



## Commentary

## SARS-CoV-2 antibody-based SURVEILLANCE: New light in the SHADOW

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Recent reports question the view that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) detection by means of RNA and antigen testing alone might suffice in tracking and containing the current coronavirus disease 2019 (COVID-19) pandemic [1,2]. Indeed, the transient nature of RNA testing for pathogen detection, its complexity and the described sources of inaccuracy [3] make it an incomplete metric of viral spread in a population. On the other hand, the accurate evaluation of SARS-CoV-2 specific antibodies provides not only important population-based data on pathogen exposure, on the prevalence of the infection, also in asymptomatic subjects, and on the selection of convalescent plasma donors, but also valuable information for tracking transmission dynamics, gaining knowledge on population immunity levels and informing disease control policies [4]. The paper by Perico and coworkers, published in this issue of *EBioMedicine*, is a comprehensive analysis of the prevalence of SARS-CoV-2 infection in the Bergamo province, an area of Italy that experienced a massive COVID-19 outbreak, with its epicenter in the whole Lombardy region. The study included 423 subjects working in two companies located in the Kilometro Rosso Scientific Park in Bergamo: the Istituto Ricerche Mario Negri and Brembo S.p.A., respectively. Health surveillance screening was offered to all workers of the two companies, with a response rate of 77%. Of the 423 subjects, 163 included in the primary study cohort tested positive at ELISA assay for SARS-CoV-2 antibodies, thus highlighting a seroprevalence of 38.5%. [5]. This percentage far exceeds not only the mean prevalence in Lombardy itself (7.5%), in Italy overall (2.5%) [6], and in other hard hit areas in the world, including New York (19.9%), London (17.5%) and Madrid (11.3%); it is also higher than the percentage (4.6%) reported in a higher risk subpopulation of healthcare workers in the Veneto region, which is relatively near to Bergamo [7]. Comparable seroprevalences have only been reported in a number of hotspots in Iran and India [5].

According to the data reported by Perico and coworkers, and further estimations conducted, 96% of infections have been undetected in the Bergamo area, thus increasing the risk of death and obfuscating essential information on the pandemic. Furthermore, in a study

performed in Iceland on the measurement of SARS-CoV-2 antibodies, it is estimated that 44% of individuals infected with the virus were not diagnosed by quantitative polymerase-chain-reaction (qPCR) thus confirming the risk of under-diagnosis on using molecular testing alone [2]. The study also shows that the highest seropositive rates were observed for IgM while only two individuals tested positive for IgG alone at ELISA; this confirms that IgG seroconversion can occur concomitantly with IgM or earlier, also in the absence of an IgM response [1,8]. No differences were found between genders for the positivity rate, while the positivity was higher in subjects living in Nembro (56.7%) than in individuals in other areas of the Bergamo province (mean prevalence 37.7%). Only 23 (5.4%) subjects had a positive rRT-PCR nasopharyngeal swab, with high cycle thresholds (Ct range, 34 - 38), and none of the 26 samples led to a detectable cytopathic effect suggesting that the previously reported range of rRT-PCR positivity (Ct between 34 and 38) lacks potential infectivity.

It is remarkable that 54% of seropositive subjects reported needing assistance from their general practitioner for symptoms such as fever, anosmia, and ageusia in addition to fatigue, muscular pain and headaches, experienced in the first two weeks of March 2020, while a subset reported symptoms attributable to COVID-19 in early February 2020. This, in turn, suggests that SARS-CoV-2 spread widely across Lombardy before the first officially reported cases (20th February 2020) in a municipality of the Lodi province.

The paper by Perico and colleagues is welcome for several reasons: first, it confirms the usefulness of SARS-CoV-2 antibody assay for a better knowledge of the spread of the infection in a specific population or subpopulation, and for avoiding the risk of under-diagnosis when using rRT-PCR testing alone. While specific antibody assay is not well suited for the early diagnosis of the infection, it is a source of valuable information for both epidemiological surveillance and probably for late case identification [9]. However, as for any diagnostic test, a careful validation of the analytical and clinical performance (in particular, sensitivity and specificity) of SARS-CoV-2 antibody testing is required in view of currently available evidence of major weaknesses in many commercialised serological tests, particularly point-of-care tests [10]. In addition, further efforts should be made to introduce valuable external quality assessment programs in order to enable clinical laboratories to understand and improve the performances of serological (and molecular) testing for a better diagnosis and monitoring of COVID-19. Finally, the study confirms recently published findings across Europe, which documented the circulation of SARS-CoV-2 at least one month before the officially recognised cases of the disease.

E-mail address: [mario.plebani@unipd.it](mailto:mario.plebani@unipd.it)<https://doi.org/10.1016/j.ebiom.2020.103087>2352-3964/© 2020 The Author. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Contributors

Mario Plebani wrote this commentary

## Declaration of Competing Interest

No interest to be declared

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