



INVITED REVIEW SERIES: COVID-19: FUNDAMENTAL REVIEWS

Epidemiology, clinical spectrum, viral kinetics and impact of COVID-19 in the Asia-Pacific region

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ABSTRACT

COVID-19 has hit the world by surprise, causing substantial mortality and morbidity since 2020. This narrative review aims to provide an overview of the epidemiology, induced impact, viral kinetics and clinical spectrum of COVID-19 in the Asia-Pacific Region, focusing on regions previously exposed to outbreaks of coronavirus. COVID-19 progressed differently by regions, with some (such as China and Taiwan) featured by one to two epidemic waves and some (such as Hong Kong and South Korea) featured by multiple waves. There has been no consensus on the estimates of important epidemiological time intervals or proportions, such that using them for making inferences should be done with caution. Viral loads of patients with COVID-19 peak in the first week of illness around days 2 to 4 and hence there is very high transmission potential causing community outbreaks. Various strategies such as government-guided and suppress-and-lift strategies, trigger-based/suppression approaches and alert systems have been employed to guide the adoption and easing of control measures. Asymptomatic and pre-symptomatic transmission is a hallmark of COVID-19. Identification and isolation of symptomatic patients alone is not effective in controlling the ongoing outbreaks. However, early, prompt and coordinated enactment predisposed regions to successful disease containment. Mass COVID-19 vaccinations are likely to be the light at the end of the tunnel. There is a need to review what we have learnt in this pandemic and examine how to transfer and improve existing knowledge for ongoing and future epidemics.

Key words: clinical spectrum, COVID-19, epidemiology, impact, viral kinetics.

INTRODUCTION

Coronaviruses had previously been considered as having a low impact on human health but drew more attention after the outbreak of severe acute respiratory syndrome (SARS) in 2003. With large genetic diversity and frequent genome recombination of circulating human coronaviruses (OC43, 229E, NL63, HKU1 and Middle East respiratory syndrome-CoV (MERS-CoV)),¹ a novel coronavirus (SARS coronavirus 2 (SARS-CoV-2)) emerged causing the coronavirus disease 2019 (COVID-19) pandemic in late 2019. The Asia-Pacific region (APR), which encompasses over half of the global population, first came under the threat of COVID-19. In response to the surging number of infections and the spread of SARS-CoV-2 to other continents, the World Health Organization (WHO) declared COVID-19 a pandemic on 12 March 2020. At the end of 2020, >70 million confirmed cases (Appendix S2 in Supplementary Information; thereafter denoted as 'cases') have been reported in more than 200 affected territories. The world has been experiencing unprecedented health, economic and social challenges from this pandemic. The International Monetary Fund estimated a reduction in gross domestic product of 6% for emerging and developed countries.² This pandemic has also affected different segments of the population and created social crises in terms of increasing inequality, exclusion, discrimination and global unemployment in the medium-to-long term.³ This article aims to provide an overview of the epidemiology, induced impact, viral kinetics and clinical spectrum of COVID-19 in the APR, focusing on regions previously exposed to SARS in 2003.

EPIDEMIOLOGY AND IMPACT OF COVID-19

Overview of affected populations

As of 31 December 2020, 21.1 million COVID-19 cases were recorded in 48 out of 59 territories in the APR,^{4,5} of whom 360 782 died.⁴ India ($n = 10\,266\,674$) had the largest number of cases followed by Russia ($n = 3\,127\,347$), Turkey ($n = 2\,208\,652$), Iran

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($n = 1\,225\,142$) and Indonesia ($n = 743\,198$)⁴ (Appendix S1 in Supplementary Information).

Cases were also identified in territories previously affected by SARS in 2003,⁶ including Australia (AU) ($n = 28\,425$), mainland China (CN) ($n = 87\,071$), Hong Kong (HK) ($n = 8847$), Taiwan (TW) ($n = 799$), Vietnam (VN) ($n = 1465$), New Zealand (NZ) ($n = 2162$), Singapore (SG) ($n = 58\,599$) and South Korea (SK) ($n = 61\,769$) (Fig. 1). In particular, SK was also exposed to MERS in 2015.^{6,7}

Situation in SARS-affected regions

Mainland China

On 31 December 2019, atypical pneumonia cases of unknown cause were identified in Wuhan, Hubei, marking the start of the nationwide epidemic in CN which sprawled to over 31 provinces at the end of January 2020.⁸ The epidemic peaked in early February 2020 with a median estimated basic reproductive

number (R) of 3.55 (interquartile range (IQR): 3.03–4.66) and an estimated effective reproductive number (R_t) of 2.19 (IQR: 1.76–2.48) after a citywide lockdown in Wuhan and neighbouring cities.⁹ In early March 2020, the daily incidence fell below 100 and since then, although there were still sporadic cases in some provinces, the number remained at a low level until the end of 2020 with 87 071 confirmed infections.⁴ Most transmissions (82.7% of secondary cases) occurred in households.¹⁰ Initial reported cases were either imported from CN or reported to have epidemiological links with travellers from CN.

Taiwan

TW experienced one major epidemic wave featured by imported cases (343/429) from January to April 2020.¹¹ Since the first case on 21 January 2020, sporadic cases were observed through to the end of February. At that time, there were 39 cases, of which 60% ($n = 23$) were

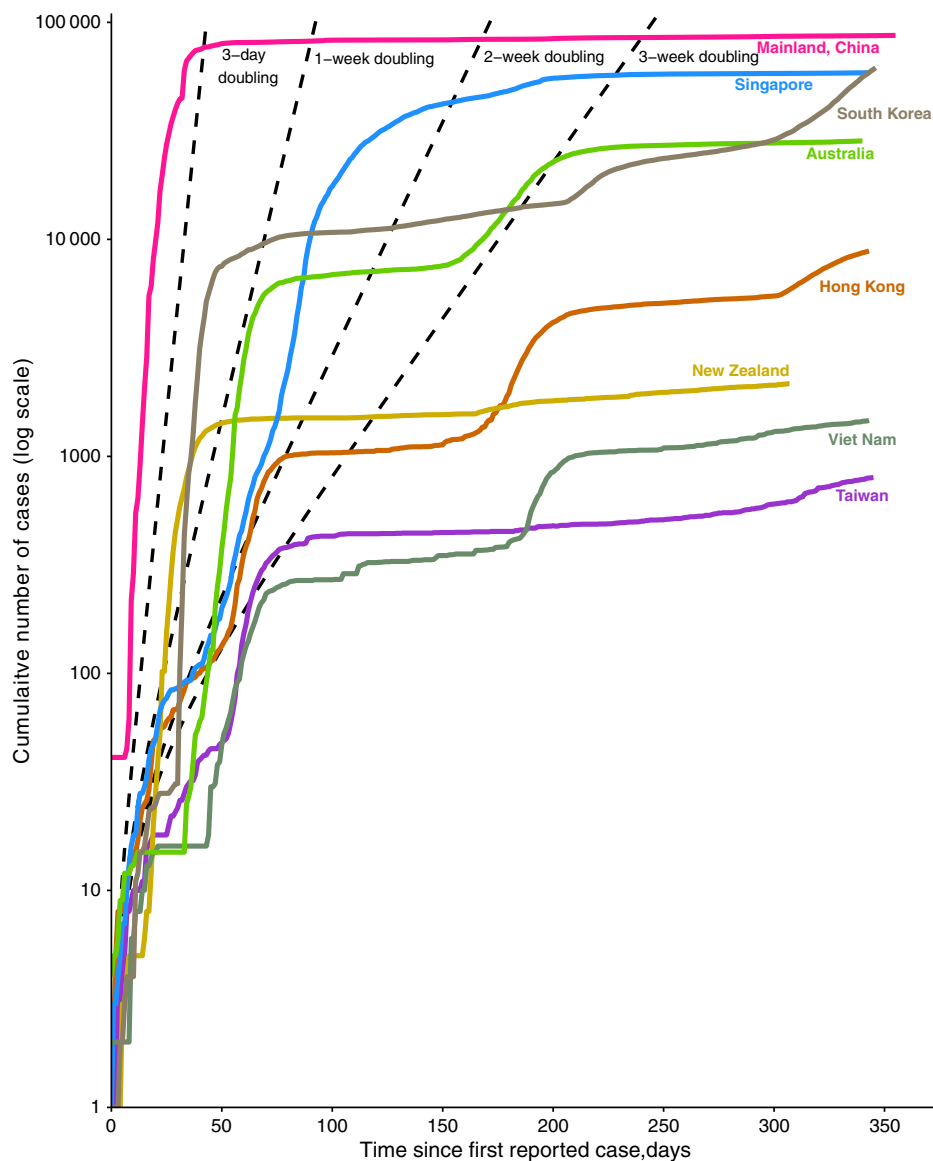


Figure 1 Cumulative number of coronavirus disease 2019 (COVID-19) cases by number of days elapsed since the first reported case in eight previous severe acute respiratory syndrome (SARS)-affected territories.⁴

attributed to three domestic families and one hospital cluster.^{12,13} Subsequently, there was another cluster with 36 infections related to naval crews of the Dunmu fleet in late April¹⁴ which did not initiate another wave. The estimated R for local community-acquired infections was 0.42.¹⁵ Since 13 April, no further local cases were reported until 22 December 2020.¹⁶

Vietnam

The occurrence of large-scale community infections marked the first epidemic wave from late January to late April 2020. Using data from the first 20-day incidence, the estimated R was 2.02.¹⁷ The largest cluster, containing 46 infections, was related to a hospital in Hanoi.¹⁸ As of 20 April 2020, VN registered 268 cases without deaths; cases were predominantly female (55.2%), aged 20–49 years (67.9%) and Vietnamese (82.5%).¹⁹ The second wave occurred between July and September 2020 and was mainly in Da Nang. The majority of infections were of the first generation (78.8%).¹⁷

Hong Kong

The first case on 23 January 2020 sparked the first epidemic wave²⁰ with two phases. Phase 1 was dominated by imported cases from CN with R estimates of 0.38 (95% credible interval (CrI): 0.35, 0.41)²¹ and 0.61 (90% CI: 0.47–0.78),²² while phase 2 was triggered by imported cases by students returning to HK from Europe and North America. About one-third of local cases were attributed to a large cluster of 103 cases with four generations of transmissions involving four pubs.²³ Using a purely contact-structured model, the R was estimated to be 2.29.²⁴ The daily incidence peaked at around 80 in March and fell below 10 in mid-April. In July, a second wave emerged, featured by locally acquired cases from several large clusters in residential care homes for the elderly (RCHE), restaurants and workplaces.²³ Sparked by a large cluster of 732 cases involving 28 dancing and singing venues, two housing estates and one RCHE, a third wave arrived in November.²⁵ As of 31 December 2020, 8847 cases (Table 1) were reported.

South Korea

The first case was identified on 20 January and the daily incidence remained low until mid-February 2020.²⁸ The first wave was initiated by a mega cluster of >5000 cases from a Shincheonji church in the city of Daegu (with a population size of 2.5 million).²⁹ The estimated R was 3.9 (95% CrI: 3.7, 4.2) and the initial doubling time was 3.80 days (95% empirical CI: 3.40–4.20); the epidemic peaked after 15 days and plateaued after 25 days.²⁹ A second wave of infections was confirmed in late June after a gradual uplift of social-distancing measures in April.³⁰ In early August, hundreds of cases from Sarang Jeil Church were found to be related to another cluster.³¹ As of 23 August, >17 000 cases were reported. The second wave peaked in late August and ended in October. Another large-scale wave arrived in early November and daily records of >1000 new cases were reported in mid-December. This wave was ongoing at the end of 2020.

Australia

AU recorded 28 425 cases and experienced two epidemic waves, one between March and April and another between late June and late September 2020.⁴ The estimated R was 2.77 (95% CI: 2.73–2.83).³² After the first COVID-19 case was reported on 25 January 2020,³³ only sporadic cases were observed from January through March. The first wave contained nearly 60% imported cases, about 25% locally acquired close contacts and around 10% domestic cases with unidentified sources.³⁴ Apart from a substantial proportion of cases from the cruise ship clusters,³⁵ some local cases were attributed to several clusters associated with airport staff,³⁶ aged care and healthcare facilities,³⁷ and private functions such as weddings.³⁷ By mid-year, >3000 cases (out of 7195) were notified by New South Wales.³⁸ However, by the end of 2020, Victoria suffered a more serious outbreak than other states and territories, reporting 20 368 cases and 820 deaths.³⁹ The sharp increase in locally acquired cases in Victoria triggered another wave. Clusters of infections and outbreaks were identified frequently in residential aged care facilities (RACF), workplaces and educational and healthcare settings.^{40,41} Locally acquired cases became the dominant infection source in the second wave.

New Zealand

NZ had one major epidemic wave from early March to early May 2020. The estimated R was 1.80.⁴² As of 10 May, there were 1503 cases, of whom 22 died. Among the dead, the mean age was 81.5 years, 50% were male and 73% lived in RACF.⁴³ About half of the cases (47%, $n = 702$) were linked to one cluster; and the 10 largest outbreaks involved multigenerational transmissions with the largest cluster having a super-spreading event at a wedding ($n = 98$), followed by outbreaks of a school ($n = 96$) and two RACFs in Canterbury ($n = 56$) and Waitemata ($n = 50$), respectively. Older age and Asian ethnicity were independently associated with locally acquired infection, and living in an RACF was associated with higher odds of severe outcomes (3.86, 95% CI: 1.59–9.35).⁴³

Singapore

SG experienced one major epidemic wave with 58 599 cases,⁴ triggered by imported cases. Subsequently, there was a substantial number of locally acquired clusters associated with business activities, family gatherings and religious events.⁴⁴ The estimated R for locally acquired infections was 2.34.²⁴ By early May, migrant workers' dormitories were the largest clusters accounting for over 85% of crude infections.⁴⁵ Under multiple control measures, specifically for clusters, the wave started to abate in early August.⁴

Highlight of epidemiological parameters

Important epidemiological time intervals or proportions that govern the disease course of COVID-19 have been widely studied (Tables 1,2). The values of these parameters vary by region. In short, the incubation period (IP) varied from 3.9 to 6.4 days, and the serial

Table 1 Cumulative number of cases, deaths and recovered, cumulative cases and deaths per 1 million population and deaths per population in eight selected previous SARS-affected territories in the Asia-Pacific region during 31 December 2019–31 December 2020^{4,26,27}

Region	Cumulative number of cases	Cumulative number of deaths	Cumulative number of recovered	Case fatality rate (%)	Cumulative cases per 1 million population	Cumulative deaths per 1 million population	Deaths per population
Australia	28 425	909	25 762	3.41	1121	35.8	1 per 27 904
Hong Kong	8847 [†]	148	7813	1.86	1178	19.7	1 per 50 726
Mainland China	87 071	4634	82 064	5.34	62.3	3.32	1 per 301 622
New Zealand	2162	25	2082	1.19	440	5.08	1 per 196 680
South Korea	61 769	917	42 953	2.09	1195	17.7	1 per 56 389
Singapore	58 599	29	58 449	0.05	10 274	5.08	1 per 196 675
Taiwan	799	7	671	1.03	33.9	0.30	1 per 3 365 891
Vietnam	1465	35	1325	2.57	15.2	0.36	1 per 2 756 060

[†]Including one possible case. SARS, severe acute respiratory syndrome.

interval (SI) ranged from 4.58 to 7.62 days. Containment delay (CD) generally ranged from 4.3 (SK) to 7.2 days (NZ) but can be up to more than 10 days among local cases (TW and SG). These time intervals are time-varying, for example, in NZ the CD decreased from 7.2 to -2.7 days with increased testing over time.⁴³

The asymptomatic proportion (AP) ranged from 27.6% (HK) to 70.0% (TW) in most countries, except CN (1.45%) and NZ (1.7%). However, in Wanzhou, CN, it surpassed 30%,⁶⁸ thus the variation in AP can be large within a country. The secondary attack rate (SAR) ranged from 3.9% (AU) to 10.3% (CN) in households, but was only 0.55% (SK) in general population. Case fatality rates (CFR) ranged from 0.05% (SG) to 5.34% (CN). AU had the highest death per populations (1 per 27 904) followed by HK (1 per 50 726) and SK (1 per 56 389).

CLINICAL SPECTRUM AND VIRAL KINETICS

Clinical spectrum

There is a wide clinical spectrum of COVID-19 ranging from asymptomatic or pre-symptomatic stage, mild, moderate and severe to critical disease with definitions as follows⁶⁹:

- *Asymptomatic or pre-symptomatic infection*: Patients who test positive for SARS-CoV-2 using a virologic test (i.e. a nucleic acid amplification test or an antigen test) but who have no symptoms of COVID-19.
- *Mild illness*: Individuals who have some symptoms and signs of COVID-19 (e.g. fever, cough, malaise,

sore throat, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and anosmia) but without evidence of viral pneumonia or hypoxia.

- *Moderate illness*: Individuals who have clinical signs of pneumonia (fever, cough, dyspnoea and fast breathing) but no signs of severe pneumonia, including SpO₂ ≥ 90% on room air.
- *Severe illness*: Individuals who have clinical signs of pneumonia (fever, cough, dyspnoea and fast breathing) plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress or SpO₂ < 90% on room air.
- *Critical illness*: Individuals who have acute respiratory distress syndrome (ARDS), septic shock and/or multiple organ dysfunction.

While the majority of patients with COVID-19 develop mild (40%) or moderate (40%) disease, about 15% develop severe disease requiring supplemental oxygen, while 5% progress to critical disease with complications such as ARDS, sepsis and septic shock, thromboembolism and/or multi-organ failure, including acute kidney injury and cardiac injury.⁷⁰ Older age, cigarette smoking and underlying co-morbid diseases, such as diabetes mellitus, hypertension, cardiac disease, chronic lung disease and malignancy, have been reported as risk factors associated with severe disease and death. Multivariable analyses have confirmed older age, higher sequential organ failure assessment (SOFA) score and D-dimer >1 µg/L on admission were associated with higher mortality. This study also observed a median duration of viral RNA detection of 20.0 days (IQR: 17.0–24.0) in survivors, while COVID-19 viral RNA was detectable until death in fatal cases.^{71,72}

Table 2 Summary of important epidemiological parameter estimates

Region	CD Estimated mean in days (95% CI)	SAR Estimated % (95% CI)	Asymptomatic proportion Estimated % (time frame)	IP Estimated mean in days (95% CI)	Serial interval Estimated mean in days (95% CI)
CN	4.6 (4.1–5.0) ^{a46}	10.3 (8.5–12.2) ^{b,c10}	1.45 ^d (April 2020) ⁴⁷	5.2 (1.8–12.4) ^{e48}	5.1 (1.3–11.6) ^{e48}
HK	6.39 (95% bCI: 5.37–7.45) ⁴⁹	11.7 (95% binCI: 7.61–16.8) ⁹⁴⁹	27.6 (November 2020) ⁵⁰	4.2 (4.0–4.5) ^{h51}	4.58 (95% bCI: 3.35–5.85) ⁴⁹
TW	3 or 10 ⁱ⁵²	0.7 (0.4–1.0) ⁹ ; 4.6 (2.3–9.3) ^{b53}	60–70 ^j (April 2020) ⁵⁴	6.0 (range: 1 to 13) ¹⁵	5.1 (range: –3 to 24) ^{k15}
VN	NA	NA	63.1 (April 2020) ¹⁹	6.4 (95% CrI: 4.89–8.5) ⁵⁵	5.83 ⁵⁶
SG	5.6 (IQR: 2–8) ^{m57}	5.9 (4.9–7.1) ^{b58}	50 (June 2020) ⁿ⁵⁹	5.54 (5.18–5.90) ⁶⁰	5.20 (95% CrI: 3.78–6.78) ^{o61}
SK	4.3 (range: 0 to 15) ^{p62}	0.55 (0.31–0.96) ⁹ ; 7.56 (3.73–14.26) ^{b63}	62.0 (July 2020) ⁶⁴	3.9 (range: 0 to 15) ⁶²	6.6 (range: 3 to 15) ^{p62}
AU	NA	3.9 (0.5–13.5) ^{b,q65}	NA	NA	7.62 (7.53–7.70) ^{r32}
NZ	7.2 (95% UI: 6.3–8.2) ^{s43}	NA	1.7 (May 2020) ⁶⁶	NA	5.0 ⁶⁷

^aStudy conducted in Shenzhen, China, from 14 January to 12 February 2020. The mean CD for cases detected via symptom-based and contact-based surveillance was 4.6 days (95% CI: 4.1–5.0) and 2.7 days (95% CI: 2.1–3.3), respectively.

^bHousehold SAR.

^cStudy was conducted in Guangzhou, China.

^dThere was a total of 81 802 COVID-19 cases by 7 April 2020, of which 1190 confirmed cases were asymptomatic after extended close follow-up and further 1095 cases tentatively were classified as asymptomatic cases but still under medical observation.

^eBased on confirmed cases reported in 30 provinces outside Hubei, China, by 17 February 2020.

^fBased on confirmed COVID-19 cases reported in HK by 13 February 2020.

^gOverall SAR.

^hEstimated median IP.

ⁱThe estimated median days from onset to report for local and imported cases were 10 and 3 days, respectively, during January to March 2020.

^jAround 60–70% of cases were regarded as asymptomatic and mild cases of COVID-19.

^kBased on cases identified in TW between 28 January and 12 April 2020.

^lBased on cases identified in VN from January to March 2020.

^mPresented as the interval from symptom onset to hospital isolation or quarantine from 2 January to 29 February 2020.

ⁿAmong all new COVID-19 cases in June 2020.

^oBased on cases confirmed in SG from 21 January to 26 February 2020 and it presented as the mean generation interval.

^pBased on cases reported in SK from 20 January to 10 February 2020.

^qStudy was conducted in the northern territory of AU.

^rPresented as generation period.

^sThe estimated mean CD during the initiation of phase 1 of control measure (i.e. travel restrictions) was 7.2 days (95% UI: 6.3 to 8.2). After the implementation of phase 4 control measures (i.e. second half of lockdown), the estimated mean CD reduced to –2.7 days (95% UI: –4.7 to –0.8).

AU, Australia; bCI, Bayesian credible interval; binCI, binomial CI; CD, containment delay; CN, mainland China; COVID-19, coronavirus disease 2019; CrI, credible interval; HK, Hong Kong; IP, incubation period; IQR, interquartile range; NZ, New Zealand; SAR, secondary attack rate; SG, Singapore; SK, South Korea; TW, Taiwan; UI, uncertainty interval; VN, Vietnam.

The median IP for COVID-19 is 4 days (IQR: 2–7 days), but can be up to 14 days.⁷³ During the ‘pre-symptomatic’ period, some infected persons can be infectious, from 1 to 3 days before symptom onset.⁷⁴ It is important to recognize that pre-symptomatic transmission occurs via infectious respiratory droplets or by direct or indirect contact with bodily fluids from an infected person while asymptomatic transmission can also occur.⁷⁵

Symptomatic transmission refers to transmission of SARS-CoV-2 from persons with symptoms to others.

Various studies have shown that transmission from symptomatic people to others predominantly occurs by close contact with respiratory droplets, by direct contact with infected persons or via contact with contaminated surfaces and objects.^{76,77}

Viral kinetics

Several viral kinetic studies with serial upper airway sampling from confirmed patients demonstrate that shedding of SARS-CoV-2 is highest in the upper respiratory

tract (URT) (nose and throat specimens) in the first week of the disease,^{78–80} peaking within the first 3 days from symptom onset, and subsequently declined with time.^{74,80,81} Another study of hospitalized patients with COVID-19 has shown very high pharyngeal virus shedding during the first week of symptoms, with a peak at 7.11×10^8 RNA copies per throat swab on day 4 while the shedding of viral RNA from sputum outlasted the end of symptoms.⁸² These data explain the high transmission potential of SARS-CoV-2 in causing community transmission among close contacts. The duration of viral RNA detection in many survivors of COVID-19 was about 37 days.^{71,72} However, patients with severe immunosuppression after receiving cellular therapies or undergoing haematopoietic stem cell transplantation may shed viable SARS-CoV-2 for no less than 2 months.⁸³ Another prospective study in New York using nasopharyngeal swab samples for patients with SARS-CoV-2 by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) has shown a significant independent association between viral load and mortality (hazard ratio (HR): 1.07 (95% CI: 1.03–1.11), $P = 0.014$), with a 7% increase in hazard for each log-transformed copy per mL.⁸⁴

The clinical course of asymptomatic and mildly symptomatic patients with COVID-19 isolated at a community treatment centre in SK was examined. Among 632 patients, 75 (11.9%) were symptomatic on admission, 186 (29.4%) were asymptomatic on arrival but became symptomatic during their stay while 371 (58.7%) remained asymptomatic throughout the entire clinical course. The mean \pm SD virologic remission period for the group was 20.1 ± 7.7 days but it was 11.7 ± 8.2 days in mildly symptomatic patients. The virologic remission period was longer in symptomatic patients than in asymptomatic patients.⁸⁵

One study based on temporal dynamics in viral shedding in patients with COVID-19 and modelling has shown the highest viral loads in throat swabs at the time of symptom onset and inferred that infectiousness peaked on or before symptom onset. The authors estimated that 44% (95% CI: 25–69%) of secondary cases were infected during the index cases' pre-symptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home.⁸⁶

In a study that examined the proportion of SARS-CoV-2 transmissions in the community that likely occurred from asymptomatic persons using decision analytical model, transmission from asymptomatic individuals was estimated to account for more than 50% of all transmissions. The study findings suggest that identification and isolation of patients with symptomatic COVID-19 alone will not control the ongoing spread of SARS-CoV-2.⁸⁷

POLICY IMPACT OF COVID-19 ON SARS-AFFECTED TERRITORIES

Health authorities of SARS-affected territories enacted interventions at the expense of social and societal benefits. Details of the interventions varied by territory but can be broadly grouped into (i) social-distancing, (ii) border control and (iii) contact-tracing and testing. Social-distancing reduces the social interaction

between individuals and is usually in the form of closing venues (such as schools and entertainment premises), work-from-home arrangements and a ban on gatherings. Border control measures block the entry of imported cases and are usually in the form of mandatory quarantine upon arrival, an entry ban for non-residents and requiring a negative test result from arrivals. Contact-tracing enables prompt identification of potential cases and digital technology greatly enhances its efficacy. SK adopted the 'corona 100m',⁸⁸ a mobile application which alerts users when they have approached locations previously visited by an infected individual. Subsequently, other countries applied similar tools (CN: Health QR Code⁸⁹; HK: LeaveHomeSafe⁹⁰; SG: Tracetoegether⁹¹; NZ: COVID-tracer⁹²; VN: Bluezone⁹³) to record the commuting history of citizens with their smartphones or a Bluetooth token to monitor whom they have contacted. The strategies for adoption and easing of control measures have varied by region and are discussed below.

Government-guided strategy

TW made a remarkable achievement in avoiding a large-scale outbreak with vigorous government-guided strategies, including prompt border control before health warnings from the WHO, social-distancing measures, a name-based rationing system for medical masks, early screening, effective methods for isolation and quarantine such as TOCC-based (travel, occupation, contact and cluster) rapid triage to arrange suspected cases with contact and travel history to outdoor clinics.⁹⁴

Suppress-and-lift strategy

The strategy involved alternate tightening and loosening of existing restrictions until the number of infections reached a low level⁹⁵ and was adopted by CN, HK, SG and VN. However, some containment measures such as mandatory mask-wearing in public areas remained in place while monitoring for possible resurgence in cases. Both the HK and SG governments provided reusable masks to all citizens for free.⁹⁶

When social-distancing measures were not sufficient in flattening the epidemic curve, CN, HK and SG adopted more stringent approaches. During the first wave, SG implemented a nationwide partial lockdown, which mainly involved a stay-at-home order and restriction of movement in specific areas⁹⁷; examples of stricter measures in HK included suspending dine-in services after 6 pm and issuing compulsory testing notices to individuals who had frequented premises related to infection clusters.⁹⁸ Similarly, CN exercised a lockdown in Wuhan and another 17 cities in Hubei and implemented active case surveillance at traffic hubs and fever clinics for suspected or confirmed cases⁸; recovered patients were suggested to perform 14-day self-health monitoring as home quarantine and have a follow-up visit on the second and fourth week after discharge.⁹⁹ With the expected daily PCR testing capacity of 10 000 in HK and 40 000 in SG,⁹⁵ high-risk groups in both territories were required to have compulsory testing to improve case identification.^{100,101} The HK

government even provided a voluntary virus testing service to all citizens to uncover hidden transmission links.¹⁰²

During the easing of restrictions, CN⁸ and HK¹⁰² used the lifting strategy, whereas SG⁹⁷ employed a three-phase plan (safe reopening, safe transition and safe nation). After the first wave ended on 1 June 2020, the first phase in SG allowed primary and secondary schools to resume face-to-face classes for students in senior forms; and in the second phase, all students were allowed to return to school.¹⁰³ Similarly, in HK, during the initially 'lift' phase in September 2020, schools were prioritized to resume for students in senior forms and (primary and secondary only) one junior form, followed by full opening in the subsequent week.¹⁰⁴ SG entered phase 3 on 28 December 2020 where social, cultural, religious and business gatherings or events resumed with limited sizes.¹⁰⁵ In HK, the maximum number of people allowed to sit at one public dining table was lifted from eight to no limit on 19 June 2020 following successful suppression of the second wave but this had led to a major upsurge of cases in the third wave which began in July 2020.²³ Dining has been banned in restaurants since 10 December 2020 as a social-distancing measure to suppress the fourth wave.¹⁰⁶ While CN resumed work and school activities in February and March, respectively,⁸ widespread active testing was first conducted at the city level (e.g. Wuhan, Beijing)^{107,108} and later expanded to the national level in August¹⁰⁹ to cover silent transmissions.

In VN, the suppress-and-lift strategy can be delineated from the border control. In the early stage of wave 1, passengers leaving international airports were screened and a stay-at-home order was enforced on citizens residing in regions or villages with active cases¹⁹; the order was later expanded to a 15-day national level lockdown in later phases of the epidemic wave in early April.¹¹⁰ Similar to SG and HK, these measures were eased in late April after the epidemic was controlled. At that time, 2119 tests were conducted per 1 million population¹⁹ which is about one-tenth of the laboratory capacity in HK and SG (HK: 21 000; SG: 24 000).¹¹¹ Subsequently, different levels of schools reopened. Domestic travel between cities resumed. A local outbreak in Da Nang and Hoi An in late July triggered the reintroduction of key interventions on 28 July. Around 80 000 people from Da Nang were evacuated to other nearby cities in early August.¹¹² Domestic air travel to and from Da Nang was suspended until 6 September.¹¹³ Thereafter, travel restrictions remained for all foreign tourists and 14-day quarantine was required among short-term business travellers arriving from designated countries.¹¹³

Trigger-based/suppression approach and alert system

Three regions used either trigger-based (SK) or suppression approaches (NZ and AU) to initiate and alert systems to ease the restrictions.

SK initially based their approach on the epidemiological threshold of an incidence of <50 cases to trigger the implementation of restrictions.⁹⁵ Alongside the general social-distancing measures, the government

adopted active contract-tracing followed by prompt isolation, treatment of cases and quick and extensive testing. In particular, the tests covered suspected cases of affected regions a few days after the outbreaks. To improve the efficiency of contact-tracing, an emergency hotline was established for health authorities to have prompt and efficient responses to individuals who had symptoms or contact with known cases.¹¹⁴ However, bans on public and religious gatherings were not imposed during the first epidemic wave.¹¹⁵ With a surge of cluster infection cases in November to initiate the third epidemic wave, several epidemiological metrics, such as the number of newly and cumulative cases and number of severe cases, were considered to revise the previous nationwide three-tier system so that the effectiveness of the interventions could be improved. A more stringent incremental physical-distancing system with a region-specific five-tier framework was implemented in early November: levels 1, 1.5, 2, 2.5 and 3 were triggered if the number of daily cases nationwide for a week was <100, >100, >300, 400–500 and 800–>1000, respectively.¹¹⁶ To limit the spread of the disease in high-risk facilities, strong restrictions were applied, such as prohibition of gatherings of >100 people in church under level 1.5 and closure of schools, restaurants, karaoke rooms, movies halls, hair salons, coffee shops and bath houses under level 3.¹¹⁷ During the Christmas and New Year holiday periods, gathering of >4 people was limited and ski resorts and tourist spots were shut down.¹¹⁸ By the end of 2020, SK had never imposed a full national lockdown.

NZ had a four-level alert system.¹¹⁹ Due to the large number of local cases observed in early March, the lockdown order was made initially on 26 March with strong containment measures, including closure of all non-essential businesses and schools to suppress or eliminate¹²⁰ to a low number or zero infections.¹²¹ Level 4 restrictions were subsequently implemented and asymptomatic testing on communities with outbreaks was conducted.^{122,123} Thereafter, community transmission started to ease. After a gradual restriction easing to level 3 on 28 April and level 2 on 2 May, NZ went to level 1 on 8 June when restrictions on gatherings, workplaces and services were lifted.¹²⁴ Following a resurgence of cases in early August, Auckland resumed level 3 restrictions.¹²⁵ On 7 October, Auckland and the rest of NZ downgraded to level 1.¹²⁶ However, NZ's borders remain closed to all foreigners and a 14-day quarantine on all returning residents is still in place as of the end of 2020.

AU had a stage 4 restriction mechanism but the link to the corresponding control measures in each stage was not explicitly mentioned.¹²⁷ A combination of key control measures mentioned earlier had likely been effective in slowing the spread of the disease in the first epidemic wave between March and April. Hotel quarantine measures were implemented on 28 March.¹²⁸ On 8 May, the government announced a state- and territory-specific three-step plan in easing restrictions in cultural venues depending on the ongoing public health situation and local epidemiology⁴¹—priority was given to libraries followed by cinemas, museums, galleries and some performing arts activities and lastly theatres inviting >100 people. A regional resurgence of

cases resulted in the lockdown in metropolitan Melbourne from 9 July¹²⁹; stage 4 and 3 restrictions were in place on 2 August in Melbourne and on 6 August in Victoria.¹³⁰ With the decline in the number of new cases, restrictions on these areas were relaxed at the end of September.¹³¹

IMPLICATION AND OUTLOOK

This review summarizes important epidemiological estimates and different bundled control and lifting measures exercised by governments at different stages of the ongoing epidemic. The end of 2020 marked the first anniversary of the COVID-19 pandemic. The territory-specific estimates of important epidemiological time intervals or proportions in the APR were very heterogeneous such that using them for inference should be handled with caution. In terms of infection rates, a contrast outcome remained substantially lower in much of the region compared to the West. Two major differences between the two hemisphere's approaches are highlighted. *First*, territories in the APR were far more attentive to COVID-19 when it first appeared due to their previous outbreak management experience of SARS in 2003 and various and recurring outbreaks of avian influenza A (H5N1), first in 1997 and then sporadically since 2002. SK even had a massive MERS outbreak in 2015. These countries became extremely vigilant and were already in a state of semi-preparedness to deal with the upcoming outbreak. Comprehensive public health infrastructure established prior to the COVID-19 pandemic allowed TW to have a prompt and coordinated response. Individuals in the APR might also have contributed to strong psychological and behavioural responses which, metaphorically, resembled a fast secondary immune response during re-exposure to the same pathogen.¹³² A comparative study between HK (a territory in APR) and the UK (a territory in the West) suggested that those who perceived severity of COVID-19 as 'high' in HK were more likely than those in the UK to adopt social-distancing measures.¹³³ *Second*, the control policies adopted in countries in the Asia-Pacific such as SG and CN were top down and citizens in this region respect authority.¹³⁴ In a controlled institution environment, the immediate implementation of draconian policies such as citywide or countrywide lockdown, compulsory quarantine of suspected cases and enforcement of visit record collection could successfully flatten the epidemic curve in a short period of time. Although implementation of some Asia-Pacific approaches used by governments in the West may induce arguments and protests from the public, the potential social and economic benefits from lockdown avoidance might lessen some objections.

With the hope of a vaccine to end this pandemic, we should review what we have learnt and examine how to transfer and improve existing knowledge for ongoing and future epidemics. Asymptomatic and pre-symptomatic transmission is a hallmark of COVID-19 and identification and isolation of patients with symptomatic COVID-19 alone will not effectively control the ongoing spread of SARS-CoV-2. For future waves,

psychological fatigue with social-distancing and new coronavirus variants may reduce the effectiveness of current control measures. For the next epidemic, early reporting of the potential disease outbreak to the WHO is essential for better containment and control; closed-loop communication between neighbouring regions is needed when a potential outbreak of infectious disease occurs to alert the healthcare system; and epidemiologists should liaise with the health department to set up a platform for real-time data access to inform prompt infection control policies. Our experience in this pandemic will ensure that we are better prepared for the next epidemic.

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Abbreviations: AP, asymptomatic proportion; APR, Asia-Pacific region; ARDS, acute respiratory distress syndrome; AU, Australia; bCI, Bayesian credible interval; CD, containment delay; CN, mainland China; COVID-19, coronavirus disease 2019; CrI, credible interval; HK, Hong Kong; IP, incubation period; IQR, interquartile range; MERS-CoV, Middle East respiratory syndrome-CoV; NZ, New Zealand; R, basic reproductive number; RACF, residential aged care facility; RCHE, residential care home for the elderly; SAR, secondary attack rate; SARS, severe acute respiratory syndrome; SARS-CoV-2, SARS coronavirus 2; SG, Singapore; SK, South Korea; SpO₂, oxygen saturation; TW, Taiwan; UI, uncertainty interval; VN, Vietnam; WHO, World Health Organization

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Supplementary Information

Additional supplementary information can be accessed via the *html* version of this article at the publisher's website.

Appendix S1. Cumulative number of cases, deaths and recovered, cumulative cases and deaths per 1 million population and deaths per population in COVID-19-affected territories (except those in Table 1) in the Asia-Pacific region during 31 December 2019–31 December 2020.

Appendix S2. Glossary of terms.