

Single Cell Multiomics in Autoimmunity - Advance Your Immunology Studies with Single Cell and Spatial Tools

Free Virtual Seminar | January 26, 2022 | 9 AM PST

There are over 80 different types of autoimmune diseases that affect about 5% of the global population. Recent studies detailing the types of cells involved in autoimmune pathology have provided a critical step in understanding how autoimmune diseases develop, and they continue to inform new therapeutic and diagnostic development avenues. We invite you to attend our webinar, sponsored by 10x Genomics, to learn how integrating these cellular profiles with epigenomic, proteomic, and spatial analysis will help provide even richer insights.

In This Webinar, You Will Learn -

- How scientists are using genomics tools to characterize, diagnose, and treat autoimmune diseases
- Single cell tools that can be used to identify cell populations that may be masked when doing bulk RNA sequencing and/or flow or mass cytometry
- Integrating multiomic profiling into your research to discover deeper insights into autoimmune disease complexity

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On the severity of COVID-19 infections in 2021 in Italy

We are close to another Christmas under the pandemic. The media are discussing the possibility of further restrictions during Christmas time to mitigate the spread of the virus. A common theme is a comparison with previous waves observed in Spring and Summer 2021. Since mid-October, we observed an increase in the number of detected cases in several European countries, with the United Kingdom and Germany reporting exceptionally high recordings. In Italy, the incidence has increased visibly, but the rate is definitely not exponential. The rise in cases is not surprising at all. We are currently living an almost normal life, with many economic activities open after the summer break, the cancellation of many social restrictions. The arrival of the cold season favors the spread of the virus, following the fact that millions of Italians are still not immunized.

The current Italian monitoring system does not strictly focus on the incidence of new cases but rather on the severity of the cases as measured by the pressure on the National Health System and the number of daily deaths. That is mainly because, unlike the previous waves, the level of severity of the COVID-19 in the last few weeks would seem to be less critical than earlier. Likely, this could be due to the high proportion of vaccinated people in Italy, around 84% with full doses at November 30, 2021 of them over 12 population (see the Italian government website, <https://www.governo.it/it/cscovid19/report-vaccini/>). Breakthrough cases are not rare in a context of high incidence, but these are primarily mild infections that only require isolation at home.

For this reason, it is crucial to analyze whether the current growth of the infection can lead to critical consequences in terms of deaths and hospitalizations, primarily focusing on the admissions in intensive care units (ICUs).

We suggest looking at three incidence-type indicators: the number of positive detected cases, the number of deaths due to COVID-19, and the number of new admissions in ICUs recorded weekly. To make their trajectories comparable over time, crude counts were scaled by the size of the respective ranges (observed in the time window considered) through the following transformation

$$\frac{Y_t - \text{Min}}{\text{Max} - \text{Min}}$$

where Y_t is any one of those three indicators, and then expressed as percentages. These indicators are shown in Figure 1, from January 3, 2021 to December 5, 2021.

Three waves are clearly visible: the first one, from the week following February 14, 2021; the second, from the week following July 4, 2021; and the third, from the week following October 17, 2021 and still active. In the first wave, the indicators referring to the number of new ICU admissions (in red) and the number of deaths (in blue) have similar trajectories to incidence (in black). Instead, after July and particularly the last wave, the slopes of both the ICU admissions and deaths indicators show patterns less steep than the growth of the incidence of the detected cases.

Very likely, these different growth levels could indicate that the composition of the contagion is currently less severe than the one observed since mid-February 2021, in which deaths and ICU admissions increased with very similar rates as the detected cases incidence rate. Furthermore, we can easily notice the (well-known) delays of around 2–4 weeks in the peaks for ICU admissions and deaths with respect to the cases peak. In other words, we know that the peak of ICU admissions will follow the peak of incidence cases by approximately 2 weeks, similarly for deaths with a lag of approximately 4 weeks.

To better describe the severity of the contagion, we consider two additional indicators: the ICU-to-case ratio and the death-to-case ratio. Here, we use the death-to-case ratio as classically defined in epidemiology,^{1,2} that is, the number of deaths assigned to the COVID-19 during a given time interval (the week), divided by the number of new cases detected in the same period. Therefore, by analogy, the ICU-to-case ratio is defined as the number of new admissions in ICUs attributed to COVID-19 each week divided by the number of new cases detected in the same week.

Note that some people counted in the numerators of both ratios may have contracted the virus weeks earlier. These indicators can be though describing the severity of the contagion^{3,4} up to detection bias; although they are not analytic indicators like the crude fatality rate, for instance.^{1,2} The death-to-case ratio and the ICU-to-case ratio are shown in Figure 2; they are both expressed $\times 1000$ incidence cases, therefore, for every week, they represent the numbers of deaths and ICU admissions respectively, in correspondence of 1000 incidence cases observed in that week.

Both ratios have opposite trends compared to the contagion's main patterns. Indeed, they tend to increase when the incidence cases decrease and vice versa. During February's wave, the levels of the death-to-case ratio and ICU-to-case ratio are approximately within the ranges 14–40 and 10–15, respectively. Then, when looking at the second and third waves, those ranges

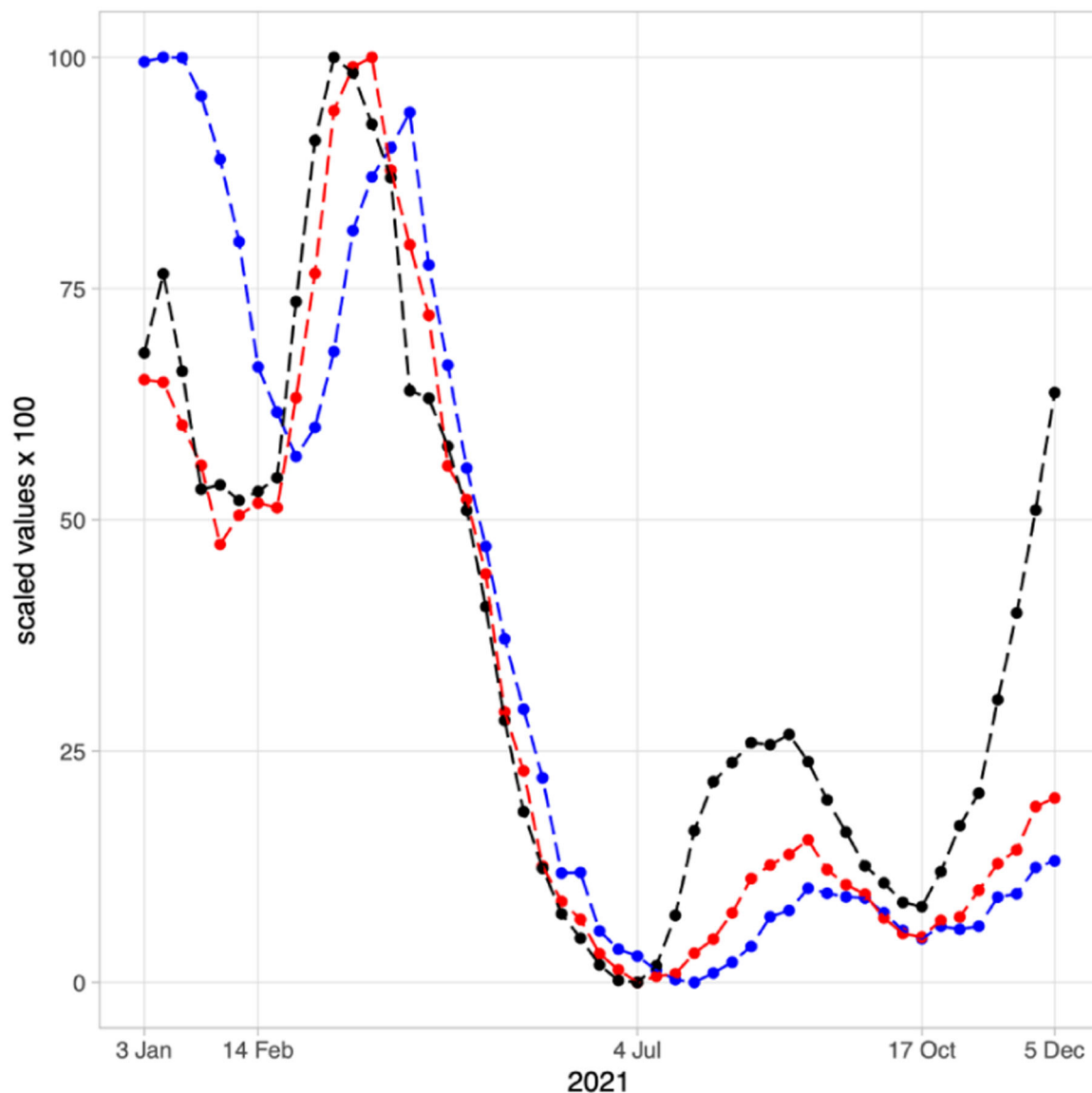


FIGURE 1 COVID-19 in Italy during 2021, incidence (black), deaths (blue), ICU admissions (red), weekly counts scaled by the size of the respective ranges and expressed as percentages (a) death-to-cases ratio, (b) ICU-to-cases ratio

substantially decrease. In terms of mean values, from the first wave to the second and third ones, the death-to-case ratio decreases on average from 28.0 to 8.7 deaths \times 1000 incidence cases (with a reduction of 69%) while the ICU-to-case ratio decreases on average from 11.5 to 5.9 ICU admissions \times 1000 cases (with a reduction of 50%).

Furthermore, concerning the current wave that started from mid-October, the death-to-case ratio decreases from around 16 deaths \times 1000 cases, at the end of September, to the current level of around 5 deaths \times 1000 cases (with a reduction of 68%). Similarly, the ICU-to-case ratio decreases from around 9 admissions in ICU \times 1000 cases, at the end of September, to the current value of around 4 admissions in ICU \times 1000 cases (with a reduction of 55%).

The epidemic is still spreading, with a relevant amount of new cases detected. However, these cases' impact on severe adverse events, like ICU admission and death, is much limited compared to what happened at the beginning of 2021 and even more during 2020. Caution should be still in place, and restrictions must apply if necessary. The reason is that an extremely high prevalence can still lead to a large number of hospitalizations, even if the individual probability of severe disease is very low. However, the situation is under control now in Italy, thanks to the current restrictions and vaccination policies. Interventions based on a misinterpretation of the data can make people worry, pandemic fatigue, and lower resilience when restrictions might be actually needed.⁵⁻⁷

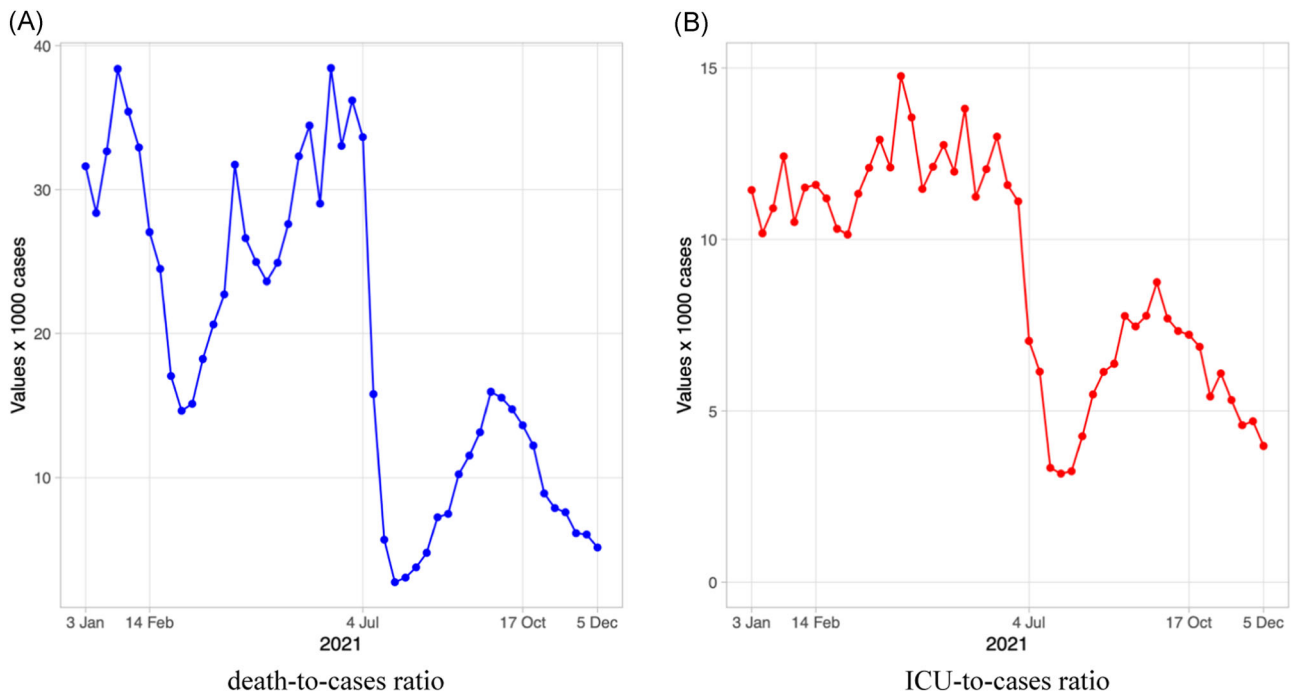



FIGURE 2 COVID-19 in Italy during 2021, (a) death-to-case ratio (blue) expressed $\times 1000$ incidence cases, (b) ICU-to-case ratio (red) expressed $\times 1000$ incidence cases.

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REFERENCES

- Choi J, Ki M, Kwon HJ, et al. Health indicators related to disease, death, and reproduction. *J Prev Med Public Health*. 2019;52(1):14-20. doi:10.3961/jpmph.18.250
- Merrill RM. *Introduction to Epidemiology*. Jones & Bartlett Learning; 2017.
- Arias-Reyes C, Carvajal-Rodriguez F, Poma-Machicao L, et al. Decreased incidence, virus transmission capacity, and severity of COVID-19 at altitude on the American continent. *PLoS One*. 2020;16(3):e0237294. doi:10.1371/journal.pone.0237294
- Wu JT, Leung K, Bushman M, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nature Med*. 2020;26:506-510. doi:10.1038/s41591-020-0822-7
- Divino F, Ciccozzi M, Farcomeni A, Jona-Lasinio G, Lovison G, Maruotti A. Unreliable predictions about COVID-19 infections and hospitalizations make people worry: the case of Italy. *J Med Virol*. 2021;94:26-28. doi:10.1002/jmv.27325
- Maruotti A, Ciccozzi M, Divino F. On the misuse of the reproduction number in the COVID-19 surveillance system in Italy. *J Med Virol*. 2021;93(5):2569-2570. doi:10.1002/jmv.26881
- Ciccozzi M, Maruotti A, Ceccarelli G, Divino F, Guarino M, Angeletti S. While we are discussing... the SARS-CoV-2 virus laughs. *J Med Virol*. 2021;93(12):6475-6476. doi:10.1002/jmv.27266