

University of Dundee

#FGDebate

Abeysekera, Kushala W. M.; Shearer, Jessica; Tavabie, Oliver D.; Dillon, John F.; Rowe, Ian A.

Published in:
Frontline Gastroenterology

DOI:
[10.1136/flgastro-2022-102330](https://doi.org/10.1136/flgastro-2022-102330)

Publication date:
2022

Licence:
CC BY-NC

Document Version
Peer reviewed version

[Link to publication in Discovery Research Portal](#)

Citation for published version (APA):

Abeysekera, K. W. M., Shearer, J., Tavabie, O. D., Dillon, J. F., & Rowe, I. A. (2022). #FGDebate: Should we focus on detecting patients at risk of liver disease in the community? *Frontline Gastroenterology*, [102330]. <https://doi.org/10.1136/flgastro-2022-102330>

General rights

Copyright and moral rights for the publications made accessible in Discovery Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from Discovery Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain.
- You may freely distribute the URL identifying the publication in the public portal.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

#FGDebate: Should we focus on detecting patients at risk of liver disease in the community

Kushala WM Abeysekera*¹, Jessica Shearer*², Oliver D Tavabie³, John F Dillon^{#4} and Ian A Rowe^{#2}

1. Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK.
2. Leeds Institute for Data Analytics, University of Leeds, Leeds, UK
3. The Sheila Sherlock Liver Centre, Royal Free Hospital, London, UK
4. Division of Clinical and Molecular Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee, UK

*=Joint first authors, #=Joint senior authors

Introduction

The #FGDebate series featured 'Controversies in detecting patients with liver disease' which was inspired by the recent review from Macpherson *et al.*(1) The debate was well attended and generated 1.35 million impressions across Twitter which placed it within the top 10 #FGDebate of all time for total impressions made. However, the main topic for debate was whether we should focus on detecting patients at risk of liver disease in the community. Here, we aim to provide arguments for and against this issue.

PRO

What is the landscape our patients find themselves in? Liver disease is a major cause of morbidity in the UK and one of the leading causes of death in 35-49 year olds. (2) The national trainee collaborative, TORCH-UK, involving 1168 patients with decompensated liver disease, across 104 acute trusts in UK, demonstrated 1 in 6 inpatients died during their admission.(3) Over 70% of new liver disease presents acutely to hospital, many dying without the chance to change.(4)

The aim must be to reduce morbidity and mortality from liver disease. The two major leading causes of this are alcohol-related liver disease (ArLD) and non-alcoholic fatty liver disease (NAFLD), both preventable liver diseases, with early intervention. Detecting liver disease early to facilitate specialist input, lifestyle and pharmacological interventions, provides a genuine opportunity to prevent patients developing decompensated cirrhosis and hepatocellular carcinoma. By doing so, we can reduce

admissions and mortality from liver disease whilst alleviating the burden on transplant services.

The standard of care for detection of liver disease has been opportunistic testing by primary care physicians who suspect their patient has liver disease. This is both inefficient and costly. Community-based early detection strategies have consistently demonstrated superiority over “standard of care” for detection of advanced fibrosis. (5-8) Furthermore, in studies that performed cost-effectiveness analyses, benefit over “standard of care” was demonstrated.(6,9,10) This was further supported by cost-comparison modelling of different strategies for detection fibrosis, supporting a two-step risk stratification model (11), now incorporated in international guidance.(12)

There are many unanswered questions. Do we utilise liver blood tests to identify fibrosis with the knowledge that many patients with cirrhosis will have normal liver biochemistry?(13) Alternatively, do we screen high risk groups e.g. patients with alcohol dependency, type 2 diabetes and obesity, which may be more labour intensive? We lack consensus on the best modality for fibrosis assessment i.e. transient elastography versus enhanced liver fibrosis test, although FIB-4 has a high negative predictive value. Prospective data will clarify the precise best combination of testing and screening for early detection of liver disease, but we already have the tools that work and we can use them to improve outcomes in the meantime.

Importantly, this cannot happen in isolation. Alcohol support services have been decimated in the last 12 years, which needs addressing. Minimum Unit Pricing for

alcohol, shown to be effective in Scotland and Wales at reducing alcohol purchases (14), is a glaring omission from the public health strategy in England.

Finally, detecting liver disease in the community is not solely the responsibility of primary care. Gastroenterologists and hepatologists must collaborate with primary care colleagues to support and identify patients with clinically significant fibrosis.

Clearly, the status quo is not working for our patients. Prospective data is vital but we already know much of what needs to be done. Detecting liver disease in patients at greatest risk early is a pragmatic and logical solution to prevent patients developing complications of liver disease and will reduce mortality.

CON

Early detection of liver disease is a key recommendation of the EASL-Lancet Commission (15) and is supported by the UK Liver Alliance. Early detection offers the opportunity to introduce lifestyle measures and treatments which may, *in theory*, alter the trajectory of disease thereby reducing morbidity and mortality. The principal issues to tackle in early detection of liver disease in persons at risk are firstly; whether there is clinical benefit to the diagnosis of liver disease, and secondly; whether the costs of detection are justified by that benefit.

The vast majority of liver disease in the UK is a result of extremely common risk factors. One in five adults drink alcohol excessively (16) and a quarter fall into the obese category (17), making the number of patients who would fulfil potential criteria for early detection interventions extremely large. The burden of this testing would fall largely to primary care clinicians, many of whom are already working beyond capacity, and this requires strong evidence to support its implementation.

Ultimately, the beneficial impact of detection or diagnosis of liver disease depends entirely on a change in treatment that favourably alters the trajectory of disease. There are no specific treatments for the patient with fatty liver due to ArLD or NAFLD and no or minimal fibrosis that depend on the diagnosis of liver disease. Reductions in alcohol consumption or dietary interventions are already recommended for those individuals to improve general health and reduce other complications of these comorbidities, questioning the impact of diagnosis. Furthermore, there is no clear evidence that the diagnosis of liver disease favourably impacts behaviour change and, in the largest primary care-based study in the UK (BALLETS) there was no net change in body weight following a diagnosis of NAFLD.(18) In the absence of specific treatment and the absence of a favourable impact of diagnosis on behaviour change it is difficult to justify the detection of *all* patients with liver disease.

With potentially only marginal benefits in the detection of liver disease it is critical to consider the costs of this approach. Without doubt, the testing strategies being advocated (and supported by national guidance) will carry substantial costs in financial terms, as well as in terms of patient and clinician time. For the commonest liver

diseases, in early stage, the overall number of patients who will go on to decompensate is unequivocally low over the medium or even longer term. There is therefore the risk of harm to the patient of receiving a diagnosis that in many cases will carry no clinical benefit.(19) In the BALLETS study there was a decrease in health-related quality of life following a diagnosis of fatty liver. Whilst this did recover over time, it is clear that there is the potential for substantial harm in the population if we make a diagnosis of NAFLD in the estimated 14.1 million prevalent patients in the UK.(20)

A focus on early detection alone will result in unnecessary investigations for the majority of individuals with the potential for harm, and at substantial cost. Rather than focussing on detection of patients at risk of liver disease in general, we need to move towards identifying those most likely to develop clinically relevant events, whilst clarifying if the interventions we offer these individuals improve outcomes at a population level. This requires prospective randomised evaluations with long-term follow-up to determine the clinical and cost-effectiveness of early detection approaches.

Conclusions

Whilst there are key differences in both sides' arguments (Table 1), it is important to firstly acknowledge areas where both agree. Liver disease in the UK is driven by both ArLD and NAFLD. Both of these diseases are preventable with alcohol cessation and

obesity management strategies undoubtedly leading to improvement in health beyond risk of liver disease complications. Detection of liver disease by the opportunistic finding of abnormal liver blood tests is unsatisfactory and can lead to under diagnosis as well as over-investigation of otherwise well individuals.

Early detection strategies have shown superiority in the detection of patients at risk of liver disease compared to the use of opportunistic abnormal liver blood tests. However, with more patients highlighted as 'at risk, there will be an increased burden at both primary and secondary care level to ensure these patients are appropriately assessed and risk-stratified. We must acknowledge the potential harm of a diagnosis of liver disease in patients at low risk of complications and aim to mitigate this within any pathway. Early detection strategies have the potential to reduce morbidity and mortality from chronic liver disease but require further finesse to allow for optimal implementation across the UK. Undoubtedly, prospective randomised controlled evaluations with appropriate follow up will provide further pertinent information to implement these strategies.

PRO	CON
UK liver disease morbidity and mortality is driven by preventable aetiologies	No specific liver disease intervention for early disease
Early recognition would allow for interventions to prevent these diseases	Risk of harm (particularly QoL) of a diagnosis in patients with limited risk of liver-related complications
Community-based screening programs perform more optimally and cost-effectively than 'standard of care'	Increased financial cost and an increase burden of work to an already stretched primary care service

Table 1. Arguments pro and con detecting patients at risk of liver disease in the community

References

1. Macpherson I, Abeysekera KWN, Harris R, *et al.* Identification of liver disease: why and how. *Frontline Gastroenterology* 2022;13:367-373
2. British Liver Trust. The alarming impact of liver disease in the UK: Facts and statistics. British Liver Trust 2019
3. TORCH-UK. O21 Chronic liver disease emergency admissions are for patients with preventable, established liver disease. *Gut.* 2022;71
4. Williams R, Aspinall R, Bellis M, *et al.* Addressing liver disease in the UK: A blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. *The Lancet.* 2014;384:1953-97.
5. Chalmers J, Wilkes E, Harris R, Kent L, Kinra S, Aithal G, *et al.* Development and implementation of a commissioned pathway for the identification and stratification of liver disease in the community. *Frontline Gastroenterology.* 2020;11:86-92
6. Dillon JF, Miller MH, Robinson EM, *et al.* Intelligent liver function testing (iLFT): A trial of automated diagnosis and staging of liver disease in primary care. *Journal of Hepatology.* 2019;71:699-706
7. Yeoman A, Yousuf F, Czajkowski MA, *et al.* GS08: Introduction of “reflex” AST testing in primary care increases detection of advanced liver disease: the Gwent AST project (GAP). *Journal of Hepatology.* 2020;73:S31
8. Srivastava A, Gailer R, Tanwar S, *et al.* Prospective evaluation of a primary care referral pathway for patients with non-alcoholic fatty liver disease. *Journal of Hepatology.* 2019;71:371-8.

9. Abeysekera KWM, Macpherson I, Glyn-Owen K, *et al.* Community pathways for the early detection and risk stratification of chronic liver disease: a narrative systematic review. *The Lancet Gastroenterology & Hepatology*. 2022;7:770-80
10. Tanajewski L, Harris R, Harman DJ, *et al.* Economic evaluation of a community-based diagnostic pathway to stratify adults for non-alcoholic fatty liver disease: a Markov model informed by a feasibility study. *BMJ Open*. 2017;7(6):e015659
11. Srivastava A, Jong S, Gola A, *et al.* Cost-comparison analysis of FIB-4, ELF and fibroscan in community pathways for non-alcoholic fatty liver disease. *BMC Gastroenterology*. 2019;19:122.
12. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis- 2021 Update. *Journal of Hepatology*. 2021;75:659-689
13. Thiagarajan P, Chalmers J, Guha IN, James MW. Detecting chronic liver disease: are liver function tests the solution? *British Journal of Hospital Medicine (Lond)*. 2020;81:1-8.
14. Anderson P, O'Donnell A, Kaner E, Llopis EJ, Manthey J, Rehm J. Impact of minimum unit pricing on alcohol purchases in Scotland and Wales: controlled interrupted time series analyses. *Lancet Public Health*. 2021;6:e557-e65.
15. Karlsen TH, Sheron N, Zelber-Sagi S, *et al.* The EASL-Lancet Liver Commission: protecting the next generation of Europeans against liver disease complications and premature mortality. *Lancet* 2022;399:61–116
16. NHS Digital. Statistics on Alcohol, England 2019. NHS Digital 2019. Accessed online 28/09/2022:- <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-alcohol/2019>

17. NHS Digital. Statistics on obesity, physical activity and diet, England 2020.
NHS Digital 2020. Accessed online 28/09/2022:- <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020>
18. Lilford RJ, Bentham L, Girling A, *et al.* Birmingham and Lambeth Liver Evaluation Testing Strategies (BALLETS): a prospective cohort study. *Health Technology Assessment* 2013;17(28)
19. Rowe IA. Too much medicine: overdiagnosis and overtreatment of non-alcoholic fatty liver disease. *The Lancet Gastroenterology & Hepatology* 2018;3:66–72
20. Estes C, Anstee QM, Arias-Loste MT, *et al.* Modelling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. *Journal of Hepatology* 2018;69:896–904.