

**Letter to the Editor: People living with HIV and NAFLD: a population left behind in
the global effort for liver fibrosis screening?**

Giada Sebastiani¹, Jovana Milic², Emmanuel A. Tsochatzis³, Catia Marzolini⁴, Michael Betel⁵, Sanjay Bhagani⁶, Caryn G. Morse⁷, Felice Cinque¹, James B. Maurice³, Patrick Ingiliz⁸, Jennifer Price⁹, Maud Lemoine¹⁰, Jürgen K. Rockstroh¹¹, Giovanni Guaraldi¹² on behalf of the Steatohepatitis in HIV Emerging Research (SHIVER) Network

¹Division of Gastroenterology and Hepatology and Division of Infectious Diseases, McGill University Health Centre, Montreal, Canada

²Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Italy

³UCL Institute for Liver and Digestive Health, Royal Free Hospital, University College London, UK

⁴Division of Infectious Diseases & Hospital Epidemiology, University Hospital Basel, Basel, Switzerland

⁵Fatty Liver Alliance, Canada

⁶Royal Free London, NHS Foundation Trust, London, UK

⁷Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA

⁸APHP Henri-Mondor University Hospital, Hepatology Department, Inserm U955, Creteil, France

⁹Department of Medicine, University of California, San Francisco, CA USA

¹⁰Department of Metabolism, Digestion and Reproduction, Division of Digestive Disease, Liver Unit, St Mary's Hospital, Imperial College London, UK

¹¹University Hospital Bonn, Germany

¹²University of Modena and Reggio Emilia, Italy

Correspondence to:

Dr. Giada Sebastiani

Division of Gastroenterology and Hepatology

Royal Victoria Hospital, McGill University Health Centre

1001 Décarie Blvd.

Montreal, QC H4A 3J1, Canada.

Email: giada.sebastiani@mcgill.ca

ACCEPTED

We read with great interest the recently released AASLD practice guidance on the Clinical Assessment and Management of nonalcoholic fatty liver disease (NAFLD)(1). The guidance includes the use of non-invasive diagnostic tests for screening of significant liver fibrosis. Surprisingly, people living with HIV (PWH) are not included among at-risk patient populations who should be screened, despite preponderant evidence about the increased frequency and severity of NAFLD(2). A recent meta-analysis showed a pooled prevalence of NAFLD and significant liver fibrosis of 34% and 12% in HIV mono-infected patients, respectively(3).

The reasons for this increased burden are related to the more complex pathogenesis of the liver disease. First, PWH have excess prevalence of classical metabolic risk factors driving the pathogenesis of NAFLD and associated liver fibrosis. Second, risk factors unique to PWH, such as exposure to certain antiretroviral drugs, immune activation and systemic chronic inflammation, create a perfect storm of etiopathogenetic pathways leading to accelerated parenchymal inflammation and liver fibrosis. Moreover, HIV itself adversely affects both hepatocytes and non-parenchymal cells(2). The European AIDS Clinical Society guidelines identify PWH as an at-risk population for NAFLD and liver fibrosis(4). Case-finding of significant liver fibrosis is recommended through stepwise care pathways utilising non-invasive diagnostic tests. The expert panel review from the American Gastroenterology Association also considers PWH a high-risk group for NAFLD(5).

We agree that the enormous and increasing burden of NAFLD warrants resource-adaptive public health management strategies, particularly those that focus on high-risk populations for NAFLD-associated significant liver fibrosis. Based on current evidence, PWH should be considered an at-risk population and targeted for screening strategies of liver

fibrosis. We believe that their inclusion into guidelines will also help address current gaps in the pathogenesis and natural history of HIV-associated NASH. Moreover, PWH are currently excluded from the global effort of therapeutic trials for nonalcoholic steatohepatitis (NASH)(2). The endorsement of the hepatological community is crucial in promoting awareness, research and public health efforts among stakeholders in HIV medicine.

ACCEPTED

References

1. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, Kleiner DE, et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 2023.
2. Guaraldi G, Maurice JB, Marzolini C, Monteith K, Milic J, Tsochatzis E, Bhagani S, et al. New Drugs for NASH and HIV Infection: Great Expectations for a Great Need. *Hepatology* 2020;71:1831-1844.
3. Kalligeros M, Vassilopoulos A, Shehadeh F, Vassilopoulos S, Lazaridou I, Mylonakis E, Promrat K, et al. Prevalence and Characteristics of Nonalcoholic Fatty Liver Disease and Fibrosis in People Living With HIV Mono-infection: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2023.
4. Ryom L, De Miguel R, Cotter AG, Podlekareva D, Beguelin C, Waalewijn H, Arribas JR, et al. Major revision version 11.0 of the European AIDS Clinical Society Guidelines 2021. *HIV Med* 2022;23:849-858.
5. Lake JE, Overton T, Naggie S, Sulkowski M, Loomba R, Kleiner DE, Price JC, et al. Expert Panel Review on Nonalcoholic Fatty Liver Disease in Persons With Human Immunodeficiency Virus. *Clin Gastroenterol Hepatol* 2022;20:256-268.

ACCEPTED

Conflict of interest

Giada Sebastiani consults for, advises, and is on the speakers' bureau for Novo Nordisk. She consults for, advises, is on the speakers' bureau for, and received grants from Merck. She consults for and is on the speakers' bureau for Gilead. She consults Intercept and Novartis. She advises Pfizer. She is on the speakers' bureau for AbbVie. She received grants from Theratechnologies.

Dr. Milic is on the speakers' bureau for Gilead and ViiV.

Emmanuel Tsochatzis consults for and is on the speakers' bureau for Novo Nordisk. He consults for Pfizer and Boehringer.

Catia Marzolini received grants from Gilead. She is on the speakers' bureau for ViiV and MSD.

Michael Betel consults for Sonic Incytes, Regeneron, Hoffmann-La Roche, and Sentrex Health Solutions.

Sanjay Bhagani advises, is on the speakers' bureau for, and received grants from Gilead. He consults for ViiV. He is on the speakers' bureau for AbbVie, MSD and Janssen.

Caryn G. Morse advises Theratechnologies and ViiV. She received grants from Gilead.

James Maurice consults for and received grants from Intercept. He consults for Advant.

Patrick Ingiliz consults for, is on the speakers' bureau for and received grants from Gilead. He consults for and is on the speakers' bureau for ViiV and AbbVie. He is on the speakers bureau for Eiger, MSD and Janssen.

Jennifer Price received grants from Gilead, Merck, Abbvie, Zydus, VIR, and Genentech.

Maud Lemoine consults for, advises and received grants from Gilead. She consults for Abbott. She received grants from ViiV.

Jürgen Rockstroh consults for and is on the speakers' bureau for Merck. He is on the speakers' bureau and consults for Gilead and ViiV. He consults for Boehringer, Gallapagos, Abivax, and Janssen.

Giovanni Guaraldi advises, is on the speakers' bureau for, and received grants from ViiV, Gilead and Merck. He received grants from Janssen.

The remaining authors have nothing to report.

Authors contributions

G.S., J.M. and G.G. conceptualized and designed the manuscript. G.S. wrote the first draft of the manuscript. J.M., E.A.T., C.M., M.B., S.B., C.G.M., J.B.M., P.I., J.P., M.L., J.K.R., G.G. revised the manuscript. All the authors contributed to discussion.

Funding

G.S. is supported by a Senior Salary Award from *Fonds de Recherche du Quebec – Sante (FRQS)* (#296306).