Institution: Queen Mary University of London		
Unit of Assessment: 1		
Title of case study: Eliminating Hepatitis C with Effective Treatment and Priority Screening		
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:**
1) Graham Foster	1) Professor of Hepatology	1) 01/2003 - present
2) Meleri Jones	2) Laboratory Manager	2) 08/2013 - present
Period when the claimed impact occurred: August 2013 - 2018		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

The World Health Organization (WHO) has issued targets to eliminate Hepatitis C Virus (HCV) by 2030 and Queen Mary's Prof. Foster is the national clinical lead for achieving these. Foster's work has revealed the aggressive nature of genotype 3 HCV, previously thought of as being 'easy to cure'. To address this, he led bespoke treatment trials that successfully defined optimal and effective regimes and have helped shape both national and international guidelines on a) HCV treatment and b) which subgroups to prioritise in HCV screening. In England, this led to an Expanded Access Programme, followed by general access, with Foster as national clinical lead. The policy is the largest ever single NHS investment in specialist services. The programme has mobilised 22 Operational Delivery Networks and successfully treated over 50,000 patients. The Public Health England HCV annual report for 2020 indicates a 20% and 44% fall in deaths and transplant listings for HCV respectively, and a 95% success rate in 'curing' patients of the virus. Foster's team has also developed a screening test for novel mutations that reduce the effectiveness of antiviral treatments, further improving HCV outcomes.

2. Underpinning research (indicative maximum 500 words)

The Hepatitis C virus (HCV) is one of the most common forms of viral hepatitis in the UK, and can cause liver scarring (cirrhosis) and failure. It has developed genetic mutations — categorised as different genotypes — over time, leading to several different manifestations of the infection. These genotypes have varying rates of prevalence in different populations, and not all respond well to treatment. 'Genotype 3' comprises of 22-30% of all HCV, and therefore is the second commonest genotype, and is even more prevalent in England and South Central Asia, at 47% and 71.6% respectively.

Prof. Foster's work on the natural history and prevalence of genotype 3 HCV has shown that:

Immigrants, not previously considered a high-risk group for this virus, have a high prevalence of infection and cirrhosis

1. *Novel viral mutations, which reduce the effectiveness of antiviral treatments, can be identified through screening* [3.1]. Foster's team, which included the PhD students Michelle Cheung and Peter Wing, has developed a test for mutations to the variant and now show that the genotype 3 mutation is associated with cellular changes associated with malignancy. This work led to a GBP2,700,000 Wellcome Trust grant to study, among other areas, this variant [EQR.1].

2. *Genotype 3 is a more aggressive strain than previously thought*. Prior to Foster's research, genotype 3 infection was regarded as 'easy to cure'. In 2013, therapy for HCV infection involved injectable 'interferon' and tablets with a high incidence of side effects. The team found that genotype 3 HCV and cirrhosis responded poorly to standard HCV interferon-based treatments, highlighting the need for genotype-specific HCV trials.

As a result of these findings, biopharmaceutical company Gilead Sciences Inc., who hold the licence for the latest HCV treatment sofosbuvir, approached Foster to lead an exploratory UK-

based study into overcoming the reduced response to the treatment seen in genotype 3 HCV. This study identified possible combinations of treatments alongside sofosbuvir that could improve treatment response [3.2]. Foster then led an international phase 3 trial in genotype 3 HCV with a newly developed combination of sofosbuvir/velpatasivir, which achieved a far greater response rate in patients [3.3]. Foster also led trials for the alternative therapeutic glecaprevir/pibrentasvir, which achieved a high response rate in patients with genotype 3 HCV without cirrhosis [3.4, 3.5].

Led by Foster, the English Expanded Access Programme achieved the first real-world confirmation that these treatments are effective and can improve life expectancy in patients with severe (decompensated) cirrhosis. Data for this programme were collected from the Medical Research Foundation (MRF)-funded HCV Research UK registry and biobank [EQR.2, 3.6]. Eligible patients were those at significant risk of death or irreversible damage from HCV infection within 12 months, irrespective of genotype. As a result, Foster's research has not only identified the most effective regimes for treatment of genotype 3 HCV, but also forms the basis of current treatment recommendations globally.

3. References to the research (indicative maximum of six references)

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chronic hepatitis C and decompensated cirrhosis. *Journal of Hepatology, 64* (6), 1224-1231. https://doi.org/10.1016/j.jhep.2016.01.029

Evidence of the quality of the research

[EQR.1] Foster, G. R. [Principal Investigator]. (2021-2025). Treating hepatitis C in Pakistan. Strategies to avoid resistance to antiviral drugs. *Wellcome Trust*. NIHR-Wellcome Trust Partnership for Global Research Collaborative Award. GBP2,791,488.

[EQR.2] Foster, G. R. [Co-Investigator]. (2011-2016). Establishment of a Resource for Long-Term Study of Hepatitis C Virus Infection in the UK [MC_EX_UU_G1000717]. *Medical Research Foundation*. Infrastructure Grant. GBP616,670.

[EQR.3] Foster, G. R. [Principal Investigator]. (2012-2017). Chronic viral hepatitis in ethnic minorities. Strategies to prevent the predicted increase in mortality [RP-PG-1209-10038]. NIHR. Research Programme Grant. GBP2,001,747.

[EQR.4] Foster, G. R. [Co-Investigator]. (2013-2018). Stratified Medicine to Optimise Treatment for Hepatitis C Virus Infection [MR/K01532X/1]. *MRC*. Research Grant. GBP4,168,144.

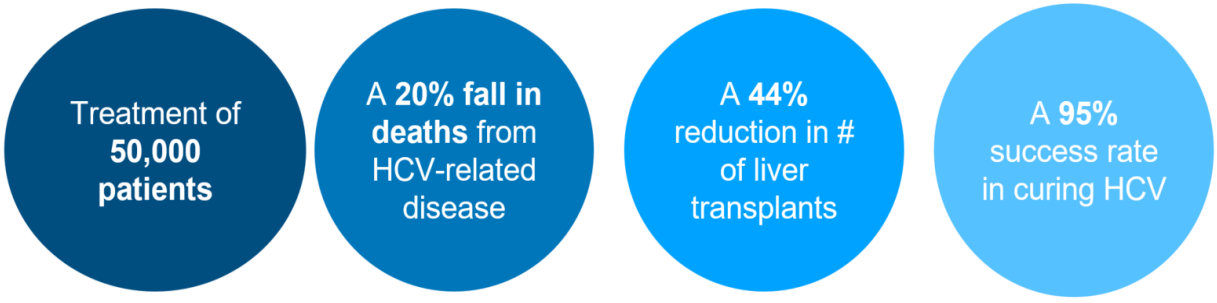
4. Details of the impact (indicative maximum 750 words)

WHO has issued targets to eliminate HCV by 2030. Queen Mary's Prof. Foster is the national clinical lead for achieving these targets. Foster and his team at Queen Mary have led successful clinical trials to define optimal and effective treatment regimes for HCV, and developed a screening test to identify novel mutations that reduce the effectiveness of antiviral treatments. Foster's work has improved HCV treatment for patients, influenced national and international guidelines for clinical practice, informed NHS commissioning and investment, and helped make HCV treatment available and cost-effective throughout the NHS, with the overall aim of eliminating the disease in England.

Improving HCV treatment for tens of thousands of patients — and targeting elimination

Foster is the national clinical lead for NHS England's HCV policy, which aims to eliminate HCV and has been a success as evidenced in 2020 with over 50,000 patients treated, a 20% fall in the number of deaths from HCV-related disease, a 44% reduction in the number of liver transplants, and a 95% success rate in 'curing' people of the virus [5.1].

NHS England's HCV elimination policy has achieved…



Influencing national and international clinical guidelines for HCV
For management of genotype 3 HCV

Foster designed and led the UK-centred BOSON trial [3.2], which informed international guidelines — such as those of India and Iran in 2016 [5.2, 5.3] — for the management of difficult-to-cure genotype 3 HCV. Foster also led the international phase 3 trial in this genotype with the newly developed treatment combination of sofosbuvir/velpatasvir [3.3], which was approved by the European and American Associations for the Study of the Liver in 2016 and 2018 respectively [5.4, 5.5]. It was approved by the National Institute for Health and Care Excellence (NICE) in 2017 [5.6]. Foster also led the successful trials for the alternative

therapeutic glecaprevir/pibrentasvir; his work [3.5] was used in the clinical and economic assessment of the combined therapy and was approved by NICE in 2018 [5.7].

For primary care screening programs

Foster's team has influenced NICE guidelines on who to test for HCV; these now include screening migrants from high-risk countries in primary care settings [5.8], with other NHS initiatives including screening of South Asian subgroups.

Informing NHS commissioning policy and guiding annual investment

In 2014, Foster co-authored a UK consensus statement as a representative of the British Association for Study of the Liver; this informed NHS England's commissioning policy [5.9] and led to the largest ever single NHS investment in specialist services. Sponsored by the Scottish government, the statement represented the opinions of the British Society of Gastroenterology Liver Committee, British Association for the Study of Liver, Scottish Society of Gastroenterology, Scottish Viral Hepatitis group, Scottish Viral Hepatitis Nurses group and British Viral Hepatitis group. NHS England's HCV policy is based on NICE recommendations of patient prioritisation [5.10], and involves 22 Operational Delivery Networks.

Making HCV medication accessible and cost-effective through the NHS

To eliminate HCV in England, NHS England undertook a unique procurement tender in which pharmaceutical companies competed to provide medication and 'case-finding' initiatives for patients with HCV. Simon Stevens, chief executive of NHS England, said "It's not often that the opportunity arises to completely eradicate a disease, but now the NHS is taking practical action to achieve exactly that*"* [5.11]. Foster helped develop the partnership between the pharmaceutical company, Gilead Sciences Inc., and the Addiction Services Provider, ChangeGrowLive, as clinical expert. The partnership was awarded the Health Service Journal's 'Best Pharmaceutical Partnership with the NHS' award in 2019 (HSJ monthly unique users: 168,000) [5.12], which celebrates the most effective private or third-sector partnerships with the NHS that bring benefit to patients and NHS organisations. According to Sir Stevens, "the NHS's sophisticated and unashamedly rigorous negotiation on behalf of both patients and taxpayers means we've now been able to strike affordable deals with our life sciences partners to save many more lives and meaningfully cut health inequalities" [5.11]. Foster also helped facilitate the partnership between NHS England, the three major pharmaceutical companies Gilead, MSD and AbbVie, and The Hepatitis C Trust, of which he was formerly a trustee. The addition of the Hepatitis C Trust is critical to eliminating the disease nationally due to its network of trained peer volunteers, who help local treatment groups identify and engage with high risk individuals [5.13].

The deal offered a unique opportunity for all stakeholders — patient organisations, pharmaceutical companies, clinicians, prison healthcare and drug misuse services — to work together to *"*reach the most marginalised and hardest-to-engage; we will ensure that no one is left behind and stop unnecessary deaths*,"* said Rachel Halford, chief executive of The Hepatitis C Trust [5.11]. She added, "the Hepatitis C Trust is delighted with this development. 69 per cent of people who have the virus are currently undiagnosed so the funding in the deal to help find those with hepatitis C and support them into treatment is groundbreaking."

5. Sources to corroborate the impact (indicative maximum of 10 references)

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[5.8] NICE. (2016). *Who should I test for hepatitis C?* https://cks.nice.org.uk/topics/hepatitis-c/diagnosis/who-to-screen-test/

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