Burden and Response: An Economic Analysis

EGYPT'S VIRAL HEPATITIS PROGRAM

THE WORLD BANK

Egypt's Viral Hepatitis Program

Burden and Response: An Economic Analysis 2017

This report is developed as part of the World Bank's Technical Assistance on Strengthening Egypt's Response to Viral Hepatitis.

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Executive Summary

Viral hepatitis is a global health problem that affects millions of people worldwide, resulting in approximately 1.4 million deaths a year. The prevalence of Hepatitis C in Egypt is the highest in the world. Over 150,000 Egyptians become infected, and about 40,000 die, annually from Hepatitis C. Access to treatment had been severely limited due to prohibitive costs but has recently improved after the arrival of highly effective antiviral treatments at low costs. These medicines now offer a route to elimination of the epidemic in the coming years.

The report seeks to inform current Hepatitis C control policies by assessing the health and economic consequences of the epidemic and the response to it. To this end, it relies on three stylized policy scenarios: a "treatment" scenario which represents a continuation of the current demand-driven treatment program; a "screening" scenario in which 10 percent of the population is tested annually; and a comprehensive "elimination" scenario in which the entire adult population is tested within 5 years.

As of 2015, Hepatitis C accounted for 7.6 percent of all deaths in Egypt, and a much higher rate for adults over age 50. The epidemic caused a loss in life expectancy of 1.8 years for men, and 1.0 years for women. The impacts of Hepatitis C on GDP per capita are very small, but the epidemic has reduced GDP by 0.3 percent as of 2015. Additionally, increased mortality owing to Hepatitis C reduces living standards by an equivalent of 1.5 percent of GDP and GDP per capita.

Current demand-driven treatment policies have the potential to reduce Hepatitis C-related mortality and new infections by about one-half by 2030. Screening – ongoing or as part of a comprehensive elimination strategy – has the potential to substantially augment these effects, averting up to two-thirds of deaths and reducing the number of new infections by around 90 percent in a comprehensive elimination scenario.

The steep declines in the costs of antiviral drugs have made treating chronic Hepatitis C infections highly cost-effective. Current spending on demand-driven treatment is refinanced by savings in costs of within 6 years, and carries a financial rate of return of 24 percent, even before taking into account the values of any health gains.

A drive to effectively eliminate Hepatitis C will also require screening policies. Such policies, in the form of an ambitious "elimination" scenario aiming to screen the entire adult population within 5 years or a more gradual screening policy, are generally not cost-saving, except when the policy is restricted to older adults (from the mid-40s). However, they are cost-effective by conventional norms, at a cost per life year gained of less than 10 percent of GDP per capita. The "elimination" scenario comes out as more effective and cost-effective compared to a gradual screening policy.

Cost-effectiveness of treatment and screening differ by age group targeted. On average, treatment at older ages is relatively more effective in terms of reducing mortality but less effective in terms of reducing the number of new infections. The cost-effectiveness of screening is low among young adults, and improves with the age of the population targeted.

From a macroeconomic perspective, treatment and screening policies achieve considerable health gains largely cost-free. Improved survival in old age results in an increase in the dependency rate and represents a drain on GDP per capita. Across the policy scenarios, this factor is offset by productivity gains from improved state of health and the financial savings owing to reduced costs of care. Additionally, reduced mortality results in a gain in living standards equivalent to 0.6 to 0.8 percent of GDP.

Introduction

Egypt faces the most severe burden from Hepatitis C globally. According to the 2015 Health Issues Survey, 7 percent of the population of ages 15-59 was chronically infected. It is estimated that Hepatitis C accounted for over 40,000 deaths in 2015, largely through cirrhosis and liver cancer, accounting for 7.6 percent of total mortality. The very high prevalence of Hepatitis C is commonly attributed to unsafe injections during mass treatments for schistosomiasis until the mid-1980s.

However, ongoing infections also play a role; an estimated 150,000-200,000 Egyptians are infected each year (corresponding to an incidence rate of 0.2 percent), mostly through unsafe medical practices. National prevention efforts focus on improving awareness, and infection control and safe injection practices at health facilities.

Access to treatment was severely limited until recently, largely owing to its high costs. However, the arrival of highly effective antiviral treatments and their availability at low costs have transformed the health outlook for people chronically infected, and have raised the prospect of eliminating the epidemic. As of end-November 2016, about 850,000 people (out of about 5 million people chronically infected) have been treated, with a success rate of well over 90 percent.

The success in extending access to treatment is creating new challenges. Much of the expansion of treatment in 2015 and 2016 affected people who knew they were infected, mostly because they had tried (or declined) earlier forms of treatment. As this pent-up demand has now been met, the future contributions of the treatment program, in terms of slowing down or stopping disease progression and reducing transmission of Hepatitis C, will largely rely on motivating people – many of whom are not aware of their infection and do not experience significant symptoms – to be tested and, if positive, obtain treatment.

This study aims to contribute to an understanding of the policy choices and opportunities by focusing on economic aspects of Hepatitis C and of Hepatitis C control policies, mainly along two lines. First, it looks at the health and economic impacts of Hepatitis C (and, by extension, the policy response) to evaluate the significance of the epidemic and the returns to investment in the

response from a broad health and development perspective. Second, it provides a forward-looking analysis of the cost-effectiveness of a continuation of the demand-driven treatment program, and of policies aiming to increase the uptake of testing and treatment (interpreted as screening across the population or for certain sub-populations).

The discussion sets out from a review of the course and state of the epidemic (Section II), covering the history of the epidemic in Egypt (and its implications for the shape of today's epidemic), the distribution of Hepatitis C across the population (e.g., by age, but also taking into account socio-economic factors), the evidence on current HCV transmission, and the implications of the national treatment programme so far. Section III discusses the health and economic impacts of Hepatitis C, drawing on empirical work as well as model-based estimates (such as those from the Global Burden of Disease), evidence on the economic impacts on people chronically infected with Hepatitis C, and providing estimates on the macroeconomic impacts. Section IV provides a snapshot of the state and objectives of Egypt's response to Hepatitis C. Section V provides a forward-looking analysis of Hepatitis C and the national policy, including projections of the course of the epidemic and how it is affected by some policies (notably the expansion of the treatment program), and estimates of the health and economic returns to investment in the response to Hepatitis C. Section VI concludes.

Course and State of Hepatitis C in Egypt

Prevalence of Hepatitis C in Egypt is the highest in the world. As of 2015 (Ministry of Health and Population and others, 2015b), 7 percent of the population at ages 15-59 were chronically infected (testing positive for viral RNA), and 10 percent carried antibodies, i.e., had been exposed to the virus or infected at some stage (Table 1). The very high prevalence rates are attributed to a history of parenteral (injected) mass treatment of schistosomiasis until the early 1980s (Frank and others (2000), Strickland (2006)), which resulted in extensive blood-borne transmission of Hepatitis C. Although ongoing infections also play a role, this history plays an important role in explaining the current profile of the epidemic, including the very high (though declining) level and the age profile of prevalence of Hepatitis C, and its regional variation.

Table 1. Prevalence of Hepatitis C Across Population Groups, 2015 (Ages 15-59, Percent)

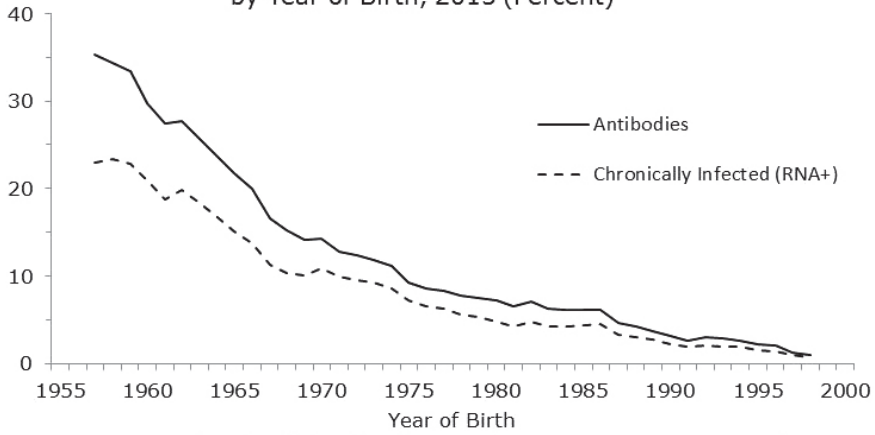
	Prevalence of Hepatitis C Antibodies			Prevalence of Hepatitis C RNA		
	Total	Men	Women	Total	Men	Women
Total	10.0	12.4	8.1	7.0	8.9	5.5
Urban	7.1	8.5	5.9	4.7	5.9	3.7
Urban poor	7.6	8.4	7.0	5.4	6.4	4.5
Urban wealthy	6.6	8.6	4.9	4.1	5.5	2.9
Rural	11.7	14.7	9.3	8.4	10.7	6.6
Rural poor	12.6	16.4	9.6	9.1	12.1	6.7
Rural wealthy	11.0	13.4	9.1	7.8	9.6	6.5
By wealth quintile						
First (poorest)	12.7	16.2	9.9	9.5	12.3	7.3
Second	11.8	15.7	8.7	8.2	10.7	6.3
Third	10.2	12.4	8.6	7.2	8.8	6.0
Fourth	9.1	10.0	8.3	6.4	7.7	5.3
Fifth (wealthiest)	6.5	8.2	4.9	3.9	5.3	2.7

Source: MoHP, El-Zanaty and Associates, and Macro International (2015, 2015b).
Note: For the urban and rural sub-populations, "poor" and "wealthy" refers to individuals with household income below or above the median for the respective sub-population. Wealth quintiles refer to the overall population.

The most comprehensive source of data on prevalence of Hepatitis C and its variation across the population is the 2015 Health Issues Survey conducted in connection with and on a subset of households from the 2014 Demographic and Health Survey. According to these data, summarized in Table 1, the socio-economic gradient of Hepatitis C is characterized by three factors. First, prevalence for men is about one-half higher than for women. Second, there is a steep rural-urban differential, with prevalence in rural areas (which were more affected by schistosomiasis) about two-thirds higher than in urban areas. Third, there is a steep wealth gradient – prevalence for the poorest quintile is about twice as high as for the wealthiest quintile. Because urban areas are much wealthier than rural areas, the wealth differentials to some extent reflect regional variations in the prevalence of Hepatitis C rather than socio-economic differences within locations. For this reason, Table 1 also divides the urban and rural sub-populations in "wealthy" and "poor" segments (with household income above or below the median for the respective sub-population), with prevalence of Hepatitis C one percentage point higher for the "poor" population across urban areas, and 1½ percentage points higher across rural areas.

The history of the epidemic – very high transmission rates linked to schistosomiasis treatment until the early 1980s, followed by ongoing transmission at a much lower rate – is reflected in the age profile of the epidemic (Figure 1).

Figure 1. Prevalence of Hepatitis C Antibodies and RNA by Year of Birth, 2015 (Percent)



Source: Ministry of Health and others (2015b). Figures show 5-year moving average around year indicated of percentage of people testing positive on an HCV antibody chemiluminescence test or an HCV RNA test.

Prevalence of Hepatitis C antibodies, i.e., having ever been infected, averages about one-third for the cohorts born before 1960, but only about 7 percent for the cohort born in the early 1980s, and near-steadily lower rates for younger cohorts. Finding a steep age gradient is typical for a chronic infection like Hepatitis C. The remarkable aspect of the data on prevalence of Hepatitis C in Egypt is the kink in the curve around 1980, consistent with the established narrative on the course of the epidemic, i.e. higher prevalence for age groups who were exposed to parenteral schistosomiasis treatment until that time.

Because of the steep age gradient in Egypt's Hepatitis C epidemic, the public health challenge posed by the epidemic is tied to demographic factors. Many people chronically infected have been infected for decades, and are now at an age when the lethal consequences of the epidemic become more common, i.e., the contribution of Hepatitis C to the burden of disease has been increasing (discussed in more detail in the next section). At the same time, high population growth and the increasing weight of younger cohorts (with much lower prevalence of Hepatitis C) means that the prevalence of Hepatitis C is decreasing even if the absolute number of people infected does not change much.

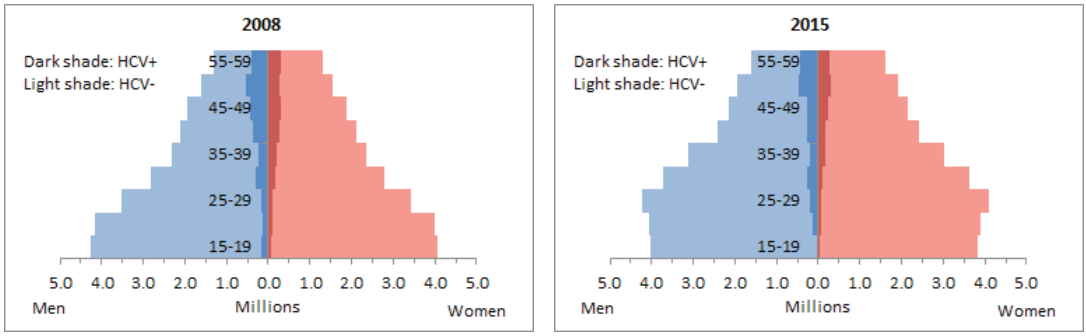
Table 2. Prevalence of Hepatitis C , 2008 and 2015 (Ages 15-59, Percent)

	Prevalence of Hepatitis C Antibodies			Prevalence of Hepatitis C RNA		
	Total	Men	Women	Total	Men	Women
2008						
Total	14.7	17.4	12.2	9.8	12.1	7.8
Urban	10.3	12.7	8.0	7.2	9.0	5.5
Rural	18.0	21.1	15.2	11.9	14.4	9.6
2015						
Total	10.0	12.4	8.1	7.0	8.9	5.5
Urban	7.1	8.5	5.9	4.7	5.9	3.7
Rural	11.7	14.7	9.3	8.4	10.7	6.6

Source: El-Zanaty and Way (2009), and MoHP, El-Zanaty and Associates, and Macro International (2015, 2015b).

Indeed, the prevalence of Hepatitis C has declined steeply – by about one-third – between the 2008 DHS and the 2015 Health Issues Survey (Table 2), from 14.7 percent to 10.0 percent (antibodies) and from 9.8 percent to 7.0 percent (RNA) for the population of ages 15-59. The extent to which this decline reflects demographic factors is apparent from Figure 2, showing changes in the population pyramid between 2008 and 2015. For ages 15-59, the number of people chronically infected with Hepatitis C declined over this period (by 19 percent), but much of this reflects that individuals born between 1948 and 1955 – an age group with very high prevalence of Hepatitis C – have aged out of the bracket covered by the DHS studies. Meanwhile, prevalence of Hepatitis C in the young cohorts which have moved into the 15-59 age bracket between the surveys (i.e., young people of ages 15 to 22 in 2015) is very low, and these cohorts carry a large weight in prevalence for the population overall because the size of the young cohorts is relatively large.

Figure 2. Age Structure of Population, HCV+ and HCV-, 2008 and 2015



Source: IHME (2016) for population size, Ministry of Health and Population, El-Zanaty and Associates, and Macro International (2015, 2015b) for prevalence of Hepatitis C. "HCV+" refers to people chronically infected with Hepatitis C (RNA-positive), "HCV-" are those not "HCV+."

Access to effective treatment used to be very limited in Egypt until recently, in light of the very high costs and poor options available. Treatment outcomes and access have been transformed by the introduction of highly effective antiviral drugs, and developments which steeply reduced the costs to the Government of Egypt of these drugs, beginning with the agreement between the government and Gilead Sciences in 2014, which made the drug sofosbuvir available at a

steeply reduced cost (US$ 300 per bottle, compared to a price of US$ 28,000 on the U.S. market. Before that, only 50,000 patients (about 1 percent of people chronically infected) received the older form of treatment annually in 2009-2011, and treatment was successful in achieving a sustained virologic response for only one-half of patients who received treatment (El Sayed and others, 2012).

From 2014, treatment with highly effective antiviral drugs became publicly available. By then, a backlog of 750,000 patients diagnosed and eligible for treatment had developed, including 150,000 patients whose earlier treatment had failed (El-Akel and others, 2017), and patients for whom the earlier treatments were deemed unsuitable or who had initially declined treatment. For these reasons, there was a steep demand for the new treatments when they became available, with waiting times of up to 6 months in some centres. By mid-2016, though, these queues disappeared, as those who had registered early eventually received treatment and some new treatment centres had been opened.

As of late 2016 (El-Akel and others, 2017), 850,000 patients had received treatment under the national program, corresponding to about one-in-six of the chronically infected. Treatment was successful for 98 percent of treatment-naïve patients and 95 percent of patients whose earlier treatment had failed (Esmat, 2016). However, there is no conclusive evidence on the population-level impact of the scaling-up of treatment yet (Kandeel and others, 2017), especially as the most recent national survey occurred very early during the scaling-up (in early 2015). By all means, though, the number of patients (especially of those already receiving care) already treated successfully represents a substantial share of the population chronically infected, and will plausibly result in declines of mortality and the number of new infections (because there are fewer people who may pass on Hepatitis C).

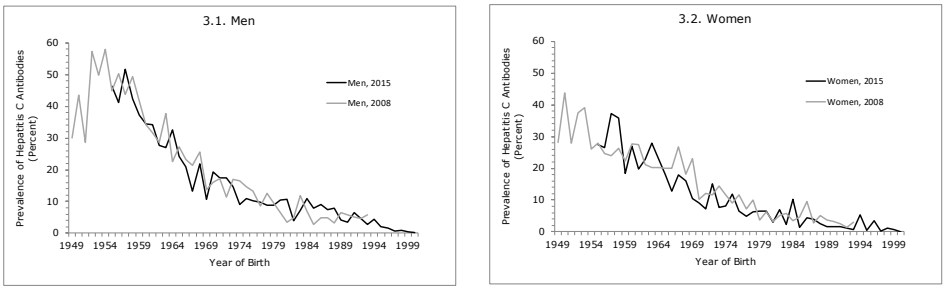
In order to project the course of the epidemic, and for an appraisal of the national response to Hepatitis C, a good understanding of the level of and factors contributing to *new infections* is important. Drawing inferences about incidence from routinely collected data is difficult; because of the very slow disease progression, individuals who test positive for Hepatitis C antibodies or viral RNA may have been infected decades ago. Current patterns of *prevalence* of Hepatitis C therefore mirror a long history of incidence, and are insufficient for

estimating the past course or current level of the incidence of Hepatitis C.

Estimates on the incidence of Hepatitis are available from three sources:

- Estimates based on national-level prevalence data
- Estimates of the rate at which people become newly infected based on repeated observations of prevalence for the same population
- Empirical work linking prevalence of Hepatitis C to various risk factors. This does not yield estimates of the level of incidence, but points to the role of various modes of transmission.

Figure 3. Prevalence of Hepatitis C Antibodies by Year of Birth and Sex, 2008 and 2015 (Percent)



Source: El-Zanaty and Way (2009); and MoHP, El-Zanaty and Associates, and Macro International, 2015.

The 2015 Health Issues Survey and 2014 DHS, together with the earlier estimates from the 2008 DHS, could be used to derive recent incidence data by comparing the prevalence of Hepatitis C antibodies by birth year between the two surveys. This is illustrated in Figure 3, which shows the prevalence of Hepatitis C antibodies by birth year for men and women. As expected in two successive population surveys, there are considerable fluctuations in prevalence between birth cohorts within surveys, and between surveys for a given birth year. Overall, the levels of prevalence by birth year are similar between the two surveys. Empirically, a comparison between the 2015 data and the 2008 data yield inconclusive results.(1)

(1) An empirical analysis, also making allowance for attrition owing to Hepatitis C (which reduces prevalence for a cohort in the absence of ongoing infections), yields statistically insignificant estimates, with error margin of a similar magnitude as estimates of the level of incidence from other sources.

Kandeel and others (2017), in a discussion of these data, also do not offer incidence estimates, but point to the steep decline in prevalence at ages 15-19 between the surveys, from 4.1 percent to 1.0 percent, and speculate that this might reflect various infection prevention and control programmes implemented since 2008.

Direct estimates of incidence of Hepatitis C, i.e., the rate at which individuals in a well-defined population become newly infected between rounds of observations, are very rare. A systematic review (Mohamoud and others, 2013) identified only 4 such incidence studies among 150 empirical studies on prevalence or incidence, with incidence at different locations in Egypt ranging from 0.8 percent to 6.8 percent per person year. As these studies refer to specific locations and the underlying data are at least 10 years old, they are not relevant with respect to current national-level incidence. One common lesson from the underlying studies (Mohamed and others (2005), Mostafa and others (2010), Saleh and others (2008, 2010)) is the difficulty of estimating incidence – as the rate and absolute number of new infections is fairly small, confidence intervals are large relative to the point estimates, and differences in estimated incidence across population sub-groups are typically not statistically significant.

Other empirical analyses may help inform incidence patterns by identifying risk factors resulting in a high prevalence of Hepatitis C. The most common – indeed universal – theme from this literature is evidence on the role of medical injections or other causes of iatrogenic transmission (i.e., transmission caused by medical examinations or treatment) of Hepatitis C.[(2)] Other factors identified – in addition to the ones discussed earlier, such as age, sex, location, and a history of schistosomiasis treatment – in at least some studies include low social status (Mohsen and others (2015), Barakat and El-Bashir (2011)).

(2) See Mohamoud and others (2013) for a review of the empirical evidence. Studies showing elevated prevalence among individuals with a history of injections and other indicators for medical services include Arafa and others (2005), Barakat and El-Bashir (2011), Habib and others (2001), Mohsen and others (2015), and Mostafa and others (2010).

Some studies attempt to estimate incidence from differences in the prevalence of Hepatitis C by age. If HIV incidence is broadly constant over time, then differences in prevalence by age indeed reflect incidence at the respective ages.[3] With this reasoning, Miller and Abu-Raddad (2010) estimate incidence of Hepatitis C at 0.7 percent annually based on various survey data (including the 2008 DHS).[4] The underlying assumption that the incidence of Hepatitis C has been constant over time, though, runs against the established narrative on the spread of the epidemic in Egypt, especially the role of parenteral schistosomiasis treatment before the early 1980s. As a consequence, the age profile of schistosomiasis is characterized by a kink around a birth year of 1980 (see Figure 1).

If incidence across age groups differed only before and after that date, the cross-sectional variation (based on the data from the 2015 Health Issues survey shown in Figure 1) would suggest an average annual incidence rate of over 1 percent before the early 1980s, and of 0.3 percent to 0.4 percent thereafter.[5] Breban and others (2013) follow a different approach, arguing that prevalence and incidence of Hepatitis C are linked, and documenting a "strong positive correlation" between the two across the few studies providing both prevalence and incidence estimates. Interpolating from these data, they arrive at an estimated national incidence rate of 0.2 percent. The forward-looking policy analysis, below, adopts a similar approach, linking the number of new infections to prevalence, with an assumed prevalence rate of 0.18 percent corresponding to 165,000 infections, well within the range of recent estimates used by national health authorities (El-Akel and others (2017), Esmat (2015)).

(3) The implied reasoning broadly is that if the pattern of incidence across age groups does not change over time, and prevalence at age 36 is 0.3 percent higher than at age 35, then incidence at age 35 is 0.3 percent.

(4) Lehmann and Wilson (2009) estimate age-specific incidence following a similar approach based on earlier data. The paper offers a discussion of the shortcomings of the methods, but does not fully recognize its implications.

(5) The kink in the age profile is statistically significant, but statistical analysis does not suggest a precise date for a break in the series (consistent with a gradual phasing out of parenteral schistosomiasis treatment in the early 1980s). The estimate of recent average annual incidence is robust to the year at which the switch is assumed to occur.

Impact of Hepatitis C

Hepatitis C most directly affects living standards in Egypt through its health impacts, i.e., increased mortality and impaired health of the chronically infected. These health consequences, in turn, may affect economic outcomes, e.g., through reduced productivity, or because of the private or public financial costs caused by the epidemic. Considering the health consequences and financial costs, what can be said about the overall impact of Hepatitis C on living standards in Egypt?

Health

Empirical evidence on the impacts of Hepatitis C on mortality in Egypt is very limited. National-level data on deaths attributed to Hepatitis C from death registries have not been recorded or compiled systematically,[6] and the availability of indirect evidence, e.g., linking overall mortality to Hepatitis C infections, is very limited and does not provide a sufficient basis for extrapolating to national-level estimates.[7] For this reason, estimates of the number of deaths attributed to Hepatitis C are generally model-generated, combining a model based on available global evidence on disease progression and other aspects of Hepatitis C with available Egyptian data, most importantly on prevalence of Hepatitis C from various population surveys.

The principal data used here on the health impacts of Hepatitis C are from the most recent Global Burden of Disease (GBD) estimates,[8] which provide estimates of the impacts of Hepatitis C (and some 300 other causes) on mortality and health impairments, by sex and age, in Egypt for the years 1990-2015.

(6) One of the objectives defined under the 2014 national "Plan of Action" is to "monitor mortality and morbidity related to viral hepatitis," and to this end to "review available mortality registries (e.g., death certificates)." Otherwise, the "Plan of Action" relies on global estimates of the mortality burden. See Ministry of Health and Population (2014).

(7) One recent empirical study (Mostafa and others, 2016), though, documents elevated mortality among people chronically infected, especially mid-age males, in three rural villages in Egypt.

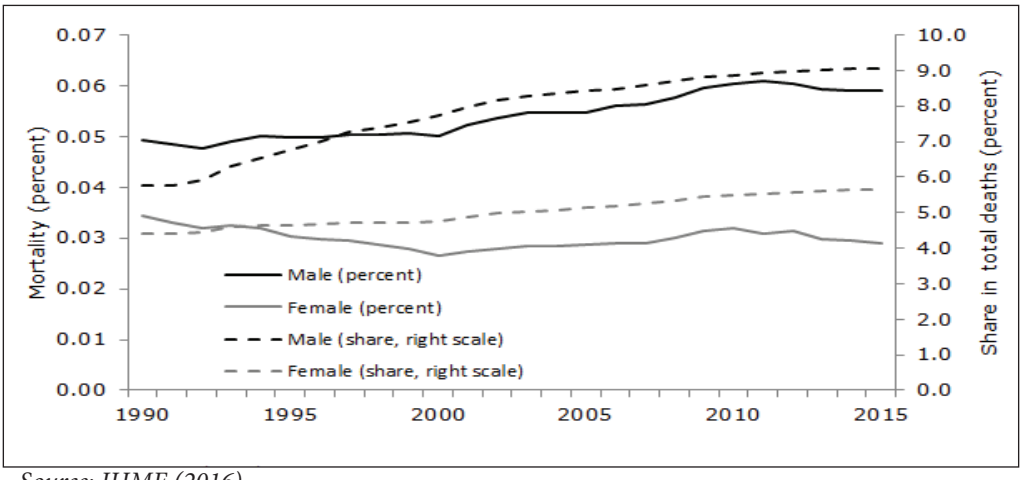
(8) These data used here are summarized and documented by Vos and others (2016) and Wang and others (2016), and are available for download through the GBD Results Tool (at http://ghdx.healthdata.org/gbd-results-tool).

Advantages of these data include availability of highly disaggregated data, in particular data by age group (which is important in light of the role of demographic factors); consistent overall and disease-specific indicators; and estimates on health impairment as well as on deaths. Also, the latest round of GBD extends through 2015, i.e., it represents the most up-to-date estimates available. However, the GBD estimates have been designed to provide estimates for any country, and may not be fully efficient in exploiting available data and accounting for idiosyncrasies of a specific country.

As of 2015, Hepatitis C accounted for about 40,000 deaths in Egypt, largely through cirrhosis (about 35,000 deaths) and liver cancer (about 5,000 deaths), according to IHME (2016). Hepatitis C is thus a significant contributor to mortality, accounting for 7.6 percent of all deaths. In line with higher prevalence of Hepatitis C among men, mortality among men (27,000 deaths, equivalent to 9.1 percent of male mortality) is much higher than for women (13,000 deaths, 5.6 percent of total).

Mortality related to Hepatitis C has increased somewhat over the last 25 years for men, but not for women (Figure 4). These trends occur against steep declines in mortality overall, the share of mortality attributed to Hepatitis C has increased considerably, from 5.8 percent in 1990 to 9.1 percent in 2015 for men, and from 4.4 percent to 5.6 percent for women.

Figure 4. Morality Due to Hepatitis C, 1990-2015 (Percent)

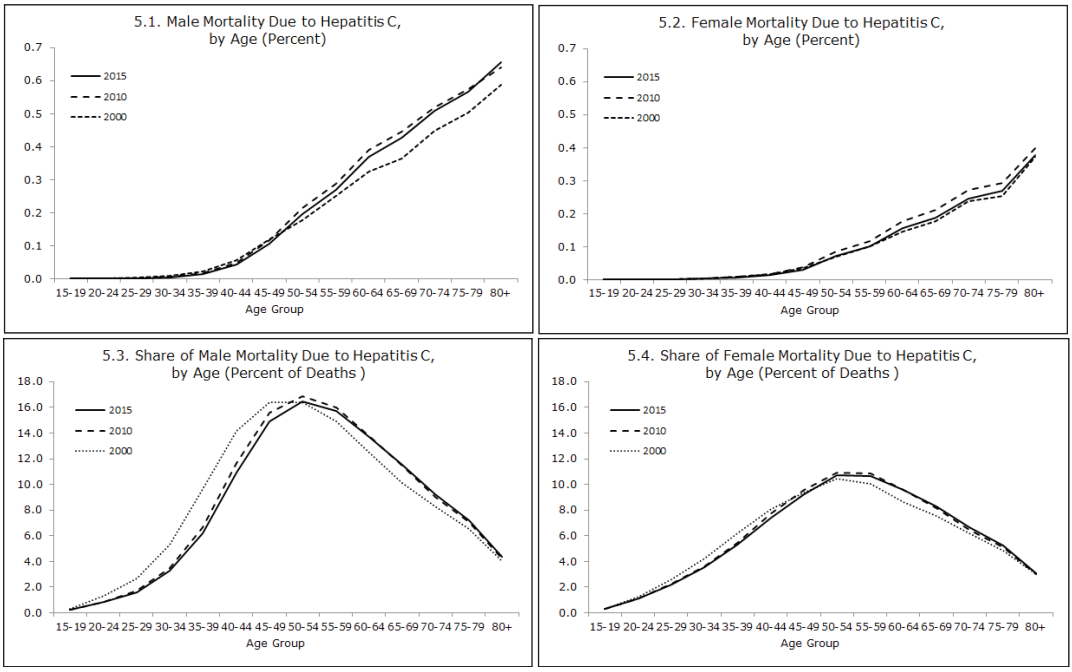


Source: IHME (2016)

Mortality related to Hepatitis C is distributed very unevenly across age groups (Figure 5), in part reflecting the profile of prevalence of Hepatitis C, but also the slow disease progression. Mortality related to Hepatitis C is very low until about age 40, then increases steeply and steadily with age. In this regard, Hepatitis C resembles many other chronic diseases which become more common at older ages. Deaths associated with Hepatitis C, though, play a relatively large role at about age 50, where they accounted for one in 6 deaths for males, and one in 9 deaths for women, in 2015. The age profile of mortality appears to have shifted to older ages (Figure 5.3 and 5.4) between 2000 and 2015, apparently a consequence of the changing age profile of the epidemic (lower prevalence in younger cohorts, compare Figure 3). An impact of the national treatment program is not obvious in the GBD mortality estimates, but will become an important factor as access to treatment increased steeply in 2016.[9]

(9) The modelling underlying the GBD data on deaths owing to Hepatitis C is geared towards attributing deaths from liver cancer and cirrhosis (estimated based on published mortality data) to causes, and does not include an explicit role for treatment of Hepatitis C. For this reason, it may be slow in reflecting ongoing changes in the policy environment such as the scaling-up of treatment.

Figure 5. Mortality Due to Hepatitis C, by Age, Various Years



Source: IHME (2016).

In addition to increased mortality, Hepatitis C also affects the state of health of those chronically infected. This point has been documented in numerous studies, although not for Egypt.

The health impacts of chronic Hepatitis C manifest themselves in reduced "health-related quality of life" (measured as an index, based on survey responses on different aspects of capabilities and well-being) as well as increased absenteeism and impaired productivity. E.g., Spiegel and others (2005) document that "patients with HCV scored lower than controls across all scales" of health-related quality of life, and that successful treatment resulted in improvements especially in physical health. The evidence of impacts on productivity is somewhat stronger. A review of this literature by Manne and others (2014) concluded "that chronic HCV infection, with and without active treatment, lead to decreased work productivity and increased absenteeism." E.g., Vietri, Prajapati, and El Khoury (2013), using European data, estimate that chronically infected patients (compared to a matched control group) lost 2.4 percent of their working time

through absenteeism, and that 10 percent of patients experienced some work impairment. Su and others (2010) estimate absenteeism at about 2 percent of working time, and reduced productivity on the job at 7.5 percent, based on data from the United States.

An alternative source of estimates on health impairments owing to Hepatitis C is the GBD study and associated database (Vos and others (2016), IHME (2016)). The GBD estimates are based on survey-based disability weights assigned to different diseases or associated states of health.[10] For health impairments owing to Hepatitis C, the most important states of health are acute Hepatitis C (immediately following infection, disability weight between 0 and 0.133), chronic Hepatitis C (in the absence of any complications, with a disability weight of 0), liver cancer owing to Hepatitis C (disability weight between 0.049 and 0.54), and uncompensated cirrhosis (disability weight of 0.178). According to the GBD estimates, the contribution of Hepatitis C to health impairments is very small overall.

For the population overall, health impairments accounted for a loss equivalent to 10.3 percent (relative to perfect health status) in 2015, but the contribution of Hepatitis C accounted for only 0.006 percentage points, and less than 0.1 percent of health impairments overall. With chronic prevalence of Hepatitis C at about 8 percent of the population in 2015 in the GBD estimates, this implied an average health impairment among people chronically infected with Hepatitis C of about 0.1 percentage point, or less than one percent of total health impairment in this sub-population.

The GBD estimates of health impairment thus differ from the empirical studies by a large margin, even though it is important to bear in mind that productivity losses and health impairments are two different concepts. One important reason that can be accounted for at least in principle is that the empirical studies focus on patient data, whereas the GBD data regard the overall population chronically infected with Hepatitis C. Nevertheless, the differences appear large and may reflect that the focus of the GBD study on the very late stages of disease, and health states characterized by very high mortality or imminent death may be too narrow.

(10) The methodology is described in more detail in the supplementary appendix to Vos and others (2016), available from the online version of the journal article. This also includes an explanation of how co-morbidities have been accounted for – in the GBD estimates, the marginal health impairment owing to a disease is smaller if health is already impaired by some other conditions, compared to the impact on an otherwise healthy person.

Economic Impact

Hepatitis C affects the economy and living standards in several ways. Most directly, it affects households of people chronically infected or who have died from Hepatitis C. Second, the costs of care and treatment, reduced productivity among chronically infected people, and demographic consequences of Hepatitis C have implications for GDP per capita. Third, care and treatment absorb resources which could be otherwise used in the absence of the epidemic. Fourth, the epidemic affects living standards through an increase in the risk of premature mortality, which can be evaluated.

On the household-level effects of Hepatitis C in Egypt, very little is known. There is a considerable literature on the household-level consequences of poor health and deaths in general (i.e., not specifically on Egypt), or for HIV/AIDS, a disease which shares some relevant characteristics with Hepatitis C (a long asymptomatic period, followed by a relatively short period of ill health and high mortality, but it is also important to note that HIV/AIDS-related deaths tend to occur at younger ages than deaths from Hepatitis C). For example, Beegle and others (2008) show that the death of a prime-age adult results in a drop in consumption of 7 per cent in the five years following the death in Tanzania, but this effect dissipates later on. Ardington and others (2014) document the impoverishing effects of deaths in KwaZulu-Natal, but point out that funeral expenses play an important role in this – a factor likely to be less relevant in Egypt.

The other cause of economic repercussions of Hepatitis C for affected households is chronic illness – income losses or the costs of care and treatment. Some evidence on this is available for Egypt regarding the consequences of chronic diseases in general (including Hepatitis C, but also diabetes or heart disease).

Rocco and others (2011) find that employment is about 7 percentage points lower among individuals affected by chronic diseases, but that wages do not differ significantly.[11]

(11) Rocco and others also report estimates using "poor health" as an instrument for chronic disease,

There are also several studies from other countries on work impairment among employees or patients with Hepatitis C. E.g., Su and others (2010) find that employees with Hepatitis C had 4 more absence days per year (about 2 percent of total working time) in the United States, and were 7.5 percent less productive on the job. Other studies also tend to find higher levels of absenteeism (several percent) for employees or patients with Hepatitis C (see Manne and others (2014) for a comprehensive survey).

Chronic diseases have also been linked to the occurrence of high household health spending. According to Rashad and Sharaf (2015), 7.4 percent of Egypt's population were impoverished by health costs (26.5 percent when accounting for health costs, 19.1 percent otherwise), and the presence of chronic diseases increases the probability of "catastrophic" health costs fivefold.12 Moreover, the vulnerability to "catastrophic" health expenditures is much higher for the lowest quintiles of the wealth distribution – a point relevant in the context of Hepatitis C, the prevalence of which is higher in poorer wealth quintiles (Table 1).

Regarding the macroeconomic effects of Hepatitis C, the neoclassical growth framework provides a useful tool for evaluating the impacts on GDP per capita. (The model is documented in the Appendix.) In this framework, Hepatitis C affects GDP per capita primarily through three channels: (1) reduced productivity among the population chronically infected, (2) changes in the dependency rate owing to Hepatitis C, and (3) the costs of care and treatment (to the extent that they crowd out investment).

■ Estimating the impacts of Hepatitis C on productivity is very difficult, because the empirical evidence focuses on patients and people knowing they are infected (and thus missing out on many people chronically infected who do not know that they are infected and who do not experience significant health impairments). The empirical evidence on labour market outcomes thus overstates the consequences of chronic infection overall. The extent to which the impacts of Hepatitis C differ across people chronically

resulting in larger estimates of economic consequences, but it is not clear if this instrument captures the effects of chronic disease.

(12) Catastrophic health costs are defined here as health costs of at least 40 percent of the households capacity to pay (total expenditure minus subsistence expenditure). Rashad and Sharaf (2015b) document similar relative increases at different poverty lines.

infected is illustrated by the Global Burden of Disease estimates (an estimate of impairment which does not necessarily translate into productivity).

Overall, chronic Hepatitis C infection results in an impairment of 1 percent, almost entirely accounted for by the consequences of uncompensated cirrhosis and liver cancer, with impairments, depending on the state of disease progression, between 5 percent and 54 percent (IHME (2016), Vos and others (2016)), although the sub-population at this advanced stage of disease account for only a small proportion of people chronically infected. Overall, we assume that chronic Hepatitis C infection reduces productivity by 2 percent, making an allowance for the consequences of advanced liver disease (an average productivity loss of 10 percent for people with cirrhosis and liver cancer, simplified from but not unlike the ones used in the GBD 2015 estimates, and broadly consistent with evidence from patient data), and for a much smaller productivity loss of about 1 percent among the population chronically infected who have not progressed to advance stages of disease. As 7 percent of the working-age population are estimated to be chronically infected, this translates into an aggregate loss in productivity and GDP per capita of 0.14 percent.

■ Based on the population figures contained in the GBD estimates, the dependency rate in 2015 was 0.619. For each working-age individual (ages 15-59), there were 0.532 young dependents, and 0.084 old dependents. Without the mortality effects of Hepatitis C, the dependency rate would be lower at 0.617 (0.530 young dependents, and 0.089 old dependents).[13] This factor increases GDP per capita by 0.19 percent.

■ For the evaluation of the macroeconomic effects of Hepatitis C so far, we assume that each death owing to Hepatitis C is associated with a cost equivalent to 1.5 times GDP per capita. This has been calculated based on estimated costs of treating cirrhosis and liver cancer, in the absence of antiviral treatment which has played a minor role until recently, using the unit costs (Table 3) and estimates and projections described later in this report, arriving at a cost per death just over US$ 5,000.

(13) The population figures were adjusted for estimates excluding the impact of Hepatitis C using survival curves. I.e., adjusted population at some age is population size times survival (excluding impact of Hepatitis C), divided by actual survival to that age. This effect may not have fully materialized so far (owing to the slow demographic dynamics), but the available mortality estimates (Figure 4), with similar rates for at least the last 25 years, suggests that the approach adopted here represents a reasonable approximation.

The evidence on the household-level costs of care is much less clear. We assume that each death is associated with a cost equivalent to 0.5 times GDP per capita (capturing preceding costs of care and funeral expenses etc.).

Because deaths owing to Hepatitis C frequently occur late in life (on average, each deaths costs about 20 life years), it is also necessary to take into account that people dying because of Hepatitis C do not die later for other causes. We assume that the costs of deaths for other causes amount to 1.0 times GDP per capita (covering treatment and all household-level costs). Applying a discount rate of 5 percent over 20 years, this saving is equivalent to 0.36 percent of GDP per capita. Overall, thus, we assume that each death owing to Hepatitis C is associated with a cost of 1.64 times GDP per capita. Using an estimate of mortality owing to Hepatitis C of 0.044 percent (IHME, 2016), this implies a cost of care and treatment of 0.07 percent of GDP. Assuming that these costs result in proportional declines in consumption and investment, this factor results in a decline in GDP per capita of 0.03 percent (see model described in Appendix).

Overall, thus, Hepatitis C has a small impact on GDP per capita. While reduced productivity and the crowding out of investment reduce GDP per capita by 0.17 percent, this effect is more or less offset by the decline in the dependency rate: The total estimated impact on GDP per capita is a small positive effect of 0.02 percent. This conclusion does not shift fundamentally if resources absorbed by care and treatment are taken into consideration. These – before the scaling up of antiviral drugs – were estimated at 0.07 percent of GDP per capita. Subtracting these from GDP per capita, the total economic costs of Hepatitis C come out as a loss of 0.05 percent of GDP per capita.

Regarding the impacts on the economy overall, we estimate that the size of the working age population is diminished by premature mortality by an estimated 0.32 percent.[14] Overall, thus, we estimate that in 2015 GDP was 0.30 percent lower than in the absence of Hepatitis C, equivalent to a loss of US$ 1.0 billion,

(14) This has been calculated similar to the effect on dependency rates. We derived a survival curve excluding the impact of Hepatitis C from GBD 2015 estimates. The size of the working-age population in the absence of Hepatitis C was then estimated by applying the increased survival rates to the respective age cohorts. This approach is suitable for analysing long-run changes (once the effects of changed mortality have materialized through the age distribution, a process that can take decades. Because mortality owing to Hepatitis C is concentrated among older adults, and as it changed only slowly over the last two decades, we believe that this approach yields a reasonably good estimate here.

or EGP 7.3 billion then (EGP 18 billion at current exchange rates). Most of this reflects the resulting changes in the size of the working-age population, while the changes in GDP per capita have been small.

In interpreting these numbers, though, it is important to remember that the economic impacts of Hepatitis C are distributed unevenly across households. The aggregate estimates do not capture the economic risks associated with the impacts of Hepatitis C, as suggested by the evidence on the role of chronic infections as a cause of poverty and "catastrophic" health expenditures (Alam and Mahal, 2014), especially for the two lowest wealth quintiles which not only are the most economically vulnerable, but also experience the highest prevalence of Hepatitis C.

Increased mortality owing to Hepatitis C affects living standards because of the risk to life prospects posed by increased premature mortality. This loss in living standards can be evaluated and compared to the economic costs by estimating an economic cost that is equivalent to the health losses caused by Hepatitis C. This approach has frequently been used in government policy evaluations, e.g., in health or environmental interventions, in evaluating gains from medical research, assessing changes in living standards across countries, or motivating investments in health.[15] The key concept is that individuals, in terms of their outlook on life, value income and the benefits that derive from it, but also the prospect of a long life and absence of an elevated risk of premature mortality.

Under this framework, an increase in mortality risk and a loss in income both reduce living standards in terms of this outlook on life, and it is possible to estimate the drop in income which is equivalent to (i.e., as bad as) an increase in mortality. Empirically, such estimates (i.e., how much of an income loss corresponds to a change in mortality) can be obtained from labour market data or policy valuations of mortality risks. Specifically, according to the GBD estimates, Hepatitis C reduced life expectancy at birth in Egypt by about one year, from 71.9 years to 70.9 years, as of 2015.16 In terms of living standards, in the concrete

(15) See Becker, Philipson, and Soares (2005), Jamison and others (2013), Murphy and Topel (2006), and Viscusi (2014) for an introduction to these methods.

(16) This has been calculated by first transforming female and male GBD mortality estimates into survival curves. Life expectancy is then calculated by adding up expected survival across ages, applying estimates of the sex ratio at birth from UNPD (2015) as weight.

sense applied here, this drop in life expectancy is equivalent to a drop in income of 1.5 percent,17 i.e., with respect to living standards, the increased mortality risks associated with Hepatitis C are equivalent to a drop in GDP of 1.5 percent, or US$ 5 billion (currently EGP 90 billion) annually.

(17) The background and methods are described in Haacker (2016, pp. 58-61). The drop in life expectancy of 1 year, or 1.4 percent, corresponds to a drop of 0.4 percent in discounted life expectancy, applying a discount rate of 3 percent. Assuming that a drop in discounted life expectancy of one percent is equivalent to a drop in income of 3.5 percent (broadly consistent with the empirical evidence), an equivalent drop in income of 1.5 is obtained.

State of Egypt's Response to Hepatitis C

Egypt's response to Hepatitis C is in transition. The introduction of highly effective new antiviral drugs has transformed the health consequences of Hepatitis C, but it has also introduced a powerful tool for controlling the spread of the epidemic, promising to reduce the number of people chronically infected with Hepatitis C as well as the number of new infections. While the latter (bringing down new infections) is a consequence of the former (few people who might pass on Hepatitis C), the prevention aspects of treatment are an important consideration in their own right for controlling transmission and have consequences for the design of the treatment program.

The scale of the Hepatitis C epidemic in Egypt has been recognized since the mid-1990s,[18] soon after the Hepatitis C virus was discovered. To address the health challenges posed by the epidemic, the National Committee for Control of Viral Hepatitis (NCCVH) was established in 2006. Important early steps in the national response to Hepatitis C were the inclusion of Hepatitis C testing in the 2008 Demographic and Health Survey (El-Zanaty and Way, 2009), providing the first nationally representative estimates of the scale and distribution of the epidemic, and the development of a National Control Strategy for Viral Hepatitis (Ministry of Health and Population, 2008). During this period, the first national treatment centers were established, and about 100,000 patients were treated by 2010 and about 360,000 by 2014 (although only about one-half achieved sustained virological control, reflecting the limited effectiveness of drugs available at the time). However, progress in infection control remained fragmented (Doss, 2016).

A new Plan of Action for the Prevention, Care and Treatment of Viral Hepatitis was introduced in 2014. This was in part motivated by the advances in the effectiveness of treatment and their costs, contributing to a shift in perspective to a "vision aimed at national eradication of viral hepatitis" (MoHP, 2014). The most significant aspects of the Plan of Action for the purposes of this study are the promotion of infection control practices, and the expansion of treatment.[19]

(18) See Frank and others (2000) for a relatively early review.

(19) Other components include the strengthening of surveillance, improvements in blood safety, elimination of the transmission of vaccine-preventable hepatitis (i.e., not Hepatitis C), education, and research.

Regarding infection control, the Plan of Action acknowledges that transmission of Hepatitis C occurs mainly through unsafe medical procedures and especially unsafe injections. The most accepted backward-looking estimates suggest that incidence remains around 0.2 percent annually (about 150,000 to 200,000 new infections, see, e.g., Breban and others (2013), El-Akel and others (2017)). However, if the perception of declining incidence (Kandeel and others, 2017) is correct, current incidence rates might be lower. In any case, these numbers need to be seen against an estimate of about 5 million people who are chronically infected: Because people chronically infected (unless treated) typically carry the virus for decades, an annual rate of onward transmission around 3 percent per person infected (=150,000 new infections, divided by 5 million chronically infected people) implies a substantial number of downstream infections.

Regarding the expansion of access to treatment, the Plan of Action was developed at the beginning of what would become a rapidly changing period for treatment. While the Plan of Action points at the role of treatment in reducing transmission of Hepatitis C (which necessitates relatively broad and early access to treatment), it also acknowledges that there is only a "small fraction of the total number of patients chronically infected with HBV and/or HCV [who] are treated annually." Referring to a number of studies suggesting that "shifting treatment to patients with more advanced forms of disease (i.e., established cirrhosis or stage 4 fibrosis […] would be more cost-effective than treating patients in earlier disease stages," it also anticipates that "new and highly-effective oral viral hepatitis therapies will soon be available."

From 2014, the arrival of new, highly effective drugs and reductions in drug prices have transformed the treatment program.[20] The government set up a web-based system to register for treatment (at the time, about 750,000 were known to be chronically infected and eligible for treatment).[21] The number of patients registering through this system considerably outstripped capacities early on, with wait times of up to half a year.

(20) See El-Akel and others (2017) for a more extensive discussion.

(21) This includes about 150,000 who had been treated before with different and less effective drugs, 150,000 who had been diagnosed but chose not be treated at the time, and about half a million for whom the interferon-based therapy was deemed unsuitable (El-Akel and others, 2017).

However, by end-November 2016, 850,000 people had been treated, with a success rate (sustained virological response) of well over 90 percent, and the backlog of patients registered but not receiving treatment had disappeared.

Looking ahead, this means that the focus of the treatment program has shifted to recruiting new patients into the system. A large share of people treated since 2014 had known about their Hepatitis C infections and were seeking treatment. For the future of the treatment program and the course of the epidemic (especially the implications of treatment for reduced transmission), it will be critical to motivate potential patients (many of whom do not experience symptoms) to be tested and – if chronically infected – to access treatment.

The forward-looking program analysis below builds on the Plan of Action by assessing the projected impacts, costs, and cost-effectiveness of the expansion of demand-driven treatment. It also addresses how the impacts could be augmented by screening for Hepatitis C across the population or for specific population groups. Additionally, it addresses the contribution of the treatment program (by reducing onward transmission of Hepatitis C) to the prevention of new infections and consequent health outcomes.

Impact of and Returns to Investment in Egypt's Response to Hepatitis C

The purpose of the analysis is to inform ongoing considerations on policies towards eliminating Hepatitis C, and to assess the effectiveness and cost-effectiveness of the main tools available, such as:

■ **Treatment:** Treatment with new highly effective antiviral drugs already has resulted in a substantial decline in the number of people chronically infected since 2014. However, much of the initial wave of people assessing treatment in 2014-2016 reflected a backlog. For this reason, and because the number of people chronically infected has already declined as a result of treatment, the pace of demand-driven treatment is set to slow down over the coming years.

■ **Screening:** To accelerate the scaling-up of treatment, and fully utilize the facilities available now, would therefore require a more activist policy to encourage people to get tested and – if testing positive – initiate treatment.

■ **Prevention:** There are two pillars of national prevention policies – measures aiming directly at reducing transmission of Hepatitis C, such as investments in safe injection practices, and treatment, which serves to "greatly improve health outcomes and prevent transmission of infection to others" (MoHP, 2014).

To analyse these different dimensions of national policies on Hepatitis C, we utilize five principal scenarios (further described in Box 1) – a scenario with "constant transmission" of Hepatitis C; a "prevention-only" scenario in which policies on blood safety, infection control, and awareness reduce transmission rates (but no treatment is available), a "treatment" scenario which additionally accounts for a continuation of the demand-driven treatment program, a "screening" scenario which additionally assumes that a certain proportion of the population is screened each year and progresses to treatment if chronically infected, and an "elimination" scenario in which the entire adult population is screened between 2017 and 2022 and treated if required. The underlying model is described in the Appendix.

These scenarios are used in various ways to assess the effectiveness and cost-effectiveness of the national policy on Hepatitis C and its components, first by comparing the projected outcomes and costs through 2030. In light of the focus on the prevention aspects of treatment in the national plan (MoHP, 2014), we also

look at the contribution of treatment to preventing new infections (in addition to infection control and other measures aiming directly to reduce incidence) in the scenarios describing the continuation and extension of the treatment program.

The discussion on various policies conducted through 2030 is complemented by an analysis of current policies, looking at the effects of implementing the treatment and screening policies in 2017 only. This analysis provides more precise estimates of the cost-effectiveness of policies considered or implemented now. In contrast, the results based on the policies implemented through 2030 represent averages of changing outcomes and costs over a fairly long period, and are imprecise especially with regard to policies implemented late within this period, of which most of the effects are cut off in the analysis (as they occur post-2030).

Box 1. Assumptions Underlying Policy Scenarios

The starting point for all scenarios is 2017. The model captures the scaling-up of treatment in 2015 and 2016, assuming that 850,000 patients were placed on treatment by end-2016 (of which 600,000 accessed treatment in 2016). Relatively more people at advanced stages of disease are assumed to seek treatment, with rates ranging from 4 percent at the earliest stage of disease (METAVIR stage F0) to 29 percent (from stage F3).

In the "constant transmission" scenario, there is no treatment, and the rate of onward transmission of Hepatitis C from people chronically infected is constant. Because prevalence is declining slowly in this scenario, this also implies a gradual decline in incidence.

The "prevention only" scenario additionally envisages that the rate of onward transmission declines by 20 percent between 2016 and 2020, and remains at this lower level thereafter. This is a working assumption – the national plan does point to the scope for and need of additional measures to reduce transmission of Hepatitis C, but does not spell out targets, and relevant national-level studies are unavailable. This scenario is used as a benchmark for the more comprehensive policies involving treatment (to avoid that outcomes are inflated by applying a baseline scenario like "constant transmission" that arguably is too pessimistic).

The "treatment" scenario additionally assumes that the demand-driven treatment program continues. However, as most of the patients treated in 2016 were previously known to be chronically infected, the rate at which new patients access treatment from 2017 is lower than in 2016, ranging from 2 percent of people at the earliest stage of disease (F0) to 15 percent from (from stage F3). This means that 7 percent of people chronically infected access treatment in 2017, and this rate declines to 5 percent by 2030 (because there are fewer chronically infected patients at advanced stages of disease). It is further assumed that 50 percent of people tested through the treatment program are chronically infected.

The "screening" scenario comprises the demand-driven "treatment" scenario. Additionally, 10 percent of the population from age 15 are assumed to be tested for Hepatitis C annually and – if chronically infected – to progress to treatment. In this scenario, the rate at which people chronically infected access treatment ranges from 7 percent at the earliest stages to 19 percent at advanced stages, and amounts to 12 percent overall in 2017, slowly declining to 10 percent by 2030 (because of the changing composition of people chronically infected).

The "elimination" scenario differs from the "screening" scenario by the pace and scale of screening, assuming that all adults are screened between 2017 and 2022 – 10 percent in 2017 (as under "screening"), 20 percent annually in 2018 to 2021, and the remainder in 2022. All people tested are registered so that there is no re-testing over this period. As there will be very few people chronically infected left after 2022, the screening program is closed, but demand-driven treatment (on a much lower scale than under "treatment") continues.

Additionally, we provide an analysis of the cost-effectiveness of treating or screening individuals at specific ages in 2017. This reflects that prevalence of Hepatitis C differs steeply across age group, and that older individuals who are chronically infected are more likely to be in advanced stages of the consequences of Hepatitis C, and experience higher mortality for other reasons. The cost-effectiveness of screening and treatment therefore differs across the population, and these differences may have implications for policy design.

Impact of Policies on State of Epidemic

From a common starting point (604,000 in 2016), the number of people receiving treatment declines to 346,000 in 2017 in the demand-driven "treatment" scenario, but it increases to about 720,000 under "screening", and further to just under one million in 2018 under the "elimination" scenario. Subsequently, the numbers accessing treatment declines, as the number of people seeking treatment or the prevalence of chronic Hepatitis C infections among people undergoing screening decline. Interestingly, the gap in the number of people receiving treatment under the "treatment" and "screening" scenarios narrows, and fewer people receive treatment with "screening" than "treatment" from 2027.

Under "elimination," the number accessing treatment declines to a trickle (about 4,000 annually) from 2023. (The "elimination" scenario does not literally end the epidemic because of treatment failure, the possibility of new infections among people already tested, and a small number of infections among children who – because of very low prevalence – are not screened under the envisaged policy.)

The continuation of the treatment program will result in steep declines in deaths owing to Hepatitis C (Figure 6.2) by about one-fifth by 2020 and one-half by 2030, relative to "prevention only." Screening augments the impact on deaths but is relatively less effective in this regard (because people recruited into treatment through screening tend to be at earlier stages of disease progression). The decline in deaths under "treatment" proportionally exceeds the decline in the size of the population chronically infected (Figure 6.4), because people at more advanced stages of disease are more likely to seek treatment than otherwise.[22]

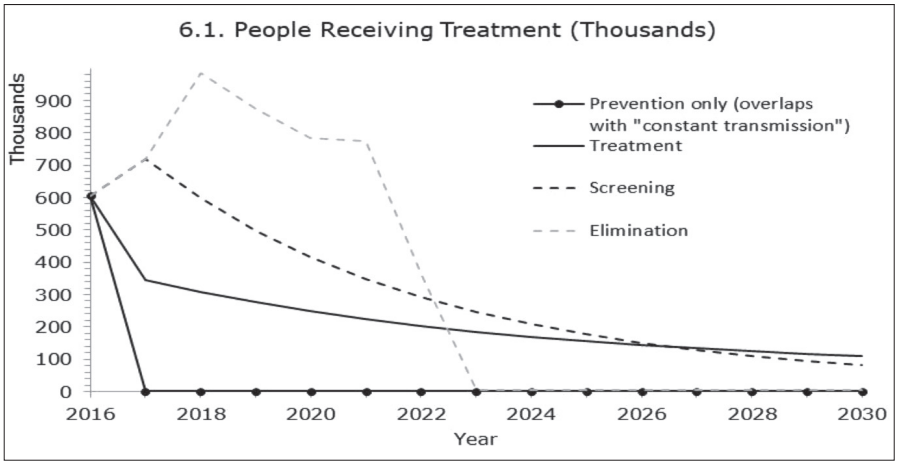
(22) On the other hand, there typically is a considerable lag between treatment and deaths averted (so that deaths would decline more slowly than the number of people chronically infected), but in our projections this factor is much weaker than the selection of relatively sick people chronically infected into treatment.

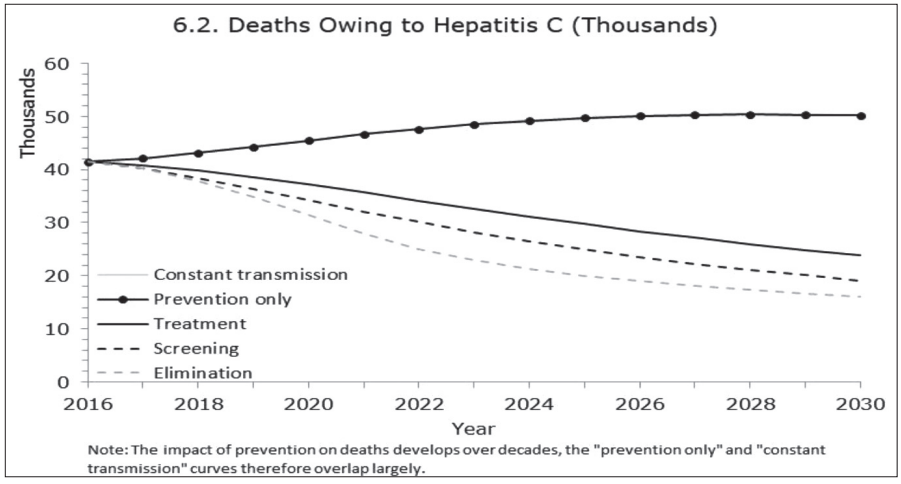
Treatment and screening (with or without "elimination") are also projected to have a major impact on the number of new infections, which declines by between one-sixth (under "treatment") and more than one-half (under "elimination") by 2020, relative to the "prevention only" scenario, because there are fewer people chronically infected to pass on Hepatitis C.[23] Screening is relatively more effective than demand-driven treatment in reducing the number of new infections because treatment tends to occur earlier with screening.

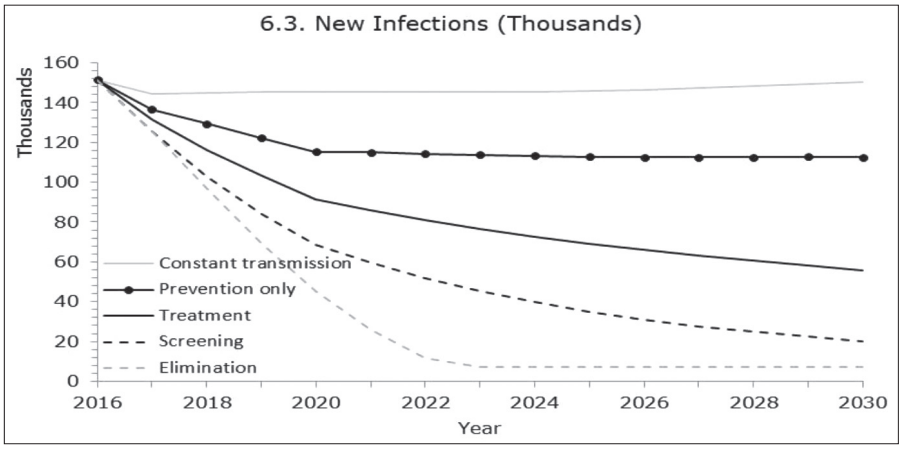
A few notes on prevention of Hepatitis C are in order. Our estimates include an allowance (an assumed decline of 20 percent by 2020) for the effects of measures under the Plan of Action directly aiming at reducing the incidence of Hepatitis C. There is some evidence suggesting that incidence has declined in the past as a consequence of improved infection control, e.g., the steep decline in the prevalence of Hepatitis C among young people observed by Kandeel and others (2017), or the increase in the adoption of infection control measures between 2003 and 2011 documented by El Sayed and others (2012). The Ministry of Health and Population (2014) considers "contact with infected blood through medical procedures (including unsafe injection practices) […] the primary mode of HCV transmission," and estimates that "8 percent of injections are unsafe." These numbers suggest that there is substantial potential for bringing down transmission rates further through infection control and other measures.

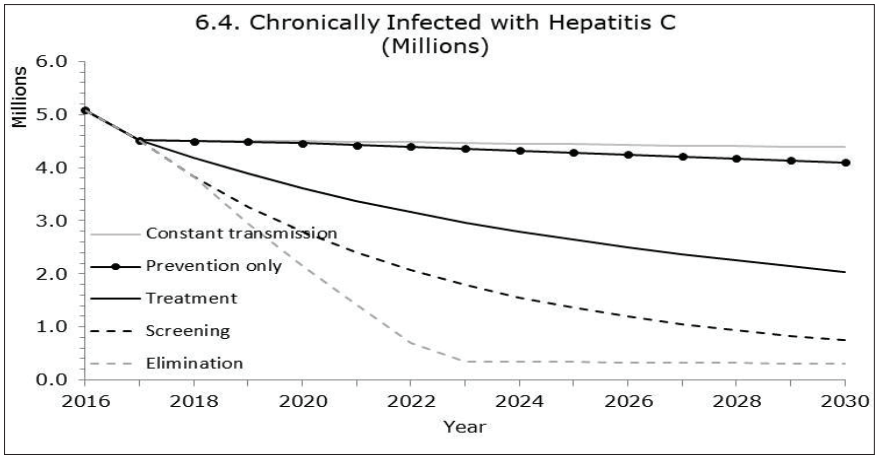
(23) More precisely, the number of new infections in our model it proportional to p*(1-p), i.e., the prevalence of people chronically infected (p) times the share of the population not chronically infected (1-p). However, with prevalence of about 6 percent and declining, the number of new infections is roughly proportional to p. See appendix for further details.

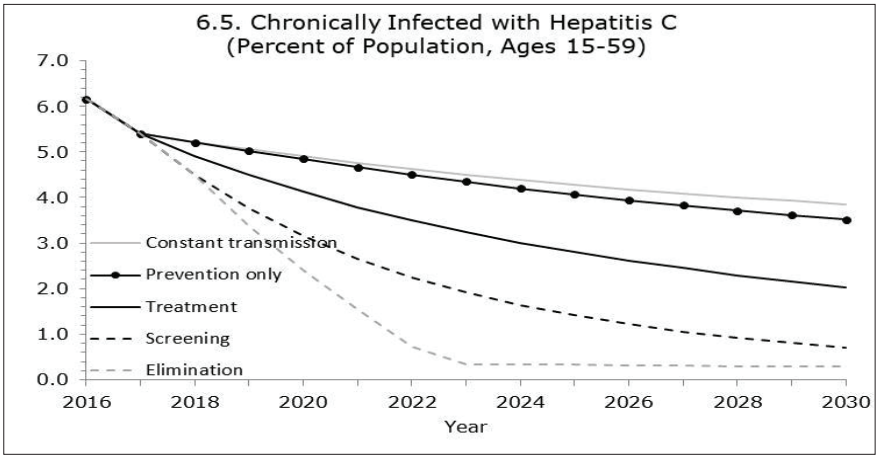
Figure 6. State and Impact of Hepatitis C, Various Scenarios, 2016-2030











However, they do not clearly translate into plausible estimates of the gains which can be achieved in immediate outcomes (like safe injections) and in transmission of Hepatitis C. Against this background, the assumed decline in incidence of 20 percent in the "prevention only" scenario is more of a memorandum item that serves two purposes. First, it documents how the effects of prevention interventions evolve. The considerable (assumed) decline in incidence due to prevention (vs. the "unchanged transmission" scenario, see Figure 6.3) translates into a very gradual decline in the number of people chronically infected (Figure 6.4), and an even slower decline in mortality (barely perceptible within the policy period through 2030 adopted here, see Figure 6.2). Second, it is used as a benchmark to evaluate the policy scenarios to avoid exaggerating policy effects by

adopting an unrealistically negative benchmark that assumes constant incidence.

It is also worth noting that the estimates summarized in Figure 6 (and Figure 7, below) may understate the potential of treatment and screening to serve as prevention. This is because infection risk (and the potential to transmit Hepatitis C) is spread unevenly across the population. E.g., Breban and others (2013) point out that "5 percent of the adult population takes more than 50 percent of all injections," according to the 2008 DHS. Targeting treatment at population sub-groups where it is most effective in reducing new infections (in addition to directly improving health outcomes) could therefore improve effectiveness and cost-effectiveness of treatment policies. This point is taken up further below with regard to the effectiveness of treatment and screening policies across age groups.

The overall impact of the policies considered on the number of people chronically infected is summarized in Figures 6.4 and 6.5. By 2030, the number of people chronically infected declines to 2.0 million in the "treatment" scenario, a reduction by one-half compared to the "prevention only" scenario. "Screening" would further reduce the number of people by two-thirds relative to treatment, and five-sixth overall. Under "elimination," the number chronically infected declines to just about 300,000. The bulk of the decline in prevalence of chronic infections can be attributed to the direct effects of treatment. Reduced incidence, whether as a result of infection control measures or a consequence of treatment, affects prevalence only very slowly, and has a small effect overall through 2030.[24]

Costs and Cost-Effectiveness of Alternative Policies

In order to obtain estimates and projections of the costs of the national response to Hepatitis C, unit cost for testing, treatment, and the most important types of treatment of the health consequences of Hepatitis were obtained (summarized in Table 3). For testing and treatment, these data were supplied by the national authorities, based on the latest available prices for the public sector. The principal

(24) The reason for this is that Hepatitis C is a chronic disease characterized by very slow disease progression (typically several decades). The number of people chronically infected (accumulated over decades) is therefore large relative to the number of new infections. In this concrete example, incidence in 2016 is estimated at 0.15 percent (3 percent of prevalence estimated at 5.4 percent). With regard to the number chronically infected, prevention measures reduce prevalence by a fraction of these 3 percent annually, while the treatment policies considered reduce the number of people chronically infected by an average of 6 percent ("treatment") and 8 percent ("screening") annually in 2017-2030.

sources of unit costs on care are a study by Estes and others (2015) and recent guidance from the Ministry of Health and Population. The estimates by Estes and others provide a good framework because the study adopts a health systems perspective, discussing not only the costs of various types of care, but also the coverage rates of these services (an important point because many people chronically infected are not aware of it, and may experience little symptoms), and documents sources of these estimates transparently. Data from the Ministry of Health and Population were used especially for items like the costs of drugs and testing, which have been subject to considerable changes. For the projections, all unit costs are held constant, i.e., projected costs are reported at 2016 prices (with exception of treatment costs, where a lower unit cost is assumed from 2017).

Table 3. Assumptions on Unit Costs

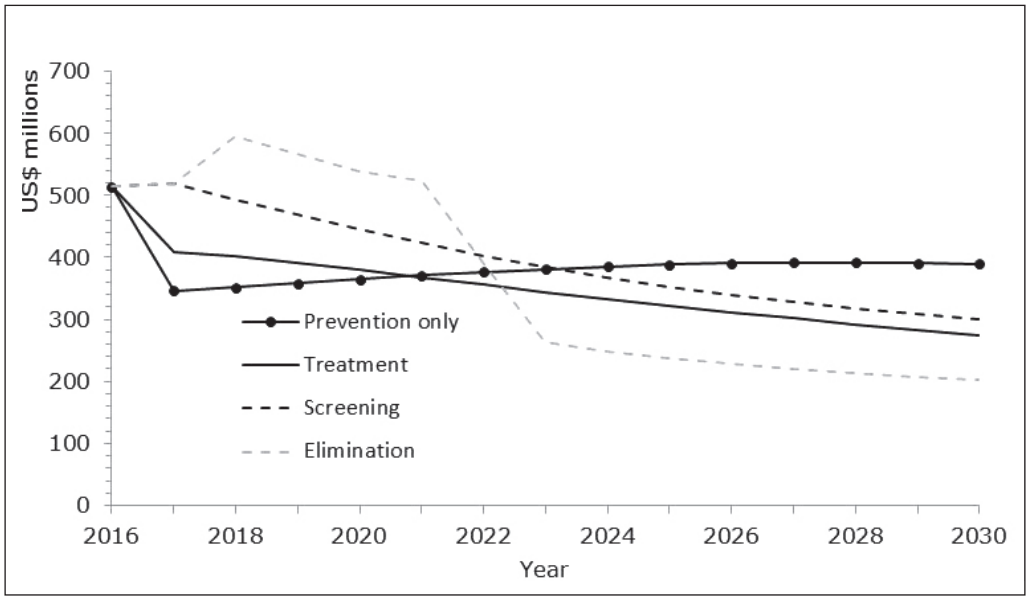
Hepatitis C Treatment 2016 From 2017	 US$ 200 US$ 98
Hepatitis C RNA Test	US$ 67
Hepatitis C Antibody Test	US$ 6
Hepatitis C testing: Fixed costs per patient, irrespective of progression to RNA test or treatment.	US$ 2
Compensated cirrhosis (average annual cost per person in health state) (Estes and others (2015), reflecting a cost per patient of US$ 685, at a coverage rate of 15 percent.)	US$ 110
Decompensated cirrhosis (average annual cost per person in health state) (Ministry of Health and Population, and Estes and others (2015), assuming a coverage rate of 60 percent.)	US$ 1,905
Hepatocellular cancer (average cost per case) (Estes and others (2015) assume an annual cost per patient of US$ 1,225, and a coverage rate of 60 percent. Annual mortality of 80 percent implies average survival of about 1.25 years.)	US$ 900
Liver transplantation (one-off) (Estes and others (2015))	US$ 42,500
Post-liver-transplantation (annual)	US$ 5,600

Sources: Ministry of Health and Population, unless stated in brackets.

The estimates and projections of the costs of the national policy on Hepatitis C are summarized in Figure 7. As of 2016, estimated spending amounted to US$ 514 million (about 0.2 percent of GDP), about one-half of which reflected the costs of demand-driven testing and treatment. Costs decline steeply in 2017 under treatment, because the unit costs of treatment have come down further between

2016 and 2017, and a projected decline in people seeking treatment, following the first wave of treatment after introduction of highly effective antiviral drugs through 2016. However, costs remain high or increase further under "screening" and "elimination," peaking at US$ 518 million (2017) and US$ 595 million (2018), respectively.

Figure 7. Projected Costs of National Policy on Hepatitis C (US$ Millions)

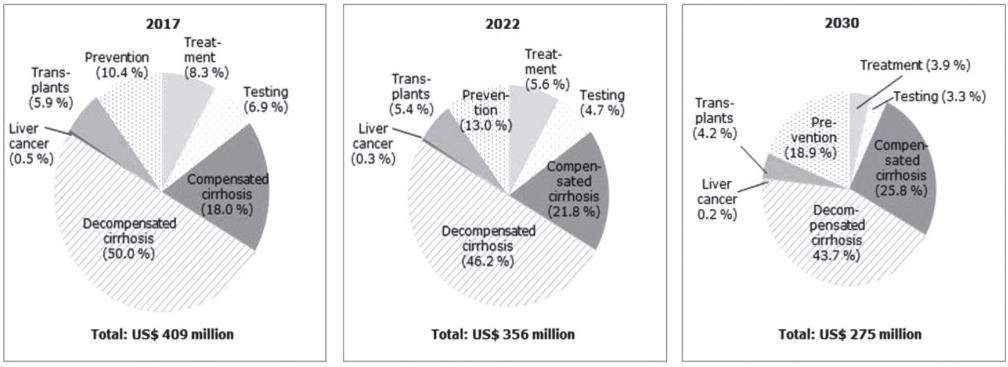


Thereafter, costs keep increasing slowly in the "prevention only" scenario – a consequence of population growth (which drives up prevention costs) and of increasing costs of care (while the number of people chronically infected declines slowly in this scenario, they tend to get sicker). In contrast, costs decline at least from 2018 under the "treatment," "screening", and "elimination" scenarios, as fewer people access treatment and the impact of treatment on disease progression reduces the costs of care, and fall below costs under the "prevention only" scenario at least from 2024. For "screening" vs. "treatment," the differences reflect initially higher treatment costs and the ongoing costs of "screening." Because the number chronically infected and progressing to treatment declines faster under "screening" than under "treatment," the cost difference narrows. Under "elimination," the initial build-up in costs reflects higher costs of screening and treatment than in the other scenarios. The savings under "elimination" from

2023 reflect that there are no more screening costs (not necessary because of very low prevalence of chronic Hepatitis C infections attained), and that treatment is reduced to a trickle (as there are very few people left to be treated).

The factors underlying these changes are illustrated in more detail in Figure 8 for the "treatment" scenario. In 2017, the most important cost component (US$ 230 million, or 56 percent of total) is the cost of care at the most advanced stages of liver disease (decompensated cirrhosis, liver cancer, and liver transplants), while testing and treatment of chronic infection accounts for only 15 percent of the costs, i.e., at current unit costs, treatment – which was prohibitively expensive a few years ago – has become a relatively small component of the overall costs of the response to Hepatitis C. By 2030, the costs of care for advanced stages of liver disease decline steeply (to US$ 132 million, or 48 percent of total costs). The costs of testing and treatment of chronic infections decline similarly. Instead, the weights of prevention increases, and the cost of care for compensated cirrhosis becomes a more important cost factor. To the extent that treatment of chronic Hepatitis C infection stops or slows down the progression of liver disease, but does not reverse it, it will be necessary to provide long-term care for the population who have suffered chronic liver damage as a consequence of an earlier infection with Hepatitis C.

Figure 8. Comosition of Spending on National Response to Hepatitis C, 2017, 2022, and 2030



Note: Estimates relate to "treatment" scenario. Size (area) of pie charts is proportional to projected spending. Prevention includes infection control, blood safety, and education.

To obtain a clearer picture of the effectiveness and especially cost-effectiveness of the stylized policy choices explored in the different scenarios, Table 4 summarizes the consequences (costs and health impacts) across scenarios. Consistent with the earlier discussion on projected costs and outcomes, the projected impact of alternative policies on health outcomes (infections and deaths averted) increases over time, while the accumulated costs shown in Table 4 under the "treatment," "screening," and "elimination" scenarios increase first, but eventually decline. For the "treatment" scenario, the accumulated savings (applying a discount rate of 5 percent) eventually more than offset the costs of treatment of chronic Hepatitis C infections, i.e., the policy saves money over a time horizon of 13 years. The "elimination" scenario saves money relative to "screening": The costs of screening under "elimination" are more front-loaded but lower overall than for the "screening" scenario, and it is more effective in identifying and treating people chronically infected and thus realizing savings in the costs of care.

Table 4 also shows that the stylized policies considered differ substantially in terms of their effectiveness and cost-effectiveness. Demand-driven treatment is the most cost-effective (and the only cost-saving) strategy, but the least effective policy towards eliminating the epidemic. Of the two policies augmenting demand-driven treatment with some "test and "treat" program, the "elimination" scenario in which the additional testing is concentrated in the first years comes out as the more cost-effective of the two, and cost-saving relative to the "screening" scenario.

One shortcoming of the results in Table 4 is the inability to clearly show differences in the effectiveness and cost-effectiveness of policies over time. For example, the cost-effectiveness of screening declines as the prevalence of chronic Hepatitis C infections declines, so more people must be screened to identify one chronically infected person. The effects over the entire policy period may therefore not offer clear guidance on the effectiveness of current policies. This point is addressed in Table 5, which summarizes the effectiveness and cost-effectiveness of policies pursued in 2017. (Note that Table 5 does not distinguish between the "screening" and "elimination" scenarios because these scenarios coincide in that year.)

Table 4. Costs and Health Impacts Across Policy Scenarios

	Accumulated costs and impacts until…					
	2017	2018	2019	2020	2025	2030
Costs (US$ millions)						
"Treatment" (vs. "prevention only")	59	104	133	146	25	-247
"Screening" (vs. "prevention only")	163	292	388	455	484	286
"Elimination" (vs. "prevention only")	163	384	565	709	563	73
"Screening" (vs. "treatment")	104	188	256	310	459	533
"Elimination" (vs. "treatment")	104	280	432	563	538	320
"Elimination" (vs. "screening")	0	92	177	254	79	-213
Infections Averted (Units)						
"Treatment" (vs. "prevention only")	4,982	16,779	33,270	52,783	182,225	326,473
"Screening" (vs. "prevention only")	10,378	34,631	67,814	106,219	345,084	588,417
"Elimination" (vs. "prevention only")	10,378	39,710	85,751	143,322	504,844	799,177
"Screening" (vs. "treatment")	5,396	17,852	34,544	53,436	162,859	261,944
"Elimination" (vs. "treatment")	5,396	22,931	52,481	90,539	322,618	472,704
"Elimination" (vs. "screening")	0	5,080	17,937	37,103	159,760	210,760
HepC-Related Deaths Averted (Units)					50,300	67,800
"Treatment" (vs. "prevention only")	1,226	4,218	9,154	15,996	71,022	138,218
"Screening" (vs. "prevention only")	1,798	6,064	12,920	22,199	92,410	173,094
"Elimination" (vs. "prevention only")	1,798	6,606	14,780	26,230	113,932	205,246
"Screening" (vs. "treatment")	572	1,846	3,766	6,203	21,389	34,877
"Elimination" (vs. "treatment")	572	2,388	5,626	10,234	42,911	67,028
"Elimination" (vs. "screening")	0	542	1,859	4,031	21,522	32,151
Costs per Infection Averted						
"Treatment" (vs. "prevention only")	11,873	6,194	3,992	2,763	136	-756
"Screening" (vs. "prevention only")	15,720	8,434	5,729	4,287	1,402	487
"Elimination" (vs. "prevention only")	15,720	9,668	6,591	4,949	1,115	92
"Screening" (vs. "treatment")	19,271	10,540	7,401	5,792	2,818	2,036
"Elimination" (vs. "treatment")	19,271	12,210	8,239	6,223	1,668	678
"Elimination" (vs. "screening")	0	18,078	9,852	6,843	496	-1,011
Costs per Death Averted						
"Treatment" (vs. "prevention only")	48,261	24,640	14,508	9,119	350	-1,786
"Screening" (vs. "prevention only")	90,734	48,169	30,067	20,513	5,235	1,655
"Elimination" (vs. "prevention only")	90,734	58,117	38,240	27,041	4,942	358
"Screening" (vs. "treatment")	181,709	101,925	67,882	49,895	21,457	15,291
"Elimination" (vs. "treatment")	181,709	117,242	76,858	55,051	12,542	4,778
"Elimination" (vs. "screening")	0	169,404	95,039	62,986	3,682	-6,626

Note: Table shows difference between scenarios in the accumulated costs and health impacts, from 2017 until year indicated, applying a discount rate of 5 percent.

Table 5. Costs and Health Impacts of Policies Pursued in 2017

	Accumulated costs and impacts until…					
	2017	2018	2019	2020	2025	2030
Net Costs (=direct costs minus subsequent savings, US$ millions)						
"Treatment" in 2017 only (vs. "prevention only")	59	54	44	32	-39	-98
"Screen"/"Elim." in 2017 only (vs. "prevention only")	163	155	141	123	14	-87
"Screen"/"Elim." in 2017 only (vs. "treatment")	104	97	89	81	46	23
Direct Costs of Treatment in 2017 (US$ millions)						
"Treatment" in 2017 only (vs. "prevention only")	59					
"Screen"/"Elim." in 2017 only (vs. "prevention only")	163					
"Screen"/"Elim." in 2017 only (vs. "treatment")	104					
Subsequent Savings in Costs of Care (US$ millions)						
"Treatment" in 2017 only (vs. "prevention only")		6	15	27	98	157
"Screen"/"Elim." in 2017 only (vs. "prevention only")		8	22	40	149	250
"Screen"/"Elim." in 2017 only (vs. "treatment")		7	15	23	58	81
Infections Averted (Units)						
"Treatment" (vs. "prevention only")	4,982	12,729	19,591	25,649	58,000	61,481
"Screen"/"Elim." (vs. "prevention only")	10,378	26,754	41,396	54,447	126,999	135,185
"Screen"/"Elim." (vs. "treatment")	5,396	13,695	20,721	26,665	54,519	57,151
HepC-Related Deaths Averted (Units)						
"Treatment" (vs. "prevention only")	1,226	3,174	5,570	8,235	22,072	32,945
"Screen"/"Elim." (vs. "prevention only")	1,798	4,658	8,192	12,148	33,412	51,597
"Screen"/"Elim." (vs. "treatment")	572	1,399	2,327	3,273	7,257	9,758
Net Costs per Infection Averted						
"Treatment" (vs. "prevention only")	11,873	4,204	2,250	1,253	-670	-1,600
"Screen"/"Elim." (vs. "prevention only")	15,720	5,788	3,405	2,263	110	-641
"Screen"/"Elim." (vs. "treatment")	19,271	7,081	4,302	3,042	850	406
Net Costs per Death Averted						
"Treatment" (vs. "prevention only")	48,261	16,860	7,913	3,902	-1,760	-2,985
"Screen"/"Elim." (vs. "prevention only")	90,734	33,241	17,206	10,143	416	-1,679
"Screen"/"Elim." (vs. "treatment")	181,709	69,329	38,314	24,780	6,386	2,376

Note: Table shows difference between scenarios in the accumulated costs and health impacts, from 2017 until year indicated, applying a discount rate of 5 percent. Unlike in other tables and figure, conflates the results for "screening" and "elimination" (as "Screen"/"Elim."), because the scenarios coincide for 2017.

According to the results summarized in Table 5, the policies under the demand-driven treatment scenario and involving screening across the population, occurring in 2017, are cost-saving interventions overall. These results are largely driven by the cost-effectiveness of treatment. An initial investment of US$ 59 million returns net savings of US$ 98 million by 2030 (evaluated at a discount rate of 5 percent). The costs of demand-driven treatment are refinanced within 6 years, and carry a financial rate of return of 24 percent,[25] even without making any allowance for the 61,500 infections and 32,900 deaths averted by 2030 as consequence of demand-driven treatment initiated in 2017.

The earlier finding that "screening" is less cost-effective than "treatment" carries through with regard to policies pursued in 2017. A policy in 2017 whereby demand-driven treatment is complemented by population testing and (for those found chronically infected) progression to treatment, as envisaged in the "screening" or "elimination" scenario, is cost-saving overall, but less so than "treatment" alone, representing a combination of cost-saving demand-driven treatment and less cost-effective screening policy. If the screening (or elimination) policy is compared with demand-driven treatment only, most of the initial investments of US$ 104 million in 2017 are offset by financial savings through 2030 (US$ 81 million, resulting in a net cost of US$ 23 million). Consequently, "screening" as of 2017 also represents very good value for money. Considering that a death from Hepatitis C costs about 20 life years, a cost per death averted of US$ 2,400 implies a cost per life year gained of only US$ 120, equivalent to about 4 percent of GDP per capita.

In summary, the results underscore the high effectiveness and cost-effectiveness of both demand-driven treatment and Hepatitis C control strategies relying on broad-based screening, which have the potential to radically change the course and impacts of the epidemic in the coming years. Thank to the effectiveness and low cost of the antiviral drugs available now, treatment per se is cost-saving and refinanced by the resulting savings in just 6 years. The effectiveness of Hepatitis C control policies would be augmented by population-based screening, contributing to a much faster progress towards eliminating the epidemic. While such broad-based screening policies are less cost-effective than demand-driven

(25) The rate of return has been calculated as the interest rate at which the discounted financial savings from 2018 just offset the initial investments in 2017.

treatment alone, they represents very good (health) value for money (at about 4 percent of GDP per capita per life year gained).

Consequences of New Infections

Complementing the findings on the consequences of alternative policies, an analysis of the consequences of new infections under the various scenarios yields some useful additional insights, e.g., about the dynamics of the epidemic and the outlook for eliminating it, the continuing health risks associated with Hepatitis C, and the returns to ongoing efforts at prevention of new infections. For this reason, Table 6 summarizes the consequences of 100 new infections with Hepatitis C, spread proportionally across the adult population (ages 20-70).

Table 6. Consequences of New Hepatitis C Infections Occurring in 2016, by Scenario

	2022	2030	2050
	(per 100 infections, ages 20-70 2/)		
Costs (US$) 1/			
"Prevention only"	177	1,362	18,666
"Treatment"	1,817	4,724	13,763
"Screening"	6,482	9,950	13,223
"Elimination"	11,916	12,121	13,136
New Infections (in addition to the 100 initial ones)			
"Prevention only"	13	31	86
"Treatment"	12	27	55
"Screening"	10	16	22
"Elimination"	7	8	11
Deaths owing to Hepatitis C			
"Prevention only"	0.0	0.4	10.8
"Treatment"	0.0	0.2	3.2
"Screening"	0.0	0.1	1.1
"Elimination"	0.0	0.1	0.6

1/ Discounted at a rate of 5 percent.

2/ Population-weighted average of consequences of 100 infections across ages 20-70.

In the "prevention only" and demand-driven "treatment" scenarios, there is substantial onward transmission of Hepatitis C. By 2030, each infection in 2016 causes an additional 0.3 infections in both scenarios. However, as people chronically infected increasingly seek treatment (as the disease progresses), the number of infections is considerably reduced by demand-driven treatment in the longer term, e.g., by about one-third by 2050. Screening is effective in disrupting transmission dynamics, reducing the number of downstream infections by 40 percent by 2030 (and 60 percent by 2050), relative to demand-driven "treatment". This happens because "screening" identifies many chronically infected people at early stages of the disease, not long after they become infected, reducing the time span during which they may pass on Hepatitis C.

The differences across scenarios in the costs caused by new infections are more complex. In the "screening" and especially the "elimination" scenario more people attain treatment, and they tend to do so earlier. For this reason, the costs caused by each new infection are initially much higher under "elimination" (US$ 119 until 2022) than under "screening" (US$ 65) and demand-driven "treatment (US$ 18). In the longer run, the costs caused by Hepatitis C infections are dominated by progression to the terminal stages of the disease and the resulting costs of care (documented in Table 3). Therefore, the costs caused by new infections increase faster in the scenarios in which progression to treatment is lowest.

There are at least two lessons complementing the preceding discussion of policy scenarios which can be drawn from these results on the consequences of new Hepatitis C infections under alternative policies. First, regarding new Hepatitis C infections, "treatment," "screening," and "elimination" are refinanced more slowly than is the case for the total costs and consequences of alternative policies. This is the case because the returns to scaling up treatment and screening across the population initially reflect that there is a relatively large number of people infected at more advanced stages of disease progression – for this population, the impacts on progression to terminal stages and corresponding costs occur more quickly than for an individual newly infected. However, even for newly infected individuals, the treatment and screening policies considered here are ultimately cost-saving, although on a longer time horizon. Second, both "treatment" and "screening" policies are effective in altering the dynamics of the epidemic and setting it on a path towards elimination, as evident from the large reductions in

the number of downstream infections caused by each additional infection.

Returns to Investments Targeting Specific Age Groups

To optimize efforts to improve uptake of treatment or screening, it is important to understand differences in prevalence, incidence and transmission patterns, and the state of the epidemic across the population. Relevant factors include regional aspects, exposure to medical procedures that carry the risk of transmission of Hepatitis C, and differences by sex and age.[26] The former two aspects are beyond the scope of this report, but the analytical framework is well suited to address differences by sex and age.

(26) See Mohamoud and others (2013) and Guerra and others (2012) on populations at high risk, and Ministry of Health and Population, El-Zanaty and Associates, and Macro International (2015b), Cuadros and others (2014), and Guerra and others (2012) on regional variations in the prevalence of Hepatitis C.

Table 7. Returns to Treatment, by Age, 2017

	Costs					Infections	HepC-Related Deaths	Cost per Infection	Cost per Death
	Testing	Treatment	Total	Savings	Net Costs	Averted	Averted	Averted	Averted
Male, Age 20	8,300	9,800	18,100	6,928	11,172	21	0.1	543	87,172
Male, Age 30	8,300	9,800	18,100	19,938	-1,838	18	1.7	-104	-1,069
Male, Age 40	8,300	9,800	18,100	39,686	-21,586	15	4.2	-1,460	-5,171
Male, Age 50	8,300	9,800	18,100	39,056	-20,956	13	4.4	-1,669	-4,794
Male, Age 60	8,300	9,800	18,100	39,469	-21,369	11	5.7	-1,936	-3,743
Male, Age 70	8,300	9,800	18,100	43,863	-25,763	9	7.2	-2,892	-3,563
Male, Age 20-70	8,300	9,800	18,100	38,101	-20,001	12	5.0	-1,627	-3,968
Female, Age 20	8,300	9,800	18,100	7,211	10,889	21	0.2	518	67,730
Female, Age 30	8,300	9,800	18,100	16,303	1,797	19	1.2	97	1,534
Female, Age 40	8,300	9,800	18,100	38,117	-20,017	15	4.0	-1,303	-5,003
Female, Age 50	8,300	9,800	18,100	37,903	-19,803	13	4.2	-1,477	-4,720
Female, Age 60	8,300	9,800	18,100	39,039	-20,939	12	5.5	-1,754	-3,818
Female, Age 70	8,300	9,800	18,100	45,122	-27,022	10	7.2	-2,746	-3,773
Female, Ages 20-70	8,300	9,800	18,100	30,062	-11,962	11	3.6	-1,049	-3,297
Average, ages 20-70	8,300	9,800	18,100	35,046	-16,946	12	4.5	-1,417	-3,763

Note: Table shows costs and consequences of placing an additional 100 individuals on treatment, evaluated around the "treatment" scenario. As in the scenario, it is assumed that 2 indivuals are tested for each person progressing to treatment. All totals are through 2030, and are discounted at a rate of 5 percent.

Tables 7 and 8 summarize our findings, showing the consequences of an increase in the uptake of demand-treatment by 100 patients, and of screening 100 additional individuals (who then progress to further testing if positive for antibodies, and to treatment if chronically infected). These changes are evaluated around the “treatment” scenario.

The issue of the effectiveness of interventions regarding Hepatitis C across age groups is complex. The prevalence of chronic infections increases steeply with age, which makes screening less effective at younger ages, and chronically infected older adults tend to be at a more advanced stage of disease progression, so that treating older adults yields more imminent health benefits such as deaths averted. On the other hand, chronically infected younger people may pass on

Hepatitis C for a longer period of time, so treating younger people would yield higher benefits in terms of infections averted.

The results on treatment (Table 7) confirm the relevance of these points.

For 100 additional individuals initiating demand-driven treatment, 12 new infections are averted on average (ages 20-70) by 2030,[27] but this number ranges from 9 (treatment of men at age 70) to 21 (treatment of men or women at age 20). At the same time, the number of deaths averted ranges from close to zero (treatment at age 20) to 7 (treatment at age 70), with an average of 4.5. Likewise, the financial savings resulting from accommodating 100 additional patients with treatment increase steeply with patients' age, from about US$ 6,900 (men at age 20) or US$ 7,200 (women at age 20) to US$ 43,900 (men) or US$ 45,100 (women) at age 70.[28] As a consequence, the cost-effectiveness of treatment, taking into account these financial savings, improves at higher ages with regard to both infections averted and death averted. This finding on infections averted is interesting because the results on effectiveness (stronger at younger ages) run against the findings on cost-effectiveness. The reason is that averting infections at young ages results in financial savings (and additional health benefits) only with a very long lag, and therefore matter little for the financial analysis, unlike deaths averted which are the dominant factor behind cost savings.

(27) The results on population averages shown in Tables 7 and 8 relate to the age groups covered in this table (ages 20 to 70). Corresponding results reported in Table 5 are slightly different because they relate to the population at ages 15+.

(28) For the older ages, this is consistent with our estimate of the average costs preceding each death owing to Hepatitis C of about US$ 5,000. For younger ages, the costs caused by new infections also play some role.

Table 8. Returns to Screening, by Age, 2017

	Costs					Infections Averted	HepC-Related Deaths Averted	Cost per Infection Averted	Cost per Death Averted
	Screening	Treatment	Total	Savings	Net Costs				
Male, Age 20	919	120	1,039	69	969	0.3	0.0	3,699	1,113,152
Male, Age 30	1,353	558	1,910	544	1,367	1.2	0.0	1,177	45,968
Male, Age 40	1,482	643	2,126	1,407	718	1.2	0.1	610	5,957
Male, Age 50	2,095	1,134	3,228	2,980	248	1.8	0.3	142	849
Male, Age 60	3,784	2,449	6,233	8,013	-1,779	3.2	1.1	-560	-1,659
Male, Age 70	4,102	2,523	6,625	10,124	-3,499	2.5	1.6	-1,402	-2,205
Male, Age 20-70	1,813	897	2,710	2,282	428	1.4	0.3	302	1,616
Female, Age 20	921	128	1,049	75	974	0.3	0.0	3,399	1,117,846
Female, Age 30	1,057	240	1,297	202	1,095	0.5	0.0	2,109	128,298
Female, Age 40	1,292	488	1,779	992	787	0.9	0.1	845	9,406
Female, Age 50	1,816	872	2,688	2,170	518	1.4	0.2	359	2,498
Female, Age 60	2,757	1,441	4,198	4,526	-328	2.0	0.6	-161	-564
Female, Age 70	2,711	1,223	3,933	4,923	-990	1.4	0.7	-732	-1,337
Female, Age 20-70	1,472	556	2,028	1,119	909	0.9	0.1	1,063	7,892
Average, ages 20-70	1,643	727	2,371	1,704	667	1.1	0.2	586	3,505

Note: Table shows costs and consequences of screening 100 individuals, and placing them on treatment if they are chronically infected with Hepatitis C, taking the "treatment" scenario as a point of departure. All totals are through 2030, and are discounted at a rate of 5 percent.

The results on screening (Table 8) are more complex because effectiveness and cost-effectiveness depend on the prevalence of chronic infections, which ranges from less than 2 percent at age 20 to well over 20 percent at age 60 (Figure 1). As a consequence, the effectiveness of screening, with regard to both infections and deaths averted, generally increases with age (except for a decline in infections averted between ages 60 and 70). Cost-effectiveness of screening also improves steadily with age, and, at least for individuals at ages 40 and above, screening is a very effective health intervention by conventional norms. E.g., a cost per death averted of around US$ 6,000 or US$ 9,400 (for screening of men and women at age 40) corresponds to a cost of about US$ 300 to US$ 470, around 10 percent to 16 percent of GDP per capita, per life year gained.

Macroeconomic Returns to Investments in Hepatitis C Control

With regard to the macroeconomic returns to investments in the Hepatitis C response, it is useful to recall the earlier argument on the macroeconomic costs of Hepatitis C. (1) With respect to GDP per capita, the negative impacts on productivity and investment are roughly offset by a decline in the dependency ratio, so that the impact on GDP per capita is very small. (2) The costs of treatment and care were found to absorb 0.07 percent of GDP or GDP per capita. (3) Premature mortality reduces living standards by an equivalent of 1.5 percent of GDP per capita. The investments in control of the epidemic will reverse these effects to a large extent, but – because the various effects play out at different speeds – the short-to-medium effects and the long-term effects differ.

Productivity effects result immediately from reduced prevalence of chronic Hepatitis C infections and improved state of health (fewer people at advanced states of the disease) among the population chronically infected. Using the same assumptions as earlier (a productivity loss of one percent across people chronically infected, and 10 percent among people at advanced stages of disease), the productivity loss of 0.14 percent of GDP or GDP per capita is reduced to 0.025 percent by 2030 in the "treatment" scenario (as the prevalence of chronic infections declines from 7 percent in 2015 to 2 percent in 2030, and the share of people at advanced stages of disease declines from 10 percent in 2015 to 2.5 percent), and to 0.01 percent in the "screening" scenario.

By 2030, the dependency ratio will be between 0.16 percent ("treatment") and 0.23 percent higher (under the "elimination" scenario) than without the expansion of treatment – because treatment focuses on the population at advanced stages of disease, and these tend to be at relatively old age, expansion of treatment has a relatively fast effect on old-age dependency ratios. In the longer run (beyond 2030), this effect loses its force, because of increasing age-related mortality among people who benefit from treatment, and because the initial effect is relatively large as treatment resolves a backlog of unmet need with immediate effects on survival.

The costs of the response to Hepatitis C affect GDP in two ways. First, to the extent that spending on Hepatitis C crowds out investment rather than consumption, the accumulation of capital is affected; lower investment reduces GDP in subsequent years. Our calculations suggest that this factor plays a

miniscule role by 2030.[29] Second, the costs of alternative policies represent an economic loss (in the sense of absorbing resources that could be used otherwise), while any savings arising from such policies represent an economic gain. Because they halt progression to the terminal stages of Hepatitis C, all policies expanding access to treatment result in financial savings by 2030, of between US$ 80 million ("screening") and US$ 120 million ("elimination"), equivalent to between 0.016 percent of GDP and 0.024 percent of GDP in that year.

These economic effects go alongside the health consequences of the alternative scenarios in terms of chronic infections and aggregate health outcomes. Earlier findings showed that Hepatitis C reduced life expectancy by about one year as of 2015, resulting in a loss in living standards equivalent to about 1.5 percent of GDP. By 2030, this loss will be reduced to between 0.45 years ("treatment") and 0.3 years ("elimination"). Compared to the "prevention only" scenario (in which the loss in life expectancy is estimated at 0.9 years as of 2030), this gain in life expectancy is equivalent to a gain of between 0.6 percent of GDP and 0.8 percent of GDP in terms of contribution to living standards (applying the same methods described earlier). This gain, equivalent to about one percent of GDP, almost entirely reflects the impacts of treatment on mortality. In the long run, the losses will be diminished further, as reduced incidence (through prevention or reduced transmission owing to treatment) will eventually result in further reductions in mortality owing to Hepatitis C. This process, however, plays out over decades and plays virtually no role until 2030.

In summary, the analysis of the costs and consequences of investments in expanding testing and access to treatment across Egypt shows that the policies considered here yield considerable health benefits, for the chronically infected population and in terms of aggregate health outcomes. The various policies are either cost-saving ("treatment," "screening") or achieve their outcomes at very low cost (about 4 percent of GDP per capita per life year gained) from a fiscal perspective, even applying a fairly short time horizon through 2030. From a macroeconomic perspective, the various policies result in a very small net cost in

(29) This is the case because later savings (positive impact on investment and eventually GDP) are to some extent offset by the higher costs of more expansive policy scenarios. For the "treatment" scenario in which net savings are highest, our calculations suggest a gain in GDP owing to higher investment in the preceding years of only US$ 3 million in 2030, for the "screening" and "elimination" scenarios they come out at zero and US$ 1 million, respectively.

terms of GDP per capita. This cost is a consequence of an increase in dependency rates by between 0.16 percent ("treatment") and 0.23 percent ("elimination") – increasing survival into retirement age means that GDP is distributed across a larger population. Improved productivity (between 0.12 and 0.14 percent) and the savings resulting from the various policies (about 0.02 percent of GDP) nearly offset this cost, so that the net macroeconomic cost of between 0.02 percent of GDP per capita ("treatment") and 0.05 percent of GDP per capita ("elimination") is negligible. To place this number into perspective, the IMF (2017) projects that GDP per capita will increase by an average 3.1 percent each year between 2017 and 2022.

Conclusions

Hepatitis C remains a serious health challenge in Egypt. However, modern antiviral drugs have transformed the treatment response to the epidemic, providing a highly effective and cost-effective tool for treating chronic Hepatitis C infection and halting disease progression. They also complement other efforts to control Hepatitis C transmission, such as infection control and prevention. This report provides an appraisal of the health and economic consequences of Hepatitis C, and assesses the effectiveness and cost-effectiveness of policies to control and end the epidemic. We find that:

- As of 2015, Hepatitis C accounted for 7.6 percent of all deaths, and a much higher rate for adults over age 50. The epidemic caused a loss in life expectancy of 1.8 years for men, and 1.0 years for women.

- The impacts of Hepatitis C on GDP per capita are very small, but the epidemic has reduced GDP by 0.3 percent as of 2015. Additionally, increased mortality owing to Hepatitis C reduces living standards by an equivalent of 1.5 percent of GDP and GDP per capita.

- Current demand-driven treatment policies have the potential to reduce mortality owing to Hepatitis C and the number of new infections by about one-half by 2030. Screening – ongoing or as part of a comprehensive elimination strategy – has the potential to substantially augment these effects, averting up to two-thirds of deaths and reducing the number of new infections by around 90 percent in a comprehensive elimination scenario.

- The steep declines in the costs of antiviral drugs have transformed treatment of chronic Hepatitis C infections in a highly cost-effective intervention. Current spending on demand-driven treatment is refinanced by savings in costs of within 6 years, and carries a financial rate of return of 24 percent, even before taking into account the values of any health gains.

▪ Eliminating Hepatitis C will require screening policies. Such policies, in the form of either an ambitious "elimination" scenario aiming to screen the entire adult population within 5 years or a more gradual screening policy, are generally not cost-saving, except when the policy is restricted to older adults (from the mid-40s). However, they are cost-effective by conventional norms, with a cost per life year gained of less than 10 percent of GDP per capita. The ambitious "elimination" scenario comes out as more effective and cost-effective compared to a more gradual screening policy.

▪ Cost-effectiveness of treatment and screening differs by age group targeted. On average, treatment at older ages is relatively more effective in terms of reducing mortality but less effective in terms of reducing the number of new infections. The cost-effectiveness of screening is low among young adults and improves with the age of the population targeted.

▪ From a macroeconomic perspective, treatment and screening policies achieve considerable health gains largely cost-free. Improved survival in old age results in an increase in the dependency rate and represents a drain on GDP per capita. Across the policy scenarios, this factor is offset by productivity gains from improved state of health and the financial savings owing to reduced costs of care. Additionally, reduced mortality results in a gain in living standards equivalent to 0.6 percent of GDP to 0.8 percent of GDP.

Appendix

Macroeconomic model

The analysis applies a version of the neoclassical growth model, described in more detail, e.g., by Romer (2011). The purpose of the analysis is to estimate the broad magnitude of the effects of Hepatitis C on GDP per capita. For this purpose, it is appropriate and sufficient to focus on the steady-state growth path of the economy, which evolves around

$$y^* = \frac{A}{1+d}\left[\frac{s}{n+g+\delta}\right]^{\frac{\alpha}{1-\alpha}}$$

,

where y^* represents GDP per capita, A represents the productivity of labor, d is the dependency ratio (the ratio of economically inactive young or old people to the working-age population), s the savings rate, n the rate of population growth, g the rate of technological progress (the rate at which A grows), d the rate of depreciation of capital, and a is a parameter describing the shape of the production function. The most plausible and tractable effects on Hepatitis C on GDP per capita discussed in this report are productivity losses (a drop in A), an change in the dependency ratio d, and changes in saving (and investment), i.e., a decline in s.

Apart from the parameters discussed in the report, it is assumed that the underlying savings rate is 15 percent, and the parameter a is equal to one-third. For the purposes of this analysis, it is not necessary to set values for the parameters n, g, and d.

Epidemiological model and demographic framework

The model used in the analysis of the effective ness and cost-effectiveness of Egypt's response to Hepatitis C is an epidemiological model of disease progression and the impacts of treatment embedded in a demographic framework.

For demographic data, we draw on the World Population Prospects (WPP) 2015 database (UNPD, 2016). Specifically, we use estimates and projections of the population size, by age, to calculate prevalence of Hepatitis C. Second, in our projections, we draw on WPP 2015 for mortality for causes other than Hepatitis C. WPP 2015, however, does not distinguish causes of mortality. To obtain an estimate of mortality for other causes for 2015 consistent with the WPP 2015 data, we apply the age-specific shares of mortality for other causes from the Global Burden of Disease 2015 database (IHME, 2016), which does not offer projections, to the WPP 2015 estimates. In our projections, mortality for causes other than Hepatitis C, by sex and age, is then assumed to change in proportion to the WPP 2015 projections on total mortality.

The population, by sex and age (in one-year increments from 0 to 99), is divided into the population who have never been infected with Hepatitis C, people carrying Hepatitis C antibodies following spontaneous clearance, people chronically infected, people who have been successfully treated, and people who have been unsuccessfully treated. The latter three categories are divided in eight states of disease progression. Disease progression (i.e., liver damage) are classified by METAVIR stage F0, F1, F2, and F3, followed by compensated cirrhosis, which might lead to decompensated cirrhosis or liver cancer (directly or following decompensated cirrhosis). Patients with decompensated cirrhosis may progress to liver transplant.

At the outset (2015), sex- and age-specific prevalence rates were taken from the 2015 DHS. The estimates on the state of disease by age group are based on two sources. Shelbaya and others (2015) were used for disease states F0 to F3 (which also implies a total for the more advanced stages of disease). The prevalence of decompensated cirrhosis and liver cancer were derived from mortality estimates from the GBD database (using our mortality estimates for the relevant population to calculate the prevalence of the respective health states consistent with the GBD 2015 mortality estimates). The resulting prevalence rates by age group (10-year-increments) were then used to create estimates by one-year increment, applying a Hodrick-Prescott filter.

The state of the epidemic evolves according to aging (in one-year increments), disease progression, mortality, treatment, and new infections.

Age-varying annual disease progression estimates were taken from Razavi and others (2014), also applying a Hodrick-Prescott filter to transform estimates by 5-year cohorts into data for one-year cohorts. After a first round of projections, it was found that these disease progression estimates were inconsistent with the estimates of mortality from liver cancer from GBD 2015. For this reason, progression to hepatic cancer was reduced by 60 percent relative to the estimates used by Razavi and others (2014), which results in a stable estimate of mortality from liver cancer close to the GBD 2015 estimates.

Treatment is assumed to be successful (achieving sustained virologic response) in 95 percent of cases (current estimates from Egypt range from 95 percent to 98 percent, see Esmat (2016)). Successful treatment is assumed to halt disease progression at stages F0 to F3, and reduce it by 70 percent at more advanced stages. This effect of treatment is at the lower end of current estimates of the effectiveness of treatment, to err on the side of caution in light of a weak evidence base so far. For similar reasons, we do not account for reversal of liver damage following treatment. Mortality owing to Hepatitis C is set at 25 percent for decompensated cirrhosis, and 70 percent for liver cancer, about consistent with GBD 2015 estimates.

The module on disease transmission assumes that each individual chronically infected passes on Hepatitis C at a rate *x*. Incidence is then calculated as x_z*p*(1-p_z), where *p* stands for prevalence, and (1-p) represents the population share not chronically infected, and *z* is an index for male adults, female adults, male children, and female children. For our purposes (initial level of *p* of about 6 percent, and declining), this implies that incidence is broadly proportional to prevalence (in line with Breban and others, 2013). The transmission parameters for children were then set to yield a prevalence rate of 0.5 percent by age 15 (in line with the 2015 DHS estimates), and transmission parameters for adults were set to yield 165,000 infections in 2015 (in line with recent authoritative estimates from Egypt, see Breban and others (2013), El-Akel and others (2017), Esmat (2015)) corresponding to a national incidence rate of 0.18 percent as of 2015 (0.21 for males, and 0.15 for females).

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