Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

benefit in efficacy, despite previous observational data suggesting the benefit of escalated ustekinumab dosing.[7] The results of an ongoing ustekinumab escalation prospective clinical trial (NCT03782376) will help clarify the effect of ustekinumab escalation.

Finally, the results of the STARDUST trial should not be seen as an argument to abandon the treat-to-target and tight control treatment paradigms in Crohn's disease. However, STARDUST raises important questions regarding the most effective strategies and populations that would most benefit from this approach. We eagerly await additional data in this area, including the REACT-2 trial (NCT01698307).

RCU has served as an advisory board member or consultant for AbbVie, Bristol Myers Squibb, Janssen, Pfizer, and Takeda; and has received research support from AbbVie, Boehringer Ingelheim, Eli Lily, and Pfizer. J-FC reports receiving research grants from AbbVie, Janssen Pharmaceuticals and Takeda; receiving payment for lectures from AbbVie, Amgen, Allergan, Ferring Pharmaceuticals, Shire, and Takeda; receiving consulting fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Eli Lilly, Ferring Pharmaceuticals, Galmed Research, GlaxoSmithKline, Geneva, Iterative Scopes, Janssen Pharmaceuticals, Kaleido Biosciences, Landos, Otsuka, Pfizer, Prometheus, Sanofi, Takeda, and TiGenix; and holds stock options in Intestinal Biotech Development. RCU is supported by an NIH K23 Career Development Award (K23KD111995-01A1).

*Ryan C Ungaro, Jean-Frederic Colombel
ryan.ungaro@mssm.edu

The Henry D Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York, USA (RCU, J-FC)

1 Colombel J-F, Narula N, Peyrin-Biroulet L. Management strategies to improve outcomes of patients with inflammatory bowel diseases. *Gastroenterology* 2017; **152:** 351–61.
2 Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. *Gastroenterology* 2021; **160:** 1570–83.
3. Danese S, Vermeire S, D'Haens G, et al. Treat to target versus standard of care for patients with Crohn's disease treated with ustekinumab (STARDUST): an open-label, multicentre, randomised phase 3b trial. *Lancet Gastroenterol Hepatol* 2022; published online Feb 1. https://doi.org/10.1016/S2468-1253(21)00474-X.
4 Colombel J-F, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. *Lancet* 2017; **390:** 2779–89.
5 Narula N, Wong ECL, Colombel J-F, et al. Early reduction in MM-SES-CD score after initiation of biologic therapy is highly specific for one-year endoscopic remission in moderate to severe Crohn's disease. *J Crohns Colitis* 2021; published online Oct 19. https://doi.org/10.1093/ecco-jcc/jjab183.
6 Waljee AK, Liu B, Sauder K, et al. Predicting corticosteroid-free biologic remission with vedolizumab in Crohn's disease. *Inflamm Bowel Dis* 2018; **24:** 1185–92.
7 Meserve J, Ma C, Dulai PS, Jairath V, Singh S. Effectiveness of reinduction and/or dose escalation of ustekinumab in Crohn's disease: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2021; published online Oct 8. https://doi.org/10.1016/j.cgh.2021.10.002.

Simplifying HCV treatment: a pathway to elimination and model for delivering health care to vulnerable populations

Published **Online** January 10, 2022 https://doi.org/10.1016/S2468-1253(21)00467-2

See **Articles** page 307

The availability of safe, effective, short-course, all oral direct-acting antivirals (DAAs) has opened the door to the possibility that chronic hepatitis C virus (HCV) infection could one day be eliminated. Consequently, in 2016, WHO set targets for the elimination of HCV as a public health threat by 2030. Achieving elimination without a vaccine requires that more than 80% of the 58 million people currently estimated to be living with chronic HCV worldwide are treated. With less than 10 years to go, the treatment gap remains enormous—only an estimated 21% of the global population with chronic HCV had been diagnosed and, of these, only 62% treated by the end of 2019.[1]

Progress towards HCV elimination has been hampered by the many steps required before HCV treatment is initiated and unduly complex follow-up that some health systems and patients cannot complete. In high-income countries, HCV principally affects those who are marginalised or disenfranchised from health services, such as people who inject drugs or those in rural or remote communities and in prisons. Low-income and middle-income countries face additional challenges. While generic drugs have become increasingly accessible and have substantially lowered the cost of treatment,[2] the cost and complexity of pre-treatment assessments such as genotyping, liver fibrosis staging, and on-treatment monitoring place considerable burden on health resources, precluding the expansion of treatment more widely.

Notwithstanding the COVID-19 pandemic, which has slowed progress towards HCV elimination worldwide by disrupting health systems and shifting health priorities,[3] there were already signs that elimination efforts had stalled. Even in countries on track to eliminate HCV, treatment rates had reached a plateau after patients who were already engaged in the health system and waiting to access treatment did so.[4] Reaching those remaining will require simplifying therapeutic models, task shifting to community and primary health-care settings, and reducing the economic burden on health systems and for patients.

As early as 2018, recommendations for simplifying the approach to initial HCV treatment for adults who do not have cirrhosis or HIV were made.[5] Indeed, a variety of real-world studies reporting on decentralised care models have shown such approaches achieve similarly high cure rates as care delivered by specialists across a range of populations and settings.[6,7] Evidence from randomised trials further supports simplified monitoring. For example, the SMART-C trial compared standard to simplified monitoring using glecaprevir–pibrentasvir, dispensing the entire 8-week treatment and requiring only two in-person visits.[8] Sustained virological response (SVR) was 92%, compared with 95% in the standard of care group, although the difference was not non-inferior. However, this trial excluded active injection drug users and people with cirrhosis, only 7% of participants had HIV infection, pre-treatment HCV genotyping was required, and the trial was conducted in high-income settings.

In *The Lancet Gastroenterology & Hepatology*, Sunil Solomon and colleagues[9] report the results of the MINMON (ACTG A5360) trial, which simplifies HCV treatment even further. All participants received the entire 12-week course of sofosbuvir–velpatasvir at entry; no pre-treatment genotyping was required; FIB-4, a simple laboratory-based test, was used to classify cirrhosis; and there were no scheduled visits or laboratory monitoring while on treatment. Two remote contacts were made using the participant's preferred method of electronic communication. Although there was no comparator arm, this trial demonstrated this highly simplified, patient-friendly approach is both feasible and results in high cure rates (SVR 95·0%, 95% CI 92·4–96·7), similar to those seen in registration trials. The trial had remarkably few dropouts (n=2) or losses to follow-up (n=2) and was conducted in low-income, middle-income, and high-income settings including participants with a wide range of HCV genotypes. The approach was not only highly effective but also safe.

This trial should have important practice-changing implications. Although the benefits for resource-constrained settings are evident, paradoxically it might be more impactful for high-income settings, which have been particularly slow to adopt decentralised models widely. Given the large proportion of participants enrolled who were co-infected with HIV (42%, 99% of whom were virologically suppressed) and a reasonable proportion (9%) with compensated cirrhosis, the study is generalisable and supports the expansion of simplified treatment to these groups.

Are there patients for whom a simplified approach might not yet be recommended? Although the trial included patients with a history of substance use, there were relatively few active users (14%). The proportion actively using injection drugs was not clear—a group for whom concerns regarding adherence and difficulties with follow-up due to a lack of mobile phones, computers, or fixed addresses are often raised. That said, only three of 20 non-responders were active substance users. This leaves relatively few patients who still require specialty care (eg, those with prior treatment, advanced cirrhosis, after transplantation, pregnancy, and other liver diseases such as hepatitis B). More research is needed to support such approaches for these special populations.

The MINMON trial adds to the growing body of evidence that DAAs can be delivered safely and simply to a wide range of populations without the need for intensive monitoring and follow-up. It is time to reframe modern HCV treatments. Aside from their continued high price tag,[10] these antivirals are more akin to antibiotics, and we should move to adopt simplification more broadly. Dispensing the full treatment course and offering flexible means of communication increases autonomy for patients and allows them to take control of an infection that remains stigmatising, without risking treatment failure. Adopting such simplified treatment can support a greater role for primary care, community-based, and nurse-led strategies, bringing treatment closer to people living with HCV. Not only can such simplified approaches advance HCV elimination efforts, but they could also serve as models for delivering health care that could change the way we manage infectious diseases affecting vulnerable populations.

MBK has received research support and consulting fees from ViiV, AbbVie, and Gilead Sciences, all outside the submitted work. MBK is supported by a Tier I Canada Research Chair.

Marina B Klein
marina.klein@mcgill.ca

Division of Infectious Diseases and Chronic Viral Illness Service, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada H4A 3J1 (MBK)

1 World Health Organization. Fact sheets. Hepatitis C. Geneva, Switzerland: World Health Organization; 2021. https://www.who.int/news-room/fact-sheets/detail/hepatitis-c (accessed Dec 1, 2021).
2 Simmons B, Cooke GS, Miraldo M. Effect of voluntary licences for hepatitis C medicines on access to treatment: a difference-in-differences analysis. *Lancet Glob Health* 2019; **7:** e1189–96.
3 Blach S, Kondili LA, Aghemo A, et al. Impact of COVID-19 on global HCV elimination efforts. *J Hepatol* 2021; **74:** 31–36.

4 Medical Journal of Australia. Australia in danger of missing 2030 hepatitis C elimination targets. https://www.mja.com.au/system/files/2020-04/FINAL%2030%20MAR%20HEPATITIS.pdf (accessed Dec 1, 2021).

5 European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2018. *J Hepatol* 2018; **69:** 461–511.

6 Oru E, Trickey A, Shirali R, Kanters S, Easterbrook P. Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. *Lancet Glob Health* 2021; **9:** e431–45.

7 Zhang M, O'Keefe D, Craig J, et al. Decentralised hepatitis C testing and treatment in rural Cambodia: evaluation of a simplified service model integrated in an existing public health system. *Lancet Gastroenterol Hepatol* 2021; **6:** 371–80.

8 Dore GJ, Feld JJ, Thompson A, et al. Simplified monitoring for hepatitis C virus treatment with glecaprevir plus pibrentasvir, a randomised non-inferiority trial. *J Hepatol* 2020; **72:** 431–40.

9 Solomon SS, Wagner-Cardoso S, Smeaton L, et al. A minimal monitoring approach for the treatment of hepatitis C virus infection (ACTG A5360 [MINMON]): a phase 4, open-label, single-arm trial. *Lancet Gastroenterol Hepatol* 2022; published online Jan 10. https://doi.org/10.1016/S2468-1253(21)00397-6.

10 Barber MJ, Gotham D, Khwairakpam G, Hill A. Price of a hepatitis C cure: cost of production and current prices for direct-acting antivirals in 50 countries. *J Virus Erad* 2020; **6:** 100001.

Endoscopic interventions for stricturing Crohn's disease

Published **Online** January 20, 2022 https://doi.org/10.1016/S2468-1253(21)00429-5

See **Articles** page 332

Cumulative bowel damage in the form of stricturing Crohn's disease remains a common complication affecting up to half of patients with Crohn's disease.[1] No selective antifibrotic therapies are available and anti-inflammatory interventions have shown limited long-term efficacy.[2] Other than surgical strictureplasty or resection, the most commonly used endoscopic therapy for fibrotic strictures is endoscopic balloon dilation (EBD). Short-term and long-term success rates and safety of EBD have mainly been established in observational retrospective studies.[3] Initial enthusiasm about intestinal stents (eg, partly or fully covered self-expanding metal stents [SEMS] and biodegradable stents) for stricturing Crohn's disease was dampened by variable success rates and high complication rates, including perforation.[4,5] No direct comparison of stenting with the current gold standard of EBD has been done to date, and most available data are based on retrospective case series and meta-analyses.

In *The Lancet Gastroenterology & Hepatology*, Carme Loras and colleagues[6] report a multicentre, randomised trial comparing the efficacy, safety, and direct costs of fully covered SEMS (FCSEMS) with EBD for patients with symptomatic Crohn's disease-associated strictures. Success rate, defined as being free from additional intervention for symptomatic recurrence at 1 year, was reported in 33 (80%) of 41 patients in EBD group and 20 (51%) of 39 patients in FCSEMS group (OR 3·9 [95% CI 1·4–10·6]; p=0·0061). In strictures longer than 3 cm there were no differences between the two methods. The mean cost of FCSEMS was 40% higher than that of EBD. The rate of adverse events was similar between the two groups.

The authors should be congratulated for the first prospective, randomised head-to-head study in the field, which enriches the area of endoscopic therapy for patients with stricturing Crohn's disease and has direct clinical implications for medical practice. EBD is more frequently used than FCSEMS; this makes these results reassuring and highlights EBD as the preferred endoscopic intervention for short strictures. For strictures longer than 3 cm, both options appear to be equally effective, but EBD had lower costs and thus might remain the procedure of choice for this group and in patients with strictures up to 5 cm length.[3]

The findings of this study are important but have several caveats that should be considered. First, radiological features of the strictures were obtained using variable radiological methods (CT or MRI) and without standardised central reading. These features are fundamental in future studies for both patient randomisation and data interpretation. Second, the study was ended before the calculated sample size was reached following an interim analysis, which showed that the researchers' hypothesis had been rejected; therefore, the study might overlook differences between study groups and make subgroup analyses more challenging. Third, FCSEMS was associated with a prohibitively high rate (around 97%) of stent migration after a mean of 2 days after the procedure, which is sufficient reason to favour EBD over stent as endoscopic therapy. Migration might drive complication rates, such as perforation, and makes additional procedures for stent removal necessary. This study also sheds light on how stents perform in a prospective controlled setting. Finally, patients and health-care providers were not masked to the intervention, which poses an inherent bias.

Of note, these data emphasise several crucial unmet needs in the field of stricturing Crohn's disease. To