Economic evaluation of direct-acting antiviral therapy in chronic hepatitis C

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Abstract

In 2011, the protease inhibitors boceprevir and telaprevir were approved in the United States and European Union for the treatment of hepatitis C infection. While remarkably effective, the newly approved therapies are also accompanied by additional side effects and considerable costs. Understanding the balance between costs and effectiveness is critical to making decisions about the optimal use of these new agents, especially for health care systems constrained by rising costs. Our goal for this review is to facilitate an understanding of the importance of cost-effectiveness analyses in guiding policy decisions about the use of newly approved drugs as well as future therapies for hepatitis C.

Introduction

For more than a decade, the standard of care for the treatment of infection with HCV has been a combination of interferon-α and ribavirin for 24 to 48 weeks depending on viral genotype [1,2]. In 2011, the first of a new class of drugs, namely the protease inhibitors boceprevir and telaprevir, were approved in the United States and European Union. These direct-acting antiviral (DAA) drugs and others to follow will revolutionize the management of HCV infection because of their superior efficacy, improved tolerability and potentially shorter treatment courses [3,4]

The environment for the introduction of these drugs is not the same as the introduction of pegylated interferon-α a decade ago. Health-care costs have risen to unsustainable levels and increasing attention is focused on demonstrating the value of new therapies [5]. Indeed, while remarkably effective, the newly approved DAA therapies are also accompanied by additional side effects and considerable costs. Furthermore, a number of studies have been published in the last several years identifying subpopulations of individuals, such as those with a rapid virological response (RVR) or CC IL28B genotype, in which interferon-α and ribavirin are highly effective when used alone [6–8]. Understanding the balance between costs and efficacy is critical to making decisions about the optimal use of these new agents, especially for health-care systems constrained by rising costs.

Our goal for this review is to facilitate an understanding of the importance of cost-effectiveness analyses in guiding policy decisions about the use of newly approved drugs as well as future therapies. To meet this goal, we will cover a number of topics: firstly, we will briefly review the global public health burden of hepatitis C, including a discussion of the economic impact of disease. Secondly, we will review the basic concepts of cost-effectiveness analysis, highlighting important assumptions about HCV that require particular attention. Thirdly, we will review studies to date on the cost-effectiveness of HCV therapy, including newly approved protease inhibitors. Finally, we will conclude with recommendations on how cost-effectiveness data may be used to prioritize patient groups for treatment and guide decisions in cost-constrained environments.

Burden of disease

Prevalence

It is estimated that between 2.2–3% of the world’s population, or roughly 130 to 170 million people, are infected with HCV [9,10]. The highest prevalence is in Africa, which has an estimated prevalence of 5.3% or 31.9 million individuals. The prevalence is higher in certain areas of the continent; for example, Cameroon is estimated to have a prevalence of 13.8% [11]. Similarly, Egypt may have the highest prevalence with close to 15% of the population, or 6.5 million individuals, infected with HCV [12]. While not as endemic as in portions of Africa, other countries such as Pakistan (4.9%), Taiwan (4.4%) and China (3.2%) also have relatively high prevalence rates.

In the United States, 1.6% of the population has antibodies to HCV with an estimated 1.3% or 3.2 million with chronic infection [13]. The true population prevalence is likely higher because these estimates do not include incarcerated or homeless individuals. Indeed, modelling estimates suggest that the prevalence of chronic HCV in the USA actually peaked in 2001 at 3.6 million individuals [14]. In Europe, the WHO estimates that 1.1–1.3%, or up to 8.8 million people, are infected, although country-specific prevalence can be as high as 5% [11,15].
The size of the population of individuals with HCV in the United States and Europe, where the newest DAAs have first been approved, is small relative to the burden of disease in countries that do not yet have access to this new class of drugs. In fact, China alone has more citizens infected with HCV (13 million) than all of Europe and the United States combined [12]. Similarly, India has an estimated 9.5 million people with chronic infection.

**Health impact**

While the incidence and prevalence of HCV infection is modelled to decrease over the next decade, complications from the disease will increase as the infected population ages. The worldwide mortality is estimated to be over 350,000 deaths per year [9]. In the United States, modelling suggests that HCV infection will result in 165,900 deaths from chronic liver disease and 27,200 deaths from hepatocellular carcinoma (HCC) from 2010 to 2019 [14,16,17]. Additionally, the proportion of patients with cirrhosis is projected to increase by 30.5% over the next decade, peaking in 2020.

Mortality predictions are dwarfed by the impact of HCV infection on quality of life. In Europe alone, almost 1.2 million disability adjusted life-years (DALYs) were lost due to HCV infection in 2002, the majority of which were attributable to HCV-related cirrhosis [15]. Furthermore, 95% of the DALYs lost were accumulated in patients with cirrhosis or HCC, suggesting that successful treatment may markedly reduce the burden of disease.

**Costs**

The economic burden of HCV infection is similarly overwhelming. Global calculations would be complex, but analyses from the United States provide context. In 2000 for example, Wong et al. [16] estimated that the direct medical costs attributable to HCV between 2010–2019 would be $10.7 billion; in 2011 dollars, this amounts to over $14.5 billion [18]. When indirect costs, including premature mortality and disability were considered, the sum rose above $100 billion. A more recent analysis of a managed care population found that annual per patient cost to payers for patients with HCV is greater than other more common medical conditions such as cardiovascular disease and diabetes [14]. In patients with HCV infection, prescription drugs and hospitalizations were key cost drivers.

**Basic concepts of cost effectiveness**

The goal of cost-effectiveness analyses is to compare the relative value of alternative interventions [19–22]. Cost-effectiveness analyses can help decision-makers make informed choices about health-care policy. In practice, however, policy making is usually much more complicated than sole consideration of cost-effectiveness and must incorporate issues of equity, affordability and unmet medical need. The current situation in HCV infection is an ideal example of where these analyses may be extraordinarily helpful. With an emerging array of potent and expensive therapies and increasingly powerful predictive tools, cost-effectiveness analyses can help provide context regarding the relative costs and health outcomes afforded by a dizzying array of options.

There are a number of basic concepts in cost-effectiveness analysis that are important to understand when interpreting these analyses. The concepts that will be covered in this section include: model construction and assumptions, utilities, costs, incremental cost-effectiveness ratios and uncertainty.

**Model construction and assumptions**

The first step in approaching a question regarding the economic evaluation of varying treatment strategies is to choose the type of analysis to perform. There are a number of options to choose from (Table 1) [19]. None of these methodologies are mutually exclusive; rather, the components of these analyses can inform each other and provide complementary information to a pertinent clinical question. Cost–benefit analyses are rarely performed in health care because of the difficulty in valuing health outcomes. Similarly, cost-minimization is also seldom used because the likelihood of treatments being equal in effectiveness is so low; even two drugs in the same class may be differentiated on their adverse event profile or convenience. Cost-effectiveness and cost–utility analyses are most commonly used in health care and are the focus of this review.

<table>
<thead>
<tr>
<th>Table 1. Types of economic analyses</th>
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<td>Taken from [19].</td>
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Once the analytic framework is clear, assumptions about perspective, time horizon and discounting for the reference, or base case, analysis must be addressed. The perspective used in a cost-effectiveness analysis is a critical feature because it determines which costs are included in the analysis and how they are valued and whose health outcomes are considered. The United States Panel on Cost-Effectiveness in Health and Medicine (US Panel) recommends using the societal perspective for the reference case [20]. More recently, a ‘limited societal perspective’ or ‘health system perspective’ has been advocated as a more appropriate choice for base case analyses of therapeutics because of the difficulty in truly understanding health costs and opportunity costs at the societal level [23]. Health system perspectives incorporate all direct medical costs inclusive of patient cost-sharing (for example, deductibles and co-payments). This differs from a health care payer perspective which may exclude patient cost-sharing and utilizes reimbursements rather than estimates of opportunity costs (that is, actual costs required to deliver medical care).

The time horizon and discount rate are also important features of the cost-effectiveness analysis. The time horizon refers to the length of time that the population being modelled will accumulate health outcomes and costs. The US Panel recommends that the time horizon be long enough to incorporate all downstream costs and health consequences. Given that complications from HCV infection may not occur until many years in the future, cost-effectiveness evaluations of HCV therapy typically require (remaining) lifetime time horizons. One of the issues with long time horizons, however, is that people value costs and health outcomes that occur in the future differently than they do in the present. Hence, costs and health outcomes should be ‘discounted’ to calculate the present value of all current and downstream costs and health consequences. To maintain the same value of purchasing health benefits over time, outcomes should be discounted at the same rate [22]. The US Panel recommends an annual discount rate for costs and outcomes of 3% for the reference case [20].
The key output in a cost-effectiveness analysis is the incremental cost-effectiveness ratio (ICER). This ratio is calculated as the difference in mean costs between a treatment and comparator group divided by the difference in mean effectiveness between a treatment and comparator group. In cases where the numerator is negative (that is, cost-savings with treatment) and the denominator is positive (that is, gains in effectiveness with treatment), ICERs are not computed and the treatment is considered economically ‘dominant’. In cases where the numerator is positive (that is, indicating incremental costs with treatment) and the denominator is negative (that is, lower effectiveness with treatment), ICERs are not computed and the treatment is considered economically ‘dominated’. Traditionally, therapies that have an ICER of less than $50,000-quality-adjusted life year (QALY) to $100,000/QALY have been considered cost-effective in the United States, although some have argued that these threshold values are too low [24-26]. Threshold ICER, or willingness-to-pay, values conferring ‘cost-effectiveness’ vary across health-care systems and are frequently not explicitly defined.

### Costs

The costs associated with an intervention, including downstream effects, are incorporated into the numerator of the cost-effectiveness ratio. Costs can include direct costs, such as direct health care costs (for example, drug costs, hospitalizations, testing) and non-health-care costs (for example, child care, transportation to clinic), and productivity costs (for example, loss of ability to work or engage in leisure or loss of productivity due to death). Productivity costs are particularly important in analyses of HCV therapy because of the significant burden of treatment on patients. Complicating comparisons of cost-effectiveness analysis is that these productivity costs can also be considered in the quality of life adjustments represented in the denominator of the ICER [27]. In fact, the US Panel recommends that productivity costs associated with morbidity and premature death should not be included in the numerator but rather represented in the quality of life weights applied in the calculation of QALYs (that is, in the denominator) [20].

The direct costs of HCV therapy include not only the high, up-front costs directly associated with treatment, but also all of the downstream costs that can result from potential complications of liver disease. Other direct costs associated with HCV therapy include costs of adjuvant therapy such as erythropoietin, costs associated with dose adjustments and costs associated with treating associated adverse events. It is important to note that with the practice of discounting future costs, the net value of liver complications is relatively small compared to the upfront cost of therapy. Cost for HCV therapy can vary significantly depending on the sources of these estimates (Tables 2 and 3). Although a detailed exploration of drug costs is outside the scope of this review [23,26-32], suffice it to say that discounts and rebates that are ubiquitous throughout the drug distribution chains obscure the true societal cost of these therapies. In reality, the final prices paid for HCV medications can vary significantly across public and private payers. In cost-effectiveness analyses, this variability is evaluated in sensitivity analyses in which drug costs are varied relative to the estimates chosen for use in the base case analysis.

### Table 2. Antiviral drug costs in US dollars

<table>
<thead>
<tr>
<th>Drug</th>
<th>Commerce cost based on average wholesale price (AWP)</th>
<th>Federal cost is based on Federal Supply Schedule</th>
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<tbody>
<tr>
<td>Peginterferon and ribavirin</td>
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</tr>
<tr>
<td>Telaprevir and boceprevir</td>
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*Commercial cost based on average wholesale price (AWP) – 19.5%, AWP obtained from Red Book [96]. Federal cost is based on Federal Supply Schedule [97].*

### Table 3. Antiviral regimen costs in US dollars

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Commerce cost based on average wholesale price (AWP)</th>
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*Commercial cost based on average wholesale price (AWP) – 19.5%, AWP obtained from Red Book [96]. Federal cost is based on Federal Supply Schedule [97].*

The perspective of the analysis is especially important when evaluating cost estimates as the costs to patients may be significantly different than the costs to insurers or health-care systems. In addition, the opportunity costs of viral resistance, an issue of significant concern with the first generation of DAAs [33], remains a challenge to incorporate into these analyses because of the unknown consequences on future therapeutic effectiveness.

### Health outcomes

Effectiveness in cost-effectiveness analyses can be measured in a number of ways. The two most common measurements, QALYs and DALYs, incorporate length and quality of life. QALYs are a measure of survival time, weighted by the quality of life experienced by patients during that time period. DALYs are based on a scale where the value of being dead is 0 and the value of perfect health is 1. Quality of life weights, also known as utilities, are derived from studies that assess patient preferences for varying health states. These studies can be based on a number of methodologies, including standard gamble and time-trade-off exercises. An alternative means of assessing utilities is to administer a multi-attribute utility assessment, such as the EQ-5D or Short-Form-36 (SF-36), from which an individual’s responses are mapped to utility weights [34]. As opposed to QALYs, which are designed to measure years of quality life gained, DALYs are designed to measure years of healthy life lost. DALYs measure the difference between current health status and the ideal status where an individual is free of premature death and disability [35]. The US Panel recommends the use of QALYs in economic analyses and thus will be discussed in further detail below [20].

There have been a number of studies assessing health state utilities in patients with HCV, although the methods have varied substantially across studies. Systematic reviews by McLernon et al. and Thein et al. [36,37] offer useful summaries for use in cost-effectiveness analyses. One important theme that emerges from these papers is that preferences derived from patients differ from physician-derived preferences [37,38], and very few studies have actually assessed utilities in community samples without HCV, the preferred source for utility weights recommended by the US Panel. Particularly in decompensated cirrhosis and HCC, expert panels
(that is, physicians) underestimate the quality of life as judged by patients. In contrast, experts tend to provide higher utility values for patients with a sustained virological response (SVR) as compared to patient-elicited utilities. These differences can have a substantial impact on the results of cost-effectiveness analysis and must be carefully addressed in sensitivity analyses. This limitation will be especially relevant when evaluating the value of future DAAs that are not more efficacious than existing therapies but may be better tolerated.

The poor reliability of utility measures is just one of the potential limitations of QALYs as a measure of health outcome. The measure itself relies on imperfect assumptions that are beyond the scope of this review [39]. Furthermore, the generalizability of utility measurements between countries is unknown, but a very relevant issue when taking into account the global nature of clinical trials [40]. Nonetheless, while not perfect, the use of QALYs in this context has been endorsed by both the US Panel and the British National Institute of Health and Clinical Excellence (NICE) and remains the standard of practice in cost-effectiveness analyses [34].

Uncertainty

Decision models are imperfect representations of reality. There are a number of different types of uncertainty associated with decision modelling [41]: methodological uncertainty refers to fundamental questions regarding the type of approach used to answer a question. For example, when evaluating the cost-effectiveness of DAAs, should the societal approach be used in countries without a nationalized health service? Another example might relate to how indirect costs of HCV therapy are accounted for in the model. Structural uncertainty refers to questions about the way in which the model is constructed; these questions may arise because of a lack of evidence or conflicting evidence. For example, different Markov models developed for hepatitis C have utilized different health states (Figure 1). How might these different models affect the results of analyses? Similarly, how might choosing treatment efficacy estimates from one country differ from estimates from another country? The third type of uncertainty, parameter uncertainty, refers to uncertainty regarding the true value of inputs used in a model. For example, point estimates of treatment efficacy, even from high-quality randomized trials, are estimates of the 'true' value in that population and do not capture the distribution and range of possible values in the population.

Uncertainty is addressed in cost-effectiveness analyses in a number of ways. First and foremost, cost-effectiveness analyses should make transparent choices that can be compared between models. Secondly, they should also provide explicit assessments about how assumptions may impact a model’s findings. For example, the exclusion of spontaneous viral resolution without treatment in HCV infection may bias the model in favour of antiviral treatment. The impact of these assumptions can be further tested using univariate or multivariate sensitivity analyses. Parameter uncertainty can be further addressed using probabilistic sensitivity analyses where inputs are modelled as distributions representing uncertainty regarding their true values and parameter estimates are simultaneously varied across simulations [42]. The range of estimates of cost-effectiveness from the simulations are then used to generate confidence intervals, cost-acceptability curves and other means of representing uncertainty associated with a model’s results.

Important assumptions in modelling the natural history of HCV

Markov models are commonly employed to represent HCV infection and its complications in cost-effectiveness analyses. Markov models are state transition models where the probability the length of time each hypothetical patient spends in each state is governed by transition probabilities and cycle length [19]. During each cycle of the model, cohorts accumulate costs and health outcomes that are then aggregated over time and compared between treatment algorithms.

Because the natural history of hepatitis C infection is not completely understood, there is some degree of structural uncertainty in all decision models developed for HCV. A good understanding of assumptions commonly applied in models of HCV is critical in evaluating its validity and credibility of its results. A number of these assumptions are discussed here.

Achievement of an SVR is equivalent to a cure

The impact of treatment, both successful and unsuccessful, on health outcomes is a critical issue in cost-effectiveness analyses of HCV infection. The durability of an SVR has been substantiated in a number of studies [43]. Furthermore, liver disease progression and incidence of HCC is markedly reduced and even reversed in patients with an SVR [43-47], supporting the assumption that SVR is equivalent to a cure. Furthermore, a number of observational studies have documented a decrease in liver-related and all-cause mortality with treatment [44,48-50], even if SVR is not attained [51,52]. However, there remains a risk of HCC in patients who are thought to be cured [49,53,54]. The degree to which this risk compares with the general population is unclear. A recent observational study in Scotland found that even non-cirrhotic SVR patients who were discharged from care after successful treatment were much more likely than the general population to experience liver-related morbidity. This excess morbidity was also seen in individuals who had spontaneous resolution of their SVR infection, presumably before the development of serious complications [55].

In models in which it is assumed that patients with SVR experience the same rate of liver-related complications as individuals in the general population, long-term costs associated with SVR are likely to be underestimated and quality of life is likely to be overestimated. This assumption may bias the analysis toward treatments that increase SVR, such as the new protease inhibitors, because the SVR state will appear less expensive than it might truly be. This assumption may not be accurate if patients who achieve SVR are left with complications from their liver disease, including ascites, encephalopathy, portal hypertensive bleeding and HCC that require continued treatment. These complications would increase costs and lower quality of life.

Non-liver mortality in HCV patients is the same as the general population
One particular challenge in modelling the natural history of patients infected with HCV is quantifying the risk of death from non-liver causes. The risk of death is significantly higher in patients with HCV as compared to the general population [50,56]. Although this higher risk of death may be driven by liver-related death [57], the contribution of non-liver causes is less clear. Chronic HCV infection has been associated with increased atherosclerotic risk, which may increase background mortality [56,58].

This assumption is important in cost-effectiveness analyses because varying estimates of background mortality can significantly affect the projections of survival in a decision model [59,60]. For example, if the background mortality is increased, fewer patients will appear to develop cirrhosis because of decreased survivorship. Any changes to the model that increase the rate of disease progression would again bias the model in favour of treatments that improve SVR.

**The natural history of chronic HCV infection is linear and homogeneous**

Modelling the progression of chronic HCV is also a significant challenge because the natural history is incompletely understood. This lack of clarity is a result of the indolent nature of the disease requiring lengthy follow-up and the fact that it is commonly not recognized until decades after infection. Much of the data on natural history is derived from retrospective studies of individuals presenting with complications of known disease though prospective studies of injection drug users and transfusion patients have also contributed to the literature [61–69]. Unfortunately, the prospective studies have been hampered by insufficient follow-up. In the situation of mixed results, meta-analyses are often helpful. Thein et al. [70] offer a meta-analysis and meta-regression that provides useful estimates for the purpose of modelling progression of chronic HCV.

Another of the difficulties encountered when modelling the natural history of disease is that the progression of disease is not homogeneous. For example, patients with HCV who are co-infected with HIV manifest a more aggressive disease course, with a higher rate of fibrosis progression and decompensated disease [71,72] as compared to mono-infected patients with HIV, although this risk may be attenuated in patients taking HAART [72,73]. Other patient factors in HCV infection, such as age of acquisition of infection, sex, race, alcohol consumption, smoking, obesity, non-alcoholic liver disease and hepatitis B infection may also alter the natural history of disease [64,74].

More complex models that adjust disease progression for individual characteristics can be developed, although the availability of data is often a limiting factor. Some progress has been made by stratifying progression rates by age, sex and year of acquisition and other factors [14,75], as have multi-state models that take into account the frequency and timing of examinations [76]. Ultimately, the impact of assumptions regarding the natural history of disease on the validity of cost-effectiveness analyses will depend on the question being addressed. In models that are attempting to predict future economic and health burdens from chronic infection, accurate modelling of the natural history is critical. In contrast, in analyses that address the cost-effectiveness of competing regimens, it is unlikely that imperfections in the modelling of the natural history of disease will be of sufficient magnitude as to affect the interpretation of the results. Sensitivity analyses are crucial in addressing this concern.

**Cost-effectiveness of HCV therapy**

The cost-effectiveness of interferon and ribavirin therapy for chronic HCV therapy has been demonstrated in multiple analyses over the past two decades. The earliest analyses in the mid-1990s assessed interferon-α alone compared to no antiviral treatment [77–79]. After the approval of ribavirin in 1998, analyses considered the addition of ribavirin to interferon therapy, primarily in comparison to interferon-α alone [80–84]. Subsequently, with the approval of pegylated interferon formulations in 2001 and 2002, cost-effectiveness analyses once again were employed to address the economic value of the new therapies [80,82,85,86]. In the majority of these analyses, the new treatments being considered proved cost-effective when compared to the standard of care because of improved efficacy and/or tolerability.

Although no new therapies became available in the decade that followed, new treatment paradigms using existing drugs were tested to optimize health outcomes. As such, decision models were adapted to evaluate the cost-effectiveness of alternative treatment pathways based on emerging clinical data. For example, Wong et al. [87] demonstrated the cost-effectiveness of treat discontinuation based on early virological response in patients with genotype 1, for patients with genotype 1, while a meta-analysis of the DAAs found that both treatments were cost-effective when compared to pegylated interferon and ribavirin naive patients for 48 weeks [89–94]. In contrast, in an analysis of telaprevir in treatment-naive genotype 1 patients with the favourable (CC) IL28B genotype, telaprevir was not cost-effective as initial therapy when it was available as salvage therapy in patients first failing interferon and ribavirin alone [95].

This latter analysis rests on the assumption that patients will be willing and able to tolerate multiple courses of antiviral therapy. In fact, the availability of DAAs may be the first opportunity in HCV therapy to choose among competing, yet equally effective, treatment strategies and it is unclear how patients, providers and insurers will respond to these options. Because cost-effectiveness analyses are designed to inform health policy decisions, they are rarely performed from the patient perspective and rather aim to maximize benefits to society, health-care system or payer.

In fact, among patients who want to receive treatment with the newest, most efficacious, and most convenient therapies, the results from decision models will often produce findings that conflict with these desires. Nonetheless, with the goal of identifying which therapies provide the greatest health gains per unit of money relative to standard care, integrating results from cost-effectiveness analyses into the development of treatment pathways helps to ensure that treatments are employed in an efficient manner. Even without consideration of costs, decision models can synthesize emerging clinical data to develop smarter treatment paradigms, thereby assisting health providers in practicing smarter medicine. For example, decision models may be particularly useful in guiding decisions about when to institute therapy; potentially attractive treatment paradigms might utilize pretreatment predictors such as patient age, gender, treatment status, degree of liver fibrosis and IL28B polymorphism to guide use of DAAs. Similarly, on-treatment response characteristics could also be helpful in determining when a DAA might be necessary.
Cost-effectiveness analyses could also help guide decisions about whether to institute any therapy at all for chronic HCV infection. For example, there may be situations where the potential prevention of liver-related complications is outweighed by the cost or complications of therapy. Examples of these situations may include early stage fibrosis, older age or advanced comorbidities. Similarly, there also may be situations where patients would be better served waiting for newer therapies.

Conclusions
The next five to ten year period in HCV management will be one of rapid innovation in antiviral therapy. More than 25 new agents are in various stages of development [33]. Decision models can help design and evaluate novel treatment paradigms that maximize benefits to society as a whole while still fostering a patient-centred health-care system. Published analyses to date suggest that there may be a population of patients, such as those with early stage fibrosis, IL-28B favourable genotype and RVR, in which currently available protease inhibitors may be best reserved for second-line use or used in shorter and more tolerable treatment algorithms. Robust and accessible clinical trial and observational data underpinning the effectiveness, cost and tolerability of these agents is critical to appropriately choosing between various options. Cost-effectiveness analyses should not be viewed as a tool designed to limit the availability of new therapies to patients; rather, they should function as tools to sustain a health-care system that can continue to reward innovation and afford the next generation of antiviral drugs.

Disclosure statement
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hepatitis C infection in individuals with the CC IL-28B polymorphism. *Hepatology* 2011; 54: 417A.


Cost-Effectiveness Analysis of Direct-Acting Antiviral Agents for Occupational Hepatitis C Infections in Germany, by Melanie Runge 1, Magdalene Krensel 2, Claudia Westermann 1,* , Dominik Bindl 3, Klaus Nagels 3, Matthias Augustin 2 and Albert Nienhaus 1,4. 1. Around 1% of the world’s population is infected with hepatitis C. The introduction of new direct-acting antiviral agents (DAAs) in 2014 has substantially improved hepatitis C treatment outcomes. Our objective was to evaluate the long-term cost effectiveness of DAAs in health care personnel (HP) with confirmed occupational diseases in Germany. Viral Hepatitis C, Direct-Acting Antivirals, Sustained Virological Response, Togo. DOI: 10.4236/ojgas.2019.97015 Jul. 10, 2019. In the event of failure of DAA therapy, it is recommended to document poor treatment adherence, drug interactions and intercurrent pathologies that may interfere with the absorption of DAAs. A non-optimal therapeutic scheme or premature discontinuation of treatment should be sought. Viral re-infection must also be ruled out [16]. Direct-acting antivirals have revolutionized the management of viral hepatitis C in the world and in Togo in particular. These drugs offer the possibility of oral therapy without interferon. This study could be extended to include a large number of patients to look for clinical, virological, and biological factors associated with SVR 12.