Title: Comprehensive large-scale nucleic acid testing strategies support China’s sustained containment of COVID-19

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To the Editor – Following identification and initial characterization of COVID-19 in late December 2019 and early January 2020, China’s containment goal has been complete interruption of local transmission of SARS-COV-2\(^1\). The nationwide epidemic wave centered on Wuhan was contained by April 2020 with non-pharmaceutical interventions (NPIs) alone, but was associated with economic loss – China’s first-quarter gross domestic product (GDP) fell 6.8% compared with first-quarter 2019\(^2\). Since containment, there have been numerous outbreaks in China caused by imported viruses with local spread, varying in size from seven to 1,200 cases, all stopped with NPIs alone\(^3\). Sustained containment has high socioeconomic value - economic activities recovered rapidly with a GDP increase of 3.2% during April-June 2020 and 4.9% during July-September\(^2\); government’s response to the pandemic was perceived positively by the Chinese public\(^4\). In this letter, we describe two large-scale PCR-based testing strategies which played critically important roles in sustaining containment since last April in mainland China - routine active PCR-based screening, and mass PCR testing during outbreak response.

With virtually all of China’s population susceptible to SARS-CoV-2 prior to induction of any vaccine-induced population immunity\(^5\), imported viruses pose an enormous threat to containment. All incoming international travelers, workers handling imported goods, medical center outpatients with fever or respiratory symptoms, and medical staff caring for patients with fever or infectious diseases are actively screened with PCR to determine if they are infected. Incoming travelers have been required to quarantine at designated hotels for 14 days following entry into China, during which time they are tested at least twice. As of 30 November 2020, 3,866 SARS-CoV-2-infected travelers were diagnosed, preventing seeding of virus in susceptible communities (Figure).

Outbreak investigations in Beijing and Dalian found that food contamination could potentially transmit SARS-COV-2\(^6\),\(^7\). Isolation of viable virus in outer packages of imported seafood in Qingdao strengthened the evidence for such transmission. Workers handling imported goods are now required to be tested weekly for SARS-COV-2, preventing several
importation-related outbreaks: for example, four dockworkers were found to have become infected in December in Dalian, and an outbreak investigation in Kashgar, Xinjiang found SARS-COV-2 importation via a contaminated cross-border truck.

Fever clinics have long been established in secondary and tertiary hospitals. Anyone with fever seeking healthcare is screened by PCR. Medical facilities admit anyone with suspected COVID-19, unexplained pneumonia, or severe acute respiratory tract infection and test the patients and accompanying persons with PCR. This screening strategy has identified index cases of several outbreaks - Xinfadi market in Beijing, Dalian, Pudong airport, Qingdao, and Manchuria.

Routine testing requires many PCR tests. Laboratories combine five or ten specimens and test the combination for SARS-CoV-2 RNA as an efficiency and cost-saving measure. If the combination tests positive, individuals whose samples were combined are tested separately to identify the infected individual(s). With a 10:1 pooled sampling approach, the average cost per person tested is approximately 9 RMB yuan ($1.50 USD) in China.

Routine PCR testing is augmented with testing of all close contacts of an infected person. Since September 2020, all close contacts of infected individuals have been required to be tested three times during a 14-day centralized quarantine period - day 1 or 2, one day later, and day 14.

Mass, community-wide PCR testing during or following outbreak response has proven to be a useful strategy to identify infected individuals, including those with no symptoms, and to determine whether a community is free of SARS-CoV-2. Once a local outbreak is identified, geographic jurisdictions are classified by epidemiologists into regions at low, moderate, or high-risk of virus transmission. Persons in high-risk settings are tested individually. In moderate-risk areas, a 5:1 or 10:1 pooled sampling approach is used to reduce the number of tests.

The first citywide mass screening was performed between May 14 and June 1, 2020 in Wuhan city, testing nearly 10 million people with PCR and identifying 300 asymptotically-
infected individuals for quarantine. The testing results were used to support full reopening of local socioeconomic activities\textsuperscript{10}. Large screening programs have been implemented following local case reports that indicated possible community transmission. For instance, during the Beijing Xinfadi outbreak, 11.9 million persons were tested between 11 June and 14 July 2020; in Dalian, 4.5 million persons were tested between 26 and 31 July; and in Qingdao, 10.9 million persons were tested between 11 and 16 October\textsuperscript{9}. These large-scale, population-wide screenings contributed to case finding and rapid control of epidemics and provided evidence for government to reopen economic activities.

Timeliness of PCR test results varies by testing purpose and epidemiologic situation. For members of the public who request PCR testing but have no symptoms or exposure history, results are to be reported within 24 hours. Results from outpatients, inpatients, caregivers, close contacts of confirmed cases, and persons residing in high-risk areas in a local outbreak setting are to be reported within 12 hours. Results for patients in fever clinics and emergency departments are to be reported within 6 hours.

In China’s new-normal situation, comprehensive, active, and innovative PCR-testing strategies are performed for targeted groups and in outbreak settings, ensuring timeliness of early case detection and interruption of local outbreaks - essential ingredients in the prevention and control strategy. Maintenance of containment has greatly reduced the impact of COVID-19 in terms of suffering, lives lost, and socioeconomic progress.

The introduction of COVID-19 vaccines globally and in China will undoubtedly improve epidemiological situations. PCR testing strategies will be adjusted to fit the changing epidemiological situations in China – likely one in which few or fewer NPIs will be needed for effective epidemic control. Inexpensive, readily available, and rapid PCR testing will continue to be essential for sensitive SARS-CoV-2 virus surveillance well into the future. Throughout 2020, PCR testing served the public well, helping to make and keep China nearly free of SARS-CoV-2, and providing socioeconomic space and time for vaccine development and long-term prevention and control of COVID-19.
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Author contributions

Zhongjie Li, Zijian Feng and George F. Gao designed and supervised the study. Zhongjie Li and Fengfeng Liu wrote the manuscript; Jinzhao Cui designed and draw the figure. Zhibin Peng, Zhaorui Chang, Qiulan Chen, Liping Wang participated in literature review and data collection. Shengjie Lai, George F. Gao commented on and revised drafts of the manuscript.

Competing interests

The authors declare no competing interests.
References


Figure legend

Local and imported COVID-19 cases from 1 April 2020 to 30 November 2020, with outbreaks and mass PCR test strategies indicated.