



**Public Participation in Decision-Making on the Coverage of
New Antivirals for Hepatitis C**

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Public Participation in Decision-Making on the Coverage of New Antivirals for Hepatitis C

Abstract

Purpose

New hepatitis C medicines such as sofosbuvir underline the need to balance considerations of innovation, clinical evidence, budget impact and equity in health priority-setting. This article examines the role of public participation in addressing these considerations.

Design/Methodology/Approach

The article employs a comparative case study approach. It explores the experience of four countries—Brazil, England, South Korea and the USA—in making coverage decisions about the antiviral sofosbuvir and involving the public and patients in these decision-making processes.

Findings

Issues emerging from public participation activities include the role of the universal right to health in Brazil, the balance between innovation and budget impact in England, the effect of unethical medical practices on public perception in South Korea, and the legitimacy of priority-setting processes in the USA. Providing policymakers are receptive to these issues, public participation activities may be reconceptualized as processes that illuminate policy problems relevant to a particular context, thereby promoting an agenda-setting role for the public.

Originality/Value

The article offers an empirical analysis of public involvement in the case of sofosbuvir, where the relevant considerations that bear on priority-setting decisions have been particularly stark. The perspectives that emerge suggest that public participation contributes to raising attention to issues that need to be addressed by policymakers. Public participation activities can thus contribute to setting policy

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3 agendas, even if that is not their explicit purpose. However, the actualization of this
4 contribution is contingent on the receptiveness of policymakers.
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8 **Keywords**

9 Hepatitis C, direct-acting antivirals (DAAs), sofosbuvir, public and patient
10 involvement (PPI), priority-setting, agenda-setting
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14 **Article Classification**

15 Case Study
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For Review Only

Introduction

In 2013 the Food and Drug Administration (FDA) in the United States of America (USA) approved sofosbuvir and simeprevir for the treatment of chronic hepatitis C infections (FDA, 2014). The regulatory agencies of other countries soon followed and the use of sofosbuvir was approved by the European Medicines Agency (EMA) in January 2014 (EMA, 2015). These medicines, along with a third called daclatasvir, were hailed as a breakthrough in the treatment of patients with chronic hepatitis C as they are considered to be highly effective antiviral agents that, for the first time, attack the hepatitis C virus (HCV) directly. These drugs are not only more effective in achieving sustained virological response—effectively curing patients—but also have fewer side effects than previous treatments. Unsurprisingly, there has been high demand for these new “cures” for hepatitis C among patients—especially given the alternative prospects of deteriorating liver function and possible liver transplantation or death, alongside the psychological distress and social stigma attached to the disease (Vietri et al, 2013; Younossi and Henry, 2015).

However, the new HCV medicines come at a price. It is a price that most countries struggle to afford, regardless of their wealth or the structure of their health system. The actual price of the regimen is hard to unveil because many health care systems engage in confidential negotiations with pharmaceutical manufacturers for discounted prices, but a 12-week treatment with sofosbuvir has been estimated to cost as much as \$84,000 in the USA (McCarthy, 2015). Policymakers or insurers face difficult decisions on whether to cover these novel and costly medicines, weighing the benefits these drugs could offer against the opportunity costs of securing health benefits for the broader population. Such challenges raise questions about what role, if any, patients and the public have in priority-setting decisions for new and expensive drugs. This article outlines how the highly innovative, but very expensive, new hepatitis C medicines have exacerbated the challenge of making prioritization decisions in health care and explores the role of patient and public involvement (PPI) in addressing this challenge.

The focus of the article arises from deliberations held at a workshop at the Brocher Foundation in Switzerland in November 2015. The workshop was dedicated to exploring ways to improve equitable access to health care through increasing public and patient involvement in prioritization decisions. It brought together

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3 academic and policy experts in health priority-setting and public involvement from 12
4 countries. Its purpose was to exchange knowledge and observations about country
5 experiences of PPI in priority-setting. One of the observations emerging from the
6 deliberations was that the new HCV medicines seem to have exacerbated the
7 challenge of making fair prioritization decisions because of the complex set of issues
8 around innovation, clinical evidence and budget impact to which they give rise. This
9 article asks what role, if any, public involvement has played in alleviating some of
10 these issues. How have countries involved the public and patients in addressing the
11 question of how to secure equitable access to new hepatitis C medicines? What can
12 we learn from this experience?
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20 In the extant literature, the importance of involving the public in health
21 priority-setting is explained with reference to the complex and multiple relevant
22 considerations that can bear on decisions. For example, to justify the model of
23 “accountability for reasonableness”, Daniels and Sabin (1997) argue that priority-
24 setting institutions must ensure fair processes. Because more than one relevant
25 consideration generally bears on priority-setting questions, relevant considerations
26 often conflict and there is no consensus among decision-makers, commentators or the
27 public at large as to how to trade them off against each other. Daniels and Sabin give
28 PPI a role in ensuring fair process and many commentators argue that it should take
29 center-stage (Emanuel, 2002; Friedman, 2008; Rid, 2009; Sabik and Lie, 2008).
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37 This article contributes to the existing debates by offering an empirical
38 analysis of public involvement in the case of sofosbuvir, where the relevant
39 considerations that bear on priority-setting decisions have been particularly stark. It
40 examines how the public has been involved in decisions on new HCV medicines in
41 four countries (Brazil, England, South Korea and the USA), thereby offering
42 comparative insights on how different health systems involve the public in complex
43 priority-setting problems, and on the perspectives that emerge. Perspectives that
44 emerge include the role of the universal right to health in Brazil, the balance between
45 innovation and budget impact in England, the effect of unethical medical practices on
46 public perception in South Korea, and the legitimacy of priority-setting processes in
47 the USA. Although these issues are contextual and not necessarily novel in the
48 individual contexts, they appear more pronounced in the case of sofosbuvir. If
49 policymakers are aware of, and receptive to, these issues, public participation
50 activities may be usefully re-conceptualized as processes that illuminate salient policy
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3 problems relevant to a particular context, thereby supporting an agenda-setting role
4 for the public. The actualization of this role is highly contingent on policymakers
5 being receptive to the issues. Given the important perspectives that emerged in the
6 case of sofosbuvir, this article concludes that further research is necessary on whether
7 they have found traction in the public policy arenas of Brazil, England, South Korea
8 and the USA.
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12 The article proceeds by providing a brief conceptual overview of health
13 priority-setting and PPI, the methods and data for the case studies, the new HCV
14 medicines generally, and of sofosbuvir particularly. These sections set the scene for
15 the discussions of the country case studies and the conclusion in the latter parts of the
16 article.
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22 **Health Priority-Setting and Patient and Public Involvement**

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26 Setting priorities in health care holds a prominent place on the policy agenda
27 in countries around the world, particularly as countries seek to achieve universal
28 health coverage. The advent of this agenda, including the creation of health
29 technology assessment (HTA) organizations, has brought about an increased interest
30 in the role of PPI in health prioritization (e.g. Martin et al., 2002; Abelson et al.,
31 2007) because decisions involve making difficult choices that cannot be made solely
32 on technical grounds and hence need to be justified and legitimized in the context of
33 social values and procedural justice (Clark and Weale, 2012; Daniels and Sabin,
34 1997).
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41 Regardless of where priority-setting takes place, it is concerned with making
42 decisions that provide a good quality, and a fair, health service while ensuring that the
43 health system is sustainable. The extant literature suggests that public input into the
44 choices made should be included as one important criterion against which to assess
45 the fairness of prioritization decisions (Sibbald et al., 2009; Kipiriri and Martin, 2010;
46 Sabik and Lie, 2008). However, barriers to public involvement exist (Goold et al.,
47 2005) and little empirical evidence is available on the effect of PPI generally, and
48 different modes of PPI such as deliberative processes specifically (Mitton et al., 2009;
49 Abelson et al., 2003).
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56 This article follows Weale et al.'s (2016, p. 5) definition of public
57 participation in priority-setting as involving "[...] individuals or groups taking part in
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3 processes of policy making that shape the determination of priorities in health care
4 and the conditions of access of different groups in society”. It is collectively-
5 orientated and excludes forms of patient involvement such as involvement in research
6 or shared decision-making as these forms of involvement are not aimed at bringing
7 about a decision that affects public policy at large. This collectively-orientated mode
8 of public participation can come in different forms such as the inclusion of patient or
9 public representatives in HTA bodies, mini-publics or consultative forums convened
10 to garner public and patient views. Importantly, it also includes more unconventional
11 forms of public participation such as protests, demonstrations, public campaigns and
12 litigation. To include these forms of involvement is crucial because in some countries
13 they have become a routinized mode of involvement that can affect priority-setting
14 decisions (Weale et al., 2016; Slutsky et al., 2016).
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24 **Methods and Data**

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28 The article employs a comparative case study approach. Its main units of
29 analysis are the country-specific processes of public participation in the case of
30 sofosbuvir. We focus on sofosbuvir because it has received substantial attention in
31 media outlets worldwide. The country case selection was informed by the aim to
32 include countries with conventional and unconventional modes of public participation
33 in health prioritization (Weale et al., 2016). For reasons of data availability, the
34 selection was restricted to the countries represented at the Brocher Foundation
35 workshop entitled “Improving equitable access to health care through patient and
36 public involvement in prioritization decisions” in Switzerland in November 2015. The
37 represented countries were Australia, Brazil, China, Colombia, Germany, New
38 Zealand, South Africa, South Korea, Sri Lanka, Thailand, the United Kingdom (UK)
39 and the United States of America (USA).
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48 Following Slutsky’s et al.’s (2016) distinction between consensus, i.e.
49 conventional, and contestatory participation, i.e. unconventional, modes of
50 participation, Brazil, England, South Korea and the USA were selected as cases.
51 England represents a system where contestatory participation is not routinized
52 (Slutsky et al., 2016), whereas Brazil and South Korea represent countries where it is
53 routinized. The USA represent a unique case in that participation is neither clearly
54 consensus nor contestatory-based because of a lack of federal prioritization decision-
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3 making in which the public participates in a routine fashion. Nevertheless, as we shall
4 see, forums for participation do exist in the form of institutes such as the Institute for
5 Clinical and Economic Review (ICER).
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8 The article draws on country data on PPI and health priority-setting that was
9 presented at the Brocher Foundation workshop. This data was supplemented by data
10 from secondary literature. At the workshop policy and academic experts presented the
11 status quo of health priority-setting and PPI in their countries following a template of
12 nine areas (see <http://www.ucl.ac.uk/socialvalues> for presentations):
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- 15 1) Overview of health system and approaches to prioritization;
- 16 2) Degree and nature of PPI in prioritization;
- 17 3) Rationale for PPI;
- 18 4) Successes and challenges;
- 19 5) A prioritization case study and impact of PPI in this case;
- 20 6) Issues highlighted by the case study;
- 21 7) Ethical or social values questions in relation to PPI;
- 22 8) Lessons learnt;
- 23 9) Future plans for PPI in prioritization.
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33 In its discussion of the country cases, this article broadly follows the outlined
34 template. Each case study begins with a brief overview of the health system and
35 approaches to PPI in health prioritization. A discussion of the rationale as well as the
36 successes and challenges of PPI is omitted because the focus is on the prioritization
37 case study (sofosbuvir) and the issues, ethical questions and lessons learnt. Unless
38 they emerge directly from PPI in the case of sofosbuvir, the category of future plans
39 for PPI is also omitted for the purpose of this paper.
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45 Due to the small number of cases included in this article, the generalizability
46 of the observations is limited. However, the purpose of this article is not to bring forth
47 generalizable claims, but to provide an insight into the role PPI has played in
48 coverage decisions on new HCV medicines. This is to gain a better understanding of
49 the contributions of PPI activities in complex prioritization decisions.
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New HCV medicines

“Hepatitis C is a virus that can infect the liver” (NHS Choices, 2015). Long-term, and potentially life-threatening complications from chronic hepatitis C infection include liver cirrhosis and liver cancer. More than 185 million people are affected by hepatitis C and approximately 350,000 people die each year as a consequence (WHO, 2014, p. 25). Hepatitis C is transmitted through contact with infected blood specimens (WHO, 2014). There are several types and subtypes of the infection, so-called genotypes.

In recent years a rapid development in treatments for chronic hepatitis C has taken place. In 2011 and 2012 the medicines telaprevir and boceprevir were introduced. Since 2013 additional medicines have been approved around the world, namely sofosbuvir, simeprevir and daclatasvir. These medicines are direct-acting antivirals (DAAs) that target the HCV itself, an innovation over previous treatments that indirectly suppressed the virus through inhibiting its replication.

This article focuses on sofosbuvir. The main clinical endpoint measured in randomized controlled trials (RCTs) on hepatitis C medicines is the sustained virological response (SVR), that is the virus being undetectable in the blood three or six months after treatment (WHO, 2014). Sofosbuvir achieved a SVR in over 90% of the patients across different genotypes of hepatitis C (WHO, 2014). Clinical experts equate the achievement of a SVR to a cure (NICE, 2015, p. 46). Arguably, providing a drug like sofosbuvir would not only yield benefits for patients, but also avert future high costs associated with liver transplants as well as generate public health benefits through reduced HCV transmission. However, there is still much uncertainty surrounding the potential of future (liver) complications for patients who have cleared the virus or the question of which patients would progress to more serious stages of liver disease if left untreated. Trials on sofosbuvir report fewer, and less severe, side effects as well as a potential reduction of the treatment cycle from 24-48 weeks to as little as 12 weeks (WHO, 2014). Additionally, sofosbuvir is administered orally in the form of a pill once a day for usually 12 weeks, whereas previous methods of administration were mostly through injections.

However, at an estimated price of \$84,000 for a 12-week treatment in the USA, sofosbuvir has been labeled the \$1,000 pill (McCarthy, 2015). The first WHO guidelines on the screening, care and treatment of patients with hepatitis C

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3 recommend access to the new medicines. In the absence of sufficient funds to treat the
4 entire patient population, they recommend to treat the sickest patients first (WHO,
5 2014). This is the way a number of countries have approached the access, for example
6 guidelines in the USA and England recommend to treat patients with cirrhosis first
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8 (McCarthy, 2014; NICE 2015).
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11 The challenge of providing access to these new medicines includes
12 considerations of cost effectiveness, affordability, health equity, public health and the
13 ethical implications of treating the sickest patients first. One of the biggest issues is
14 how to resolve the perceived tension between cost effectiveness and affordability. The
15 approach to prioritization in many tax-based health systems focuses on the assessment
16 of cost effectiveness, with an assumption - explicit or implicit - that treatments should
17 be made available to all patients for whom they deliver outcomes whose cost
18 effectiveness exceeds a pre-determined threshold. But when the total budget impact of
19 such a treatment is large, its adoption may require significant re-direction of
20 resources, either from other areas of health spending, and/or from areas of non-health
21 expenditure (Claxton et al., 2015; Ward, 2015). A re-direction of resources raises
22 questions of equity with regard to the patient groups who lose out as a result. It
23 therefore requires debate and resolution in the political space, which may or may not
24 include the wider public.
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35 The above issues are complicated by the fact that Hepatitis C is already
36 strongly associated with health inequities. It disproportionately affects populations in
37 low and middle income countries (Graham and Swan, 2015), which to date have not
38 had much access to available treatments due to the challenging screening and
39 monitoring requirements. Moreover, sofosbuvir and other DAAs have been labeled a
40 cure, a label that few other medical innovations achieve. Familiar issues of pricing
41 and the current patent system are also surfacing. For example Argentina, Brazil,
42 China, Russia and the Ukraine are challenging the current patent for the new hepatitis
43 C drugs (Bagcchi, 2015). Similarly, a non-governmental organization of doctors in
44 France that provides healthcare for vulnerable populations worldwide, the Médecins
45 du Monde, is challenging the patent at the European Patent Office (EPO) (Boseley,
46 2015). Given this mix of complex issues, the question arises if PPI can help
47 adjudicate between the different issues. What has the experience of involving the
48 public and patients been in the case of sofosbuvir?
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Public Participation in the Case of Sofosbuvir

Brazil

The Brazilian Public Health System, better known by the acronym SUS (Sistema Único de Saúde; Unified Health System) was established under the Federal Constitution of Brazil in 1988. Enshrined in the Constitution is a right to health care and a governmental duty to guarantee universal and equal access to services and activities that promote, protect and restore health (Paim et al., 2011). Brazil's forums for public participation include municipal and state health councils comprised of members of the public and patient representatives. Through these councils health care planners are held to account by the citizenry (Dall'Agnol Modesto et al., 2007). Brazil's tradition of public involvement is also reflected in the way the public is involved in the SUS. The National Health Council, which consists of a mix of representatives of service user organizations (50%), health care worker representatives (25%), government and health service providers (25%), holds monthly meetings in which proposals are deliberated (Dall'Agnol Modesto et al., 2007).

In the case of sofosbuvir, the National Commission on Technology Incorporation in the National Health System (CONITEC), the HTA body in Brazil, decided unanimously to recommend the inclusion of sofosbuvir, daclatasvir and simeprevir for the treatment of chronic HCV (CONITEC, 2015). The recommendation was preceded by a public consultation on HTA report. Public contributions were made through submissions to the CONITEC website.

During the process of assessing sofosbuvir, CONITEC also presented revised Clinical Protocol and Therapeutic Guidelines (PCDT) for the disease, with new guidance on treating the condition. The assessment process did not evoke as much public protest and engagement as did the revised PCDT. According to the revised protocol, the degree of fibrosis determines the group of patients who are eligible to be treated with the new antiviral agents under the SUS, excluding patients at fibrosis stages F1 and F2 (PCDT, 2015).

The Brazilian Movement of the Fight against Viral Hepatitis voiced its dissatisfaction with the protocol and invoked the constitutional universal right to health, claiming that the patient groups included in the protocol "represent less than 4% of the current need and means tearing the principle of universality of access to

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3 health”¹ (MBHV, 2015). The official estimate is that 60,000 patients will be treated
4 with sofosbuvir in the next two years. To the Work Group of Intellectual Property
5 (GTPI), “this is less than 1/3 of the related demand [...]” (GTPI, 2015).
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8 The fact that the Brazilian Movement of the Fight against Viral Hepatitis
9 invoked the constitutional universal right to health reflects a prominent feature of
10 many health systems in Latin America where the right to health is enshrined in the
11 Constitution. Reimbursement decisions on medicines are made through benefit plan
12 assessments (BPA), following the principles of financial sustainability and of clinical
13 efficiency. For a molecule to be considered for BPA, it generally has to overcome the
14 HTA hurdle. In order to ensure financial sustainability some countries perform
15 different degrees of Budget Impact Analysis (BIA) (e.g. Ministerio de Salud de
16 Colombia, 2015). In this setting there is an inherent tension between the HTA results
17 and the BPA results that may yield that a cost effective technology is unaffordable for
18 the entire system, which is why CONITEC recommended restricting access to
19 sofosbuvir according to fibrosis stage.
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28 Given the constitutional protection of the right to health, Latin American
29 individuals and campaign groups can resort to courts to challenge the results of the
30 HTA and BPA. Every year thousands of Latin Americans resort to this
31 unconventional form of PPI and more often than not judges rule in favor of the
32 avalanche of plaintiffs (Cubillos et al., 2012). The effect that easy litigation has on the
33 incentives to participate in the more established PPI mechanisms is unclear. If one can
34 almost certainly win a case in less than two weeks, why join a process that may take
35 months or years and that may not lead to your desired outcome? Policymakers in
36 Latin America continue to grapple with the constraining effects of the constitutional
37 right to health on priority-setting decisions.
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46 *England*

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49 The National Health System (NHS) is a tax-based health system in which
50 national and local structures share decision-making responsibility. At local level, 211
51 clinical commissioning groups (CCGs) are responsible for commissioning (Thorlby
52 and Arora, 2014), i.e. buying, health services from public, private or non-profit health
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58 ¹ Translated by one of the authors of this article.
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3 care providers. At the national level, NHS England oversees spending and allocation
4 of resources (NHS England, 2016). CCGs and NHS England are supported by the
5 National Institute for Health and Care Excellence (NICE), an organization responsible
6 for appraising the clinical and cost effectiveness of new medicines. If NICE makes a
7 positive recommendation on a new drug, then commissioners are under a legal
8 obligation to make the treatment available (NICE, 2016). NICE makes its appraisals
9 on the basis of clinical and cost effectiveness considerations as well as social value
10 judgements (Rid et al., 2015).

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16 NICE conducts a public consultation process for every treatment it appraises.
17 In this process there are two groups that are allowed to participate, namely consultees
18 and commentators. Consultees include patient and professional organizations, the
19 pharmaceutical manufacturer, government and NHS entities (NICE, 2013, p. 4).
20 Commentators include manufacturers of comparator technologies or research groups
21 who are allowed to comment, but do not have a right to appeal the decision. The
22 wider public can submit comments on NICE's website (NICE, 2016a).

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28 NICE made a positive recommendation for the use of sofosbuvir, although the
29 use of sofosbuvir in genotypes 4, 5 and 6 was only recommended in patients whose
30 infection had already progressed to liver cirrhosis (NICE, 2015). The contentious
31 issues did not arise as a result of NICE's appraisal of sofosbuvir, but as a result of
32 NICE's decision to grant NHS England an extension to the normal implementation
33 period in which a NICE-recommended treatment has to be made available on the
34 NHS. Usually NHS commissioners have to ensure that patients receive access to the
35 recommended treatment within three months after it has been recommended (NICE,
36 2016). In the case of sofosbuvir a waiver of this period was sought by NHS England
37 (NICE, 2014a). Four reasons were provided: First, NHS England argued that the
38 health service had to be reworked in order to provide access to the new medicines
39 through specialized treatment centers. Second, a substantial increase in demand for
40 treatment could be expected, making it necessary for NHS England to ensure it could
41 accommodate this demand. Third and fourth, networks for service provision would
42 have to be created in order to guarantee that appropriate screening and monitoring
43 structures were in place for hepatitis C patients (NICE, 2014a).

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56 Although NHS England's request downplayed the expected budget impact of
57 sofosbuvir as a reason for the request—because budget impact is not an eligible reason
58 for such extensions under the legal framework set by the government—the ensuing
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3 protest suggests that stakeholders agreed that it was a veiled request based on
4 concerns about budget impact (NICE, 2014b). The submissions by NHS England
5 suggest that such views were not far-fetched. According to NHS England's
6 submission: "[...] at the prices proposed by the manufacturer in their NICE
7 submission, this technology is not affordable at the quantum of new expenditure it
8 would represent" (NICE, 2014, p. 8). Consultees were given the opportunity to
9 comment on NHS England's request. One patient organization summarized the
10 problems as follows:
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16 The Hepatitis C Trust objects in the strongest possible terms to any attempt to
17 introduce budget as a factor. If we are going to change our health care
18 resource allocation model to one based on arbitrary consideration of this
19 year's budget, then this should be debated nationally, preferably through an
20 election manifesto. Either NICE has a mandate to decide resource allocation
21 or it doesn't (The Hepatitis C Trust, 2014, p. 6).
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24 The submissions in response to NHS England's request to delay the date by
25 which sofosbuvir has to be made accessible highlights complex questions about the
26 how the ability of NICE's decision-making framework to accommodate cost
27 effectiveness and affordability is perceived by stakeholders. The patient
28 representatives raised the issue that if budget impact is an implicit consideration in
29 cases such as sofosbuvir, then this has to be made explicit and deserves debate in the
30 wider public and political policymaking arena.
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38 *South Korea*

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41 The Republic of Korea has a National Health Insurance Service (NHIS) that
42 covers 96.6% of the population (OECD, 2012). The rest of the population is covered
43 "[...] by a medical aid plan which is directly funded by [...] the national and local
44 governments [...]" (Ahn, 2012, p. 344). While the NHIS is known for its population-
45 based universal coverage, the benefits that are covered are limited and out-of-pocket
46 payments were at 36.9% in 2013 (OECD, 2015) even though the benefit coverage has
47 expanded since the 1990s.
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53 In 2012 the NHIS set up a lay citizen's council, the Citizen Committee for
54 Participation, made up of lay members of the public who are selected following an
55 application process. Although still in its early years, the decision-making mechanism
56 of the Committee, and its influence on the final decisions by the Health Insurance
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3 Policy Committee (HIPC), are considered significant. In its first year 69% of newly
4 covered services were originally chosen and recommended by the Citizen Committee
5 (Oh et al., 2015). However, except for the Citizen Committee, PPI is not prominent in
6 Korea unless a nationwide interest develops that puts pressures on adopting new
7 health technologies, especially pharmaceuticals. Such was the case with sofosbuvir.
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11 The case of sofosbuvir reached the public agenda not through the Citizen
12 Committee, but through a scandal that rocked a clinic in Seoul in November 2015.
13 Sofosbuvir was approved by the regulatory authority in September 2015 (MFDS,
14 2015). A scandal arose in a neighborhood in Seoul when an outbreak of HCV was
15 tied to the re-use of disposable needles at a local clinic specializing in intravenous
16 (IV) injection services (Ah-young, 2015). According to the Korea Times (Ah-young,
17 2015a), a total of 78 HCV infections were confirmed until the fourth of December
18 2015 and 55 out of 78 patients were found to have type 1a, which is usually prevalent
19 in less than 1% of the hepatitis C patients in Korea (Seong et al., 2013). Many
20 Koreans learned about the disease and the treatment option of sofosbuvir and its
21 combination drug from news reporting on a massive scale and they were sympathetic
22 to the victims of unethical medical practices. The incident elevated the issue of
23 sofosbuvir to the national political arena, with public and advocacy groups
24 campaigning for access to the new medicines. The coincidence of this event and the
25 reimbursement review process of these drugs finally resulted in the Ministry of Health
26 and Welfare asking for a faster review of sofosbuvir (The DailyPharm, 2015).
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30 The Korean experience highlights additional ethical issues that characterize
31 the debate on new hepatitis C drugs, namely issues of fairness, government
32 accountability and public responsibility when infections occur due to unsafe medical
33 practices. This is the case in the recent scandal in Korea, but similar examples can be
34 found in other countries, for example in the UK where contaminated blood
35 transfusions in the 1980s led to increased HCV infections. Even though this issue did
36 not emerge as a result of formalized PPI processes, the public outcry in Korea
37 underlines the effectiveness of public campaigns in the face of such scandals. The
38 final reimbursement decision is outstanding at the time of writing, but given the
39 scandal and the ensuing public reaction, it is unlikely that the formalized PPI process,
40 if pursued by the decision-making authorities, will lead to any recommendation other
41 than to reimburse sofosbuvir.
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The USA: The Institute for Clinical and Economic Review

Due to the fragmented nature of the American health care system there is no one government-mandated institution for health priority-setting. Following the introduction of the Patient Protection and Affordable Care Act in 2010, the health care system remains a predominantly private system but the percentage of uninsured continues to drop (The Commonwealth Fund, 2015). There are two publicly subsidized and federally managed health care programmes, namely Medicare for the elderly population over 65 and Medicaid for families meeting low-income eligibility criteria (The Commonwealth Fund, 2015). Given the lack of institutionalized priority-setting, this section examines the experience of an independent research body, the Institute for Clinical and Economic Review (ICER)², that produces evidence reports on new medicines, on which payer organizations such as insurers draw.

The Institute for Clinical and Economic Review is an independent research institute funded largely by non-profit foundations. It produces evidence reports on medical technologies to help guide the application of evidence to clinical practice and insurance coverage policy (ICER, 2014). The Institute has created regional committees of independent clinicians and public representatives, called Comparative Effectiveness Public Advisory Councils (CEPAC), who are convened to deliberate on evidence reports in meetings open to the public (ICER, 2016). The meetings are spent debating the evidence, after which the CEPAC votes on whether the evidence is adequate to demonstrate that a new technology is as good or better than other options available to patients. The reports include evidence on cost effectiveness and potential budget impact and the Institute asks the CEPAC groups to vote on the "value" of new interventions.

The Institute's draft evidence report on the HCV medicines received criticism from patient advocacy groups focused predominantly on the results of the economic analyses that found that these drugs would not reduce long-term costs in the health care system while presenting huge potential short-term costs that could overwhelm health care budgets (ICER, 2014a). At the public CEPAC meeting, the CEPAC voted that the evidence was adequate to demonstrate the clinical superiority of the new

² In order to avoid confusion between the incremental cost effectiveness ratio (ICER) and the Institute for Clinical and Economic Review (also ICER), this article does not use the 'ICER' abbreviation for the Institute, but refers to it as the 'Institute' or spells out its full name.

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3 drugs but that they represented a "low" value to the health care system³ (ICER,
4 2014b). The voting stage of the meeting was followed by a so-called policy
5 roundtable, an invited group composed of representatives from insurers,
6 manufacturers, clinical experts and patients. The roundtable included the leader of one
7 of the patient groups. This representative criticised the vote of the CEPAC and sought
8 to cast aspersions on the clinical expertise, primary motives, and financial interests of
9 all involved (ICER, 2014c). The clinical experts responded by expressing their belief
10 that, for clinical and economic reasons, the most reasonable path forward was to
11 prioritize patients for treatment, with sicker patients receiving treatment first (ICER,
12 2014c). They felt this was reasonable not only because the short-term clinical risks
13 were minimal, but because there was inadequate infrastructure to treat all patients
14 immediately and because the financial repercussions of immediate treatment for all
15 eligible patients was unrealistic (ICER, 2014c).
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24 The recommendation to use severity of initial liver damage as a method of
25 prioritizing patients was the recommendation that was included in the final CEPAC
26 report (ICER, 2014). The patient advocacy organizations did not accept this
27 recommendation and opposed it in the press (Clary, 2015). But private and
28 public health insurers felt empowered to establish their initial coverage
29 recommendations to mirror this approach, and many cited the CEPAC report as
30 justification (e.g. UnitedHealthcare, 2014). Anecdotally, many insurers informed the
31 Institute that having a transparent, independent process for evidence review was
32 important to their decision-making. Even if patient advocacy groups disagreed with
33 the result, insurers felt that the overall process had enough legitimacy to serve as a
34 cornerstone of their coverage policies.
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43 The case underlines complex questions about the purpose of PPI and the
44 legitimacy of prioritization decisions. While insurers found the Institute's process
45 helpful, the protests by patient advocacy groups suggest that they did not view the
46 CEPAC vote as a fair outcome of a legitimate process. The extant literature on the
47 legitimacy of decision-making processes in health priority-setting converges on the
48 idea that outcomes of decisions are more legitimate if the public has been involved
49 (Daniels and Sabin, 1997; Abelson et al., 2007; Parkinson, 2003). However, the
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56 ³ Please note that this section is an account from one of the co-authors who is the Director of
57 the Institute and was present in the deliberations. The full summary of the proceedings can be
58 found on the Institute's website (ICER, 2015).
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3 experience of the Institute for Clinical and Economic Review in the case of HCV
4 medicines suggests that enhancing the legitimacy of decision-making processes of
5 independent review bodies in the eyes of public and patient representatives remains a
6 challenging issue.
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10 11 **Discussion and Conclusion** 12

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15 Examining PPI in the case of sofosbuvir across multiple and diverse settings
16 highlights that none of the countries included in this paper diverted from their
17 established modes of involving the public and patients. These modes need to be
18 viewed in the political and historical contexts of the respective countries. They led to
19 different, yet very important, questions that need to be addressed. In England,
20 stakeholders stressed the controversies that arise when cost effective medicines are
21 not covered within the statutory timeframe due to budget impact concerns, even
22 though such a delay is statutorily permitted in certain circumstances. This suggests
23 that the methodological approach employed by NICE does not sit easily with
24 stakeholders. The public consultation process highlighted this issue, but it cannot be
25 resolved in the currently available PPI forums. It is a political question that needs to
26 be addressed in the wider public space.
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32 In South Korea, a scandal pre-empted potential deliberations by the
33 established Citizen Committee of Participation. The Korean example brings to the
34 forefront the importance of what Slutsky et al. (2016) label ‘contestatory
35 participation’ and of the significant pressure that media campaigns can exert on
36 decision-making in health priority-setting. It remains to be seen how the story
37 unfolds, but it seems likely that the established forums of PPI will not deviate from
38 the public perception that the novel HCV medicines should be made available in the
39 light of unethical medical practices. The Korean example is as much a story of
40 successful pressure exerted through media spaces as it is an example of how an issue
41 can reach the policy agenda and exacerbate the challenges faced by policymakers.
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52 The experiences of the USA and Brazil countries underline the importance of
53 national context. The deliberative meetings held by the Institute for Clinical and
54 Economic Review fill a void in a fragmented health system in which insurers, the
55 public and patient advocacy groups have little guidance on which to draw when
56 making tough decisions or engaging with each other. The Institute’s experience
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3 accentuates the role that deliberative processes can play in evaluating evidence.
4 However, it also shows how challenging it is for these processes to be viewed as
5 legitimate by all those involved (Kieslich and Littlejohns, 2015), and failing to
6 establish legitimacy is a real barrier to the contribution that public participation
7 activities can make. In Latin America, PPI takes places in the context of national
8 health systems that guarantee a right to health. The public and the patients insist on
9 their right to health and policymakers are faced with the constraints that this system
10 puts on policies that seek to introduce efficiency savings.

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16 In conclusion, has the PPI experience in Brazil, England, South Korea and the
17 USA helped address some of the difficult challenges that arise in the case of
18 sofosbuvir? The short answer is no. The country experiences are as much a tale of
19 challenges that arise when making difficult prioritization decisions as they are a tale
20 of agenda-setting. With regard to the unconventional modes of participation such as
21 protests and litigation, this observation is not surprising as they tend to receive much
22 attention in the media. However, with regard to the more conventional modes of
23 participation through consultation and deliberation, this observation is interesting as it
24 may suggest an agenda-setting role for the public even when this is not the explicit
25 purpose of these modes of participation. PPI on sofosbuvir has brought a number of
26 issues to, or back on, the policy agenda. In England, policymakers need to address
27 what NICE's cost effective paradigm implies for a cash-strapped NHS. The American
28 experience suggests it may be time for policymakers to think about how they can help
29 insurers and providers establish decision-making processes that are perceived as
30 legitimate by the public. In South Korea, the importance of combining ethical and
31 budgetary considerations has been underlined, especially when patients are infected
32 with HCV through no fault of their own. In Latin America policymakers are having to
33 strike the balance between realizing the right to health and the necessity to ensure the
34 sustainability of health care systems (Ferraz, 2011). Of course, whether these issues
35 find traction on the policy agenda depends on the receptiveness and willingness of
36 policymakers to engage with them, and this question is an area for further research.

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The possible role of issue characteristics (Lowi, 1964; Burgin, 1995) also
merits attention in future research. Lowi (1964) argues that variations in policy-
making processes can be explained with reference to the character and type of issues
that are being addressed. In the case of pharmaceutical products issue characteristics
include the disease area, the population affected, cost effectiveness, budget impact

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3 and questions of equity. The question that demands further exploration is whether
4 certain characteristics of issues brought forth by cases such as the new HCV
5 medicines call for a stronger, or a particular mode of public involvement. Given its
6 large budget impact, views from the wider public could be gained on the kind of
7 trade-offs they would be willing to make if access to the new hepatitis C medicines is
8 to be provided. However, constructing a case for a stronger, or a particular mode of
9 public involvement, will rest on the resolution of at least three arguments against it.
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14 First, the discussed issues are not new or unique to HCV medicines. They are
15 simply more pronounced in this case. The novel HCV drugs have brought to light the
16 challenging issues that have long concerned policymakers, practitioners and
17 academics. To use these challenges as an argument for going beyond existing modes
18 of PPI would run the risk of establishing a case of exceptionality that may not be
19 justified. Second, existing modes of involvement or participation all come with their
20 own advantages, disadvantages and risks (Weale et al., 2016). Regardless of how
21 carefully a particular mode of involvement is chosen, chances are that none of them
22 can address the entire breadth of issues. Third, isolating the situations in which issue
23 characteristics exacerbate the challenges of decision-making to such an extent that
24 warrants for taking the issues to the public at large would be difficult. Nevertheless,
25 the complex trade-offs emerging in priority-setting decisions on HCV medicines
26 suggest that the normative and empirical role of issue characteristics is worth
27 exploring.
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