Vaccination strategy and challenges for consolidating successful containment of covid-19 with population immunity in China

Zijian Feng and colleagues argue that sustained elimination of SARS-CoV-2 in China offers flexibility in covid-19 vaccination policy and discuss the anticipated challenges and systematic monitoring necessary to keep the immunisation component of the response on track.

The epidemiology of covid-19 in China is unusual but not unique. SARS-CoV-2 was contained by April 2020 through a population response comprising non-pharmaceutical interventions. The overarching policy adopted from the start of the epidemic was “zero tolerance for local transmission.” Although successful and able to be sustained for 18 months with only two post-containment covid-19 deaths (fig 1), zero tolerance has major implications for the maintenance of elimination and for China’s covid-19 vaccination strategies.

The goal of China’s covid-19 response has always been to minimise morbidity, mortality, and socioeconomic damage—reflecting the values of human health, unimpeded societal functioning, and economic health. Carefully monitored use of the new covid-19 vaccines to build population immunity and protect people is integral to China’s response. We describe analyses of the epidemiological situation in China that are important for vaccination strategy and discuss the challenges and systematic monitoring necessary to keep the immunisation component of the response on track.

Analysis

Three characteristics of the post-containment epidemiology of SARS-CoV-2 inform vaccination strategy: total population susceptibility; effective but imperfect protection from imported virus through an international border quarantine programme; and a SARS-CoV-2 effective reproduction number ($R_e$) greater than 1, despite routine use of individual, environmental, and population non-pharmaceutical interventions.

Representative serological surveys taken one month after containment showed that 4.4% of Wuhan’s population, 0.4% of Hubel’s population outside of Wuhan; and less than 0.1% of the rest of China’s population had been infected, indicating that over 99.9% of the population was susceptible to SARS-CoV-2.

Every month, border quarantine stops over 700 infected people from entering China, but the process is imperfect—more than 20 outbreaks were caused by imported virus in 2020. Although stopped while small (6 to 1064 cases), each outbreak required enormous effort to contain, including test and trace, smartphone identification of close contacts, quarantine of contacts, and isolated management of infected people; some outbreaks also required total population PCR screening to identify asymptomatic infections.

**KEY MESSAGES**

- Elimination of SARS-CoV-2 from China is providing a window of time to consolidate containment by building population immunity through vaccination.
- China’s population was virtually entirely susceptible after containment, making this window of protection fragile and dependent on continued strong use of non-pharmaceutical interventions while building immunity.
- Premature lifting of non-pharmaceutical interventions invites loss of epidemic control and morbidity and mortality from covid-19, especially among elderly people and those with comorbidities.
- Sustained containment allows flexibility to logically sequence target populations for building immunity and to ultimately lift the policy of “zero tolerance for local transmission” with minimal covid-19 morbidity and mortality.
- Assessing real world vaccine performance for updating policy and vaccines is reliant, in part, on overseas studies owing to the paucity of domestic infections.
This huge effort shows that routinely used non-pharmaceutical interventions such as masks, physical distancing, travel restrictions, and hand hygiene are inadequate to stop community transmission, so $R_t$ remained $>1$ in China in the period after containment but before vaccination.

**Strategy**

Experience with other diseases that are preventable by vaccines tells us that only a major vaccination effort can make it safe to lift the zero tolerance policy without substantial loss of life and societal damage. Emerging variants may be able to break through border protection more easily, transmit more efficiently, cause more severe illness, or even escape vaccine induced immunity. Containment bought China precious time to strengthen its non-pharmaceutical interventions and develop vaccines, but it needed to be consolidated with vaccination as soon as possible.

In July 2020, after three vaccines (two inactivated and one adenovirus) were approved for overseas phase III clinical trials, China’s regulatory authority allowed their emergency use in mainland China (fig 2). Only people in occupations at risk of infection were vaccinated, such as healthcare workers in direct contact with patients and people working overseas. After successful phase III trials, conditional market authorisation was granted at the end of 2020, starting a large, carefully sequenced vaccination effort. As global public goods, the approved vaccines are also exported to meet overseas commitments as well as being used domestically.

There are three epidemiologically distinct but partially overlapping populations to consider in the vaccination strategy: people at occupational or residential risk of SARS-CoV-2 infection, people at increased risk of serious illness if infected, and people at risk of transmitting SARS-CoV-2 once infected.

People at occupational risk of infection and workers essential to maintaining social functions were vaccinated in the first quarter of 2021. The first large population to be vaccinated consisted of working age adults in broadly defined border communities—cities with international airports or ports and provinces with international borders, workers in service and high density industries, and students and staff in universities. This group is the most vulnerable to importation outbreaks and is at the highest risk of transmission to others if infected; people in this group were vaccinated by June 2021 in a time of increasing vaccine supply. The remaining working age adults and older adults rounded out the second stage of the campaign, which was completed in September 2021. Children aged 18 years and under complete the third stage, starting from adolescents aged 12-17 (who have been vaccinated) and working down in age (currently under way) (fig 2).

This sequencing is different from that recommended by the World Health Organization for countries with community transmission, in that people at the greatest risk of severe illness were not targeted immediately after healthcare workers. Having zero tolerance for local transmission effectively protects older adults, people with comorbidities, and children in the first, second, and third stages of the campaign. Vaccinating working age adults protects those who make society function and those who can more readily transmit the virus. After adults are vaccinated, children will be the only wholly susceptible population, and emerging SARS-CoV-2 variants could cause severe illness in children. Three covid-19 inactivated vaccines are approved for children aged 3 years and older. Although a decision for children under 12 has not been made yet, they are certain to follow adults in China’s vaccination campaign.

**Strategy evaluation**

The vaccination campaign is concurrent with the zero tolerance policy—how can policy makers determine whether the vaccination strategy is working in a country with little local transmission?

China relies on widespread, routine PCR testing in medical facilities, workplaces, environmental surfaces, and other accessible places to identify infections. To ensure that no infections or outbreaks are missed, the Protocol for Prevention and Control of Covid-19, has been frequently updated to incorporate increasingly sensitive population and environmental testing strategies.

If the sequencing strategy is working, deaths and hospital admissions from covid-19 should remain at or near zero. Vaccination of those at occupational risk should strengthen border quarantine protection, making importations less frequent. In contrast to the 20 importations in the last eight months of 2020, there have been four in the first eight months of 2021 (in Yunnan, Guangdong, Jiangsu, and Yunnan again). Measured $R_t$ should fall as population immunity is built, and when we have identified laboratory correlates of protection, serological surveys will be useful for determining population protection. After the zero tolerance policy is lifted, importation and transmission
and emerging SARS-CoV-2 variants can be
the
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are needed so that SARS-CoV-2 transmis-
epidemic control and what levels of cover-
enter communities without causing loss of
guarding when it is safe to stop the

Lifting “zero tolerance”
China currently has no deadline for lift-
with vaccine induced population immunity
and sustaining protective immunity using
emerging scientific evidence to adjust
vaccines, vaccination schedules, policy,
and the vaccination programme is a key
part of China’s path out of the pandemic.

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Box 1: Challenges of China’s vaccination campaign

- Inability to conduct large vaccine
  effectiveness studies in China owing to
  little local transmission
- Deciding when it is safe to stop the
  international border quarantine
  programme
- Ensuring that emerging SARS-CoV-2
  variants do not escape vaccines or non-
  pharmaceutical interventions
- Sustaining confidence in a lengthy
  vaccination campaign

will occur, but hospital admissions, severe
ilnesses, and deaths should remain low.

Vaccine evaluation
Vaccine performance and the vaccination
campaign must be monitored closely. Phase
III clinical trials showed vaccine efficacies
in WHO’s acceptable range, but too few par-
ticipants had comorbidities or were older.
Given ethical problems and the impracti-
calities of conducting placebo controlled
tests when vaccines are widely available,
real world evaluation is essential to fill evi-
dence gaps.

Vaccine effectiveness against current
and emerging SARS-CoV-2 variants can be
assessed overseas⁶ and in China. Vaccine
effectiveness against imported variants that
escape border quarantine can be assessed in
close contacts,⁷ as was done in Guangdong,
showing 70% effectiveness against the delta
variant.¹¹ We don’t yet know how well China’s
covid-19 vaccines prevent transmission
of SARS-CoV-2. As with routine childhood
vaccines, some indirect protection will
likely be seen with many covid-19 vaccines;
evidence is emerging.¹² Optimal dosing is
yet to be determined—specifically whether
a third dose will be needed for effective
and longer term protection.¹³

Vaccine safety is monitored by the Chinese
Center for Disease Control and Prevention
and the National Center for Adverse Drug
Reaction Monitoring using a passive adverse
events system that was established 15 years
ago.¹⁵ A characteristic of the system is that
all serious adverse events are evaluated for
causality. For covid-19 vaccines, the system
was modified to identify adverse events of
special interest, and active vaccine safety
is being pilot tested.¹⁶ To date, no serious
safety problem has been identified beyond
severe allergic reactions that are associated
with all vaccines.

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 mathematical transmission models that use
vaccine performance characteristics, local
vaccine coverage, and demographic data.⁸
Models can be refined with real world expe-
rience. Vaccine coverage is known and
monitored in detail in China, making it fea-
sible to construct high resolution maps of
R, and the consequences of spread to help
policy makers safely retire non-pharmaceu-
tical interventions.

Building population immunity
with vaccines requires a high degree of
compliance with vaccination
recommendations, which is challenged
by vaccine hesitancy or refusal due to
complacency about low risk of infection or
concerns about vaccines. China does not
have vaccine mandates, but vaccination
is considered by law to be a shared duty
between the public and the government.
Before any covid-19 vaccines were
approved, China had the highest rate of
demand among 19 large countries
with covid-19 epidemics.¹⁷ But confidence
is volatile, potentially changing with
external events.¹⁸ Articulating clearly
why it is important to get vaccinated and
that vaccine safety and effectiveness are
monitored carefully will help sustain
confidence. Vaccination is enabled by a
strong local public health workforce,¹⁹
making vaccines readily and freely available for all. Incentives, such as vaccine
passports, are not currently national
policy, but requiring proof of vaccination
is becoming more common and may help
attain and sustain immunity.

A corollary to Walt Orenstein’s
admonition that “vaccines don’t save
lives; vaccinations save lives”²⁰ is that
vaccines don’t build population immunity;
and sustaining confidence in a lengthy
vaccination campaign

1 Zhou L, Wu Z, Li Z, et al. One hundred days of
coronavirus disease 2019 prevention and control
in China. Clin Infect Dis 2021;73:332-9. doi:10.1093/
cid/ciaa725

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2 Li Z, Guan X, Mao N, et al. Antibody seroprevalence in the epicenter Wuhan, Hubei, and six selected provinces after containment of the first epidemic wave of covid-19 in China. Lancet Reg Health West Pac 2021;8:100094. doi: 10.1016/j.lamrhc.2021.100094

3 Li Z, Liu F, Cui J, et al. Comprehensive large-scale nucleic acid-testing strategies support China’s sustained containment of covid-19. Nat Med 2021;27:740-2. doi:10.1038/s41591-021-01308-7

4 World Health Organization. Tracking SARS-CoV-2 variants. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

5 Covid-19 Vaccines Technical Working Group. Technical vaccination recommendations for covid-19 vaccines in China (first edition). China CDC Weekly 2021;3:459-461. doi:10.46234/ccdcw2021.083.

6 World Health Organization. WHO SAGE roadmap for prioritizing uses of covid-19 vaccines in the context of limited supply. https://www.who.int/publications/i/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply.

7 Liu FT, Zheng C, Wang LP, et al. Interpretation of the protocol for prevention and control of covid-19 in China (edition 8). China CDC Weekly 2021;3:527-530. doi:10.46234/ccdcw2021.138.

8 Pan A, Liu L, Wang C, et al. Association of public health interventions with the epidemiology of the covid-19 outbreak in Wuhan, China. JAMA 2020;323:1915-23. doi: 10.1001/jama.2020.6130

9 Jara A, Undurraga EA, Gonzalez C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. N Engl J Med 2021;385:875-84. doi:10.1056/NEJMoa2107715

10 Li Y, Liu J, Yang Z, et al. Transmission of severe acute respiratory syndrome coronavirus 2 to close contacts, China, January-February 2020. Emerg Infect Dis 2021;27:2288-93. doi:10.3201/eid2709.202035

11 Kang M, Yi Y, Li Y, et al. Effectiveness of inactivated covid-19 vaccines against covid-19 pneumonia and severe illness caused by the B.1.617.2 (delta) variant: evidence from an outbreak in Guangdong, China. SSRN 2021:3895639 [Preprint]. http://dx.doi.org/10.2139/ssrn.3895639.

12 Dagan N, Bara N, Kepten E, et al. BNT162b2 mRNA covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med 2021;384:1412-23. doi:10.1056/NEJMoa2101765

13 World Health Organization. Strategic advisory group of experts on immunization. Covid-19 vaccines technical documents. https://www.who.int/gROUPS/strategic-advisory-group-of-experts-on-immunization/covid-19-materials.

14 Li MJ, Yang J, Wang L, et al. A booster dose is immunogenic and will be needed for older adults who have completed two doses vaccination with CoronaVac: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial.medRxiv 2021. doi:10.1101/2021.08.03.21261544.

15 Liu D, Wu W, Li K, et al. Surveillance of adverse events following immunization in China: Past, present, and future. Vaccine 2015;33:4041-6. doi:10.1016/j.vaccine.2015.04.060

16 Liu Z, Meng R, Yang Y, et al. Progress of active surveillance for vaccine safety in China. China CDC Weekly 2021;3:581-3. doi:10.46234/ccdcw2021.150

17 Lazaru JV, Ratzan SC, Palayew A, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med 2021;27:225-8. doi:10.1038/s41591-020-1124-9

18 Larson HJ, Broniatowski DA. Volatility of vaccine confidence. Science 2021;371:1289. doi:10.1126/science.abi6488

19 Li Z, Gao GF. Strengthening public health at the community-level in China. Lancet Public Health 2020;5:e629-30. doi:10.1016/S2468-2667(20)30266-8

20 Orenstein W. Vaccines don’t save lives. Vaccinations save lives. Hum Vaccin Immunother 2019;15:2786-9. doi:10.1080/21645515.2019.1682360

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