

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.

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It is crucial to communicate the goal and the advantage of low case numbers clearly to foster public cooperation. The success of these measures depends crucially on the cooperation and involvement of the public. Making the case for the economic and social benefits of reducing case numbers will, if clearly communicated, greatly foster public cooperation.

Controlling COVID-19 will become easier. In the near future, increased immunisation, more testing, and an improved understanding of mitigation strategies will further facilitate the control of COVID-19.

We urge governments throughout Europe to agree on clearly formulated common goals, coordinate their efforts, develop regionally adapted strategies to reach the goals, and thereby work resolutely towards low case numbers.

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- 1 Dorn F, Fuest C, Göttert M, et al. The economic costs of the coronavirus shutdown for selected European countries: a scenario calculation (No. 25). Munich: EconPol Europe, 2020.
- 2 Kretzschmar ME, Rozhnova G, Bootsma MC, van Boven M, van de Wijgert JH, Bonten MJ. Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study. Lancet Public Health 2020; 5: e452-59.
- Maier BF, Brockmann D. Effective containment 3 explains subexponential growth in recent confirmed COVID-19 cases in China. Science 2020; 368: 742-46.
- Alwan NA, Burgess RA, Ashworth S, et al. 4 Scientific consensus on the COVID-19 pandemic: we need to act now. Lancet 2020; **396:** e71–72.
- Dehning J, Zierenberg J, Spitzner FP, et al. 5 Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions, Science 2020; 369: eabb9789

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- Giordano G, Blanchini F, Bruno R, et al. Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. Nature Medicine 2020; 26:855-60
- Haug N, Geyrhofer L, Londei A, et al. Ranking the effectiveness of worldwide COVID-19 government interventions. Nature Human Behavior 2020; 4: 1303-12.
- Dykstra P, Fortunato E, Grobert N, et al. Independent expert report. Improving pandemic preparedness and management: lessons learned and ways forward. Nov 11, 2020. https://ec.europa.eu/info/sites/ info/files/research\_and\_innovation/groups/ sam/jointopinion\_improvingpandemic preparednessandmanagement\_ november-2020.pdf (accessed Dec 15, 2020).

## Infectivity of asymptomatic versus symptomatic COVID-19

Asymptomatic cases of COVID-19 are a potential source of substantial spread within the community setting.<sup>1</sup> However, little information is available about the infectivity and epidemiological significance of people with asymptomatic COVID-19.2

Singapore's testing strategy for severe acute respiratory syndrome coronavirus 2 is designed to detect infection in both symptomatic and asymptomatic people. Various methods are used. Workers in specific industries, such as construction, marine, and process industries, are routinely tested once per week or every two weeks, and all close contacts of those who test positive for COVID-19 are tested as well. All COVID-19 case detection, regardless of symptom status, triggers public health actions, including contact tracing and the quarantining of close contacts. A close contact generally refers to a person who was within 2 m of the index case for at least 30 min (or for shorter durations in high-risk settings).<sup>3</sup> All quarantined people are tested by PCR at the end of their guarantine period, and are only released from quarantine when they test negative for COVID-19. Serology tests are also done in most people who are infected, to determine the possible duration of their COVID-19 infection, and to assist with epidemiological investigations and containment efforts.<sup>3</sup> As COVID-19 viral load is typically higher before seroconversion than after, seronegative cases are thought to be more infectious than seropositive cases.<sup>4,5</sup>

To identify the relative infectivity of people with COVID-19 on the basis of their symptom and serology status, we studied all people who completed their quarantine between Aug 1 and Oct 11, 2020, as a result of being close community contacts of people who were infected and who had also



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undergone serology tests as part of their COVID-19 status assessment. Close contacts who lived in migrant worker dormitories were excluded from this analysis because their living environments were contextually different from community close contacts and because there were separate challenges in identifying cases and their close contacts within the dormitories. Negative binomial regression was done using Python version 3.7.1 (Python Software Foundation, Wilmington, DE, USA) to calculate the incidence rate ratios of a guarantined person from the community testing positive for COVID-19, adjusting for the symptom and serology status of the index case; two-tailed statistical significance was set at 0.05. 628 people with COVID-19 were

See Online for appendix

For the **2014 ELSO** anticoagulation guideline see https://www.elso.org/portals/0/ files/elsoanticoagulationguideline8-2014-table-contents.pdf included in this analysis (appendix). 3790 people were close contacts of an index case and were quarantined. On average, 6.0 people from the community were quarantined per index case. Overall, 89 (2%) of 3790 close community contacts developed COVID-19 while in quarantine. Of these, 50 (56%) of 89 contacts were guarantined because of an asymptomatic index case, whereas 39 (44%) contacts were quarantined because of a symptomatic case. 43 (48%) contacts were guarantined because of a seronegative index case, whereas 46 (52%) were quarantined because of a seropositive index case.

Negative binomial regression revealed that when adjusted for age, gender, and serology of index case, the incidence of COVID-19 among close contacts of a symptomatic index case was 3.85 times higher than for close contacts of an asymptomatic index case (95% CI 2.06-7.19; p<0.0001; appendix).

Our findings suggest that people with asymptomatic COVID-19 are infectious but might be less infectious than symptomatic cases. We also identified that the proportion of close contacts who became infected did not depend on the serology status of the index case. One reason for this observation could be that close contacts tend to live or work with the index case and are exposed because of their regular contact with a person who was infectious before turning seropositive.

The main limitation of this analysis is that cycle threshold values and viable shedding data were not available for all individuals included. Future studies should explore the relationship between viral loads, viable shedding, and transmission. Nevertheless, these findings suggest that where resources permit, contact tracing should proactively seek people with asymptomatic COVID-19 because they can transmit disease and will need to be contained if a national policy objective is to minimise cases and transmission. However, if resources are limited, then focusing contact tracing around symptomatic people who are easy to identify (by way of them seeking health care) might be more resource-effective in reducing transmission at the population level.

We declare no competing interests.

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- Kronbichler A, Kresse D, Yoon S, Lee KH, Effenberger M, Shin JI. Asymptomatic patients as a source of COVID-19 infections: a systematic review and meta-analysis. Int J of Inf Dis 2020; 98: 180–86.
- 2 Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. *Respiratory Medicine* 2020; **169:** 1–5.
- 3 Yong SEF, Anderson DE, Wei WE, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. *Lancet* 2020; 20: 809–15.
- 4 Peeling RW, Weddenburn CJ, Garcia PJ, et al. Serology testing in the COVID-19 pandemic response. *Lancet* 2020; **20:** e245–49.
- 5 Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infec Dis* 71: 2027–34.

# ECMO support for COVID-19: a balancing act

We read with great interest the analysis of data from the Extracorporeal Life Support Organization (ELSO)<sup>1</sup> Registry. It provides valuable data that support the use of extracorporeal membrane oxygenation (ECMO) for patients with COVID-19. However, it is widely acknowledged that many critically ill patients with COVID-19 present with coagulation abnormalities that include thrombotic microangiopathy and venous and arterial thromboembolic complications.<sup>2,3</sup> Hence, anticoagulants have been used in these critically ill patients both therapeutically and prophylactically.4,5

During ECMO support, continuous contact of circulating blood cells with the surface of the extracorporeal circuit leads to the hypercoagulable state. As a result, anticoagulant therapy is necessary. Although heparin dosage, monitoring assays, and target values selected by most centres are specified in the 2014 ELSO anticoagulation guideline, balancing thrombosis and haemostasis under the double hit of COVID-19 and ECMO is a big challenge for clinicians.

For these reasons, it would have been valuable to record the types and dosages of anticoagulants, the anticoagulant monitoring methods, and the target values.

The big data survey and the authoritative statistical analysis of the ELSO Registry data would make it clear whether patients with COVID-19 who receive ECMO require higher doses of heparin to increase clinical benefits and which monitoring method is most suitable.

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