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Detecting HCV infection by means of mass population SARS-CoV-2 screening: a pilot experience in Northern Italy

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To the Editor

We read with interest the paper by Crespo et al., who suggested that mass severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) testing offers a unique opportunity to screen for viral hepatitis, particularly hepatitis C virus (HCV) infection [1].

As the COVID-19 pandemic has overwhelmed entire national healthcare systems and severely strained their ability to manage patients with chronic diseases, such as those with chronic viral hepatitis [2], we agree that access to screening programmes and subsequent linkage to care would possibly turn the challenges of the pandemic in new opportunities.

Mass serological SARS-CoV-2 screening has been capable of revealing the spread of the disease in Europe [3]. After our first successful attempt at using rapid immunochromatographic testing (RICT) to screen for SARS-CoV-2 antibodies in Castiglione d’Adda, an area of early viral circulation in Northern Italy [4], we not only extended the programme to five other towns in Lombardy, but also included rapid HCV screening in three: San Pellegrino Terme (4,840 inhabitants) and Suisio (3,828 inhabitants) in the province of Bergamo north-east of Milan, and Sordio (3,429 inhabitants) in the province of Lodi south-east of Milan. With the full support and collaboration of the local authorities, all of the inhabitants of these three towns were invited to undergo voluntary screening in suitably adapted, publicly owned buildings (schools and sports centres) at the beginning of August (Suisio), the end of September (Sordio), or between the end of October and mid-November (San Pellegrino Terme). After giving their informed consent, they underwent RICT for SARS-CoV-2 antibodies (PrimaLab COVID-19 IgG/IgM Rapid Test, Balerna, Switzerland in Suisio; Technogenetics Rapid Test COVID-19 IgM/IgG, Milan, Italy in Sordio and San Pellegrino Terme), and those aged >50 years (or younger if they explicitly requested it) underwent RICT for HCV antibodies (Meridian Bioscience OraQuick HCV-Rapid Antibody Test Cincinnati, OH, USA). They also completed a questionnaire to ascertain whether they were aware of a previous HCV infection.
A total of 5,152 subjects (42.6% of the inhabitants of the three towns together) underwent SARS-CoV-2 screening, and almost half of these (n=2,505, 48.6%) also underwent HCV screening, including 79.3% of those aged >50 years. Table 1 shows the results of the HCV tests: 72 subjects (2.9%, 95% confidence interval [CI] 2.3-3.6%) were positive for HCV antibodies (ranging from 2.1% [95% CI 1.1-3.6%] in Sordio to 3.4% [95% CI 2.4-4.6%] in San Pellegrino Terme). Fewer than half (46.1%) of these were aware of their serostatus.

On the basis of historical data, the overall seroprevalence of HCV in Italy is about 2% (1.6-7.3%), with the vast majority of infections reported in subjects aged >60 years, and an increasing gradient from northern to southern Italy [5]. The 2.9% seroprevalence observed in our study is similar to the northern Italian general population estimates made about 20 years ago (3.3%) [6].

The fact that 53.9% of the HCV-positive subjects were unaware of their serostatus may seem high but it is lower than the estimated 66% made by a European study in 2015 [7].

The limitations of this study include the absence of simultaneous HCV-RNA testing, although all of the positive subjects were counselled and given prescriptions for diagnostic investigations (including HCV-RNA testing) and subsequent linkage to care. Unfortunately, due to the limited time available, the questionnaire ascertained only whether participants were aware of a previous HCV infection, while no information regarding previous HCV treatments was recorded among those tested positive. Secondly, the reported sensitivity and accuracy of the test in a low prevalence setting [8] may have led to false negative results as 11 of the subjects who tested negative reported a previously treated HCV infection. On the other hand, this is not a surprising finding given the well-known time-dependent reduction in HCV antibodies after HCV eradication [9].

Our findings revealed a fair number of HCV infections in people who were unaware of their serostatus, thus suggesting that rapid HCV testing in the context of SARS-CoV-2 screening programmes is a further means of achieving the WHO’s 2030 HCV elimination target [10].
successful, other screening programmes for communicable diseases such as HIV infection could benefit from the same strategy.

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Declarations

Conflict of interest: AG has received consultancy fees from Mylan, and educational and grant support from Gilead. MG has received grants and fees for speaker bureaux, advisory boards and CME activities from BMS, Viiv, MSD, AbbVie, Gilead, Janssen and Roche. GP, FC and CB have nothing to declare.

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**Author’s contribution:** All of the authors were involved in writing the manuscript, have approved the final version as submitted, and have agreed to be accountable for all aspects of the work.
| Town (residence, domicile, or workplace) | All screened for SARS-CoV-2-Ab n=5152 | Tested for HCV n=2505 (48.6%) | HCV-Ab positive n=72 (2.9%) | HCV-Ab negative n=2433 (97.1%) |
|---------------------------------------|----------------------------------------|--------------------------------|--------------------------------|--------------------------------|
|                                       | n (%) or median (IQR)                  | n (%) or median (IQR)         | n (%) or median (IQR)         | n (%) or median (IQR)         |
| Suisio                                | 1126 (21.9)                            | 735 (29.3)                    | 20 (27.8)                     | 715 (29.4)                    |
| Sordio                                | 1393 (27.0)                            | 585 (23.4)                    | 12 (16.7)                     | 573 (23.6)                    |
| San Pellegrino Terme                  | 2633 (51.1)                            | 1185 (47.3)                   | 40 (55.6)                     | 1145 (47.1)                   |
| Age (years)                           | 50 (34-65)                             | 61 (53-71)                    | 63.5 (56-75)                  | 61 (52-71)                    |
| Males                                 | 2350 (45.6)                            | 1118 (44.6)                   | 37 (51.4)                     | 1081 (44.4)                   |
| Morbidities                           |                                        |                                |                                |                                |
| Smoking                               | 919 (17.8)                             | 428 (17.1)                    | 16 (22.2)                     | 412 (16.9)                    |
| Cardiovascular disease                | 1314 (25.5)                            | 957 (38.2)                    | 32 (44.4)                     | 925 (38.0)                    |
| Rheumatic diseases                    | 250 (4.9)                              | 165 (6.6)                     | 10 (13.9)                     | 155 (6.4)                     |
| Diabetes mellitus                     | 242 (4.7)                              | 183 (7.3)                     | 10 (13.9)                     | 173 (7.1)                     |
| Chronic lung diseases                 | 364 (7.1)                              | 177 (7.1)                     | 8 (11.1)                      | 169 (6.9)                     |
| Oncological diseases                  | 248 (4.8)                              | 173 (6.9)                     | 7 (9.7)                       | 166 (6.8)                     |
| Onco-hematological diseases           | 38 (0.7)                               | 26 (1.0)                      | 1 (1.4)                       | 25 (1.0)                      |
| Solid neoplasms                       | 214 (4.2)                              | 150 (6.0)                     | 6 (8.3)                       | 144 (5.9)                     |
| Ever tested for HIV                   | 644 (25.7)                             | 23 (31.9)                     | 621 (25.5)                    |                               |
| HIV positive                          | 6 (0.2)                                | 2 (2.8)                       | 4 (0.2)                       |                               |
| HCV risk factors                      |                                        |                                |                                |                                |
| Piercings or tattoos                  | 115 (4.6)                              | 7 (9.7)                       | 108 (4.4)                     |                               |
| Ever received blood transfusions      | 114 (4.6)                              | 11 (15.3)                     | 103 (4.2)                     |                               |
| Ever had sexual intercourse without a condom | 8 (0.3) | 2 (2.8) | 6 (0.2) |                               |
| Intravenous drug use                  | 0 (0.0)                                | 0 (0.0)                       | 0 (0.0)                       |                               |

Table 1. Characteristic of subjects screened for SARS-CoV-2 and HCV antibodies by HCV findings.

N = number; IQR = inter-quartile range.