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International Journal of Infectious Diseases 100 (2020) 490–496

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

The costs of an expanded screening criteria for COVID-19: A modelling study

Jue Tao Lim[a,1], Borame L. Dickens[a,1], Alex R. Cook[a,*], Ai Leng Khoo[b], Yock Young Dan[c], Dale Andrew Fisher[d,1], Paul Anantharajah Tambyah[d,1], Louis Yi Ann Chai[d]

[a] Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore
[b] Pharmacy and Therapeutics Office, Group Health Informatics, National Healthcare Group, Singapore
[c] Division of Gastroenterology and Hepatology, National University Health System, Singapore and Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[d] Division of Infectious Diseases, University Medicine Cluster, National University Health System, Singapore and Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

ARTICLE INFO

Article history:
Received 17 June 2020
Received in revised form 28 July 2020
Accepted 8 August 2020

Keywords:
SARS-CoV-2
COVID-19
Extended screening criteria
Nosocomial infection

ABSTRACT

Objectives: Nosocomial infection is an ongoing concern in the COVID-19 outbreak. The effective screening of suspected cases in the healthcare setting is therefore necessary, enabling the early identification and prompt isolation of cases for epidemic containment. We aimed to assess the cost and health outcomes of an extended screening strategy, implemented in Singapore on 07 February 2020, which maximizes case identification in the public healthcare system.

Methods: We explored the effects of the expanded screening criteria which allow clinicians to isolate and investigate patients presenting with undifferentiated fever or respiratory symptoms or chest x-ray abnormalities. We formulated a cost appraisal framework which evaluated the treatment costs averted from the prevention of secondary transmission in the hospital setting, as determined by a branching process infection model, and compared these to the costs of the additional testing required to meet the criteria.

Results: In the base case analysis, an $\boldsymbol{R}_0$ of 2.5 and incubation period of 4 days, an estimated 239 (95% CI: 201–287) cases could be averted over 150 days within the hospital setting through ESC. A corresponding $2.36 (2–2.85) million USD in costs could be averted with net cost savings of $124,000 (95% CI: −334,000 to 516,000). In the sensitivity analyses, when positive identification rates (PIR) were above 7%, regardless of $\boldsymbol{R}_0$ and incubation period, all scenarios were cost-saving.

Conclusion: The expanded screening criteria can help to identify and promptly isolate positive COVID cases in a cost-saving manner or within acceptable cost margins where the costs incurred from the testing of negative patients could be negated by the averted costs. Outbreak control must be sustainable and effective; the proposed screening criteria should be considered to mitigate nosocomial transmission risk within healthcare facilities.

Background

Since its emergence in Wuhan, Hubei Province, China, the Coronavirus Disease 2019 (COVID-19) has continued to spread with escalating numbers of cases and countries affected. (Dong et al., 2020) To prevent ongoing transmission, effective screening of suspected cases is necessary which enables the early identification and prompt isolation of cases for epidemic containment. These screening measures for testing have been largely guided by the World Health Organization's (WHO) case definitions (Anon, 2020a), which serve as a valuable epidemiologic tool for public health officials to track the disease and is regularly updated with the changing epidemiology and demographics of the disease. This definition includes the presentation triad of fever, chest symptoms as well as a positive contact with an active infection or travel to an area with confirmed local transmission.

COVID-19 shares many clinical similarities to other respiratory and febrile illnesses, creating significant uncertainty at the point of testing as to whether cases should be treated as a potential positive

* Corresponding author at: Saw Swee Hock School of Public Health, National University of Singapore, Tahir Foundation Building, 12 Science Drive 2, #09-01, Singapore 117549.
E-mail address: ephcar@nus.edu.sg (A.R. Cook).
[1] These authors contributed equally.

https://doi.org/10.1016/j.ijid.2020.08.025

infection. Although symptom case reports have emerged over the ongoing outbreak (Zhou et al., 2020; Wang et al., 2020; Guan et al., 2020), the case definition is dynamic, being continually updated using clinician feedback through research or policymakers who collate and publish. Both pathways however have an inevitable time delay in information dissemination. This affects clinicians and healthcare workers (HCWs) at the front line who rely on the case definition to screen and triage patients, where this epidemiologic case definition lag can lead to problems of case misclassification. The screening process should therefore maximise sensitivity to minimise the number of missed cases and risk of nosocomial transmission, which occurred in Singapore during another coronavirus outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 (Gopalakrishna et al., 2004). During this outbreak, frequent inadequately protected patient-to-HCW interactions among untested and unidentified cases (Gopalakrishna et al., 2004; Tan, 2006) led to 97 HCWs becoming infected (Koh, 2018). Due to the presence of nosocomial transmission, clinicians at the National University Hospital, Singapore (NUHS) quickly responded with a revised testing protocol. They screened patients with a substantial expansion of the admission and isolation criteria to quickly identify and isolate infected individuals whose symptom profiles were too mild to be considered for testing (Li et al., 2003; Singh et al., 2003) or for patients who sought medical attention with atypical disease presentations, especially in the pediatric or geriatric population (Chen et al., 2020). The implementation of this expanded screening criteria (ESC) placed all patients with undifferentiated fever or respiratory symptoms or chest x-ray abnormalities in isolation until all symptoms and fever were resolved or an alternative diagnosis was proven, regardless of travel history or confirmed previous exposure. Using ESC, NUH clinicians were able to identify and isolate 13 patients who did not fit the WHO SARS criteria but were eventually confirmed to have SARS, who would have otherwise been potential spreaders (the number of positive and negative cases for SARS are presented in Supplementary Table 1) (Chai, 2014).

Clinicians responded to the COVID-19 crisis similarly, implementing ESC on 7th February 2020, which was approximately three weeks after the first imported case. With widespread concerns raised regarding the low detection rate of infected travellers where most present mild symptoms (12.1% with no fever, 67.7% with cough) (World Health Organisation, 2020a) and high asymptomatic rates (Mizumoto et al., 2020) there was an estimated 1.8% ascertainment rate in Wuhan (Wu et al., 2020a).

A wider screening policy for COVID-19 and future novel respiratory viruses requires assessment in terms of its efficacy and costs. The clinical management and costs of a large proportion of negative outcomes comes at the expense of resources which can be invested in other parts of the healthcare system. The efficacy of the ESC in the long term should thus be assessed in terms of its prevention of nosocomial transmission, which may not only negate these costs but also save resources for the healthcare system. This paper therefore assesses the practicality of ESC through a cost-effectiveness analysis by estimating the number of cases that can be averted through ESC, and calculating the associated costs from the testing of negatives and cost savings from potentially averted cases.

Methods

The first case definition used by the Ministry of Health, Singapore for the testing of suspect COVID-19 cases was based on WHO and other international bodies recommendations (Chinese Communicable Disease Center, 2020). This centered on the presence of fever, respiratory illness or pneumonia, and recent travel to Wuhan, China (namely, regions with reported infections) or close contact with a COVID-19 patient (Anon, 2020b) (Table 1). Recognizing the limitations of these case definitions and extending from our experience from SARS (Tan, 2006; Chai, 2014), we proposed an expanded screening criteria (ESC) simplified for execution at the hospital triage, which was then implemented on 7 February 2020 with immediate effect. Any patients with undifferentiated fever OR respiratory symptoms OR chest x-ray abnormalities are placed into isolation on admission with respiratory precautions, and investigated until symptoms and fever resolve or an alternative diagnosis was determined (Table 1). We used our institution in Singapore, a 1000-bed tertiary hospital, as a study example (Anon, 2020c). From 8 February 2020 to 21 February 2020, 14 cases were identified through ESC which would have otherwise been missed.

We determined the total number of infected cases that could occur from each non-identified admitted COVID-19 case in a hospital setting using a branching process infection model (Figure 1), which estimates the number of new infections at each generation. Each day, a set of imported cases is designed to be able to start multiple generations of transmission. The model characterizes this influx of cases into the hospital and subsequent infections that may occur. The baseline generation represents the first COVID-19 positive case which is not deemed to be a suspected case under the non-ESC criteria (WHO criteria until 31 January 2020 or Ministry of Health criteria until 25 January 2020) but would otherwise have been isolated under ESC. Under non-ESC screening, the daily influx of symptomatic and positive cases is parameterised by a binomial distribution with a probability

Table 1
Working criteria and expanded screening criteria for evaluating patients who may be ill with or have been exposed to 2019 Novel Coronavirus (COVID-19) (Wang et al., 2020).

	World Health Organization 31 January 2020 (Anon, 2020a)	Ministry of Health, Singapore 25 January 2020	Expanded Screening Criteria for admission and isolation
A	Severe acute respiratory infection AND has history of travel to or residence in China during the 14 days prior to symptom onset	Pneumonia OR severe respiratory infection with breathlessness AND has history of travel to mainland China during the 14 days prior to symptom onset	Undifferentiated fever OR respiratory infection OR abnormal chest x-ray
B	Acute respiratory illness AND has contact with a confirmed or probable case of COVID-19 infection OR worked in or attended a health care facility where patients with confirmed or probable COVID-19 patients were being treated during the 14 days prior to symptom onset	Acute respiratory illness of any degree of severity AND has history of travel to Wuhan city or Hubei Province, China OR has been to a hospital in mainland China OR had close contact with a case of COVID-19 infection during the 14 days prior to symptom onset	

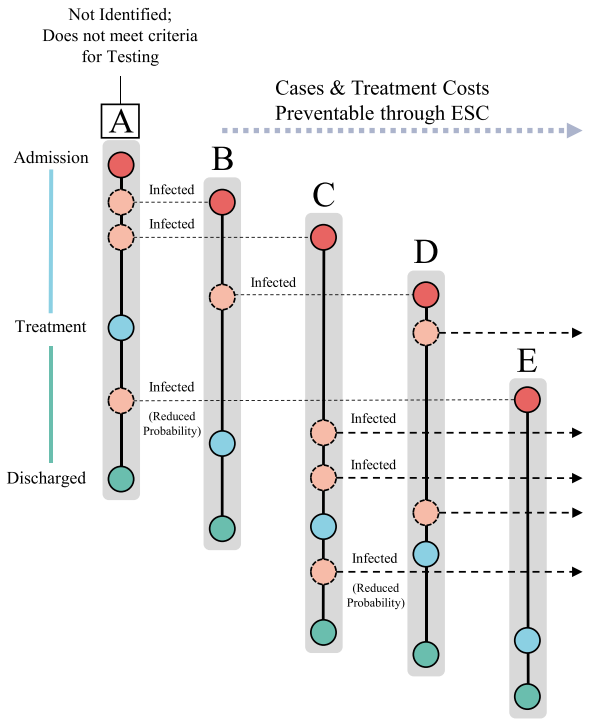

Figure 1. Branching Process SIR Model simulating secondary case generation in the hospital setting without the implementation of ESC. Multiple infection events can occur per individual over time, leading to primary, secondary and tertiary generations of cases.

determined by the positive identification rate (PIR), otherwise referred to as the proportion p of confirmed symptomatic cases observed out of the total number of observed respiratory illness cases n. All symptomatic and asymptomatic cases are assumed to be able to transmit the infection due to the closed environment within the hospital setting so are not distinguished. The number of importations γ in the hospital facility is therefore,

$$\gamma_t \sim \text{Bin}(n, p).$$

The number of infections incurred from these daily incoming non-isolated cases is determined by a Poisson distribution with a rate of infection λ, and the incubation period length which determines the infectiousness period j. Therefore the total number of infections Z at time t, to time t and incubation period j, is defined as

$$Z_{t=t:t+j} = \sum_{i=1}^{j} X_{k,i}$$

where $X_{k,i}$ denotes the size of the generation k descending from ancestor i, and determined by

$$X_{k,i} \sim \text{Poisson}(\lambda).$$

After each newly infected person's incubation period, the individual is assumed to be in the process of being identified and to have a decreasing rate of infectiousness of 10% until their end point T at 20 days. After the period $j+1$, an individual's infectiousness is consequently greatly reduced, where a person is expected to have follow up with the development of new symptoms or unexpected ongoing symptoms from the new infection of COVID-19 and is consequently isolated, or if asymptomatic, is discharged. Therefore, Z is updated to

$$Z_{t=t+j+1:T} = \sum_{i=j+1}^{T} X_{k,i}, \; X_{k,i} \sim \text{Poisson}(\lambda \times 0.1).$$

For the main analysis, we ran 50 simulations with a set of parameters taken from literature; a rate of infection (λ) of 2.5 and incubation period (IP) of 4 days (Wu et al., 2020b), and PIR rate 8.0% which is based on the upper bound for case identification in the SARS epidemic in 2003 (Rainer et al., 2007; Chowell et al., 2015; Chan et al., 2004; Assiri et al., 2013; Mohd et al., 2016; Chang et al., 2005). The full analysis was run for different parameter distributions (Table 2). For each independent combination, 50 simulations were run where the incubation period j was varied between 4–8 days, the rate of infection λ from 1.5 to 3.5 increments, and the rate of influx p from 1.0% to 30.0% in 1.0% increments based on a range of positive identification rates (PIRs) from literature on COVID-19, CoV-SARS and CoV-Middle East Respiratory Syndrome (Rainer et al., 2007; Chowell et al., 2015; Chan et al., 2004; Assiri et al., 2013; Mohd et al., 2016; Chang et al., 2005). All simulations were run across 150 days (approximately 5 months) and performed in R Version 3.6.3.

After determining the number of new cases occurring within healthcare facilities, we assessed the healthcare system costs and outcomes of implementing the proposed ESC and followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). The cost framework examined the impact of the ESC on hospitalization and testing costs while considering the transmission dynamics and importation rates of COVID-19 cases in a hospital setting. A constant daily influx of 84 patients was assumed across 150 days based on 1182 general ward patients being admitted across 14 days (8 February 2020 to 21 February 2020, Supplementary Table 2). The total number of patients being admitted to the isolation wards for undifferentiated fever or respiratory infection or an abnormal chest x-ray according to the ESC was taken to be 14.7% (174 isolated out of 1182 admitted patients, Supplementary Table 2). A proportion of these, according to the PIR, will be COVID-19 positive.

Table 2
Parameters used within the branching process model for the baseline and sensitivity analyses.

Parameter	Notation	Value	Source
Daily number of admitted patients to isolation ward	n	84	NUH
Baseline			
Positive identification rate	p	0.02	NUH
Rate of infection	λ	2.5	Wu et al. (2020b)
Incubation period	j	4 days	Anon (2020d), Linton et al. (2020)
Sensitivity analysis			
Positive identification rate	p	0.01–0.30	Rainer et al. (2007), Chowell et al. (2015), Chan et al. (2004), Assiri et al. (2013), Chang et al. (2005), Chang et al. (2005)
Rate of infection	λ	1.0–3.5	Wu et al. (2020b)
Incubation period	j	4–8 days	Anon (2020d), Linton et al. (2020)

All costs presented are in US Dollars with no discounting for the year 2020. The net cost of ESC is calculated as the total hospitalization costs for the isolation of negative patients subtracted from the total hospitalization costs averted from the isolation of positive cases which would have otherwise been missed by a non ESC criteria. For the former, the total hospitalisation cost for the isolation of negative cases was the total number of negative diagnoses at the cost of $1201 each, as all patients receive 2 Coronavirus Polymerase Chain Reaction (PCR) tests and a respiratory isolation room cost (Supplementary Table 3). This represents the costs to the healthcare system which should be minimised as they require no further isolation measures. For the latter, the total cost averted from the isolation of positive cases under the ESC was determined by the branching process model with an associated testing and treatment cost each. These COVID-19 positive patients inherit the same initial costs as negative patients at the testing phase and have subsequent treatment costs depending on whether they require Intensive Care Unit (ICU) stay with a probability of 26.6% based on patient outcome profiles from literature (Wang et al., 2020; Anon, 2020e). Those who do not require ICU admission had treatment costs totalling $8630 each. Procedures included weekly chest x-rays, liver function tests and cardiac enzymes assessments, twice weekly C-Reactive Protein tests, full blood count tests and PCR tests to examine viral clearance rates, and one CT Thorax on admission across 14 days (Supplementary Table 4). Patients who required ICU care received an additional cost for 7 days of intensive care management, followed by the standard respiratory isolation procedures for a non-ICU patient at a total of $12 658 (Supplementary Table 5).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

At an R_0 of 2.5 and incubation period (IP) of 4 days, approximate to estimates by Wu et al. (2020c) for Wuhan, an estimated 240 (95% CI: 200–290) cases would be prevented over 150 days through ESC by isolating patients presenting fever or respiratory symptoms such as cough with their travel and exposure profile not considered (Table 3). With an observation of 84 patients being admitted per day into hospital and a corresponding total of 12,600 across the 150-day period (Supplementary Table 2), 1900 patients would be expected to enter respiratory isolation of which 200 (95% CI: 170–230) to 300 (95% CI: 250–370) would be COVID-19 positive, depending on the R_0 (Table 2). A total cost between $2.0 million (95% CI: 1.7–2.3 million) to $3.0 million (95% CI: 2.5–3.7 million) could be potentially averted from the isolation of these patients. A corresponding cost saving at an R_0 of 2.5 or greater can be achieved with $120,000 (95% CI: −330,000 to 520,000) to $740,000 (95% CI: 120,000–1,400,000) saved. Of note, if the proportion of positive cases is taken to be 8.0%, which represents the upper bound of SARS patient identification during the testing period for the 2003 epidemic (Rainer et al., 2007; Chowell et al., 2015; Chan et al., 2004; Assiri et al., 2013; Mohd et al., 2016; Chang et al., 2005), the total cost of testing for negative patients is $1.9 million at this PIR.

When increasing the PIR from 1.0% to 30.0%, the number of COVID-19 infected individuals averted at the hospital drastically increases from 29 (95% CI: 18–48) to 900 (95% CI: 840–1000) at $R_0 = 2.5$ and IP of 4 days (Figure 2A–F), with substantial increases averted when R_0 increases from 1.0 to 3.5. Increasing the R_0 or decreasing the IP resulted in a greater number of infections, although the latter parameter had a smaller effect. For example, at a PIR of 5.0%, IP of 8 days and R_0 of 1.0 versus 3.5, there was an average of 0.68 (95% CI: 0.34–0.82) to 1.02 (95% CI: 0.85–1.21) infected patients arriving daily (Supplementary Figure 1A and B). At the higher R_0 of 2, PIR of 5.0% and IP of 6 versus 8, 0.83 (95% CI: 0.73–1.01) to 0.79 (95% CI: 0.66–0.92) infected patients were expected to enter a hospital facility (Supplementary Figure 1C and D). In contrast, increasing the PIR from 1.0% to 20.0% had a more dramatic increase from 0.15 (95% CI: 0.09–0.26) to 3.23 (95% CI: 3.00–3.92) patients, when keeping the R_0 fixed at 2 and IP at 4 days (Supplementary Figure 1E and F).

With an incubation period of 4–8 days, the net cost savings of ESC are $7.5 million (95% CI: $7.1–$8.6 million) at R_0 of 2.5 and ranged between −$2.1 million (95% CI: −$2.2 to −$2.0 million) to $10.4 (95% CI: 8.1–$11) million for an R_0 of 1.0–3.5 (Figure 3A). A higher R_0 causes ESC to yield larger cost savings with this difference in cost savings being more pronounced at higher PIR values. At a PIR of 1.0%, having an R_0 of 1.5 versus 3.5 increases the cost savings by $153,000 with 14 more infections averted (Figure 3B) but at a PIR of 30.0%, this difference widens to $5.0 million (Figure 3A) with 440 more infections averted (Figure 3B). However, provided that the PIR is above 8.0%, regardless of R_0, cost savings can be achieved through ESC implementation. Notably, less than a 3.0% difference was recorded in net cost savings across the R_0 of 1–3.5 at a PIR of 1.0%, with the largest change being a −$49,000 decrease in net cost savings at the R_0 of 3.5. Across all R_0 and PIR

Table 3
The net cost of expanding the screening criteria (ESC) for different basic reproduction values at a positive identification rate of 8.0%, which represents the upper bound for SARS infection identification rates in the 2003 pandemic. (Rainer et al., 2007; Chowell et al., 2015; Chan et al., 2004; Assiri et al., 2013; Mohd et al., 2016; Chang et al., 2005) All costs are rounded to the nearest ten if greater than 10, nearest hundred if greater than 100, thousand if greater than 10,000, and hundred thousand if greater than one million. Costs are also in USD.

Variable	Values					
For the basic reproduction number:	Non- specific	1.5	2	2.5	3	3.5
Number of patients being admitted per day	84					
Total number of patients at 150 days	12 600					
Total number in respiratory isolation at 150 days	1900					
Cost of respiratory isolation $ Million	2.2					
Total number of COVID-19 positive cases prevented	–	200 (170–230)	220 (190–240)	240 (200–290)	280 (210–330)	300 (250–370)
Costs averted from isolation of cases under ESC $ million	–	2.0 (1.7–2.3)	2.2 (1.9–2.4)	2.4 (2.0–2.9)	2.7 (2.1–3.3)	3.0 (2.5–3.7)
Net cost of expanding transmission criteria $ thousand	–	−270 (−670 to 370)	−80 (−430 to 20)	120 (−330 to 520)	450 (−210 to 920)	740 (120 to 1400)

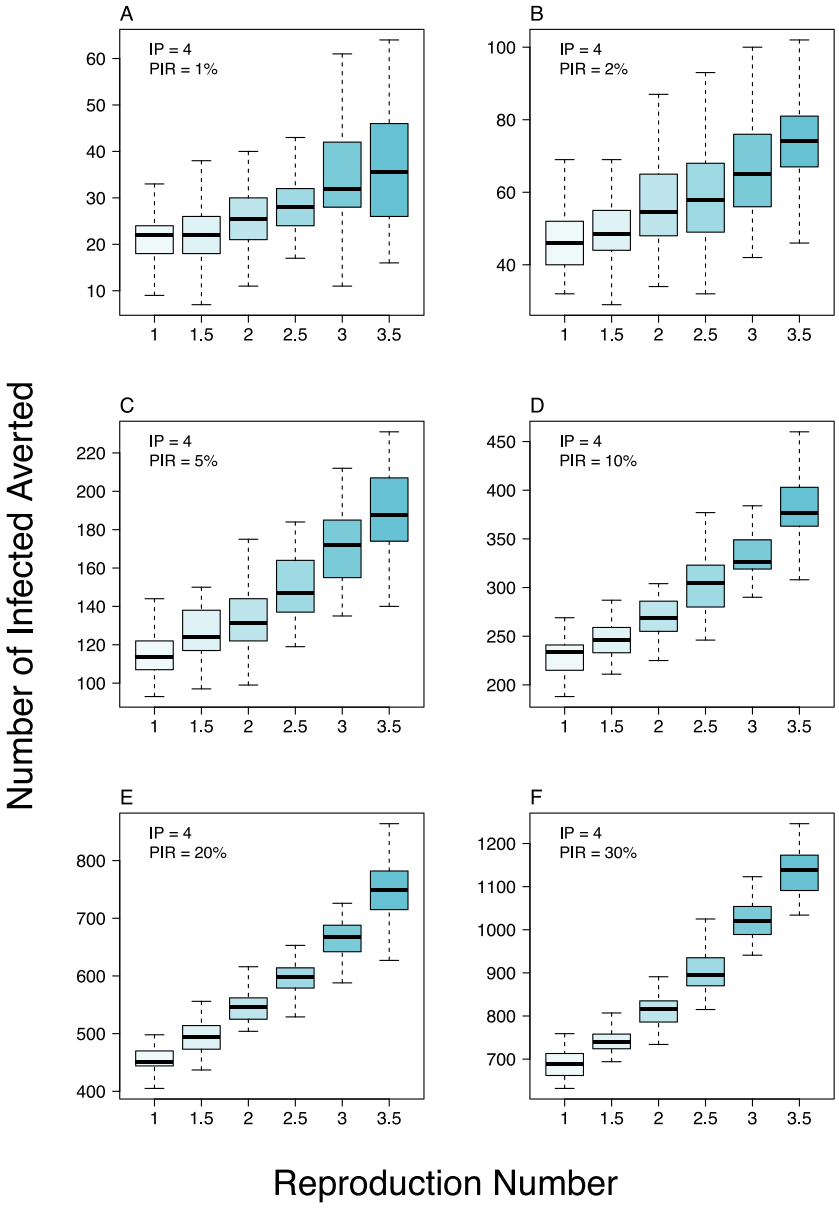

Figure 2. Boxplots of the number of infections averted with a 4 day incubation period (IP) across a range of basic reproduction numbers () 1.0–3.5 and positive identification rates (PIR) of (A) 1.0%, (B) 2.0%, (C) 5.0%, (D) 10.0%, (E) 20.0% and (F) 30.0%.

values, changing the IP from 4 to 8 days decreased the net cost savings of ESC by an average of −$52,000.

Discussion

Among the lessons learned during the SARS epidemic of 2003–2004 was the importance of adapting official case definitions to provide effective triage and screening (Tan, 2006), especially as the definitions are expected to rapidly evolve for a new disease. For the current COVID-19 outbreak, all early diagnosed patients had travelled from China but by the 4th Feb 2020, suspected local transmission was evident, therefore negating the usefulness of this travel history (Anon, 2020f). Furthermore, as symptom profiles were identified as being very heterogeneous with the two dominant symptoms fever and cough at 88.7% and 67.8% prevalence among 1099 patients in mainland China (Guan et al., 2020), the expanded screening criteria (ESC) was designed to capture all of these patients to reduce the risk of nosocomial transmission.

As of 7 February 2020, ESC was implemented as an emergency response to operate alongside intense contract tracing (Pung et al., 2020) and social distancing (Koo et al., 2020; Lim et al., 2020). The results demonstrate that provided the positive identification rate (PIR) is sufficiently high at 7% or greater, costs-savings can be created across the R_0 values 1.0–3.5, making the screening strategy sustainable for the healthcare system in the long term. At lower PIR vales and low R_0 values, the strategy should still be considered by policymakers during the initial part of the epidemic to ensure the majority if not all cases are captured at healthcare facilities. Nosocomial transmission should also be prevented through the isolation of these cases at the point of admission during testing with the costs accounted for. The prevention of 200–300 COVID-19 infections in a hospital at an R_0 of 2.5 and incubation period (IP) of 4 days can also prevent transmission within the community and relieve the need for PPE resources which are already under strain (World Health Organisation, 2020b). The branching process shows the rapidity of infection spread and highlights the urgency of enhancing hospital surveillance to detect any potential

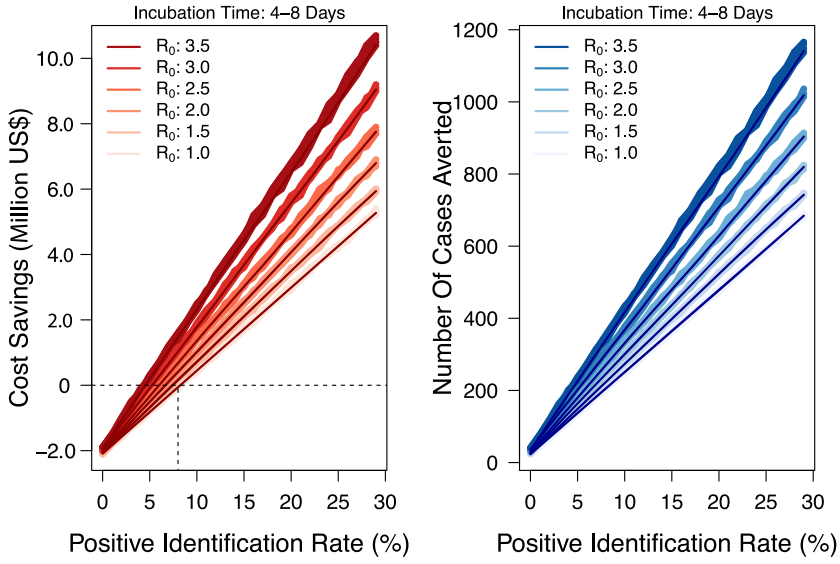

Figure 3. The (A) cost savings in US$ millions when comparing the costs of additional testing from the expansion of screening criteria (ESC) to the treatment costs avoided from preventing secondary transmission in the hospital setting and (B) total number of cases averted. The threshold value for cost-saving (set as 0 dollars) for all basic reproduction values is presented as a black dotted line in panel A with the minimum positive identification rate at 8.0% necessary for cost-saving highlighted for the lowest $\boldsymbol{R}_0$ at 1.0.

transmission chains when a case is identified, which is already carried out for all atypical pneumonias, some upper respiratory illnesses and hospitalized acute respiratory illnesses (Pung et al., 2020).

Our findings are relevant to cities and highly urbanized regions with well-developed healthcare infrastructure and resources to undertake considerable epidemiological investigation for suspected cases. The costs for areas with fewer resources or different health systems however are likely to be considerably lower but potentially at the cost of a lower PIR. A total of 40,000 cases have been confirmed in Singapore to date (25th March 2020; a full case listing is provided by gov.sg (Anon, 2020g)) with limited local transmission currently suspected. Elsewhere, ~8 million cases and over 435,000 deaths have been confirmed across 6 WHO regions (World Health Organisation, 2020c). The analysis performed here can be utilised for all countries regardless of outbreak stage as it can prevent nosocomial transmission at hospitals with incoming cases of local transmission and prevent imported cases from establishing transmission chains altogether. It also supports the general body of literature highlighting the importance of a highly sensitive standardised criteria for case identification in an epidemic involving a new infectious pathogen. For COVID-19, this has been particularly challenging as it shares symptoms with many respiratory illnesses, making it difficult for practitioners to distinguish positive cases. Similar issues already exist for influenza between national and regional surveillance programmes where most use measured or reported fever with cough and/or sore throat (Fitzner et al., 2018). During the initial wave of the 2009 influenza A H1N1 pandemic in Singapore, serological surveillance on 727 patients from June to October 2009 demonstrated that the revised WHO definition had the highest reported positive predictive value (PPV) in comparison to three others (Jiang et al., 2015). This variety in case definition across institutions demonstrates the ongoing challenges in place for both diagnosis and surveillance, which can be difficult for practitioners to interpret and implement. For COVID-19, complete case finding is being prioritised where possible in Singapore as PPV will substantially change with increasing disease prevalence. Provided the case definition is highly sensitive, it can continue to be rapidly updated with greater specificity over time as symptom profile data continues to be shared and assessments carried out on missed cases, therefore sensitivity at the initial phases should be greatly prioritised.

The model can be used by policy makers to estimate the costs saved using ESC within the hospital setting for the ongoing COVID-19 pandemic. ESC is cost-effective in the long term, especially at higher $\boldsymbol{R}_0$ and PIR values, preventing undiagnosed cases from infecting other individuals, which is especially important during the initial outbreak phase or where the epidemic is suppressed from lockdown measures. It should be noted however that there are several limitations in our analysis, primarily due to the ongoing uncertainties regarding the parameters of the COVID-19 infection profile and differing operational procedures in hospitals. Firstly, the PIR is currently unknown and the $\boldsymbol{R}_0$ is likely to vary considerably in space and time across Singapore. Infectiousness will also vary between HCWs and patients, which may not be fully explained by the branching process. Second, the asymptomatic rate has yet to be determined as part of the continually evolving symptomatic profile (Anon, 2020h; Nishiura et al., 2020). Third, we only considered the hospital costs for the institution and did not account for the productivity and economic losses from unnecessary isolation or those saved from averting of nosocomial cases. This also includes the excess manpower costs from HCWs who are currently working long hours to ensure patient wellbeing. Fourth, revisions may be required to make these findings applicable to other countries or cities through adaption of the isolation and testing procedures. Lastly, the potential for superspreading events, as witnessed in SARS (Shen et al., 2004), has not been accounted for as the movement patterns of HCW were not modelled.

ESC should be implemented in the early phase of an epidemic where local community transmission is suspected or where imported cases are being repeatedly recorded. Cost-savings or relatively minor costs are expected to occur whilst reducing the risk of uncontrolled outbreaks occurring in nosocomial settings. This is critical considering the ongoing anxiety and strain on healthcare systems worldwide, which are reflected within the public and impossible to fully quantify (Boccuzzi, 2003; Ernst, 2006). Measures such as ESC, which can aid national control

efforts, should be considered in order to relieve this pressure through the exhaustive testing and isolation of individuals which have good potential to be positive (Anon, 2020c).

Contributors

JTL, BLD, LYAC designed the experiments, JTL, BLD, ARC created the models, BLD, JTL, LYAC, ARC, ALK, YYD, DAF, PAT interpreted the results, BLD, JTL, LYAC, ARC wrote the manuscript, ALK and LYAC performed data collection for the models.

Conflict of interest

None declared.

Funding source

Singapore Population Health Improvement Centre (NMRC/CG/C026/2017_NUHS) and grant no. COVID19RF-004 to BLD, JTL and ARC. Clinician Scientist Award (CSA) funded by the National Medical Research Council to LYAC.

Ethical approval

Ethical approval was not required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2020.08.025.

References

Surveillance Case Definitions for Human Infection with Novel Coronavirus. https://www.who.int/docs/default-source/coronaviruse/surveillance-case-definitions-for-human-infection-with-novel-coronavirus.pdf?sfvrsn=2cc7104e_2 [Accessed 11 February 2020].

Global Surveillance for 2019-nCoV. https://www.who.int/docs/default-source/coronaviruse/20200121-global-surveillance-for-2019-ncov.pdf [Accessed 11 February 2020].

MOH | Updates on 2019 Novel Coronavirus (2019-nCoV) Local Situation. https://www.moh.gov.sg/2019-ncov-wuhan [Accessed 11 February 2020].

The Incubation Period of COVID-19 From Publicly Reported Confirmed Cases | Annals of Internal Medicine | American College of Physicians. https://annals.org/AIM/FULLARTICLE/2762808/INCUBATION-PERIOD-CORONAVIRUS-DISEASE-2019-COVID-19-FROM-PUBLICLY-REPORTED [Accessed 7 April 2020].

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study-Lancet. https://www-thelancet-com.libproxy1.nus.edu.sg/journals/lancet/article/PIIS0140-6736(20)30211-7/fulltext [Accessed 6 February 2020].

MOH | News Highlights: Confirmed Cases of Local Transmission of Novel Coronavirus Infection in Singapore. https://www.moh.gov.sg/news-highlights/details/confirmed-cases-of-local-transmission-of-novel-coronavirus-infection-in-singapore [Accessed 12 February 2020].

332019 Novel Coronavirus: Cases in Singapore. http://www.gov.sg/article/2019-ncov-cases-in-singapore [Accessed 11 February 2020].

Eurosurveillance | Pattern of Early Human-To-Human Transmission of Wuhan 2019 Novel Coronavirus (2019-nCoV), December 2019 to January 2020. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.4.2000058 [Accessed 12 February 2020].

Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. Lancet Infect Dis 2013;13:752–61.

Boccuzzi SJ. Indirect health care costs. In: Weintraub WS, editor. Cardiovascular Health Care Economics. Totowa, NJ: Humana Press; 2003. p. 63–79.

Chai LYTP. An expanded screening criteria may be requisite for novel coronavirus: lesson learnt from SARS. 2014. International Conference on Emerging Infectious Diseases. .

Chan TY, Miu KY, Tsui CK, Yee KS, Chan MH. A comparative study of clinical features and outcomes in young and older adults with severe acute respiratory syndrome. J Am Geriatr Soc 2004;52:1321–5.

Chang S-M, Liu C-L, Kuo H-T, et al. Comparative study of patients with and without SARS WHO fulfilled the WHO SARS case definition. J Emergency Med 2005;28:395–402.

Chen Z-M, Fu J-F, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr 2020;, doi:http://dx.doi.org/10.1007/s12519-020-00345-5 published online Feb 5.

Chinese Communicable Disease Center. http://www.chinacdc.cn/en/aboutus/bri/ [Accessed 6 February 2020].

Chowell G, Abdirizak F, Lee S, et al. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. BMC Med 2015;13:210.

Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020; S1473309920301201.

Ernst R. Indirect costs and cost-effectiveness analysis. Value Health 2006;9:253–61.

Fitzner J, Qasmieh S, Mounts AW, et al. Revision of clinical case definitions: influenza-like illness and severe acute respiratory infection. Bull World Health Organ 2018;96:122–8.

Gopalakrishna G, Choo P, Leo YS, et al. SARS transmission and hospital containment. Emerg Infect Dis 2004;10:395–400.

Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; NEJMoa2002032.

Jiang L, Lee V, Lim W, et al. Performance of case definitions for influenza surveillance. Eurosurveillance 2015;20:21145.

Koh D. 9 Occupational health aspects of emerging infections–SARS outbreak affecting healthcare workers. Semi–Plenary Sessions. BMJ Publishing Group Ltd; 2018 A14.1-A14.

Koo JR, Cook AR, Park M, Sun Y, Sun H, Lim JT, Tam C, Dickens BL. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. Lancet Infect Dis 2020;.

Li G, Zhao Z, Chen L, Zhou Y. Mild severe acute respiratory syndrome. Emerg Infect Dis 2003;9:1182–4.

Lim JT, Dickens BSL, Choo ELW, Chew LZX, Koo JRH, Tam C, Cook AR. Revealing regional disparities in the transmission potential of SARS-CoV-2 from interventions in Southeast Asia. Proc R Soc B 2020;287(1933):20201173.

Linton NM, Kobayashi T, Yang Y, et al. Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: a statistical analysis of publicly available case data. J Clin Med 2020;9:538.

Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Eurosurveillance 2020;25, doi:http://dx.doi.org/10.2807/1560-7917.ES.2020.25.10.2000180.

Mohd HA, Memish ZA, Alfaraj SH, et al. Predictors of MERS-CoV infection: a large case control study of patients presenting with ILI at a MERS-CoV referral hospital in Saudi Arabia. Travel Med Infect Dis 2016;14:464–70.

Nishiura H, Kobayashi T, Yang Y, et al. The rate of underascertainment of novel coronavirus (2019-nCoV) infection: estimation using Japanese passengers data on evacuation flights. J Clin Med 2020;9:419.

Pung R, Chiew CJ, Young BE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. Lancet 2020;395:1039–46.

Rainer TH, Lee N, Ip M, et al. Features discriminating SARS from other severe viral respiratory tract infections. Eur J Clin Microbiol Infect Dis 2007;26:121.

Shen Z, Ning F, Zhou W, et al. Superspreading SARS events, Beijing, 2003. Emerg Infect Dis 2004;10:256–60.

Singh K, Hsu L-Y, Villacian JS, Habib A, Fisher D, Tambyah PA. Severe acute respiratory syndrome: lessons from Singapore. Emerg Infect Dis 2003;9:1294–8.

Tan C-C. SARS in Singapore–key lessons from an epidemic. Ann Acad Med Singapore 2006;35:5.

Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;, doi:http://dx.doi.org/10.1001/jama.2020.1585 published online Feb 7.

World Health Organisation. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). 16-24 February,. 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.

World Health Organisation. Rational Use of Personal Protective Equipment (PPE) for Coronavirus Disease (COVID-19). Interim Guidance 19 March. 2020. https://apps.who.int/iris/bitstream/handle/10665/331498/WHO-2019-nCoV-IPCP-PE_use-2020.2-eng.pdf.

World Health Organisation Coronavirus disease 2019 (COVID-19). Situation Report–77. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200406-sitrep-77-covid-19.pdf?sfvrsn=21d1e632_2.

Wu JT, Leung K, Bushman M, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. Nat Med 2020a;, doi:http://dx.doi.org/10.1038/s41591-020-0822-7 published online March 19.

Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 2020b; S0140673620302609.

Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 2020c;, doi:http://dx.doi.org/10.1016/S0140-6736(20)30260-9 published online Jan 31.

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.