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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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3 **GLOBAL, REGIONAL, AND NATIONAL TRENDS IN STATIN UTILIZATION IN**
4 **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 countries (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 countries (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 2019¹ 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

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3 Analysis System, MIDAS) from January 2015 to October 2020. These countries represent
4 approximately 90% of the global population older than 40 years of age.¹⁶ IQVIA samples
5 pharmaceutical sales from multiple distribution channels (e.g., manufacturers, wholesalers, and
6 medical facilities) to develop nationally representative estimates of retail and non-retail
7 pharmaceutical sales in each country.¹⁷ If necessary, IQVIA projects its samples to represent
8 100% of the retail and non-retail sales in each country and reports >90% global precision in
9 recent years.¹⁷ However, IQVIA does not publicly disclose detailed information on data
10 collection, projection, and validation.
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14 Several sources were used to further characterize these countries. Countries were grouped based
15 on their income and geographical regions per the World Bank (2020).¹⁸ Population estimates and
16 age-standardized IHD mortality rates were obtained from the Global Burden of Disease (GBD)
17 (2015-2019).¹⁶ Health expenditures (total, public, out-of-pocket) were also obtained from the
18 World Bank (2015-2018).¹⁹ We projected the values of these estimates through 2020 by applying
19 the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on data
20 availability). Finally, whether statins were included in national essential medicine lists was
21 determined, for reference, using the Global Essential Medicines database (2017).⁹
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24 *Measuring Statin Utilization*

25 We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating
26 to statins (C10AA). As IQVIA does not report country-specific data for six countries in Centra
27 America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and twelve
28 countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Democratic
29 Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined these
30 countries in aggregate. We examined total market data, or retail and non-retail statin sales, for 52
31 countries (**eTable A**). In the 23 countries/groups that lack non-retail sector data, utilization was
32 estimated by interpolation, using the ratio of statin consumption in the retail and non-retail
33 sectors for other countries in their region for which data was available (85% of all statins were
34 dispensed through the retail sector).
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38 To enable international comparisons over time, we converted statin sales (expressed in
39 milligrams) into defined daily doses (DDD) using the Anatomical Therapeutic Chemical
40 Classification System developed by the WHO Collaborating Centre for Drug Statistics
41 Methodology.²⁰ To account for differences in population size and age distribution, we report
42 statin utilization as DDDs per 1000 population ≥ 40 years per day (TPD) for each country.
43 Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating
44 statin sale and population estimates.
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47 *Statistical Analysis*

48 Descriptive statistics were used to examine trends and disparities in statin utilization from 2015
49 to 2020. Simple linear regressions were used to determine statistical significance in trends and
50 disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-
51 COVID-19 (April 2020 to October 2020) periods were also evaluated.
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54 Fixed-effects panel regression analysis was used to quantify the association between economic
55 and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin
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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 $p < 0.05$). 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 $\geq 10\%$ 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 world⁴—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 (NCD) Action Plan 2013-2020 aimed for a 25% reduction in premature deaths from NCD, 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

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3 increases in recent years.¹⁶ These countries, with worsening IHD mortality, have comparatively
4 low statin utilization in given their regional and income group averages. However, Venezuela
5 has also experienced substantial declines in statin utilization in this period—aggravating the IHD
6 burden experienced by its populace.
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9 Among LMICs, we found that every \$100 increase in per capita health spending was associated
10 with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-
11 pocket health spending was associated with an 11% decline. These findings suggest that policy
12 efforts to address global disparities in statin utilization, may need to increase health spending
13 while shifting the burden of health spending from individuals to the public sector (either via the
14 direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public
15 investment in health (as measured by government health spending as a percentage of total
16 expenditures) has declined in LMICs during the last two decades.²² Only high-income and upper-
17 middle countries have seen moderate increases in government health spending,²² countries that
18 consume a disproportionate share of statins. Out-of-pocket spending as a share of total health
19 spending has remained stubbornly high in LMICs (above 40% and twice the percentage in HICs)
20 during this period.²² International aid—a major source of health spending in LMICs—is
21 disproportionately directed to communicable diseases,²² and these policies may aggravate global
22 disparities in the use of essential medicines, including statins, and hinder efforts to reduce CVD
23 mortality. International aid for health, which could alleviate costs of essential medicines for
24 governments and the public, has also stagnated since 2013.²²
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28 Economic or political crises, which are often followed by sharp declines in total health spending,
29 may also impact access to essential medicines. The starkest example is Venezuela, where statin
30 utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010
31 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as
32 well as widespread and chronic shortages of essential medicines in the past decade.^{19,23}
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35 Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of
36 medicines that impact domestic and international markets, transportation hurdles, and restrictions
37 on movement (internationally and domestically and by providers and patients).²⁴ For example,
38 early in the pandemic, active pharmaceutical ingredient production in China was severely
39 curtailed—leading to shortages and delays in the production of medicines throughout the world,
40 including in the United States, the European Union, and India.²⁵
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43 During the first six months of COVID-19 pandemic, statin utilization declined by more than 5%
44 in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the
45 post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more
46 severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the
47 pandemic.²⁶ However, the most severe disruptions in individual countries occurred in LMICs,
48 which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe
49 (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the
50 Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic
51 declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19
52 disparities, including inequitable access to vaccinations,²⁶ may result in persistent disruptions to
53 statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the
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3 COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and
4 country level CVD disparities between HIC and LMICs.
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6 7 *Limitations*

8 This study had several limitations. First, comparisons between regions, income groups, and
9 countries should be interpreted in the context of the available data and total market coverage of
10 the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91
11 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and
12 we account for missing non-retail sales through interpolation (using the ratio of statin
13 consumption in the retail and non-retail sectors for other countries in their region for which data
14 was available). Second, IQVIA does not provide sales data for most low-income countries;
15 therefore, this study may underestimate the magnitude of statin utilization disparities between
16 HICs and LMICs. Finally, relationships between changes in statin utilization and country-level
17 characteristics are not casual. However, the trends and disparities in statin utilization described in
18 this study help evaluate the global progress in ensuring equitable access to essential medicines
19 and inform efforts to reduce the global burden of CVD.
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21

22 23 **Conclusion**

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

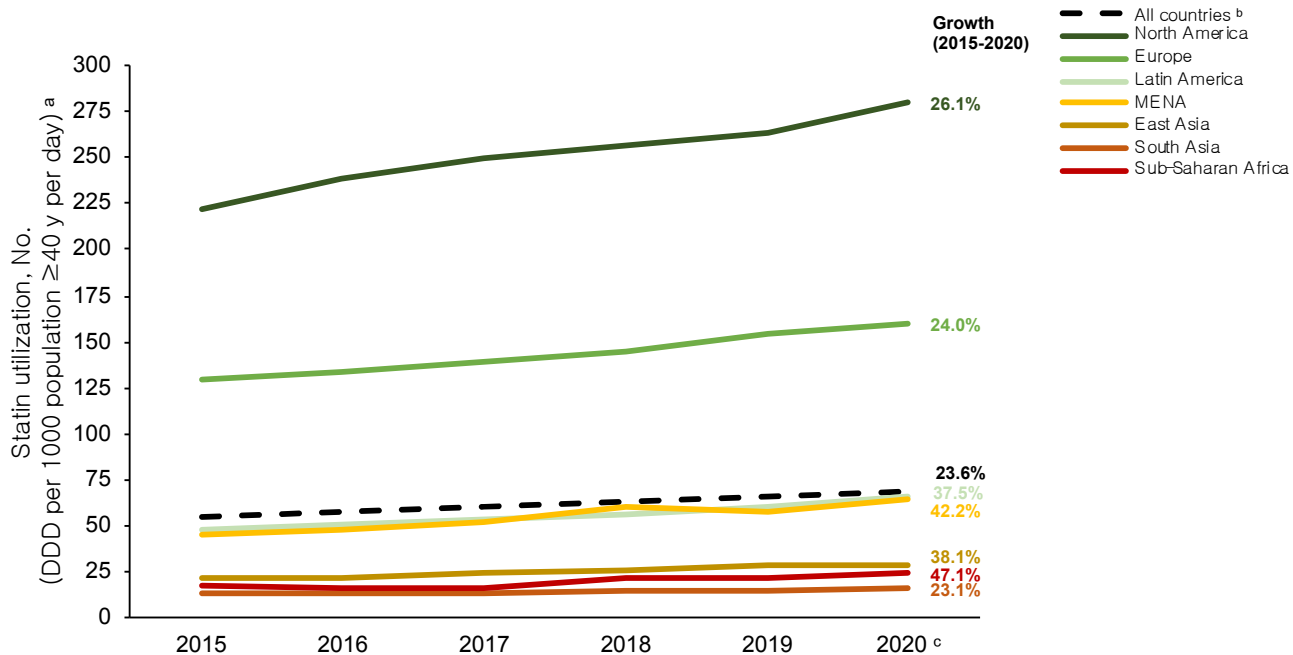
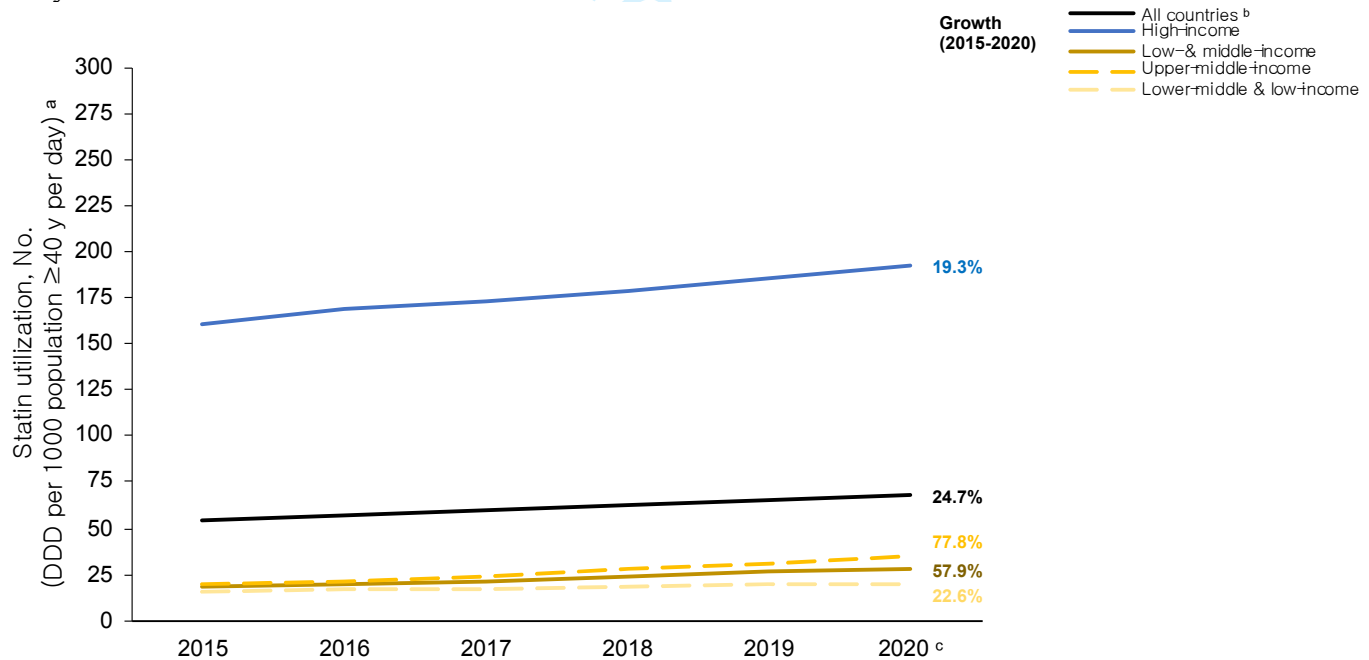
a All trends in statin utilization were statistically significant ($p < 0·05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

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 $< \frac{1}{2}$ 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.

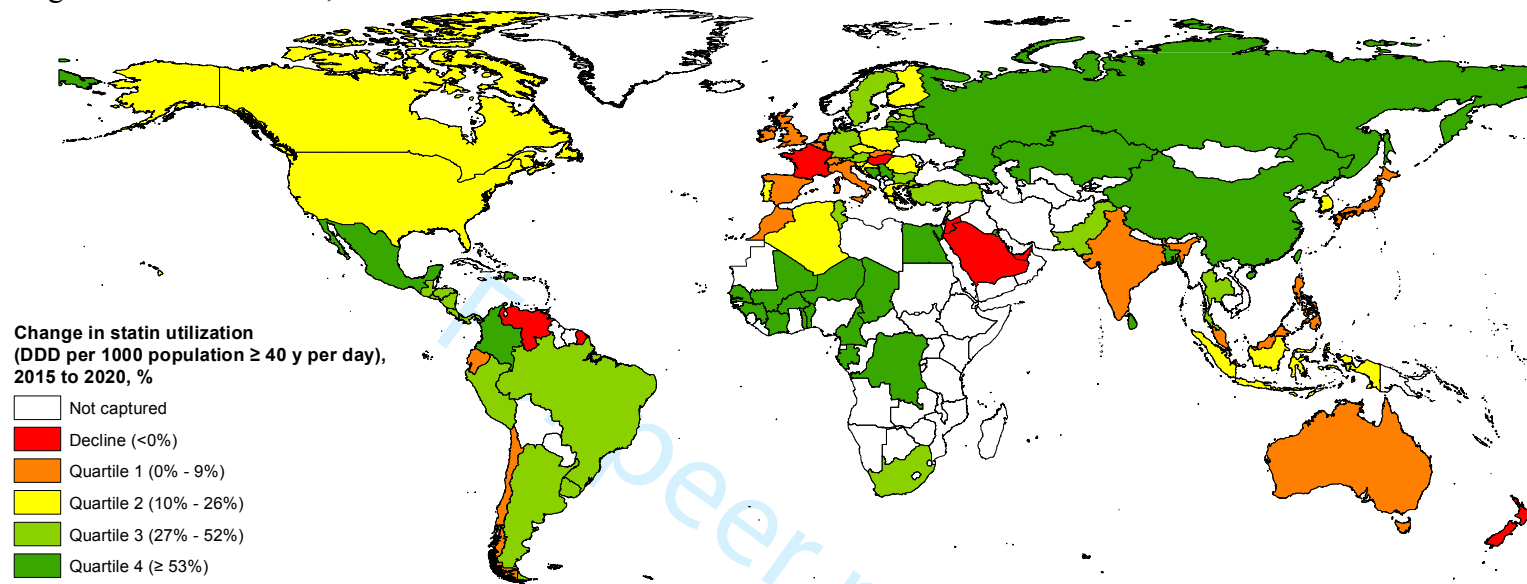
Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020**a. By Region****b. By Income**

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.

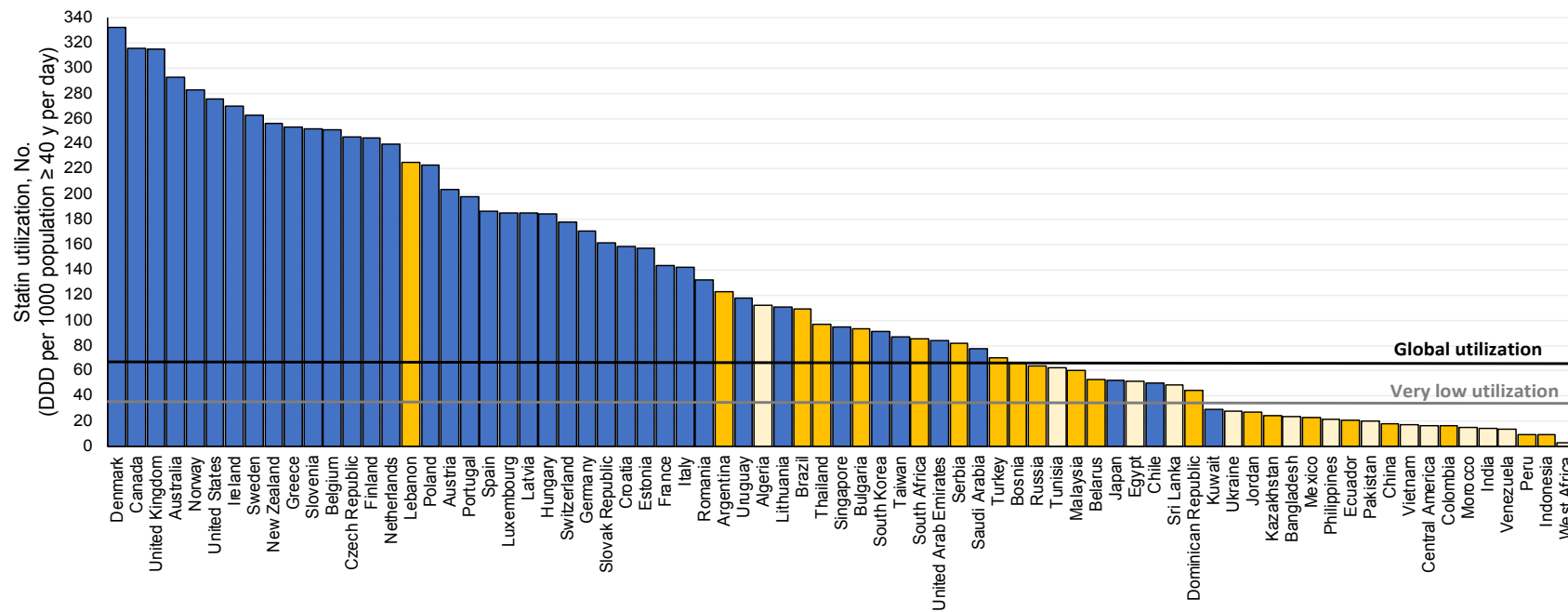
a All trends in statin utilization were statistically significant ($p<0.05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by County, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

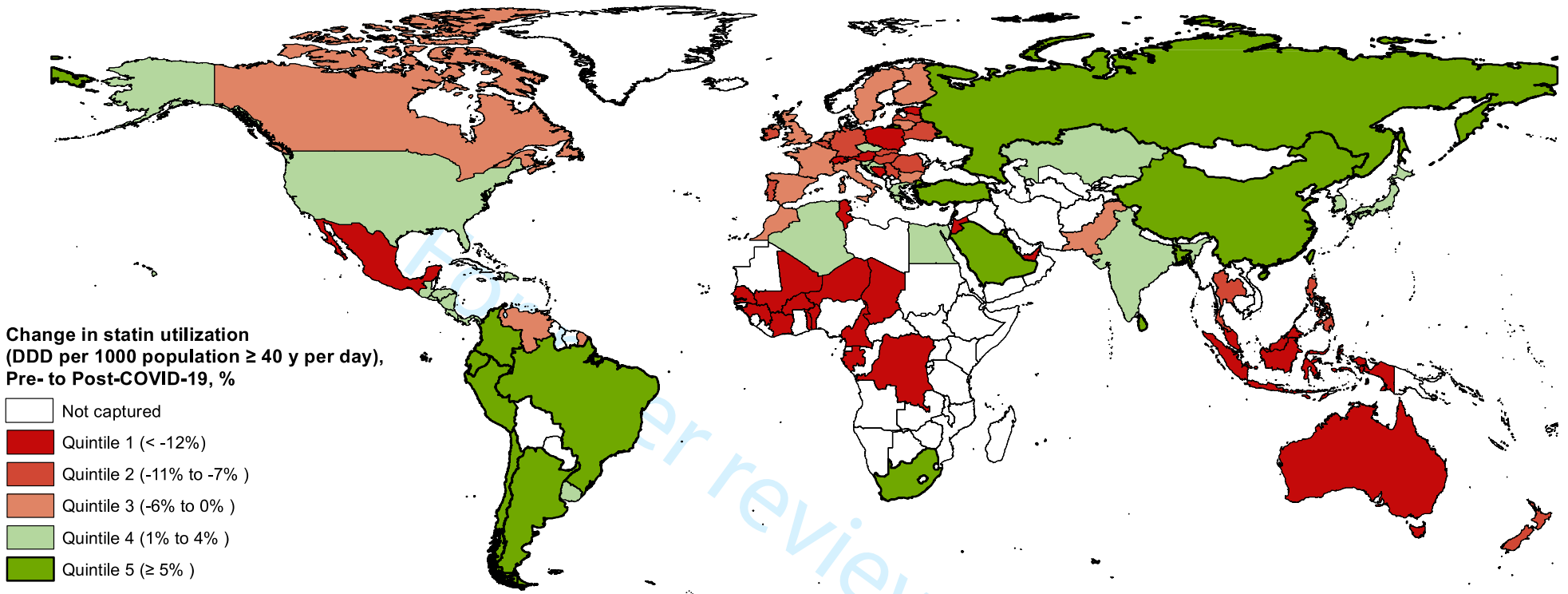


b. Statin utilization, 2020



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

<i>Countries/Regions</i> ^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)	<i>p</i>	Growth, %
	Denmark	331.7	326.1	0.73
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

<i>Countries/Regions</i> ^b	Statin utilization, No. (DDD per 1000 population \geq 40 y) ^a			Growth, %
	Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	<i>p</i>	
	Mexico	28.4	23.8	
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 \geq 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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1
2
3 47 **Abstract**

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5 49 **Background**

6 50 Prior studies have reported inequitable global access to essential medicines for cardiovascular
7 51 disease (CVD) prevention, especially statins. We examine recent trends and disparities in statin
8 52 utilization at the income group, regional, and country levels.

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10 54 **Methods**

11 55 Pharmaceutical sales data was used to examine statin utilization in 41 high-income countries
12 56 (HICs) and 50 low- and middle-income countries (LMICs) from 2015 to 2020. Utilization was
13 57 measured using defined daily doses (DDD) per 1000 population ≥ 40 years per day (TPD). Fixed-
14 58 effects panel regression analysis was used to examine associations between statin utilization and
15 59 country-level factors.

16 60

17 61 **Findings**

18 62 Globally, statin utilization increased 24.7% from 54.7 DDD/TPD in 2015 to 68.3 DDD/TPD in
19 63 2020. However, regional and income group disparities persisted during this period. In 2020,
20 64 statin utilization was more than six-times higher in HICs than LMIC (192.4 vs. 28.4 DDD/TDP,
21 65 $p < 0.01$). Substantial disparities were also observed between LMICs, ranging from 3.1
22 66 DDDs/TDPs in West African nations to 225.0 DDD/TDP in Lebanon in 2020. While statin
23 67 utilization increased in most LMIC between 2015 to 2020, several experienced declines in
24 68 utilization, most notably Venezuela (-85.1%, from 92.3 to 14.0 DDD/TPD). In LMICs, every
25 69 \$100 increase in per capita health spending was associated with a 17% increase in statin
26 70 utilization, while every 10% increase in out-of-pocket health spending was associated with a
27 71 11% decline (both $p < 0.05$).

28 72

29 73 **Interpretation**

30 74 Despite global increases in statin utilization, there are substantial regional and country-level
31 75 disparities between HIC and LMICs. To address global CVD disparities, policymakers should
32 76 promote increased and equitable access to statins in LMICs.

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Strengths and Limitations

- Pharmaceutical sales data was used to examine statin utilization in 41 high-income countries (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.

90 INTRODUCTION

91
92 Cardiovascular disease (CVD)—primarily ischemic heart disease (IHD)—causes approximately
93 one-third of deaths worldwide.[1] While age-standardized CVD mortality rates have declined
94 globally, the number of deaths due to CVD has increased from 12.1 million in 1990 to 18.6
95 million in 2019[1] and substantial regional, income group, and country level disparities
96 exist.[2,3] For example, age-standardized CVD mortality rates were lowest in high-income
97 countries (HICs) in Asia-Pacific, Europe, and North America and highest in low- and middle-
98 income countries (LMICs) in Eastern Europe, Middle East and North Africa, and South Asia.[4]
99 Moreover, the CVD burden has increased in nearly every LMIC during the past three decades.[1]
100 Currently, LMICs account for approximately 80% of global CVD deaths.[2]

101
102 Medicines, alongside lifestyle changes such as diet, exercise, and smoking cessation, are a
103 cornerstone of CVD prevention.[5] Statins (HMG-CoA reductase inhibitors) are particularly
104 important because they are widely recommended for primary and secondary prevention—that is,
105 among adults with and without known CVD.[5–7] Statins have been included in the World
106 Health Organization (WHO) Model Essential Medicines List (EML)—used to develop national
107 EMLs that guide public procurement—since 2007.[8] Despite statins steadily losing patent
108 protections throughout the world since 2006,[8] only 60% of LMICs include these medicines in
109 their EMLs as of 2017.[9] As medicines included in EMLs have higher availability in the private
110 and public sectors,[10] these policies—as well as differences in income, health spending, and
111 disease burden—may result in global disparities in statin utilization.

112
113 While utilization of preventative cardiovascular medicines, including statins, has increased
114 globally in the past decade, large disparities exist.[11,12] For example, a study using
115 pharmaceutical sales data from 65 countries found that consumption of cardiovascular medicines
116 was approximately six-times higher in HICs than in LMICs in 2018.[11] A separate study using
117 sales data from 83 countries found that consumption of lipid-lowering medicines was at least
118 three-times higher in HICs than in LMICs in 2018.[12] However, these studies do not focus on
119 the population at greatest need, adults older than 40 years,[6,7] nor do they evaluate country-
120 level factors associated with statin utilization. Furthermore, an updated analysis of statin
121 utilization is imperative considering the ongoing COVID-19 pandemic that has caused severe
122 disruptions to the pharmaceutical supply chain and the provision of healthcare.[13–15]

123
124 This study used global pharmaceutical sales data to estimate statin utilization per population
125 aged 40 years and older in 91 countries from 2015 to 2020. Disparities across and within regions
126 and income groups were examined over time, including in the six months prior to and following
127 the start of the COVID-19 pandemic. To inform global efforts to improve access to essential
128 medicines, we also examined the extent to which country-level factors, such as gross domestic
129 product (GDP), health spending, and underlying IHD burden, are associated with statin
130 utilization.

131 **Methods**

132 *Design and Data Sources*

133 We conducted a cross-sectional study examining trends and disparities in statin utilization in 91
134 countries using pharmaceutical sales data collected by IQVIA (Multinational Integrated Data
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3 136 Analysis System, MIDAS) from January 2015 to October 2020. These countries represent
4 137 approximately 90% of the global population older than 40 years of age.[16] IQVIA samples
5 138 pharmaceutical sales from multiple distribution channels (e.g., manufacturers, wholesalers, and
6 139 medical facilities) to develop nationally representative estimates of retail and non-retail
7 140 pharmaceutical sales in each country.[17] If necessary, IQVIA projects its samples to represent
8 141 100% of the retail and non-retail sales in each country and reports >90% global precision in
9 142 recent years.[17] However, IQVIA does not publicly disclose detailed information on data
10 143 collection, projection, and validation.
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13 145 Several sources were used to further characterize these countries. Countries were grouped based
14 146 on their income and geographical regions per the World Bank (2020).[18] Population estimates
15 147 and age-standardized IHD mortality rates (GBD 2019 causes of death were mapped to
16 148 International Classification of Diseases[19]were obtained from the Global Burden of Disease
17 149 (GBD) (2015-2019).[16] Health expenditures (total, public, out-of-pocket) were also obtained
18 150 from the World Bank (2015-2018).[20] We projected the values of these estimates through 2020
19 151 by applying the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on
20 152 data availability). Finally, whether statins were included in national essential medicine lists was
21 153 determined, for reference, using the Global Essential Medicines database (2017).[9]
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24 155 *Measuring Statin Utilization*

25 156 We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating
26 157 to statins (C10AA).[21] As IQVIA does not report country-specific data for six countries in
27 158 Centra America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and
28 159 twelve countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire,
29 160 Democratic Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined
30 161 these countries in aggregate. We examined total market data, or retail and non-retail statin sales,
31 162 for 52 countries (eTable A). In the 23 countries/groups that lack non-retail sector data, utilization
32 163 was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail
33 164 sectors for other countries in their region for which data was available (85% of all statins were
34 165 dispensed through the retail sector).
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37 167 To enable international comparisons over time, we converted statin sales (expressed in
38 168 milligrams) into defined daily doses (DDD) using the Anatomical Therapeutic Chemical
39 169 Classification System developed by the WHO Collaborating Centre for Drug Statistics
40 170 Methodology.[21] To account for differences in population size and age distribution, we report
41 171 statin utilization as DDDs per 1000 population ≥ 40 years per day (TPD) for each country.
42 172 Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating
43 173 statin sale and population estimates.
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46 175 *Statistical Analysis*

47 176 Descriptive statistics were used to examine trends and disparities in statin utilization from 2015
48 177 to 2020. Simple linear regressions were used to determine statistical significance in trends and
49 178 disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-
50 179 COVID-19 (April 2020 to October 2020) periods were also evaluated.
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3 181 Fixed-effects panel regression analysis was used to quantify the association between economic
4 182 and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin
5 183 utilization estimates were logged in these models to enable interpretation as percent change
6 184 associated with each unit of the independent variables examined. The independent variables
7 185 included time-varying health expenditure per capita, out-of-pocket health expenditure (as a
8 186 percentage of total expenditure), and age-standardized IHD mortality rate. Errors were clustered
9 187 by year and country to account for serial correlation.
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11 189 All *p*-values are two-sided. STATA version 17.1 was used for all statistical analyses.
12 190

13 191 This study was considered exempt by the Institutional Review Board at the University of
14 192 Southern California because this study was not considered human subjects research.
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16 194 No patients or members of the public were involved in the design of this study
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18 196 RESULTS

19 197 As shown in **Figure 1**, global statin utilization increased 24.7% from 54.7 DDD/TPD in 2015 to
20 198 68.3 DDD/TPD ($p<0.01$). While statin utilization increased, to varying degrees, in all regions
21 199 and income groups (all $p<0.05$), disparities persisted. In 2020, statin utilization was highest in
22 200 North America and Europe (279.7 and 159.9 DDD/TPD, respectively) and substantially lower in
23 201 Latin America, MENA, East Asia, South Asia, and sub-Saharan Africa (66.1, 64.1, 29.3, 16.1,
24 202 and 24.7 DDD/TPD, respectively). From 2015 to 2020, statin utilization increased substantially
25 203 in HICs (19.3% from 161.3 to 192.4 DDD/TPD) and LMICs (57.9% from 18.0 to 28.4
26 204 DDD/TPD). However, disparities by income group remained throughout this period—by 2020,
27 205 statin utilization was seven times greater in HICs than in LMICs.
28 206

29 207 **Figure 2** depicts country-specific variation in statin utilization. From 2015 to 2020, statin
30 208 utilization increased or remained stable in most HICs, except Singapore (125.2 to 95.0, -24.1%,
31 209 $p=0.27$), the United Arab Emirates (104.4 to 83.9, -19.7%, $p=0.02$), Luxembourg (216.6 to
32 210 185.3, -14.4%, $p<0.01$), and New Zealand (295.4 to 256.0, -13.4%, $p=0.12$). HICs located in
33 211 North America and Europe have substantially higher statin utilization than comparable countries
34 212 located in other regions. For example, in 2020, statin utilization in HICs ranged from over 300
35 213 DDD/TPD in Denmark, Canada, and United Kingdom to less than 50 DDD/TPD in Japan, Chile,
36 214 and Kuwait.
37 215

38 216 From 2015 to 2020, statin utilization increased by more than 10% in nearly all LMICs.
39 217 Exceptions included India (12.9 to 14.1, 9.1%, $p=0.02$), Malaysia (57.8 to 60.0, 3.9%, $p=0.41$),
40 218 Ecuador (20.2 to 20.9, 3.6%, $p=0.09$), and Jordan (28.6 to 27.1, -5.4%, $p=0.20$), where
41 219 utilization remained relatively stable, and Venezuela, where utilization sharply declined (92.3 to
42 220 13.8, -85.1%, $p<0.01$). Several LMICs had higher statin utilization than the global average in
43 221 2020, including Lebanon, Algeria, Brazil, Thailand, and South Africa (224.9, 111.8, 109.3,
44 222 96.8, and 85.4 DDD/TPD, respectively). Statin utilization is lower than 34 DDD/TPD
45 223 (approximately half the global average) in 35 LMICs, including some of the most populous
46 224 nations, such as China, India, Indonesia, Pakistan, Bangladesh, and Mexico.
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226 **Table 1** presents factors associated with changes in statin utilization. In HICs, only health
227 expenditure per capita was significantly and positively associated with statin utilization. In
228 LMICs, every \$100 increase in health expenditure per capita was associated with a 17% increase
229 in utilization, while every 10% increase in out-of-pocket health expenditure (as percentage of
230 total health expenditure) was associated with a 11% decline in utilization (both $p < 0.05$). Greater
231 rates of IHD mortality were also positively associated with more statin utilization in LMICs.

232
233 Compared with the pre-COVID-19 period, statin utilization declined by more than 5.0% in 41
234 countries, including 19 HICs and 22 LMICs (**Figure 3**). Severe disruptions in statin utilization—
235 or $\geq 10\%$ decline—were found in 13 HICs, including Australia (327.5 to 265.2 DDD/TPD, -
236 19.0%), the United Arab Emirates (92.7 to 77.8 DDD/TPD, -16.1%), and Germany (180.6 to
237 160.6 DDD/TPD, -11.1%) (**eTable B**). Some of the most severe disruptions in statin utilization
238 were observed among LMICs, including in Tunisia (76.5 to 52.7 DDD/TPD, -31.1%), Vietnam
239 (23.3 to 17.2 DDD/TPD, -26.3%), Ukraine (32.1 to 26.1 DDD/TPD, -18.7%), and Mexico
240 (28.4 to 23.8 DDD/TPD, -16.3%).

241 242 **DISCUSSION**

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

252
253 Statin utilization is also substantially lower in countries with disproportionately high age-
254 standardized CVD mortality rates, namely LMICs in South Asia, MENA, and sub-Saharan
255 Africa.[4] The WHO Global Non-Communicable Disease (NCD) Action Plan 2013-2020 aimed
256 for a 25% reduction in premature deaths from NCD, especially CVD, from 2010 to 2025 by
257 ensuring that at least half of adults at high CVD risk receive cardiovascular medicines and that
258 80% of public and private facilities have these essential medicines available on-site.[22] Growth
259 in statin utilization in LMICs was concentrated among those countries with worsening IHD
260 mortality—suggesting reactionary policies for the management of CVD morbidity and mortality
261 versus preventative strategies for the provision of essential medicines. Together, our findings
262 suggest that global efforts to reduce the burden of CVD need to be strengthened—statin
263 utilization remains inequitable and suboptimal in LMICs, including those with worsening rates
264 of CVD mortality.

265
266 Importantly, there is a substantial gap between CVD burden and statin utilization between HIC
267 and LMICs. For example, statin utilization is very low (less than half the global average) in 70%
268 of the LMICs examined, yet account for 68% of the global population of middle aged and older
269 adults and 55% CVD deaths worldwide.[16] Forty-two percent of CVD deaths occur in China
270 (25%), India (14%), and Indonesia (4%),[16] all of whom have very low statin utilization and
271 together account for less than 11% of statins dispensed in the world. From 2015 to 2019, the IHD

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3 272 mortality rate has declined or remained stable in most LMICs, with notable exceptions of
4 273 Bangladesh (5%), Malaysia (5%), and Venezuela (10%) that have experienced substantial
5 274 increases in recent years.[16] These countries, with worsening IHD mortality, have
6 275 comparatively low statin utilization in given their regional and income group averages. However,
7 276 Venezuela has also experienced substantial declines in statin utilization in this period—
8 277 aggravating the IHD burden experienced by its populace.
9 278

10 279 Among LMICs, we found that every \$100 increase in per capita health spending was associated
11 280 with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-
12 281 pocket health spending was associated with an 11% decline. These findings suggest that policy
13 282 efforts to address global disparities in statin utilization, may need to increase health spending
14 283 while shifting the burden of health spending from individuals to the public sector (either via the
15 284 direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public
16 285 investment in health (as measured by government health spending as a percentage of total
17 286 expenditures) has declined in LMICs during the last two decades.[23] Only high-income and
18 287 upper-middle countries have seen moderate increases in government health spending,[23]
19 288 countries that consume a disproportionate share of statins. Out-of-pocket spending as a share of
20 289 total health spending has remained stubbornly high in LMICs (above 40% and twice the
21 290 percentage in HICs) during this period.[23] International aid—a major source of health spending
22 291 in LMICs—is disproportionately directed to communicable diseases,[23] and these policies may
23 292 aggravate global disparities in the use of essential medicines, including statins, and hinder efforts
24 293 to reduce CVD mortality. International aid for health, which could alleviate costs of essential
25 294 medicines for governments and the public, has also stagnated since 2013.[23]
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27 296 Economic or political crises, which are often followed by sharp declines in total health spending,
28 297 may also impact access to essential medicines. The starkest example is Venezuela, where statin
29 298 utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010
30 299 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as
31 300 well as widespread and chronic shortages of essential medicines in the past decade.[20,24]
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33 302 Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of
34 303 medicines that impact domestic and international markets, transportation hurdles, and restrictions
35 304 on movement (internationally and domestically and by providers and patients).[25] For example,
36 305 early in the pandemic, active pharmaceutical ingredient production in China was severely
37 306 curtailed—leading to shortages and delays in the production of medicines throughout the world,
38 307 including in the United States, the European Union, and India.[26]
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40 309 During the first six months of COVID-19 pandemic, statin utilization declined by more than 5%
41 310 in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the
42 311 post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more
43 312 severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the
44 313 pandemic.[27] However, the most severe disruptions in individual countries occurred in LMICs,
45 314 which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe
46 315 (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the
47 316 Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic
48 317 declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19
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3 318 disparities, including inequitable access to vaccinations,[27] may result in persistent disruptions
4 319 to statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the
5 320 COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and
6 321 country level CVD disparities between HIC and LMICs.
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9 323 *Limitations*

10 324 This study had several limitations. First, comparisons between regions, income groups, and
11 325 countries should be interpreted in the context of the available data and total market coverage of
12 326 the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91
13 327 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and
14 328 we account for missing non-retail sales through interpolation (using the ratio of statin
15 329 consumption in the retail and non-retail sectors for other countries in their region for which data
16 330 was available). Second, IQVIA does not provide sales data for most low-income countries;
17 331 therefore, this study may underestimate the magnitude of statin utilization disparities between
18 332 HICs and LMICs. Finally, relationships between changes in statin utilization and country-level
19 333 characteristics are not casual. However, the trends and disparities in statin utilization described in
20 334 this study help evaluate the global progress in ensuring equitable access to essential medicines
21 335 and inform efforts to reduce the global burden of CVD.
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25 337 **Conclusion**

26 338 Despite a 25% increase in global statin utilization from 2015 to 2020, there are substantial and
27 339 persistent regional and country-level disparities between HIC and LMICs. To address worsening
28 340 CVD disparities, global, regional, and national policymakers should promote increased and
29 341 equitable access to statins in LMICs.
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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 \geq 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. * $p < 0\cdot05$

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.

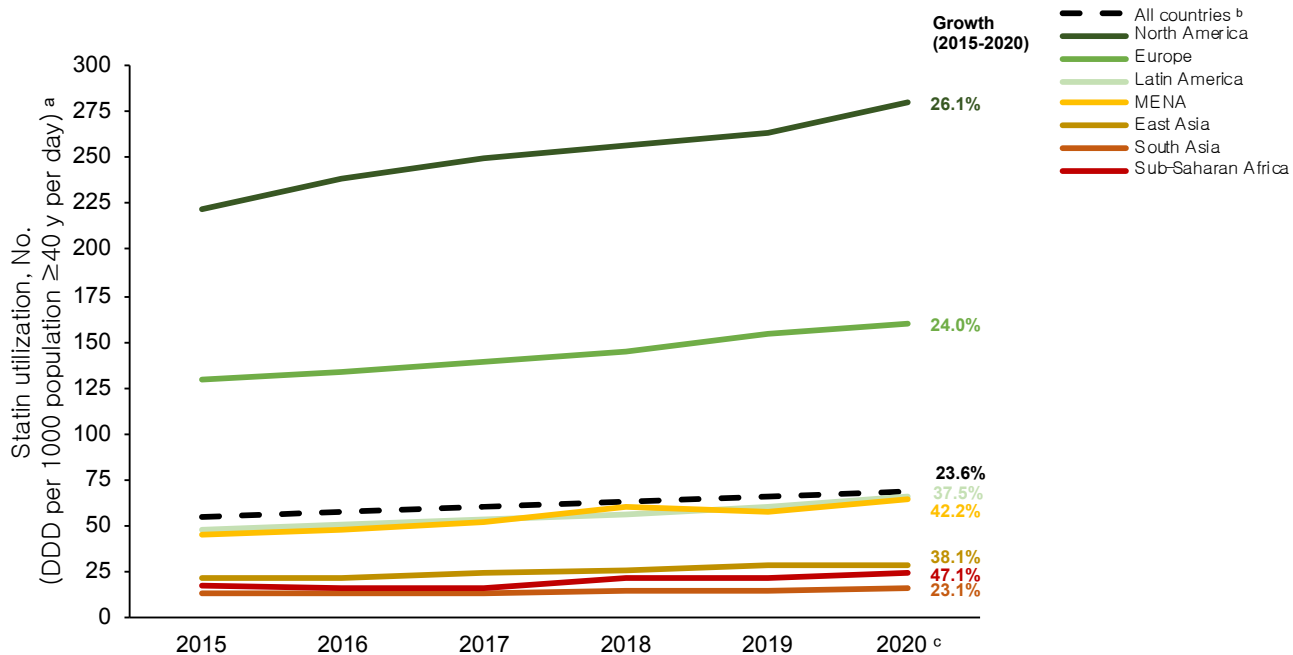
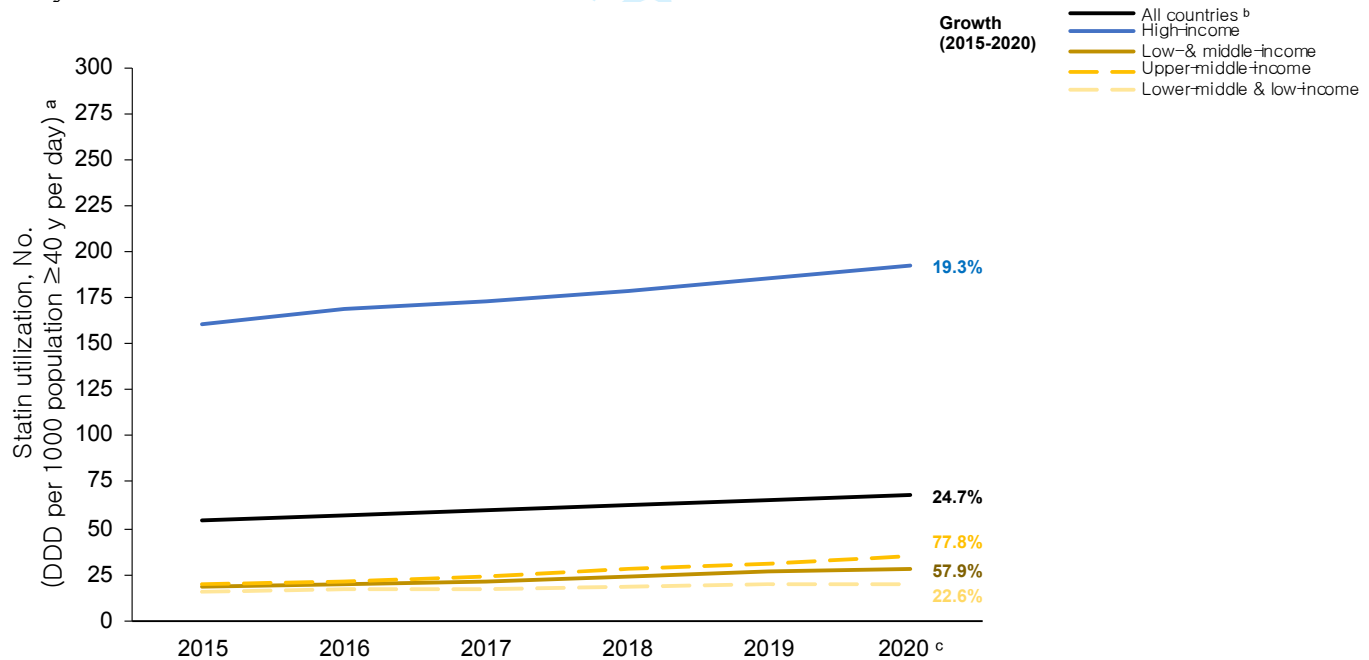
a All trends in statin utilization were statistically significant ($p < 0\cdot05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

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 $< \frac{1}{2}$ 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.

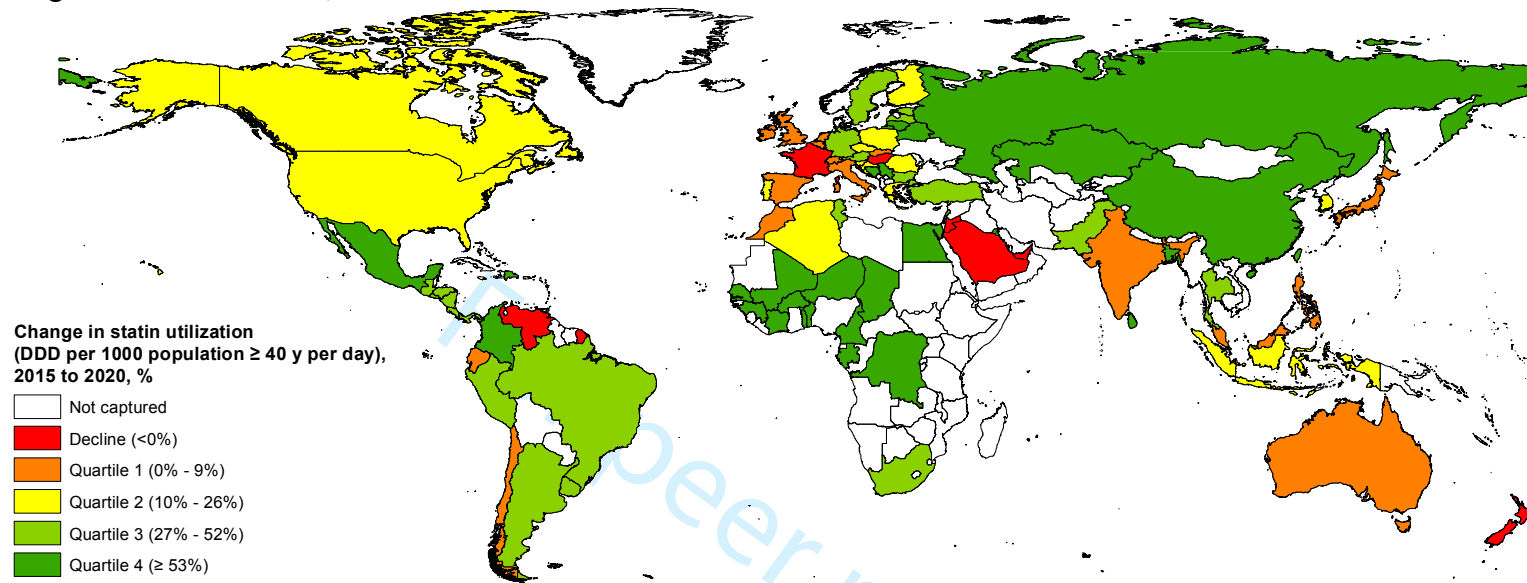
Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020**a. By Region****b. By Income**

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.

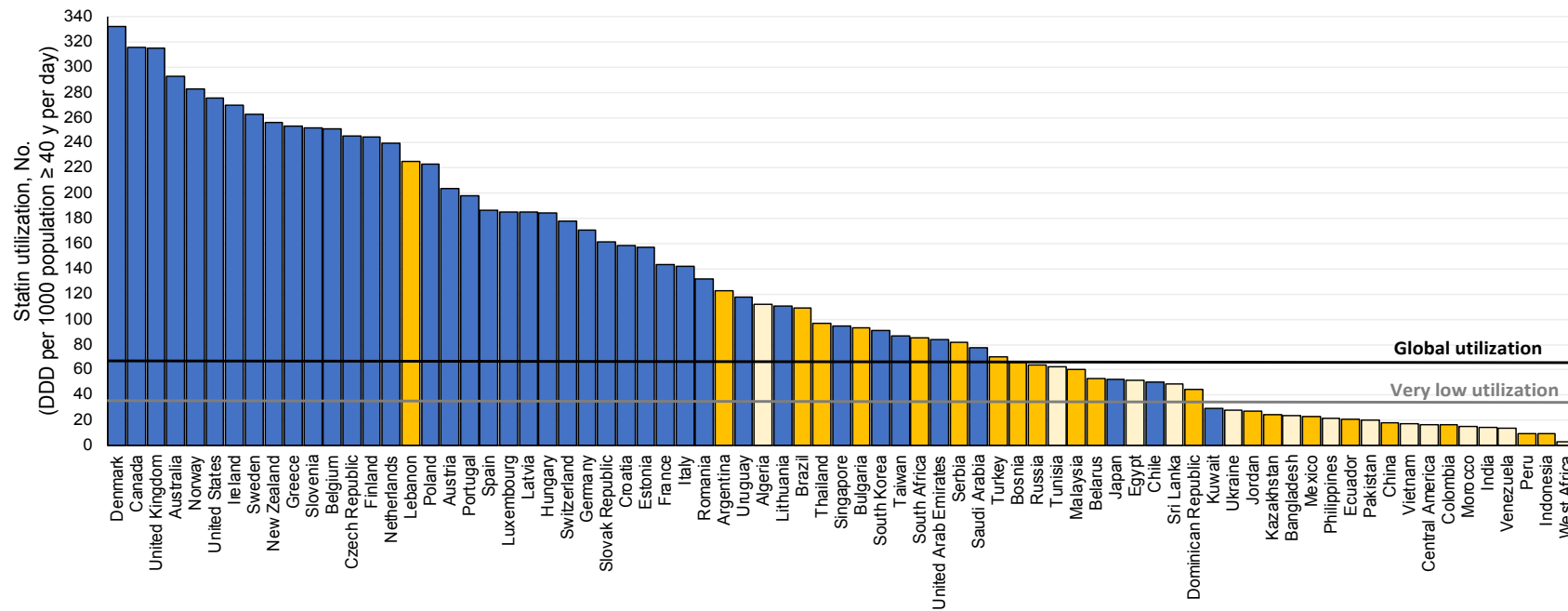
a All trends in statin utilization were statistically significant ($p < 0.05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by Country, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

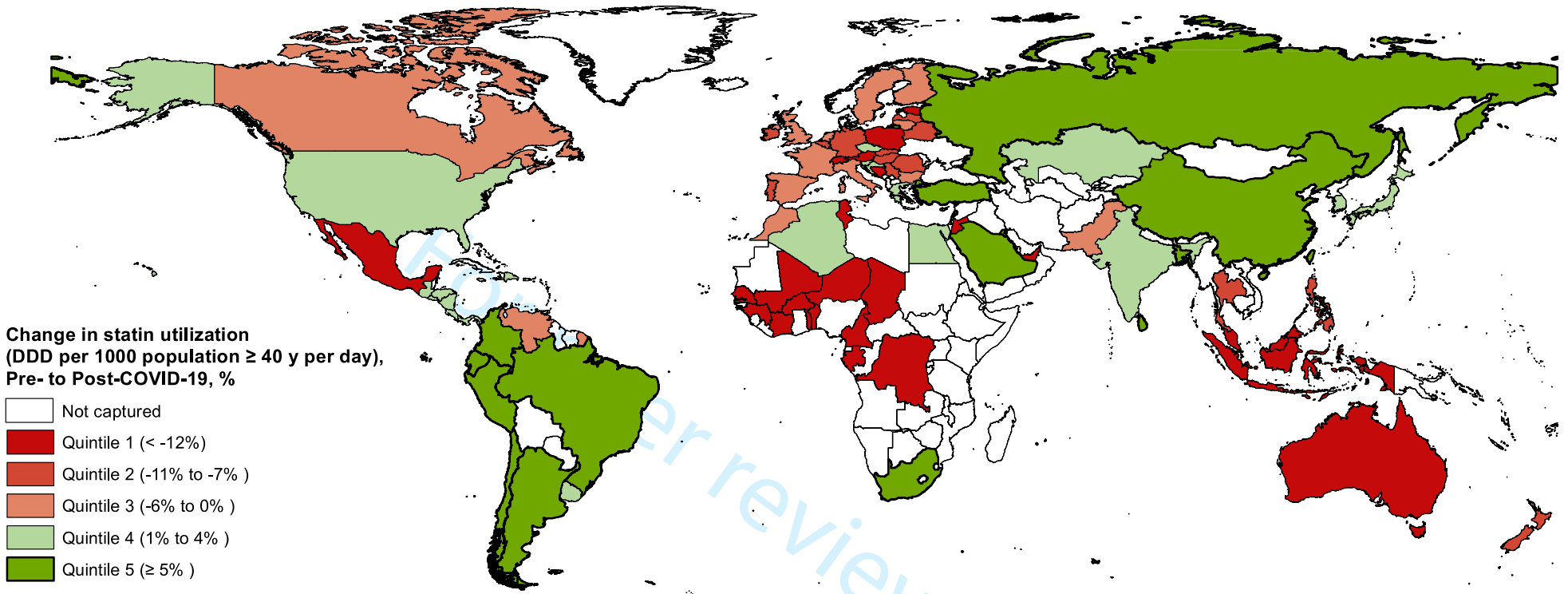


b. Statin utilization, 2020



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

<i>Countries/Regions</i> ^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)	<i>p</i>	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			Growth, %
	Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	<i>p</i>	
	Mexico	28.4	23.8	
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 $\geq 5\%$. **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.

BMJ Open

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

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 countries (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 countries (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/TPD, $p < 0.01$). Substantial disparities were also observed between LMICs, ranging from 3.1 DDDs/TPDs in West African nations to 225.0 DDD/TPD 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 countries (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

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3 140 Analysis System, MIDAS) from January 2015 to October 2020. These countries represent
4 141 approximately 90% of the global population older than 40 years of age.[16] IQVIA samples
5 142 pharmaceutical sales from multiple distribution channels (e.g., manufacturers, wholesalers, and
6 143 medical facilities) to develop nationally representative estimates of retail and non-retail
7 144 pharmaceutical sales in each country.[17] If necessary, IQVIA projects its samples to represent
8 145 100% of the retail and non-retail sales in each country and reports >90% global precision in
9 146 recent years.[17] However, IQVIA does not publicly disclose detailed information on data
10 147 collection, projection, and validation.
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14 149 Several sources were used to further characterize these countries. Countries were grouped based
15 150 on their income and geographical regions per the World Bank (2020).[18] Population estimates
16 151 and age-standardized IHD mortality rates (GBD 2019 causes of death were mapped to
17 152 International Classification of Diseases[19]were obtained from the Global Burden of Disease
18 153 (GBD) (2015-2019).[16] Health expenditures (total, public, out-of-pocket) were also obtained
19 154 from the World Bank (2015-2018).[20] We projected the values of these estimates through 2020
20 155 by applying the county-specific growth rates observed from 2015 to 2018 or 2019 (depending on
21 156 data availability). Finally, whether statins were included in national essential medicine lists was
22 157 determined, for reference, using the Global Essential Medicines database (2017).[9]
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24 159 *Measuring Statin Utilization*

25 160 We extracted country-level dispensing for WHO Anatomic Therapeutic Chemical codes relating
26 161 to statins (C10AA).[21] As IQVIA does not report country-specific data for six countries in
27 162 Centra America (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama) and
28 163 twelve countries in West Africa (Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire,
29 164 Democratic Republic of Congo, Gabon, Guinea, Mali, Niger, Senegal, and Togo), we examined
30 165 these countries in aggregate. We examined total market data, or retail and non-retail statin sales,
31 166 for 52 countries (eTable A). In the 23 countries/groups that lack non-retail sector data, utilization
32 167 was estimated by interpolation, using the ratio of statin consumption in the retail and non-retail
33 168 sectors for other countries in their region for which data was available (85% of all statins were
34 169 dispensed through the retail sector).
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38 171 To enable international comparisons over time, we converted statin sales (expressed in
39 172 milligrams) into defined daily doses (DDD) using the Anatomical Therapeutic Chemical
40 173 Classification System developed by the WHO Collaborating Centre for Drug Statistics
41 174 Methodology.[21] To account for differences in population size and age distribution, we report
42 175 statin utilization as DDDs per 1000 population ≥ 40 years per day (TPD) for each country.
43 176 Global, regional, and income group statin utilizations in DDD/TPD were derived by aggregating
44 177 statin sale and population estimates.
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47 179 *Statistical Analysis*

48 180 Descriptive statistics were used to examine trends and disparities in statin utilization from 2015
49 181 to 2020. Simple linear regressions were used to determine statistical significance in trends and
50 182 disparities. Changes in statin utilization in the pre- (October 2019 to March 2020) and post-
51 183 COVID-19 (April 2020 to October 2020) periods were also evaluated.
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3 185 Fixed-effects panel regression analysis was used to quantify the association between economic
4 186 and health indicators and the statin utilization from 2015 to 2020. Annual, country-level statin
5 187 utilization estimates were logged in these models to enable interpretation as percent change
6 188 associated with each unit of the independent variables examined. The independent variables
7 189 included time-varying health expenditure per capita, out-of-pocket health expenditure (as a
8 190 percentage of total expenditure), and age-standardized IHD mortality rate. Errors were clustered
9 191 by year and country to account for serial correlation.
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11 193 All *p*-values are two-sided. STATA version 17.1 was used for all statistical analyses.
12 194

13 195 This study was considered exempt by the Institutional Review Board at the University of
14 196 Southern California because this study was not considered human subjects research.
15 197

16 198 *Patient and Public Involvement*

17 199 No patients or members of the public were involved in the design of this study
18 200

19 201 **RESULTS**

20 202 As shown in **Figure 1**, global statin utilization increased 24.7% from 54.7 DDD/TPD in 2015 to
21 203 68.3 DDD/TPD ($p<0.01$). While statin utilization increased, to varying degrees, in all regions
22 204 and income groups (all $p<0.05$), disparities persisted. In 2020, statin utilization was highest in
23 205 North America and Europe (279.7 and 159.9 DDD/TPD, respectively) and substantially lower in
24 206 Latin America, MENA, East Asia, South Asia, and sub-Saharan Africa (66.1, 64.1, 29.3, 16.1,
25 207 and 24.7 DDD/TPD, respectively). From 2015 to 2020, statin utilization increased substantially
26 208 in HICs (19.3% from 161.3 to 192.4 DDD/TPD) and LMICs (57.9% from 18.0 to 28.4
27 209 DDD/TPD). However, disparities by income group remained throughout this period—by 2020,
28 210 statin utilization was seven times greater in HICs than in LMICs.
29 211

30 212 **Figure 2** depicts country-specific variation in statin utilization. From 2015 to 2020, statin
31 213 utilization increased or remained stable in most HICs, except Singapore (125.2 to 95.0, -24.1%,
32 214 $p=0.27$), the United Arab Emirates (104.4 to 83.9, -19.7%, $p=0.02$), Luxembourg (216.6 to
33 215 185.3, -14.4%, $p<0.01$), and New Zealand (295.4 to 256.0, -13.4%, $p=0.12$). HICs located in
34 216 North America and Europe have substantially higher statin utilization than comparable countries
35 217 located in other regions. For example, in 2020, statin utilization in HICs ranged from over 300
36 218 DDD/TPD in Denmark, Canada, and United Kingdom to less than 50 DDD/TPD in Japan, Chile,
37 219 and Kuwait.
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39 221 From 2015 to 2020, statin utilization increased by more than 10% in nearly all LMICs.
40 222 Exceptions included India (12.9 to 14.1, 9.1%, $p=0.02$), Malaysia (57.8 to 60.0, 3.9%, $p=0.41$),
41 223 Ecuador (20.2 to 20.9, 3.6%, $p=0.09$), and Jordan (28.6 to 27.1, -5.4%, $p=0.20$), where
42 224 utilization remained relatively stable, and Venezuela, where utilization sharply declined (92.3 to
43 225 13.8, -85.1%, $p<0.01$). Several LMICs had higher statin utilization than the global average in
44 226 2020, including Lebanon, Algeria, Brazil, Thailand, and South Africa (224.9, 111.8, 109.3,
45 227 96.8, and 85.4 DDD/TPD, respectively). Statin utilization is lower than 34 DDD/TPD
46 228 (approximately half the global average) in 35 LMICs, including some of the most populous
47 229 nations, such as China, India, Indonesia, Pakistan, Bangladesh, and Mexico.
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231 **Table 1** presents factors associated with changes in statin utilization. In HICs, only health
232 expenditure per capita was significantly and positively associated with statin utilization. In
233 LMICs, every \$100 increase in health expenditure per capita was associated with a 17% increase
234 in utilization, while every 10% increase in out-of-pocket health expenditure (as percentage of
235 total health expenditure) was associated with a 11% decline in utilization (both $p < 0.05$). Greater
236 rates of IHD mortality were also positively associated with more statin utilization in LMICs.

237
238 Compared with the pre-COVID-19 period, statin utilization declined by more than 5.0% in 41
239 countries, including 19 HICs and 22 LMICs (**Figure 3**). Severe disruptions in statin utilization—
240 or $\geq 10\%$ decline—were found in 13 HICs, including Australia (327.5 to 265.2 DDD/TPD, -
241 19.0%), the United Arab Emirates (92.7 to 77.8 DDD/TPD, -16.1%), and Germany (180.6 to
242 160.6 DDD/TPD, -11.1%) (**eTable B**). Some of the most severe disruptions in statin utilization
243 were observed among LMICs, including in Tunisia (76.5 to 52.7 DDD/TPD, -31.1%), Vietnam
244 (23.3 to 17.2 DDD/TPD, -26.3%), Ukraine (32.1 to 26.1 DDD/TPD, -18.7%), and Mexico
245 (28.4 to 23.8 DDD/TPD, -16.3%).

246 247 **DISCUSSION**

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

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258 Statin utilization is also substantially lower in countries with disproportionately high age-
259 standardized CVD mortality rates, namely LMICs in South Asia, MENA, and sub-Saharan
260 Africa.[4] The WHO Global Non-Communicable Disease (NCD) Action Plan 2013-2020 aimed
261 for a 25% reduction in premature deaths from NCD, especially CVD, from 2010 to 2025 by
262 ensuring that at least half of adults at high CVD risk receive cardiovascular medicines and that
263 80% of public and private facilities have these essential medicines available on-site.[22] Growth
264 in statin utilization in LMICs was concentrated among those countries with worsening IHD
265 mortality—suggesting reactionary policies for the management of CVD morbidity and mortality
266 versus preventative strategies for the provision of essential medicines. Together, our findings
267 suggest that global efforts to reduce the burden of CVD need to be strengthened—statin
268 utilization remains inequitable and suboptimal in LMICs, including those with worsening rates
269 of CVD mortality.

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271 Importantly, there is a substantial gap between CVD burden and statin utilization between HIC
272 and LMICs. For example, statin utilization is very low (less than half the global average) in 70%
273 of the LMICs examined, yet account for 68% of the global population of middle aged and older
274 adults and 55% CVD deaths worldwide.[16] Forty-two percent of CVD deaths occur in China
275 (25%), India (14%), and Indonesia (4%),[16] all of whom have very low statin utilization and
276 together account for less than 11% of statins dispensed in the world. From 2015 to 2019, the IHD

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3 277 mortality rate has declined or remained stable in most LMICs, with notable exceptions of
4 278 Bangladesh (5%), Malaysia (5%), and Venezuela (10%) that have experienced substantial
5 279 increases in recent years.[16] These countries, with worsening IHD mortality, have
6 280 comparatively low statin utilization in given their regional and income group averages. However,
7 281 Venezuela has also experienced substantial declines in statin utilization in this period—
8 282 aggravating the IHD burden experienced by its populace.
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11 284 Among LMICs, we found that every \$100 increase in per capita health spending was associated
12 285 with a 17% increase in statin utilization and that every 10% increase in the proportion of out-of-
13 286 pocket health spending was associated with an 11% decline. These findings suggest that policy
14 287 efforts to address global disparities in statin utilization, may need to increase health spending
15 288 while shifting the burden of health spending from individuals to the public sector (either via the
16 289 direct provision of healthcare and medicines or via insurance schemes). Unfortunately, public
17 290 investment in health (as measured by government health spending as a percentage of total
18 291 expenditures) has declined in LMICs during the last two decades.[23] Only high-income and
19 292 upper-middle countries have seen moderate increases in government health spending,[23]
20 293 countries that consume a disproportionate share of statins. Out-of-pocket spending as a share of
21 294 total health spending has remained stubbornly high in LMICs (above 40% and twice the
22 295 percentage in HICs) during this period.[23] International aid—a major source of health spending
23 296 in LMICs—is disproportionately directed to communicable diseases,[23] and these policies may
24 297 aggravate global disparities in the use of essential medicines, including statins, and hinder efforts
25 298 to reduce CVD mortality. International aid for health, which could alleviate costs of essential
26 299 medicines for governments and the public, has also stagnated since 2013.[23]
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29 301 Economic or political crises, which are often followed by sharp declines in total health spending,
30 302 may also impact access to essential medicines. The starkest example is Venezuela, where statin
31 303 utilization declined 85% between 2015 to 2020. The ongoing sociopolitical crisis began in 2010
32 304 and has spiraled into a sustained period of hyperinflation, a 75% decline in health spending, as
33 305 well as widespread and chronic shortages of essential medicines in the past decade.[20,24]
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37 307 Pharmaceutical supply chain disruptions have resulted from slowdowns in the production of
38 308 medicines that impact domestic and international markets, transportation hurdles, and restrictions
39 309 on movement (internationally and domestically and by providers and patients).[25] For example,
40 310 early in the pandemic, active pharmaceutical ingredient production in China was severely
41 311 curtailed—leading to shortages and delays in the production of medicines throughout the world,
42 312 including in the United States, the European Union, and India.[26]
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45 314 During the first six months of COVID-19 pandemic, statin utilization declined by more than 5%
46 315 in 41 countries. As a whole, HICs experienced greater declines in statin utilization during the
47 316 post-COVID-19 period (-2% versus -4% observed worldwide). Perhaps, because HICs had more
48 317 severe restrictions on movement to mitigate COVID-19 spread than LMICs early in the
49 318 pandemic.[27] However, the most severe disruptions in individual countries occurred in LMICs,
50 319 which may be more vulnerable to supply chain disruptions. Several countries in Eastern Europe
51 320 (*e.g.*, Serbia, Bosnia, Belarus, and Ukraine), Southeast Asia (*e.g.*, Thailand, Malaysia, the
52 321 Philippines, Vietnam, and Indonesia), and MENA (*e.g.*, Tunisia and Jordan) saw dramatic
53 322 declines in statin utilization, as did West Africa as a region and Mexico. Global COVID-19
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3 323 disparities, including inequitable access to vaccinations,[27] may result in persistent disruptions
4 324 to statins access in LMICs, as countries prioritize acute health needs. If these trends continue, the
5 325 COVID-19 pandemic may halt or reverse gains in statin utilization and worsen regional and
6 326 country level CVD disparities between HIC and LMICs.
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8 328 *Limitations*

9 329 This study had several limitations. First, comparisons between regions, income groups, and
10 330 countries should be interpreted in the context of the available data and total market coverage of
11 331 the included countries. For example, IQVIA does not provide non-retail sales for 39 of the 91
12 332 countries examined. However, 85% of all statins were dispensed through retail pharmacies, and
13 333 we account for missing non-retail sales through interpolation (using the ratio of statin
14 334 consumption in the retail and non-retail sectors for other countries in their region for which data
15 335 was available). Second, IQVIA does not provide sales data for most low-income countries;
16 336 therefore, this study may underestimate the magnitude of statin utilization disparities between
17 337 HICs and LMICs. Finally, relationships between changes in statin utilization and country-level
18 338 characteristics are not casual. However, the trends and disparities in statin utilization described in
19 339 this study help evaluate the global progress in ensuring equitable access to essential medicines
20 340 and inform efforts to reduce the global burden of CVD.
21 341

22 342 **Conclusion**

23 343 Despite a 25% increase in global statin utilization from 2015 to 2020, there are substantial and
24 344 persistent regional and country-level disparities between HIC and LMICs. To address worsening
25 345 CVD disparities, global, regional, and national policymakers should promote increased and
26 346 equitable access to statins in LMICs.
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3 347 **Contributorship Statement**

4 348 Dr. Guadamuz developed the methodology, conducted the analyses, wrote the first draft, and
5 349 received funding for the study. Mr. Shooshtari provided administrative support and supplied
6 350 suggestions for the analyses, data interpretation, and article drafting. Dr. Qato provided critical
7 351 revisions to the article resulting in improvements to the design, analyses, and interpretations, and
8 352 received funding for the study. All authors reviewed, revised, and approved the final version of
9 353 the article.
10 354

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15 359 Data Science Research Collaborative in the Era of COVID-19. The funders, the Robert Wood
16 360 Johnson Foundation, and IQVIA, had no role in the design and conduct of the study, analysis or
17 361 interpretation of the data, and preparation, or final approval of the article before publication.
18 362

19 363 **Competing Interests Statement**

20 364 Dr. Guadamuz current reports employment with Flatiron Health, Inc, which is an independent
21 365 subsidiary of the Roche Group. Flatiron Health, Inc., had no role in the design and conduct of the
22 366 study, analysis or interpretation of the data, and preparation, or final approval of the article
23 367 before publication.
24 368

25 369 **Ethical Approval Statement**

26 370 This study was considered exempt by the Institutional Review Board at the University of
27 371 Southern California because this study was not considered human subjects research.
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29 373 **Data Sharing Statement**

30 374 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 \geq 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. * $p < 0\cdot05$

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.

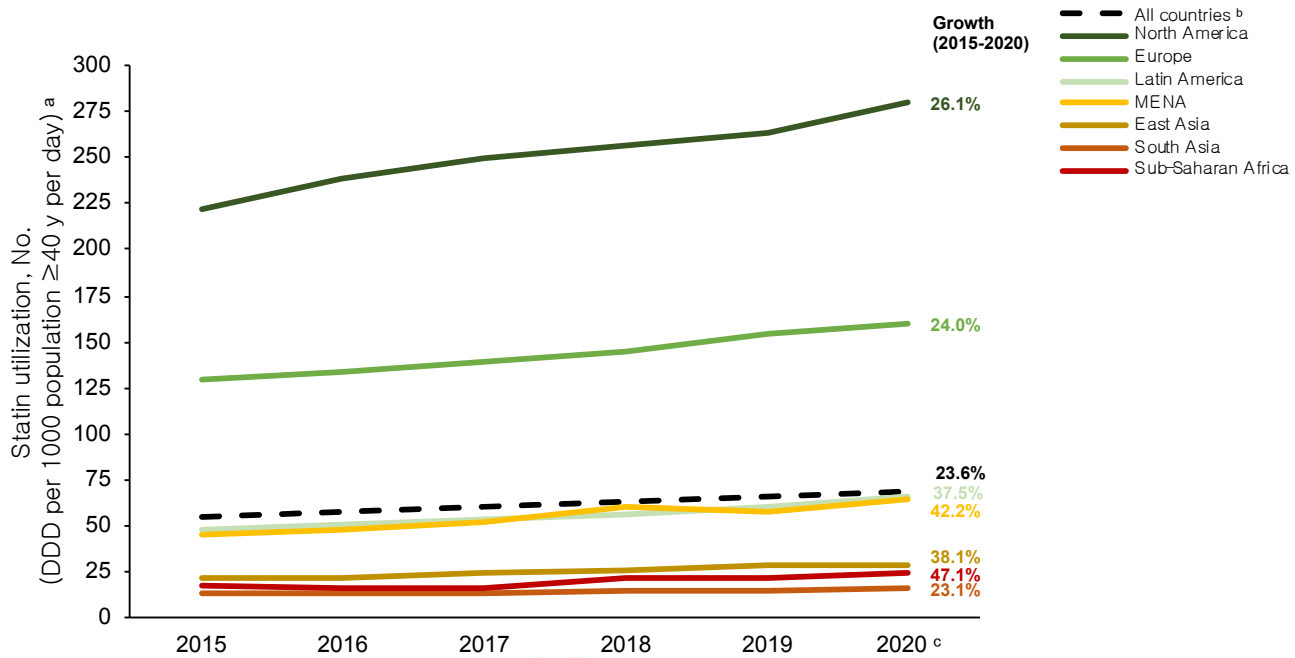
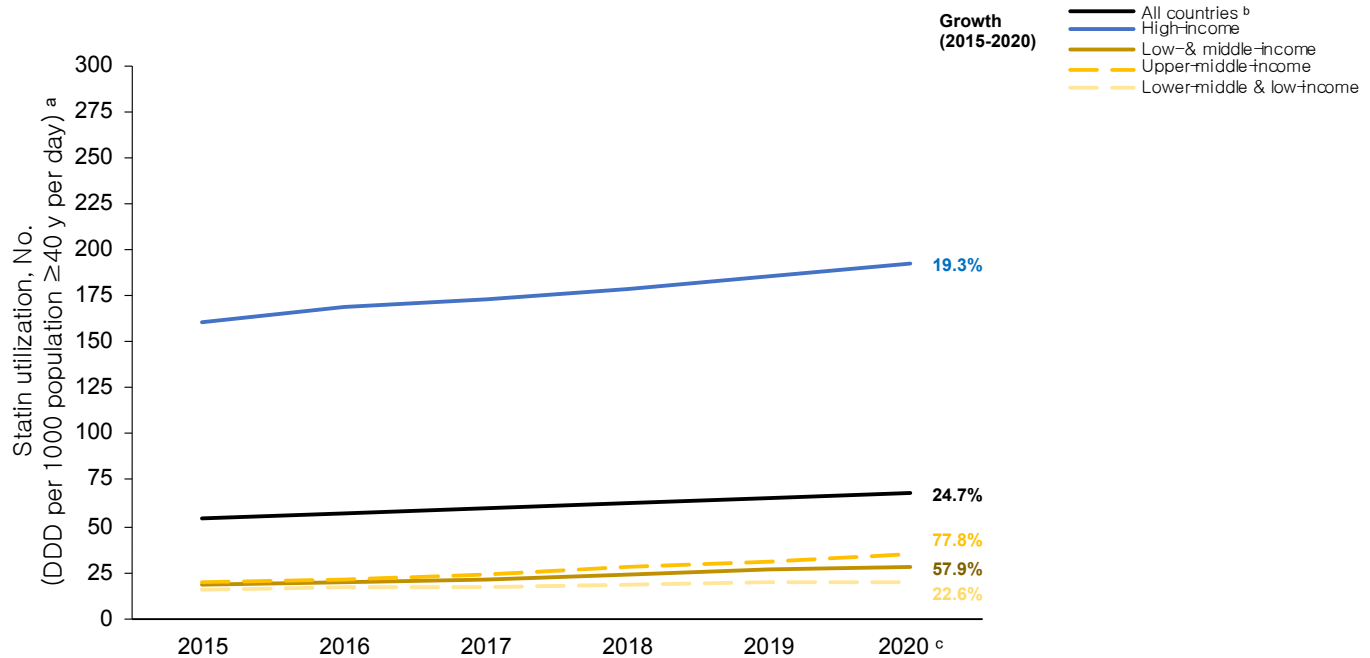
a All trends in statin utilization were statistically significant ($p < 0\cdot05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020

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 $< \frac{1}{2}$ 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.

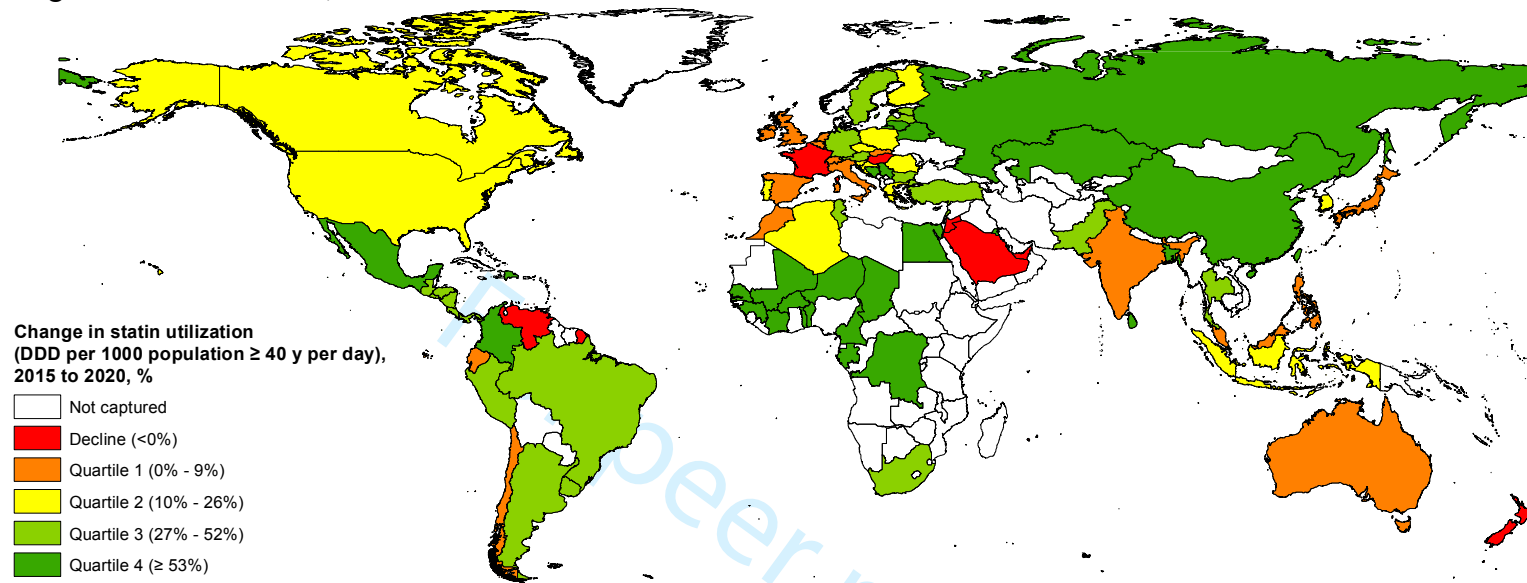
Figure 1. Statin Utilization by Geographical Region and Income, 2015 to 2020**a. By Region****b. By Income**

Notes: DDD=defined daily doses; MENA=Middle East and North Africa; No.=number.

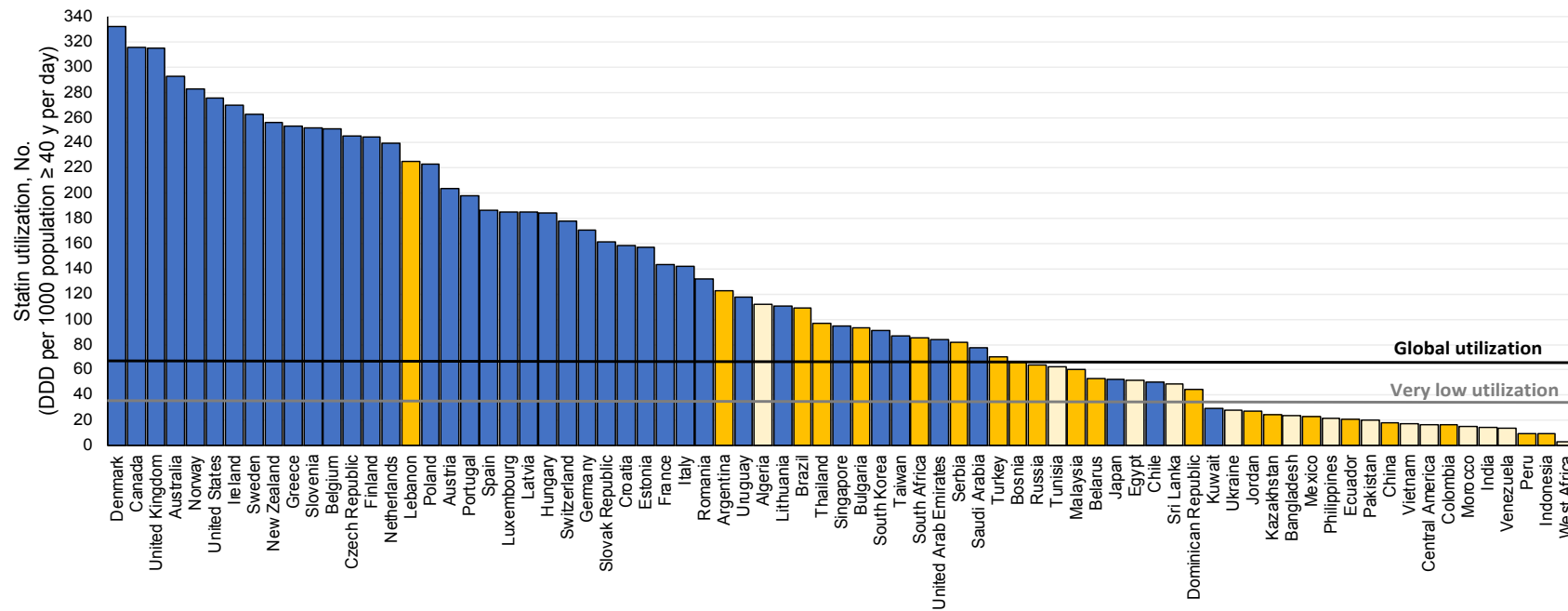
a All trends in statin utilization were statistically significant ($p < 0.05$), per simple linear regression. **b** We captured statin utilization for 91 countries. **c** Based on data from January to September 2020.

Figure 2. Statin Utilization by Country, 2015 to 2020

a. Change in statin utilization, 2015 to 2020

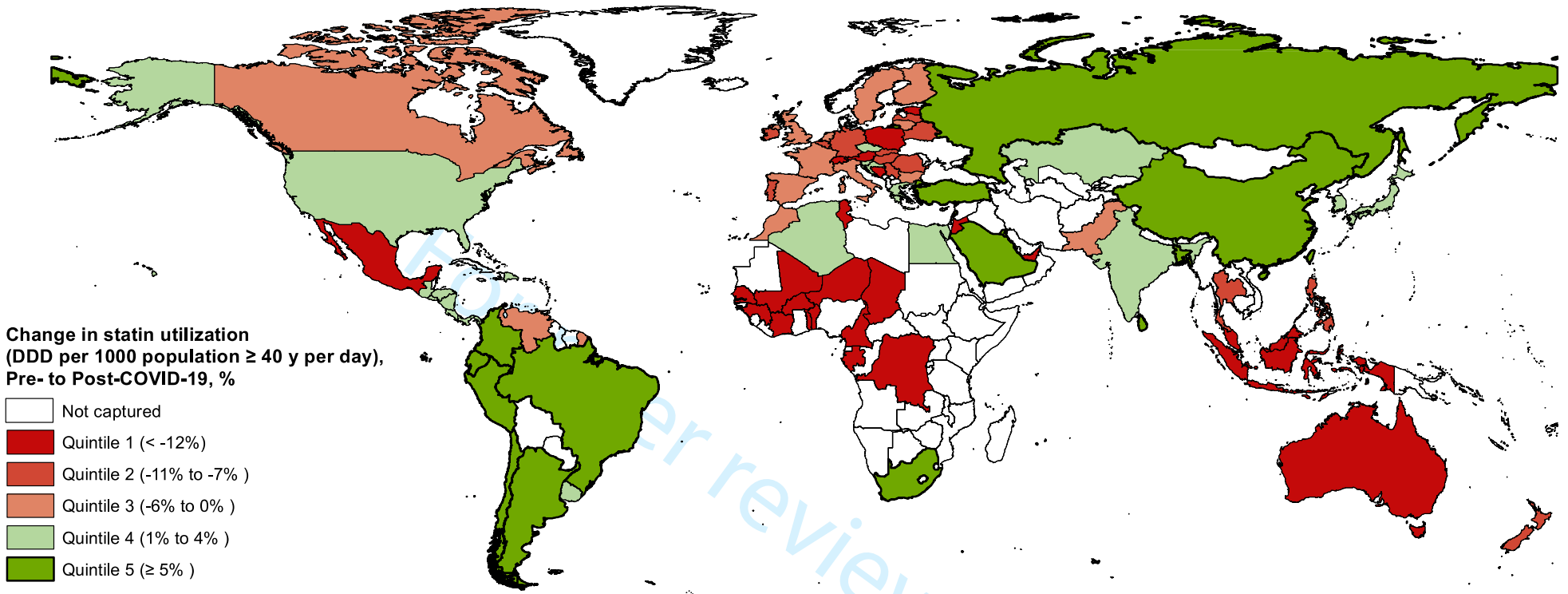


b. Statin utilization, 2020



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 ⁹	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

<i>Countries/Regions</i> ^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)	<i>p</i>	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

<i>Countries/Regions</i> ^b	Statin utilization, No. (DDD per 1000 population \geq 40 y) ^a			Growth, %
	Pre-COVID-19 (10/19 to 03/20)	Post-COVID-19 (04/20 to 09/20)	<i>p</i>	
	Mexico	28.4	23.8	
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 \geq 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.