

of the use of intravenous immunoglobulins, unplanned hospitalisations, and emergency department visits after CAR T-cell therapy will provide cost and QOL estimations.

The data behind inflated valuations related to the industry-sponsored estimate of average research costs to get a drug to market are discussed elsewhere.<sup>13</sup> Although it can be argued that the high costs of CAR T-cell therapy could be justified by the value it provides, data related to the cost-effectiveness of the treatment are awaited. In the wake of substantially rising health-care expenditure on cancer care, largely driven by the costs of a small number of approved drugs, it is imperative that the regulatory bodies monitor industry-sponsored, early-phase clinical trials with a patient-centric lens so that engineered and genetically modified products in the therapeutic pipeline benefit the patients in the greatest need without clinically significant toxicity and compromise to QOL.<sup>10</sup>

It is crucial that early-phase clinical trials report efficacy, toxicity, and survival outcomes in all patients undergoing apheresis after a clinically meaningful length of follow-up to establish durability and details related to treatment-associated adverse events after CAR T-cell therapy. Acknowledging that early-phase studies are distinctive to registration trials and might not capture mortality with a short follow-up, non-relapse mortality should be reported whenever applicable.

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Muhammad Bilal Abid

mabid@mcw.edu

Division of Infectious Diseases and Division of Hematology and Oncology, BMT & Cellular Therapy Program, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI 53226, USA

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## Learning from serosurveillance for SARS-CoV-2 to inform pandemic preparedness and response

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See Online for appendix

The COVID-19 pandemic underlined the importance of serosurveillance as an evidence-based tool to understand population immunity, track viral transmission, and guide public health decision making.<sup>1</sup> Since the start of the COVID-19 pandemic more than 4200 seroprevalence studies were done in over 145 countries by testing blood specimens from more than 34 million people.<sup>2</sup> In early 2023, the Robert Koch Institute, Germany's national public health institute, convened a online symposium about international serological studies that involved research organisations, national public health agencies, institutes, and regional

public health agencies from low-income and middle-income countries and invited participants to reflect on lessons learned and draw practical conclusions on challenges, opportunities, and next steps (the participating groups are listed in the appendix). Attendees had implemented seroprevalence studies at the national or regional level since the start of the COVID-19 pandemic, and collectively addressed the questions on how to use this investment to maximise continued public health benefits and to inform future pandemic preparedness and response. Here, we discuss the primary lessons identified by the meeting attendees.

First, serosurveillance data during the early phase of the COVID-19 pandemic was useful to understand national and regional outbreak dynamics, but its utility for public health decision making has now decreased with much of the world's population having been infected or immunised against SARS-CoV-2.<sup>1</sup> Serological studies now require a more tailored focus on vulnerable populations and also the inclusion of other pathogens. An important area of their application is to guide ongoing vaccination strategies. Here, seroprevalence studies need to focus on providing data to better understand protection of vulnerable populations, such as older people and those who are immunocompromised. This is of particular value in settings where constrained health-service provision or low vaccination uptake led to a low (continuous) vaccine coverage, that could be targeted by seroprevalence led vaccination strategies.<sup>3</sup> To further increase our understanding of immunity towards COVID-19, serological research needs to focus on quantitative antibody measurements and correlates of protection, such as the seroconversion and waning of antibodies against SARS-CoV-2. Additionally, the infrastructure developed for seroprevalence studies on SARS-CoV-2 now offers the potential to support multi-pathogen serosurveillance. Testing for different pathogens or biomarkers of chronic disease would maximise the benefit of collected biosamples.

Second, reflecting on the multitude of serosurveillance studies conducted during the pandemic, common methodological challenges were evident, notably the limitations of one-time assessments (eg, cross-sectional studies) and delays in study implementation and results sharing,<sup>4</sup> which hampered the use of the results of seroprevalence studies in continuing surveillance and comparison of population immunity over time and across contexts. These challenges were compounded by the low comparability between studies with varied protocols and quality. This experience highlights that in any new pandemic scenario, resources need to be available immediately to enable rapid research decision making and underscores the importance of a coordinated approach as early as possible, such as piloted by the WHO Unity Studies during the COVID-19 pandemic.<sup>5</sup> The national and regional protocols for serosurveillance studies developed by public health

actors globally provide an important starting point. These should be collected and retained in a global or regional operational repository of open source protocols for SARS-CoV-2 and other pathogens. Such a repository would help address a range of public health questions to be shared, adapted, and implemented in a timely manner for preparedness and response to future pandemics.

Third, biobanking is widely neglected but vital for pandemic preparedness, because it allows for retention of valuable samples from seroprevalence investigations. These samples can serve as a baseline for existing or endemic pathogen immunity levels, negative controls to develop serological assays for a novel pathogen, and aid in chronic disease surveillance through biomarker testing.<sup>6</sup> Indeed, when the question about re-infection with SARS-CoV-2 emerged in 2020 the pandemic, the scarcity of stored respiratory samples hindered a timely answer to this question.<sup>7</sup> Moderate investment in strengthening biobank infrastructure regionally and globally has the potential to yield considerable public health gains and enable more rapid responses in the future. The World Bank's Pandemic Fund could provide resources to help to retain and improve in-country biobanking capacity as part of preparedness activities.

These practical lessons highlight areas for continued use of serosurveillance for preparedness and response to ongoing and future pandemics that require action now (panel). There are already initiatives under way to support this agenda and provide important steps

#### **Panel: Actions to take now to improve pandemic preparedness through serosurveillance**

##### **Refine the focus of ongoing serological studies on SARS-CoV-2**

- Guidance for ongoing vaccination strategies
- Research on COVID-19 immunity
- Shift towards multi-pathogen serosurveillance

##### **Build an operational protocol repository**

- Coordinated and timely response
- Designated funding for use in current (eg, outbreaks and seasonal epidemics) and future applications

##### **Strengthen the global infrastructure of national and regional biobanks to harness the potential of samples collected**

- Baseline immunity to emerging or endemic pathogens
- Development of tests for novel pathogens
- Surveillance through testing for biomarkers

to overcome methodological challenges and delays in study implementation and sharing of results. These initiatives include work by the WHO to establish an international framework and network to conduct seroepidemiological investigations and studies,<sup>8</sup> including an operational repository of protocols and reporting and dissemination tools that can be adapted by countries to enhance analysis.<sup>5</sup> There are also other for-profit and non-profit efforts to visualise and analyse multi-pathogen serological investigations. Additionally, the global community can benefit from current investment in human and laboratory capacities, but should call for the availability of ready-to-use funds for coordinated and timely response following the example of the Coalition for Epidemic Preparedness Innovations, an alliance to finance and coordinate the development of new vaccines to prevent and contain infectious disease epidemics.<sup>9</sup> Most importantly, these funds should account for global strengthening of biobank infrastructure, including multi-pathogen serosurveillance and the storing of samples. Sustaining and building on the investments in serosurveillance made over the past 3 years will be crucial for strengthening pandemic preparedness and response and improving global public health.

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# Public Health Collaborators on Serosurveillance for Pandemic Preparedness and Response PHSerPPR muellers@rki.de

The members of the Public Health Collaborators on Serosurveillance for Pandemic Preparedness and Response PHSerPPR are Sophie A Müller, Ambrose Agweyu, Olusola A Akanbi, Mary A Alex-Wele, Kokou N Alinon, Rahul K Arora, Saidou Balam, Bernard Barekye, Amen Ben Hamida Isabel Bergeri, Nicki Boddington, Lena Böff, Idesbald Boone, Andelé Conradie, Anahit Demirchyan, Sandra Dudareva, Charbel El Bcheraoui, Megan Evans, Elise Farley, , Iris Hunger, Jefferson M Jones, E Wangeci Kagucia, Makobu Kimani, Hannah C Lewis, Festo Mazuguni, Solomon Mwakasungula, Jason M Mwenda, Olena Nesterova, Emmanuel Nepolo, Natasha Nghitukwa, James Nyagwange, Ruth Offergeld, Tochi J Okwor, Felix Reichert, Serine Sahakyan, Sabah Shaikh, Kaveto A Sikuvu, Sabrina Weiss, Mairead Whelan, Christian H Winter, Abdhalah K Ziraba, and Johanna Hanefeld.

Robert Koch Institute, 13353 Berlin, Germany (SAM, LB, IBo, AC, SD, CEB, ME, IH, RO, FR, SW, CHW, JH); KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya (AA, EWK, MK, JN); London School of Hygiene and Tropical Medicine, London, UK (AA, JH); Nigeria Centre for Disease Control and Prevention, Abuja, Nigeria (OAA, TJO); University of Port Harcourt, Port Harcourt, Nigeria (MAA-W); University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria (MAA-W); Africa Centres for Disease Control and Prevention, Addis Ababa, Ethiopia (KNA, BB, FM); SeroTracker, Centre for Health Informatics, University of Calgary, Calgary, AB, Canada (RKA, SS, MW); University of Sciences of Techniques and Technologies of Bamako, Bamako, Mali (SB); WHO Unity Studies, WHO, Geneva, Switzerland (IB, NB, HCL); Turpanjian College of Health Sciences, American University of Armenia, Yerevan, Armenia (AD, SSA); WHO Regional Office for Africa, Brazzaville, Republic of Congo (EF, JMM); US Centers for Disease Control and Prevention, Atlanta, GA, USA (ABH, JMJ); Ifakara Health Institute, Ifakara, Tanzania (SM); State Institution "Public Health Center of the Ministry of Health of Ukraine", Kyiv, Ukraine (ON); School of Medicine, University of Namibia, Windhoek, Namibia (ENO); Namibian Ministry of Health and Social Services, Windhoek, Namibia (NN, KAS, CHW); African Population and Health Research Center, Nairobi, Kenya (AKZ)

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