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whether they were unilateral, bilateral, or multilateral. It provides information about the location and geography of the ceasefire; the ceasefire's content (eg, what acts will be included and when it will start), with a link to a statement if one publicly exists; some indication of the conflict context; and links to previous ceasefires and peace agreements available on the PA-X Peace Agreement Database. Importantly, the tracker enables ceasefires to be viewed alongside COVID-19 infection and death data pulled in real-time from the application programming interface of the Johns Hopkins University Center for Systems Science and Engineering COVID-19 Dashboard.<sup>3</sup> The ceasefire tracker is available free-of-charge in three different views: a filterable timeline of ceasefires, a searchable database, and a map view in which the COVID-19 death and infection rates can be toggled on and off.

Several aspects of the tracker shed light on the relationship between the pandemic and conflict resolution efforts (appendix). Notably, the UN Secretary General's global call was not a game changer in terms of conflict globally: despite initial ceasefire responses, the number of ceasefire declarations has decreased over time and fewer ceasefires are referencing COVID-19. Non-state armed actors have disproportionately responded, often with unilateral ceasefires that have not been reciprocated, sometimes for strategic reasons such as raising their profile internationally. However, in some areas where infection rates are high (eg, northern Syria), humanitarian ceasefires have been called.<sup>4</sup>

The ceasefire tracker forms part of a growing number of trackers that track not just health data relating to the pandemic, but also social science data focused on the political fall out of the virus, such as conflict patterns or civic freedom—which themselves will have public health consequences. It forms part of the University of Edinburgh's

growing PeaceTech approach to harnessing data and technology innovation to support peacebuilding initiatives and illustrate how data from different expert domains and of different types can be integrated and visualised.<sup>5</sup>

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## Anti-SARS-CoV-2 antibodies in healthy donor plasma pools and IVIG products

The persistent worsening of the COVID-19 pandemic demands greater efforts for epidemiological

surveillance.<sup>1,2</sup> Few studies have assessed the seroprevalence of anti-SARS-CoV-2 antibodies in the general population. These studies have generally had small sample sizes or been restricted to specific, well-defined individuals.<sup>3,4</sup> Given that more than 1000 donors contribute to a plasma pool, the antibody profile of the pool could be considered a representation of the epidemiological status of the population at the time of donation.

In May, 2020, Grifols established a programme for continuous monitoring with ELISA<sup>5</sup> of the fractionation plasma pools collected in Spain, Germany, Czech Republic, Slovakia, and the USA to track the incorporation of anti-SARS-CoV-2 antibodies into these pools and, consequently, into the resulting batches of intravenous immunoglobulin (IVIG). The first pools testing positive for anti-SARS-CoV-2 antibodies in plasma collected in Spain and the USA were detected from July to early September, 2020 (appendix pp 1–2). From mid-September to November, 2020, most pools in both countries were positive for anti-SARS-CoV-2 antibodies, with increased titres compared with earlier in the pandemic. By contrast, the first plasma pool to test positive for anti-SARS-CoV-2 antibodies in central European countries was detected in mid-November, 2020 (appendix p 3). This difference might reflect a different epidemiological status of the population in Germany, Czech Republic, and Slovakia compared with Spain and the USA.

The anti-SARS-CoV-2 antibody titres measured in the final IVIG products are also shown in the appendix (pp 1–2). Specific anti-SARS-CoV-2 antibodies were first detected in batches of IVIG products manufactured from plasma collected in the USA in September, 2020, with increased titres observed in October, 2020. Plasma from the USA is placed on an inventory hold for 60 days for traceability purposes. In addition, there is a span of 1–2 months between plasma

For the Ceasefires in a Time of COVID-19 tracker see <https://pax.peaceagreements.org/static/covid19ceasefires>

See Online for appendix

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pool preparation and the release of manufactured IVIG.

These results suggest that plasma pools for fractionation might mirror the immunogenic status of the general population regarding SARS-CoV-2. Consequently, anti SARS-CoV-2 antibodies are being increasingly integrated into therapeutic IVIG products and, presumably, into intramuscular and subcutaneous immunoglobulin products. Since these products are indicated for immunodeficient patients and other therapeutic or prophylactic approaches, a close follow-up of the progression of the presence of anti-SARS-CoV-2 antibodies in both plasma pools and IgG products is recommended.

All authors are employees of Grifols, a manufacturer of IVIG products and other blood plasma derivatives.

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## Diagnostic dilemma in COVID-19-associated pulmonary aspergillosis

We thank the community for rapid recognition and characterisation of COVID-19-associated pulmonary aspergillosis (CAPA), increasingly observed in people with severe SARS-CoV-2 infection. Consistent

with previous efforts to standardise definitions for invasive fungal infections,<sup>1–3</sup> Philipp Koehler and colleagues<sup>4</sup> propose new definitions for CAPA and provide management recommendations. We have questions and concerns for feedback.

Although we agree that standardised definitions are necessary to facilitate enrolment into clinical trials, consensus definitions for invasive fungal infections were historically supported by observational studies and not intended to guide clinical care.<sup>1,2</sup> As a newly recognised syndrome, we worry that the proposed definitions for CAPA are not adequately supported by evidence; premature confidence in definitions risks biasing outcomes of future research and directing inappropriate management, without first establishing a requisite level of evidence.

The proposed CAPA definitions are highly reliant on bronchoscopy, which is variably used, especially in surge conditions with strained infection control. A bronchoscopy-driven approach will inevitably underestimate the burden of CAPA and potentially skew trial enrolment towards people with more invasive disease.

Also, we have concerns with the biomarker cutoffs proposed. Whereas investigators have done detailed studies to determine cutoffs for galactomannan enzyme immunoassays using appropriate measures (ie, receiver operating characteristic curves) in other populations,<sup>3,5</sup> we are not aware of similar data to support recommendations for positivity at the multiple levels proposed by Koehler and colleagues, combined with requirements for repeated testing. This expert proposal is particularly problematic when cutoffs are not aligned with local regulatory recommendations. Should clinicians and investigators ignore their regulatory-cleared biomarker cutoffs in the absence of supportive evidence? Moreover, Koehler and colleagues proposed various cutoffs

for non-bronchoalveolar lavage biomarkers, which have not been cleared or validated. Although this proposal is reasonable to generate data in early research settings, one can hardly say that we have enough evidence to derive consensus.

Multiple issues arise with using definitions in different clinical and research contexts. For instance, conservative definitions are not actionable for clinical care or prevention studies—settings where the earliest therapy is essential to improve clinical outcomes. We thank our colleagues for early efforts to understand and define this new entity, but fear that more caution is needed to acknowledge critical gaps in data. We believe that establishing consensus definitions for CAPA requires more efforts, especially those directed towards deriving biomarker performance characteristics.

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