5,091	$526	54	8	Yes	81·4
West Africa [g]	Retail only								
Gabon		Sub-Saharan Africa	Upper middle	$7,006	$218	59	23	-	117·4
Benin		Sub-Saharan Africa	Lower middle	$1,291	$31	20	45	-	113·1
Cameroon		Sub-Saharan Africa	Lower middle	$1,499	$54	6	76	-	115·5
Côte d'Ivoire		Sub-Saharan Africa	Lower middle	$2,326	$72	29	39	-	122·0
Senegal		Sub-Saharan Africa	Lower middle	$1,488	$59	24	56	-	117·6
Burkina Faso		Sub-Saharan Africa	Low	$831	$40	43	36	-	130·2
Chad		Sub-Saharan Africa	Low	$614	$29	17	62	-	120·1
Democratic Republic of the Congo		Sub-Saharan Africa	Low	$557	$19	15	42	-	114·7
Guinea		Sub-Saharan Africa	Low	$1,194	$38	16	61	-	123·7
Mali		Sub-Saharan Africa	Low	$859	$35	28	34	-	116·0
Niger		Sub-Saharan Africa	Low	$565	$30	33	49	-	118·1
Togo		Sub-Saharan Africa	Low	$915	$42	17	56	-	134·9

Notes: EML=essential medicines list, IHD=ischemic heart disease, MENA=Middle East and North Africa, OOP=out-of-pocket. **a** Based on "sell-in" data or the volume purchased by retail (*e.g.*, pharmacies) or non-retail (*e.g.*, hospitals) sectors. As an exception, we used "sell-out" data, or the volume dispensed to patients, in the United Kingdom. We present data on the total market, or retail and non-retail drug sales, for 52 countries. In the 39 countries lacking non-retail sector data, utilization was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail sectors for other countries in their region for which data was available. In 2020, 85% of statins were dispensed via retail sectors (based on countries with data for retail and non-retail sectors). **b** World Bank. **c** World Health Organization. **d** Global Burden Disease, age-standardized IHD mortality rate. **e** Republic of China (Taiwan), Statistical Bureau. **f** Australian Department of Foreign Affairs & Trade, Venezuela Fact Sheet. **g** IQVIA does not provide country specific utilization for this region.

eTable B. Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Denmark	331·7	326·1	0·73	-1·7
Canada	322·9	314·3	0·68	-2·7
United Kingdom	324·5	308·8	0·14	-4·8
Australia	**327·5**	**265·2**	**0·26**	**-19·0**
Norway	**304·7**	**274·4**	**0·26**	**-9·9**
United States	271·6	271·2	·98	-0·1
Ireland	**280·3**	**257·8**	**0·38**	**-8·0**
Sweden	265·0	255·5	0·61	-3·6
New Zealand	**275·3**	**243·6**	**0·74**	**-11·5**
Greece	250·5	253·7	0·33	1·3
Slovenia	250·8	256·1	0·55	2·1
Belgium	**271·5**	**243·0**	**0·14**	**-10·5**
Czech Republic	241·7	248·3	0·15	2·7
Finland	253·0	243·2	0·47	-3·9
Netherlands	248·8	237·9	0·22	-4·4
Lebanon	201·9	232·4	0·17	15·1
Poland	**241·2**	**202·5**	**0·32**	**-16·0**
Austria	**223·5**	**190·8**	**0·18**	**-14·7**
Portugal	**205·4**	**184·8**	**0·43**	**-10·0**
Spain	188·6	180·1	0·51	-4·5
Luxembourg	**198·1**	**176·2**	**0·21**	**-11·0**
Latvia	**193·1**	**174·8**	**0·40**	**-9·5**
Hungary	**192·9**	**175·0**	**0·30**	**-9·3**
Switzerland	**202·8**	**170·1**	**0·15**	**-16·1**
Germany	**180·6**	**160·6**	**0·27**	**-11·1**
Slovak Republic	**175·5**	**155·2**	**0·09**	**-11·6**
Croatia	156·5	158·3	0·67	1·2
Estonia	**174·5**	**148·9**	**0·39**	**-14·7**
France	145·8	141·8	0·17	-2·7
Italy	**144·7**	**135·1**	**0·52**	**-6·6**
Romania	**141·6**	**125·4**	**0·34**	**-11·4**
Argentina	108·7	130·2	0·03	19·8
Uruguay	116·1	118·1	0·35	1·8
Algeria	108·9	111·6	0·88	2·5
Lithuania	**113·8**	**106·0**	**0·52**	**-6·8**
Brazil	107·0	112·0	0·25	4·7
Thailand	**102·6**	**92·9**	**0·34**	**-9·4**
Singapore	96·6	93·4	0·59	-3·3
Bulgaria	94·0	90·8	0·50	-3·4
South Korea	90·5	91·4	0·72	1·0
Taiwan	87·0	86·8	0·96	-0·2
South Africa	83·9	87·8	0·64	4·6
United Arab Emirates	**92·7**	**77·8**	**0·60**	**-16·1**
Serbia	**85·1**	**78·7**	**0·25**	**-7·5**
Saudi Arabia	72·1	81·1	0·26	12·4
Turkey	65·0	73·1	0·04	12·4
Bosnia	**70·5**	**61·2**	**0·37**	**-13·2**
Russia	58·6	66·2	0·08	13·0
Tunisia	**76·5**	**52·7**	**0·05**	**-31·1**
Malaysia	**65·9**	**53·7**	**0·21**	**-18·6**
Belarus	**55·0**	**51·0**	**0·25**	**-7·2**
Japan	53·2	54·1	0·82	1·7
Egypt	51·4	53·3	0·50	3·7
Chile	45·5	50·6	0·25	11·4
Sri Lanka	44·5	50·0	0·14	12·4
Dominican Republic	44·7	44·7	0·00	0·0
Kuwait	26·3	27·7	0·84	5·4
Ukraine	**32·1**	**26·1**	**0·22**	**-18·7**
Jordan	**28·7**	**24·1**	**0·50**	**-16·1**
Kazakhstan	22·8	22·9	0·97	0·8
Bangladesh	20·9	24·9	0·17	19·3

eTable B (continued). Statin Utilization in Pre- and Post-COVID-19, October 2019 to September 2020

Countries/Regions [b]	Statin utilization, No. (DDD per 1000 population ≥ 40 y) [a] Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	*p*	Growth, %
Mexico	**28·4**	**23·8**	**0·60**	**-16·3**
Philippines	**23·2**	**21·3**	**0·54**	**-8·1**
Ecuador	18·1	22·3	0·30	23·6
Pakistan	20·4	19·4	0·40	-4·8
China	16·2	18·3	0·17	13·3
Vietnam	**23·3**	**17·2**	**0·38**	**-26·3**
Central America [c, d]	16·1	16·7	0·75	4·0
Colombia	14·3	17·3	0·08	20·7
Morocco	**15·5**	**15·1**	**0·75**	**-3·1**
India	13·7	14·3	<0·01	4·3
Venezuela	**14·5**	**14·4**	**0·95**	**-0·9**
Peru	5·9	10·3	0·41	74·7
Indonesia	**10·9**	**8·9**	**0·32**	**-18·3**
West Africa [c, e]	**4·0**	**2·8**	**0·04**	**-30·1**

Notes: DDD=defined daily doses; No.=number.

a Statistical significance was determined using simple linear regression. Countries in bold declined ≥5%. **b** Sorted based on statin utilization in 2020, refer to **Error! Reference source not found.**. **c** IQVIA does not provide country specific utilization for this region. **d** Central American countries included Costa Rica, El Salvador, Honduras, Guatemala, Nicaragua, and Panama. **e** West African countries included Benin, Burkina Faso, Cameroon, Chad, Democratic Republic of the Congo, Gabon, Guinea, Ivory Coast, Mali, Niger, Senegal, and Togo.