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only three of the seven babies were tested, and the possibility of vertical transmission has since been raised in larger studies.⁴ Finally, SARS-CoV-2 infection induces a hypercoagulable state, including elevated levels of D-dimer and fibrinogen, and sometimes progresses to disseminated intravascular coagulation;⁵ this complication could be especially dangerous in pregnancy, given a normal underlying hypercoagulable state. The case series by Yu and colleagues provides a starting point for epidemiological studies, but the medical community needs to be circumspect in their conclusions and protect vulnerable workers until safety can be established for both mother and baby.



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Seroconversion in household members of COVID-19 outpatients

We read with interest the Article by Qifang Bi and colleagues,¹ in which they reported a household secondary

attack rate, as detected by repeated RT-PCR tests, of approximately 11%. We have found substantially higher attacks rates in western Norway through detection of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The first case of COVID-19 in Norway was identified in Bergen on Feb 28, 2020, before the outbreak was declared a pandemic, allowing rigorous testing of suspected cases before and during the rise in confirmed cases. All suspected COVID-19 cases in the peak period between Feb 28 and April 4 were referred to the Bergen municipality emergency room for centralised evaluation and testing according to a strict exposure likelihood algorithm, allowing an overview of the early virus spread in the population. If a family was exposed, only the index case was tested for SARS-CoV-2 infection. Both cases and household members were tested for specific antibodies to the receptor binding domain of SARS-CoV-2, as described by Stadlbauer and colleagues,² at 6 weeks after the index patient tested positive by RT-PCR.

Of 158 cases, 125 (79%) tested positive for antibodies and 12 (8%) were defined as borderline. In 77 household members, 24 (31%) tested positive and two (3%) were borderline. Our results show that detection of seroconversion might provide a more accurate picture of attack rates in households than intermittent RT-PCR testing.

FK reports that an assay used to screen for seroconversion was developed in his laboratory and that Mount Sinai has filed patent applications to protect that assay, has licensed its use for several companies, and is commercialising the assay. All other authors declare no competing interests.

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Appropriate selection of convalescent plasma donors for COVID-19

We read with considerable interest the Comment from Long Chen and colleagues¹ about the potential use of convalescent plasma for the treatment of COVID-19. Chen and colleagues mention the earlier pragmatic WHO recommendation for the use of convalescent plasma as therapy in Ebola virus disease.² The absence of a clinically relevant therapeutic benefit in patients with Ebola virus infection described by Griensven and colleagues,³ and more recently the finding of no therapeutic benefit in a small trial in patients with COVID-19 in Zhengzhou, China,⁴ will be used to question the usefulness of convalescent plasma in COVID-19. In the Guinea-Bissau Ebola study,³ no attempt was made to select donors for the potency of their neutralising antibody. In the COVID-19 study,⁴ seropositive donors were recruited only after IgM antibody to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was no longer detected, and no attempt to quantify the antibody response was reported. We previously described the levels of detectable antibody and the inferred level of neutralising antibody in convalescent plasma donors for patients with Ebola virus disease in Sierra Leone,⁵ showing 100-fold

differences in the level of neutralising antibody. We described a strategy for selecting donors with the highest levels of neutralising antibody, which was not undertaken in donors in the Guinea-Bissau or Zhengzhou studies. For planned interventions in the treatment of patients with COVID-19 severe disease, we strongly recommend selection and qualification only of donors who carry the highest levels of detectable neutralising antibody to SARS-CoV-2. In this respect, we have data which indicate that quantification of specific antibody to the receptor-binding domain will indicate levels of neutralising antibody (unpublished). Commercial assays based on the receptor-binding domain alone, although not intended for the purpose of identifying suitable convalescent plasma donors, will probably be able to serve this need.

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Underlying factors in paediatric invasive pneumococcal disease in Belgium

In their Article, Stefanie Desmet and colleagues¹ describe changes in paediatric invasive pneumococcal disease in Belgium following sequential use of the seven-valent, 13-valent, and ten-valent (also known as pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine [PHiD-CV]) pneumococcal conjugate vaccines (PCV7, PCV13, and PCV10, respectively). The authors cautiously hypothesise that the observed rise in invasive pneumococcal disease in children (mostly due to serotype 19A) might be linked to the PCV13-to-PCV10 switch. We would like to highlight an aspect of the Belgian setting to help contextualise these findings.

Sequential use of PCVs in a national immunisation programme is not unique to Belgium. Other countries or regions (eg, New Zealand, Sweden, Quebec in Canada, Piedmont in Italy, and Morocco) have implemented a PCV13-to-PCV10 switch, mainly driven by cost-effectiveness and the similar effects of both PCVs on reducing the overall pneumococcal disease burden—the ultimate goal of a PCV programme. The limited data available from some of these countries or regions indicate that dynamics as seen in Belgium were not observed.² Unique to Belgium is that, despite 11 years of universal PCV use and high vaccination coverage, the overall incidence of invasive pneumococcal disease in children younger than 2 years remains three to four times higher than in other European countries with similarly mature PCV programmes and reliable surveillance (appendix).^{1,3–5} Possible explanations for this high incidence are Belgium's high population density (among the highest in Europe) and widespread day-care attendance, which favour high pneumococcal transmission and disease pressure. This

hypothesis is also supported by the observation of fast replacement disease by non-PCV13 serotypes in children younger than 2 years following PCV13 implementation in Belgium.¹ After the PCV13-to-PCV10 switch, the increasing trend in non-PCV13 serotypes no longer continued and was replaced by an increase in non-PCV10 serotypes, particularly 19A.¹

Ultimately, local disease biology might be the key factor to understanding invasive pneumococcal disease dynamics following vaccine implementation. Given the high number of potentially pathogenic pneumococcal serotypes, the effect of PCVs on overall invasive pneumococcal disease might be more affected by transmission and disease pressure than by the vaccines' effects on specific serotypes. Which serotypes have a selective advantage might depend on vaccine composition, but the dynamics of replacement by non-vaccine serotypes—which determine overall disease impact—largely depend on local disease and transmission patterns, as observed in this high disease-incidence setting in Belgium. Therefore, the invasive pneumococcal disease dynamics following PCV changes in Belgium cannot be transposed to other countries.

Further monitoring of invasive pneumococcal disease epidemiology is important, but future interpretation of the dynamics of invasive pneumococcal disease following the recent PCV10-to-PCV13 switch in Belgium might be obscured by COVID-19 measures, such as physical distancing.

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See Online for appendix