Institution:
Glasgow Caledonian University (GCU)

Unit of Assessment:
3: Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study:
Major reduction in hepatitis C infected people presenting with serious liver disease following an evidenced-based public health strategy in Scotland

Period when the underpinning research was undertaken:
2013-2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Prof Sharon Hutchinson	Professor of Epidemiology	2013 to date
Prof David Goldberg	Professor of Public Health	2013 to date
Dr Hamish Innes	Research Fellow	2013 to date
Dr Scott McDonald	Research Fellow	2013 to date
Dr Esther Aspinall	Senior Clinical Fellow	2013 to date
Dr Norah Palmateer	Senior Research Fellow	2016 to date
Dr Kevin Pollock	Senior Research Fellow	2018 to 2019
Dr Alan Yeung	Research Fellow	2019 to date
Heather Valerio	Research Associate	2013 to 2018
Shanley Smith	Research Associate	2016 to date

Period when the claimed impact occurred:
2015–2020

Is this case study continued from a case study submitted in 2014?
No

1. Summary of the impact

Professors Hutchinson and Goldberg established a research programme on hepatitis C virus (HCV) that has shaped Scotland's public health response and led to major health benefits. Their epidemiological studies and modelling– addressing the knowledge gap in how to scale-up therapy for greatest health gain– underpinned Scottish Government's HCV strategy and setting of targets on treatment. HCV treatment targets have been met, and lead to reductions in liver-related failure (67%), cancer (69%) and death (49%). Over 300 cases of liver failure have been averted in the first four years of the national HCV strategy, translating to £30million saving to the NHS.

2. Underpinning research

The research has been led by Professors Hutchinson and Goldberg at GCU, and funded through collaborative research grants with Health Protection Scotland (HPS, a division of NHS Scotland) totalling over £2.5 million during 2013-2020 [G1-G3]. An aim of these grants was to inform Scottish Government's strategy on HCV through a combination of mathematical modelling and epidemiological studies evaluating interventions to prevent infection and disease. These grants have funded 14 researchers and yielded 115 peer-reviewed journal articles during 2013-20; ten of these researchers are listed above, having either led or contributed to selected papers [R1-R6].

During 2013-15, Hutchinson and Innes employed mathematical modelling to inform Scottish Government's strategy on new highly-effective HCV interferon-free therapies [R1]. A Markov simulation model was created to forecast the population-level impact of different prioritisation strategies for scaling-up these new but expensive HCV therapies; while the model was parameterised to Scotland, the findings were translatable to other resource rich countries. Key

strengths of the work included a) a synthesis of a vast array of observational data from Scotland's surveillance systems (lacking elsewhere) to parameterise the model, and b) the adoption of a dynamic approach (rarely employed in previous HCV studies due to complexity) modelling both transmission and disease progression simultaneously. Results indicated that treatment of HCV-infected patients with moderate/severe liver disease needed to be increased 3-fold to make a 75% reduction in incidence of HCV-related liver failure within 5 years. This key finding directly informed Government's policy (2015) on prioritising the new therapies to those with moderate/severe liver disease and new national targets for HCV treatment and disease.

The GCU team have also been at the forefront of research examining the clinical benefit of HCV antiviral therapy. During 2013-15, research led by Innes and Hutchinson involved (i) comprehensive statistical analysis of liver and non-liver related outcomes associated with treatment for a large real-world national cohort, and (ii) a Markov-chain Monte Carlo simulation of the patient-important benefits of treatment [R2,R3]. Evidence from these studies - that the short-term benefit of therapy was greatest for patients with moderate/severe liver disease - further informed Scottish Government's HCV treatment strategy (2015).

During 2015-20, the GCU team have evaluated the impact of the Scottish strategy to prioritise new HCV therapies to those with moderate/severe liver disease. Through record-linkage and statistical analysis of population-level surveillance data and individual-level clinical cohort data (lacking elsewhere), Hutchinson and Goldberg demonstrated the first country-level evidence of major population impact of the new HCV therapies to reduce (and avert) presentations of liver failure [R4]. Further, McDonald and Hutchinson showed that clearance of HCV infection following treatment with the new therapies was associated with a lower risk of severe liver complications (including liver cancer) and improved survival among patients with cirrhosis [R5].

In recognition of the insights of international relevance from GCU's research on HCV, Hutchinson was commissioned by the International Journal of Drug Policy to review the Scottish experience of translating research on treatment and management of HCV infection into public health policy and impact [R6].

3. References to the research

The research, funded by NHS Scotland via Health Protection Scotland [G1,G2,G3], provided the evidence to inform the national public health response to Hepatitis C in Scotland. The research involved advanced statistical analysis of public health surveillance data, including novel record-linkage and national clinical cohort studies to inform the extent and nature of hepatitis C infection in Scotland, and the effectiveness of antiviral treatments [R2,R4,R5,R6]. Our research is unique in its analysis of national clinical data – covering all clinics across the country, lacking elsewhere – to determine the 'real-world' effectiveness of therapies and thus is not subject to selection biases of most other studies confined to specialist academic centres. Our analysis yielded the most comprehensive understanding of clinical benefit of HCV therapies, with a large sample size and in excess of 5 years per-patient follow-up afforded the statistical power for the first examination of a diverse range of outcome events in different patient groups (vis-à-vis mild versus moderate/severe liver disease) [R2]. Major strengths of the mathematical modelling work for Scotland was the synthesis of a vast array of observational data from these surveillance systems and clinical cohort data to parameterise the model [R1,R3]. Further the adoption of a dynamic modelling approach to robustly account for HCV transmission and disease progression simultaneously [R1], in contrast to previous models focussing on one of these outcomes, was a key advancement that provided crucial insight to healthcare policymakers. Our recent research "provided the first evidence of a major population impact of new direct-acting antiviral therapies in averting HCV-related decompensated cirrhosis [liver failure]" [R4], and was selected as part of the Best at the International Liver Congress (involving over 10,000 delegates) in 2018 [C6] and was the subject of a keynote presentation at the First WHO Europe Regional meeting on Viral Hepatitis [C9]. The research has been published in leading hepatology journals (including the BMJ journal Gut and Journal of Hepatology, both with an impact factor of 20).

Peer-reviewed Research Papers:

- [R1] Innes H, Goldberg D, Dillon J, Hutchinson SJ. Strategies for the treatment of Hepatitis C in an era of interferon-free therapies: what public health outcomes do we value most? Gut. 2015 Nov; 64(11): 1800-9. https://doi.org/10.1136/gutjnl-2014-308166

- [R2] Innes HA, McDonald SA, Dillon JF, Allen S, Hayes PC, Goldberg D, Mills PR, Barclay ST, Wilks D, Valerio H, Fox R, Bhattacharyya D, Kennedy N, Morris J, Fraser A, Stanley AJ, Bramley P, Hutchinson SJ. Toward a more complete understanding of the association between a hepatitis C sustained viral response and cause-specific outcomes. Hepatology. 2015 Aug; 62(2):355-64. https://doi.org/10.1002/hep.27766

- [R3] Innes H, Goldberg D, Dusheiko G, Hayes P, Mills PR, Dillon JF, Aspinall E, Barclay ST, Hutchinson SJ. Patient-important benefits of clearing the hepatitis C virus through treatment: a simulation model. J Hepatol. 2014 Jun;60(6):1118-26. https://doi.org/10.1016/j.jhep.2014.01.020

- [R4] Hutchinson SJ, Valerio H, McDonald SA, Yeung A, Pollock K, Smith S, Barclay S, Dillon JF, Fox R, Bramley P, Fraser A, Kennedy N, Gunson R, Templeton K, Innes H, McLeod A, Weir A, Hayes PC, Goldberg D. Population impact of direct-acting antiviral treatment on new presentations of hepatitis C-related decompensated cirrhosis: a national record-linkage study. Gut. 2020 Dec; 69(12): 2223-2231. https://doi.org/10.1136/gutjnl-2019-320007

- [R5] McDonald SA, Pollock KG, Barclay ST, Goldberg DJ, Bathgate A, Bramley P, Dillon JF, Fraser A, Innes HA, Kennedy N, Morris J, Went A, Hayes PC, Hutchinson SJ. Real-world impact following initiation of interferon-free hepatitis C regimens on liver-related outcomes and all-cause mortality among patients with compensated cirrhosis. J Viral Hepat 2020 Mar; 27(3): 270-80. https://doi.org/10.1111/jvh.13232

- [R6] Hutchinson SJ, Dillon JF, Fox R, McDonald SA, Innes HA, Weir A, McLeod A, Aspinall EJ, Palmateer NE, Taylor A, Munro A, Valerio H, Brown G, Goldberg DJ. Expansion of HCV treatment access to people who have injected drugs through effective translation of research into public health policy: Scotland's experience. Int J Drug Policy. 2015 Nov;26(11):1041-9. https://doi.org/10.1016/j.drugpo.2015.05.019

Research Grants awarded to Hutchinson as PI to inform and evaluate Scotland's strategy on Hepatitis C and other blood borne viruses:

- [G1] Hutchinson SJ (PI), Goldberg DJ. Analytical research to inform on the effectiveness of services to prevent, diagnose and treat blood borne viruses in Scotland using data collected as part of the Scottish Government's Sexual Health & BBV Framework (2015-2020). (Funded by Health Protection Scotland, 2015-2020, £1,805,110)

- [G2] Hutchinson SJ (PI), Goldberg DJ. Research to estimate the number of people in Scotland to be initiated onto antiviral therapy for hepatitis C. (Funded by Health Protection Scotland, 2013-2015, £75,000)

- [G3] Hutchinson SJ (PI), Goldberg DJ. Analytical research to inform on the effectiveness of services to prevent, diagnose and treat blood borne viruses in Scotland using data collected as part of the Scottish Government's Sexual Health & BBV Framework. (Funded by Health Protection Scotland, 2013-2015, £709,720)

4. Details of the impact

The GCU research directly informed Scottish Government (SG) health policy on HCV, specifically on the scale-up of new therapies and setting of National Targets on treatment and

disease in 2015. This evidence-based strategy led to changes in treatment practice that is estimated to have averted over 300 cases of liver failure in Scotland in the first 4 years, translating to ~£30 million saved by NHS Scotland. Evaluation of the clinical impact of these new therapies by the GCU team has informed the latest SG strategy published in 2019 to eliminate HCV by 2024.

Impact Pathway: In 2014, SG established an expert advisory group– Hepatitis C Treatment and Therapies Group– to provide recommendations on the delivery of new HCV therapies. GCU researchers chaired (Goldberg) and were members (Hutchinson and Innes) of this group [C1, page 14]. Hutchinson was funded by Health Protection Scotland (HPS) to undertake research to inform the group [G2,G3]. In late 2014, key stakeholders (150 service users and providers) were consulted at a National Symposium on the research findings and recommendations of the advisory group [C1 (page 2)]; GCU researchers chaired and presented at the event. The report of the advisory group [C1] was adopted as policy by SG in 2015 (see below). Thereafter, Hutchinson was funded to evaluate the impact of these new therapies on clinical practice and outcomes [G1]; the findings [R4,R5] summarised below underpin Scotland's latest policy to eliminate HCV by 2024 (see below) [C3].

Impact on Scottish Health Policy (2015): SG first published a report from the Hepatitis C Treatment and Therapies Group in 2015 [C1], which recommended prioritisation of the new therapies to those with moderate/severe liver disease and new national targets on (a) numbers to be treated (50% increase to 1,500 in 2015/16, and rising thereafter to 2,000 by 2018/19) and (b) reductions in new presentations of HCV-related liver failure (75% reduction by 2020). The prioritised approach and new targets were set based on the GCU mathematical modelling [R1]. Government policy documents [C1 pages 10-13; C2 pages 36-37] reference the GCU research [R1,R2,R3,R6] and state: "Modelling work undertaken by GCU estimates that a minimum of 1500 treatment initiates per year during 2015-2020 is required to stand a chance of reducing the number of new liver failure presentations from the current level of nearly 200 to 50 by 2020" and that "of the annual number of people initiated onto antiviral therapy, 1500 should belong to the F2-F4 liver fibrosis category [i.e. moderate/severe liver disease] at time of treatment".

Impact on Clinical Practice and Outcomes (2015-2018): The SG National Target on treatment, informed by GCU research [R1], has been exceeded each year between 2015/16 and 2018/19 [C3, pages 14-15]. In the four years since the introduction of the new therapies, ~6,900 people were initiated on treatment in Scotland and an estimated 6,100 persons were cured of their HCV infection (i.e. no longer at increased risk of liver disease) [C5,R4]. In line with the Government's policy [C1], the scale-up in new therapies was greatest for those with severe liver disease (cirrhosis): ~1,800 initiated in the first 4 years with 1,600 estimated to have achieved cure, representing a 3.2-fold and 5.9-fold rise respectively compared to the 4 years prior to the new therapies [C5,R4]. As a result of the major scale-up in therapy among those with severe liver disease and as predicted by the GCU modelling [R1], the numbers presenting to hospital with chronic HCV-related liver failure reduced by 67% between 2014 and 2018 [C5,R4]. Through time-series analysis published in the BMJ journal Gut, an estimated 330 cases of liver failure have been averted in Scotland since the introduction of new therapies [C5,R4]. The life-time cost of managing a case of liver failure is ~£95,000, thus the 330 cases averted translates to ~£30 million expense avoided to the NHS [C3]. Further, surveillance data also shows that presentations of HCV-related liver cancer have reduced by 69% and HCV-related deaths have reduced by 49% [C3].

Impact on Scottish Health Policy (2019): GCU research [R4,R6] demonstrating impact of HCV therapies on clinical outcomes has informed Scotland's recent HCV Elimination strategy [C3], where SG has endorsed new targets to eliminate HCV infection and disease by the year 2024 [C4], in advance of the WHO global target by 2030. Scotland's evidenced-based strategy on HCV and associated clinical impact has been recognised as best practice at the International Liver Congress [C6], by the World Innovation Summit on Health [C7,C8] and WHO Europe [C9,C10].

5. Sources to corroborate the impact

- [C1] The Scottish Government Hepatitis C Treatment and Therapies Group Report 2015 (http://www.hepatitisscotland.org.uk/files/2814/4431/5598/treatment_and_therapies_group.pdf) references the GCU research [R1,R2,R3,R6] on page 11, and lists that GCU researchers (Goldberg (chaired), Hutchinson and Innes) as members of the Advisory Group on page 12.
- [C2] The Scottish Government Sexual Health and Blood Borne Virus Framework 2015-2020 (www.gov.scot/publications/sexual-health-blood-borne-virus-framework-2015-2020-update/) references the GCU research on page 36 [R1] and page 37 which states "Reports published in the world's leading liver disease journals have not only informed and evaluated policy and practice in Scotland, but internationally" [R6].
- [C3] Scotland's HCV Elimination Strategy (2019-2024) references the key GCU research [R1-R6] in respect of impact on clinical practice and outcomes (pages 5 and 14-19) (https://hpspubsrepo.blob.core.windows.net/hps-website/nss/2840/documents/1_hcv-elimination-Scotland-v2.pdf). Pages 17, 18 and 22 highlight the life-time cost of managing a case of liver failure (i.e. £95,000) and "potential avoidance of in excess of £30 million to the NHS in caring for patients with liver failure" from the estimated 330 cases averted through the scale-up in new therapies (and references the paper [R4] by GCU published in Gut in 2020).
- [C4] Scottish Government's press release 'Eliminating hepatitis C' (https://www.gov.scot/news/eliminating-hepatitis-c/) in which Scotland's Public Health Minister endorses the above report [C3] and commits to increase the number of people treated for HCV to at least 3,000 annually from 2020 to eliminate the condition by 2024.
- [C5] The research paper [R4] is peer-reviewed evidence detailing the impact on clinical practice and clinical outcomes: Hutchinson SJ, et al. Population impact of direct-acting antiviral treatment on new presentations of hepatitis C-related decompensated cirrhosis: a national record-linkage study. Gut. 2020 Dec; 69(12): 2223-2231. doi: 10.1136/gutjnl-2019-320007 (https://gut.bmj.com/content/gutjnl/69/12/2223.full.pdf)
- [C6] Hutchinson's presentation on Scotland's HCV strategy and impact was selected as part of the Best at the International Liver Congress in 2018 (Slide 23 in https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Feasl.eu%2Fwp-content%2Fuploads%2F2018%2F09%2FBest-of-ILC2018-Viral-hepatitis_FINAL.pptx)
- [C7] Scotland's HCV strategy is in the 2018 report on Viral Hepatitis for the World Innovation Summit on Health: https://www.wish.org.qa/wp-content/uploads/2018/11/IMPJ6078-WISH-2018-Viral-Hepatitis-181026.pdf. On page 7, the Scottish Minister for Public Health MSP Aileen Campbell is quoted as saying "The Scottish Government's investment in the new highly effective hepatitis C therapies has led to a major reduction in people presenting with the life-threatening consequences of this disease. This will create considerable future savings for healthcare".
- [C8] Scotland's evidenced-based strategy to HCV is recognised in this peer-reviewed paper: Schröeder SE, Pedrana A, Scott N, et al. Innovative strategies for the elimination of viral hepatitis at a national level: A country case series. Liver Int. 2019 Oct; 39(10): 1818–1836. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6790606/pdf/LIV-39-1818.pdf
- [C9] Hutchinson's keynote presentation of the impact of Scotland's HCV strategy at the First WHO Regional meeting on Viral Hepatitis is referenced by WHO here: http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/news/news/2019/3/first-regional-consultation-on-viral-hepatitis-in-europe-shows-progress-and-reaffirms-countries-commitment-to-elimination
- [C10] Scotland's evidenced-based HCV strategy and impact is included in WHO Europe's 'Compendium of good practices in the health sector response to viral hepatitis in the WHO European Region' (pages 91-95) https://apps.who.int/iris/bitstream/handle/10665/333494/9789289055161-eng.pdf?sequence=1&isAllowed=y