by converting existing public facilities (ie, exhibition centres) into a medical setting. In Fangcang shelters, basic medical care, frequent monitoring, and rapid referral are effectively provided and implemented while relieving the burden of local medical capacities.[3] This type of clinical management for patients who recovered from COVID-19 might effectively reduce the possibility of additional virus transmission when SARS-CoV-2 re-emerges. During this follow-up study, three patients who were discharged were not able to take part in retesting because two patients died, one from comorbid coronary heart disease and another from acute respiratory distress syndrome, and the third patient had a cardiac arrest. Among patients with a negative retest, one patient had leg thrombosis that necessitated amputation.

Our finding that among patients with a positive retest 52% had IgG anti-viral antibodies and 30% had IgM antibodies suggests partial immune system recognition of SARS-CoV-2. Because 35% of patients with a positive retest had one or more COVID-19-related symptoms, the usefulness of viral antibodies in COVID-19 clearance remains in question, and the potential for continued virus transmission after hospital discharge warrants additional investigation. To prevent a second wave of COVID-19 infections, we recommend a minimum period of 14-day clinical observation in a Fangcang-like medical setting after recovery from COVID-19.

We declare no competing interests. The study was funded by Public Health and Family Planning Research Project of Hubei Province (NO.WJ2019M128), Natural Science Foundation of Hubei Province (NO.2019CFB449), and General program of National Natural Science Foundation of China (NO. 81372664). This study was approved by the institutional ethics board of Wuhan Pulmonary Hospital, Wuhan, China (2020 [7]). All participants agreed to take part in this study. QM and JuL contributed equally.

*Qi Mei, Jun Li, Ronghui Du, *Xianglin Yuan, *Ming Li, Jian Li*
yuanxianglin@hust.edu.cn, 95252925@qq.com

Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 430030 Wuhan, China (QM, XY); Department of Respiratory and Critical Care Medicine, Wuhan Pulmonary Hospital, Wuhan, China (JuL, RD, ML); and Institute for Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-University Munich, Munich, Germany (JiL)

1 WHO. Situation reports. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports (accessed June 11, 2020).
2 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395:** 1054–62.
3 Chen S, Zhang Z, Yang J, et al. Fangcang shelter hospitals: a novel concept for responding to public health emergencies. *Lancet* 2020; **395:** 1305–14.

Elimination of COVID-19: what would it look like and is it possible?

Published Online
August 6, 2020
https://doi.org/10.1016/S1473-3099(20)30633-2

In countries that have achieved a low incidence of COVID-19 infection, such as Australia and New Zealand, disease elimination has been proposed.[1,2] Yet we do not have a definition of elimination for COVID-19. Both these countries implemented early, widespread, and strict disease mitigation strategies. With low cumulative incidence, most of the population in these countries remain susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Before the availability of a vaccine, implementing exit strategies that ease social distancing restrictions will probably result in epidemics if a low level of community transmission remains or is imported through travel, as seen with the resurgence in the state of Victoria, Australia in July 2020. For other respiratory transmitted infections, such as measles, mumps, and smallpox, the prevaccine era saw recurrent epidemic cycles,[3] and a similar pattern is projected for unmitigated SARS-CoV-2 transmission, depending on the duration of immunity.[4] Reduced case counts, flattened epidemic curves, and longer interepidemic periods are also dependent on achieving immunisation coverage and reduced transmission through implementation of non-pharmaceutical interventions (NPIs).[5]

The concepts of disease elimination and eradication mostly relate to immunisation programme outcomes. Disease eradication is the global reduction of infection to zero cases, whereas disease elimination is the absence of sustained endemic community transmission in a country or other geographical region.[6] With ongoing global SARS-CoV-2 transmission, reduction to zero cases in a defined region is only possible with stringent travel restrictions. For COVID-19, modelling estimates suggested that sustained restrictions that reduced travel by 90% to and from Wuhan, China, early in the spread of SARS-CoV-2, only modestly affected the epidemic trajectory to other regions of China.[7] However, in Australia, travel bans were highly effective in controlling the spread of SARS-CoV-2 into Australia and averted a much larger epidemic.[8]

After the eradication of smallpox was declared in 1980, the global eradication of polio and the regional elimination of measles have been goals of WHO. Some countries have achieved the elimination of polio and measles, but eradication remains elusive, especially with global resurgence of measles in 2018–19.[9] Although the regional elimination of a pathogen can be achieved through continued control efforts, eradication of a disease in humans might only be feasible if humans are the only host.[10] Pathogen extinction includes destruction of all natural and laboratory stored samples. Advances in synthetic biology and genetic engineering make extinction of any human pathogen unlikely.[11]

Elimination of any infectious disease is an ambitious strategy, requiring substantial resources to achieve. The WHO criteria for elimination of measles are: evidence of low incidence, high quality surveillance with rapid outbreak response, and high population immunity.[6] Without a vaccine, the criteria of low incidence and high population immunity are mutually exclusive propositions. The basic reproduction number (R_0) for COVID-19 probably lies between 2 and 3;[12] therefore, more than 60% population immunity is required to induce herd immunity.[3] Less than 5% of the population are estimated to have been infected in high burdened countries, such as Italy,[13] excluding any consideration of plans to allow unmitigated transmission of COVID-19. Only vaccination can purposefully achieve a sustained and sufficiently high population immunity to eliminate epidemic respiratory infections such as COVID-19. Until then, NPIs flatten the epidemic curve and can lengthen the interepidemic period.

Elimination criteria require evidence of the maintenance of R_0 below 1 in a health system with the capacity to detect a case of infection if it does occur. For measles, an adequate surveillance system is measured by an annual rate of two negative measles tests per 100 000 population.[6] For infections with presymptomatic and asymptomatic transmission, such as COVID-19, several generations of transmission can occur without detection.[14] Capacity to detect COVID-19 has been estimated to require weekly COVID-19 testing rates of the population with symptoms of fever and cough of approximately 2000 tests per million population,[15] although currently achievable in some countries, this rate of testing might be difficult to maintain in the long term.

In the absence of a WHO goal for COVID-19 elimination, individual countries should instead develop their own criteria for control. This should include extensive surveillance and criteria for differentiating sustained community transmission from sporadic, non-sustaining outbreaks. A low threshold definition of sustained community transmission for COVID-19 could be at least three generations of transmission from an index case or a specified period, such as 3 months, without new cases. Periods shorter than 3 months might not be meaningful, and declarations of elimination might result in a false sense of security for the population. Setting clear parameters for defining resurgence can provide a flag for the start of a potential epidemic period and signal the need for increased use of NPIs. Without country-wide elimination, it is likely that continued management and control of COVID-19 with intermittent periods of restrictions is required until a vaccine is available.[4]

AEH reports grants from GSK, outside the submitted work. CRM reports grants from Sequirus, Sanofi, and National Health and Medical Research Council, outside the submitted work.

Anita E Heywood, C Raina Macintyre
a.heywood@unsw.edu.au

School of Public Health and Community Medicine, University of New South Wales Sydney, Sydney, NSW 2052, Australia (AEH); and The Kirby Institute, University of New South Wales Sydney, Sydney, NSW, Australia (CRM)

1 Cousins S. New Zealand eliminates COVID-19. *Lancet* 2020; **395:** 1474.
2 Group of Eight Australia. COVID-19 Roadmap to Recovery: a report for the Nation, 2020. https://go8.edu.au/research/roadmap-to-recovery (accessed July 23, 2020).
3 MacIntyre CR. On a knife's edge of a COVID-19 pandemic: is containment still possible? *Public Health Res Pract* 2020; **30:** 3012000.
4 Kissler SM, Tedijanto C, Goldstein E, Grad YH, Lipsitch M. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science* 2020; **368:** 860–68.
5 Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? *Lancet* 2020; **395:** 931–34.
6 WHO. Framework for verifying elimination of measles and rubella. *Wkly Epidemiol Rec* 2013; **88:** 89–99.
7 Chinazzi M, Davis JT, Ajelli M, et al. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science* 2020; **368:** 395–400.
8 Costantino V, Heslop DJ, MacIntyre CR. The effectiveness of full and partial travel bans against COVID-19 spread in Australia for travellers from China during and after the epidemic peak in China. *J Travel Med* 2020; published online May 22. https://doi.org/10.1093/jtm/taaa081.
9 Holt E. Global surge in measles should be "a wake-up call". *Lancet* 2019; **394:** 2137.
10 Dowdle WR. The principles of disease elimination and eradication. *Bull World Health Organ* 1998; **76** (suppl 2)**:** 22–25.
11 Noyce RS, Evans DH. Synthetic horsepox viruses and the continuing debate about dual use research. *PLoS Pathog* 2018; **14:** e1007025.
12 Li Q, Guan X, Wu P, et al. Early Transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; **382:** 1199–207.

13 Lavezzo E, Franchin E, Ciavarella C, et al. Suppression of COVID-19 outbreak in the municipality of Vo, Italy. medRxiv 2020; published online April 18. https://doi.org/10.1101/2020.04.17.20053157 (preprint).
14 Peak CM, Childs LM, Grad YH, Buckee CO. Comparing nonpharmaceutical interventions for containing emerging epidemics. *Proc Natl Acad Sci USA* 2017; **114:** 4023–28.
15 Lokuge K, Banks E, Davis S, et al. Exit strategies: optimising feasible surveillance for detection, elimination and ongoing prevention of COVID-19 community transmission. *medRxiv* 2020; published online April 23. https://doi.org/10.1101/2020.04.19.20071217 (preprint).

Inclusion of pregnant women in COVID-19 vaccine development

Published **Online** August 11, 2020
https://doi.org/10.1016/S1473-3099(20)30638-1

On Dec 31, 2019, the Wuhan Municipal Health Commission (Wuhan, China), reported a cluster of cases of pneumonia to WHO. A novel coronavirus was identified—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—and the outbreak was declared as a Public Health Emergency of International Concern in January, 2020. The virus subsequently spread rapidly throughout China and other countries worldwide, and on March 11, 2020, the outbreak was declared a pandemic. Since March 11, 2020, the virus has continued to spread, causing substantial morbidity and mortality in many countries.

In previous outbreaks of other coronavirus infections, such as severe acute respiratory syndrome and Middle East respiratory syndrome, serious complications were reported in pregnant women.[1,2] During the 2009 influenza A H1N1 pandemic, pregnant women accounted for 5% of US deaths, while representing only 1% of the US population.[3] However, despite more than 18 million reported cases of COVID-19 worldwide,[4] understanding of the effect of SARS-CoV-2 on pregnant women, fetuses, and infants is incomplete.

A systematic review and meta-analysis of mainly small case series reported that a high proportion of women with confirmed COVID-19 infection had preterm birth (<37 weeks [22%]) and caesarean delivery (48%).[5] Estimated rates of admission to the intensive care unit among pregnant women (7%) were higher than those of non-pregnant women (4%) and around 1·9% of infants born to these women tested positive for SARS-CoV-2.[5] Thus far, the literature has focused on symptomatic women with confirmed infection, however, this might underestimate the rates of admission, since many individuals are asymptomatic.[6]

Many important questions remain unanswered, including the extent of asymptomatic or mild infection and the effect of COVID-19 on miscarriage, intrauterine fetal growth restriction, congenital anomalies, long-term growth, and neurodevelopmental outcomes. The effects of Zika virus infection in pregnancy are a sobering reminder of the possible burden of viral infection in pregnant women.[7]

A comprehensive document published by the Pregnancy Research Ethics for Vaccines, Epidemics, and New Technologies Working Group in 2019 provided ethical guidance for preparedness, research, and response for pregnant women and vaccines against emerging epidemic threats.[8] The document identified a number of specific strategies to promote the ethically responsible, socially just, and respectful inclusion of the interests of pregnant women in the development and deployment of vaccines against emerging pathogens. The WHO Scientific Advisory Group of Experts welcomed this initiative and suggested it should be extended to include lactating women.[9]

The need for a vaccine against COVID-19 is indisputable. A particular consideration is that for many of the vaccine candidates and platforms being actively considered, such as nucleic acids, viral vectors, and novel adjuvants, no trials have been done in pregnant women.[10]

At present, the evidence base for pregnant women and COVID-19 is limited. Although pregnant women are not considered to be at increased risk of complications compared with non-pregnant women, they seem to be (at least) of similar risk. An additional consideration for pregnant women with COVID-19, especially among those with severe infection, is that access to effective drugs might be restricted, considering the scarcity of data on most drugs in pregnancy. The need for intensive care support among patients with COVID-19 is of particular concern for pregnant women who reside in low-income and middle-income countries.[5] These factors suggest that pregnant women should be