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.

Authors' contributions

FB: Patient care, writing of the manuscript, and revision of the final version of the manuscript. SAD: Pathology reading, and revision of the final version of the manuscript. MD: Patient care, and revision of the final version of the manuscript. DMF: Patient care, and revision of the final version of the manuscript.

Supplementary data

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Let's leverage SARS-CoV2 vaccination to screen for hepatitis C in Spain, in Europe, around the world

To the Editor:

Since 2015, Spain has had a national strategic plan for tackling HCV and has been recognised as one of the best positioned countries in the world for achieving HCV elimination.[1] Its innovative strategies (*e.g.* one-step diagnosis, alert systems from microbiology laboratories, point-of-care diagnostics and simplified patient care pathways) have substantially decreased the delay between diagnosis and treatment by greatly improving linkage to care through more patient-centred approaches. At the start of 2020, HCV elimination appeared to be within grasp, but the COVID-19 pandemic has derailed this progress in Spain and the rest of the world.[2] In addition, the SARS-CoV-2 infection has exacerbated heath inequalities[3]; and many HCV patients are marginalized and thus highly vulnerable.

The real impact of the COVID-19 pandemic remains unknown but HCV programmes, from micro-elimination efforts to larger awareness campaigns, have come to a standstill. We read with interest the article by Blach *et al.* evaluating the impact of COVID-19 on global HCV elimination efforts.[4] Based on mathematical modelling, the authors suggest that a 1-year hiatus in HCV elimination programmes could result in 72,300 excess liver-related deaths and 44,800 excess liver cancers globally over the next 10 years. Along this line, Buti *et al.* have recently modelled the magnitude of the impact in Spain on HCV burden of the delay in its diagnosing and treating, also showing a marked increase in HCV-related morbidity-mortality.[5] Blach *et al.* conclude that attention should shift back to hepatitis programming as soon as it becomes safe to do so.[4] We believe that that time is now and we must and can combat the dual threats of SARS-CoV-2 and HCV infection jointly, as has recently been suggested.[6]

The majority of the European population will be vaccinated against SARS-CoV-2 by the end of 2021. This presents a window of opportunity to combine HCV detection with COVID-19 vaccination efforts and may allow us to hit two targets with one shot: eliminate a slow and deadly epidemic, HCV; and mitigate a fast and deadly pandemic, COVID-19. Thanks to HCV point-of-care tests, in particular dried-blood-spots, this approach does not involve major logistical issues or major additional costs to vaccination campaigns. Indeed, HCV screening strategies have been shown to be cost-effective across all age cohorts.[7] The 15-20 minutes that patients wait after vaccination is an ideal time

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to test for HCV. While there are other health conditions that may also warrant linked testing to COVID-19 testing and vaccination, and this should be determined at the local level, we argue that HCV be considered given the world's commitment (assumed by WHO) to eliminating HCV as a public health threat by 2030. Momentum needs to be renewed and given the challenge in reaching both the general population and, particularly, marginalized populations, this is a unique opportunity. The HCV field is uniquely positioned to reach difficult-to reach populations like people who inject drugs and some migrant populations. COVID-19 efforts can leverage the expertise and experience of the hepatitis C community, and this would be a mutually beneficial relationship. It is critical to vaccinate as many people as possible, and reaching vulnerable populations is always challenging but always possible with committed stakeholders involved.

Taking this public health approach into account, and aiming to prevent an increase in the social inequities and delayed HCV elimination, 17 Spanish scientific societies and patient associations, part of the Spanish Alliance for Viral Hepatitis Elimination (AEHVE), have released a position statement calling on Spain to capitalise on this historic opportunity and: i) revitalise HCV management, including diagnosis, referrals and treatment initiation; ii) immediately restart HCV micro-elimination programmes, particularly those devoted to marginalised populations; and iii) offer hepatitis B and C screening to anyone undergoing any SARS-CoV-2 serological diagnosis.[8] The AEHVE position statement is in alignment with the position paper released by the European Association for the Liver Study and the European Society of Clinical Microbiology and Infectious Diseases.[9]

This ambitious proposition has already borne fruit: in a pilot study in a region of Northern Italy.[10] Giacomelli *et al.* included rapid HCV screening in 2,505 individuals during a program of mass serological SARS-CoV-2 screening. They detected 72 individuals (2.9%) with HCV antibodies, most of them were unaware of their serostatus. And there is another inspiring example in Cantabria, a region in the north of Spain, where a pioneering initiative will be launched to create a multipurpose population cohort for clinical research, taking advantage of the COVID-19 vaccination campaign. In this cohort, HCV infection will be tested in 50,000 individuals with the support and collaboration of the local political and health authorities. This is a good example of the implementation of public health measures during the pandemic. We must now urgently move from positioning ourselves to taking concrete action to further HCV elimination efforts.

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Age and comorbidity are central to the risk of death from COVID-19 in liver transplant recipients

To the Editor:

Our understanding of the impact of COVID-19 on liver transplant recipients has recently advanced significantly. In August 2020 Colmenero *et al.* published data on behalf of the Spanish Liver Transplant Society (SETH) in the *Journal of Hepatology*.[1] The authors reported data on 111 LT recipients with SARS-CoV-2 infection and concluded that these patients were at no greater risk of severe COVID-19 than the general population. Furthermore, within LT recipients, comorbidity, male sex, and mycophenolate mofetil (MMF) use were reported as associated with severe disease. We congratulate our Spanish colleagues for rapidly conducting their comprehensive study in the midst of the pandemic.

Helpfully, Colmenero *et al.* provided an extract of their dataset: an important gesture in an era of rapid-fire reports. Having examined this, we feel a number of points would benefit from further exploration. We have also made comparisons with our own analysis of 151 LT recipients with SARS-CoV-2 infection (data extract supplied).[2] A key difference is that Colmenero *et al.* used a composite endpoint of death, intensive care unit (ICU) admission, or mechanical ventilation, whereas we used death alone; neither showed a significant difference between LT and non-LT patients. This is in contrast to the high rates of mortality in patients with cirrhosis.[3]

The first point of note is that only 4/20 (20%) SETH patients who died were admitted to ICU, compared to 22/28 (79%) in our cohort; overall mortality was similar at 18% and 19%, respectively. Although the reasons for this are not apparent, those who died in the SETH cohort without ICU admission were older and had higher Charlson comorbidity index (CCI) scores, which may suggest that ICU admission was thought inappropriate. Within our cohort, 9% of LT recipients deemed in need of ICU due to severe enough disease were not admitted due to this being deemed inappropriate. ICU admission reflects a combination of patient and clinician factors and is therefore an imperfect marker of COVID-19 disease severity.

Second, although Colmenero *et al.* report a univariable association between age and severe COVID-19, their multivariable analysis shows no significant association with age in contrast to the general literature.[4,5] On closer analysis, the authors have included age both alone and as a component of the CCI in their analysis, thus masking age as an independent variable. The same issue exists for diabetes and renal function, which are both components of the CCI.[6]

Third, Colmenero *et al.* reported a correlation between male sex and severe COVID-19 consistent with findings from other large non-LT datasets.[7] However, comparing their Table 1, Table 2, and the raw dataset demonstrates that the association of poor outcome is in fact with *female* sex [12/79 (15%) men died *vs.* 8/32 (25%) women] and that there has been a transcription error.

Fourth, the multivariable analysis includes a number of variables that change over the disease course of COVID-19, such as immunosuppression withdrawal, and oxygen saturations at diagnosis. Patients were diagnosed with SARS-CoV-2 at varying time points, with time from diagnosis to ICU admission ranging from -1 to 11 days, with ICU admission not being universal as above. Furthermore, patients not hospitalized were excluded. This makes the use of a composite endpoint and time-dependent analysis (*e.g.* Cox regression) more difficult to interpret.

Considering the points above, we re-examined the SETH dataset in relation to the single endpoint of death. We adjusted reported CCI scores to remove age, and only considered baseline variables. To permit comparison, we retrospectively applied the same calculations to our own cohort, using diagnosis as the point-of-entry for both cohorts. We then performed a multivariable logistic regression analysis in each cohort and both cohorts combined, with death as the dependent variable and age, sex, CCI (without age), hypertension, and baseline tacrolimus, azathioprine, ciclosporin, MMF, everolimus, and corticosteroid use as independent variables (Fig. 1A). When analyzed in this way, with backwards selection at p <0.1, age and CCI were significantly associated with death whereas no significant associations remained with immunosuppressive regimens (Fig. 1A). A limitation of our registry was that the precise duration from laboratory diagnosis to death was not known, thus preventing the performance of a time-dependent analysis. Our instructions to submitting physicians specified that patients should be followed until mortality or resolution of COVID-19 and both cohorts allowed inclusion of patients presenting at any time point.

To explore the relationship between age, co-morbidity and death we plotted age against CCI according for both LT cohorts (Fig. 1B,C). Notably, no patient from either cohort with a CCI of 0 died. Conversely, patients who died were older with higher CCI scores. For the SETH cohort, the CCI threshold for death was <3. In our cohort, 6 patients died with a CCI <3 however in 4 cases an additional important cofactor not captured by CCI was identified (Fig. 1C). The pattern of increasing mortality

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