

## Impact case study (REF3)

<b>Institution:</b> University of Bristol		
<b>Unit of Assessment:</b> 2) Public Health, Health Services and Primary Care		
<b>Title of case study:</b> Towards global elimination of Hepatitis C: Bristol research informs prevention and treatment strategies		
<b>Period when the underpinning research was undertaken:</b> 2010 - 2020		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Peter Vickerman	Professor in Infectious Disease Modelling	10/2013 - present
Matthew Hickman	Professor in Public Health and Epidemiology	09/2005 - present
<b>Period when the claimed impact occurred:</b> 2014 - 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> No		

## 1. Summary of the impact

Hepatitis C Virus (HCV) is a blood-borne infection that causes considerable global morbidity. Research from the University of Bristol on the impact and cost-effectiveness of HCV treatment, especially in preventing HCV transmission has:

- guided the World Health Organisation's (WHO) treatment guidelines (2018) that expand HCV treatment to all patient groups;
- underpinned the WHO's Global Health Strategy (2016) to eliminate HCV as a public threat by 2030, initiating a global expansion in HCV treatment;
- guided over ten countries' HCV elimination initiatives.

Early data suggest that elimination strategies in Australia and Scotland have respectively decreased chronic HCV prevalence by 42% and 71% among people who inject drugs, the most affected patient group.

## 2. Underpinning research

HCV is an important cause of liver disease. In high-income countries, most chronic HCV is among people who inject drugs (PWID) whereas more disseminated epidemics involving other transmission routes (mainly through unsafe medical injections and procedures) can occur in low- and middle-income countries. Amongst PWID, needle and syringe programmes and opioid substitution therapy are the primary HCV prevention interventions but, prior to our research, evidence quantifying their impact and cost-effectiveness for reducing HCV transmission was minimal. Although HCV is a curable infection, the coverage of HCV treatment has traditionally been low and not recommended among people with risk of re-infection, such as PWID.

Since 2010, Vickerman and Hickman at the University of Bristol (UoB) have led a substantial body of work, including intervention studies, epidemiological analyses, systematic reviews, infectious disease and economic modelling, that has transformed the evidence base for the prevention and treatment of HCV among PWID and other groups at risk of HCV transmission.

### HCV prevention and treatment among PWID and other high-risk groups

UoB researchers produced the first strong evidence (culminating in a Cochrane systematic review (1), published 2017) that needle and syringe programmes and/or opioid substitution therapy can reduce the risk of HCV acquisition amongst PWID by over 50%. This evidence was used in our modelling, which showed that needle and syringe programmes and opioid substitution therapy are highly cost-effective in the UK and USA. UoB developed the first dynamic model of HCV transmission that showed the potential prevention impact of HCV antiviral treatment and that treatment scale-up among PWID could eliminate HCV (2). UoB researchers found that treating PWID who have active infection risk is likely to be more cost-effective than treating people with no infection risk and could avert up to two new HCV infections for each person treated (3). We also identified the importance of combining the scale-up of HCV

## Impact case study (REF3)

treatment with opioid substitution therapy and needle and syringe programmes for reducing HCV transmission and minimising the need for re-treatment (4), showing that ambitious HCV elimination targets could not be achieved without this scale-up. In the UK, we projected that from 5 to 10% of PWID with chronic HCV need treating each year to eliminate HCV by 2030. We have produced similar models for 11 sites and countries in Europe and 21 countries worldwide. UoB researchers also investigated the HCV epidemic among men who have sex with men (MSM) and found that, among this group, HCV elimination is possible with achievable scale-up of HCV treatment.

### HCV prevention around the world

UoB research has demonstrated the large prevention impact that HCV treatment could have across the world (5,6) and showed that it is cost-effective to test and treat in lower- and middle-income countries. However, our analyses emphasise that achieving HCV elimination will always need a focus on PWID given their large global contribution to HCV transmission; a recent analysis by UoB suggests PWID contribute 43% of incident infections globally (7).

## 3. References to the research

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1. Platt L, Minozzi S, Reed J, **Vickerman P**, Hagan H., **French C**, Jordan A, ...**Hickman M** (2017). Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database Systematic Review*, 9: 1-89. DOI:[10.1002/14651858.CD012021.pub2](https://doi.org/10.1002/14651858.CD012021.pub2)
2. Martin NK, **Vickerman P**, Grebely J, Hellard M, Hutchinson SJ, Lima VD, Foster GR, Dillon JF, Goldberg DJ, Dore GJ, **Hickman M**. (2013). HCV treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. *Hepatology*, 58(5): 1598-1609. DOI:[10.1002/hep.26431](https://doi.org/10.1002/hep.26431)
3. Martin NK, **Vickerman P**, Dore GJ, Grebely J, Miners A, Cairns J, Foster GR, Hutchinson SJ, Goldberg DJ, Martin TCS, Ramsay M, **Hickman M**. (2016). Prioritization of HCV treatment in the direct-acting antiviral era: An economic evaluation. *J. Hepatology*. 65:17-25. DOI:[10.1016/j.jhep.2016.02.007](https://doi.org/10.1016/j.jhep.2016.02.007)
4. Martin NK, **Hickman M**, Hutchinson SJ, Goldberg D, **Vickerman P**. (2013). Combination Interventions to Prevent HCV Transmission among People Who Inject Drugs: Modeling the Impact of Antiviral Treatment, Needle and Syringe Programs, and Opiate Substitution Therapy. *Clinical Infectious Diseases*, 57(2): S39-45. DOI:[10.1093/cid/cit296](https://doi.org/10.1093/cid/cit296)
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6. **Trickey A, Fraser H, Lim A, Walker J**, Peacock A, College S, Leung J, Grebely J, Larney S, Martin NK, Degenhardt L, **Hickman M, May MT, Vickerman P**. (2019). Modelling the potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional and country levels: A modelling study. *J. Viral Hepatitis*, 26:1388-1403. DOI:[10.1111/jvh.13187](https://doi.org/10.1111/jvh.13187)
7. **Trickey A, Fraser H, Lim A**, Peacock A, College S, **Walker J**, Leung J, Grebely J, Larney S, **Martin N, Hickman M**, Degenhardt L, **May MT, Vickerman P**. (2019). The Contribution of Injection Drug Use to Hepatitis C Virus Transmission Globally, Regionally, and at Country Level: A Modelling Study. *Lancet Gastroenterol Hepatol*, 4(6), 435-44. DOI:[10.1016/S2468-1253\(19\)30085-8](https://doi.org/10.1016/S2468-1253(19)30085-8)

## 4. Details of the impact

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Globally, HCV affects 71 million infected individuals and causes 400,000 deaths each year. UoB research has made an important contribution to reducing this burden through research that has defined effective and cost-effective interventions that has underpinned the development of global and national strategies to manage and eliminate HCV. These have led to measurable improvements in patient health.

### Impact on HCV prevention guidelines

UoB research strengthened the weak evidence for the impact and cost-effectiveness of opioid substitution therapy and needle and syringe programmes. This evidence has been central to HCV prevention guidelines around the world [D,E,Hi,Ii]. In the UK, UoB's modelling and evidence synthesis underpins UK National Institute for Health and Care Excellence (NICE) Public Health Guidance (2008 and 2014) on needle and syringe programmes and has influenced recent recommendations for the crucial role of needle and syringe programmes and opioid substitution therapy for achieving HCV elimination in England (2019) [E], Scotland (2019) [Ii] and Georgia (2017) [Hi]. It has also underpinned recommendations to scale-up needle and syringe programmes in the US (2019) [D].

### Impact on HCV treatment guidelines

UoB research on the impact and cost-effectiveness of HCV treatment as prevention among PWID and MSM has been instrumental in changing HCV-treatment guidelines globally. In 2017, WHO commissioned modelling research from UoB, which showed that a 'treat-all' policy would achieve prevention benefits; this formed part of the evidence used to change WHO's HCV treatment guidelines published in 2018 [C] to a treat-all policy. These new guidelines contrasted with prior guidance that had restricted HCV treatment to people based on disease stage. Further, the European Association for the Study of the Liver (2018) [A], and the American Association for the Study of Liver Disease (2020) [B] have both primarily used UoB modelling evidence to advocate for the prevention benefits of HCV treatment and to recommend treatment for patient groups at risk of re-infection, including PWID [A,B] and MSM [A].

These new treatment guidelines have been central to development of national HCV elimination strategies in Georgia, Scotland and Australia, which now recommend the prioritisation of HCV treatment to PWID alongside scaling up other prevention interventions [Hi,Ii, Ji].

### Impact on elimination strategies

UoB research uncovered the extent to which treatment and prevention scale-up will be needed to reduce HCV-transmission to negligible levels in different global settings. In particular, the research was crucial for the WHO 2016 Global Health Sector Strategy (GHSS) on Viral Hepatitis [Fi], which proposed the elimination of viral hepatitis as a major public health threat by 2030. Our modelling showed elimination was possible by 2030 and was used to produce the prevention and treatment targets needed for eliminating HCV as proposed by WHO [Fii]. The WHO strategy to eliminate HCV has been instrumental for many countries developing National HCV elimination initiatives (124 by February 2019 [Fiii]), resulting in substantial increases in treatment in many countries (including Georgia and Australia, see Figure 1) and globally [Fiii]. Our prevention and treatment targets are the foundation for all National HCV elimination initiatives.

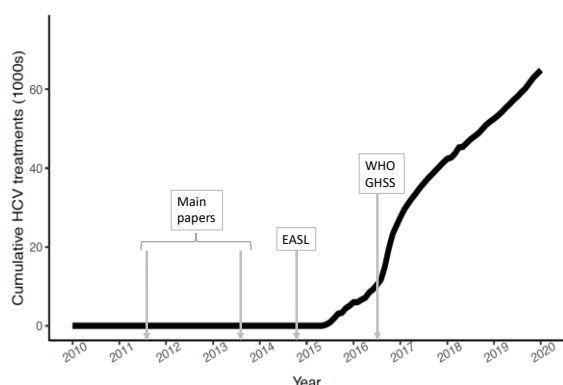
UoB research has also guided HCV elimination programmes in Georgia (through their yearly technical advisory group) [Hi,Hii], Scotland (strategy cites nine UoB studies) [Ii], Australia (strategy cites UoB research (1) as primary evidence for using HCV treatment as a prevention strategy among PWID) [Ji] and Pakistan [G]. The UoB researchers presented their findings on how to optimise the costs of achieving HCV elimination in Pakistan at an invitation-only Technical Meeting for World Hepatitis Day in 2019. This policy-shaping meeting was hosted by WHO and the Pakistan Ministry of National Health Services, Regulations and Coordination (NHSRC). The outcome of the Meeting was the Islamabad Declaration for Hepatitis Elimination 2019 and an official announcement by Dr Arif Alvi (President of Pakistan) of a Prime Minister's plan for eliminating viral hepatitis in Pakistan [Gii]. Our work has supported Pakistan's treatment targets and budget requirements for achieving HCV elimination, published in Lancet Global Health (5) with associated press articles in all major English language newspapers in Pakistan [Giii].

## Impact case study (REF3)

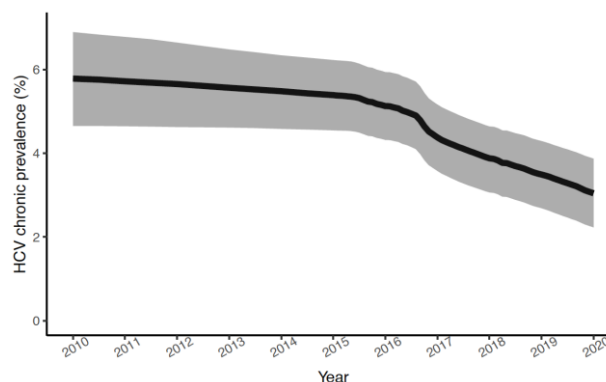
## Impacts on patient health

There is empirical evidence from Scotland and Australia that national elimination strategies, underpinned by UoB's research, have had a profound effect on the number of PWID who have been treated over time (Fig.1). Emerging data from Scotland shows that after four years of treatment scale-up in Tayside (2017-2020; Fig.1e/f), chronic HCV prevalence fell by 71% among PWID, as motivated and predicted by UoB research [Iii]. Similarly, chronic HCV prevalence decreased by 42% in the first two years (2016-2017; Fig.1c/d) of scaling up HCV treatment in Australia [Jii]. In Georgia, our modelling suggests chronic HCV prevalence has reduced by 37% and mortality by 14% by February 2019 (Fig.1a/b) as published in Lancet Global Health [Hii].

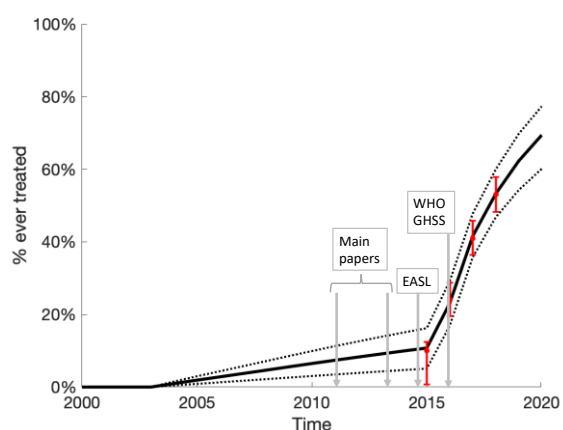
(a) Georgia treatment scale-up



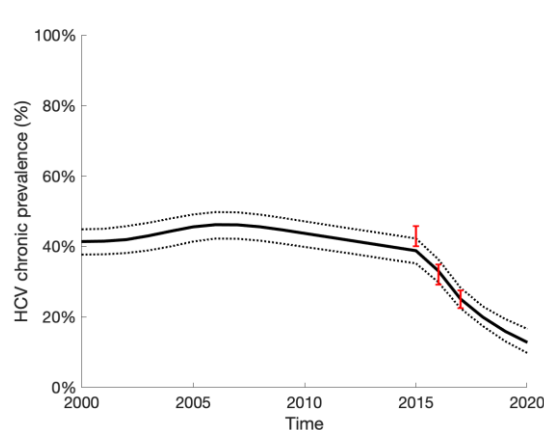
(b) Chronic prevalence in Georgia



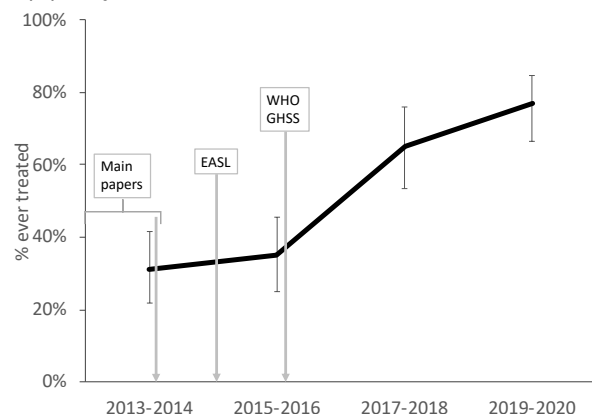
(c) Australia treatment scale-up in PWID



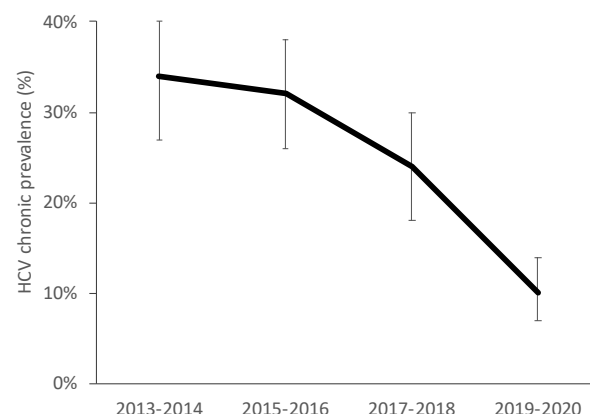
(d) Chronic prevalence in PWID in Australia



(e) Tayside treatment scale-up in PWID



(f) Chronic prevalence in PWID in Tayside



**Figure 1:** Treatment scale-up and impact in **Georgia** (a and b; modelling from [Hii]), **PWID in Australia** (c and d; data adapted from [Jii]), and **PWID in Tayside, Scotland** (e and f; extension of data from [Iii]). Treatment figures also show dates over which our initial **Main papers** were published (2011-2013), when **EASL** (European Association for the study of the Liver) first recommended treating PWID (August 2014), and when WHO published their Global Health Strategy to eliminate HCV (June 2016; **WHO GHSS**).

## 5. Sources to corroborate the impact

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- [A] European Association for the study of the Liver (EASL) (2018). [Recommendations on Treatment of Hepatitis C](#). See refs 216-218, 253 and 254 (p.35), including (2) and (4) above. *Our studies are used as main evidence for prevention benefits of treating PWID, and that this can result in achieving elimination if also scale up needle and syringe programmes.*
- [B] American Association for the Study of Liver Disease (AASLD) (2020). [HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C](#). See pp.194-197 (3 papers by Martin and Fraser, including 2 and 4 above) for Guidelines for PWID and pp.201 (2 papers by Martin) for Guidelines for MSM. *Our studies are used as main evidence for showing treating MSM or PWID can have impact and be cost-effective.*
- [C] WHO (2018). [Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Virus Infection](#). See p.viii for acknowledgement of UoB's modelling and web Annex 4 for our modelling as in ref (6) above.
- [D] CDC (2019). [Summary of Information on The Safety and Effectiveness of Syringe Services Programs \(SSPs\)](#). See refs 8 and 22 (1 and 4 above) - evidence for benefits of SSP for HCV.
- [E] PHE (2019). [Hepatitis C in England 2019 Working to eliminate hepatitis C as a major public health threat](#). See refs 44, 48 and 49 (p.27), including (1) above.
- [F] i) WHO (2016). [Global Health Sector Strategy on Viral Hepatitis 2016-2021. Towards Ending Viral Hepatitis](#). UoB modelling used to develop the strategy to eliminate HCV as discussed in the WHO testimonial letter [Fii].  
 ii) WHO (2020). Testimonial letter - Unit Head, Strategic Information, Analysis and Data Use HIV, Hepatitis and STI Department  
 iii) WHO (2019). Presentation: [Global progress towards hepatitis elimination – An update](#) Slide 5 gives increasing number of countries that have a national hepatitis plan and slide 7 gives increase in global treatments from 2015 to 2017.
- [G] i) The Economist Intelligence Unit (2019). [A Renewed Commitment: Pakistan's policy response to hepatitis B and C](#). See p.4 modelling as in ref (5) above.  
 ii) WHO (2019). Press release: [15 million people affected with hepatitis B and C in Pakistan: Government announces ambitious plan to eliminate hepatitis](#)  
 iii) Media reports for ref (5).
- [H] i) Georgia's Ministry of Labour, Health, and Social Affairs (2017). [National Hepatitis C Virus Elimination Progress Report, 2015-2017](#). See pp.69-70 for UoB modelling results, and recommendation 2A.1 on page 16.  
 ii) Walker J,... Vickerman P (2020). Interim effect evaluation of the hepatitis C elimination programme in Georgia: a modelling study. *Lancet Global Health*, 8(2): e244-e253. DOI:[10.1016/S2214-109X\(19\)30483-8](#)
- [I] i) Health Protection Scotland (2019). [Scotland's Hepatitis C Action Plan: Achievements of the First Decade and Proposals for a Scottish Government Strategy \(2019\) for the Elimination of both Infection and Disease](#) Nine UoB studies (including 2 and 4 above) cited advocating for prevention and treatment interventions among PWID for achieving elimination.  
 ii) Hickman et al. (2019). Evaluating the Population Impact of Hepatitis C Direct Acting Antiviral Treatment as Prevention for People Who Inject Drugs (Epitope) - a Natural Experiment (Protocol). *BMJ Open*, 9(9): e029538. DOI:[10.1136/bmjopen-2019-029538](#)  
 iii) Palmateer et al. (2020). Reductions in the population prevalence of HCV viraemia among people who inject drugs associated with scale-up of direct-acting antiviral therapy in community drug services: Real world data. Unpublished. *Two papers present data showing decline in HCV prevalence among PWID when scale up treatment and our modelling that underpinned this.*
- [J] i) Gastroenterological Society of Australia (2018). [Australian recommendations for the management of hepatitis C virus infection: a consensus statement \(September 2018\)](#). UoB research (2) is ref 5 (p.4).  
 ii) Iversen et al. (2019). Association between Rapid Utilisation of Direct Hepatitis C Antivirals and Decline in the Prevalence of Viremia among People Who Inject Drugs in Australia. *J Hepatol*, 70(1): 33-39. DOI:[10.1016/j.jhep.2018.09.030](#) Paper presents data showing decline in HCV prevalence among PWID when scale up treatment