

How best to use limited tests? Improving COVID-19 surveillance in long-term care

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ABSTRACT

Background: Long-term care facilities (LTCFs) are particularly vulnerable to nosocomial outbreaks of coronavirus disease 2019 (COVID-19), with high rates of transmission and mortality. Timely epidemiological surveillance is essential to detect and respond to outbreaks, but testing resources are highly limited in the current pandemic context.

Methods: We used an individual-based transmission model to simulate COVID-19 spread along inter-individual contact networks in the LTCF setting. A range of surveillance strategies were evaluated for their ability to detect simulated outbreaks, assuming limited availability of standard RT-PCR tests. Various epidemiological scenarios were considered, including COVID-19 importation from patient transfers or staff members infected in the community.

Findings: We estimated a median delay of 7 (95% uncertainty interval: 2-15) days from importation of an asymptomatic COVID-19-infected patient to first presentation of COVID-19 symptoms among any patients or staff, at which point an additional 7 (0-25) individuals were infected but did not (yet) show symptoms. Across a range of scenarios, the reference surveillance strategy (testing individuals with COVID-like symptoms with signs of severity) took a median 11–21 days to detect an outbreak. Group testing (pooling specimens from multiple individuals for a single RT-PCR test) patients and staff with any COVID-like symptoms was both the most timely and efficient strategy, detecting outbreaks up to twice as quickly as the reference, and more quickly than other considered strategies while using fewer tests. Maximizing use of available tests via testing cascades was more effective

than group testing only when substantial testing resources were available (on the order of 1 test/20 beds/day). Including not merely those with symptoms but also newly admitted patients in group tests and testing cascades reduced delays in outbreak detection for LTCFs actively admitting patients potentially already infected with COVID-19.

Interpretation: Improving COVID-19 surveillance can alert healthcare institutions to emerging outbreaks before they escalate, informing a need for urgent public health intervention in settings with ongoing nosocomial transmission.

Keywords: SARS-CoV-2, surveillance, healthcare-associated infection, mathematical modelling, individual-based model, contact networks, group testing

RESEARCH IN CONTEXT

Evidence before this study

On April 18 2020 we searched PubMed and MedRxiv for articles published since January 1 2020 and containing the terms ("COVID" OR "coronavirus" OR "nCoV" OR "SARS-CoV-2) AND ("long-term care" OR "LTCF"). We identified 16 articles published in academic journals, mostly outbreak reports and editorials describing a need for improved testing and control measures. Very few of the 179 identified preprints were studies of COVID-19 in long-term care. A separate search for the same COVID terms AND ("transmission model" OR "mathematical model" OR "dynamic model") returned 29 published articles, including an evaluation of surveillance strategies in airports, and a range of transmission models at the country or community levels, but none specifically tailored to healthcare settings, whether hospitals, LTCFs or otherwise. Among 776 preprints, we identified a large number of studies assessing and projecting COVID-19 burden in hospital systems, but only two transmission models specific to healthcare settings, neither of which addressed long-term care settings nor options for epidemiological surveillance. Together, this suggests a lack of research on the unique transmission dynamics and surveillance considerations for COVID-19 in healthcare settings. This gap is further highlighted by extensive study of nosocomial outbreaks of other zoonotic coronaviruses (SARS-CoV, MERS-CoV).

Added value of this study

Our study is among the first to model nosocomial transmission of COVID-19, and highlights an important role for asymptomatic and pre-symptomatic transmission, as well as unique challenges for epidemiological surveillance that result from lags between infection and symptom onset. Our study is also among the first to evaluate different surveillance strategies for COVID-19 in the healthcare setting, in the context of optimizing highly limited testing resources. We include group testing, which has recently been proposed as a cost-effective strategy for COVID-19 surveillance, but which has been little implemented in practice. Our findings provide an evidence base for how to tailor surveillance to COVID-19's unique epidemiological characteristics, and ultimately how to improve allocation of limited tests in healthcare settings. We conclude with tangible recommendations for decision-makers.

Implications of all the available evidence

LTCFs are uniquely vulnerable to COVID-19 outbreaks, owing to frail and elderly patient populations and limited resources for testing and outbreak response. We show that differences in allocation of limited tests can have important public health consequences. Improving outbreak detection (e.g. by group testing and/or expanding testing criteria) allows outbreaks to be detected sooner, facilitating timely interventions such as patient isolation, enhanced infection prevention measures and contact tracing. Delaying these responses by a matter of days could make the difference between isolated cases and full-blown nosocomial outbreaks. As the COVID-19 pandemic continues to unfold, improving outbreak detection with the limited resources available remains a central priority for healthcare institutions worldwide.

INTRODUCTION

The ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by novel human coronavirus SARS-CoV-2, is a public health emergency of international concern. COVID-19 is highly transmissible with a wide clinical spectrum, ranging from asymptomatic respiratory tract infection to progressive

pneumonia and death.¹ Older patients and those with comorbidities are at greatest risk of severe outcomes,² making healthcare settings such as long-term care facilities (LTCFs) particularly vulnerable to COVID-19.³ From rehabilitation hospitals to nursing homes, a growing number of LTCFs worldwide are reporting catastrophic outbreaks, with high rates of infection and mortality among patients and healthcare workers (HCWs) alike.^{3–5}

Timely detection of nosocomial COVID-19 outbreaks is essential to protect patients and HCWs and to slow contagion. Yet COVID-19 surveillance is limited by available testing resources. The current standard RT-PCR (reverse transcriptase polymerase chain reaction) test is laborious and expensive, and is in some settings subject to specific guidelines. For instance, in LTCFs in countries such as France, the Netherlands, the UK and the USA, tests have been limited only to individuals presenting with characteristic COVID-19 symptoms or signs of severity.^{3,6–8} Yet symptomatic cases represent just the tip of the iceberg: infectious individuals with no, mild, or as-yet undeveloped symptoms are common in COVID-19 outbreaks, and can easily go undetected by syndromic surveillance systems while nonetheless seeding chains of transmission.^{9–11} Recent studies have indicated that surveillance strategies such as group testing may represent effective and resource-efficient alternatives to standard syndromic surveillance,^{12–15} but few settings have adopted such practices.

In order to mitigate and prevent further nosocomial outbreaks, there is an urgent need to improve COVID-19 surveillance, taking into account both limited testing resources and the unique transmission dynamics and clinical characteristics of COVID-19. Here, we investigated the efficacy and timeliness of a range of COVID-19 surveillance strategies using simulations from a dynamic COVID-19 transmission model among patients and HCWs in the LTCF setting.

METHODS

Surveillance strategies for COVID-19 in long-term care

We used simulated epidemics (described below) to evaluate a range of surveillance strategies for detecting introductions of COVID-19 into the LTCF setting (Table 1). Surveillance strategies varied according to who received conventional RT-PCR tests and with what priority, assuming limited testing resources fixed at a maximum of 1, 2, 4 or 8 tests per day (for the 170-bed LTCF simulated in the main analysis, this corresponds to roughly one test per day per 170, 85, 43 or 21 beds). We assumed a one-day lag between a test and its result, a low test sensitivity upon initial infection, and subsequently a high sensitivity upon symptom onset (see all parameter values in Table S1).

Individuals were selected for testing according to three clinical indications: presentation of COVID-like symptoms (mild or severe), hospital admission, or belonging to a particular demographic (e.g., patients, HCWs). Symptom-based tests were administered on the first day that symptoms appeared. COVID-19 may clinically resemble other acute respiratory infections,¹ so individuals with COVID-like or actual COVID-19 symptoms were both indicated for symptom-based testing. Average daily incidence of influenza-like illness among older adults in French emergency departments (50-99 years, 2008-2017) was used as a proxy attack rate for patients and staff presenting with COVID-like symptoms of other aetiologies, 20% of whom were assumed to develop signs of severity.

The reference strategy in the current resource-limited pandemic context was taken as testing upon presentation of COVID-like symptoms with signs of severity. Three groups of alternative strategies were also evaluated: (i) testing for other indications (any COVID-like symptoms, hospital admission), (ii) maximizing daily testing capacity via testing cascades, or (iii) group testing. To reach daily testing capacity, cascades of priority apportioned tests first to those with severe symptoms and then other indications (e.g. mild symptoms, admission) until all tests were used. For group testing, clinical specimens from multiple individuals were pooled and tested as one (up to, but not necessarily reaching a maximum of 2, 4, 8 or 16 specimens per test). Although such a group testing procedure can not reveal which individual(s) is (are) potentially infected, it can save cost and time and is widely used in screening for rare diseases, quality control in manufacturing, and computational biology. COVID-19 group testing also comes at the cost of reduced test sensitivity,¹³ which was assumed to decrease linearly with each additional true negative sample as

$$s_g = s_i - (r \times \frac{S}{P})$$

where s_g and s_i are group- and individual-level test sensitivities, r is the discounting rate for each additional negative sample, S is the number of specimens, and P is the number of true positive specimens. As with standard RT-PCR testing, group testing for COVID-19 is very highly specific,¹⁵ so perfect specificity was assumed. For all group testing strategies, we assumed that tests were first reserved for individuals presenting with severe symptoms, and that a group test was then conducted only if any tests remained.

Table 1. Surveillance strategies considered for detection of COVID-19 outbreaks. Symptoms refer specifically to COVID-like symptoms among anyone in the hospital (patients or staff). Admission refers to patients newly admitted to the LTCF that same day. Arrows (\rightarrow) indicate order of priority for testing cascades.

Surveillance strategy	Description	Indications evaluated	Daily testing capacity always reached?
Baseline indication-based testing	Administer RT-PCR tests to any individuals indicated for testing, up to the daily testing capacity	Symptoms (severe) [reference strategy]	No
		Symptoms (any)	No
		Admission	No
		Random (patients)	Yes
		Random (healthcare workers)	Yes
		Random (all)	Yes
Testing cascades	Administer RT-PCR tests to individuals according to cascades of priority, until daily testing capacity is reached. First priority is always given to individuals presenting with severe COVID-like symptoms.	Symptoms (severe) \rightarrow Symptoms (mild) \rightarrow Random (patients)	Yes
		Symptoms (severe) \rightarrow Symptoms (mild) \rightarrow Admission \rightarrow Random (patients)	Yes
		Symptoms (severe) \rightarrow Admission \rightarrow Random (patients)	Yes
		Symptoms (severe) \rightarrow Admission \rightarrow Symptoms (mild) \rightarrow Random (patients)	Yes
Group testing	First administer individual RT-PCR tests to anyone presenting with severe COVID-like symptoms. Subsequently, if any tests remain, pool clinical specimens together up to a maximum of 2, 4, 8 or 16 specimens, and run one RT-PCR test across all specimens	Symptoms (any)	No
		Admission	No
		Random (patients) (always maximizes number of specimens per group test)	No

Surveillance strategies were evaluated based on their ability to detect nosocomial outbreaks using three measures of timeliness and efficacy: (i) detection probability, the probability of detecting an outbreak t days from the index case at $t=1$; (ii) detection lag, the number of days from the index case to outbreak detection (first positive test result); and (iii) outbreak size upon detection, the cumulative number of undetected COVID-19 cases among patients and staff in the hospital upon first positive test result. Testing strategies were only evaluated for simulations in which the initial index case resulted in an outbreak (defined as simulations with ≥ 1 nosocomial transmission event), and we defined a maximum outbreak detection lag of 21 days, after which all outbreaks were assumed to be detected, regardless of the surveillance strategy used.

Simulating nosocomial COVID-19 spread

COVID-19 epidemics were simulated using a dynamic, stochastic, individual-based transmission model, describing dynamic inter-individual contacts among and between hospital patients and personnel in a five-ward, 170-bed LTCF.¹⁶ There were on average 154 patients and 239 members of staff present in the hospital per day, the latter partitioned across 13 distinct categories (e.g. nursing, administrative or operations staff). Both patients and staff could potentially become infected with COVID-19 and/or experience COVID-like symptoms. Hospital structure, demographics, and dynamic contact networks were estimated from close-proximity interaction data, measured via sensors worn by all patients and personnel over a 12-week period in a five-ward rehabilitation hospital in northern France (described elsewhere)¹⁷. Distinct contact patterns among and between individuals reflect both inherent differences in behaviour as well as different amounts of time spent in the hospital (e.g., patients are admitted and discharged but typically spend 24 hours per day in the hospital, whereas staff are present according to their standard working hours).

Clinical progression of COVID-19 was characterized by: (i) a non-infectious incubation period of 2-5 days, (ii) an infectious pre-symptomatic period of 1-3 days, (iii) an on-average 7-day symptomatic period, and (iv) eventual recovery with full immunity. For (iii), we estimated that 70% of COVID-19 patients develop clinical symptoms,^{18,19} and that 20% of symptomatic patients develop severe (including critical) symptoms.²⁰ To reflect rapid pulmonary deterioration characteristic of severe COVID-19, we assumed no difference in average time to symptom onset across cases. As surveillance strategies were evaluated only for detection of outbreaks, death and potential long-term clinical outcomes were not explicitly simulated. All clinical and epidemiological parameters are presented in supplementary table S1.

All simulations began with an asymptomatic index case of COVID-19 imported into the LTCF on day one (t_1), but five distinct epidemiological scenarios were considered to account for variable outbreak onset: (i) one infected patient admitted at t_1 , (ii) one infected patient admitted at t_1 and subsequently once weekly, (iii) one staff member infected in the community at t_1 , (iv) one staff member infected in the community at t_1 and subsequently once weekly, and (v) either one infected patient or one staff member introduced at t_1 and subsequently once weekly (assuming 50% probability of patient or staff). Index cases, whether at t_1 or later, had equal probabilities of being in the incubating, pre-symptomatic or asymptomatic stages of infection. Visitors were excluded from the model to represent common practices in the current context of pandemic COVID-19, though no additional COVID-specific interventions were implemented. For each outbreak simulation (100 per

importation scenario), the stochastic surveillance algorithm was run 100 times (=10,000 simulations × 5 scenarios) for each surveillance strategy. Resulting simulation uncertainty in model outcomes is expressed as 95% uncertainty intervals (UI).

The per-contact transmission rate of COVID-19 was estimated assuming a basic reproduction number of $R_0 = 3$. We assumed that

$$R_0 = p \times n \times d \times \tau$$

where p is the per-minute probability of transmission between susceptible and infectious individuals in contact with one another; n is the average number of daily contacts per individual; d is the average duration of these contacts; and τ is the duration of the infectious period. Based on data from a contact survey in the French general community ($n = 8$ contacts/days, $d = 30$ minutes) and assuming an infectious period of $\tau = 9$ days,^{21,22} we calculated a transmission probability of $p = 0.14\%$ per minute spent in contact. We further set a saturation threshold at one hour of contact, such that the per-contact transmission probability was at most 8.3% per contact between any two individuals.

Sensitivity analyses were conducted to account for model and parameter uncertainty. First, we simulated a smaller, single-ward, 30-bed geriatric LTCF, with on average 26 patients and 80 staff per week, and fewer and longer contacts (but a similar total duration of contact) between patients. Second, outbreaks were simulated assuming alternative transmission rates ($p=0.07\%/\text{min of contact}$, $p=0.28\%/\text{min of contact}$; derived from $R_0 = 1.5$, $R_0 = 6$).

RESULTS

COVID-19 spreads quickly, but symptoms lag

In our simulations, COVID-19 spread quickly but with a great degree of stochasticity upon its introduction to the LTCF and in the absence of surveillance or control measures (Figure 1). Transfer of a single asymptomatic infected patient always resulted in an outbreak (100% of simulations). Outbreaks were characterized by a median time lag of 7 (2-15) days between the index case entering the facility and the first appearance of any COVID-19 symptoms among any infected patients or staff (Figure 1). By this time, 7 (0-25) additional patients and/or staff had acquired COVID-19 but did not

(yet) show symptoms. The lag until first onset of severe COVID-19 symptoms was greater (12 days from index case, 4–21) and coincided with a greater number of undetected infections (23, 2–73).

When COVID-19 was introduced by an asymptomatic infected staff member, outbreaks were less likely to occur than when patients introduced the virus (64% of simulations). Outbreaks caused by staff were further characterized by fewer transmission events on average and a greater lag between the index case and symptom onset among anyone infected, but similar mixes of patients and staff became infected regardless of who initiated the outbreak (Figure S1).

The reference strategy is never the best one, whatever the number of tests

Across five scenarios of COVID-19 importation into the LTCF (Figure 2A), surveillance strategies varied greatly in their ability to detect COVID-19 outbreaks (Figure 2B). We first examined indication-based testing strategies individually, prior to testing cascades or group tests. Across scenarios and testing capacities, the reference strategy (severe symptoms) was always outperformed, with lags in onset of severe symptoms entailing lags in outbreak detection. When COVID-19 was imported by patient transfer, testing patients upon hospital admission facilitated rapid outbreak detection, but at the cost of failing to detect ongoing outbreaks already underway in the facility. Conversely, testing patients and staff with any COVID-like symptoms was the strategy most likely to detect ongoing outbreaks, but like the reference strategy was hindered by lags between outbreak onset and the appearance of symptoms.

Increase testing capacity to improve outbreak detection

Increasing testing capacity generally led to more rapid outbreak detection, but some strategies benefited more from increased capacity than others (Figure S2). The reference strategy benefited the least: owing to a low average daily incidence of severe COVID-like symptoms (1·0, 0·6–1·8 for scenario five), increasing capacity above 2 tests/day rarely resulted in more tests being used and had a negligible impact on outbreak detection. A similar threshold was observed for testing upon admission, owing to a limited number of new patients admitted per day (2·0, 0·0–7·0). Relative efficacies of different surveillance strategies thus depended not only on daily testing capacity but on the number of individuals indicated for testing, and in turn the number of tests actually used each day.

Cascades and group tests detect outbreaks sooner

Testing cascades and group testing detected outbreaks more quickly than traditional indication-based testing, but for different reasons. For cascades, increasing testing capacity always resulted in more individuals being tested and hence a greater probability of outbreak detection. The relative efficacies of different cascades depended on the order of priority given to different indications (Figure S3). As with individual-based tests, prioritizing admissions was advantageous for outbreaks only caused by patient transfer, whereas prioritizing symptoms was advantageous for outbreaks only caused by staff (Figure 3).

Group testing strategies detected outbreaks more quickly than cascades when testing capacity was limited (Figure 3). By pooling multiple specimens per test, group testing resulted in a greater probability of testing an infected patient or member of staff and ultimately of detecting the presence of COVID-19 in the facility, despite reduced test sensitivity. Outbreak detection was improved by increasing the maximum allowable number of specimens per group test, up to a threshold set by the number of individuals potentially indicated for inclusion, e.g. in our simulations a daily average incidence of 5·4 (3·9–7·6) individuals presenting with any COVID-like symptoms over the first three weeks of the outbreak (Figure S4). Again, group testing of admitted patients was preferable when outbreaks were only caused by patient transfers, and of individuals presenting with any COVID-like symptoms when only caused by staff (Figure 3). Group testing strategies required on average just two tests per day, explaining minimal benefit to further increased capacity.

Group testing is the most resource-efficient strategy

Group testing was more efficient than other surveillance strategies, requiring fewer tests (Figure 4) and, in some instances, fewer specimens than other strategies (Figure S5) to detect outbreaks on average up to twice as quickly as the reference strategy. In particular, group testing patients and staff with any COVID-like symptoms was the most effective and efficient strategy under limited testing capacity for outbreaks potentially caused by either patients or staff (scenario five). In this scenario, cascades required a high daily testing capacity and on average up to three times as many tests to outperform group testing. The number of specimens per group test was ultimately limited by the number of individuals indicated for inclusion, explaining variability in the number of specimens collected across different group testing strategies.

Detection lags entail larger outbreaks

The longer outbreaks went undetected, the more undocumented infections accumulated. Due to the exponential nature of emerging outbreaks, delays of only one or two days sometimes resulted in tens more infections. By detecting outbreaks more quickly, group testing and testing cascades coincided with fewer infections upon outbreak detection than simple indication-based strategies, across a range of testing capacities (Figure S6).

Sensitivity analyses

When assuming lower or higher transmission rates, the sizes and durations of outbreaks varied, entailing overall longer and shorter lags until outbreak detection, respectively. However, across transmission rates, group testing patients and staff with any COVID-like symptoms remained the fastest and most efficient means of detecting an outbreak when testing capacity was limited (Figures S7, S8).

In a smaller LTCF with only one ward and 30 beds, COVID-19 introductions were less likely to result in outbreaks (96% vs 100% of simulations when introduced by a newly admitted patient, and 24% vs 64% when introduced by a member of staff). For similar per-bed testing capacities, efficacies of surveillance strategies were similar to the larger LTCF, with group testing strategies proving both the most effective and most efficient under limited testing resources (Fig S9). However, unlike in the larger LTCF, group testing random patients generally led to more rapid outbreak detection than symptomatic individuals due to the small ward size.

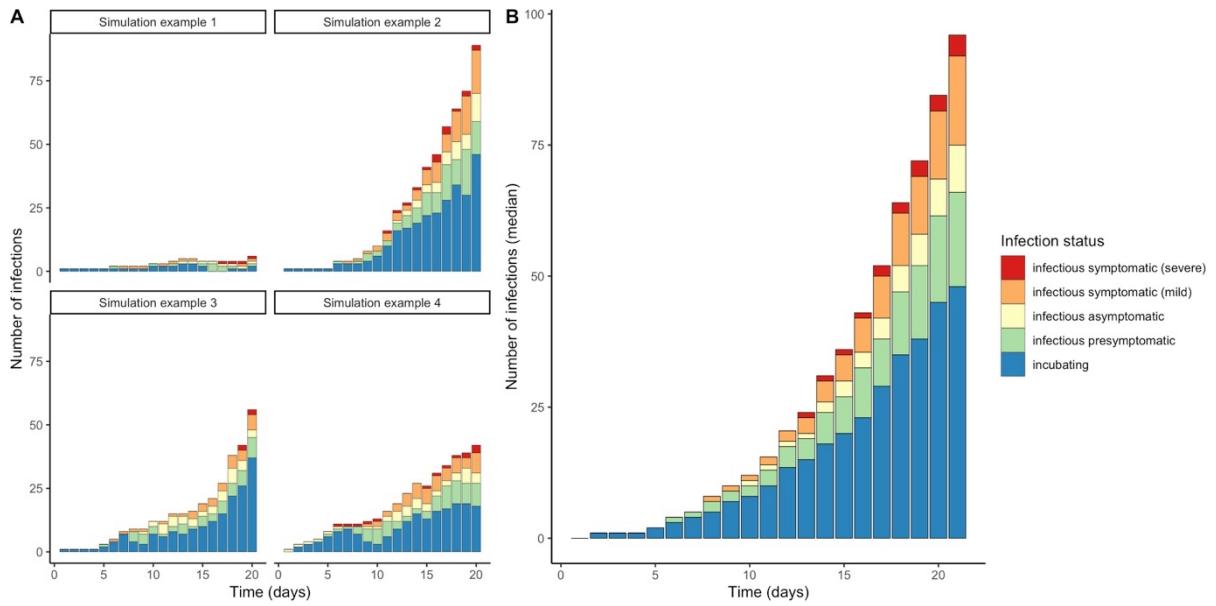


Figure 1. Epidemic curves resulting from stochastic simulations of COVID-19 transmission in a five-ward LTCF over the potential outbreak detection period of 21 days. Relative to all infections, symptomatic cases represent just the ‘tip of the iceberg’. Here, all simulations began with transfer of a single asymptomatic infected patient to the facility on day one (t_1). **A)** Four examples of epidemic simulations, displaying variation in outbreak velocity and lags until first appearance of any individuals with mild (orange) or severe (red) COVID-19 symptoms. **B)** Median epidemic curve across all epidemic simulations.

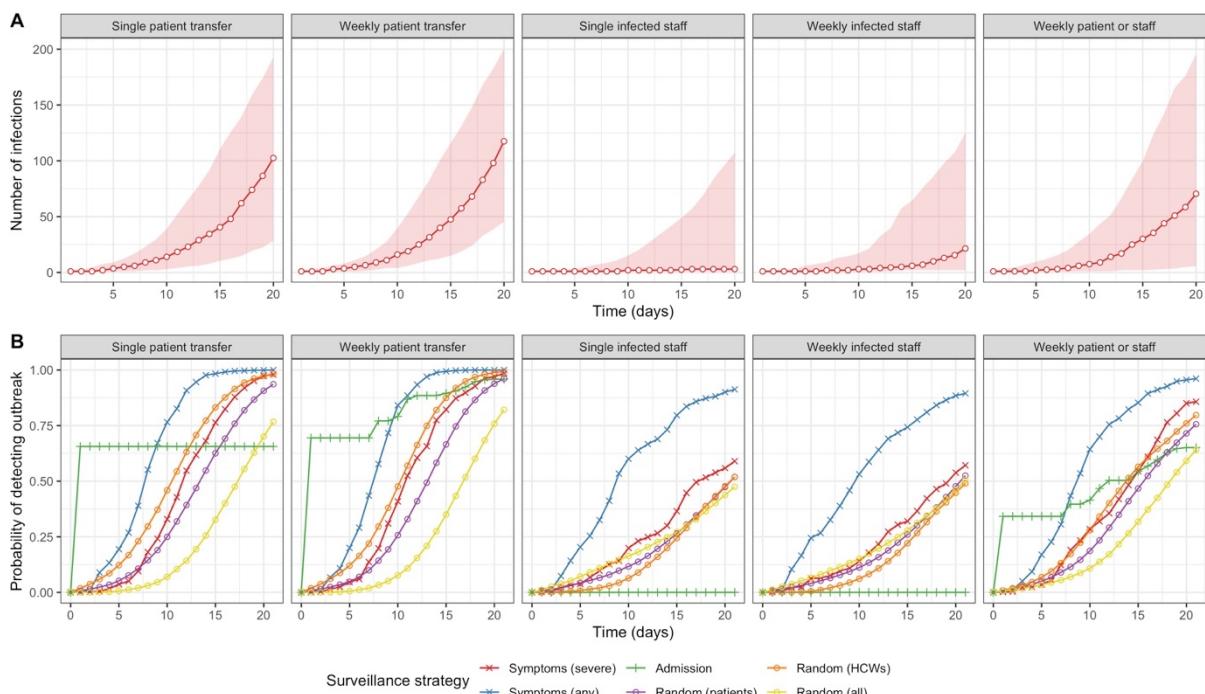


Figure 2. Outbreak trajectories and detection efficacies of indication-based surveillance strategies. **A)** Cumulative case counts for simulations resulting from five distinct scenarios of COVID-19 importation into a LTCF. Shaded areas represent 95% uncertainty intervals resulting from stochasticity in the transmission model. **B)** Probability of detecting COVID-19 outbreaks using different surveillance strategies over time for each importation scenario. Here we assume a maximum of four tests per day. Each colour represents a different surveillance strategy, and similar strategies are grouped by point shape. Detection probability was computed over 10,000 simulations per scenario.

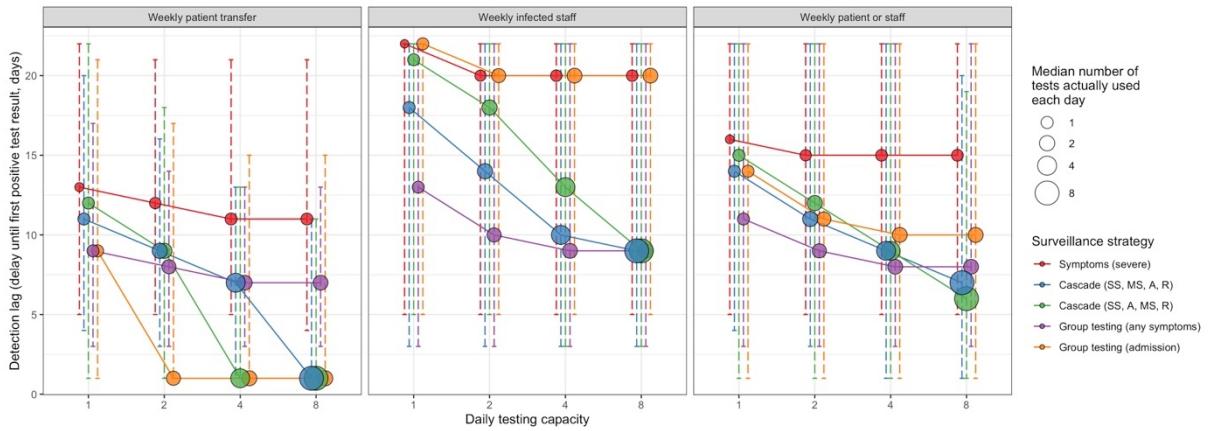


Figure 3: Comparing group tests and testing cascades in different outbreak settings. Here, detection lag is a function of daily testing capacity, comparing selected group tests and cascades to the reference strategy across three scenarios of COVID-19 importation into a LTCF (panels). For group testing, individual tests were first given to anyone presenting with severe COVID-like symptoms, and subsequently to the indicated group if any tests remained (here, to a maximum of eight individual specimens per group test). For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients). Circles represent median, error bars represent 95% uncertainty intervals.

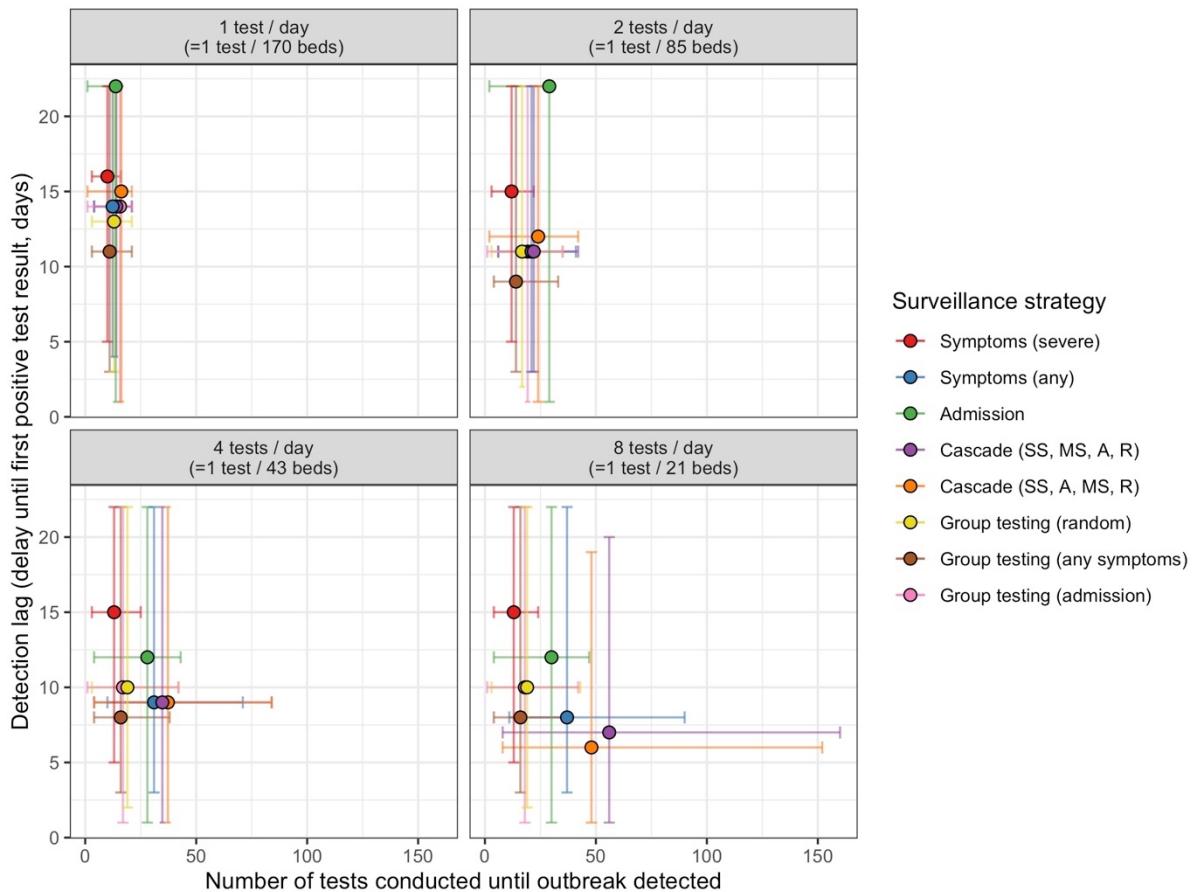


Figure 4. Efficacy-efficiency plots of competing surveillance strategies. For COVID-19 importation scenario five (random importation by both patients and staff), comparison of the efficacy (y-axis) and efficiency (x-axis) of selected surveillance strategies across different daily testing capacities (panels). Circles represent medians and

error bars represent 95% uncertainty intervals. For group testing strategies, individual tests were first apportioned to any individuals presenting with severe COVID-like symptoms. Overlapping circles were shifted along the x-axis by up to 5 units (tests conducted) and can be identified by reduced size of error bar whiskers. For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients).

DISCUSSION

COVID-19 outbreaks in LTCFs can be catastrophic, with rapid transmission and high rates of mortality among particularly frail and elderly patients.^{3–5} This motivates a need for timely and effective surveillance strategies that optimize limited testing resources to detect outbreaks as quickly as possible. In the current pandemic context, the standard-of-care in many settings is to only test individuals presenting with COVID-19 symptoms with signs of severity.^{6–8} Yet active syndromic surveillance is hampered by reportedly large proportions of mild and asymptomatic infections, and by delays between infection and symptom onset.^{9,10,18,19} We used mathematical modelling to compare a range of strategies for how to distribute limited RT-PCR tests to optimize COVID-19 outbreak detection in a LTCF under a range of epidemiological scenarios. Our work suggests that the reference standard-of-care is a comparatively poor strategy. Under limited testing capacity, group testing symptomatic patients and staff was both the timeliest and most efficient strategy considered, in most scenarios requiring fewer tests and in some cases fewer clinical specimens to detect outbreaks more quickly than other strategies. Maximizing use of available tests via testing cascades was inefficient, but even more effective than group testing for timely outbreak detection when large numbers of tests were available (on the order of 1 test/20 beds/day). In addition to those with symptoms, including newly admitted patients in group tests and testing cascades substantially reduced delays in outbreak detection, but only for LTCFs actively admitting patients potentially already infected with COVID-19.

Our simulations predicted large nosocomial outbreaks of COVID-19 in the absence of specific control strategies. This is consistent with large outbreaks recently observed in LTCFs worldwide, including an infamous outbreak in King County, Washington that resulted in 167 confirmed infections within three weeks of the first reported case.⁴ We further predicted larger and more rapid outbreaks when COVID-19 was introduced through admission of an infected patient, rather than through an infected member of staff. This is probably due to the nature of human interactions in LTCFs (patient-patient contacts are particularly long and numerous)¹⁷ and highlights both (i) a need to screen incoming patients potentially exposed to or infected with COVID-19,²³ and (ii) the importance of interventions to limit contact between patients (e.g. isolation of retirement home residents), as already recommended for affected facilities in the current pandemic context.³

Our simulations were further characterized by delays between COVID-19 introductions and symptom onset, during which time new infections not (yet) showing symptoms accumulated. This is consistent with (i) a reportedly substantial proportion of asymptomatic cases, and (ii) an important role for pre-symptomatic transmission.²⁴ Recent modelling studies estimate that 44% of secondary infections among hospital transmission-pairs resulted from pre-symptomatic transmission,²² and that, early on in COVID-19 outbreaks, transmission events occur on average two to three days prior to symptom onset.¹¹ These findings highlight epidemiological challenges associated with detecting emerging outbreaks using symptoms alone. We further found that testing patients and healthcare workers with any, and not only severe COVID-like symptoms can substantially improve outbreak detection, supporting recent recommendations to expand testing criteria in LTCFs to include individuals with atypical signs and symptoms of COVID-19, such as muscle aches, sore throat and chest pain.²³

Resource limitations for COVID-19 surveillance can in part be overcome by pooling specimens from multiple individuals together in the form of group tests, which in our analysis was the most efficient surveillance strategy. Recent mathematical modeling results have also suggested that group testing could be highly cost-effective for COVID-19 screening in large populations.¹² However, our analysis was limited to one-stage group testing, in which infected individuals were not specifically identified. This strategy is pertinent for outbreak detection but is problematic for subsequent infection control (e.g., who to isolate). In two-stage group testing, initially proposed by Dorfman in 1943 for syphilis screening among soldiers,²⁵ individual samples are re-tested after a positive group result to determine who is infected. Other strategies have also been proposed that involve split samples and simultaneous multi-pool samples.²⁶ Such strategies may be considered by facilities conducting group tests to facilitate subsequent case identification. Under the assumptions made in our analysis, including a one-day delay between identifying individuals for testing and receiving the test result, group testing is still likely to be more timely than other strategies when accounting for additional delays in obtaining second-stage test results. Decision-makers should consider the trade-off between conducting fewer tests and the potential consequences of delays in knowing which patient(s) from the group sample are positive.

This work has several limitations. First, substantial uncertainties remain regarding epidemiological characteristics of COVID-19, including its transmissibility in particular settings such as LTCFs, and a potential role for environmental acquisition,^{27,28} which was not included in our model. Furthermore, many LTCFs have already implemented control measures, such as interruption of social activities and provisioning of personal protective equipment, that should act to reduce transmission from baseline. We conducted sensitivity analyses to consider unusually high and low transmission rates to reflect

these uncertainties. Although outbreaks spread more or less quickly, the relative efficacies of surveillance strategies were largely unchanged in these analyses, resulting in identical conclusions for optimizing use of limited testing resources, regardless of non-pharmaceutical interventions potentially already put in place or a role for environmentally-mediated transmission.

Second, LTCFs represent a diverse range of healthcare institutions, each with unique specializations, patient populations and living conditions, and the generalizability of our findings across these settings is not clear. Although our main analysis was informed using data from a large, five-ward rehabilitation hospital in France, we conducted a scenario analysis for a smaller, single-ward geriatric facility, and reached similar conclusions. However, we found that conducting group tests among randomly selected individuals may be preferable to symptomatic or newly admitted individuals in small facilities. This is because a large proportion of individuals could potentially be included in a daily group test that randomly samples among all individuals in the facility, improving the probability of including infected individuals in tests without a need for exceedingly large numbers of clinical specimens.

Finally, the testing landscape for COVID-19 is due to shift quickly, with increased testing capacity and alternative testing technologies, such as rapid diagnostic tests, likely to become available in the coming months. However, uptake of new technologies is certain to be heterogeneous, and testing resources may remain limited for the foreseeable future. Although we explicitly modelled standard RT-PCR testing, our findings may be broadly generalizable to other COVID-19 testing technologies with limited capacity. Findings for group testing, however, necessarily assume that pooling samples from multiple individuals is both logically feasible and retains sufficient test sensitivity, as demonstrated for RT-PCR.¹³ Further, even in settings with abundant testing capacity, limiting the number of tests necessary to detect an outbreak may remain a priority given health-economic concerns.

In conclusion, our results have potentially important implications for COVID-19 surveillance in the long-term care setting. With limited resources available to detect and manage burgeoning outbreaks, LTCFs may continue to be hardest hit by COVID-19, even as non-pharmaceutical interventions such as lockdowns and quarantines come to slow transmission in the community. Broadening testing guidelines to include both (i) newly admitted patients, and (ii) patients and staff presenting with any COVID-like symptoms could reduce lags in outbreak detection. Furthermore, group testing in particular could allow LTCFs to detect outbreaks days, if not weeks earlier than traditional surveillance practices, all while preserving precious testing resources.

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Contributors

LO and LT conceived the study. AD programmed the transmission model and DS programmed surveillance algorithms. DS, AD, LO and LT interpreted the results. KP, BTH, DG and JF consulted on analyses. DS wrote the article. All authors edited and revised the article.

Declarations of interest

None declared.

SUPPLEMENTARY MATERIALS

Table S1. Model parameter estimates.

Parameter	Value (distribution)	Source
Parameters for estimation of COVID-19 transmission rate per minute of contact (in the community)		
COVID-19 basic reproduction number (R_0)	3 (1.5, 6 in sensitivity analysis)	Assumed
COVID-19 average infectious period (τ)	9 days	²²
Average number of contacts per day per individual (n)	8	²¹

Average duration per contact (d)	30 minutes	²¹
COVID-19 epidemiological and clinical parameters		
COVID-19 transmission rate per minute of contact	0.00139 (0.00070, 0.00278 in sensitivity analysis)	Estimated
Duration of incubation period	2-5 days (uniform)	^{10,29}
Duration of presymptomatic period	1-3 days (uniform)	^{10,29}
Duration of symptomatic period (whether asymptomatic, mild symptomatic or severe symptomatic)	7 days (log-normal, $\sigma^2 = 7$)	³⁰
Proportion of COVID-19 infections presenting any symptoms	0.7	^{18,19}
Proportion of symptomatic COVID-19 infections with severe symptoms	0.2	²⁰
Testing and surveillance parameters		
Daily incidence of non-COVID, COVID-like symptoms	0.011	Estimated from ³¹
Proportion of non-COVID, COVID-like symptoms with signs of severity	0.2	Assumed
Delay from test to test result	1 day	Assumed
Test sensitivity (infectious periods)	90%	³²
Test sensitivity (incubation period)	30%	Assumed
Daily testing capacity (tests/day)	1, 2, 4, 8	Assumed
Maximum number of specimens per group test	2, 4, 8, 16	Assumed
RT-PCR sensitivity discounting rate per additional true-negative specimen	0.3125%	¹³

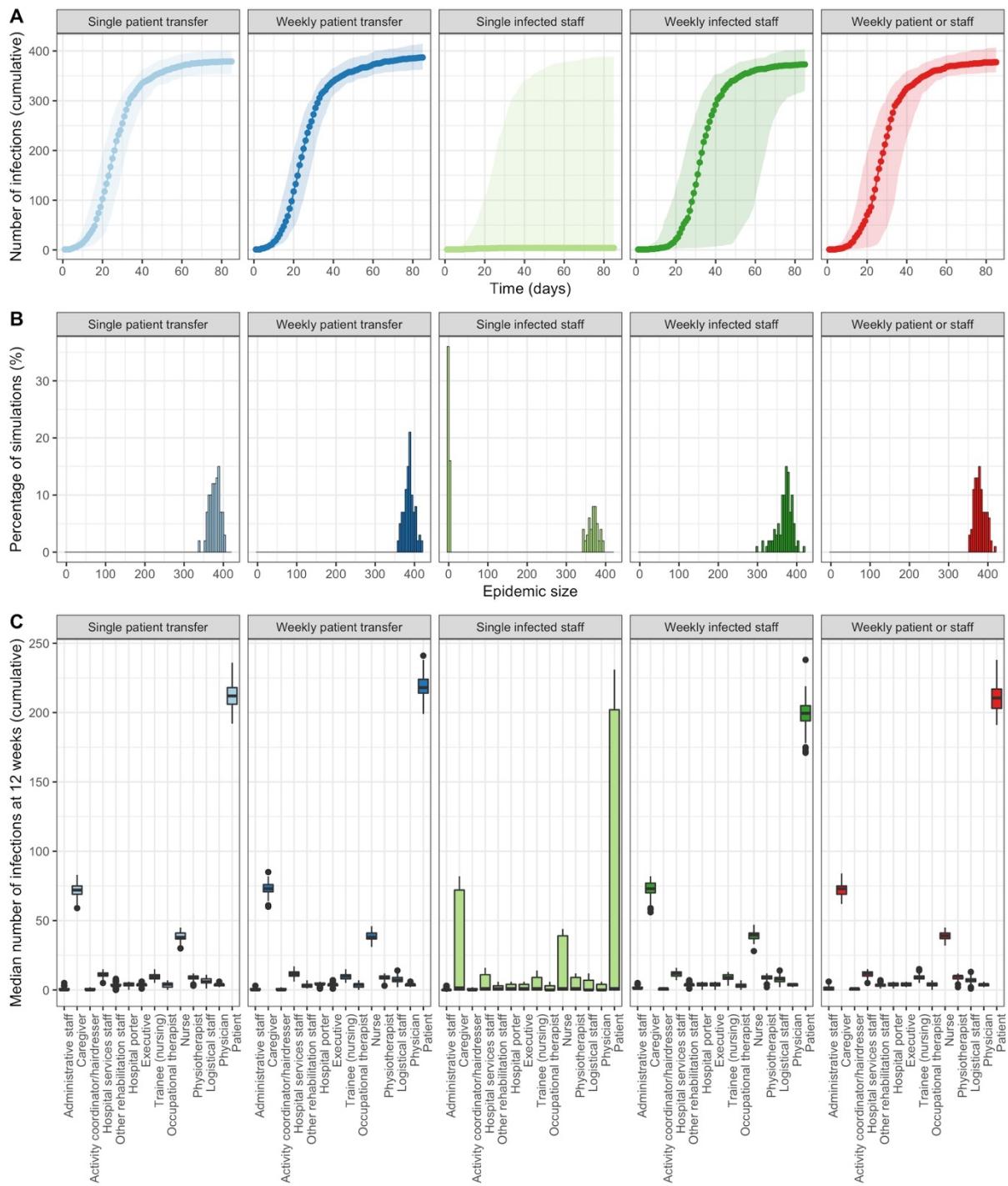


Figure S1. Epidemiological characteristics of COVID-19 epidemics simulated over a 12-week period in the LTCF setting, in the absence of any surveillance, control measures or interventions, and comparing different importation scenarios in each column. **A)** The cumulative number of infections among patients and staff in the hospital over the 12-week simulation period. Coloured bands represent 95% uncertainty intervals from stochastic simulations. **B)** Histograms of the final epidemic size at 12 weeks (NB: data are naturally censored by the 12-week simulation period). **C)** Distributions of cumulative infection totals at 12 weeks among the fourteen different categories of individuals present in the hospital.

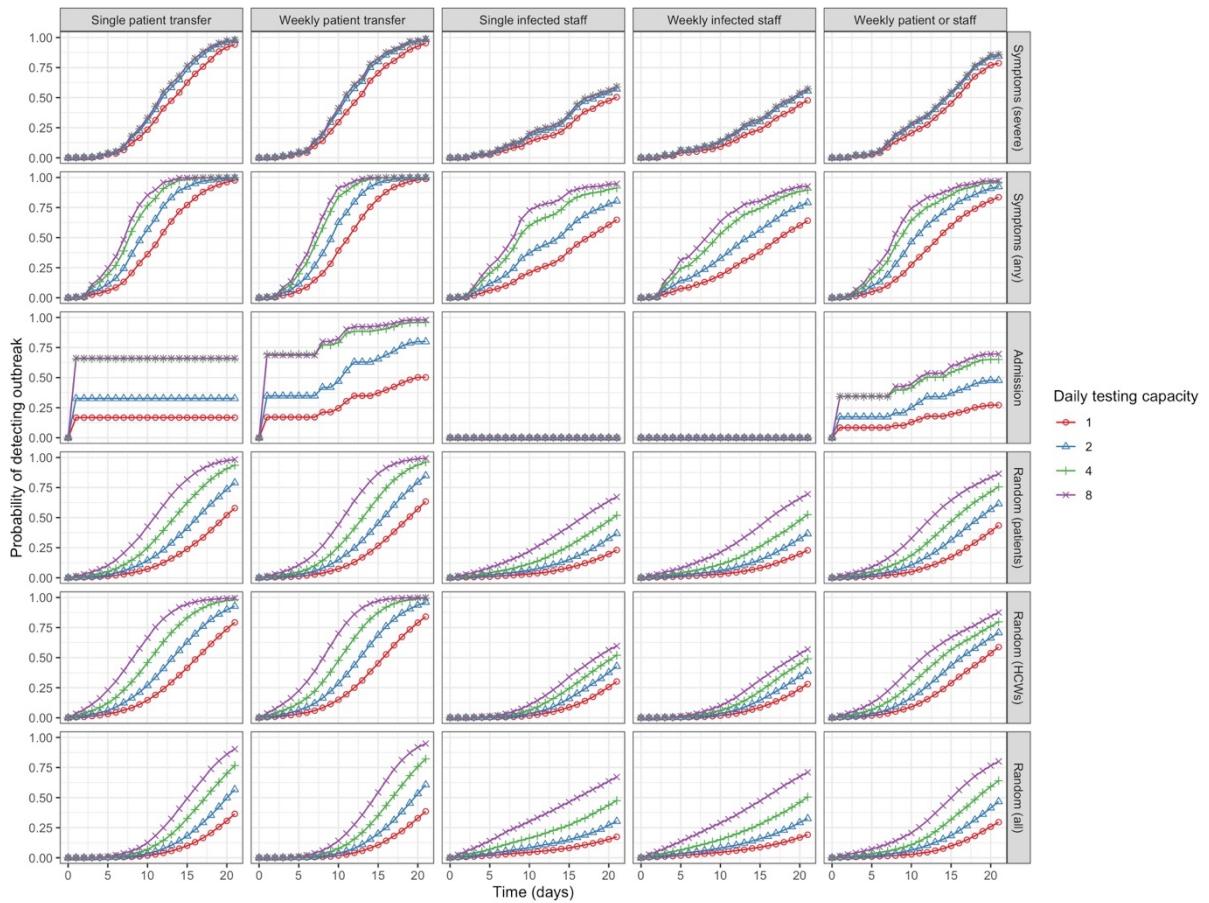


Figure S2. Probability of detecting COVID-19 over time for each importation scenario, here demonstrating the impact of daily testing capacity on detection probability for individual indication-based strategies. Each colour and shape represents a different testing capacity. Detection probability was computed over 10,000 simulations per scenario.

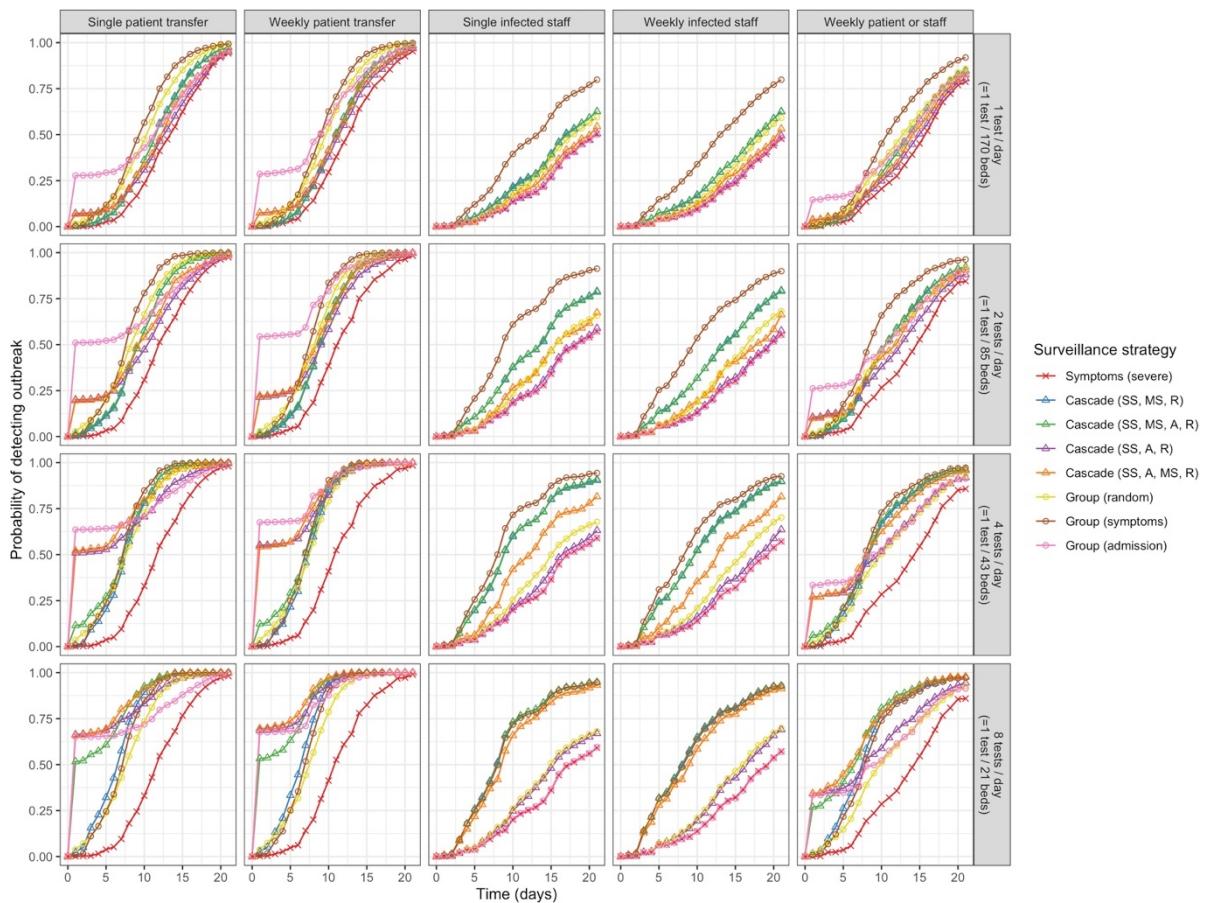


Figure S3. Probability of detecting COVID-19 outbreaks using different surveillance strategies over time for each importation scenario, here comparing the reference strategy (red crosses) to selected cascade (triangles) and group testing (squares) strategies. Detection probability was computed over 10,000 simulations per scenario.

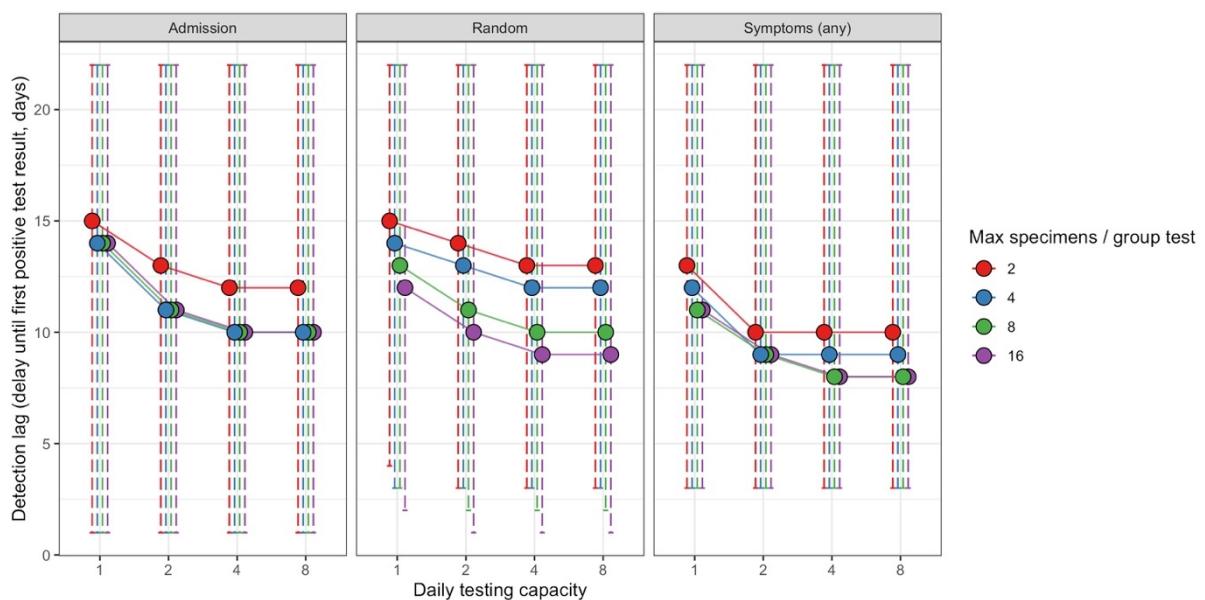


Figure S4. Efficacy of group-based testing depends on the targets of group testing (here, newly admitted patients, random individuals, individuals with any COVID-like symptoms), daily testing capacity (x-axis), and the maximum number of specimens included per group test (colours). Here, estimates are for importation scenario five. Circles represent medians and error bars represent 95% uncertainty intervals.

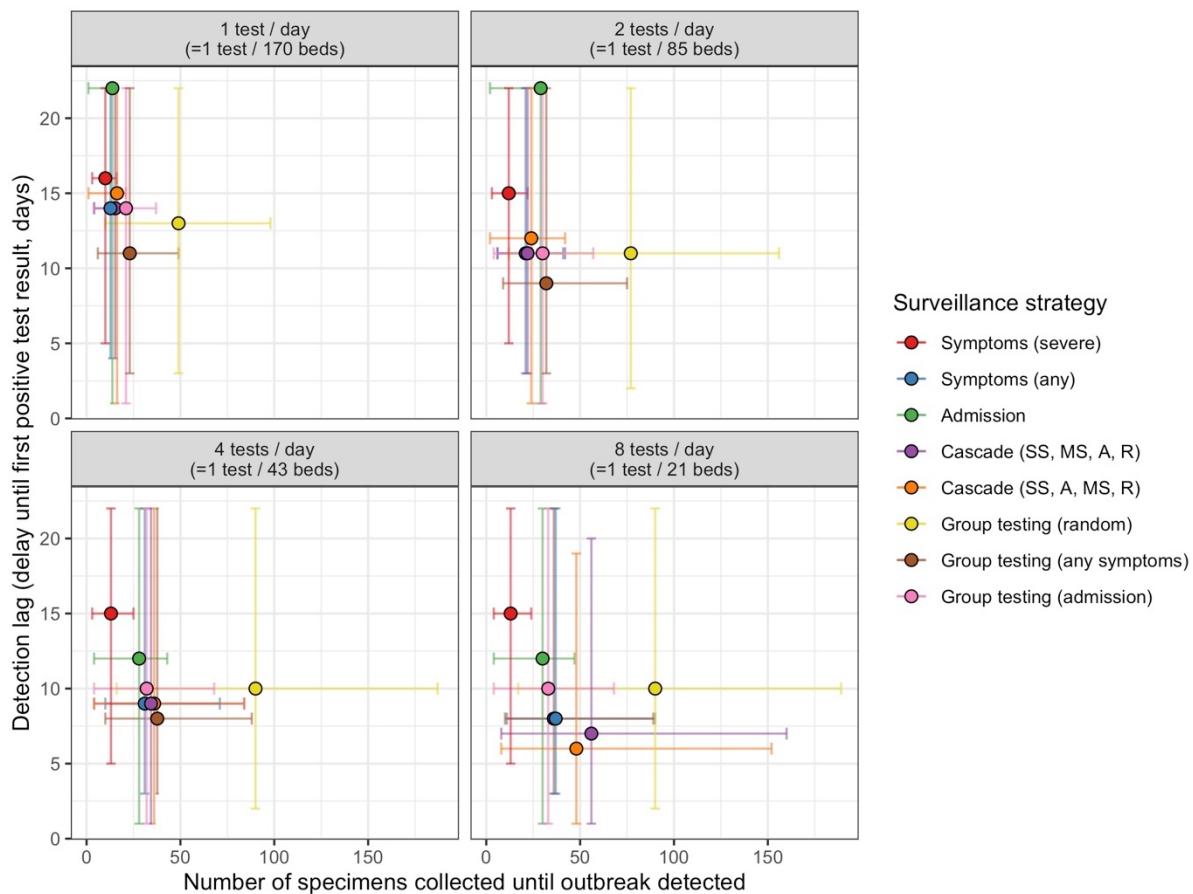


Figure S5. For selected surveillance strategies, comparison of surveillance efficacy (y-axis) and efficiency (x-axis), here in terms of the number of clinical specimens (swabs) collected until the outbreak was detected, for COVID-19 importation scenario five (random importation by both patients and staff). Circles represent medians and error bars represent 95% uncertainty intervals. For group tests, individual tests were first apportioned to any individuals presenting with severe COVID-like symptoms. Overlapping circles were shifted along the x-axis by up to 5 units and can be identified by reduced size of error bar whiskers. For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients).

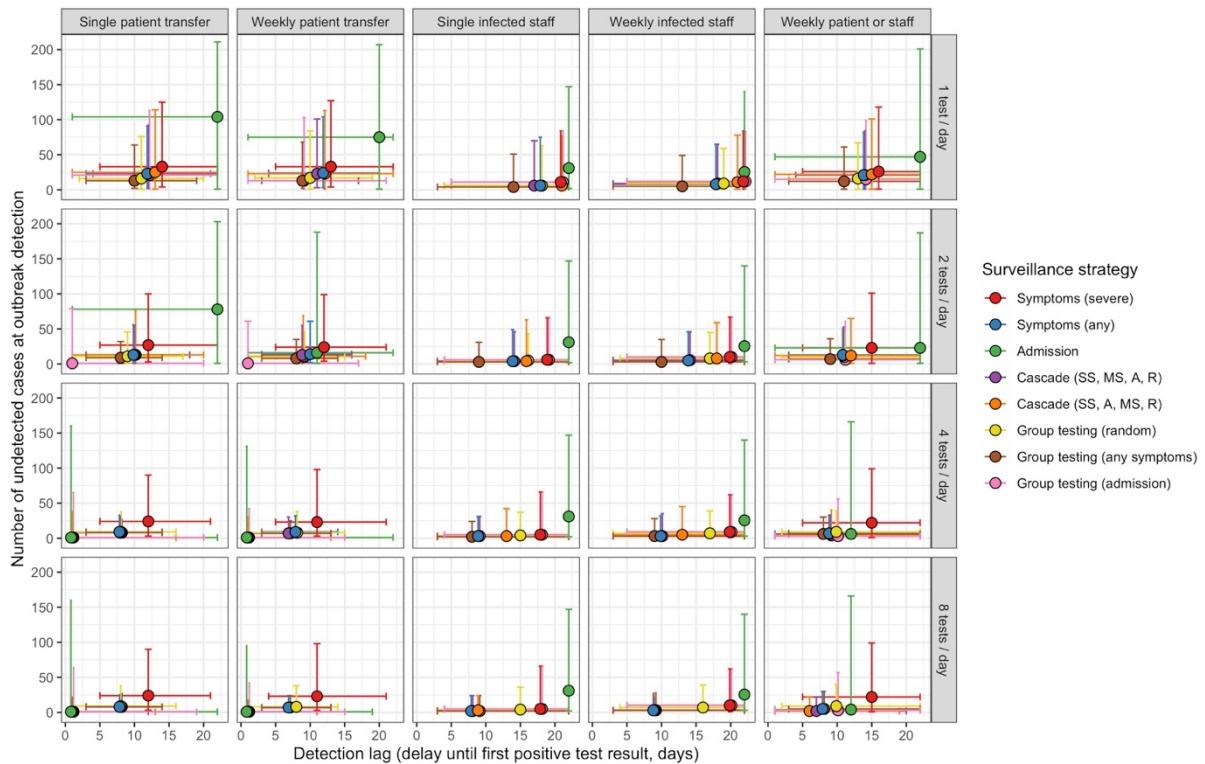


Figure S6. Relationship between detection lag (x-axis) and the number of undetected cases upon outbreak detection (y-axis), for selected surveillance strategies (colours), importation scenarios (columns) and testing capacities (rows). Circles represent medians and error bars represent 95% credible intervals. Note that some circles overlap.

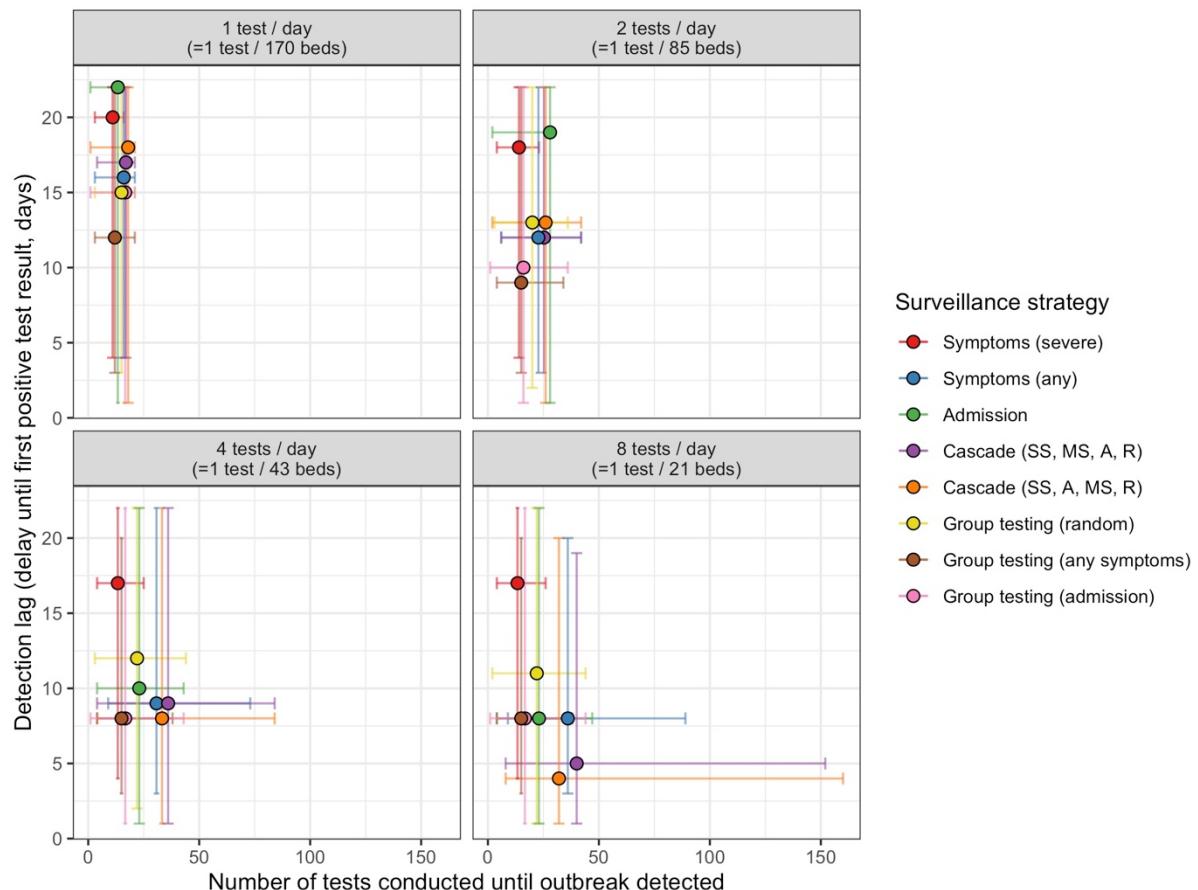


Figure S7. For a sensitivity analysis with a low transmission rate (estimated from $R_0 = 1.5$), comparison of surveillance efficacy (y-axis) and efficiency (x-axis) for COVID-19 importation scenario five (random importation by both patients and staff). Circles represent medians and error bars represent 95% uncertainty intervals. For group tests, individual tests were first apportioned to any individuals presenting with severe COVID-like symptoms. Overlapping circles were shifted along the x-axis by up to 5 units and can be identified by reduced size of error bar whiskers. For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients).

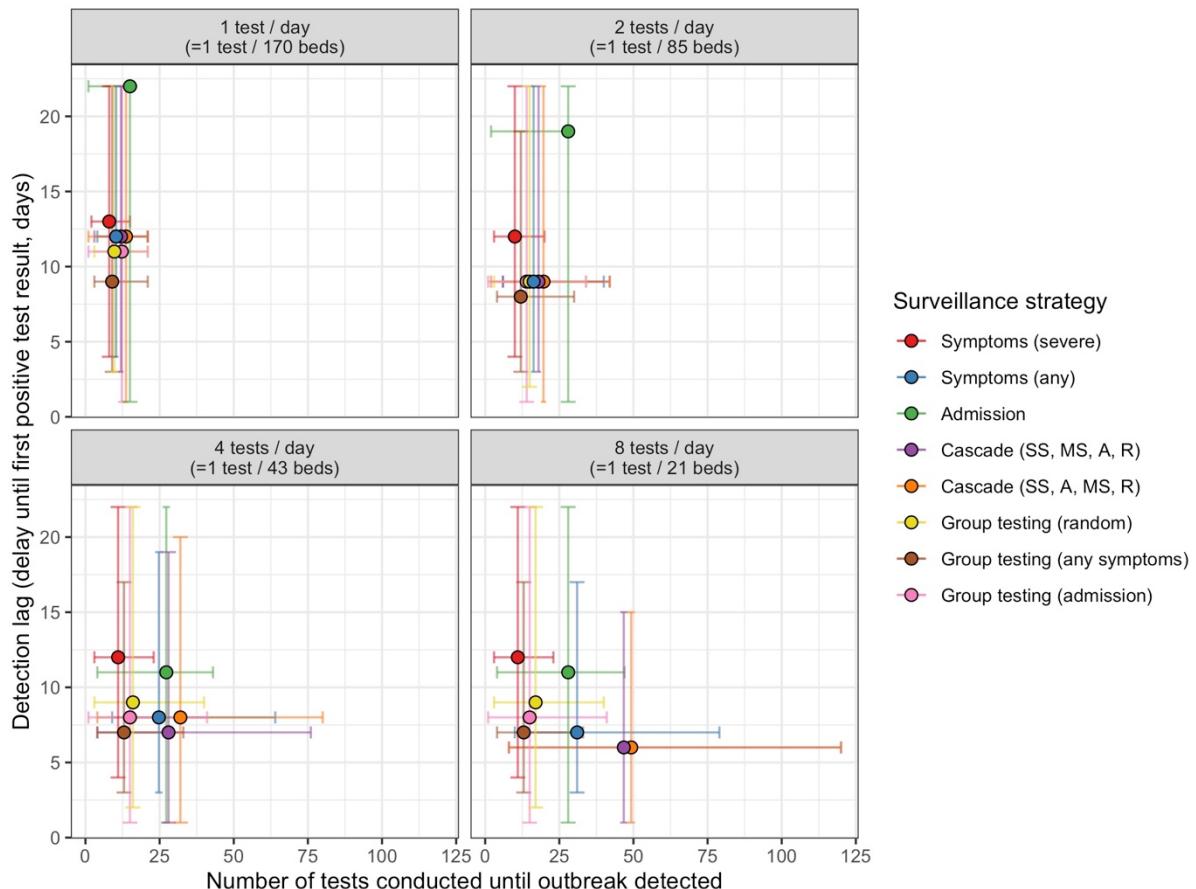


Figure S8. For a sensitivity analysis with a high transmission rate (estimated from $R_0 = 6$), comparison of surveillance efficacy (y-axis) and efficiency (x-axis) for COVID-19 importation scenario five (random importation by both patients and staff). Circles represent medians and error bars represent 95% uncertainty intervals. For group tests, individual tests were first apportioned to any individuals presenting with severe COVID-like symptoms. Overlapping circles were shifted along the x-axis by up to 5 units and can be identified by reduced size of error bar whiskers. For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients).

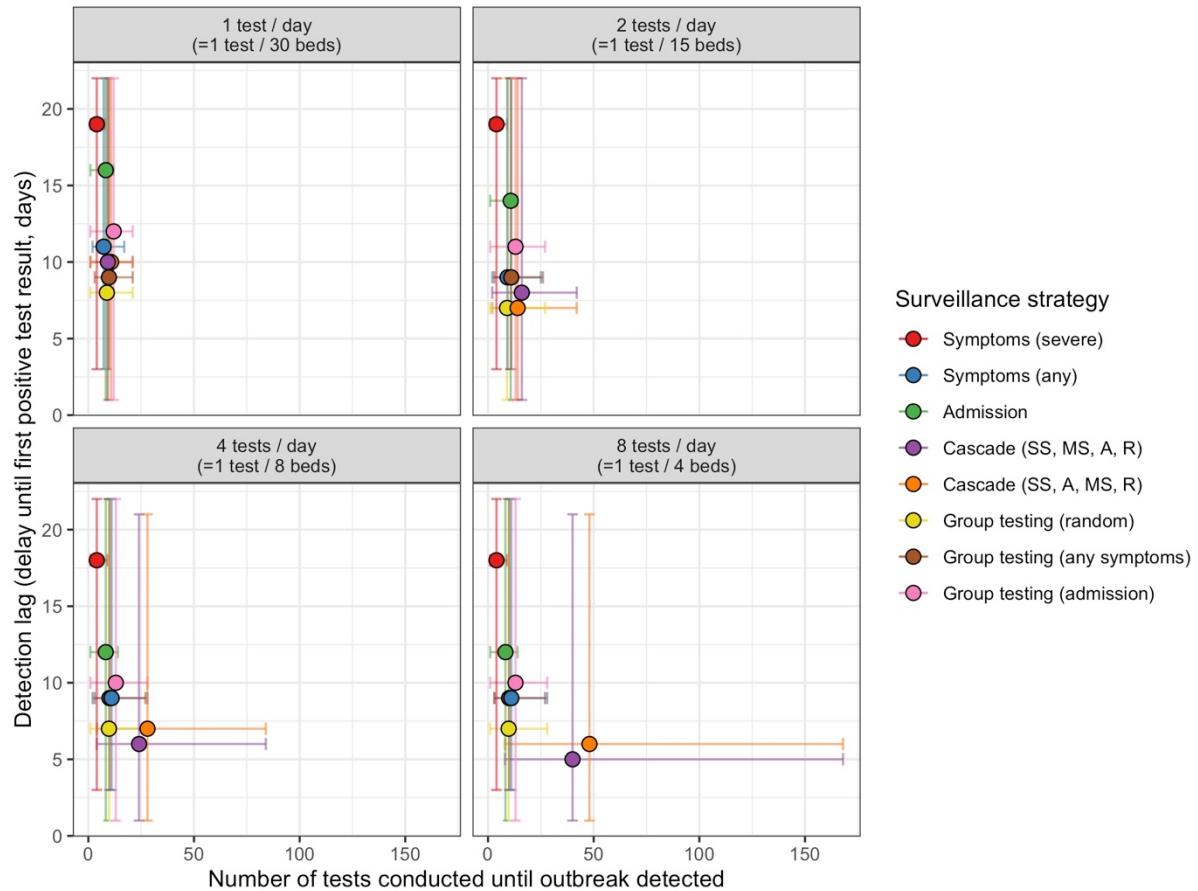


Figure S9. For a sensitivity analysis in a smaller LTCF (one ward, 30 beds), comparison of surveillance efficacy (y-axis) and efficiency (x-axis) for COVID-19 importation scenario five (random importation by both patients and staff). Circles represent medians and error bars represent 95% uncertainty intervals. For group tests, individual tests were first apportioned to any individuals presenting with severe COVID-like symptoms. Overlapping circles were shifted along the x-axis by up to 5 units and can be identified by reduced size of error bar whiskers. For cascades: SS=severe symptoms, MS=mild symptoms, A=admission, R=random (patients).

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