A model of the economic benefits of global hepatitis C elimination: an investment case

Nick Scott, Christian Kuschel, Alisa Pedrana, Sophia Schroeder, Jessica Howell, Alexander Thompson, David P Wilson, Margaret Hellard**

Major gains in reducing the burden of hepatitis C are now possible because of the discovery of a cure. The prevention of premature deaths and increased workforce participation among people who are cured are likely to provide substantial indirect economic benefits. We developed an investment case for hepatitis C for the six WHO world regions, which, to our knowledge, is the first to consider both indirect and direct economic benefits in this context. Scaling up of testing and treatment to reach the 2030 WHO hepatitis C elimination targets was estimated to prevent 2·1 million (95% credible interval 1·3–3·2 million) hepatitis C-related deaths and 10 million (4–14 million) new hepatitis C virus infections globally between 2018 and 2030. This elimination strategy was estimated to cost US$41·5 billion (33·1–48·7 billion) in testing, treatment, and health care between 2018 and 2030 ($23·4 billion more than the status quo scenario of no testing or treatment scale up), with a global average of $885 (654–1189) per disability-adjusted life-year averted at 2030. Compared with the status quo scenario, the elimination scenario generated $46·1 billion (35·9–53·8 billion) in cumulative productivity gains by 2030. These indirect costs made elimination cost-saving by 2027, with a net economic benefit of $22·7 billion (17·1–27·9 billion) by 2030. This model shows that countries might be underestimating the true burden of hepatitis C and will benefit from investing in elimination.

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Introduction

Hepatitis C is a blood-borne infection transmitted through injection drug use, unsafe medical procedures, and other community exposures.[1] Globally, more than 70 million people are infected with hepatitis C virus (HCV)[2] and nearly 400 000 people die annually because of hepatitis C-related cirrhosis, liver failure, or liver cancer.[1] Individuals infected with HCV experience a reduction in quality of life[3,4] and might require health-care services to manage their disease. Most of these health-care needs typically occur 10–20 years after initial infection with the onset of cirrhosis and liver cancer, which can result in large costs to a country's health system.[5] Newly available, direct-acting antiviral treatments that can cure hepatitis C can successfully prevent the adverse outcomes of liver failure and liver cancer[6–8] and improve quality of life in patients.[3,4] Scaling up of testing and treatment could therefore avert longer-term direct costs, but this approach requires short-term investment.

Many low-income and middle-income countries do not spend money on viral hepatitis prevention or care, meaning that any upscaling of programmes as part of an elimination strategy will be new costs with little immediate, direct economic benefit. However, countries underestimate how much money they might already be losing on chronic HCV infection, since it decreases workforce participation and creates economic productivity losses.[9–12] As well as preventing longer-term direct health-care costs, scaled-up testing and treatment can produce indirect economic benefits because of increased workforce participation, both among people who are cured and from the prevention of premature deaths, and by improving the health security of the individual, their family, and their country.

Mathematical models can quantify the economic benefits of hepatitis C programmes, compared with the status quo of continuing to passively manage disease and to test and treat people without any scale-up. Many studies have evaluated the cost-effectiveness or cost of scaling up hepatitis C treatment,[13–15] but these studies have only considered direct health costs. As data emerge about the productivity losses associated with HCV infection and the improvements in productivity after cure,[9–12] quantifying the economic productivity losses attributable to hepatitis C becomes possible,[16,17] and hence so does quantifying the indirect economic benefits of investment in testing and treatment.

Before the discovery of direct-acting antiviral treatments, there was minimal investment in hepatitis C. As a consequence, globally, 80% of people with hepatitis C are undiagnosed, and hepatitis C-related deaths have been increasing steadily.[2] With deaths from viral hepatitis (B and C combined) now outnumbering those associated with HIV, tuberculosis, or malaria,[18] there is global recognition of viral hepatitis as a considerable global public health threat. Advancements in diagnostics and the discovery of a cure for HCV infection mean that major gains are now possible over short time periods, provided investment can be catalysed. Investment cases are needed to inform governments and funding agencies on the cost, cost-effectiveness, and economic benefits of the commitment to eliminate hepatitis C;[19] however, investment cases for this disease can substantially underestimate the benefits by failing to account for productivity gains from an increased workforce.

In this study, we used mathematical and economic modelling to estimate the impact, cost, cost-effectiveness, and economic benefits of two investment strategies for hepatitis C: first, an elimination strategy scaling up HCV testing and treatment to reach WHO targets of diagnosing 90% of people living with hepatitis C and 80% of people diagnosed started on treatment by 2030;[20] and second, a progress strategy scaling up hepatitis C testing and treatment to have 45% of people living with

hepatitis C diagnosed and 80% of diagnosed individuals started on treatment by 2030. The progress scenario definition was based on WHO recommendations that HCV testing of the general population only occurs in settings with 2% or more hepatitis C prevalence,[15,21] and that globally, countries with 2% or higher prevalence were estimated to contain approximately 45% of people living with hepatitis C. We assessed both of these strategies for each of the six WHO world regions, accounting for direct and indirect costs.

Model design

A mathematical model of hepatitis C transmission, disease progression, and treatment was calibrated to the HCV epidemic in each WHO region on the basis of previous modelling work (appendix pp 1–3).[22–24]

See Online for appendix

The number of people in each population group (people who inject drugs, people who formerly injected drugs, and other) was tracked according to infection status (susceptible, acutely infected, and chronically infected) and stage of liver disease. Population data comes from the UN Population Division and the United Nations Office on Drugs and Crime World Drug Reports (2013–2017), with the proportion of people in each liver disease stage calibrated to fit mortality data from the Global Burden of Disease study (accessed from the Global Health Data Exchange; appendix p 6).[25–27] The model accounted for patients' progression through the hepatitis C care cascade (undiagnosed, diagnosed hepatitis C antibody positive, diagnosed hepatitis C RNA positive, on treatment, or cured) and engagement in care (engaged in care or lost to follow-up), with individuals only able to access testing and treatment or incur direct health-care costs if they were engaged in care.

For this analysis, transmission was only modelled for people who inject drugs, however in many low-income and middle-income countries general population transmission (ie, related to non-injection drug use) is occurring. At a regional level, not everyone is likely to be at risk of infection and there are probably additional, smaller subpopulations who are at risk (eg, men who have sex with men, specific villages, or geographical areas). Therefore, in place of directly modelling transmission among the general population, the population of people who inject drugs was interpreted more generally as a collective risk population for transmission in each region, and was adjusted to account for this difference in the calibration procedure (appendix pp 1–2). Model parameters and sources, which came from a variety of settings, are provided, along with a detailed model description in the appendix (appendix pp 1–11).

Testing efficiency

Data for the total number of antibody and PCR tests were unavailable, and so we could not directly estimate the efficiency of testing to diagnose people (test positivity rate). Therefore, the efficiency of hepatitis C antibody testing was assumed on the basis of the prevalence of infection in the populations being tested; for populations at risk of transmission, this efficiency was based on prevalence (ie, in a risk group with 50% prevalence, an average of two tests would be required to obtain one positive result), and for the general population, testing was assumed to be done twice as well as random selection (ie, if the prevalence in the general population was approximately 1%, 50 tests would be required to obtain one positive result). Based on an approximate 25% spontaneous clearance rate, it was assumed that three-quarters of hepatitis C RNA tests among people diagnosed as antibody positive resulted in one positive result.[28]

Status quo scenario

Baseline projections were done for all regions to estimate epidemiological outcomes (hepatitis C prevalence, incidence, mortality, and disability-adjusted life-years [DALYs]) and economic outcomes (costs associated with testing, treatment, disease management, and lost productivity) in a scenario where testing and treatment rates were maintained as per those recorded in 2016 (from the WHO Global Hepatitis Report[2]). In this scenario, the small number of treatments were allocated in the model to patients with advanced liver disease (from most to least severe).

Progress and elimination scenarios

Sequential model simulations were run, with the annual number of tests and treatments available in the model increased until they were sufficient to reach the 2030 progress targets (45% diagnosed and 80% of those diagnosed treated), or the 2030 elimination targets (90% diagnosed and 80% of those diagnosed treated). Scale-up of testing and treatment included prioritisation to key populations: when treatment numbers were less than the total number of people diagnosed, treatments were first allocated to people with stage F3 liver disease or worse (to prevent deaths), then to key transmission risk populations to prevent new infections (constrained so that individuals could be tested a maximum of once per year), and then to the rest of the general population with liver disease stages F0–F2.

The algorithm for scaling up treatment was implemented so that the target of 80% of diagnosed people commenced on treatment was achieved by 2022 (after 5 years), compared with the diagnosis target that was modelled to be achieved by 2030. This adjustment was done because many settings have already established that people can start direct-acting antiviral treatments rapidly after diagnosis.[29]

Direct costs

Direct costs included antibody and RNA testing and treatment (commodities and region-specific staffing costs; appendix pp 5–6) and disease management

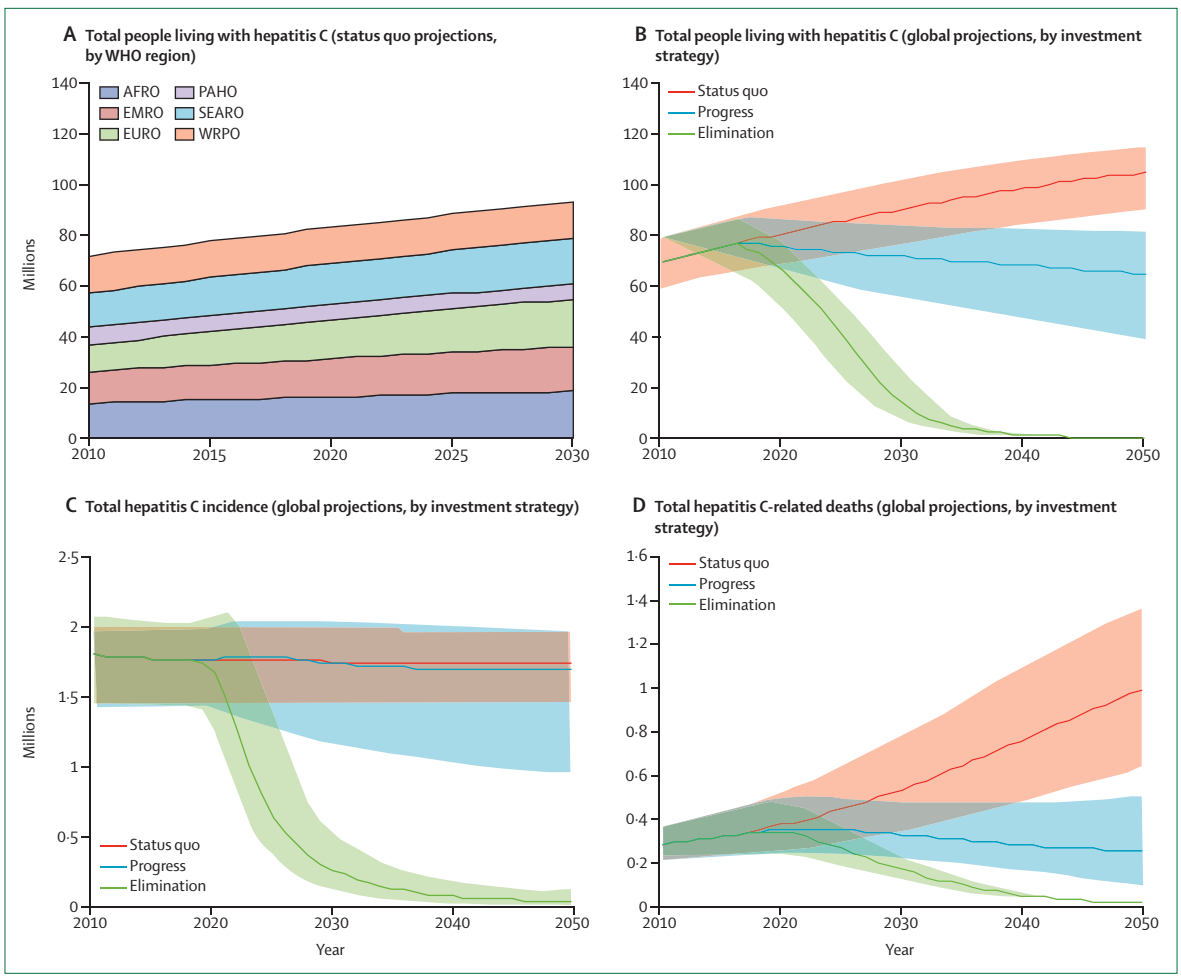

Figure 1: **Projected impact of the status quo, progress, and elimination scenarios on the projected number of people living with hepatitis C (A, B), hepatitis C incidence (C), and hepatitis C mortality (D)**

AFRO=African region. EMRO=Eastern Mediterranean region. EURO=European region. PAHO=region of the Americas. SEARO=South-East Asia region. WPRO=Western Pacific region.

(region-specific by disease stage; appendix p 6). Costs were discounted at a rate of 3% to more heavily weight shorter term costs as recommended by WHO (the same rationale for 3% discounting was applied for all outcomes).[30]

Commodity (ie, consumable) costs were based on generic WHO pricings of US$1·1 per antibody test, $20 per RNA test, and $105 per treatment course (appendix pp 5–6). Staffing costs were calculated by assuming that 2 h of provider time would be required for each interaction (testing and treatment), with per capita gross domestic product (GDP) used as a proxy for providers' wages (appendix pp 5–6). Our projections assume that half of the human resource requirements for testing and treatment activities could be absorbed by staff in the context of universal health care; however, separate scenarios were projected in the sensitivity analysis where 0% or 100% of staffing costs were included (appendix p 18).

Because of differing global access to care and engagement in care, the fraction of disease management costs that should be included for people in different stages of the care cascade is unclear (undiagnosed, diagnosed, or cured). Therefore three scenarios were run to generate an estimate, with upper and lower bounds: first, in which no disease management costs were considered (ie, applied to 0% of diagnosed people; testing and treatment costs only); second, in which disease management costs were applied to 25% of diagnosed people (and 25% of undiagnosed or cured people with decompensated cirrhosis or hepatocellular carcinoma); and finally, in which disease management costs were applied to 50% of diagnosed people (and 50% of undiagnosed or cured people with decompensated cirrhosis or hepatocellular carcinoma). Infrastructure costs were excluded because infrastructure was considered to become increasingly available with the Sustainable Development Goals universal health care coverage target of 3.8.

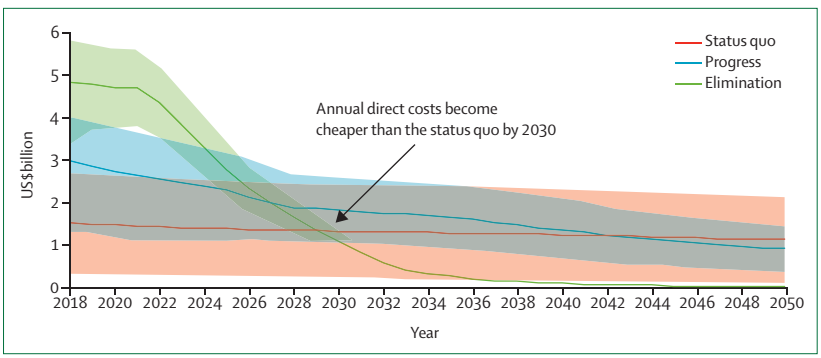

Figure 2: **Estimated annual direct costs of the status quo, elimination, and progress scenarios at the global level**
Lines show estimates assuming 25% of people with hepatitis C incur disease management costs (ie, the costs of managing hepatitis C-related illness, separate to testing and treatment costs), whereas the upper bounds assume 50% and the lower bounds 0% (ie, testing and treatment costs only). All costs include discounting at 3% per annum. Disease management costs were taken from the Hep C calculator tool,[5] with country-specific estimates used to generate population-weighted averages for each WHO region.

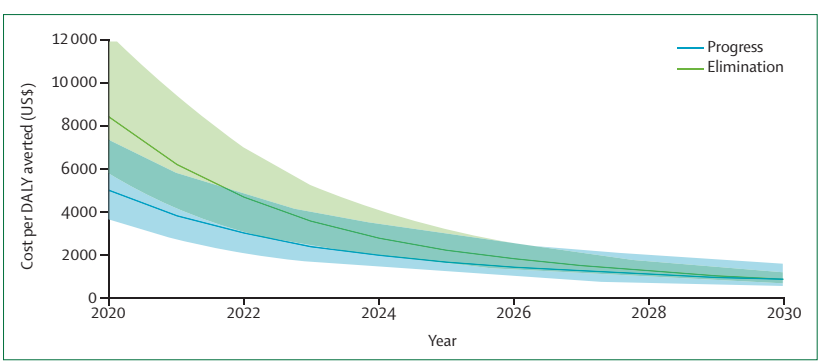

Figure 3: **Cost-effectiveness (cost per disability-adjusted life-year [DALY] averted) of the progress and elimination investment scenarios compared with the status quo**
The shaded region shows the point estimate and 95% CrI. Data are aggregated over the six WHO world regions. Costs include testing, treatment, and disease management, and exclude indirect economic benefits. Cost and DALYs were discounted at 3% per annum. DALY=disability-adjusted life-year.

Cost-effectiveness of the progress and elimination scenarios

Disability weightings for each disease stage were taken from the Global Burden of Disease study[31] and were added to the estimated years of life lost due to hepatitis C-related mortality to generate DALY outcomes for each scenario. The incremental cost-effectiveness ratio (difference in direct costs divided by difference in DALYs) was calculated for the progress and elimination scenarios compared with the status quo. DALYs were discounted at a rate of 3%.

Productivity losses from absenteeism and presenteeism

For each WHO region and scenario, an independent mathematical model was used to calculate hepatitis C-attributable productivity losses due to absenteeism (resulting from a reduced workforce or from individuals working reduced hours), and presenteeism (in which individuals are less productive at work because of their illness; appendix p 4). The model accounted for differential employment opportunities among people who inject drugs, as well as differential productivity and treatment uptake by cirrhosis status. The human capital approach[32] was used to estimate the number of years of potential productive life lost among people with hepatitis C before and after cure, which were converted to economic outcomes with population-weighted average per capita GDP. Parameters and sources for productivity losses are provided (appendix p 7).

Productivity losses from premature deaths

For each WHO region and scenario, total hepatitis C-related deaths in a given year were taken from the epidemic model projections. Because a disproportionate number of these deaths occur among older age groups (appendix p 8 shows the estimated 2016 age distribution of deaths related to hepatitis C for each region[33]), only a fraction were assumed to result in years of productive life lost. For each year in the projection timeframe (2018–50), the productive life lost from premature deaths in that year was calculated based on age-specific assumptions (appendix p 4).

Years of productive life lost due to premature death were converted to economic outcomes with population-weighted average per capita GDP for each region. Future economic gains were discounted at 3%.

Calculating the economic benefits over time

The net economic benefits of the progress and elimination scenarios over time were calculated as:

(cumulative testing, treatment, health care, and lost productivity costs in the status quo scenario) – (cumulative testing, treatment, health care, and lost productivity costs in the investment scenario [progress and elimination])

For the sensitivity analysis, we generated a net economic benefit curve for the elimination scenario under alternate plausible assumptions: 0% or 100% of staffing costs included, rather than 50%; test positivity among the general population equally as well as random selection, rather than twice as well as random selection; 0% or 50% of disease management costs included, rather than 25%; and drug costs of $1000 or $5000 in high-income countries, rather than prices of generic drugs.

Model results

Our model projected that, if hepatitis C testing and treatment were scaled up according to the elimination strategy, an 85% (95% credible interval [CrI] 70–92) reduction in annual hepatitis C incidence and a 47% (27–63) reduction in annual hepatitis C-related mortality could be achieved by 2030, relative to 2015 (the reference year for the WHO incidence and mortality reduction targets; figure 1). Compared with the status quo scenario, this strategy was estimated to prevent a cumulative 2·1 million (95% CrI 1·3–3·2 million) hepatitis C-related

deaths and 10 million (4–14 million) new HCV infections between 2018 and 2030, and to substantially reduce the overall number of people living with hepatitis C (figure 1).

In the progress scenario, minimal impact was made on incidence (figure 1). This result is because of the high prevalence of hepatitis C among risk populations, which meant that re-infection rates were high enough to negate the benefits of treatment as prevention among populations such as people who inject drugs.

The status quo, progress, and elimination scenarios resulted in 6%, 57%, and 70% of the global adult population being tested by 2030 (appendix p 12). The elimination scenario cost a cumulative $41·5 billion (95% CrI 33·1–48·7 billion) in testing, treatment, and health care globally between 2018 and 2030 ($23·4 billion more than the costs incurred by the status quo scenario). To control the epidemic, an initial investment scale-up was required at a peak of $4·8 billion (3·2–5·7 billion) globally in 2019 (figure 2), before the annual direct costs became less than in the status quo scenario by 2030 and reduced to $16·0 million by 2050.

By 2026, both the progress and elimination scenarios had incremental cost-effectiveness ratios of under $2000 per DALY averted, reducing to $842 (95% CrI 514–1613) per DALY averted in the progress scenario and $885 (654–1189) per DALY averted in the elimination scenario, by 2030 (figure 3). This outcome does not include indirect economic benefits.

As a result of the cumulative averted morbidity and mortality, the indirect economic benefits from scaling up hepatitis C programmes continued to grow over time, leading to a larger and more productive workforce (annual gains are shown in figure 4). Most of these benefits came from the European region because of the higher per capita GDP (appendix p 7). The elimination scenario produced a cumulative economic productivity gain of $46·1 billion (95% CrI 35·9–53·8 billion) between 2018 and 2030 (by reducing cumulative productivity losses from $273·8 billion [95% CrI 214·1–335·1] in the status quo to $227·7 billion [178·2–281·3; appendix pp 14–17]).

When the cumulative $46·1 billion in productivity gains from elimination were considered alongside the additional $23·4 billion in direct costs required (compared with the status quo scenario), investment in hepatitis C elimination was estimated to become cost saving by 2027 and lead to a net global economic benefit of $22·7 billion (95% CrI 17·1–27·9 billion) by 2030 (figure 5). The progress scenario was estimated to become cost saving earlier than the elimination scenario, but in the longer term the elimination scenario provided far greater economic benefits, since the ongoing transmission occurring in the progress scenario resulted in perpetual treatment costs.

Important differences were observed between regions. For example, elimination took the longest to become cost saving and produced the smallest economic benefit in the South-East Asia region because of a combination of low per capita GDP reducing productivity gains, below-average diagnosis rates meaning that more testing was required to reach the targets, and below-average disease management costs reducing the cost of the status quo (appendix pp 14–17). Conversely, net economic benefits were greatest in the region of the Americas because of high disease management costs and above average status quo diagnosis rates. Economic productivity gains from elimination were the highest in the European region, as a result of higher per capita GDP. These differences show the importance of more in-depth, setting-specific analyses to inform policy.

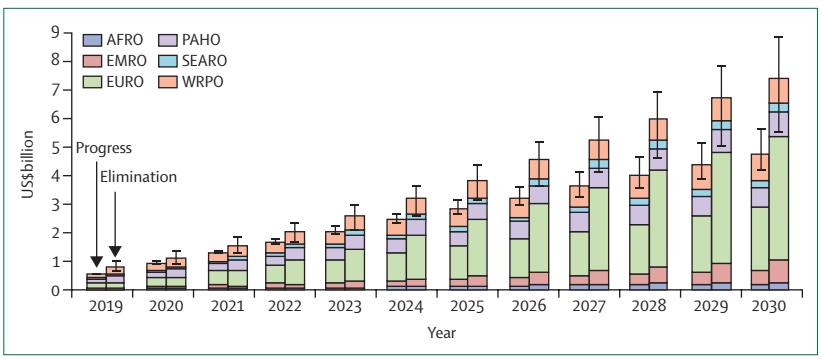

Figure 4: **Estimated annual economic productivity gains from the elimination and progress investment scenarios**

All costs include discounting at 3% per annum. AFRO=African region. EMRO=Eastern Mediterranean region. EURO=European region. PAHO=region of the Americas. SEARO=South-East Asia region. WPRO=Western Pacific region.

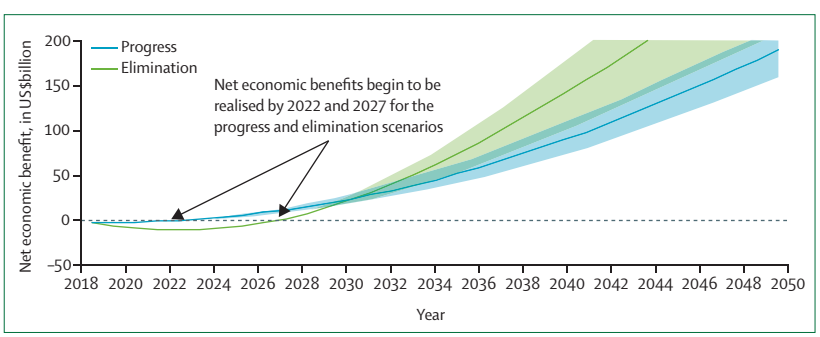

Figure 5: **Net economic benefit of the elimination and progress investment scenarios compared with the status quo**

The shaded region shows the point estimate and 95% CrI. Data are aggregated over the six WHO world regions. Calculated as (cumulative testing, treatment, health care, and lost productivity costs in the status quo) – (cumulative testing, treatment, health care, and lost productivity costs in the investment scenario [progress or elimination]). All costs include discounting at 3% per annum. Upfront investment is required, resulting in negative benefit (below $0).

Sensitivity analysis

Without staffing costs included, investment to eliminate hepatitis C became cost saving almost immediately (2019) compared with 2027 with 50% of staff costs or 2030 with 100% of staff costs included (appendix p 18). The proportion of disease management costs included in the model (ie, 0%, 25%, or 50%) had less of an impact on the year investment would become cost saving, largely

because these costs were incurred in both the status quo and elimination scenarios (eg, post cure). If test positivity rates among the general population were halved, the year that investment would become cost saving changed from 2027 to 2030. If human resource costs were not included, the cost of the elimination strategy was reduced by $8·4 billion. Procuring drugs at generic pricings was crucial to ensuring that investment became cost saving earlier, with elimination estimated to take until 2030 to become cost saving if drugs were $1000 or 2037 if drugs were $5000 in high-income countries. This finding highlights the importance of continued global efforts to universally reduce drug costs.

Discussion

This economic modelling provides evidence that a finite period of investment in hepatitis C could generate a net economic benefit of $22·7 billion globally by 2030 and lead to considerable reductions in transmission and mortality, with very little ongoing costs. Our models estimate that the annual direct costs of the elimination scenario could reach a maximum of $4·8 billion in 2019, before reducing to $16·0 million by 2050 and continuing to decline, and that the total cost of the elimination scenario between 2018 and 2030 is approximately $41·5 billion. This analysis is an advancement on other work[14,15] because it is, to our knowledge, the first investment case for hepatitis C elimination that considers the indirect economic benefits attributable to the prevention of premature deaths and increased workforce participation. We have shown that when these important factors are considered, global investment in hepatitis C could become cost saving by 2027.

The required investment for the global elimination scenario is small compared with the $343·2 billion that would be spent on HIV, tuberculosis, and malaria over the same time period (ie, 2018–2030), assuming the current investment levels in these diseases were maintained ($19 billion on HIV,[34] $6·9 billion on tuberculosis,[35] and $2·7 billion on malaria[36]), and particularly when considering that the current expenditure on HIV, tuberculosis, and malaria is unlikely to lead to an end to those epidemics by 2030.[37] Moreover, tools are available that can benchmark the effect of this investment against the effects of existing health interventions to assess whether this strategy represents better or worse value for money. The global impact of existing health expenditure is estimated to be approximately $2900 per DALY averted, meaning that investment in the progress and elimination scenarios would have a similar cost-effectiveness by 2022 and 2024, respectively (figure 3), and are more cost-effective if considered for longer time periods, allowing more benefits from averted disease to accrue.

Staffing costs associated with testing and treatment vary by region, but are estimated to be more than double the commodity costs required for diagnosis and treatment. Our projections assume that half of the testing and treatment appointments could be undertaken by existing staff in the context of universal health care; however, given the simplicity of hepatitis C testing and treatment, the availability of adequate human resources for all of these services is possible. If hepatitis C testing and treatment did not require specific workforce expansion, then this would reduce the projected costs of the elimination scenario by $8·4 billion. Any investment in staffing costs for hepatitis C elimination that cannot be absorbed among the existing health-care workforce will make a positive impact on the provision of health care for other diseases and contribute to broader universal health-care targets.[19]

This study identified a number of key parameters that have insufficient or no data available to inform them, and which should be prioritised to improve the validity of cost estimations. In particular, investment cases for hepatitis C could be greatly improved by filling data gaps on the effectiveness of testing programmes at identifying people living with hepatitis C (test positivity rate), the infrastructure and staffing costs associated with testing and treatment scale up, and the proportion of people diagnosed with HCV who are engaged in care. Our sensitivity analysis shows that when the models were run with alternate assumptions for these parameters, the year that hepatitis C elimination became cost saving ranged between 2019 and 2030, compared with 2027 when best estimate parameters were used. Therefore, ensuring that testing of the general population is as targeted as possible and using an existing health-care workforce as much as possible should be given consideration in the implementation of hepatitis C elimination strategies.

The regional models we have used do not capture the considerable heterogeneity between countries within the same region, including differences in epidemic characteristics, prevention, populations, costs, and existing health systems (including the capacity to achieve the assumed high testing coverage and accurate treatment targeting among specific populations), in particular the differences between high-income and low-income countries. Moreover, countries with missing data were excluded from regional averages, biasing projections towards the epidemiological situations of countries with better surveillance and reporting systems. As new data and updated estimates become available, these data could change the regional model inputs that are used in future analyses. Although our credible intervals are likely to capture much of this uncertainty, the purpose of this study was to use global datasets to show the type of evidence that modelling can provide to support hepatitis C elimination. We therefore urge individual countries to develop their own investment cases on the basis of locally obtained and validated data.

Very few studies estimate the indirect consequences of treating hepatitis,[13] making productivity losses difficult to

accurately estimate. For hepatitis C, the only model parameters available came from studies done in the USA[9] and Europe (Germany, France, Spain, Italy, and the UK).[11] Although this limits the generalisability of these parameters, it might also make them conservative, because health systems in these high-income countries might have the capacity to manage hepatitis C-related symptoms and facilitate continued work compared with low-income and middle-income countries. In many low-income and middle-income countries with high hepatitis C prevalence, cirrhosis and liver cancer are important causes of lost productivity and early death, with downstream effects on family and village-level financial security. Our estimation of productivity losses has also assumed that employment opportunities would become available for people with the capacity to work, rather than increasing unemployment, and we have excluded productivity losses from people in unpaid work (appendix p 4). These factors would largely depend on country and cultural contexts, and should be considered for individual country investment cases. Finally, we did not consider infrastructure costs, under the assumption that facilities and access to facilities would become available with universal health care. Viral hepatitis was included in the political declaration on universal health care that was adopted by the United National General Assembly in September, 2019, and there are increasing numbers of countries integrating hepatitis C elimination programmes into this framework.[29]

Conclusion

These findings show that a finite period of investment in hepatitis C could generate a net economic benefit of $22·7 billion globally by 2030 and lead to considerable reductions in transmission and mortality. Countries should consider hepatitis C investment cases to catalyse early financing for greater long-term economic benefits.

Contributors

NS designed the model and drafted the manuscript. CK performed the epidemiological modelling and NS performed the productivity modelling. MH and DPW conceived the study. AP, SS, JH, DPW, and MH provided critical review of the modelling assumptions, inputs, outcomes, and interpretation. All authors were involved in revising the manuscript.

Declaration of interests

The Qatar Foundation provided funding for the initial World Innovations Summit for Health report to the Burnet Institute. NS receives investigator-initiated research funding from Gilead Sciences unrelated to this work. AP has received investigator-initiated research funding from Gilead Sciences, AbbVie, and Merck, and honoraria from Gilead Sciences. JH received the Gilead Sciences Australia fellowship (2017) and honoraria from Gilead Sciences. AT has received investigator-initiated research funding from Gilead Sciences, AbbVie, and Merck; is an advisory board member for Gilead Sciences, AbbVie, Merck, BMS, Bayer, and Eisai; and is a speaker for Gilead Sciences, Abbvie, Merck, Bayer and BMS. MH and the Burnet Institute receive investigator-initiated research funding from Gilead Sciences, AbbVie, and BMS unrelated to this work. CK, SS, and DPW declare no competing interests.

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