OPINION EDITORIAL

Sofosbuvir: The Creation of an [In]Valuable Medicine for Hepatitis C

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On a crisp December morning, Maria left Romania to travel to Egypt. Never having flown before, she knew that without this journey she might never be cured [1]. On a plane Tim also saw an advertisement for a tour that could save his life [2]. Neither ancient pyramids nor sunny beaches attracted Maria and Tim to Egypt, but '*Tour n' Cure*', a travel programme offering affordable sofosbuvir-based treatment for Hepatitis C virus (HCV) when their own countries' health systems could not [2]. In contrast to existing interferon therapies, which have low response rates and toxic side effects, sofosbuvir promised to be the first cure HCV [3–6]. Although Romania has Europe's highest HCV prevalence [7], sofosbuvir cost approximately €47,100 as of 2018 [1]. The UK's National Health Service rations sofosbuvir, which cost £38,980 in 2016 [8,9], and Tim would have had to pay out-of-pocket to access treatment [2]. Yet, because of '*Tour n' Cure*', both are now virus-free. Sofosbuvir-based HCV medications, initially seen as a medical breakthrough, are unaffordable for many patients and health systems alike [10,11]. According to Médecins Sans Frontières, sofosbuvir at its original price was 67 times more expensive than gold per gram [12]. In over half of the countries where data were available, initial cost of sofosbuvir exceeded Gross Domestic Product (GDP) per capita [13]. Between 2016-2018 the price in some low- and middle-income countries has dropped by 75% due to voluntary licenses by Gilead, the originator company, and World Health Organization (WHO)-prequalified generic production [14]. However, amongst higher income countries, a price inequality persists, where richer countries pay less than countries with a lower GDP [13]. This paper examines how sofosbuvir became '[in]valuable', by tracing the research and development (R&D) of this life-saving yet unaffordable cure. Contrasting its 'value' from commercial and public health perspectives, it examines how despite significant public investment in R&D, access barriers exist.

Originally from Egypt himself, Schinazi, one of the main researchers behind sofosbuvir, co-authored a breakthrough paper on a precursor molecule whilst employed by Emory University and the U.S. Veterans Affairs Medical Centre [3]. Yet, neither Emory nor the public institutions that funded its development owned sofosbuvir's intellectual property rights (IPR), but the private spin-off company Pharmasset, founded by Schinazi and colleagues whilst working at the university [15]. The university laboratory from which Pharmasset emerged relied on public investments from the U.S. Veterans Administration and the National Institutes of Health (NIH) [16]. The NIH also conducted the phase II clinical trials of sofosbuvir and provided an additional grant of more than $2 million to Pharmasset [16]. In 2012, Pharmasset and IPR for sofosbuvir were sold to Gilead Sciences, a California based pharmaceutical company, for $11 billion. Schinazi personally received $440 million, of which he re-invests $4 million annually into his laboratories at Emory [10,17,18]. Gilead invested <$300 million into sofosbuvir's R&D [16], but by acquiring Pharmasset Gilead could determine sofosbuvir's price, setting it at $84,000 for a 12-week-course instead of $36,000 considered by Pharmasset [5]. By 2016's first quarter, Gilead had earned $35 billion from sofosbuvir-based medicines, forty times more than the total R&D costs of Gilead and Pharmasset

combined [10]. An investigation by the Senate Finance Committee [2015] into the pricing and marketing of sofosbuvir-based medicines concluded that Gilead's "*primary focus was outmanoeuvring potential competitors to ensure its drugs had the greatest share of the market, for the highest price, for the longest period of time.*"[19].

Considering Gilead's 2015 revenue on HCV drugs of $19 billion, equalling approximately two-thirds of the NIH annual budget, royalties from sofosbuvir would have been considerable. However, sofosbuvir's profits failed to feed back into public funds to support further R&D. Furthermore, the Bayh-Dole Act [1980] allows the NIH to intervene if federally funded innovations are not made accessible to the public, but the NIH failed to exercise this right for sofosbuvir [15,20]. Provisions tied to public funding should have demanded an appropriate share of the profits from any final compounds and that such products would be accessible to the public at an affordable price [15]. According to the latest WHO report, only 7% of HCV patients have received direct-acting antivirals to date, with pricing remaining one of the access barriers [14].

Selling Pharmasset to Gilead allowed for the extortionately pricing of sofosbuvir, making the treatment unaffordable for millions of HCV patients including Maria and Tim. However, Schinazi was personally involved in negotiations lowering sofosbuvir's price to $11 per pill in Egypt [17]. Egyptians can access HCV treatment at 1% of the price for American patients [21]. While the use of unsterilised needles in governmental schistosomiasis campaigns in the 1970 left Egypt with the world's highest HCV prevalence, the country has the highest cure rates of the disease globally because of this access deal [21,22]. An agreement between the Egyptian government, Gilead, and local generic manufacturers pushed down the price further to $80 for a three-month-course, available in state clinics [23,24]. In access agreements like these, stringent measures are taken to prevent cheaper, generic drugs from being exported to high-income countries where prices are higher. Yet, the Egyptian ministries of Health, Tourism, and Aviation united forces to bring HCV patients from wealthy countries to Egypt instead [25]. *Tour n' Cure* offers packages at $5000, which include sofosbuvir treatment, a five-star hotel, and a sightseeing tour of Egypt [23,25]. Using the hashtag 'Stop The Wait', *Tour n' Cure* hired the footballer Messi for a promotional video, which has >5.6 million views on YouTube [26]. Long-time sufferers of HCV like Maria and Tim now travel from high-income countries, where the treatment is prohibitively expensive, to Egypt for treatment.

Sofosbuvir shows how local decisions on the commercializtion of biomedical innovations have global impacts. In a world ruled by market forces, new medicines are judged by their commercial success and return to shareholders [15,27]. From this perspective, sofosbuvir is a successful and valuable medicine that generated an extraordinary profit. Using the term 'value-based pricing', pharmaceutical companies argue that high prices reflect advances in public health and economic value compared to prior standards of care [15]. Next to commercial value, sofosbuvir also held significant public health value, as it was one of the first direct-acting antivirals for HCV, changing the prognosis of HCV patients. However, because of the prices asked to reflect this advancement in 'value', 71 million people suffering from HCV across the world were struggling to pay the initial $1000 per pill [16,28], and health systems could not finance its procurement. Sofosbuvir's minimum production price is <$50 per 12-week course, which means that four months of Gilead's revenue from HCV medications could treat every individual suffering from HCV worldwide [4].

This case study shows how 'value' has contradictory meanings from commercial and public health perspectives.Commercial and health interests are often in opposition with one another, which is why innovation that has the potential to save lives should be driven by public health needs rather than market incentives [8,15,29]. Due to the way this invention was commercialized, sofosbuvir could not fulfil its public health value. Instead of bringing benefit to the global community, the creation of this 'valuable' medicine perpetuated existing health inequalities that became embodied in the experiences of people like Maria and Tim.

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