Trends in PCSK9 Inhibitor Utilization in the United States, Europe and Other Countries: An Analysis of International Sales Data

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HIGHLIGHTS

- Large disparities in PCSK9 inhibitor utilization were observed between and within regions.
- Among regions, the US has the highest absolute and relative share of PCSK9 inhibitor consumption.
- By 2018-2019, population-standardized consumption in the Netherlands and Austria exceeded that in the US.
- Total expenditures using list prices on PCSK9 inhibitors from 2015-2019 were 3.4 billion international dollars.
- Countries with larger current health expenditures as % GDP and lower prevalence of ischemic heart disease tended to have greater utilization of PCSK9 inhibitors.

ABSTRACT

First approved in July 2015, proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors are costly lipid-lowering drugs. Their utilization has important policy and clinical implications but has not been assessed across different geographical regions. The objective of this study was to describe trends in PCSK9 inhibitor adoption and utilization between 2015 and 2019 in the United States, Europe and other countries.

Keywords

alirocumab; evolocumab; PCSK9 inhibitor; drug utilization; drug consumption; drug expenditures; lipid-lowering drugs; commercial phenomena; developed countries; developing countries; healthcare disparities.

INTRODUCTION

Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors were first approved in the United States (US) and Europe in July 2015. These branded, biologic, lipid-lowering drugs have similar indications in the US and Europe: treatment of familial hypercholesterolemia, treatment of patients with intolerance or inadequate response to statins and secondary prevention of cardiovascular events in patients with atherosclerotic cardiovascular disease. In Canada and Europe, initial list prices for PCSK9 inhibitors were only half the price in the US.(1) The budget impact and number of patients using PCSK9 inhibitors during the first five years after approval in the US were predicted to be $100 billion and 2.6 million persons.(2,3) However, use of PCSK9 inhibitors has been much lower than analysts predicted, likely due to high prices and formulary restrictions designed to manage their budget impact.(4)

Growth in global consumption of lipid-lowering drugs over the past decade has outpaced other major classes of cardiovascular drugs.(5) While consumption of PCSK9 inhibitors in the US has increased,(6,7) no studies have compared their utilization across regions. Given diversity in national prices, pharmaceutical price regulations, approved indications and clinical practice guidelines, it is unknown to what extent the uptake and utilization of PCSK9 inhibitors varies between the US, Europe and other countries.

In this study, we analyzed pharmaceutical market sales data to describe international trends in PCSK9 inhibitor utilization. Cross-country comparisons can provide insights

on the uptake of new treatments, explore reasons for variability in consumption across countries, identify disparities in treatment access, inform future policy decisions and help generate hypotheses for future research on the appropriateness, effectiveness, safety and economic impact of PCSK9 inhibitor use.

METHODS

Study Design and Data Sources

We conducted cross-country comparisons using monthly pharmaceutical sales data from July 2015 to July 2019. Data on the number of PCSK9 inhibitor units sold and expenditures, in current local currency and converted to US dollars at a fixed exchange rate, were obtained from IQVIA's Multinational Integrated Data Analysis System (MIDAS). Details about the MIDAS data are found in Supplementary Table 1. MIDAS country panels can be individual countries, regions or territories. National data are collected by IQVIA from multiple distribution channels such as wholesalers, direct distribution from manufacturers, retail and hospital pharmacies and vary by country and data source. If required, the sampled data are projected to represent 100% of the total sales channel in each country. Product information is grouped according to its main indication, and undergoes various quality-control checks. IQVIA annually validates its data using manufacturer sales, with 95% global precision in most years.(8) Sources of additional data used in the analysis are described in the Supplementary Methods. Individual-level data about patients or prescribers was not available; therefore, this study was exempt from ethics approval.

Classification of Countries

Each MIDAS country was classified into one of three mutually exclusive geographical regions: the US, defined as the US and Puerto Rico; Europe, defined as countries whose drugs are evaluated by the European Medicines Agency; and other countries, defined as the remaining countries in the data set (Supplementary

Table 1). Countries were also classified according to their age-standardized prevalence of ischemic heart disease (IHD), selected as a proxy for the population eligible for PCSK9 inhibitor treatment, and their current health expenditure as percentage of gross domestic product (CHE%GDP), selected as a financial indicator of resources spent on health.

Measures of PCSK9 Inhibitor Utilization

Consumption

The primary outcome of interest was PCSK9 inhibitor consumption, defined as the absolute number of standard units (SU) sold and standardized per 1000 inhabitants aged ≥ 40 years per year. A SU is the smallest common physical dosage form for a specific product. For evolocumab and alirocumab, each SU is equal to one pre-filled syringe or one auto-injector cartridge. We estimated overall person-years of PCSK9 inhibitor exposure and the number of individuals using PCSK9 inhibitors in the last month of the study by dividing total units sold by 26 or units sold in July 2019 by 2. This assumed each person used an every 2 weeks dosing regimen, or equivalently consumed 26 PCSK9 inhibitor SU per year (52 weeks/2 weeks).

Expenditures and Unit Prices

Exploratory outcomes included expenditures (absolute and population standardized) and average price per SU. Monthly expenditures in MIDAS are list prices at the manufacturer sales level (i.e., the manufacturer sales price or wholesaler purchase price). In the main analysis, expenditures were converted from local currency using purchasing power parity (PPP) factors to international dollars (ID; Supplementary

Table 2 and Supplementary Methods). Calculations were repeated using US dollar constant currencies as a sensitivity analysis.

Data Analysis

Data for alirocumab and evolocumab were summed up to provide total consumption and expenditures for PCSK9 inhibitors. When reporting yearly measures, monthly data were aggregated into four 12-month periods (e.g., 2018-2019 aggregates monthly sales inclusive of August 2018 to July 2019). In stratified analyses, we summed up the population of each constituent country ≥ 40 years for each category or region by year. In a given period, price per SU was estimated by dividing total expenditures by the total number of SU sold. Analyses were conducted using R software version 3.6.1 (R Core Team; Vienna, Austria).

Role of the Funding Source

No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

RESULTS

49 (73%) out of 67 countries in our data set reported PCSK9 inhibitor sales and were included for analysis. Total sales in these countries were 8,471,379 SU, equivalent to 325,822 person-years of treatment. Among regions, the US consistently utilized more PCSK9 inhibitor units and had the largest expenditures each year than all other countries combined, on both the absolute and population-standardized scales (Table 1 and Supplementary Table 3). The US also rapidly adopted PCSK9 inhibitors, with monthly absolute consumption consistently outpacing Europe and other countries (Figure 1). In stratified analyses, the US, countries with the lowest age-standardized prevalence of IHD and those with the highest CHE%GDP had the greatest annual rates of consumption (Figure 2).

During the last month of available data (July 2019), an estimated 216,844 people used a PCSK9 inhibitor globally, of whom 125,504 (57.9%) were people in the US, 66,961 (30.9%) in Europe and 24,379 (11.2%) in other countries. At country-level, PCSK9 utilization was highly variable. By 2018-2019, consumption in the Netherlands and Austria exceeded the US and was the highest amongst all countries (Table 1).

Total expenditures on PCSK9 inhibitors were 3.4 billion ID (Supplementary Table 3). The US accounted for 2.6 billion ID (75.6%) spent on PCSK9 inhibitors. In stratified analyses, annual expenditures on PCSK9 inhibitors were greatest in the US, countries with the lowest age-standardized prevalence of IHD and those with the

highest CHE%GDP (Supplementary Figure 1). Average prices varied widely across countries and ranged from in 949 ID/SU in Argentina to 127 ID/SU in Korea (Supplementary Table 3). Results for the sensitivity analysis using constant US dollars were similar although there was less variability in average unit prices (Supplementary Table 4 and Supplementary Figure 1).

DISCUSSION

From 2015 to 2019, the US had the most rapid uptake and consistently consumed more PCSK9 inhibitor units than all other countries combined. Quick uptake of new treatments in the US may contribute to higher expenditures and prices, and this pattern of utilization has been observed with the introduction of other lipid-lowering drugs such as lovastatin and ezetimibe.(9–11) Yet by the end of the study period, population-standardized consumption in Austria and the Netherlands exceeded that in the US.

Our previous research found that international PCSK9 inhibitor consumption increased at a compound annual growth rate of 104% between 2016 to 2018.(12) During the same period, Sumarsono and colleagues reported similar increasing trends in PCSK9 inhibitor utilization among US Medicare Part D beneficiaries by 144% from 25,569 to 62,476.(7) Our current study adds additional evidence regarding the overall absolute and population-standardized trends in PCSK9 inhibitor utilization in the US since it is not restricted to a subset of Medicare Part D beneficiaries.

We observed large variability in PCSK9 inhibitor consumption, expenditures and prices across geographical regions. This variation suggests disparities in access to PCSK9 inhibitors since greater utilization tended to be in countries with a larger ability, and perhaps willingness, to pay, as measured by CHE%GDP, and not the burden of IHD. Examples of the mismatch between potential need and observed

utilization were apparent amongst regions. For example, Puerto Rico has 2-times the prevalence of IHD than the US mainland, yet PCSK9 inhibitor consumption was 8-times greater in the US mainland in 2018-2019. Similarly, countries in Eastern Europe and the Middle-East, such as Estonia, Slovenia, Turkey and Jordan, have a greater prevalence of IHD but limited utilization of PCSK9 inhibitors.

When assessed using list prices, the US has the largest share of global expenditures on PCSK9 inhibitors, and paid some of the highest average prices. A few other high-income countries, namely Germany, the Netherlands, Spain, Canada and Japan, also had high relative and population-standardized expenditures. Price per SU in this study can serve as a benchmark for international reference pricing particularly for low- and middle-income countries who may soon evaluate adopting PCSK9 inhibitors within their health systems but likely have less purchasing power for these medications than high-income countries. More broadly, decision makers, whether individual clinicians, formulary committees, insurers or national governments, may need to re-assess how PCSK9 inhibitors are priced and accessed in order to achieve appropriate use of these safe and effective drugs.

Limitations

Comparisons among countries should be interpreted in the context of the available data and total pharmaceutical market coverage. Less than 100% market coverage could underestimate the true utilization of PCSK9 inhibitors. Although we stratified according to the age-standardized prevalence of IHD, this does not account for patients with familial hypercholesterolemia and other clinical manifestations of

atherosclerotic cardiovascular disease who may also receive PCSK9 inhibitors. Individual-level data were not available in this study so we could not assess the appropriateness of PCSK9 inhibitor prescribing, which remains an important question for future drug utilization research. Since MIDAS only contains data on list prices at the manufacturer sales level, we could not determine prices at other sales levels such as procurement, reimbursement or out-of-pocket costs paid by patients and health plans. The expenditure and pricing results therefore should be interpreted as exploratory because they do not reflect net prices which account for off-invoice discounts and rebates. Lastly, unit prices should be interpreted with some uncertainty, since the method of their calculation, using PPP or constant US dollars, influenced the results.

CONCLUSIONS

PCSK9 inhibitor consumption and expenditures have risen rapidly, especially in the US, from 2015 to 2019. Given the evidence that these drugs improve cardiovascular outcomes, disparities in PCSK9 inhibitor utilization amongst countries is a barrier to global efforts to treat and prevent cardiovascular disease.

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Conflict of Interest Disclosures

Dr Chan and Professor Wong have received research grants from Amgen.

Author Contributions

Mr Blais and Ms Wei had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conceptualization: Blais, Chan, Knapp.

Formal Analysis: Blais, Y. Wei.

Funding acquisition: Chan, Wong.

Resources: Chan, Wong.

Visualization: Blais.

Supervision: Chan.

Writing - original draft: Blais, Knapp.

Critical revision of the manuscript for important intellectual content: All authors.

Data Sharing

MIDAS data were licensed from IQVIA and the terms of our agreement do not permit disclosure, sub-licensing or publishing of raw data.

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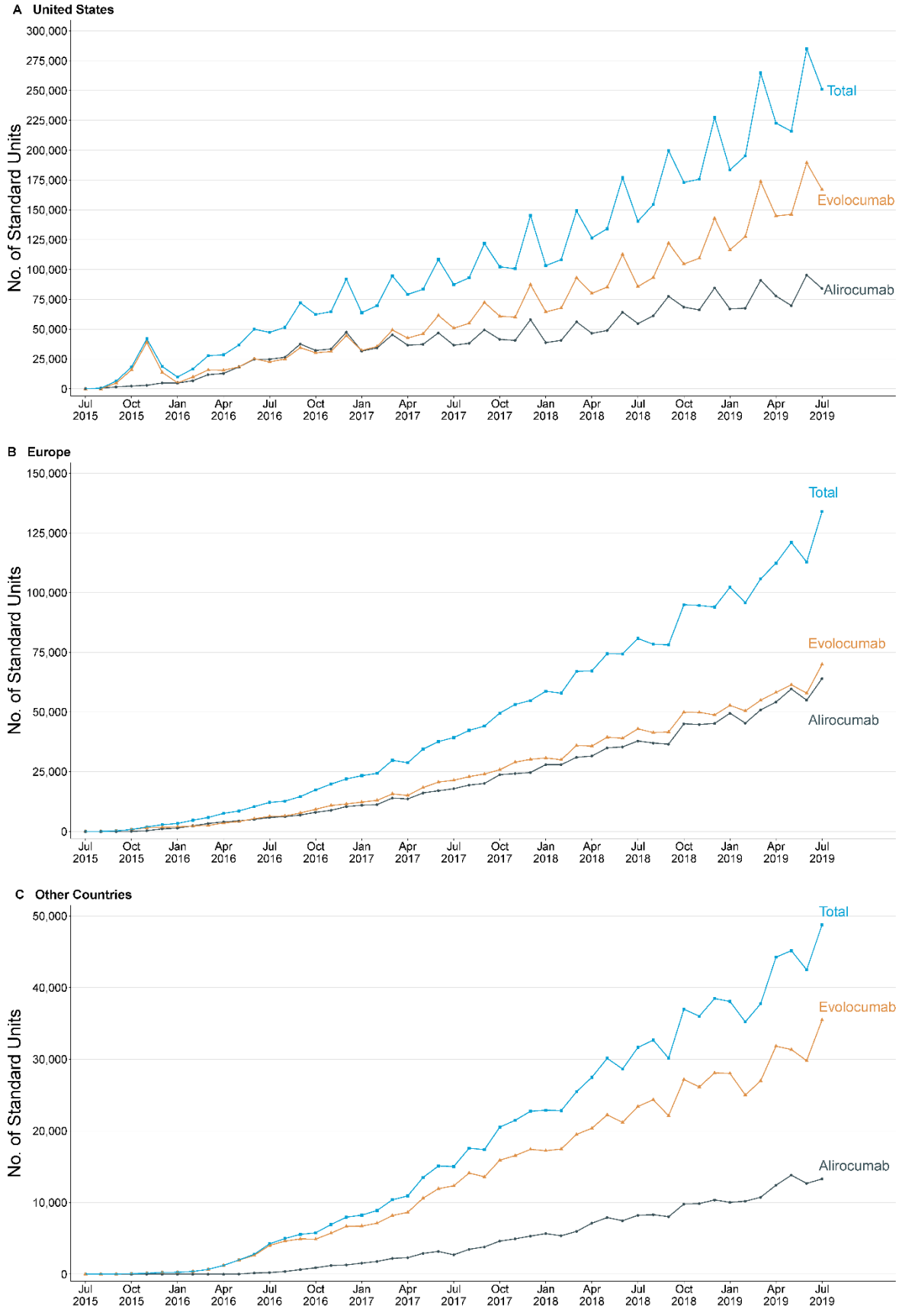
FIGURES

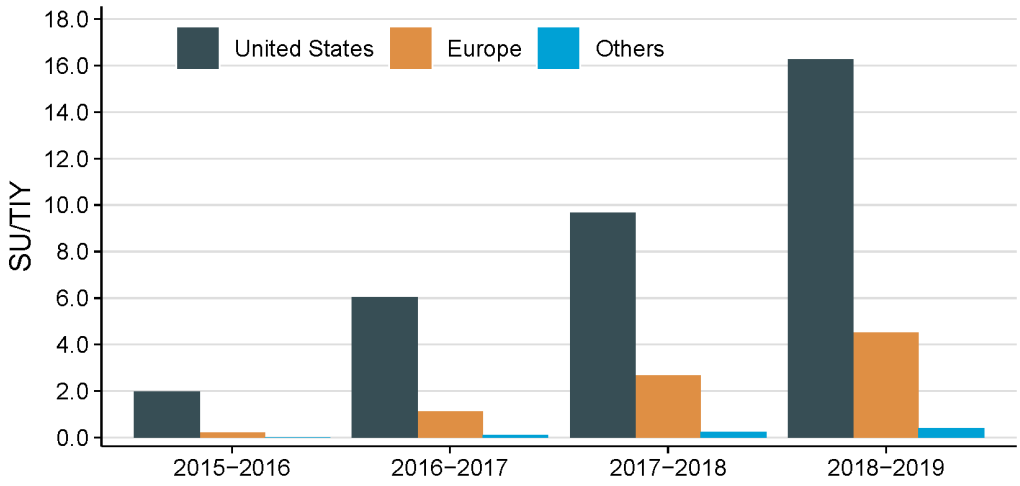
Figure 1. Monthly PCSK9 Inhibitor Consumption in the United States, Europe and Other Countries from July 2015 to July 2019


A United States
No. of Standard Units
300,000
275,000
250,000
225,000
200,000
175,000
150,000
125,000
100,000
75,000
50,000
25,000
0
Total
Evolocumab
Alirocumab
Jul 2015
Oct 2015
Jan 2016
Apr 2016
Jul 2016
Oct 2016
Jan 2017
Apr 2017
Jul 2017
Oct 2017
Jan 2018
Apr 2018
Jul 2018
Oct 2018
Jan 2019
Apr 2019
Jul 2019
B Europe
No. of Standard Units
150,000
125,000
100,000
75,000
50,000
25,000
0
Total
Evolocumab
Alirocumab
Jul 2015
Oct 2015
Jan 2016
Apr 2016
Jul 2016
Oct 2016
Jan 2017
Apr 2017
Jul 2017
Oct 2017
Jan 2018
Apr 2018
Jul 2018
Oct 2018
Jan 2019
Apr 2019
Jul 2019
C Other Countries
No. of Standard Units
50,000
40,000
30,000
20,000
10,000
0
Total
Evolocumab
Alirocumab
Jul 2015
Oct 2015
Jan 2016
Apr 2016
Jul 2016
Oct 2016
Jan 2017
Apr 2017
Jul 2017
Oct 2017
Jan 2018
Apr 2018
Jul 2018
Oct 2018
Jan 2019
Apr 2019
Jul 2019

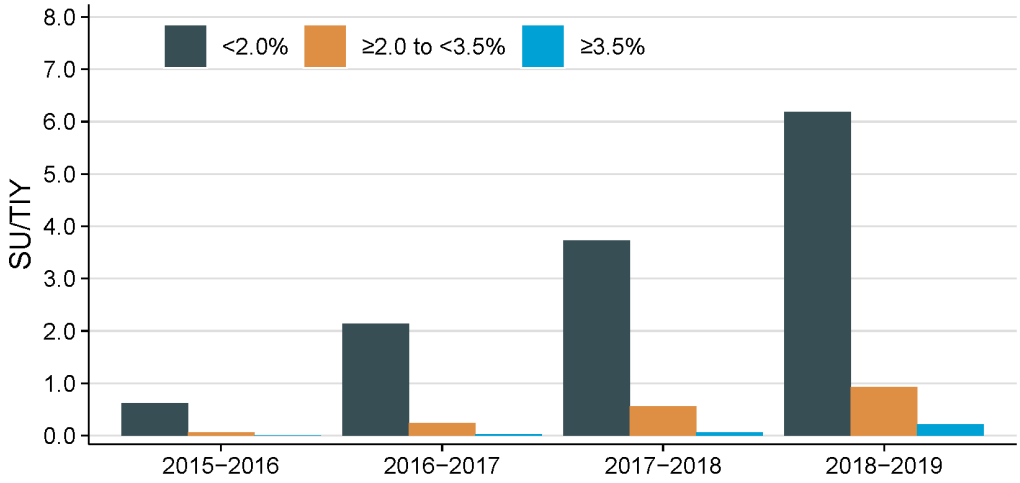
Number of alirocumab, evolocumab and total (both agents) standard units sold monthly in the United States (**A**), in Europe (**B**) and in other countries (**C**). The y-axis has been rescaled in each panel to better visualize absolute consumption within each region.

Figure 2. Annual PCSK9 Inhibitor Consumption in 49 Countries from 2015 to 2019, Standardized for Population

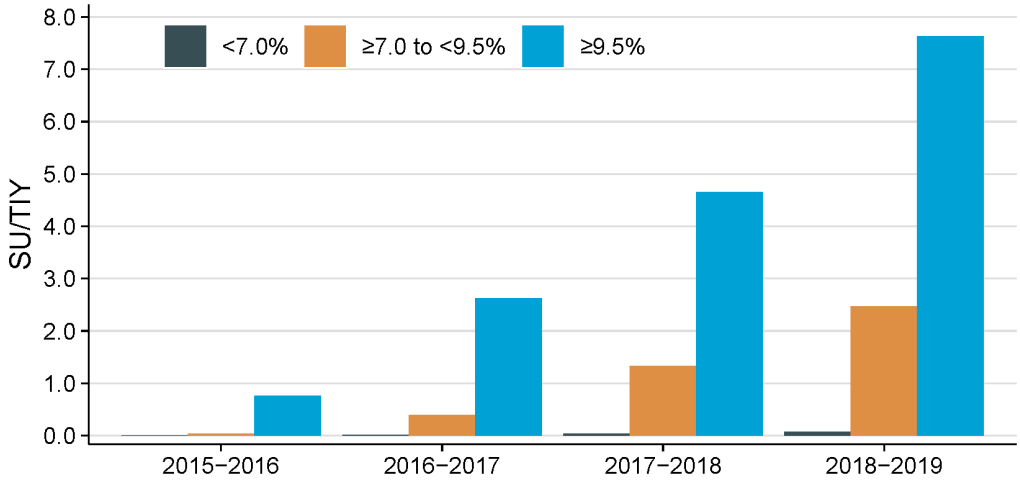
A


United States
Europe
Others
SU/TIY
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
2015–2016
2016–2017
2017–2018
2018–2019

B


<2.0%
≥2.0 to <3.5%
≥3.5%
SU/TIY
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
2015–2016
2016–2017
2017–2018
2018–2019

C


<7.0%
≥7.0 to <9.5%
≥9.5%
SU/TIY
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
2015–2016
2016–2017
2017–2018
2018–2019

Abbreviation: SU/TIY, standard unit per 1000 inhabitants ≥ 40 years per year.

A, Stratified by region. **B**, Stratified by the age-standardized prevalence of ischemic heart disease in 2018. **C**, Stratified by current health expenditures as a percentage of gross domestic product in 2018. Monthly sales data in MIDAS were aggregated for each 12-month period from August to July and standardized per 1000 inhabitants ≥ 40 years per year. For example, 2015-2016 includes monthly sales from August 2015 to July 2016.

TABLE

Table 1. Absolute (No. of standard units), Relative (%) and Population-Standardized (SU/TIY) PCSK9 Inhibitor Consumption in the United States, Europe and Other Countries, 2015 to 2019

	2015-2016			2016-2017			2017-2018			2018-2019			Total	
	No.	%	SU/TIY	No.	%	SU/TIY	No.	%	SU/TIY	No.	%	SU/TIY	No.	%
United States														
United States	302,440	81.1	2.0	927,409	68.9	6.1	1,500,113	59.7	9.8	2,544,682	60.0	16.4	5,274,644	62.3
Puerto Rico	272	0.1	0.2	1,525	0.1	0.9	1,573	0.1	1.0	3,103	0.1	1.9	6,473	0.1
Total	302,712	81.1	2.0	928,934	69.0	6.0	1,501,686	59.7	9.7	2,547,785	60.1	16.3	5,281,117	62.3
Europe														
Germany	41,619	11.2	0.9	126,539	9.4	2.7	231,338	9.2	4.9	349,635	8.3	7.4	749,131	8.8
Netherlands	4,265	1.1	0.5	53,152	3.9	5.9	127,585	5.1	14.1	208,363	4.9	22.8	393,365	4.6
Spain	2,372	0.6	0.1	42,981	3.2	1.7	103,290	4.1	4.0	171,800	4.1	6.5	320,443	3.8
Italy	774	0.2	0.0	10,317	0.8	0.3	72,547	2.9	2.0	153,684	3.6	4.2	237,322	2.8
United Kingdom	1,217	0.3	0.0	25,488	1.9	0.8	66,550	2.6	2.0	103,646	2.4	3.1	196,901	2.3
Austria	2,529	0.7	0.5	17,422	1.3	3.7	45,911	1.8	9.6	85,178	2.0	17.6	151,040	1.8
Belgium	0	0.0	0.0	8,244	0.6	1.4	25,039	1.0	4.2	38,866	0.9	6.5	72,149	0.9
Sweden	1,010	0.3	0.2	5,913	0.4	1.2	15,528	0.6	3.1	31,235	0.7	6.1	53,686	0.6
Norway	3,999	1.1	1.6	10,145	0.8	3.9	16,458	0.7	6.3	25,511	0.6	9.7	56,113	0.7
Slovakia	0	0.0	0.0	1,702	0.1	0.6	9,670	0.4	3.5	18,582	0.4	6.7	29,954	0.4
France	0	0.0	0.0	0	0.0	0.0	3,081	0.1	0.1	16,294	0.4	0.5	19,375	0.2
Czech	0	0.0	0.0	176	0.0	0.0	224	0.0	0.0	5,514	0.1	1.0	5,914	0.1
Slovenia	220	0.1	0.2	394	0.0	0.3	1,932	0.1	1.7	4,104	0.1	3.5	6,650	0.1
Bulgaria	34	0.0	0.0	94	0.0	0.0	1,562	0.1	0.4	3,576	0.1	0.9	5,266	0.1
Finland	348	0.1	0.1	604	0.0	0.2	2,064	0.1	0.7	3,540	0.1	1.2	6,556	0.1
Luxembourg	0	0.0	0.0	6	0.0	0.0	234	0.0	0.8	2,154	0.1	7.3	2,394	0.0
Poland	61	0.0	0.0	431	0.0	0.0	744	0.0	0.0	776	0.0	0.0	2,012	0.0
Portugal	0	0.0	0.0	0	0.0	0.0	198	0.0	0.0	567	0.0	0.1	765	0.0
Croatia	0	0.0	0.0	12	0.0	0.0	0	0.0	0.0	502	0.0	0.2	514	0.0
Hungary	64	0.0	0.0	92	0.0	0.0	174	0.0	0.0	298	0.0	0.1	628	0.0
Estonia	0	0.0	0.0	0	0.0	0.0	9	0.0	0.0	57	0.0	0.1	66	0.0
Romania	0	0.0	0.0	16	0.0	0.0	14	0.0	0.0	44	0.0	0.0	74	0.0
Lithuania	1	0.0	0.0	0	0.0	0.0	16	0.0	0.0	25	0.0	0.0	42	0.0
Ireland	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	1	0.0	0.0	1	0.0
Latvia	0	0.0	0.0	7	0.0	0.0	0	0.0	0.0	0	0.0	0.0	7	0.0
Total	58,513	15.7	0.2	303,735	22.6	1.1	724,168	28.8	2.7	1,223,952	28.9	4.5	2,310,368	27.3

	2015-2016			2016-2017			2017-2018			2018-2019			Total	
	No.	%	SU/TIY	No.	%	SU/TIY	No.	%	SU/TIY	No.	%	SU/TIY	No.	%
Others														
Canada	6,270	1.7	0.3	42,831	3.2	2.3	95,845	3.8	5.1	164,400	3.9	8.7	309,346	3.7
Japan	3,236	0.9	0.0	45,459	3.4	0.6	118,154	4.7	1.5	156,263	3.7	2.0	323,112	3.8
Switzerland	1,110	0.3	0.3	12,614	0.9	2.8	31,800	1.3	7.0	51,330	1.2	11.2	96,854	1.1
Australia	1,122	0.3	0.1	3,743	0.3	0.3	16,471	0.7	1.4	29,398	0.7	2.5	50,734	0.6
Mexico	110	0.0	0.0	5,425	0.4	0.1	11,780	0.5	0.3	20,920	0.5	0.5	38,235	0.5
Brazil	0	0.0	0.0	1,655	0.1	0.0	6,790	0.3	0.1	13,182	0.3	0.2	21,627	0.3
Saudi Arabia	0	0.0	0.0	0	0.0	0.0	2,080	0.1	0.2	9,999	0.2	0.9	12,079	0.1
United Arab Emirates	54	0.0	0.0	1,062	0.1	0.4	3,420	0.1	1.3	6,072	0.1	2.3	10,608	0.1
Taiwan	0	0.0	0.0	24	0.0	0.0	1,141	0.0	0.1	3,998	0.1	0.3	5,163	0.1
China	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	3,872	0.1	0.0	3,872	0.0
Russian Federation	0	0.0	0.0	44	0.0	0.0	653	0.0	0.0	2,381	0.1	0.0	3,078	0.0
Thailand	0	0.0	0.0	0	0.0	0.0	16	0.0	0.0	950	0.0	0.0	966	0.0
Egypt	12	0.0	0.0	244	0.0	0.0	164	0.0	0.0	886	0.0	0.0	1,306	0.0
Kuwait	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	688	0.0	0.4	688	0.0
Turkey	0	0.0	0.0	31	0.0	0.0	250	0.0	0.0	591	0.0	0.0	872	0.0
Lebanon	0	0.0	0.0	122	0.0	0.1	246	0.0	0.1	556	0.0	0.2	924	0.0
Colombia	0	0.0	0.0	0	0.0	0.0	24	0.0	0.0	128	0.0	0.0	152	0.0
Serbia	0	0.0	0.0	0	0.0	0.0	8	0.0	0.0	126	0.0	0.0	134	0.0
New Zealand	0	0.0	0.0	2	0.0	0.0	2	0.0	0.0	100	0.0	0.0	104	0.0
Argentina	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	30	0.0	0.0	30	0.0
Korea	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	6	0.0	0.0	6	0.0
Jordan	0	0.0	0.0	0	0.0	0.0	4	0.0	0.0	0	0.0	0.0	4	0.0
Total	11,914	3.2	0.0	113,256	8.4	0.1	288,848	11.5	0.3	465,876	11.0	0.4	879,894	10.4
All Countries														
Total	373,139	100.0	0.2	1,345,925	100.0	0.9	2,514,702	100.0	1.6	4,237,613	100.0	2.7	8,471,379	100.0

Abbreviations: SU/TIY, standard unit per 1000 inhabitants ≥ 40 years per year.
Monthly sales data were aggregated for each 12-month period. For example, 2015-2016 includes monthly sales from August 2015 to July 2016.

SUPPLEMENTARY MATERIAL

Supplementary Methods

Supplementary Table 1. Regional Grouping, Income Category and Total Pharmaceutical Market Coverage of the Included MIDAS Countries

Data in sales channels (retail and hospital) that do not have 100% audit coverage are projected by IQVIA. Excluded channels are those not covered in MIDAS country audits or that were not available in our data set. Prices in MIDAS do not include rebates or off-invoice discounts. Figures in brackets indicate the number of MIDAS countries included within each region. Income category was defined according to the World Bank Fiscal Year 2020 (calendar year 2018).[1]

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
United States (2)	July 2015	Puerto Rico	High	Yes	Yes	Mail order and non-reporting wholesalers	93	Not projected
		United States	High	Yes	Yes	Others	89	Indirect sales projected, direct sales are not projected
Europe (25)	August 2015	Austria	High	Yes	Yes	None	100	Yes, except for dispensing doctors
		Belgium	High	Yes	Yes	Physicians (<1%)	>99	Yes

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
		Bulgaria	Upper middle	Yes	Yes	Others	98	Not projected
		Croatia	High	Yes	Yes	Others	98	Not projected
		Czech	High	Yes	Yes	Specialist distribution channels, welfare centers and army	95	Not projected
		Estonia	High	Yes	No	Hospitals	88	Yes
		Finland	High	Yes	Yes	None	100	Not projected
		France	High	Yes	Yes	None	100	Yes
		Germany	High	Yes	Yes	None	100	Projected and not projected depending on source
		Hungary	High	Yes	Yes	None	100	Not projected
		Ireland	High	Yes	Yes	None	100	Not projected
		Italy	High	Yes	Yes	Government, charity organizations	99	Yes
		Latvia	High	Yes	Yes	None	100	Yes

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
		Lithuania	High	Yes	Yes	None	99	Yes (hospital)
		Luxembourg	High	Yes	No	Hospitals	98	Indirect sales not projected, direct sales are projected
		Netherlands	High	Yes	Yes	Others	91	Yes, depending on data source
		Norway	High	Yes	Yes	None	100	Not projected
		Poland	High	Yes	Yes	None	100	Yes
		Portugal	High	Yes	Yes	Some specialized hospitals	100	Yes
		Romania	Upper middle	Yes	Yes	None	100	Yes (retail)
		Slovakia	High	Yes	Yes	Special distribution channels and army	97	Not projected
		Slovenia	High	Yes	Yes	Exports	98	Not projected
		Spain	High	Yes	Yes	Military, prisons	99	Yes
		Sweden	High	Yes	Yes	None	100	Not projected

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
		United Kingdom	High	Yes	Yes	Internet pharmacies, private hospitals, military, home care	89	Yes
Others (22)	September 2015 (Canada)	Argentina	Upper middle	Yes	No	Hospitals, institutions, supermarkets	73	Yes
		Australia	High	Yes	Yes	Clinics, prisons, government, day surgeries	90	Yes, depending on data source
		Brazil	Upper middle	Yes	No	Insurers, supermarkets	44	Yes
		Canada	High	Yes	Yes	Internet pharmacy sales	100	Yes
		China	Upper middle	Yes	Yes	Small hospitals, community health centers	72	Yes
		Colombia	Upper middle	Yes	No	Hospitals, physicians, private institutions	71	Yes
		Egypt	Lower middle	Yes	No	Hospitals, tenders, army	75	Yes, depending on data source

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
		Japan	High	Yes	Yes	None	100	Yes
		Jordan	Upper middle	Yes	No	Hospitals, government institutions, healthcare centers	71	Yes, depending on data source
		Korea	High	Yes	No	Hospital (in-patient), exports, military, others	65	Yes
		Kuwait	High	Yes	No	Hospitals, government institutions, health centers	35	Yes
		Lebanon	Upper middle	Yes	No	Hospitals, government institutions, health centers	77	Yes, depending on data source
		Mexico	Upper middle	Yes	No	Hospitals, government tender, others	61	Yes
		New Zealand	High	Yes	Yes	Government, health store, optometrists, grocery, veterinary, others	97	Yes, depending on data source

Region	Month and year of first PCSK9 inhibitor sale	MIDAS country	Income category	Retail sector	Hospital sector	Sectors not covered	Coverage (% of total market)	Projection
		Russia Federation	Upper middle	Yes	Yes	Penitentiary hospitals, others	97	Yes (retail)
		Saudi Arabia	High	Yes	No	Institutions, government & semi-government hospitals	45	Yes, depending on data source
		Serbia	Upper middle	Yes	Yes	Military, homes for the elderly, others	93	Not projected
		Switzerland	High	Yes	Yes	None	100	Not projected
		Taiwan	High	No	Yes	Drugstores, dispensing doctors, dental clinics, military	83	Yes
		Thailand	Upper middle	No	Yes	Health centers, private clinics, drugstores	71	Yes
		Turkey	Upper middle	Yes	Yes	Military, government	100	Not projected
		United Arab Emirates	High	Yes	No	Hospitals, government institutions, health centers	45	Yes

Data Sources

In addition to the pharmaceutical sales data from IQVIA, we obtained publicly available national data from other sources. Population estimates by age group for both sexes were obtained from the United Nations World Population Prospects report.[2] Purchasing power parity (PPP) conversion factors for household final consumption expenditure were obtained from the World Bank.[3] Current health expenditure as percentage of gross domestic product (CHE%GDP) in 2018 were obtained from the World Health Organization (WHO) Global Health Observatory.[4] CHE%GDP reflects how a society prioritizes health as measured in monetary terms.[5] Data on the age-standardized prevalence of ischemic heart disease in 2018 were obtained from the Global Burden of Disease Study.[6]

Expenditure Calculations

To permit international comparisons, sales in current local currency (indicative of list prices at the manufacturer sales level during the month of sale) were adjusted using purchasing power parity (PPP) factors to international dollars. Calculating expenditures with PPP controls for the differences in prices between countries, thereby allowing comparable volume comparisons in expenditures. An international dollar would therefore "buy in the cited country a comparable amount of goods and services a US dollar would buy in the United States."[7] Given that there are advantages and disadvantages of converting currency using PPP or to a common currency,[8] we also analyzed PCSK9 inhibitor expenditures in US dollar constant currency as a sensitivity analysis (Supplementary Table 4). Sales in constant US dollars were available in MIDAS which converted sales in local currency at a fixed exchange rate using Q3 2019 average exchange rates. The results using international dollars and constant US dollars were similar (Supplementary Tables 3-4 and Supplementary Figure 1).

Expenditures in local currency were converted using PPP according to the methods described in the Health Action International/WHO Guidebook and were not adjusted for inflation.[9]

An example of converting local currency expenditures for Mexico in 2018:

$$\frac{Total\ expenditures\ in\ local\ currency\ 2018{-}2019}{PPP_{2018}} = Total\ expenditures\ in\ international\ dollars$$

99,875,086 Peso Mexicano/10.448015 = 9,559,240 international dollars

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Supplementary Table 2. Additional National Data Used in the Analyses: Population ≥ 40 years (thousands), Current Health Expenditure (CHE) as % Gross Domestic Product (GDP), Age-standardized Prevalence of Ischemic Heart Disease (IHD) and Purchasing Power Parity (PPP) Factors

Country	Population, 2015	Population, 2016	Population, 2017	Population, 2018	CHE as % GDP, 2018	Prevalence of IHD (%), 2018	PPP, 2015	PPP, 2016	PPP, 2017	PPP, 2018
Argentina	15,603	15,893	16,203	16,529	9.6	1.1	8.0	10.8	10.8	10.8
Australia	11,081	11,272	11,445	11,609	9.3	3.2	1.5	1.5	1.6	1.5
Austria	4,726	4,763	4,799	4,834	10.3	2.0	0.9	0.8	0.8	0.8
Belgium	5,849	5,901	5,949	5,998	10.3	2.1	0.9	0.9	0.9	0.8
Brazil	73,667	75,551	77,506	79,530	9.5	1.8	2.1	2.2	2.3	2.4
Bulgaria	3,963	3,971	3,972	3,972	7.3	3.2	0.8	0.7	0.7	0.7
Canada	18,204	18,448	18,682	18,916	10.8	1.8	1.3	1.3	1.3	1.2
China	639,448	651,020	661,258	670,491	5.4	2.5	4.0	4.1	4.1	4.1
Colombia	16,262	16,702	17,187	17,703	7.6	1.9	1,305.8	1,398.7	1,462.4	1,440.9
Croatia	2,284	2,290	2,291	2,295	6.8	3.1	4.0	3.9	3.9	3.7
Czech	5,550	5,636	5,718	5,804	7.6	3.7	14.2	13.9	13.9	13.3
Egypt	23,504	24,106	24,812	25,594	4.9	5.9	2.3	2.6	3.4	3.8
Estonia	686	692	696	700	6.7	4.7	0.6	0.6	0.6	0.6
Finland	2,895	2,912	2,929	2,946	9.0	2.1	1.0	1.0	0.9	0.9
France	33,312	33,579	33,814	34,027	11.3	1.8	0.9	0.8	0.8	0.8
Germany	47,167	47,278	47,414	47,543	11.4	2.2	0.8	0.8	0.8	0.7

Country	Population, 2015	Population, 2016	Population, 2017	Population, 2018	CHE as % GDP, 2018	Prevalence of IHD (%), 2018	PPP, 2015	PPP, 2016	PPP, 2017	PPP, 2018
Hungary	5,152	5,202	5,252	5,301	6.7	3.5	148.0	146.4	152.4	147.6
Ireland	2,056	2,102	2,158	2,216	6.9	2.0	1.0	1.0	1.0	0.9
Italy	35,461	35,803	36,078	36,290	8.7	2.2	0.8	0.8	0.8	0.7
Japan	76,396	76,953	77,419	77,799	11.0	1.2	109.0	114.9	115.7	109.6
Jordan	2,051	2,158	2,257	2,348	7.8	5.4	0.4	0.4	0.3	0.3
Korea	26,088	26,630	27,145	27,632	7.6	1.0	959.7	967.1	988.8	938.8
Kuwait	1,280	1,391	1,498	1,601	5.0	6.0	0.2	0.2	0.2	0.2
Latvia	1,072	1,068	1,060	1,052	6.2	3.9	0.6	0.6	0.6	0.5
Lebanon	2,049	2,141	2,215	2,272	8.4	5.3	793.8	761.7	761.8	788.9
Lithuania	1,572	1,567	1,561	1,549	6.6	3.6	0.5	0.5	0.5	0.5
Luxembourg	276	284	290	295	5.3	1.7	1.0	1.0	1.0	0.9
Mexico	38,439	39,493	40,555	41,633	5.4	2.2	9.4	9.5	10.1	10.4
Netherlands	8,946	9,007	9,068	9,125	10.0	2.5	0.9	0.9	0.9	0.8
New Zealand	2,156	2,191	2,216	2,240	9.2	2.6	1.6	1.6	1.6	1.5
Norway	2,542	2,578	2,613	2,641	10.0	1.8	10.6	10.7	10.4	9.8
Poland	18,852	19,065	19,264	19,464	6.3	2.3	1.9	1.8	1.9	1.8
Portugal	5,823	5,871	5,918	5,965	9.4	1.5	0.7	0.7	0.7	0.6
Puerto Rico	1,601	1,607	1,602	1,594	10.5	3.8	1.0	1.0	1.0	1.0
Romania	10,351	10,424	10,480	10,526	5.6	3.1	1.9	1.8	1.9	1.8
Russian Federation	69,576	70,024	70,488	70,966	5.3	3.9	25.3	25.8	25.7	25.2

Country	Population, 2015	Population, 2016	Population, 2017	Population, 2018	CHE as % GDP, 2018	Prevalence of IHD (%), 2018	PPP, 2015	PPP, 2016	PPP, 2017	PPP, 2018
Saudi Arabia	9,191	9,675	10,170	10,671	6.4	5.5	1.7	1.8	1.7	1.7
Serbia	4,506	4,522	4,534	4,548	8.5	4.0	48.4	48.0	48.8	46.1
Slovakia	2,641	2,679	2,724	2,764	6.7	3.0	0.5	0.6	0.6	0.6
Slovenia	1,124	1,137	1,149	1,161	8.3	3.1	0.7	0.7	0.6	0.6
Spain	25,304	25,698	26,100	26,511	9.0	1.9	0.7	0.7	0.7	0.7
Sweden	4,996	5,040	5,077	5,108	10.9	2.0	9.3	9.3	9.5	9.0
Switzerland	4,408	4,466	4,521	4,571	11.9	1.8	1.4	1.4	1.4	1.3
Taiwan	11,670	11,892	12,141	12,405	6.1	2.3	16.4	16.6	16.6	16.6
Thailand	32,054	32,704	33,327	33,918	3.8	1.6	13.0	13.1	13.3	13.1
Turkey	26,838	27,722	28,647	29,589	4.1	3.4	1.4	1.6	1.7	1.8
United Arab Emirates	2,433	2,530	2,610	2,671	4.2	5.5	2.8	2.9	2.8	2.9
United Kingdom	32,940	33,221	33,502	33,781	10.0	1.8	0.8	0.8	0.8	0.7
United States	150,602	152,184	153,670	155,124	16.9	1.8	1.0	1.0	1.0	1.0

Supplementary Table 3. Absolute (No. of international dollars), Relative (%) and Population-Standardized (ID/TIY) PCSK9 Inhibitor Expenditures and Price per Standard Unit (ID/SU) in the United States, Europe and Other Countries from 2015 to 2019. Absolute figures are in thousands of international dollars.

	2015-2016				2016-2017				2017-2018				2018-2019				Total		
	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/SU
United States																			
United States	154,756	88.0	1,027.6	512	483,570	81.6	3,177.5	521	793,989	75.6	5,166.8	529	1,139,015	71.8	7,342.6	448	2,571,330	75.5	487
Puerto Rico	152	0.1	95.2	560	912	0.2	567.6	598	1,002	0.1	625.7	637	1,603	0.1	1,005.5	517	3,670	0.1	567
Total	154,908	88.0	1,017.8	512	484,482	81.8	3,150.3	522	794,992	75.7	5,120.0	529	1,140,618	71.9	7,278.2	448	2,575,000	75.6	488
Europe																			
Germany	14,451	8.2	306.4	347	41,340	7.0	874.4	327	75,330	7.2	1,588.8	326	113,301	7.1	2,383.1	324	244,421	7.2	326
Netherlands	978	0.6	109.4	229	12,301	2.1	1,365.7	231	29,852	2.8	3,292.0	234	50,139	3.2	5,494.7	241	93,270	2.7	237
Spain	662	0.4	26.2	279	12,329	2.1	479.8	287	30,043	2.9	1,151.1	291	52,296	3.3	1,972.6	304	95,330	2.8	297
Italy	271	0.2	7.6	350	2,974	0.5	83.1	288	18,340	1.7	508.3	253	41,600	2.6	1,146.3	271	63,185	1.9	266
United Kingdom	224	0.1	6.8	184	4,780	0.8	143.9	188	12,545	1.2	374.4	188	20,692	1.3	612.5	200	38,241	1.1	194
Austria	810	0.5	171.4	320	4,093	0.7	859.3	235	10,568	1.0	2,202.1	230	20,634	1.3	4,268.6	242	36,105	1.1	239
Belgium	0	0.0	0.0	NA	2,145	0.4	363.5	260	6,153	0.6	1,034.3	246	10,052	0.6	1,675.9	259	18,350	0.5	254
Sweden	205	0.1	41.1	203	1,127	0.2	223.6	191	2,918	0.3	574.8	188	6,166	0.4	1,207.1	197	10,416	0.3	194
Norway	749	0.4	294.5	187	1,857	0.3	720.4	183	2,946	0.3	1,127.3	179	4,794	0.3	1,815.3	188	10,346	0.3	184
Slovakia	0	0.0	0.0	NA	607	0.1	226.5	356	3,017	0.3	1,107.7	312	5,891	0.4	2,131.4	317	9,515	0.3	318
France	0	0.0	0.0	NA	0	0.0	0.0	NA	846	0.1	25.0	274	4,843	0.3	142.3	297	5,688	0.2	294
Czech	0	0.0	0.0	NA	80	0.0	14.3	456	102	0.0	17.9	457	1,972	0.1	339.8	358	2,155	0.1	364
Slovenia	88	0.1	78.6	402	132	0.0	116.3	335	534	0.1	464.5	276	1,203	0.1	1,036.6	293	1,958	0.1	294
Bulgaria	21	0.0	5.2	612	53	0.0	13.3	562	651	0.1	163.8	417	1,918	0.1	482.9	536	2,642	0.1	502
Finland	83	0.0	28.8	240	149	0.0	51.2	247	432	0.0	147.6	210	728	0.0	247.0	206	1,393	0.0	212
Luxembourg	0	0.0	0.0	NA	1	0.0	4.2	198	47	0.0	161.3	200	464	0.0	1,573.0	215	512	0.0	214
Poland	30	0.0	1.6	485	193	0.0	10.1	449	316	0.0	16.4	425	330	0.0	17.0	425	869	0.0	432
Portugal	0	0.0	0.0	NA	0	0.0	0.0	NA	68	0.0	11.5	343	205	0.0	34.4	362	273	0.0	357
Croatia	0	0.0	0.0	NA	5	0.0	2.3	430	0	0.0	0.0	NA	185	0.0	80.8	369	191	0.0	371
Hungary	45	0.0	8.8	709	66	0.0	12.7	717	120	0.0	22.8	689	191	0.0	36.1	642	423	0.0	673
Estonia	0	0.0	0.0	NA	0	0.0	0.0	NA	3	0.0	4.6	356	20	0.0	29.0	356	23	0.0	356
Romania	0	0.0	0.0	NA	8	0.0	0.8	505	7	0.0	0.7	493	21	0.0	2.0	472	36	0.0	483
Lithuania	0	0.0	0.3	445	0	0.0	0.0	NA	7	0.0	4.6	449	12	0.0	7.6	469	19	0.0	461
Ireland	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	0	0	0.0	0
Latvia	0	0.0	0.0	NA	3	0.0	2.7	412	0	0.0	0.0	NA	0	0.0	0.0	NA	3	0.0	412
Total	18,618	10.6	70.1	318	84,244	14.2	314.6	277	194,844	18.6	722.0	269	337,659	21.3	1,242.0	276	635,365	18.7	275
Others																			
Canada	1,338	0.8	73.5	213	9,461	1.6	512.8	221	20,693	2.0	1,107.6	216	35,448	2.2	1,874.0	216	66,940	2.0	216
Japan	540	0.3	7.1	167	7,185	1.2	93.4	158	19,602	1.9	253.2	166	30,849	1.9	396.5	197	58,176	1.7	180
Switzerland	219	0.1	49.7	197	2,473	0.4	553.6	196	5,483	0.5	1,212.9	172	9,413	0.6	2,059.3	183	17,588	0.5	182
Australia	231	0.1	20.9	206	712	0.1	63.2	190	3,004	0.3	262.5	182	5,632	0.4	485.2	192	9,579	0.3	189
Mexico	51	0.0	1.3	465	2,614	0.4	66.2	482	5,427	0.5	133.8	461	9,559	0.6	229.6	457	17,651	0.5	462

	2015-2016				2016-2017				2017-2018				2018-2019				Total		
	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/TIY	ID/SU	No.	%	ID/SU
Brazil	0	0.0	0.0	NA	653	0.1	8.6	395	2,580	0.2	33.3	380	5,059	0.3	63.6	384	8,292	0.2	383
Saudi Arabia	0	0.0	0.0	NA	0	0.0	0.0	NA	1,085	0.1	106.7	522	4,651	0.3	435.9	465	5,736	0.2	475
United Arab Emirates	28	0.0	11.7	525	441	0.1	174.4	415	1,022	0.1	391.6	299	1,826	0.1	683.6	301	3,317	0.1	313
Taiwan	0	0.0	0.0	NA	9	0.0	0.8	374	440	0.0	36.2	385	1,496	0.1	120.6	374	1,945	0.1	377
China	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	847	0.1	1.3	219	847	0.0	219
Russian Federation	0	0.0	0.0	NA	28	0.0	0.4	644	320	0.0	4.5	490	1,139	0.1	16.1	478	1,488	0.0	483
Thailand	0	0.0	0.0	NA	0	0.0	0.0	NA	9	0.0	0.3	544	547	0.0	16.1	576	556	0.0	576
Egypt	10	0.0	0.4	843	155	0.0	6.4	635	81	0.0	3.3	492	480	0.0	18.7	542	726	0.0	556
Kuwait	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	224	0.0	140.1	326	224	0.0	326
Turkey	0	0.0	0.0	NA	14	0.0	0.5	436	81	0.0	2.8	322	194	0.0	6.6	328	288	0.0	331
Lebanon	0	0.0	0.0	NA	52	0.0	24.4	427	103	0.0	46.5	419	231	0.0	101.9	416	387	0.0	418
Colombia	0	0.0	0.0	NA	0	0.0	0.0	NA	11	0.0	0.6	456	64	0.0	3.6	498	75	0.0	492
Serbia	0	0.0	0.0	NA	0	0.0	0.0	NA	3	0.0	0.8	431	57	0.0	12.6	455	61	0.0	454
New Zealand	0	0.0	0.0	NA	0	0.0	0.0	0	0	0.0	0.2	215	21	0.0	9.5	213	22	0.0	209
Argentina	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	28	0.0	1.7	949	28	0.0	949
Korea	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	1	0.0	0.0	127	1	0.0	127
Jordan	0	0.0	0.0	NA	0	0.0	0.0	NA	2	0.0	1.0	542	0	0.0	0.0	NA	2	0.0	542
Total	2,418	1.4	2.2	203	23,796	4.0	21.1	210	59,946	5.7	52.3	208	107,769	6.8	92.5	231	193,929	5.7	220
All Countries																			
Total	175,944	100.0	115.4	472	592,522	100.0	382.5	440	1,049,782	100.0	667.8	417	1,586,046	100.0	995.1	374	3,404,294	100.0	402

Abbreviations: ID/TIY, international dollar per 1000 inhabitants ≥ 40 years per year; NA, not applicable; ID/SU, international dollar per standard unit.
Monthly sales data were aggregated for each 12-month period. For example, 2015-2016 includes monthly sales from August 2015 to July 2016. Expenditures were obtained from monthly sales data in MIDAS and are list prices at the manufacturer sales level. These list prices do not account for rebates or off-invoice discounts. Expenditures were converted from local currency to international dollars (thousands) using purchasing power parities. Price per standard unit was estimated by dividing expenditures (international dollars) by the number of standard units sold in each year or overall.

Supplementary Table 4. Absolute (No. of US dollars), Relative (%) and Standardized (USD/TIY) PCSK9 Inhibitor Expenditures and Price per Standard Unit (USD/SU) in the United States, Europe and Other Countries from 2015 to 2019. Absolute figures are in thousands of US dollars.

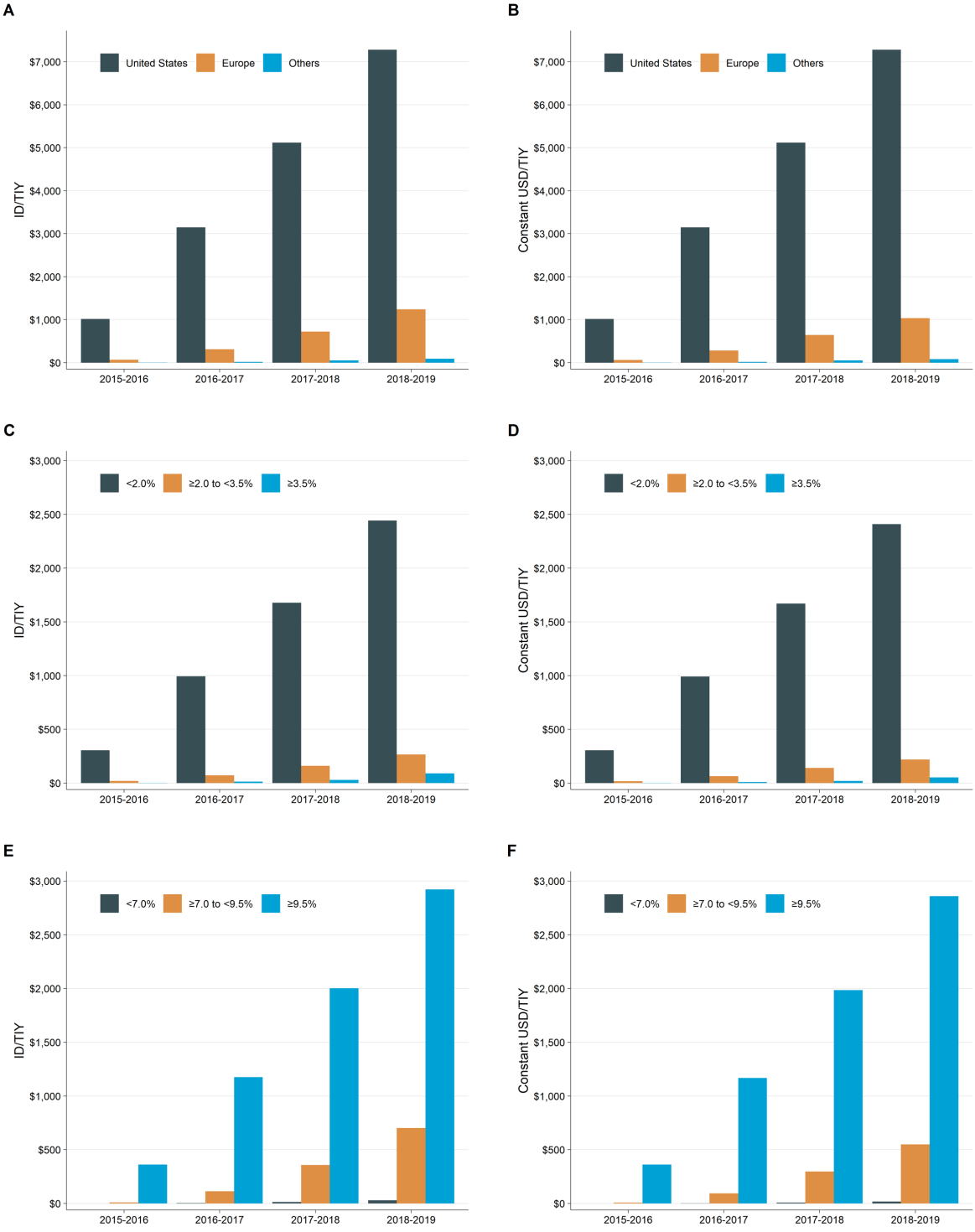
	2015-2016				2016-2017				2017-2018				2018-2019				Total		
	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/SU
United States																			
United States	154,756	88.5	1,027.6	512	483,570	82.8	3,177.5	521	793,989	77.3	5,166.8	529	1,139,015	74.9	7,342.6	448	2,571,330	77.8	487
Puerto Rico	149	0.1	92.8	546	885	0.2	550.6	580	979	0.1	611.3	623	1,566	0.1	982.3	505	3,578	0.1	553
Total	154,904	88.6	1,017.7	512	484,455	82.9	3,150.1	522	794,968	77.4	5,119.8	529	1,140,581	75.0	7,277.9	448	2,574,908	77.9	488
Europe																			
Germany	13,395	7.7	284.0	322	37,122	6.4	785.2	293	66,782	6.5	1,408.5	289	93,827	6.2	1,973.5	268	211,126	6.4	282
Netherlands	967	0.6	108.1	227	11,948	2.0	1,326.5	225	28,509	2.8	3,143.9	223	44,711	2.9	4,899.8	215	86,134	2.6	219
Spain	548	0.3	21.7	231	9,937	1.7	386.7	231	23,879	2.3	914.9	231	39,718	2.6	1,498.2	231	74,082	2.2	231
Italy	252	0.1	7.1	326	2,623	0.4	73.3	254	15,952	1.6	442.2	220	33,793	2.2	931.2	220	52,621	1.6	222
United Kingdom	225	0.1	6.8	185	4,702	0.8	141.5	184	12,274	1.2	366.4	184	19,123	1.3	566.1	185	36,324	1.1	184
Austria	768	0.4	162.6	304	3,792	0.6	796.1	218	9,821	1.0	2,046.5	214	18,143	1.2	3,753.2	213	32,524	1.0	215
Belgium	0	0.0	0.0	NA	2,038	0.3	345.4	247	5,850	0.6	983.4	234	8,987	0.6	1,498.4	231	16,875	0.5	234
Sweden	198	0.1	39.6	196	1,090	0.2	216.2	184	2,861	0.3	563.5	184	5,755	0.4	1,126.6	184	9,903	0.3	184
Norway	885	0.5	348.2	221	2,214	0.4	858.8	218	3,402	0.3	1,301.8	207	5,249	0.3	1,987.7	206	11,750	0.4	209
Slovakia	0	0.0	0.0	NA	396	0.1	148.0	233	2,069	0.2	759.4	214	3,874	0.3	1,401.6	208	6,339	0.2	212
France	0	0.0	0.0	NA	0	0.0	0.0	NA	802	0.1	23.7	260	4,339	0.3	127.5	266	5,141	0.2	265
Czech	0	0.0	0.0	NA	48	0.0	8.5	274	61	0.0	10.7	274	1,131	0.1	194.8	205	1,240	0.0	210
Slovenia	66	0.0	58.6	299	96	0.0	84.7	244	384	0.0	334.5	199	818	0.1	704.8	199	1,365	0.0	205
Bulgaria	9	0.0	2.3	266	22	0.0	5.6	237	280	0.0	70.4	179	778	0.1	196.0	218	1,089	0.0	207
Finland	91	0.1	31.4	261	158	0.0	54.2	261	450	0.0	153.7	218	713	0.0	242.0	201	1,412	0.0	215
Luxembourg	0	0.0	0.0	NA	1	0.0	4.5	212	50	0.0	172.8	214	471	0.0	1,597.1	219	523	0.0	218
Poland	15	0.0	0.8	240	94	0.0	4.9	217	156	0.0	8.1	209	155	0.0	8.0	200	419	0.0	208
Portugal	0	0.0	0.0	NA	0	0.0	0.0	NA	51	0.0	8.6	256	142	0.0	23.9	251	193	0.0	252
Croatia	0	0.0	0.0	NA	3	0.0	1.3	253	0	0.0	0.0	NA	102	0.0	44.5	203	105	0.0	205
Hungary	23	0.0	4.4	357	33	0.0	6.3	357	62	0.0	11.8	357	96	0.0	18.1	322	214	0.0	341
Estonia	0	0.0	0.0	NA	0	0.0	0.0	NA	2	0.0	3.1	239	13	0.0	18.9	232	15	0.0	233
Romania	0	0.0	0.0	NA	4	0.0	0.3	219	3	0.0	0.3	219	9	0.0	0.8	203	16	0.0	210
Lithuania	0	0.0	0.2	247	0	0.0	0.0	NA	4	0.0	2.5	247	6	0.0	4.0	247	10	0.0	247
Ireland	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	0	0	0.0	0
Latvia	0	0.0	0.0	NA	2	0.0	1.7	257	0	0.0	0.0	NA	0	0.0	0.0	NA	2	0.0	257
Total	17,443	10.0	65.7	298	76,321	13.1	285.0	251	173,704	16.9	643.6	240	281,955	18.5	1,037.1	230	549,423	16.6	238
Others																			
Canada	1,369	0.8	75.2	218	9,395	1.6	509.2	219	20,451	2.0	1,094.7	213	33,797	2.2	1,786.7	206	65,011	2.0	210
Japan	554	0.3	7.3	171	7,773	1.3	101.0	171	21,338	2.1	275.6	181	31,824	2.1	409.1	204	61,490	1.9	190
Switzerland	314	0.2	71.1	282	3,459	0.6	774.6	274	7,605	0.7	1,682.1	239	12,275	0.8	2,685.5	239	23,653	0.7	244
Australia	242	0.1	21.8	216	739	0.1	65.6	197	3,169	0.3	276.9	192	5,732	0.4	493.8	195	9,882	0.3	195
Mexico	25	0.0	0.6	223	1,256	0.2	31.8	232	2,786	0.3	68.7	236	5,074	0.3	121.9	243	9,140	0.3	239

	2015-2016				2016-2017				2017-2018				2018-2019				Total		
	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/TIY	USD/SU	No.	%	USD/SU
Brazil	0	0.0	0.0	NA	366	0.1	4.8	221	1,495	0.1	19.3	220	2,967	0.2	37.3	225	4,828	0.1	223
Saudi Arabia	0	0.0	0.0	NA	0	0.0	0.0	NA	499	0.0	49.0	240	2,138	0.1	200.4	214	2,637	0.1	218
United Arab Emirates	22	0.0	9.0	405	343	0.1	135.6	323	789	0.1	302.3	231	1,418	0.1	530.8	233	2,572	0.1	242
Taiwan	0	0.0	0.0	NA	5	0.0	0.4	200	235	0.0	19.3	206	799	0.1	64.4	200	1,039	0.0	201
China	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	509	0.0	0.8	131	509	0.0	131
Russian Federation	0	0.0	0.0	NA	12	0.0	0.2	262	130	0.0	1.8	199	454	0.0	6.4	191	595	0.0	193
Thailand	0	0.0	0.0	NA	0	0.0	0.0	NA	4	0.0	0.1	234	233	0.0	6.9	245	237	0.0	245
Egypt	1	0.0	0.1	119	25	0.0	1.0	101	17	0.0	0.7	101	110	0.0	4.3	124	153	0.0	117
Kuwait	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	136	0.0	84.7	197	136	0.0	197
Turkey	0	0.0	0.0	NA	4	0.0	0.1	120	24	0.0	0.8	97	63	0.0	2.1	107	91	0.0	104
Lebanon	0	0.0	0.0	NA	26	0.0	12.3	216	52	0.0	23.5	212	121	0.0	53.3	218	200	0.0	216
Colombia	0	0.0	0.0	NA	0	0.0	0.0	NA	5	0.0	0.3	208	29	0.0	1.6	224	34	0.0	221
Serbia	0	0.0	0.0	NA	0	0.0	0.0	NA	2	0.0	0.4	199	25	0.0	5.5	198	27	0.0	198
New Zealand	0	0.0	0.0	NA	0	0.0	0.0	0	0	0.0	0.2	226	21	0.0	9.5	213	22	0.0	209
Argentina	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	7	0.0	0.4	242	7	0.0	242
Korea	0	0.0	0.0	NA	0	0.0	0.0	NA	0	0.0	0.0	NA	1	0.0	0.0	101	1	0.0	101
Jordan	0	0.0	0.0	NA	0	0.0	0.0	NA	1	0.0	0.4	252	0	0.0	0.0	NA	1	0.0	252
Total	2,526	1.4	2.3	212	23,402	4.0	20.8	207	58,601	5.7	51.1	203	97,733	6.4	83.9	210	182,262	5.5	207
All Countries																			
Total	174,873	100.0	114.7	469	584,178	100.0	377.1	434	1,027,273	100.0	653.5	409	1,520,269	100.0	953.9	359	3,306,593	100.0	390

Abbreviations: USD/TIY, constant US dollars per 1000 inhabitants ≥ 40 years per year; NA, not applicable; USD/SU, constant US dollars per standard unit.
Monthly sales data were aggregated for each 12-month period. For example, 2015-2016 includes monthly sales from August 2015 to July 2016. Expenditures were obtained from monthly sales data in MIDAS and are list prices at the manufacturer sales level. These list prices do not account for rebates or off-invoice discounts. Expenditures were converted from local currency to constant US dollars using a fixed exchange rate. Price per standard unit was estimated by dividing expenditures (constant US dollars) by the number of standard units sold in each year or overall.

Supplementary Figures

Supplementary Figure 1. Annual PCSK9 Inhibitor Expenditures Using List Prices at the Manufacturer Sales Level in 49 Countries from 2015 to 2019



Abbreviations: ID/TIY, international dollars per thousand inhabitants ≥ 40 years per year; USD/TIY, US dollars per thousand inhabitants ≥ 40 years per year. Stratified by region in international dollars (**A**) and constant US dollars (**B**). Stratified by the age-standardized prevalence of ischemic heart disease in 2018 in international dollars (**C**) and constant US dollars (**D**). Stratified by current health expenditures as a percentage of gross domestic product in 2018 in international dollars (**E**) and constant US dollars (**F**). Monthly sales data in MIDAS were aggregated for each 12-month period from August to July and standardized per 1000 inhabitants ≥ 40 years per year. For example, 2015-2016 includes monthly sales from August 2015 to July 2016.