Editorial

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Targeted direct-acting antiviral treatment for chronic hepatitis C: A financial reality or an obstacle to elimination?

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In the article "Are targeted treatment recommendations in chronic hepatitis C tailored to diagnostic methods of fibrosis?" Deuffic-Burban *et al.* examined different policy scenarios for giving individuals with chronic hepatitis C infection access to direct-acting antiviral (DAA) treatments. The authors used a Markov model to estimate the 5-year reduction in the incidence of cirrhosis, liver complications and liver deaths compared to no treatment under three different rules for access: providing therapy only to patients with ⩾F3 fibrosis scores, providing therapy only to patients with ⩾severe F2 fibrosis scores, and providing universal therapy. Non-invasive diagnostic tests of fibrosis and their limitations were modelled when determining who actually received the targeted therapy. Universal therapy was found to be the most effective strategy for reducing the 5-year incidence of cirrhosis, liver complications and liver deaths. This was followed by targeting individuals with ⩾F2 fibrosis scores, which still reduced these outcomes but not to the same extent as universal treatment. Targeting individuals with ⩾F3 fibrosis scores did not reduce the incidence of cirrhosis, and only moderately impacted on liver complications. When yearly assessment of fibrosis (something the authors acknowledged as being unrealistic) was introduced into the model, the impact of the targeted therapy scenarios improved.

The authors conclude that quantifying the impact of different scenarios of treatment access will help health agencies and experts to draft therapeutic guidelines. An important question to consider is whether it is reasonable and ethical to develop therapeutic guidelines that restrict an individual's access to hepatitis C treatment when cure rates are over 95% [1,2]. This is particularly the case in developed countries that have the resources to support universal treatment.

As noted by Deuffic-Burban *et al.*, on World Hepatitis Day 2016 the World Health Organization announced elimination targets for hepatitis C, which include reducing HCV-related deaths by 65% and new chronic hepatitis C infection by 80% by 2030 [3]. Whilst ambitious, these targets are achievable, particularly in developed countries with strong health infrastructure. However, the 2030 targets will not be reached without unrestricted universal access to DAAs for hepatitis C because in the vast majority of developed countries, such as the UK, France and Italy (the countries Deuffic-Burban *et al.* considered), hepatitis C transmission is predominately due to unsafe injecting drug use [4]. If treatment is withheld from people who inject drugs (PWID), due to restrictions based on fibrosis stage or caps on the total number of people who can access treatment each year, there will be no or minimal reduction in new hepatitis C infections through treatment-as-prevention [5,6] and as a consequence it will not be possible to reach the 2030 elimination goals.

Mathematical modellers have explored the issue of treatment-as-prevention, predominately focusing on PWID, in both the interferon treatment era and the DAA treatment era [5–10]. All have shown significant reductions in hepatitis C prevalence over 10 to 15 years with relatively modest levels of hepatitis C treatment among PWID. Moreover, these and other models suggest that treatment for all people is highly cost-effective, and in fact over this longer time period, universal treatment will be more economical and have greater benefits than prioritised treatment [8], both in terms of reducing morbidity and hepatitis C prevalence. Deuffic-Burban *et al.* agree, stating "A prioritization strategy of hepatitis C treatment for patients with advanced disease would decrease the overall impact of treatment on morbidity and mortality."

A vitally important issue when discussing treatment allocation, modelling and cost-effectiveness of hepatitis C treatment is to recall that we are talking about individuals with a chronic blood-borne infection that has a one-in-ten chance of causing them significant ill health and premature death, with a lifetime risk (>5%) of hepatocellular carcinoma. It is difficult to think of other diseases whose sufferers are restricted from accessing treatment until they are at high risk of serious adverse health outcomes such as cirrhosis and liver cancer, despite the availability of a highly effective and tolerable cure.

There is also increasing evidence, and anecdotal reports, that curing an individual's hepatitis C infection has a broader impact on their health than simply stopping the progression of liver disease. A 2015 study found that people treated with DAAs had increased health-related quality of life and mental health scores following treatment [11]. Further consideration should also be

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given to the intangible benefits of cure, such as the reduction in stigma associated with having a blood-borne virus infection, or diminished anxiety due to the elimination of concern about transmitting their virus to another person, be it a family member, friend or stranger.

A reason commonly offered to justify restricted hepatitis C treatment access is that although universal access is cost-effective, the total cost is too high given the large numbers of people infected and the high cost of treatment. However, this argument lacks merit as it is dependent on governments' decisions for prioritising health care funding (and indeed other components of their national budgets), and begs the question: how much is too much, and for whom? The lowest gross domestic product of the three countries considered in Deuffic-Burban *et al.'s* article was around $1.8 trillion (US) (for Italy, in 2014 – the 8th highest globally), of which around 7% is spent on health annually [12,13]; undoubtedly these nations care about health.

A second reason to discount the "total cost" argument is that treatment costs have fallen substantially from their original price of over $80,000 a treatment course when DAAs first came onto the market to as low as $400–500 dollars in some countries. Whilst government health departments and insurance companies in developed countries like France, Italy and the UK are unlikely to negotiate prices down to as low as $400, there is evidence that pharmaceutical companies are prepared to negotiate on drug price to enable universal treatment access. For example, the Australian Government has invested around $1 billion (AUD) (approximately $720 million (US) in March 2016) in an initial 5-year program involving a risk-sharing arrangement with pharmaceutical companies, ensuring major discounts on drug prices and a maximum expenditure per year but no cap on treatment numbers. It is estimated that since March 1st 2016 (when universal treatment became available) and the end of July, over 25,000 people (more than 10% of those with chronic hepatitis C infection in Australia) received hepatitis C treatment [14]. Major discounts on drug pricing in Portugal have also led to universal treatment access; since February 2015, individuals with chronic hepatitis C have had non-restricted access to sofosbuvir-based DAA regimens. Although treatment uptake has not been as dramatic as in Australia, over 6500 Portuguese initiated treatment in the first nine months of the scheme [15].

Patients in many developed countries without universal access are voting with their feet, accessing discounted treatments online from manufacturers of generic medications in India and China through buyers' clubs [16]. Whilst the available evidence suggests that the vast majority of treatments accessed through these channels are bioequivalent to the brand-named treatments [16], it seems extraordinary that individuals are being forced to engage in "disruptive economies" to secure health care that they should reasonably expect to obtain from standard and legitimate health services in their own country. Rather than restricting treatment access, government officials need to return to the negotiating tables to obtain a better price for treatment for their citizens. Whilst acknowledging that some countries have perceived or real legislative restrictions on price negotiations for medications, limiting their capacity to negotiate on price, the current situation provides an argument for changing those restrictions, rather than accepting them as the status quo. In developing countries where cost and affordability are more legitimate barriers to universal access, innovative funding schemes such as low-interest loans and microfinancing could facilitate greater access to treatments.

History shows we have had very few opportunities to eliminate a chronic infection that causes considerable morbidity and mortality globally. Hepatitis C elimination is achievable but requires universal treatment access; restricting treatment is simply placing obstacles on the path to elimination. Therapeutic guidelines that include pegylated interferon and ribavirin as treatment options have quickly become relics – dinosaurs that will soon be extinct; so too should guidelines that restrict access to DAAs.

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Authors' contributions

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