

Number of people treated for hepatitis C virus infection in 2014-2023 and applicable lessons for new HBV and HDV therapies

Authors

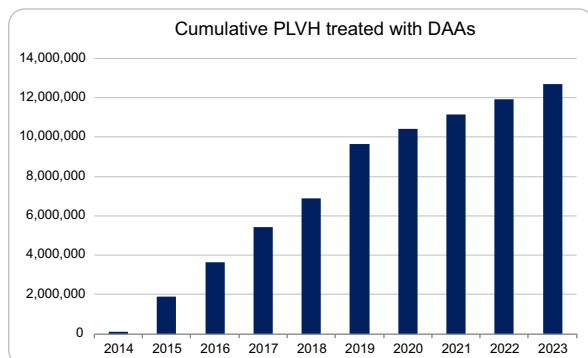
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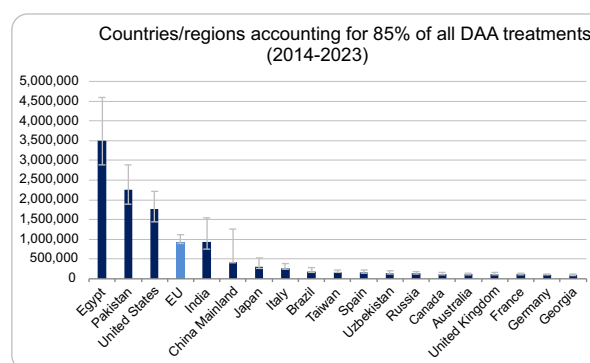
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Graphical abstract

Over the last 10 years, 12.7 million people living with hepatitis C viral (PLHCV) infections were treated with direct acting antivirals (DAAs)



Egypt, Pakistan, the U.S. and the E.U. accounted for 67% of this total



Highlights

- Since 2014, 12.7 out of the starting 61 million HCV infections were treated with direct-acting antivirals which cured 21% of total global infections.
- Egypt accounted for 27% of total treatments while Egypt, Pakistan, the US and the EU accounted for 67% of total treatments.
- Increases in treatment in nearly every country were followed by a drop as the pool of warehoused patients was depleted.
- After the drop, the launch of screening programs was associated with a treatment rebound as more individuals were diagnosed.

Impact and implications

Long-term hepatitis C virus (HCV) infection can lead to cirrhosis and liver cancer. Since 2014, these infections can be effectively treated with 8-12 weeks of oral therapies. In 2015, the World Health Organization established targets to eliminate HCV by 2030, which included treatment targets for member countries. The current study examines HCV treatment patterns across 119 countries and regions from 2014 to 2023 to assess the impact of national programs. This study can assist physicians and policymakers in understanding treatment patterns within similar regions or income groups and in utilizing historical data to refine their strategies in the future.

Number of people treated for hepatitis C virus infection in 2014–2023 and applicable lessons for new HBV and HDV therapies

The Polaris Observatory Collaborators^{*,†}

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See Editorial, pages 283–285

Background & Aims: The year 2023 marked the 10-year anniversary of the launch of direct-acting antivirals (DAAs) for the treatment of hepatitis C virus (HCV). Monitoring HCV treatment trends by country, region, and globally is important to assess progress toward the World Health Organization's 2030 elimination targets. Additionally, historical patterns can help predict the uptake of future therapies for other liver diseases.

Methods: The number of people living with HCV (PLHCV) treated between 2014–2023 across 119 countries was estimated using national HCV registries, reported DAA sales data, pharmaceutical companies' reports, and estimates provided by national experts. For the countries with no available data, the average estimate of the corresponding Global Burden of Disease region was used.

Results: An estimated 13,816,000 (95% uncertainty intervals: 13,221,000–16,415,000) PLHCV were treated, of whom 12,748,000 (12,226,000–15,231,000) were treated with DAAs, of which 11,081,000 (10,542,000–13,338,000) were sofosbuvir-based DAA regimens. Country-level data accounted for 97% of these estimates. In high-income countries, there was a 41% drop in treatment from its peak, and reimbursement was a large predictor of treatment. In low- and middle-income countries, price played an important role in expanding treatment access through the public and private markets, and treatment continues to increase slowly after a sharp drop at the end of the Egyptian national program.

Conclusions: In the last 10 years, 21% of all HCV infections were treated with DAAs. Regional and temporal variations highlight the importance of active screening strategies. Without program enhancements, the number of treated PLHCV stalled in every country/region, which may not reflect a lower prevalence but may instead reflect the diminishing returns of existing strategies.

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Introduction

The year 2023 marked the 10-year anniversary of the launch of direct-acting antivirals (DAAs) for the treatment of hepatitis C virus (HCV), an infection that affects 50 million people globally and leads to 244 thousand deaths annually, primarily from cancer and cirrhosis.¹ Compared to their predecessors, DAAs are characterized by high sustained viral responses (>95%), minimal side effects, and short treatment durations (~8–12 weeks).

The 69th World Health Assembly endorsed the World Health Organization's (WHO's) Global Health Sector Strategy for Viral Hepatitis with the goal of eliminating hepatitis infection as a public health threat by 2030.² This was followed by the WHO's global targets for management of HCV infections, including

diagnosing and treating 90% and 80%, respectively, of all people living with HCV (PLHCV).³ As such, estimates of treated PLHCV need to be tracked to determine how countries and regions are progressing toward achieving the elimination targets.^{4,5}

Analysis of the trends in HCV treatment is also important since curative therapies for other viral infections (hepatitis B virus [HBV] and hepatitis delta virus [HDV]) are also in development. A study of HCV treatment patterns can help to prepare and forecast the uptake of these new therapies once approved.

The objectives of this study were to estimate the total number of DAA-treated PLHCV by country, region, and globally and to examine the treatment patterns across different regions.

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Materials and methods

The number of treated PLHCV between 2014–2023 in each country was estimated using the following sources in descending order of priority: 1) national prescription drug/national registries, 2) reported DAA sales data, as provided by manufacturers under a confidentiality agreement and converted to treated PLHCV, 3) pharmaceutical companies' presentations to investors and analysts where their estimated number of treated PLHCV was reported, 4) pharmaceutical companies' local country office treatment estimates, 5) estimates provided by national experts working at major treatment centers via the annual Polaris Observatory update.

Priority was given to source 1 when it was clear that the public health system was accountable for treating PLHCV in the country (e.g., Australia, Egypt, France, Georgia, Iceland, Italy, Norway, Spain, and the United Kingdom). For source 2, when sales data were reported by the number of pills, they were divided by 28 to convert to bottles. The number of bottles sold was then converted to treated PLHCV by dividing the number of bottles of sofosbuvir/velpatasvir, sofosbuvir/ledipasvir, elbasvir/grazoprevir, and ombitasvir/paritaprevir by 3 (12 weeks average duration of treatment) and of glecaprevir/pibrentasvir by 2 (8 weeks of treatment). For multi-pill combinations that also used daclatasvir, ravidasvir, ledipasvir, dasabuvir, ribavirin, and ritonavir, the unit sales of the nucleoside (e.g., sofosbuvir, ombitasvir/paritaprevir) were used to estimate the number of treated PLHCV. Since sofosbuvir-based treatment accounted for most of all HCV treatments, the proportion of PLHCV on sofosbuvir-based regimens was calculated as a percentage of PLHCV on DAAs. In countries with access to generic sofosbuvir and daclatasvir,⁶ it was assumed that all PLHCV were treated with sofosbuvir-based regimens. If a country had not reported their number of treated PLHCV in 2023, it was assumed to be the same as 2022 with the same percentage of DAA- and sofosbuvir-based regimens.

Sofosbuvir/velpatasvir/voxilaprevir was used as a second-line treatment and was not included in this analysis to prevent double counting. Similarly, 24 weeks of sofosbuvir/daclatasvir was used for treatment failures but was not considered in this analysis. The use of sofosbuvir/pegylated interferon/ribavirin was small relative to DAA therapies over the 10-year period and was also ignored. Traditional medicines, such as herbal therapies, were not considered.

To estimate the global and regional number of treated PLHCV, the regional treatment rate based on available country data for the Global Burden of Disease (GBD) regions⁷ was used for countries with missing data. The following countries were excluded from the regional estimates due to their high treatment rate: Australia, Denmark, Egypt, Finland, France, Georgia, Iceland, Japan, Malaysia, New Zealand, the Netherlands, Norway, Portugal, the Republic of Korea, Rwanda, Saudi Arabia, the Seychelles, Slovenia, Spain, Sweden, Taiwan, and the United Kingdom; since in given years, they treated $\geq 10\%$ of their HCV-infected population, which would not be representative of the countries with missing data in the same region.

For the base case estimate, the data source from the highest priority data source was selected (e.g., national registry, method 1, was selected over sales data, method 2, and method 2 was selected over method 3). The data from the different sources were used to develop uncertainty intervals (UIs).

Uncertainty analysis was conducted using Monte Carlo simulation with Latin Hypercube (a sampling size of 500) after running 10,000 trials in Crystal Ball® (Release 11.1.3708.0), an Excel® add-in by Oracle®. A binomial distribution was used for low (25% probability), base (50% probability), and high (25% probability) treatment estimates, with the 95% UI selected as the output. Given the asymmetry of the low, base, and high treated PLHCV estimates, UIs were deemed more appropriate than confidence intervals.

Results

An estimated 13,816,000 (95% UI: 13,221,000–16,415,000) PLHCV were treated in the last 10 years, of whom 12,748,000 (12,226,000–15,231,000) were treated with DAAs, including 11,081,000 (10,542,000–13,338,000) with sofosbuvir-based DAA regimens (Fig. 1A). In the last 10 years, 21% of the starting 62 million⁸ HCV infections were treated with DAAs. Most of these estimates (97%) came from country-level data (Table 1), with 3% of the regional and global estimates from extrapolation of GBD regional treatment rate data. Country-reported treated patients accounted for 63% of the total estimates, followed by analysis of drug sales data (19%), company-reported estimates (14%), and expert inputs (4%).

The annual number of treated PLHCV is shown in Fig. 1B, demonstrating a rapid switch to DAAs in 2015, when they were approved widely, and a peak in 2019 due to the expansion of the Egyptian HCV elimination program in that year. The cumulative number of DAA treatments is shown in Fig. 1C, which demonstrates that by 2023, 87% were on a sofosbuvir-based regimen.

The annual regional and global estimates of DAA treatment are shown in Table 2, indicating the high treatment in WHO's Eastern Mediterranean region, lower middle-income group, and Asia. All the above came about due to the programs in Egypt and Pakistan (Fig. 2). Fig. 3 shows the annual number of treated PLHCV by World Bank income groups, demonstrating the treatment trends. This figure excludes the annual number of treated HCV infections in Egypt. In high-income countries (HICs), the number of treatments peaked in 2016, but it had already declined by 8% before the COVID-19 pandemic in 2020 resulted in a further 29% decline (Table 1). Similarly, in lower middle-income countries (excluding Egypt), treatment peaked in 2016 and declined by 22% before the COVID-19 pandemic resulted in an additional 44% decline in 2020. On the other hand, COVID-19's impact in the other regions was less pronounced. In 2020, treatment increased by 16% in upper middle-income countries and 650% in low-income countries. Finally, Fig. 2 shows the countries that accounted for 85% of all DAA treatments between 2014–2023. Egypt, Pakistan, the United States, and the European Union (EU) accounted for 67% of all HCV treatments. The EU was added to this graph due to its high treatment rate as a region, but the numbers reported for the EU overlap those of the EU member countries shown on the same graph.

Discussion

This study is unique as it presents the treatment pattern for the highly curative HCV therapies by country and region, and the described methodology can be used to monitor progress in

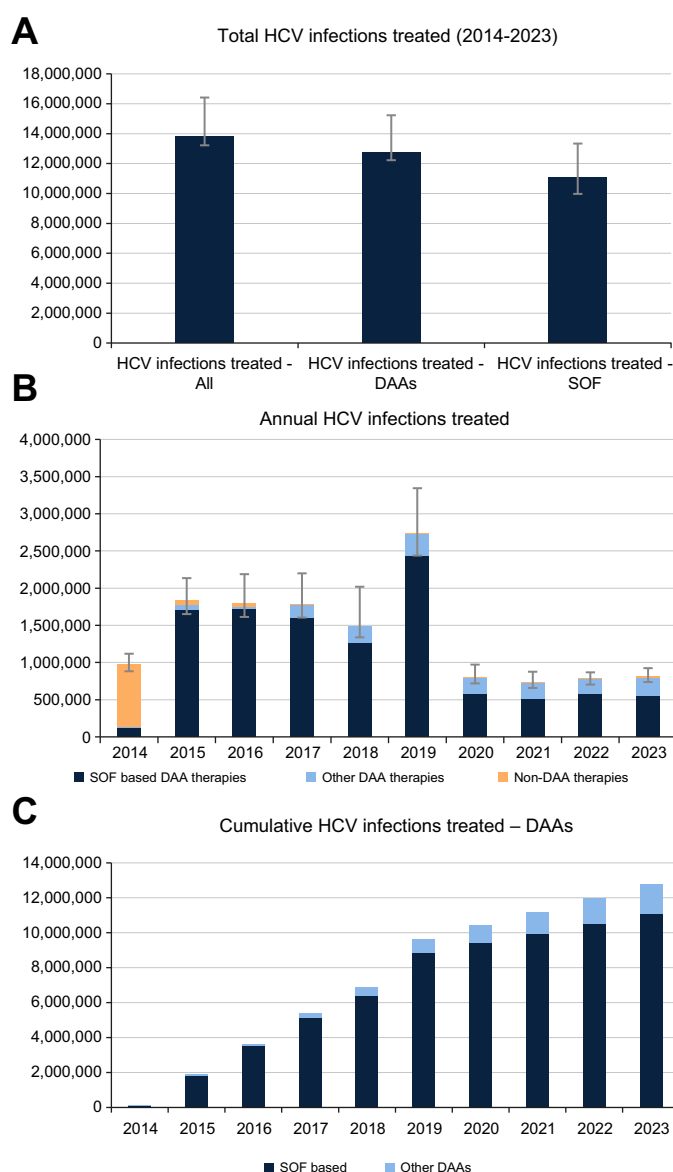


Fig. 1. Number of HCV infections treated globally in 2014-2023. (A) Total treated PLHCV between 2014-2023. (B) Annual number of treated PLHCV between 2014-2023. (C) Cumulative number of PLHCV treated with SOF-based regimens broken out. SOF-based = sofosbuvir-containing regimens. Other DAAs = elbasvir/grazoprevir, ombitasvir/paritaprevir, and glecaprevir/pibrentasvir-based therapies. Non-DAA therapies include interferon and protease-based therapies. DAAs, direct-acting antivirals; HCV, hepatitis C virus; PLHCV, people living with hepatitis C virus; SOF, sofosbuvir.

access to treatment. The lessons from this study may be applicable to new therapies being developed for other liver diseases.

Treated PLHCV

At the global level, the annual number of treated PLHCV peaked in 2019 (Table 2) when the Egyptian program was

expanded, but the number of treatments did rebound in 2022 after the end of the Egyptian program and recovery from the COVID-19 pandemic.

At the WHO regional level, the increase in 2020 in the African Regional Office (AFRO) was mainly due to the expansion of Rwanda's national program (Tables 1 and 2). Rwanda was also responsible for the growth in treatment shown in low-income countries. The Eastern Mediterranean region's treated PLHCV estimate was dominated by the Egyptian and Pakistan programs, and the region accounted for 46% of global treated PLHCV between 2014-2023. The European region's treatment estimates peaked in 2019 coinciding with the expanded treatment in Uzbekistan, Ukraine, and Russia, while the EU's treatment estimates peaked in 2017, when treatment restrictions were removed. The EU accounted for 55% of the treated PLHCV in the European region. The Pan American Health Organization (PAHO) showed a peak in treatment in 2016 as a result of high treatment in the United States, as well as an expansion of treatment in Brazil. India was responsible for a treatment peak in 2016 in the Southeast Asian region. The Western Pacific region's treatment peaked in 2015 with the launch of Japan's program as well as an increase in DAA treatment in China. The WPRO region saw large fluctuations in treatment with the launch of national programs in Australia, Cambodia (Médecins Sans Frontières/UNITAID), Malaysia, Mongolia, New Zealand, the Philippines, and Vietnam.

At the national level, a discussion of global treatment of PLHCV starts with Egypt, as it alone accounted for 27% of all those treated in the studied period. As shown in Table 1, the country started its DAA treatment program in October 2014, but the annual number of treated PLHCV dropped by 18% as the pool of those diagnosed, motivated, and warehoused was successfully treated. In 2018, the country initiated a national screening and treatment program, which led to 1.6 million Egyptians being treated in 2019 alone. The high uncertainty shown in Fig. 2 was due to the higher proportion of private-market HCV treatment before the national program kicked off.

The Egyptian national program⁹ exemplifies the importance of: 1) a country's commitment to elimination – which led to removal of obstacles as they emerged (e.g., initiating national screening as the number of treated cases declined), 2) adequately financing the national program, 3) implementing awareness and linkage to care programs, 4) negotiating with pharmaceutical companies to get access to the latest therapies as soon as they were launched in HICs, 5) collaborating with licensed and local drug manufacturers to ensure a steady supply of medicine at a low cost, 6) negotiating with diagnostic companies to get a steady supply of lab reagents, 7) training enough healthcare and community workers to support a national rollout, 8) creating a robust health information system to track progress, and 9) decentralizing service delivery to enable screening and linkage to care in rural villages and small towns. The Egyptian program showed that a passive HCV elimination program that focuses on treatment only will result in declining treatment numbers, and a full elimination program must be coupled with active screening, awareness, and linkage to care programs to achieve the WHO elimination goals.

Table 1. HCV infections treated with DAAs by country and region.

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Afghanistan	DS			12 (11–15)	12 (11–15)	20 (18–30)	20 (18–30)	30 (30–40)	80 (70–100)	460 (410–580)	460 (410–580)	1,100 (980–1,400)
Algeria	DS		1,400 (1,300–2,000)	2,900 (2,600–4,200)				70 (60–100)				4,400 (3,900–6,400)
Argentina	20			2,200 (2,000–3,100)	2,200 (2,000–3,100)	2,300 (2,100–3,200)	2,160 (2,000–3,000)	1,900 (1,800–2,600)	1,400 (1,300–1,900)	1,700 (1,600–2,400)	1,700 (1,600–2,400)	15,600 (14,500–21,600)
Armenia	NCID				2,000 (2,000–3,400)	1,000 (1,000–1,700)	1,100 (1,100–1,800)	1,200 (1,200–2,000)	1,700 (1,700–2,800)	1,100 (1,100–1,800)	100 (100–170)	8,200 (8,200–13,700)
Australia	21–23	901 (810–1,200)	3,439 (3,100–4,400)	33,200 (29,900–42,500)	21,000 (18,900–26,900)	15,200 (13,700–19,500)	11,300 (10,200–14,500)	8,200 (7,400–10,500)	6,600 (5,900–8,500)	5,200 (4,700–6,700)	5,500 (5,000–7,000)	111,000 (99,500–142,000)
Austria	DS		2,000 (1,800–2,800)	2,000 (1,800–2,800)	2,000 (1,800–2,800)	1,900 (1,700–2,700)	1,800 (1,600–2,500)	1,200 (1,100–1,700)	1,100 (990–1,500)			12,000 (10,800–16,700)
Azerbaijan	DS			13 (10–30)		1 (1–3)	1,600 (1,300–4,000)		4 (3–10)	690 (550–1,700)	690 (550–1,700)	3,000 (2,400–7,500)
Bahrain	EC		50 (50–80)	150 (140–230)	100 (90–150)	100 (90–150)	100 (90–150)	100 (90–150)				600 (540–900)
Bangladesh	DS			110 (90–280)	2,000 (1,600–5,000)	5 (4–13)	100 (80–250)	200 (160–500)				2,400 (1,900–6,000)
Belarus	DS			30 (30–50)	150 (140–240)	1,500 (1,400–2,400)	4,600 (4,100–7,300)	1,600 (1,400–2,500)		6 (5–10)	6 (5–10)	7,900 (7,100–12,500)
Belgium	24		1,300 (1,200–1,700)	810 (730–1,000)	1,800 (1,600–2,300)	990 (890–1,300)	2,500 (2,300–3,200)	1,700 (1,500–2,200)	950 (860–1,200)	810 (730–1,000)	810 (730–1,000)	11,700 (10,500–15,000)
Bénin	MoH					16 (15–20)	140 (130–190)	80 (70–110)	40 (40–50)	160 (150–220)	60 (60–80)	500 (460–680)
Bolivia	DS						40 (40–60)	270 (240–390)		70 (60–100)	70 (60–100)	450 (410–650)
Bosnia and Herzegovina	DS				55 (50–70)	70 (60–90)	90 (80–110)	70 (60–90)	110 (100–140)			400 (360–490)
Brazil	25		7,459 (6,700–11,100)	41,260 (37,100–61,600)	15,200 (13,700–22,700)	12,200 (11,000–18,200)	36,700 (33,000–54,800)	19,200 (17,300–28,700)	14,900 (13,400–22,300)	16,200 (14,600–24,200)	16,400 (14,800–24,500)	180,000 (162,000–268,000)
Bulgaria	26,27		179 (160–220)	698 (630–870)	1,400 (1,300–1,800)	1,200 (1,100–1,500)	930 (840–1,200)	810 (730–1,000)	810 (730–1,000)			6,000 (5,400–7,500)
Burkina Faso	DS			10 (9–13)		830 (750–1,100)	830 (750–1,100)	2,600 (2,300–3,400)	3,300 (3,000–4,300)	2,800 (2,500–3,600)	2,800 (2,500–3,600)	13,200 (11,900–17,100)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Burundi	DS			630 (570–990)	1,200 (1,100–1,900)	270 (240–420)	280 (250–440)	360 (320–570)	470 (420–740)	80 (70–130)	80 (70–130)	3,400 (3,000–5,300)
Cambodia	NDB, ^{28,29}		50 (50–60)	310 (280–400)	3,000 (2,700–3,900)	8,600 (7,700–11,100)	5,400 (4,900–7,000)	2,800 (2,500–3,600)	2,000 (1,800–2,600)	280 (250–360)	400 (360–520)	22,800 (20,600–29,400)
Cameroon	DS			1,200 (1,100–2,300)	1,900 (1,700–3,600)	4,000 (3,600–7,600)		810 (730–1,500)	540 (490–1,000)	540 (490–1,000)	540 (490–1,000)	9,500 (8,600–18,200)
Canada	³⁰ , EC		11,100 (10,000–14,100)	10,500 (9,500–13,400)	14,900 (13,400–19,000)	17,900 (16,100–22,800)	16,300 (14,700–20,800)	11,300 (10,200–14,400)	11,000 (9,900–14,000)	11,000 (9,900–14,000)	11,000 (9,900–14,000)	115,000 (104,000–146,000)
Chad	DS							1 (1–3)		310 (250–780)	310 (250–780)	620 (500–1,600)
Chile	DS		120 (100–300)	60 (50–150)	60 (50–150)	260 (210–650)	220 (180–550)		1 (1–3)			720 (580–1,800)
China Mainland	DS		70,000 (66,400–212,000)		200 (190–610)	390 (370–1,200)	1,000 (950–3,000)	52,100 (49,400–158,000)	93,000 (88,200–281,000)	94,700 (89,800–287,000)	94,700 (89,800–287,000)	406,000 (385,000–1,229,000)
Colombia	³¹			550 (500–750)	560 (500–770)	1,100 (990–1,500)	580 (520–790)	490 (440–670)	670 (600–920)	890 (800–1,200)	1,200 (1,100–1,600)	6,000 (5,400–8,300)
Congo, Republic of the	DS			30 (30–40)		70 (60–90)	50 (50–60)	13 (12–16)	60 (50–80)	2 (2–3)	2 (2–3)	230 (200–280)
Côte d'Ivoire	DS			50 (40–130)		5,000 (4,000–12,500)						5,100 (4,000–12,600)
Croatia	EC		99 (90–130)	179 (160–230)	340 (310–430)	440 (400–560)	474 (430–600)	360 (320–460)	340 (310–430)	250 (230–320)	300 (270–380)	2,800 (2,500–3,500)
Cuba	EC			15 (14–20)		5 (5–7)	80 (70–110)					100 (90–130)
Czechia	²⁷ , EC		257 (230–320)	570 (520–720)	620 (560–780)	650 (590–820)	1,400 (1,300–1,800)	2,300 (2,100–2,900)	1,700 (1,500–2,100)	2,600 (2,400–3,300)	2,600 (2,400–3,300)	12,700 (11,500–16,000)
Denmark	INFcare		630 (570–790)	510 (460–640)	450 (410–560)	750 (680–940)	2,000 (1,800–2,500)	800 (720–1,000)	500 (450–630)	500 (450–630)	500 (450–630)	6,600 (6,000–8,300)
Dominican Republic	EC		41 (30–100)	300 (240–750)	800 (640–2,000)	1,200 (960–3,000)	1,800 (1,400–4,500)					4,100 (3,300–10,400)
Egypt	⁹		827,000 (744,000–1,087,000)	342,000 (308,000–450,000)	479,000 (431,000–630,000)	226,000 (203,000–297,000)	1,600,000 (1,440,000–2,103,000)	15,000 (13,500–19,700)	5,000 (4,500–6,600)	3,000 (2,700–3,900)	310 (280–410)	3,497,000 (3,148,000–4,597,000)
Eritrea	DS						100 (90–130)			270 (240–340)	270 (240–340)	640 (580–800)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Estonia	32		450 (410–650)	604 (540–870)	562 (510–810)	950 (860–1,400)	980 (880–1,400)	630 (570–910)	1,200 (1,100–1,700)		780 (700–1,100)	6,200 (5,500–8,900)
Ethiopia	DS		2,000 (1,800–2,800)	850 (770–1,200)		320 (290–450)		620 (560–880)	890 (810–1,300)	1,200 (1,100–1,700)	280 (250–400)	6,200 (5,600–8,700)
Finland	EC		75 (70–100)	160 (140–210)	300 (270–380)	1,368 (1,200–1,800)	1,970 (1,800–2,500)	2,000 (1,800–2,600)	2,100 (1,900–2,700)	2,000 (1,800–2,600)	1,700 (1,500–2,200)	11,700 (10,500–15,000)
France	INVS		19,400 (17,500–24,900)	16,000 (14,400–20,500)	19,600 (17,600–25,100)	14,000 (12,600–18,000)	11,400 (10,300–14,600)	7,100 (6,400–9,100)	5,900 (5,300–7,600)	5,500 (5,000–7,100)	5,500 (5,000–7,100)	104,000 (94,000–134,000)
Georgia	Georgia CDC		6,000 (5,400–7,500)	21,600 (19,400–27,100)	15,000 (13,500–18,800)	10,300 (9,300–12,900)	12,400 (11,200–15,600)	8,500 (7,700–10,700)	4,000 (3,600–5,000)	4,400 (4,000–5,500)	4,400 (4,000–5,500)	86,600 (77,900–109,000)
Germany	DS		21,500 (19,400–27,000)	14,200 (12,800–17,800)	12,800 (11,500–16,100)	10,600 (9,500–13,300)	9,700 (8,700–12,200)	7,600 (6,800–9,500)	5,600 (5,000–7,000)	6,000 (5,400–7,500)	7,900 (7,100–9,900)	95,900 (86,300–121,000)
Ghana	DS			4 (3–10)	1,300 (1,000–3,300)		17 (14–40)	17 (14–40)	30 (20–80)	310 (250–780)	310 (250–780)	2,000 (1,600–5,000)
Greece	EC		1,500 (1,400–2,100)	1,500 (1,400–2,100)	1,900 (1,700–2,600)	1,600 (1,400–2,200)	1,200 (1,100–1,600)	1,300 (1,200–1,800)	1,200 (1,100–1,600)	1,100 (990–1,500)	1,600 (1,400–2,200)	12,900 (11,600–17,700)
Guatemala	DS			10 (9–13)	40 (40–50)				1,800 (1,600–2,300)			1,900 (1,700–2,300)
Guinea	DS					2 (2–5)		3 (2–8)		270 (220–680)	270 (220–680)	550 (440–1,400)
Guyana	DS				1 (1–3)				1 (1–3)	1,700 (1,400–4,300)	1,700 (1,400–4,300)	3,400 (2,700–8,500)
Haiti	DS					3 (2–8)		90 (70–230)	16 (13–40)			110 (90–270)
Hong Kong	EC		85 (80–130)	124 (110–190)	16 (14–20)	40 (40–60)	7 (6–11)	390 (350–590)				660 (600–1,000)
Hungary	27,33			931 (840–1,200)	923 (830–1,200)	2,479 (2,200–3,100)	1,400 (1,300–1,800)	900 (810–1,100)	500 (450–630)	750 (680–950)	650 (590–820)	8,500 (7,700–10,800)
Iceland	Trap HepC		30 (30–40)	480 (430–620)	170 (150–220)	100 (90–130)	80 (70–100)	80 (70–100)	50 (50–60)	70 (60–90)	70 (60–90)	1,100 (1,000–1,500)
India	DS		60,200 (54,200–98,100)	194,000 (175,000–316,000)	182,000 (164,000–297,000)	180,000 (162,000–293,000)	90,000 (81,000–147,000)					706,000 (636,000–1,151,000)
Indonesia	34		1,300 (1,200–4,400)	6,600 (5,900–22,100)	1,400 (1,300–4,700)	2,000 (1,800–6,700)	2,200 (2,000–7,400)	310 (280–1,000)	1,600 (1,400–5,400)	1,600 (1,400–5,400)	1,600 (1,400–5,400)	18,600 (16,700–62,300)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Iran	EC		5,300 (5,100– 8,600)	2,545 (2,400– 4,100)	5,949 (5,700– 9,700)	4,856 (4,700– 7,900)			2,400 (2,300– 3,900)			21,000 (20,200– 34,200)
Iraq	DS		240 (220– 850)	2,000 (1,800– 7,100)	60 (50– 210)	40 (40– 140)	100 (90– 350)	60 (50– 210)	20 (18– 70)	20 (18– 70)	20 (18– 70)	2,600 (2,300– 9,000)
Ireland	HSE		350 (320– 470)	540 (490– 720)	1,100 (990– 1,500)	1,600 (1,400– 2,100)	1,200 (1,100– 1,600)	530 (480– 710)	530 (480– 710)	530 (480– 710)	570 (510– 760)	7,000 (6,300– 9,300)
Israel	EC		1,500 (1,400– 1,900)	1,800 (1,700– 2,300)	1,500 (1,400– 1,900)	3,400 (3,100– 4,300)	2,400 (2,200– 3,000)	1,700 (1,600– 2,100)	1,200 (1,100– 1,500)	1,000 (930– 1,300)	1,000 (930– 1,300)	15,500 (14,300– 19,400)
Italy	35		31,200 (28,100– 46,800)	34,400 (31,000– 51,600)	44,400 (40,000– 66,600)	56,300 (50,700– 84,400)	36,300 (32,700– 54,400)	15,400 (13,900– 23,100)	14,500 (13,100– 21,700)	13,100 (11,800– 19,600)	13,100 (11,800– 19,600)	259,000 (233,000– 388,000)
Japan	MHLW & NDB		92,200 (83,000– 163,000)	63,400 (57,100– 112,000)	34,900 (31,400– 61,900)	36,800 (33,100– 65,200)	20,400 (18,400– 36,200)	15,100 (13,600– 26,800)	12,400 (11,200– 22,000)	9,200 (8,300– 16,300)	9,200 (8,300– 16,300)	294,000 (264,000– 520,000)
Jordan	DS			400 (360– 580)	500 (450– 720)	420 (380– 610)						1,300 (1,200– 1,900)
Kazakhstan	rceз.kz		450 (410– 1,200)	450 (410– 1,200)	1,900 (1,700– 5,100)	2,000 (1,800– 5,300)	15,400 (13,900– 41,100)	7,700 (6,900– 20,600)	6,600 (5,900– 17,600)	6,800 (6,100– 18,200)	11,000 (9,900– 29,400)	52,300 (47,100– 140,000)
Kenya	DS		40 (40– 120)	570 (510– 1,700)	90 (80– 280)	30 (30– 90)	1,200 (1,100– 3,700)	1,200 (1,100– 3,700)	190 (170– 580)	1,600 (1,400– 4,900)	1,600 (1,400– 4,900)	6,500 (5,900– 20,000)
Korea, Republic of	KCDC		1,500 (1,400– 1,900)	13,200 (11,900– 16,900)	13,000 (11,700– 16,700)	12,600 (11,300– 16,200)	12,200 (11,000– 15,700)	7,600 (6,800– 9,800)	6,100 (5,500– 7,800)	5,600 (5,000– 7,200)	5,500 (5,000– 7,100)	77,300 (69,600– 99,300)
Kyrgyzstan	DS			1,100 (990– 1,400)	1,000 (900– 1,200)	970 (870– 1,200)	1,800 (1,600– 2,200)	2,300 (2,100– 2,900)	450 (410– 560)			7,600 (6,900– 9,500)
Laos	DS			1 (1– 3)	3 (2– 8)	50 (40– 130)	690 (570– 1,700)	3,900 (3,200– 9,800)	530 (440– 1,300)	1 (1– 3)	1 (1– 3)	5,200 (4,300– 12,900)
Latvia	27,36		910 (820– 1,100)	410 (370– 510)	1,260 (1,100– 1,600)	1,700 (1,500– 2,100)	2,500 (2,300– 3,100)	2,600 (2,300– 3,300)	1,500 (1,400– 1,900)	1,100 (990– 1,400)	1,100 (990– 1,400)	13,100 (11,800– 16,300)
Lebanon	DS			330 (330– 650)	220 (220– 430)			10 (10– 20)	10 (10– 20)	30 (30– 60)	30 (30– 60)	630 (630– 1,200)
Liberia	DS							970 (870– 1,200)				970 (870– 1,200)
Libya	DS		1,700 (1,500– 2,600)					970 (870– 1,500)	830 (750– 1,300)			3,500 (3,200– 5,300)
Lithuania	27,37		423 (380– 530)	332 (300– 420)	766 (690– 960)	1,176 (1,100– 1,500)	1,900 (1,700– 2,400)	930 (840– 1,200)	950 (860– 1,200)	1,600 (1,400– 2,000)	3,200 (2,900– 4,000)	11,300 (10,100– 14,100)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Luxembourg	DS		150 (140–190)	300 (270–380)	200 (180–250)	130 (120–170)	180 (160–230)	120 (110–150)	130 (120–170)	150 (140–190)	130 (120–170)	1,500 (1,300–1,900)
Malaysia	³⁸ , EC			330 (310–420)	330 (310–420)	1,200 (1,100–1,500)	3,200 (3,000–4,000)	3,504 (3,300–4,400)	4,200 (3,900–5,300)	4,800 (4,500–6,100)	4,800 (4,500–6,100)	22,400 (20,800–28,300)
Malta	DS		40 (30–100)	70 (60–180)	100 (80–250)			1 (1–3)				210 (170–530)
Mauritania	DS			220 (200–270)								220 (200–270)
Mauritius	DS			300 (240–750)	6 (5–15)	100 (80–250)	4 (3–10)					410 (330–1,000)
Mexico	MoH			2,400 (2,200–3,300)	1,035 (970–1,400)	2,700 (2,500–3,700)	4,320 (4,000–5,900)	5,500 (5,200–7,500)	5,500 (5,200–7,500)	15,000 (14,100–20,500)	7,900 (7,400–10,800)	44,400 (41,600–60,600)
Moldova	DS			4 (3–10)			3,200 (2,600–8,000)	400 (320–1,000)	130 (100–330)			3,700 (3,000–9,300)
Mongolia	NCCD		280 (250–390)	10,400 (9,400–14,400)	17,700 (15,900–24,500)	15,600 (14,000–21,600)	10,800 (9,700–15,000)	6,900 (6,200–9,600)	1,100 (990–1,500)	2,100 (1,900–2,900)	2,100 (1,900–2,900)	67,000 (60,300–92,700)
Morocco	MoH			1,600 (1,500–2,400)	1,600 (1,500–2,400)	1,300 (1,200–1,900)	1,200 (1,100–1,800)	1,000 (950–1,500)	1,000 (950–1,500)			7,700 (7,400–11,500)
Myanmar	DS		1,900 (1,700–4,200)	17,500 (15,800–38,400)	8,000 (7,200–17,600)	7,000 (6,300–15,400)	3,000 (2,700–6,600)	3,700 (3,300–8,100)	1,300 (1,200–2,900)	680 (610–1,500)	680 (610–1,500)	43,800 (39,400–96,000)
Nepal	DS		3,300 (3,000–4,100)	1,700 (1,500–2,100)	230 (210–290)	340 (310–430)	170 (150–210)	210 (190–260)	1,600 (1,400–2,000)			7,600 (6,800–9,400)
Netherlands	³⁹	58 (50–70)	819 (740–1,000)	1,509 (1,400–1,900)	600 (540–760)	529 (480–670)	355 (320–450)	241 (220–310)	218 (200–280)	186 (170–240)	132 (120–170)	4,600 (4,200–5,900)
New Zealand	DS		534 (480–800)	1,412 (1,300–2,100)	1,486 (1,300–2,200)	840 (760–1,300)	3,500 (3,200–5,300)	1,000 (900–1,500)	810 (730–1,200)	710 (640–1,100)	710 (640–1,100)	11,000 (9,900–16,500)
Nicaragua	DS									50 (40–130)	50 (40–130)	100 (80–250)
Nigeria	DS		740 (670–930)	1,200 (1,100–1,500)	1,800 (1,600–2,300)	400 (360–500)	400 (360–500)	4,200 (3,800–5,300)	270 (240–340)			9,000 (8,100–11,300)
Norway	⁴⁰	740 (670–950)	861 (770–1,100)	974 (880–1,200)	1,849 (1,700–2,400)	3,098 (2,800–4,000)	2,100 (1,900–2,700)	1,300 (1,200–1,700)	930 (840–1,200)	768 (690–980)	850 (770–1,100)	13,500 (12,100–17,300)
Oman	EC		70 (60–100)	410 (370–580)	500 (450–700)	500 (450–700)	500 (450–700)	200 (180–280)	200 (180–280)	500 (450–700)	300 (270–420)	3,200 (2,900–4,500)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Pakistan	41		228,000 (205,000– 291,000)	360,000 (324,000– 459,000)	349,000 (314,000– 445,000)	354,000 (319,000– 452,000)	324,000 (292,000– 413,000)	154,000 (139,000– 196,000)	143,000 (129,000– 182,000)	176,000 (158,000– 225,000)	194,000 (175,000– 247,000)	2,282,000 (2,054,000– 2,911,000)
Peru	DS				6 (5– 15)	6 (5– 15)	6 (5– 15)	1 (1– 3)	290 (230– 730)			310 (250– 770)
Philippines	DS		130 (120– 170)	180 (160– 230)	2,300 (2,100– 2,900)	5,100 (4,600– 6,500)	1,500 (1,400– 1,900)	640 (580– 820)	3,700 (3,300– 4,700)	210 (190– 270)	210 (190– 270)	14,000 (12,600– 17,800)
Poland	42		4,100 (3,700– 5,300)	8,000 (7,200– 10,400)	11,115 (10,000– 14,400)	6,816 (6,100– 8,900)	8,330 (7,500– 10,800)	3,100 (2,800– 4,000)	2,600 (2,300– 3,400)	3,100 (2,800– 4,000)	3,400 (3,100– 4,400)	50,600 (45,500– 65,700)
Portugal	Atlas ECDC		9,700 (8,700– 12,100)	6,800 (6,100– 8,500)	4,900 (4,400– 6,100)	4,700 (4,200– 5,900)	3,900 (3,500– 4,900)	2,300 (2,100– 2,900)	2,300 (2,100– 2,900)	2,200 (2,000– 2,800)	2,200 (2,000– 2,800)	39,000 (35,100– 48,800)
Qatar	DS		237 (210– 310)	360 (320– 470)	550 (500– 720)	320 (290– 420)	600 (540– 790)	150 (140– 200)	130 (120– 170)	130 (120– 170)	130 (120– 170)	2,600 (2,300– 3,400)
Romania	43		286 (260– 380)	5,478 (4,900– 7,300)	10,200 (9,200– 13,600)	5,800 (5,200– 7,700)	14,400 (13,000– 19,100)	6,900 (6,200– 9,200)	4,400 (4,000– 5,800)	5,900 (5,300– 7,800)	5,900 (5,300– 7,800)	59,300 (53,300– 78,700)
Russia	EC			4,540 (4,100– 6,200)	7,901 (7,100– 10,700)	7,129 (6,400– 9,700)	12,066 (10,900– 16,400)	22,230 (20,000– 30,200)	22,892 (20,600– 31,100)	23,463 (21,100– 31,900)	30,400 (27,400– 41,400)	131,000 (118,000– 178,000)
Rwanda	44		800 (720– 2,100)	1,000 (910– 2,600)	3,300 (3,000– 8,500)	6,600 (6,000– 16,900)	800 (720– 2,100)	16,900 (15,300– 43,400)	17,400 (15,800– 44,700)	23,100 (20,900– 59,300)	2,200 (2,000– 5,600)	72,100 (65,300– 185,000)
Saudi Arabia	MoH			7,500 (7,000– 10,300)	4,600 (4,300– 6,300)	2,400 (2,200– 3,300)	1,800 (1,700– 2,500)	1,300 (1,200– 1,800)	780 (730– 1,100)	1,700 (1,600– 2,300)	1,500 (1,400– 2,100)	21,600 (20,200– 29,700)
Seychelles	DS			70 (60– 180)	70 (60– 180)		2 (2– 5)		130 (120– 330)			270 (240– 680)
Singapore	DS			90 (80– 130)	550 (500– 760)	30 (30– 40)	1,400 (1,300– 1,900)	940 (850– 1,300)	90 (80– 130)	9 (8– 13)	9 (8– 13)	3,100 (2,800– 4,300)
Slovakia	27,45			405 (360– 510)	350 (320– 440)	396 (360– 500)	400 (360– 510)	230 (210– 290)	230 (210– 290)	270 (240– 340)	360 (320– 460)	2,600 (2,400– 3,300)
Slovenia	EC		129 (120– 180)	178 (160– 250)	260 (230– 370)	250 (230– 360)	102 (90– 150)	100 (90– 140)	120 (110– 170)		140 (130– 200)	1,300 (1,200– 1,800)
South Africa	EC, MoH			100 (90– 150)	300 (270– 440)	250 (230– 370)	200 (180– 290)	250 (230– 370)	800 (720– 1,200)	3,400 (3,100– 5,000)	6,100 (5,500– 9,000)	11,400 (10,300– 16,800)
Spain	46		29,100 (26,200– 39,300)	28,700 (25,800– 38,800)	29,000 (26,100– 39,200)	26,600 (23,900– 36,000)	15,900 (14,300– 21,500)	8,400 (7,600– 11,400)	7,400 (6,700– 10,000)	7,000 (6,300– 9,500)	6,000 (5,400– 8,100)	158,000 (142,000– 214,000)
Sri Lanka	DS			12 (10– 30)	60 (50– 150)	70 (60– 180)	50 (40– 130)	2,300 (1,800– 5,800)	130 (100– 330)	280 (220– 700)	280 (220– 700)	3,200 (2,600– 8,000)
Suriname	DS									80 (60– 200)		80 (60– 200)

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Table 1. (continued)

Country	Source	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Sweden	47,48	1,300 (1,200– 1,600)	2,300 (2,100– 2,900)	2,500 (2,300– 3,100)	2,100 (1,900– 2,600)	5,800 (5,200– 7,300)	4,800 (4,300– 6,000)	2,400 (2,200– 3,000)	2,100 (1,900– 2,600)	1,700 (1,500– 2,100)	1,800 (1,600– 2,300)	26,800 (24,100– 33,500)
Switzerland	DS	528 (480– 820)	2,300 (2,100– 3,600)	1,900 (1,700– 3,000)	3,000 (2,700– 4,700)	3,200 (2,900– 5,000)	1,800 (1,600– 2,800)	980 (880– 1,500)	880 (790– 1,400)	710 (640– 1,100)	790 (710– 1,200)	16,100 (14,500– 25,100)
Taiwan	EC		500 (450– 680)	899 (810– 1,200)	10,536 (9,500– 14,300)	19,600 (17,600– 26,700)	45,800 (41,200– 62,300)	36,200 (32,600– 49,200)	20,000 (18,000– 27,200)	15,800 (14,200– 21,500)	13,800 (12,400– 18,800)	163,000 (147,000– 222,000)
Tajikistan	DS			1,000 (900– 1,300)	1,500 (1,400– 2,000)	2,000 (1,800– 2,700)	480 (430– 640)	6,400 (5,800– 8,600)	410 (370– 550)	70 (60– 90)	70 (60– 90)	11,900 (10,700– 16,000)
Tanzania	DS						1 (1– 3)	2,100 (1,700– 5,300)		1 (1– 3)	1 (1– 3)	2,100 (1,700– 5,300)
Thailand	DS				3,000 (3,000– 5,400)	2,200 (2,200– 3,900)	3,800 (3,800– 6,800)	2,700 (2,700– 4,800)				11,700 (11,700– 21,000)
Tunisia	DS					1,100 (990– 1,400)	80 (70– 100)	120 (110– 150)	240 (220– 300)			1,500 (1,400– 1,900)
Türkiye	DS		4,900 (4,400– 7,200)	5,600 (5,000– 8,200)	5,300 (4,800– 7,800)	5,300 (4,800– 7,800)	5,500 (5,000– 8,100)	5,600 (5,000– 8,200)	5,600 (5,000– 8,200)	2,700 (2,400– 4,000)	3,100 (2,800– 4,600)	43,600 (39,200– 64,200)
Turkmenistan	DS		420 (380– 530)	380 (340– 480)	540 (490– 680)	170 (150– 210)	780 (700– 980)	11,900 (10,700– 14,900)	6,600 (5,900– 8,300)	20 (18– 30)	20 (18– 30)	20,800 (18,700– 26,000)
Uganda	DS		40 (30– 100)	30 (20– 80)	30 (20– 80)	100 (80– 250)	30 (20– 80)	3,400 (2,700– 8,500)	60 (50– 150)	4 (3– 10)	4 (3– 10)	3,700 (3,000– 9,200)
Ukraine	DS		550 (500– 1,300)	2,400 (2,200– 5,500)	749 (670– 1,700)	1,156 (1,000– 2,600)	8,640 (7,800– 19,700)	8,600 (7,700– 19,600)	16,300 (14,700– 37,200)	12,800 (11,500– 29,200)		51,200 (46,100– 117,000)
United Kingdom	49– 52		8,100 (7,300– 10,800)	12,100 (10,900– 16,200)	14,600 (13,100– 19,500)	15,200 (13,700– 20,300)	15,400 (13,900– 20,600)	9,200 (8,300– 12,300)	11,500 (10,400– 15,400)	11,000 (9,900– 14,700)	11,000 (9,900– 14,700)	108,000 (97,300– 144,000)
United States	DS	126,000 (113,000– 158,000)	260,000 (234,000– 325,000)	231,000 (208,000– 289,000)	208,000 (187,000– 260,000)	187,000 (168,000– 234,000)	195,000 (176,000– 244,000)	147,000 (132,000– 184,000)	133,000 (120,000– 166,000)	142,000 (128,000– 178,000)	142,000 (128,000– 178,000)	1,771,000 (1,594,000– 2,214,000)
Uzbekistan	EC			15,000 (13,500– 22,600)	9,300 (8,400– 14,000)	8,500 (7,700– 12,800)	29,100 (26,200– 43,800)	9,900 (8,900– 14,900)	11,500 (10,400– 17,300)	14,500 (13,100– 21,800)	36,200 (32,600– 54,400)	134,000 (121,000– 202,000)
Vietnam	DS		4,500 (4,100– 10,000)	5,100 (4,600– 11,300)	10,800 (9,700– 24,000)	12,000 (10,800– 26,600)	10,000 (9,000– 22,200)	12,900 (11,600– 28,600)	3,000 (2,700– 6,700)	60 (50– 130)	60 (50– 130)	58,400 (52,600– 130,000)
Zimbabwe	DS			60 (50– 150)			19 (16– 50)			5 (4– 13)	5 (4– 13)	90 (70– 220)
Other	DS			169,000 (152,000– 264,000)	132,000 (119,000– 207,000)	102,000 (91,800– 160,000)	59,300 (53,400– 92,800)					462,000 (416,000– 723,000)

DAA, direct-acting antivirals; DS, drug sales data; EC, expert consensus; HCV, hepatitis C virus; HSE, National Hepatitis C Treatment Programme, Ireland; INVS, Institut de Veille Sanitaire; MHLW, Ministry of Health, Labor and Welfare; MoH, Ministry of Health; MSF, Médecins Sans Frontières; NCCD, National Center for Communicable Diseases; NCID, National Center for Infectious Diseases; NDB, National Database; PHAC, Public Health Agency Canada.

Table 2. HCV infections treated with DAAs by WHO regions, World Bank income group, the European Union, continent, and globally.

WHO region	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
African regional office (AFRO)		8,400 (7,800–9,400)	10,400 (9,800–11,700)	18,800 (17,900–21,900)	23,200 (22,000–26,500)	6,100 (6,000–32,800)	37,100 (35,900–84,800)	27,200 (25,100–52,400)	38,300 (33,400–45,100)	19,300 (18,300–42,000)	189,000 (182,000–318,000)
Eastern Mediterranean regional office (EMRO)		1,066,000 (856,000–1,329,000)	721,000 (582,000–895,000)	844,000 (773,000–1,050,000)	594,000 (535,000–961,000)	1,930,000 (1,549,000–2,411,000)	178,000 (175,000–242,000)	157,000 (128,000–230,000)	184,000 (149,000–230,000)	200,000 (162,000–253,000)	5,873,000 (4,913,000–7,602,000)
European regional office (EURO)	2,600 (2,200–3,100)	157,000 (155,000–192,000)	201,000 (190,000–254,000)	223,000 (216,000–273,000)	218,000 (216,000–306,000)	247,000 (241,000–294,000)	175,000 (172,000–223,000)	152,000 (144,000–166,000)	143,000 (138,000–157,000)	168,000 (159,000–187,000)	1,688,000 (1,654,000–1,989,000)
The Pan-American Health Organization (PAHO)	126,000 (101,000–158,000)	280,000 (228,000–347,000)	290,000 (241,000–357,000)	245,000 (201,000–315,000)	226,000 (200,000–297,000)	262,000 (223,000–319,000)	188,000 (158,000–229,000)	171,000 (142,000–208,000)	195,000 (164,000–235,000)	187,000 (159,000–230,000)	2,170,000 (1,820,000–2,692,000)
South East Asia regional office (SEARO)		84,100 (69,700–118,000)	220,000 (179,000–392,000)	197,000 (160,000–332,000)	192,000 (156,000–322,000)	99,500 (86,100–192,000)	65,600 (54,300–110,000)	68,200 (57,900–107,000)	80,400 (67,500–100,000)	89,600 (75,100–111,000)	1,096,000 (910,000–1,747,000)
Western Pacific regional office (WPRO)	910 (730–1,100)	173,000 (158,000–226,000)	135,000 (122,000–378,000)	105,000 (96,400–369,000)	108,000 (100,000–311,000)	81,400 (76,100–255,000)	116,000 (105,000–176,000)	134,000 (115,000–171,000)	124,000 (105,000–150,000)	124,000 (105,000–150,000)	1,101,000 (1,052,000–2,160,000)
World Bank income group	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
High income	130,000 (104,000–161,000)	510,000 (461,000–602,000)	512,000 (461,000–662,000)	489,000 (447,000–608,000)	475,000 (453,000–545,000)	470,000 (439,000–538,000)	336,000 (310,000–397,000)	289,000 (262,000–342,000)	291,000 (263,000–337,000)	301,000 (271,000–348,000)	3,803,000 (3,483,000–4,506,000)
Upper middle income		105,000 (90,600–138,000)	116,000 (107,000–278,000)	85,600 (82,300–306,000)	74,800 (72,200–333,000)	127,000 (120,000–323,000)	147,000 (139,000–205,000)	175,000 (156,000–210,000)	176,000 (158,000–209,000)	163,000 (147,000–199,000)	1,169,000 (1,144,000–2,156,000)
Lower middle income		1,145,000 (960,000–1,403,000)	944,000 (826,000–1,202,000)	1,058,000 (983,000–1,294,000)	819,000 (756,000–1,212,000)	2,071,000 (1,730,000–2,552,000)	281,000 (270,000–377,000)	238,000 (202,000–335,000)	279,000 (235,000–337,000)	328,000 (281,000–391,000)	7,163,000 (6,343,000–8,903,000)
Low income		9,200 (8,500–10,200)	7,500 (7,000–8,400)	11,400 (10,700–12,800)	12,700 (12,400–15,200)	4,300 (4,100–28,200)	32,300 (31,000–69,200)	27,400 (25,200–52,100)	32,800 (27,800–39,300)	11,000 (10,500–33,000)	149,000 (140,000–267,000)
European Union	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
European Union	1,300 (1,100–1,700)	127,000 (124,000–150,000)	128,000 (117,000–177,000)	149,000 (139,000–189,000)	149,000 (143,000–172,000)	126,000 (122,000–141,000)	70,100 (66,400–93,900)	58,800 (54,900–65,600)	58,900 (55,300–65,500)	62,800 (59,400–69,700)	930,000 (887,000–1,121,000)
Continent	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Africa		839,000 (673,000–1,046,000)	356,000 (288,000–442,000)	499,000 (496,000–621,000)	252,000 (207,000–533,000)	1,608,000 (1,288,000–2,031,000)	56,300 (53,600–103,000)	34,300 (32,000–59,900)	42,700 (38,200–50,400)	21,000 (20,800–45,900)	3,708,000 (3,106,000–4,921,000)
Asia		504,000 (456,000–605,000)	744,000 (675,000–1,079,000)	694,000 (624,000–1,032,000)	702,000 (670,000–1,027,000)	1,111,000 (550,000–868,000)	426,000 (417,000–541,000)	403,000 (373,000–514,000)	427,000 (382,000–495,000)	480,000 (432,000–556,000)	4,991,000 (4,645,000–6,596,000)
Australia and New Zealand	910 (730–1,100)	4,000 (3,200–6,200)	34,600 (27,700–43,300)	22,500 (18,000–29,200)	16,000 (14,700–21,500)	14,800 (14,100–18,500)	9,200 (8,900–13,900)	7,400 (7,100–9,200)	5,900 (5,800–7,400)	6,200 (5,800–7,800)	121,000 (106,000–158,000)

(continued on next page)

Table 2. (continued)

WHO region	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Europe	2,600 (2,200– 3,100)	143,000 (140,000– 167,000)	154,000 (143,000– 205,000)	183,000 (175,000– 227,000)	185,000 (181,000– 213,000)	177,000 (173,000– 221,000)	116,000 (112,000– 159,000)	114,000 (107,000– 126,000)	110,000 (106,000– 122,000)	108,000 (101,000– 121,000)	1,293,000 (1,254,000– 1,530,000)
Latin America and the Caribbean		9,100 (7,600– 11,100)	49,000 (40,500– 60,500)	21,700 (18,600– 43,300)	21,900 (19,400– 49,300)	49,700 (41,900– 62,400)	29,700 (25,400– 35,600)	26,600 (22,900– 33,100)	41,300 (35,700– 48,900)	33,600 (30,400– 44,600)	283,000 (246,000– 386,000)
Northern America	126,000 (101,000– 158,000)	271,000 (219,000– 339,000)	242,000 (194,000– 305,000)	223,000 (179,000– 279,000)	204,000 (177,000– 256,000)	212,000 (175,000– 265,000)	158,000 (129,000– 198,000)	144,000 (115,000– 180,000)	153,000 (125,000– 192,000)	153,000 (125,000– 192,000)	1,888,000 (1,538,000– 2,362,000)
Global	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2014–2023
Global	130,000 (104,000– 161,000)	1,770,000 (1,589,000– 2,068,000)	1,748,000 (1,666,000– 2,144,000)	1,777,000 (1,725,000– 2,192,000)	1,484,000 (1,451,000– 2,015,000)	2,731,000 (2,433,000– 3,340,000)	796,000 (804,000– 968,000)	729,000 (703,000– 874,000)	780,000 (732,000– 867,000)	802,000 (760,000– 907,000)	12,748,000 (12,226,000– 15,231,000)

AFRO, African region; DAAs, direct-acting antivirals; EMRO, Eastern Mediterranean region; EURO, European region; HCV, hepatitis C virus; PAHO, Pan American Health Organization; SEARO, Southeast Asian region; WPRO, Western Pacific region.

HCV infections treated with DAAs by income group (e.g. Egypt)

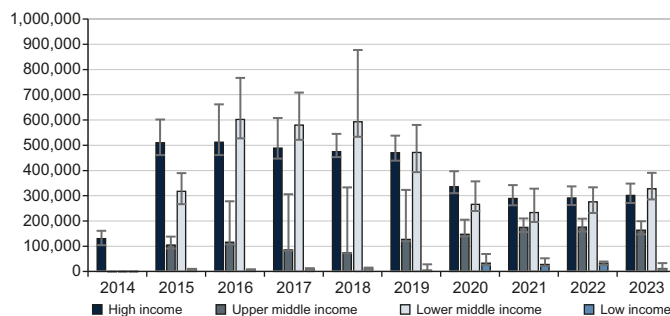


Fig. 2. Countries/regions accounting for 85% of all DAA treatments globally in 2014–2023. DAAs, direct-acting antivirals; EU, European Union.

Pakistan, the country with the second largest number of treated PLHCV after Egypt (Fig. 2), is a special case as more than 70% of all its HCV treatments were purchased in the private market. This model required the availability of treatments at an affordable price, demonstrating the importance of the private market to support the national elimination efforts. Pakistan has shown that at affordable prices, some portion of the population can afford to purchase the medicine on their own. Pakistan's treatment numbers did peak in 2018, but the Prime Minister's plan is underway to expand their national elimination program under the public health system.

The United States and the EU had the next largest number of DAA-treated infections (Fig. 2). In the United States, the number of treated cases peaked in 2015 shortly after their launch, while in the EU, the peak occurred in 2017 when nearly all member states removed treatment restrictions after price negotiation and reimbursement approval. The same pattern was observed in other HICs: a peak in treatment when DAAs were reimbursed, followed by a steady decline (Table 1).

The number of DAA-treated PLHCV in India (Fig. 2) was difficult to estimate due to exports of DAAs to other countries for sale in the private market by individuals. Initially, these reports were discounted, but a review of the national program and adjustments of sales in India's private market could only account for 90,000–194,000 treated PLHCV in years 2016–2019 (Table 1). The remaining DAAs, which could have treated an

Countries/regions accounting for 85% of all DAA treatments (2014–2023)

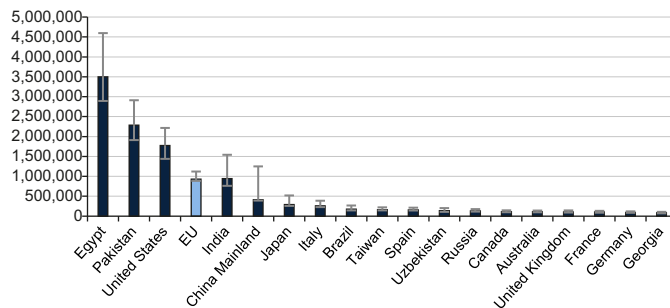


Fig. 3. Total PLHCV treated with DAAs by World Bank income group regions (excluding treatments in Egypt). DAAs, direct-acting antivirals; HCV, hepatitis C virus; PLHCV, people living with hepatitis C virus.

additional 463,000 PLHCV, were classified as “other” since their whereabouts could not be accounted for in India. DAA sales data for India was not available after 2019.

The number of DAA-treated PLHCV in China was also very difficult to estimate since locally manufactured treatment was being used for internal consumption. IQVIA DAA sales data were used to estimate the total number of treated PLHCV, but it led to a gross underestimation. We estimate that 93,000–95,000 PLHCV have been treated with DAAs annually since 2020. Other countries with a high number of treated PLHCV (Japan, Italy, Brazil, Spain, and Taiwan) all had funded national strategies in place, which explains their high numbers (Italy has the highest number of treated PLHCV in the EU) (Fig. 2).

Impact of price and reimbursement

The number of DAA-treated PLHCV in HICs peaked in 2016 (Fig. 3), when the prices of DAAs were near their peak, and the number of treated cases dropped by 47% while the prices of DAAs declined over the 2014–2023 period. In the EU countries, there was an immediate increase in the number of treated PLHCV as soon as DAA treatment for those with fibrosis scores of F0–F2 was reimbursed in 2017, with some countries (e.g., the Netherlands) starting earlier. However, in HICs, there was no increase in DAA treatment as prices declined. These trends suggest that in HICs, price negotiations were important to reach the cost-effectiveness and reimbursement thresholds. Further price reductions were used to expand related activities, but the price reduction did not lead to an increase in the number of treated PLHCV. Thus, in HICs, a threshold price was needed for reimbursement, and treatment reimbursement itself was the key predictor of an increase in treatment.

On the other hand, the relationship between DAA prices was strongly correlated with the number of treatment initiations in low- and middle-income countries (LMICs). The number of treated PLHCV in upper middle-income countries increased as DAA prices dropped and countries like China, Russia, Malaysia, and Brazil continued to expand their treatment programs. The number of treated PLHCV also increased in low-income countries (Table 2) as the prices of DAAs dropped. In lower middle-income countries, a similar relationship was observed; however, this trend peaked in 2018 (Fig. 3) when the pool of diagnosed and motivated PLHCV who were able to pay for their treatment was depleted in Pakistan and India. These trends suggest that traditional price elasticity of demand applies in LMICs, where an increase in the number of treated PLHCV was observed with lowering prices until the initial warehoused pool of PLHCV was depleted.

Treatment in the absence of a screening program

The number of treated PLHCV stagnated/declined in every country/region irrespective of income level (Table 1). This trend was observed much faster in HICs, while in LMICs (e.g.,

Pakistan and Indonesia), it took longer to manifest. This trend may be the result of the depletion of the pool of PLHCV waiting for treatment who can pay (in countries where PLHCV must pay out of pocket). The decline in the number of treatments has led to the conclusion, in some countries, that HCV prevalence must be lower than originally estimated. However, declining numbers of treated PLHCV may be more indicative of exhausting the efficacy of existing strategies rather than a lower HCV prevalence.

To achieve the WHO elimination targets, countries should consider expanding screening programs. This was best demonstrated in the Egyptian program, where adoption of a national screening campaign in 2019 resulted in a very large increase in treatment. In the United Kingdom, England initiated a wide-scale screening program to maintain their treatment numbers. Similarly, after Germany initiated a one-time screening of adults in 2022, an increase in the number of treated PLHCV was observed. The recommendations to screen adults for HCV in the United States also led to an increase in treatment initiations.

PLHCV segmentation

Countries are finding that treating 80% of all diagnosed PLHCV is difficult, as more recent studies suggest that one-third of diagnosed individuals are motivated to come in for a curative treatment within the first 1–3 years,^{10,11} one-third can be connected to care via awareness and linkage to care programs,¹² and the last third will require additional programs to be linked to care. The low linkage to care in the general population may be explained by low awareness of HCV and its relation to liver cancer. A survey by the World Hepatitis Alliance found that only 42% of all respondents knew of a relationship between viral infection and liver cancer,¹³ while a similar study in Brazil found that only 23% of the respondents attributed HCV infection to liver cancer.¹⁴ Similarly, a study in Uzbekistan found that 42% of PLHCV lost to follow-up did not know their infection could lead to liver cancer.¹⁵ Although screening for HCV is important to meet the WHO elimination targets, awareness programs will be needed to motivate PLHCV to seek treatment. In addition, linkage to care programs will be needed to bring in those who are less motivated to seek care. Studies have shown that it is possible to bring >30% of lost-to-follow-up PLHCV back into care through active linkage to care initiatives.^{12,16,17}

Relevant lessons for other liver diseases

An analysis of HCV treatment is timely as several products are in development for the functional cure of HBV. In addition, there is already a product on the market for the treatment of HDV, while several pipeline products are targeting HDV treatment. The same concerns that were present before the launch of DAAs are being voiced again. Will the new treatments put an undue burden on national healthcare budgets? Are there

enough specialists to treat the new wave of patients coming in for treatment as these products launch? And how will we deal with the large burden of these diseases in LMICs? The historical trends in HCV treatment can provide lessons that could be applicable to the pipeline therapies.

When DAAs launched, there was much concern about health systems being severely economically challenged due to their high prices and the instant inflow of PLHCV to be treated. The history of DAA treatment seems to suggest that in HICs, the national reimbursement agencies are competent and only approve treatments once they are cost-effective. In LMICs, price does play an important role, and treatments will remain limited until prices drop sufficiently.

Another concern raised before the launch of DAAs was that countries may not have enough specialists to treat the large inflow of new patients as new therapies are launched. This can apply to HBV as well. The HCV experience has taught us that only a fraction of all diagnosed patients will come in for treatment, and in fact, much effort (screening, awareness, and linkage to care) is needed to bring in patients for treatment. Treatment simplification can also help engage other healthcare professionals (general practitioners and nurses) to treat a portion of the population.

There is a key distinction between HCV and HBV (and HDV) that is worth noting. The HCV diagnosis rate was already much higher at the time when DAAs were launched. In comparison, HBV diagnosis rates are close to half those of HCV, and the HDV diagnosis rate is low.^{4,18} The launch of new therapies for HBV and HDV will require collaborations between hospitals, major clinics, universities, and national governments to screen for these diseases, but more importantly, countries need national registries to keep track of the positive and negative test results for linkage to care and retention in care programs once new treatments are available.

Study limitations

There were several challenges with our study. Our methodology was highly dependent on national reporting. Biases in these estimates would carry over to our analysis as well. Unit sales data from IQVIA were only reliable in HICs. In LMICs, this data captured only specific channels (e.g. hospital sales) and had to be adjusted for the portion of total sales represented by those channels to generate more accurate treatment estimates.

The review of companies' presentations to investors was helpful in the years 2014–2019 when companies reported the number of treated PLHCV for their products and the entire market in the United States and the EU. For our study, we did not purchase and analyze financial analysts' reports.

In LMICs, the majority of HCV treatment occurred at a handful of tertiary centers. Physician interviews and a review of hospital records provided a reasonable estimate of the total number of treated PLHCV in the country when compared to drug sales data. This approach, however, was less successful in HICs where PLHCV had access through multiple channels (tertiary hospitals, clinics, prisons, harm reduction centers, and pharmacies).

Export/import data were analyzed by country, but they significantly underestimated the number of bottles shipped to each country when compared to the data reported by generic manufacturers to patent holders. There were also large discrepancies between the treated PLHCV estimated via sales figures, the national programs, and those provided by national experts in LMICs. A significant amount of DAAs purchased (estimated more than 15%) in LMICs appear to be expiring, presumably due to the products not being distributed to hospitals, complex treatment algorithms, a shortage of related supplies (e.g., PCR reagents, antibody tests, etc.), and an insufficient number of diagnosed PLHCV coming in for treatment. The upper bound of our UIs did include purchases that may have expired unless the country specifically notified us of the volume of products that had expired. In that case, the expired products were subtracted from our estimates.

The "other" group captured treated PLHCV who could not be allocated to a specific country. The example of India was discussed above, but there were also shipments of generic DAAs to European and Middle Eastern countries that were clearly used in programs run by international agencies like Médecins Sans Frontières. Those shipments were all captured under "other". Thus, there could be some double counting of treated PLHCV when the countries being serviced by these organizations reported their estimates separately.

Another limitation was not taking into consideration a longer duration of therapy (with or without ribavirin) for treatment of patients with cirrhosis or retreatment of DAA treatment failures. Doing so would result in a lower number of calculated treated PLHCV, as they would require an additional number of bottles to treat the same individual. However, only 19% of the total estimates came from analysis of DAA sales data, and if 25% of all DAAs sold in these countries used double the duration of treatment for the above populations, our overall estimates would be 2.5% lower. This is well within our confidence UIs.

Our analysis also did not take into consideration retreatment of reinfections. Doing so would result in a lower number of calculated treated PLHCV, as they would be counted multiple times if the national registry is only reporting treatment initiation. This is important in countries where the epidemic is predominantly driven by injecting drug use and access to needle and syringe programs, or opioid substitution therapy is not available or is limited. Although reinfection rates are relatively high (6.6/100 person-years; 95% CI 3.4–12.7) in these settings,¹⁹ the percentage of total PLHCV who are actively injecting, are reinfected, and are subsequently treated will be small and well within our confidence UIs.

Finally, the adjustment of bottles sold to treat PLHCV assumed 8–12 weeks of treatment, depending on the regimen. However, PLHCV may not be 100% treatment compliant. This would result in a higher number of HCV treatments than shown here.

Conclusions

In the last 10 years, DAAs have cured 21% of the infected population worldwide and 30% of the target population (taking

into consideration 90% diagnosis and 80% treatment targets). However, 7 years remain to treat the remaining 70% of the

target population. To accomplish this, expanded access, active HCV screening, and linkage to care may be required.

Abbreviations

DAAs, direct-acting antivirals; EU, European Union; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis delta virus; HICs, high-income countries; LMICs, low- and middle-income countries; PLHCV, people living with hepatitis C virus; WHO, World Health Organization; UI, uncertainty interval.

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Conflict of interest

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

HR conceived the study, designed the methodology, and was responsible for the project administration. HR, DMR-S, and IG conducted the formal analysis. HR wrote the original draft and updated it after feedback from all first authors (IW, HQ, LAK, ASD, SA, JT, JVL, DLB). HR, IG, DMR-R, ASV, SH, and KR-S had access to the underlying data and verified the data. All authors curated and validated the data, as well as reviewed and edited the manuscript. All authors had full access to the data for their country and accepted the responsibility to submit their data for publication.

Data availability statement

All data presented in this article is accessible through the Polaris Observatory website (<https://cdfaound.org/polaris/database-query/>).

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Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2025.01.013>.

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