

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. 5 Brignardello-Petersen R, Izcovich A, Rochwerg B, et al. GRADE approach to drawing conclusions from a network meta-analysis using a partially contextualised framework. BMJ 2020; 371: m3907.

Authors' reply

We thank Meixuan Li and colleagues for their interest in our study¹ and for highlighting an interesting topic regarding network meta-analyses and the ranking methods used in many of them.

Published Online February 22, 2022 https://doi.org/10.1016/ S2468-1253(22)00054-1

Surface under the cumulative ranking (SUCRA) curves have become a popular ranking method in network meta-analyses.² However, as Li and colleagues point out, SUCRAs should be interpreted with caution for several reasons.³⁴ One of the most important reasons is that SUCRAs can be derived from studies in which the certainty of the evidence is low or very low. Hence, SUCRAs do not consider that chance might explain differences between treatments.

In our study, the inclusion criteria and the quality analysis that followed GRADE recommendations allowed us to include studies with at least a moderate-to-high level of confidence in their results, which could have decreased the chance of SUCRA misinterpretation. Nevertheless, this might not be enough to reduce bias, and the approach suggested by the authors to rank treatments and to reduce bias in SUCRA interpretation is interesting, although bias can still occur. Furthermore, there is no consensus on clinically meaningful differences in SUCRA values between different interventions,⁵ which makes SUCRA rankings less relevant.

Finally, we believe it is essential to highlight that appropriate interpretation of network metaanalyses implies reviewing both direct and indirect comparisons, the network meta-analysis estimates, and their associated certainty estimates. SUCRA values and their visual display, when taken together with these other elements, can help in the interpretation of network meta-analysis results. However, given their intrinsic limitations, we strongly suggest caution in interpreting the results of our study solely on the basis of SUCRA values and rankings.

JSL reports consulting fees from AbbVie and honoraria from Janssen. PAO reports consulting fees from AbbVie, Takeda, and Janssen; honoraria from Takeda and Janssen; and financial support for attending meetings, travel, or both from AbbVie, Takeda, Janssen, and Ferring. LP-B reports grants from AbbVie, MSD. Takeda, and Fresenius Kabi: consulting fees from Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillots, Celltrion, Takeda, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Inotrem, Allergan, MSD, Roche, Arena, Gilead, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius Kabi, OSE Immunotherapeutics, Enthera, Theravance, Pandion Therapeutics, Gossamer Bio, Viatris, and Thermo Fisher; honoraria from AbbVie, Galapagos, Janssen, Ferring, Tillots, Celltrion, Takeda, Pfizer, Sandoz, Biogen, MSD, Arena, Gilead, Amgen, Vifor, and Viatris; financial support for attending meetings, travel, or both from AbbVie, Galapagos, Janssen, Ferring, Tillots, Celltrion, Takeda, Pfizer, Sandoz, Biogen, MSD, Arena, Gilead, Amgen, and Vifor; participation on a data safety monitoring board or advisory board for Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillots, Celltrion, Takeda, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Inotrem, Enterome, Allergan, MSD, Roche, Arena, Gilead, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius Kabi, OSE Immunotherapeutics, Enthera, Theravance, Pandion Therapeutics, Gossamer Bio, Viatris, and Thermo Fisher; and stock options from CTMA

Juan S Lasa, Pablo A Olivera, *Laurent Peyrin-Biroulet peyrinbiroulet@gmail.com

IBD Unit, Gastroenterology Section, Department of Internal Medicine, Centro de Educación Médica e Investigación Clínica (CEMIC), Buenos Aires, Argentina (JSL, PAO); Gastroenterology Department, Hospital Británico de Buenos Aires, Buenos Aires, Argentina (JSL); Zane Cohen Centre for Digestive Diseases, Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada (PAO); Division of Gastroenterology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada (PAO); INSERM NGERE and Department of Hepatogastroenterology, Nancy University Hospital, Lorraine University, Vandoeuvre-lés-Nancy F-S4511, France (LP-B)

- 1 Lasa JS, Olivera PA, Danese S, Peyrin-Biroulet L. Efficacy and safety of biologics and small molecule drugs for patients with moderate-to-severe ulcerative colitis: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol 2022; **7**: 161–70.
- Mills EJ, Thorlund K, Ioannidis JPA. Demystifying trial networks and network meta-analysis. *BMJ* 2013; **346**: f2914.
 Bafeta A, Tringuart L, Seror R, Ravaud P.
- Bafeta A, Trinquart L, Seror R, Ravaud P. Reporting of results from network metaanalyses: methodological systematic review. BMJ 2014; **348:** g1741.

- 4 Mbuagbaw L, Rochwerg B, Jaeschke R, et al. Approaches to interpreting and choosing the best treatments in network meta-analyses. Syst Rev 2017; 6: 79.
- 5 Singh S, Murad MH, Fumery M, Dulai PS, Sandborn WJ. First- and second-line pharmacotherapies for patients with moderate to severely active ulcerative colitis: an updated network meta-analysis. *Clin Gastroenterol Hepatol* 2020; **18**: 2179–91.

Uptake of third doses of SARS-CoV-2 vaccines among people with inflammatory bowel disease in Ontario, Canada

Patients with inflammatory bowel disease (IBD) are often treated with immunosuppressive medications, which are associated with decreased antibody response to initial SARS-CoV-2 vaccination and waning antibody levels following a second dose.^{1,2} The province of Ontario, Canada began offering third doses of SARS-CoV-2 vaccines to priority groups, including individuals with IBD on immunosuppressive therapy, beginning Sept 14, 2021,3 followed by everyone aged 18 years and older on Dec 20, 2021.4 We describe and compare vaccine uptake in people with and without IBD as of Jan 9, 2022.

We used health administrative data from Ontario, Canada for this population-based retrospective cohort study. Data include demographic characteristics, healthcare encounters, and SARS-CoV-2 vaccinations for all provincial residents eligible for universal health-care coverage (>99% of the population). We identified all patients with IBD aged 18 years or older living in Ontario as of Sept 1, 2021 using validated algorithms^{5,6} and compared them with people without IBD. Vaccination status was obtained from COVaxON, a comprehensive registry containing information on vaccine product, date of administration, and dose number for all vaccines administered in the

province. COVaxON also includes outof-province vaccinations reported to local public health units.

We determined overall and agespecific weekly cumulative incidence of first, second, and third doses of vaccination against SARS-CoV-2. We calculated the relative risk (RR) and corresponding 95% CI of vaccination. Third doses were assessed in the full population and among those with two doses. Analyses were done with SAS version 9.4 and R software.

Among 107059 patients with IBD, 89.9% had one dose of a SARS-CoV-2 vaccine, 88.6% had two doses, and 58.3% had three doses as of Jan 9, 2022. Among 12145893 individuals without IBD, 85.6% had one dose, 83.8% had two doses, and 44.3% had three doses (RR for third doses 1.32, 95% CI 1.31-1.32; appendix). Among individuals with IBD, those between 18 and 39 years of age were least likely to receive a third dose (41.4%) but this age group had the highest uptake of third doses relative to the general population (RR 1.47, 95% CI 1.45-1.49).

In conclusion, in Ontario, Canada, where universal vaccination is available, there is higher uptake of third doses of SARS-CoV-2 vaccines among patients with IBD relative to the general population, but coverage remains suboptimal. Although the number of people with third doses is climbing, we expect these rates to plateau in both populations. As with first and second doses, we expect patients with IBD to have higher uptake of third doses than those without IBD. Efforts should be made to understand reasons for third dose vaccine hesitancy in patients with IBD, particularly in the Omicron era.

SB reports grants from the Public Health Agency of Canada. GGK has received honoraria for speaking or consultancy from AbbVie, Janssen, Pfizer, and Takeda; research support from Janssen, AbbVie, GlaxoSmithKline, Merck, and Shire; and shares ownership of a patent for treatment of inflammatory disorders, autoimmune disease, and PBC (UTI Limited Partnership, assignee. Patent 62/ 555,397). EIB has acted as a legal consultant for Hoffman La-Roche Limited and Peabody & Arnold LLP and consultant for McKesson Canada for matters unrelated to a medication used to treat inflammatory bowel disease or COVID-19. All other authors declare no competing interests. This project was supported by funding from the Public Health Agency of Canada, through the Vaccine Surveillance Reference group and the COVID-19 Immunity Task Force. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada. The study is supported by ICES, which is funded by the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care. Parts of this material are based on data and information compiled and provided by MOH and the Canadian Institute for Health Information. The opinions, results, and conclusions reported in this paper are those of the authors and are independent of the data sources: no endorsement is intended or should be inferred. JW receives support from the Arthritis Society Stars Career Development Award (STAR-19-0610).

M Ellen Kuenzig, Jessica Widdifield, Sasha Bernatsky, Gilaad G Kaplan, *Eric I Benchimol

eric.benchimol@sickkids.ca

SickKids Inflammatory Bowel Disease Centre, Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON M5G 1X8, Canada (MEK, EIB); Child Health Evaluative Sciences, SickKids Research Institute, Toronto, ON, Canada (MEK, EIB); Institute of Health Policy Management and Evaluation University of Toronto, Toronto, ON, Canada (JW, EIB); Sunnybrook Research Institute, Holland Bone & Joint Program, Toronto, ON, Canada (JW); ICES, Toronto, ON, Canada (JW, EIB); Divisions of Rheumatology and Clinical Epidemiology, Department of Medicine, McGill University Health Centre, Montréal, QC, Canada (SB); Departments of Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada (GGK); Department of Paediatrics, University of Toronto, Toronto, ON, Canada (EIB)

- Quan J, Ma C, Panaccione R, et al. Serological responses to SARS-CoV-2 vaccination in patients with inflammatory bowel disease: a prospective cohort study. *Gastroenterology* 2022; **162**: 548.
 Alexander II. Konnedy NA. Ibrahaim H et al.
- Alexander JL, Kennedy NA, Ibraheim H, et al. COVID-19 vaccine-induced antibody responses in immunosuppressed patients with inflammatory bowel disease (VIP): a multicentre, prospective, case-control study. Lancet Gastroenterol Hepatol 2022; published online Feb 3. https://doi.org/10.1016/ S2468-1253(22)00005-X.
- 3 Government of Ontario. Expanded eligibility for third doses of the COVID-19 vaccine. Queen's Printer for Ontario. Sept 14, 2021. https://news. ontario.ca/en/backgrounder/1000805/ expanded-eligibility-for-third-doses-of-thecovid-19-vaccine (accessed Feb 8, 2022).
 - Government of Ontario. All Ontarians 18+ eligible for COVID-19 booster appointments at three-month interval. Queen's Printer for Ontario. Dec 15, 2021. https://news.ontario. ca/en/release/1001352/all-ontarians-18eligible-for-covid-19-booster-appointmentsat-three-month-interval (accessed Feb 8, 2022).

4

- 5 Benchimol EI, Guttmann A, Griffiths AM, et al. Increasing incidence of paediatric inflammatory bowel disease in Ontario, Canada: evidence from health administrative data. Gut 2009; 58: 1490–97.
- 6 Benchimol EI, Guttmann A, Mack DR, et al. Validation of international algorithms to identify adults with inflammatory bowel disease in health administrative data from Ontario, Canada. J Clin Epidemiol 2014; 67: 887–96.

See Online for appendix