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Can community pharmacists treat hepatitis C virus?

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Andrew Radley and colleagues[1] present the findings of a real world, cluster-randomised controlled trial in *The Lancet Gastroenterology & Hepatology*, investigating the effects of pharmacists providing direct-acting antiviral drugs to people receiving opioid substitution treatment therapy in Scottish community pharmacies. In both study groups, community pharmacists offered opportunistic screening for hepatitis C virus (HCV) with dried blood spot tests to people receiving opioid substitution therapy. People were more than twice as likely to be cured of HCV if their test and direct-acting antiviral drug prescription was provided by their community pharmacist (intervention group) than if they were referred to a multidisciplinary team at a local treatment centre (conventional care group). In both groups, antiviral treatment was dispensed as daily modified directly observed therapy with opioid substitution therapy at the community pharmacy. The findings of this study are highly relevant, because increasing access to care for HCV is key to achieving the WHO 2030 elimination goals.[2]

The model of care for HCV in Scotland is unusual. Throughout most of Europe, prescription of direct-acting antiviral drugs is limited to specialist hepatologists and infectious disease physicians.[3] However, in Scotland, general practitioners, nurses, and pharmacists can also prescribe direct-acting antiviral drugs. It should be noted that the conventional care used as a comparator in Radley and colleagues' study[1] consisted of a community based, multidisciplinary service that included nurses who prescribed direct-acting antiviral drugs. It is likely that the intervention effect would have been greater if the study had been done in a region in which standard of care consisted of specialists prescribing from tertiary referral centres. Few countries have used community pharmacists as a means to reach people who would benefit from HCV testing and treatment. In the USA, pharmacists can provide direct-acting antiviral drugs if operating under a collaborative care agreement with a physician. Such models, in both the Veterans Affairs health-care network and in open systems, result in cure rates that are similar to those in specialist care.[4] For decades, pharmacists have provided essential care as part of community management of chronic disease. The role of pharmacists in the provision of pre-exposure prophylaxis for HIV is being investigated with the potential for expansion, and Radley and colleagues' study puts HCV testing and treatment on the agenda as well.[5]

A cornerstone of the viral hepatitis global health sector strategy is provision of equitable health service coverage to people in need. In many countries, people who inject drugs are the population most in need of HCV services. Substantive evidence now shows that, for many reasons, people who inject drugs are more likely to have HCV testing and treatment if these services are provided within a pre-existing health-care relationship in a familiar setting (eg, their drug and alcohol service, needle and syringe programme, general practice, community pharmacy) than if patients are referred to a new service.[6,7] Models of care that meet the needs of people who inject drugs are needed to achieve elimination of HCV in this important group of patients. Decentralised care also acts to mitigate against geographic inequity. French and Australian data have shown that people living in rural and regional areas where there are fewer specialists have lower rates of HCV treatment.[8,9] Lower-middle-income countries with few specialists would also be well served by task shifting to accessible health-care workers.

For the benefits of direct-acting antiviral drugs to be fully realised, models of care should target the needs of the people who are most likely to be infected. Studies have found that provision of community-based HCV treatment increases treatment uptake without compromising cure outcome.[6] Specialists should adapt in response to the evidence, be agents of change, and create collaborative networks with local health-care providers to support community-based HCV testing and treatment. Policy makers should act on the evidence and enable a broader workforce to provide direct-acting antiviral drugs.

Health-care systems have been impacted by the emergence of the COVID-19 pandemic. Before the pandemic, five countries were on track to deliver the WHO HCV elimination targets by 2030, and a further 12 were working towards elimination.[10] The ability to get on track, or stay on track, to eliminate HCV is now uncertain as treatment and harm reduction services adjust to the existence of severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2). Because access to hospital-based care is restricted, and many people fear attending hospital for non-COVID-19 related health problems, community-based HCV testing and treatment have become even more important. Now, more than ever, health-care workers and policy makers need to be collaborative, innovative, and determined to achieve the WHO vision—elimination of HCV as a public health threat.

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Ozanimod in Crohn's disease: a promising new player

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Over two decades since the introduction of infliximab, the drug armamentarium to treat patients with inflammatory bowel disease is still expanding, despite the implementation of new strategies to increase efficacy of current drugs, such as the avoidance of autoantibody formation by combination therapy and pro-active drug optimisation. Next to primary and secondary loss of response within the first year of therapy,[1] therapy side-effects and compliance issues contribute to the continuous need for newer and more selective drugs. Expanding therapeutic opportunities are enabled by improved insights into the dysregulated immune mechanisms that are important in the pathogenesis of inflammatory bowel disease.

In *The Lancet Gastroenterology & Hepatology*, Brian Feagan and colleagues describe the first results of the efficacy of ozanimod in Crohn's disease and show endoscopic, histological, and clinical improvements in their phase 2 uncontrolled STEPSTONE study.[2] The oral sphingosine 1-phosphate receptor modulator ozanimod selectively targets surface receptor isoforms 1 and 5, causing their degradation on the cell surface of lymphocytes and vascular endothelial cells. Subsequently, lymphocyte trafficking from lymph nodes to the circulation and site of inflammation is inhibited.[3,4]

The advantage of ozanimod is its oral administration, which minimises patients' burden related to subcutaneous injections and infusions. The STEPSTONE trial demonstrates that oral medication once daily benefits drug compliance at least in the first 12 weeks of treatment. Whether compliance is sustained after remission needs to be confirmed in phase 3 clinical trials.

The introduction of novel small molecules in inflammatory bowel disease treatment reopens research challenges in the era of drug physiology. Given that small changes in exposure can have clinically meaningful effects on efficacy and safety, research on the effect of patient-related factors influencing transit time and absorbing functionality of the gastrointestinal tract are, in addition to drug-related factors, relevant to optimise the delivery of adequate concentrations of ozanimod. In addition, on the basis of the observed differences in endoscopic outcomes between disease locations in the STEPSTONE trial, it could be hypothesised that ozanimod induces a local effect; however, more research is needed to the elucidate the possible presence of sphingosine 1-phosphate receptors in the intestinal epithelium.[5]