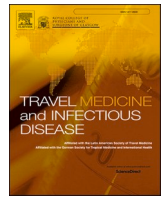




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Experience from five Asia-Pacific countries during the first wave of the COVID-19 pandemic: Mitigation strategies and epidemiology outcomes

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ABSTRACT

Background: With no vaccines or specific treatments, non-pharmaceutical interventions are the only tools for controlling the human-to-human transmission of the COVID-19 disease, which appeared in Wuhan, China last December and has spread globally since. Here we describe and compare the first-wave mitigation strategies and epidemiology of five Asia-Pacific countries that responded rapidly to the epidemic.

Methods: From January to April 2020, mitigation measures and epidemiological data for Singapore, South Korea, Japan, Taiwan, Hong Kong were screened from official local government websites and a review of investigational studies was conducted. Daily case reports and mitigation measures information were extracted. Epidemiological estimates were calculated and compared between countries.

Results: All five countries combined measures, focusing on contact tracing, testing, isolation efforts and health-care management. Epidemiological data varied temporally and geographically: incubation period ranged 3.9–7.1 days, effective reproduction number at time t (R_t) ranged 0.48–1.5, with intensive care admissions 1–3% of hospitalised patients, and case fatality rates were 0.1–3%. Extrinsic estimates to the virus were lower than global estimates.

Conclusion: Implemented mitigation strategies in these countries allowed a rapid and successful control or delay of the first COVID-19 pandemic wave. These are valuable examples to inform subsequent waves.

1. Introduction

The Asia-Pacific region is considered a primary source of global influenza epidemics and other new viruses due to its large and highly interactive human and animal populations [1,2]. This region contains an estimated population of 4.6 billion inhabitants, representing 59% of the world's population [3], with the vast majority living in high-density

urban areas [4].

In December 2019, human cases of pneumonia (later called COVID-19 disease) of unknown origin were reported in Wuhan City, Hubei Province of China. Neighbouring countries were quickly alerted because of past epidemics outbreak experiences originating from China—the avian influenza A (H7N9) virus in 2013 [5], and a previous coronavirus: the SARS-CoV in 2003 causing Severe Acute Respiratory Syndrome

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(SARS) [6]. Another coronavirus, MERS-CoV, causing the Middle East Respiratory Syndrome, emerged in 2012 in Saudi Arabia. Although both SARS and MERS caused illness ranging from common cold to more severe disease, the coronaviruses presented limited human-to-human transmission rates [6–8].

The new coronavirus, later named SARS-CoV-2, identified as the causative agent of COVID-19 by Chinese Authorities [9], has spread globally, resulting in more than 6.3 million confirmed COVID-19 cases across 188 countries/regions of the world and all Asia-Pacific countries by beginning of June 2020 [10].

The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020 by the World Health Organization (WHO) [11]. At this date, the epidemic had already been declared an emergency by official authorities of several Asian countries.

As a transmissible disease without vaccines and specific treatments, non-pharmaceutical interventions (NPI) are the only available tools to reduce human-to-human transmission of COVID-19. These include measures such as isolation of confirmed cases, social distancing, community containment measures, and quarantine [12]. For isolation to be successful at preventing transmission, early case detection is crucial, i.e., before the onset of viral shedding or at least before the onset of peak viral shedding [13]. This is particularly difficult for COVID-19 because shedding starts in the pre-symptomatic period [14], and a number of infections remain asymptomatic [15]. Laboratory testing for COVID-19 enables the identification of infected people, and tracing and quarantining of their contacts [16]. Initially, tests were recommended by the WHO for suspected cases who presented with an acute respiratory tract infection (ARI) correlated with a travel history or residence in a country/area with reported community transmission of SARS-CoV-2. Once local community transmission had been reported in a country/area, all patients presenting with ARI were considered as suspected cases and recommended to be tested [17,18]. In fact, across different countries, testing coverage ranged from more than 100 tests per 1,000 population in Iceland to only 0.1 tests per 1,000 population in Indonesia in end of April [19].

As SARS-CoV-2 spread globally, public health authorities and healthcare systems faced several challenges to make the right mitigation measure choices, complicated by the need to balance the risks to both population health and the economy. So far, some publications have reported synthesis of mitigation strategies defined by countries to reduce the impact of the epidemic [20,21], but to our knowledge no analyses have been undertaken focusing on Asia Pacific countries. Despite Asia Pacific experiencing some of the earliest cases due to strong travel links with China, several countries in the region have been commended as exemplars of early and effective implementation of mitigation measures during an epidemic [22,23].

The main objectives of this study were to describe the mitigation strategies used by selected Asia-Pacific countries outside of China to control the spread of the epidemic in their territories and to provide a synthesis of epidemiological data and their evolution, to inform modelling studies and facilitate future policy decisions.

2. Methods

2.1. Country selection

We chose five countries in the Asia-Pacific region – Singapore, South Korea, Japan, Taiwan and Hong Kong – which reported early cases of COVID-19 disease in January 2020 and that responded rapidly with implementation of mitigation measures. These countries were also chosen due to their quality of surveillance reporting with detailed measures and daily number of cases confirmed, allowing longitudinal time and country comparisons. For this analysis, Hong-Kong and Taiwan were considered separately from China as they have their own public health decision-making bodies.

2.2. Information and data sources

From January to April 2020, COVID-19 epidemiological and mitigation measures information was identified from three sources: official local government websites, English language peer-reviewed articles and press/media reports.

The mitigation strategies information was gathered by screening of official public COVID-19 information from disease control centres or Ministry of Health websites institutions locally on a daily basis. In addition, we screened main local English online newspapers for complementary information on the context of measure implementations and concerns raised at the national level.

Epidemiological data were extracted from official institutions reports according to available public updates. To complement official information, we conducted a literature review of English language peer-reviewed articles using Embase. Emtree terms are provide in supplementary material. Only information from observational studies were collected. We did not include modelling studies as COVID-19 has been evolving rapidly in the first months of the pandemic. We also hand-searched relevant articles presenting epidemiological data from observational studies using MedRxiv [24], the pre-print server for health sciences.

The period of search and data collection lasted from 01 January to 30 April 2020.

2.3. Mitigation strategies

Mitigation strategies using NPI have been previously defined for Pandemic Influenza preparedness [25] and describe the actions that persons and communities can take to help slow the spread of respiratory virus infections. To help comparison between countries, we combined the reported implemented measures into six groups:

1. Tracing and tracking of new cases through the identification of index cases and close contacts, temperature check measures in public and workplaces and the support of new digital technologies to trace contacts.
2. Laboratory SARS-CoV-2 virus testing strategies, including systematic or targeted testing.
3. Individual hygiene measures such as mask wearing for all or for symptomatic cases only and hand sanitiser use
4. Travel restrictions and border control measures to detect and manage imported cases.
5. Social distancing measures to avoid close contact between people. These include distancing or closures in schools and universities, workplaces, leisure and cultural locations (e.g. theatres, exhibitions, museums, etc.), or stricter confinement measures implemented for the whole population.
6. Management of healthcare facilities, including triage of mild versus more severe cases to different locations to control the disruption of the healthcare system.

2.4. Epidemiological data

Epidemiological data were collected from official institutions reports and from the literature review articles. From official reports, we extracted the number of daily confirmed cases, the number of hospitalised cases, the number of cases in critical care or intensive care units (ICU), the number of recovered patients and the number of COVID-19 associated deaths.

From observational studies, we extracted information on the natural history of the disease such as the incubation period (defined as the duration between estimated dates of infection and reported symptom onset), the serial interval (duration between transmission pairs in a household cluster), the duration of infectiousness, and disease transmission parameters including the Basic Reproduction number (R0)

(defined as the average number of secondary infections produced by a typical case of an infection in a population where everyone is susceptible), and the effective Reproduction number (R_t) (defined as the average number of secondary cases per infectious case in a population comprising of both susceptible and non-susceptible hosts) [26,27]. We also extracted the estimated proportion of asymptomatic cases, the crude case fatality rate and ICU proportion of hospitalised cases.

2.5. Quality control

Quality control of information and data extracted were performed by cross-checking different sources and followed by a global versus local comparison of sources.

2.6. Statistical methods

We calculated cumulative incidence estimates as the number of cumulative confirmed cases as of 30 April 2020, divided by the population size [28,29]. Case fatality ratios (CFR) were calculated as the cumulative number of deaths divided by the cumulative number of confirmed cases as of 30 April 2020.

We also estimated the testing capacity using the number of people tested for SARS-CoV-2 per 1,000 population in Singapore, South Korea, Japan, and the total number of tests performed per 1,000 population in Hong Kong and Taiwan by 30 April 2020.

Descriptive analyses were performed using Excel and graphs were made using Word with Microsoft Office 365® Pro Plus Version 1908.

2.7. Ethical considerations

This article is based on previously conducted studies or publicly available information and does not contain any individual information of human participants in studies. Therefore, no patient consent was required to perform the study.

2.8. Patient and public involvement

Patients were not involved in this study. The public has not been directly involved but a public health perspective has been considered in the formulation of research objectives and communication of the findings.

3. Results

The five countries included in our analysis: Singapore, South Korea, Japan, Taiwan, and Hong Kong, have been reporting their mitigation measures and the number of confirmed cases on a daily basis through official disease control centres or Ministry of Health websites.

3.1. Overview of number of reported confirmed cases, hospitalisations, deaths and recovered patients by country

First cases in each of these countries were detected between 16 and 23 January 2020. Over the following months, the epidemic curve has evolved differently between countries, Singapore and Japan still experiencing outbreaks in end of April whereas South Korea, Hong Kong and Taiwan passed the first wave (Figs. 1 and 2). The crude attack rates have progressively increased in each country and as of 30 April 2020, the highest cumulative incidence estimate was reported in Singapore (283.66/100,000 population) and the lowest in Taiwan (1.80/100,000 population). On 30 April 2020 the lowest CFR was reported in Singapore with 15 deaths and a CFR of 0.1%, followed by Hong Kong with 4 deaths and a CFR of 0.4%, while the highest was reported in Japan with 415 deaths and a CFR of 3.0%. CFR tend to be an underestimate especially in Singapore, Japan given the ongoing outbreaks at this time. The proportion of ICU admissions among hospitalisations were reported as 1% in Singapore, 2% in Hong Kong, and 3% in Japan on 30 April 2020. Concomitantly during this period, the proportion of recovered patients increased to be as high as 84% in South Korea but remains low in Singapore (8%), reflective of the different stage of the epidemic (Table 1).

3.2. Implementation of public health measures to control the outbreak and evolution of the testing strategies

The time interval between the first imported COVID-19 case and the start of mitigation measures was 17 days for Japan, whereas mitigation measures started before first cases were reported in Hong Kong (22 days), Singapore (21 days), South Korea (18 days) and Taiwan (1 day).

The evolution of cases and the testing capacity coverage have differed across the five Asian countries (Figs. 1 and 2, brown bars). Other key mitigation measures are detailed in Figs. 1 and 2, triangles; and Supplementary Figs. 1–5.

For Singapore, three different periods can be distinguished with regards to the evolution of cases and testing (Fig. 1A). During period 1 (20 Jan–06 Feb), symptomatic cases and close contacts were systematically tested. The Disease Outbreak Response System Condition (DORSCON), developed following the significant SARS outbreak in 2003, allowed to delay the need for lockdown through a rapidly wide-reaching response system, associating tracking, and tracing of cases. Temperature screening was quickly made mandatory in airports and extended to schools, workplaces, public buildings and healthcare settings. Progressive border control resulted in stay-home-notices (SHN) first at home and later in designated facilities for residents traveling from all countries and entry refusing for foreigners. During period 2 (07 Feb–21 Mar) with the increase of imported cases, extensive testing was deployed. Over 800 public health preparedness clinics (PHPC) screened patients with influenza-like symptoms together with recommendations of SHN to

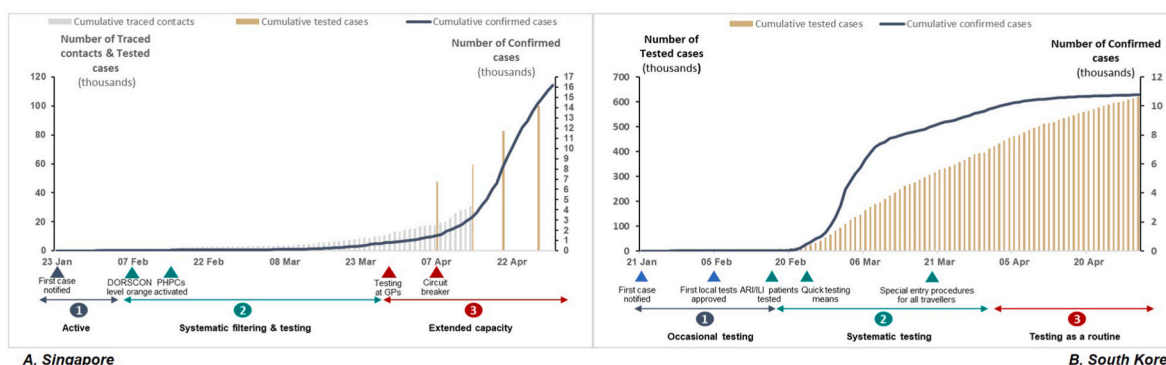


Fig. 1. Evolution of the testing strategy by country and associated number of reported cases: A. Singapore, B. South Korea.

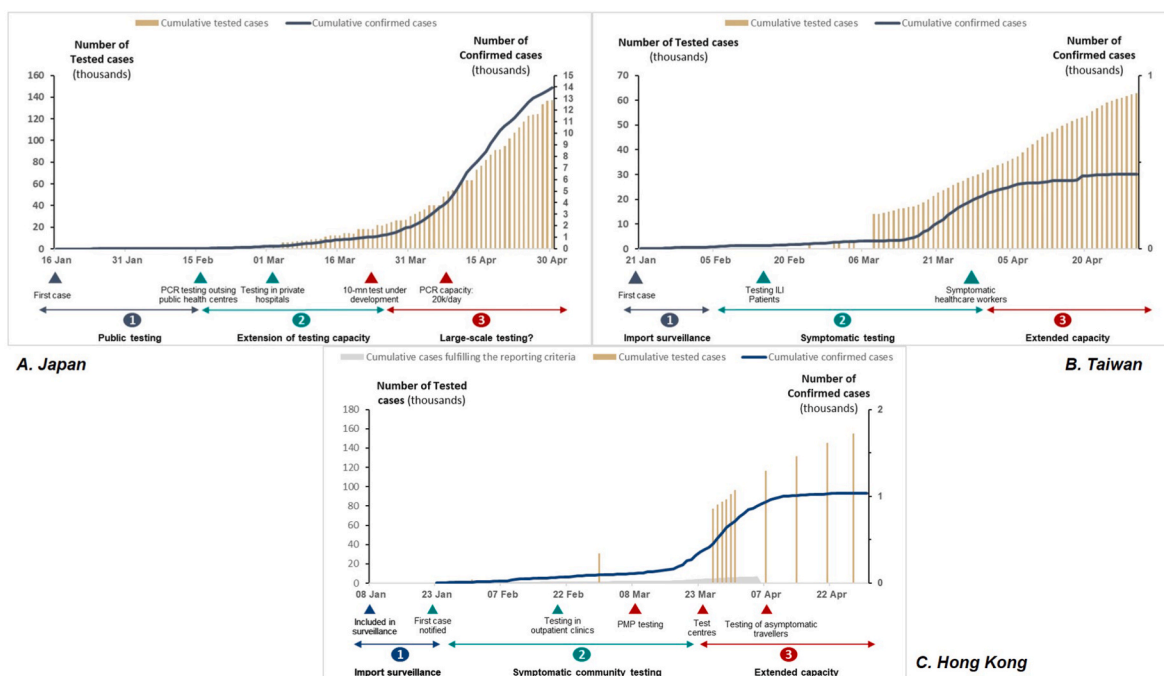


Fig. 2. Evolution of the testing strategy by country and associated number of reported cases: A. Japan, B. Taiwan, C. Hong Kong. ARI/ILI, acute respiratory infection/influenza-like illness; DORSCON, Disease Outbreak Response System Condition; GP, general practitioner; PHPC, Public Health Preparedness Clinic; ILI, influenza-like illness; PCR, polymerase chain reaction; PMP, private medical practitioner.

Table 1

Cumulative number of COVID-19 confirmed cases and epidemiological data from first case reported from January to 30 April 2020 by country.

Country	Population size (million)	First detected case (date, 2020); Time interval* (days)	Cumulative number tests n (tests per 1,000 population)	Cumulative number of people tested n (people tested per 1,000 population)	Cumulative number of infected cases n (crude incidence estimates/100,000 pop.)	Cumulative number of hospitalisations n (ICU %)	Cumulative number of deaths n (CFR %)	Cumulative number of recovered cases n (%)
Japan	126.5	16 Jan (+17)	n.k.	137,338 (1.08)	13,929 (11.01)	11,275 (3)	415 (3.0)	3,449 (25)
Taiwan	23.8	21 Jan (- 19)	62,844 (2.6)	n.k.	429 (1.80)	101 (n.k.)	6 (1.4)	322 (75)
South Korea	51.6	21 Jan (-18)	n.k.	619,881 (12.01)	10,765 (20.86)	n.k.	247 (2.3)	9,059 (84)
Hong Kong	7.4	23 Jan (-19)	160,055 (21.48)	n.k.	1,037 (14.01)	188 (2)	4 (0.4)	846 (82)
Singapore	5.7	23 Jan (-21)	143,919 (25.2)	99,929 (17.5)	16,169 (283.67)	1,708 (1)	15 (0.1)	

CFR, case fatality ratio; ICU, intensive care unit; n.k., not known; pop.: population; *Time interval: Time between the first Covid-19 confirmed case reported and the start of mitigation measures implemented by the country.

avoid over-burdening of hospitals. Singapore developed also a system of ‘Community Isolation Facilities’ for mild-symptom patients. In period 3 (21 Mar–30 Apr), the systematic tracing of contacts with immediate isolation was powered through a digital tracking method (Trace-Together app) and allowed a systematic testing of suspect cases people tested translating to 17.5 persons tested per 1,000 population (as of 27 April 2020). After a surge with new imported cases and a community spread, Singapore initiated a lockdown on 07 April 2020, with strict confinement and social distancing measures named the ‘Circuit Breaker’ (CB). On 21 April 2020, new several clusters were reported in workers’ dormitories, particular crowded areas. With the hundreds of new cases reported per day, the government reinforced and extended the CB. In end April, a total of only 15 deaths was reported and with the stricter measures, a quite stable number (around 500) of new cases per day mainly from dormitories was maintain and less than twenty new cases per day in the community [19,30].

South Korea reported the first COVID-19 case on 21 January- 2020. Three different periods can be described in line with the testing strategies: occasional testing (from 21 Jan–18 Feb), systematic large-scale testing (18 Feb–05 Apr) and routine testing (after 05 Apr) (Fig. 1B).

The outbreak was initially slow, until the patient 31 on 18 February 2020, attending a church service and leading to a sharp increase of cases in Daegu city, the epicentre. At this point, with the rapid increase of new cases, the government reacted with an aggressive testing strategy. It was the first country to introduce a drive-in testing method with a wide testing campaign (619,881 persons tested as of 30 April 2020), translating to 12.01 per 1,000 population. Every person in contact with a positive case, those coming back from other countries or presenting with symptoms were tested free of charge. Important element of the strategy included a detailed digitally tracking of movements using CCTV, phone data and credit card records and subsequent information of potential contact cases. South Korea also prioritised hospital beds for in-critical condition patients, and repurposed dormitories called ‘Life Treatment Centres’ for others. Finally, social distancing has been in place in period 2, with mask wearing in public transports and taxis, but no confinement measures. As of 30th April, South Korea has controlled the first wave of the epidemic, with only four new cases on 30 April 2020, down from the peak of 1,062 total reported cases on 02 March 2020 [19,31].

In Japan (Fig. 2A) there was no broad community testing strategy, but a systematic identification of disease clusters and rigorous tracing of

Table 2
Epidemiological parameters reported by investigational epidemiological studies (as of 30 April 2020).

Epidemiological parameter	Estimates	Country	Short description of the study	Source
Incubation period (days)	Mean: 3.9 (range 0–15) and Median: 3.0	South Korea	Analysis of 28 cases confirmed (between 20 Jan and 10 Feb 2020)	[Ki 2020] [35]
	Median: 4.0 (IQR 3–6)	Singapore	Investigation study of 3 clusters (n = 19) (15 Feb 2020)	[Pung 2020] [37]
	Mean: 5.1 (95% CI, 4.5–5.8 days)	All 5 countries	Included data from 181 confirmed cases from 24 countries outside China and 25 provinces within mainland China. Singapore (n = 16), Japan (n = 13), Taiwan (n = 10), Hong Kong (n = 8), South Korea (n = 8).	[Lauer 2020] [53]
Serial interval (days)	Mean: 7.1 (95% CI 6.13–8.25)	Singapore	Analysis of an outbreak (n = 93) from 19 Jan to 26 Feb 2020	[Tindale 2020] [36]
	Range: 3–8	Singapore	Investigation of 3 clusters (n = 19) (15 Feb 2020)	[Pung 2020] [37]
	Median: 4.0 (95% CI, 3.1–4.9)	Several, includes South Korea	Analysis of 28 infector–infectee pairs in several countries (China, Vietnam, South Korea, Germany, Taiwan, Singapore)	[Nishiura 2020] [39]
	Median: 4.4 (95% CI, 2.9–6.7)	Hong Kong	Analysis of 21 transmission chains from 16 Jan to 15 Feb 2020	[Zhao 2020] [38]
	Mean: 4.5 (95% CI 2.69–6.42)	Singapore	Analysis of an outbreak (n = 93) from 19 Jan to 26 Feb 2020	[Tindale 2020] [36]
Duration of infectiousness	No information			
	Mean: 5.2 (95% CI: –3.35–13.94)	Singapore	Estimation based on outbreak data from clusters (n = 54)	[Ganyani 2020] [54]
Reproduction number (R0)	Mean: 6.6 (range 3–15) and Median 4.0	South Korea	Among only 28 cases confirmed (between 20 Jan and 10 Feb 2020)	[Ki 2020] [35]
Effective Reproduction number at time t (Rt)	2.6 (95% CI: 2.4–2.8)	Japan	Estimated using real-time data (15 Jan to 29 Feb 2020)	[Kuniya 2020] [40]
	0.48 (95% CI 0.25–0.84)	South Korea	Analysis as of 28 confirmed cases (20 Jan to 10 Feb 2020)	[Ki 2020] [35]
	0.54 (95% CI: 0.24–0.98)	Hong Kong	Estimated on 11 Apr based on real-time data since February	[HKU Med 2020] [51]
	0.9 (95% CI: 0.7–1.0)	Singapore	Estimation from publicly available data of 247 confirmed cases between 23 Jan–17 Mar 2020	[Tariq 2020] [55]
	0.9 (95% CI: 0.7–1.1) vs 0.7 (95% CI: 0.4–0.9)	Japan	Estimate from Hokkaido City before (16–28 Feb 2020) and during (29 Feb–12 Mar 2020) the state of	[MoHLW 2020] [56]

Table 2 (continued)

Epidemiological parameter	Estimates	Country	Short description of the study	Source
Proportion of ICU patients (%)	1.28 (95% CI 1.26–1.30) before school closures and 0.72 (0.70–0.74)	Hong Kong	emergency respectively The estimated Rt was 1.28 (95% CI 1.26–1.30) during the 2-week period before the start of the school closures on Jan 22th and 0.72 (0.70–0.74) during the first 2 weeks of school closures after 22 Jan	[Cowling 2020] [42]
	1.5 (95% CI: 1.4–1.6)	South Korea	Based on analysis of 6,284 cases including 42 deaths (26 Feb 2020)	[Shim 2020] [41]
	10	Singapore	Field-report of mitigation measures implemented in Singapore and reported estimates in the period of mid-March	[Lin 2020] [50]
Proportion of asymptomatic cases (%)	11	Japan	Among 516 confirmed cases (infectious disease trend and active epidemiological survey), as of 23 Mar 2020	[NIID 2020] [45]
	1.9	South Korea	Analysis of an outbreak in a call center (1,143 tests, 97 confirmed cases, 94 working in call center with 216 employees)	[Park 2020] [57]
	7.1	South Korea	Analysis of first 28 patients nationwide, (2/28 presented no symptoms)-re-analysis in April	[Kim 2020] [44]
Duration of infectiousness	10.7	South Korea	Among 28 cases of laboratory-confirmed coronavirus 2019 by 10 Feb 2020 (3/28 presented no symptoms)	[Ki 2020] [35]
	13.1	Hong Kong	Analysis of 715 cases of SARS-CoV-2, 94 were reported as asymptomatic infections as of 31 Mar 2020	[Cowling 2020] [42]
	16.7	Hong Kong	Analysis of a household cluster of 6 persons (1/6 had no symptoms)	[Chan et al.] [49]
	18	Japan	Among 516 confirmed cases (infectious disease trend and active epidemiological survey), as of 23 Mar 2020	[NIID 2020] [45]
	33	South Korea	Based on investigation into Sejong City/ Ministry of Oceans	[KCDC 2020] [31]

(continued on next page)

Table 2 (continued)

Epidemiological parameter	Estimates	Country	Short description of the study	Source
Crude Case Fatality Ratio (CFR) (%)	33	Japan	and Fisheries clusters Analysis of 566 charter flight returnees from Wuhan (4/12 infected cases) were asymptomatic	[NIID 2020] [58]
	35	Japan	Estimate of true proportion of asymptomatic individuals of the Diamond Princess cruise Ship	[Mizumoto 2020] [47]
	0.4	Hong Kong	Mortality rate estimate as of 11 Apr 2020	[HKU Med] [51]
	0.7	South Korea	Overall Case Fatality Rate based on MoHW data as of 10 Mar 2020	[Kim 2020] [59]
	0.9	South Korea	Mortality rate as of 16 Mar 2020, for 8,236 confirmed patients	[Kang 2020] [60]
	0.9	South Korea	Report of the first 7,755 patients with confirmed COVID-19 in South Korea as of 12 Mar 2020. A total of 66 deaths have been recorded	[61]
	1.19 (males) vs 0.52 (females)	South Korea	Based on 7,555 cases as of 11 Mar 2020 including 62 female cases vs 38 male cases	[Dudley 2020] [62]
	1.5	Taiwan	Mortality rate estimate as of 14 Apr 2020	[Taiwan CDC 2020] [63]
	2.1	South Korea	Estimate as of 14 Apr 2020 (222 deaths/10,564 infected cases)	[MoHW 2020] [64]
	2.4	South Korea	Age-adjusted case fatality rate based on MoHW data and demographic data as of 24 Mar 2020	[Kim 2020] [59]
2.6 (IC 95%: 0.89–6.7)	Japan	Case fatality ratio estimate using age-adjusted data from the outbreak on the Diamond Princess cruise ship, Feb 2020	[Russell 2020] [52]	

CDC, Center for Disease Control; CI, confidence interval; IQR, Interquartile Range; HKU, Hong Kong University; KCDC, Korean Center for Disease Control; MoHW, Ministry of Health and Welfare, MoHLW, Ministry of Health, Labour and Welfare NIID: National Institute of Infectious Diseases.

contact cases for testing with an initial 500–1,500 people tested per day in period 1 (16 Jan–15 Feb) and gradual increase with 20,000 testing capacity during period 2 (16 Feb–20 Mar) and period 3 (20 Mar–30 Apr). The number of people tested was 137,338 as of 30 April 2020, translated to 1.08 per 1,000 population [32]. The Government provided a quick response on basic public health protection measures: hand sanitisers, and social distancing in period 1. The cultural norm of mask wearing (e.g., existing hay fever masks used during the winter period) helped compliance for the whole population. Japan limited use of hospital capacity for severe cases only. Confinement measures were limited to clusters. After a regular increase in the number of cases on 7 April

2020, during period 2, an emergency declaration pushed for further confinement, but it was not possible to legally enforce a complete lockdown. Investment to increase hospital beds and artificial ventilators was actioned. Measures allowed to manage the epidemic but new cases continued to be reported in period 3 reaching 13,929 cumulative cases on 30 April 2020, with less than 300 new cases per day since 27 April. In end April, it is unclear whether the epidemiological curve of cases reached a plateau [19,32].

Taiwan (Fig. 2B), combined early measures of universal mask usage, border control, and strict quarantine measures with the use of data and digital technologies. They have avoided a complete lockdown situation, even as a neighbouring country to China. An open and transparent information platform the ‘Central Epidemic Situation Command Centres’ (CECC) early in period 1 (21st Jan.–05th Feb), was established with the use of digital technologies for proactive case identification and quarantine of suspected cases since the first imported case. The CECC included LINE, a messaging app used by 21 million people and databases of the National Health Insurance Administration, National Immigration Agency and Customs Administration, allowing artificial intelligence and big data techniques to identify greater risk people based on travel and medical history. The government also controlled medical supplies and availability of masks to the general public, while building capacity for these resources and implementing a ban on export. Healthcare preparedness developed emergency response in hospitals, inventory of clinical beds and principles for patient diversion and transfers. Testing has always been focused on symptomatic cases and people with travel history from high-risk countries. Indeed, in period 1 (21 Jan–05 Feb), Taiwan tested symptomatic cases with a 14-day travel history or contact with travellers. In period 2 (05 Feb–29 Mar), testing capacity was increased and testing of (1) flu-negative patients presenting with Influenza-Like Illness (ILI), (2) pneumonia clusters or cases with no improvement after 3 days, and (3) healthcare workers with pneumonia symptoms, were added. In period 3 (29th Mar.–30th Apr.), the number of tests performed extended to reach 2.6 tests per 1,000 population. All these measures have contributed to case number remaining very low, with only 429 total confirmed cases at 30th April, the lowest of the five countries. The plateau in cumulative number was reached around mid-April, with no new cases detected on 30 April 2020 [19,33].

Hong Kong (Fig. 2C), which shares a land border of 30 km with Southern China, was able to contain the outbreak during the period 1 (08–23 Jan) by preparing a tracing/tracking scheme, implementing hygiene measures and border controls very early before the first case was reported on 23 January, Hong Kong reported only 1,037 cumulative cases and no new daily cases on 30 April 2020. During period 2 (23 Jan–23 Mar), schools were closed, staff (including government employees) were asked to work from home, religious services were conducted online and festivals/sporting events were cancelled. Border control measures with China were taken initially, followed later by banning entry to all foreign travellers. Hong Kong was the first country to practice ‘universal mask wearing’ [34] while at this time Singapore and Taiwan were instructing the wearing of masks for sick people only. There was a spike in new cases during late March (period 3, 23 Mar–20 Apr) (Fig. 2C) while the relaxing of measures, which led to tightening up once again. For individuals under quarantine, electronic bracelets were introduced (wristbands), connected to a mobile phone app (StayHomeSafe) that reported the user’s whereabouts and sent a text message alerts when users strayed too far from their quarantine zone. Hong Kong released live details of buildings with confirmed COVID-19 cases displayed in an interactive map as green and red zones which guided the movement of the general public. The testing capacity increased during this period to reach a cumulative number of tests per 1,000 population of 21.48 (as of 30 April 2020), which, along with Singapore, represented at this time the highest test coverage among the five Asia-Pacific countries analysed here [19,34].

3.3. Epidemiological data (Table 2)

We identified and extracted a total of 28 references published between 01 January and 30 April 2020.

With regards to the natural history of the disease, the incubation period has been reported in four studies investigating clusters at the beginning of the epidemic in February 2020 and has varied between 3.9 days (range 0–15) in South Korea [35] to 7.1 days (95% CI 6.13–8.25) in Singapore [36]. Chain of transmission or the serial interval between two clusters was estimated in six investigation studies in different countries and reported to vary in a range of 3–8 days in a study in Singapore [37], 4.4 days (95% CI, 2.9–6.7) in Hong Kong [38] and 6.6 days (range 3–15) in South Korea [35]. A multicentre study of 28 infector/infectee pairs including Singapore, South Korea and Taiwan reported a median serial interval of 4.0 days (95% CI, 3.1–4.9) [39]. Information on the duration of infectiousness was not available in these countries.

The R_0 was reported in Japan only and was 2.6 (95% CI: 2.4–2.8) [40]. The R_t , was reported at different dates and in different countries. In South Korea R_t has been reported as 0.48 (95% CI 0.25–0.84) from 20 January to 10 February 2020 [35] to 1.5 (95% CI: 1.4–1.6) from 20 Jan. to 6 Mar in different studies and settings [41]. In Hong Kong, although increased numbers of unlinked COVID-19 cases have been detected since early March 2020, R_t has remained around the critical threshold of 1 from 03 February until 29 March 2020 (last data available) [42].

Regarding asymptomatic cases, more than 20% of initially asymptomatic cases reported by the Korea Centres for Disease Control and Prevention following extensive testing, did not develop symptoms during hospitalisation [43], while in retrospective multicentre studies of early cases in South Korea, 10–11% of patients were asymptomatic [35, 44]. In Japan, the reported rate of infection in patients without symptoms at testing was 18% (among 516 cases) [45] but rose to 33% (8/12 cases) in a study of Japanese evacuees from Wuhan [46] and 35% based on the investigation of the Diamond Princess Cruise ship [47]. In smaller investigation studies, in Taiwan, asymptomatic cases were also reported: in the first ten SARS-CoV-2 infected patients, one patient presented with only a sore throat [48]. Similarly, in Hong Kong, one asymptomatic case was found in a household cluster of six [49] while in a larger study 13% (of 715 positive cases) were found asymptomatic [42].

Regarding severity and CFR, the severity estimated by the proportion of ICU patients was reported in only two observational studies with 10% and 11% of patients admitted to ICU in Singapore [50] and Japan [45], respectively, although at a national level from government data in Singapore and Japan on 30 April 2020, the percentage of patients in ICU were only 1% and 3% (Table 1). Case fatality ratios have been reported by the Ministry of Health, centres for disease controls and investigation studies, varying between 0.4% in Hong-Kong [51] to 1.6% in Japan [52] at different dates and in different settings.

4. Discussion

4.1. Common strategy

Singapore, South Korea, Japan, Taiwan and Hong Kong managed to control or delay their first pandemic wave. New cases per day have been decreasing since mid-April, except in Singapore and reached no new cases by 30 April in Hong-Kong and Taiwan. The main commonality in the response to COVID-19 has been to combine different types of measures, with a focus on reporting and contact tracing efforts, using new digital means. All countries initially implemented limited social distancing measures, instead focusing on quarantine and isolation of contact cases and travellers, as well as on identification of symptoms. Countries have also carefully managed the use of hospital beds: in Singapore and South Korea through isolation of mild cases in less care-intensive facilities (Community Isolation Facilities, Life Treatment Centres), in Japan with an increase of treatment capacity (artificial ventilators and hospital beds), Hong Kong with second-tier isolation

beds and Taiwan with capacity tracking. All five countries responded rapidly, with Singapore, Taiwan, and Hong Kong putting measures in place before the first case was reported in their territories.

Taiwan, with a population of 24 million living only 140 km away from mainland China, was expected to be substantially affected, but reported the lowest number of confirmed cases and the lowest cumulative incidence estimate in Asia. Early implementation of tracking and quarantine of travellers from high-risk areas may have been key to avoiding widespread introduction into the community. In addition, individual prevention measures such as the wearing of masks were systematically adopted, facilitated by good national supply capacity and a cultural acceptance of this measure –face masks are used by unwell individuals in the general community and by those particularly vulnerable to respiratory illness [42]. In Taiwan, community-wide mask wearing may thus have contributed to the early control of COVID-19 by reducing virus in saliva and respiratory droplets from individuals with subclinical or mild infection [65]. In Hong Kong, more specific non-pharmaceutical interventions (including border restrictions, quarantine and isolation, distancing, and changes in population behaviour) have been demonstrated to be associated with reduced transmission [42].

At the end of April, all countries implemented additional social distancing measures, most were relatively low-level distancing measures (e.g. no confinement of the population) rather than full lockdowns. Japan and Singapore, the two countries that managed to slow the spread of disease but not overcome the first peak with their measures, implemented community wide restrictions, which were the Circuit Breaker in Singapore, and Japan's emergency declaration, but with no legal ability to enforce a lockdown. In Hong Kong, more specific non-pharmaceutical interventions (including border restrictions, quarantine and isolation, distancing, and changes in population behaviour) have been demonstrated to be associated with reduced transmission [42].

4.2. Main differences in strategies and limitations

An important difference between countries mitigation strategies lies in large-scale testing in Singapore (17.5/1,000 population), South Korea (12.01/1,000 population) and Hong Kong (21.48 per 1000 population), while testing has remained limited in Japan (1.08/1,000 population) and targeted in Taiwan (2.6/1000 population). Comparisons of testing strategies should be cautiously interpreted as countries are reporting testing coverage or testing capacity information in different ways: in our study we found that Taiwan and Hong Kong report the number of tests performed, South Korea report the number of people tested, while Singapore and Japan report both. This distinction is important as people may be tested several times, and the number of tests a person takes is likely to vary across countries. Where testing coverage is higher and testing strategy is broader in the population, the sample of tested people may provide a less biased estimate of the incidence of the virus. Taiwan presented with a much more targeted approach where efforts of testing have focused on symptomatic cases and people with travel history from high-risk countries. Border control measures with China were taken earlier in Taiwan than in other countries allowing a better control of imported cases. Also, the number of cases reported may have been impacted by the sensitivity of the RT-PCR test and numbers should be therefore interpreted with caution [66]. Indeed, the sensitivity of RT-PCR on viral RNA swabs in clinical practice has been reported to vary depending on the site sampling: in one study (n = 205 patients), sensitivity of RT-PCR was 93% for broncho-alveolar lavage, 72% for sputum, 63% for nasal swabs, and only 32% for throat swabs [67].

Despite important efforts made to control and sequence their mitigation measures implementation, strategies presented some limitations. Except Taiwan, countries did not differentiate their approach towards at-risk versus lower risk populations. For example, other options could have included stricter confinement measures for people living in high-density areas, or to prioritise testing for populations with comorbidities and elderly people who have been early reported to be at higher risk

of hospitalisations [68]. In Singapore, the upsurge of cases in April shows that the situation of close contacts in foreign workers dormitories and the associated increased risk of COVID-19 transmission was underestimated in the initial strategy of the country. Finally, while extensive contact tracing using an app presents the advantage to help the early identification of cases and their historical contacts, the implementation of apps or extensive measures on public movements using CCTV, bank and phone data of people needs to consider privacy related concerns and their adoption limited, if not adequately addressed [69].

4.3. Epidemiological parameters

We developed a pragmatic review during the first epidemic wave and when information was scarce or rapidly evolving, grey literature such as government reports, dashboards and MedRxiv sources, have constituted an important part of our body of evidence. The lack of peer review of these sources with no risk bias assessment is an important limitation to the conclusions and needs to be considered when interpreting the information.

We found an incubation mean period range between 3.9 days and 7.1 days, which is consistent with the WHO estimate of 'around 5–6 days' and in the range of 1–14 days [70].

The proportion of ICU admissions differ between observational studies (10% in Singapore, 11% in Japan) and official numbers of reported ICU admissions (1% in Singapore to 3% in Japan). Official reports, as long as reporting is complete which is believed to be the case here, are more representative than observational studies which are developed at a specific point of time and not analysing the whole infected population. The 1%–3% ICU admissions proportions reported are lower when compared to global numbers. Indeed, although rates largely vary globally, up to one quarter of hospitalised patients, on average, have needed an ICU admission, representing 5%–8% of the total infected population [71]. ICU admissions are dependent on the severity of illness and the ICU capacity of the healthcare system [72], which may suggest that the differentiated healthcare management of cases had a positive impact on the reported severity of the disease.

We reported a lower CFR both from official reports (0.1% in Singapore to 2.3% in South Korea) and observational studies (0.4% in Hong Kong to 2.6% in Japan) compared to the WHO estimated global CFR of 3.4% at the beginning of March [23,73]. CFR estimates have varied in the first months of the epidemic due to differences between countries' control measures, management of severe patients, and reporting of cases. Also, early CFR were calculated based on small cohorts at the start of the epidemic [61]. It is expected that CFR will continue to evolve as asymptomatic cases of COVID-19, patients with mild symptoms, or individuals who are misdiagnosed, have been left out of the denominator leading to an underestimation of infected cases and an overestimation of the CFR [74]. The reported number of cases is highly dependent on the ability of the country to confirm and report their cases in a timely manner. For CFR calculations, attributable deaths may be difficult to calculate in real time, and death is associated with previously infected cases. Then, at a time point a ratio of deceased patients over the cumulative number of cases is questionable, but this similar calculation between countries might provide indicative information for comparison. For mortality estimates, denominators should consider all causes of deaths in the proportion of attributable COVID-19 deaths.

The R_0 of 2.6 found in Japan [40] is well-aligned with the reported R_0 which ranges between 2.2 and 6.4 over the past few months [75]. As R_t is time- and implementation of control measures-dependent, the variation we found between 0.48 and 1.5 is not unexpected for these countries where mitigation strategies have been put in place early at the start of the outbreak. An $R_t < 1$ indicates that the number of new cases decreases over time and, if maintained, the outbreak will be brought under control, but release of mitigation measures could allow R_t to

increase and further outbreaks to occur in the future [76].

The proportion of asymptomatic cases ranged between 1.9% and 35% of infected patients. This result is consistent with the report from Heneghan et al. that between 5% and 80% of people testing positive for SARS-CoV-2 may be asymptomatic [15]. So far, there is not one reliable study to determine the number of asymptomatic cases since they were enrolled mainly because of close contact with a person positive for COVID-19, and were incidentally found themselves with positive RT-PCR but presented no sign of the clinical features (fever, fatigue, dry cough, dyspnoea, abdominal pain) commonly attributed to the virus [75]. One possibility to elucidate the proportion of asymptomatic patients is to undertake population-based antibody testing through seroprevalence studies. This can help to discriminate between seroconverted and non-seroconverted individuals as a public health element to respond to the epidemic in hard-hit regions [77].

Interestingly, the Ferguson et al. COVID-19 model has suggested that while social distancing reduces the spread of the virus in the first months, the lifting of these measures might also allow a second wave of the pandemic later in 2020 or in 2021 [78] making the experience of countries important for national deciders to prevent the reintroduction of COVID-19.

In the absence of treatments or vaccines for a new virus, rapid and effective implementation of a combination of key mitigation measures such as contact tracing, case isolation [16] and monitoring of international arrivals was enough to control the first wave of this new virus outbreak.

5. Conclusion

With early exposure to the disease, and rapid decision needed to protect populations, South Korea, Singapore, Taiwan, Hong Kong, and Japan are a benchmark to understand potential differences in the spread of the disease and the mitigation strategies possible to implement to face the epidemic at country level. Strategies developed to control the outbreak have been a combination of measures: first targeting imported cases, testing and isolation of clusters, and healthcare management of infected cases, which have reduced or delayed the need to progress to stricter measures such as community-level lockdowns. The multi-faceted implemented mitigation strategies with the use of new digital technologies allowed a rapid and successful control or delay of the first pandemic wave. These are valuable examples that can inform public health preparedness of future waves in these and other countries.

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Data availability statement

All data relevant to the study are included in the article or uploaded as supplementary information.

Declaration of competing interest

CEG, GN, RH are employees of Sanofi Pasteur, which is developing vaccines against COVID-19. LC, OV are employees of Corporate Value Associates. CS has no competing interest to declare. PV received grants from ANIOS, consulting fees from GSK, PFIZER ASTELLAS, Biosciences.

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Appendix A. Supplementary data

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