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David R M Smith, David R M Smith, David R M Smith, Audrey Duval ...+7 more authors

Institutions: Conservatoire national des arts et métiers, Université Paris-Saclay, Pasteur Institute, University of Paris

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Rapid antigen testing as a reactive public health response to surges in SARS-CoV-2 outbreak risk in healthcare settings

David R. M. Smith[1,2,3]*, Audrey Duval[1,2,4]*, Jean Ralph Zahar[4,5], Lulla Opatowski[1,2,3]§, Laura Temime[3,6]§

* contributed equally
§ contributed equally

1. Institut Pasteur, Epidemiology and Modelling of Antibiotic Evasion (EMAE), Paris, France
2. Université Paris-Saclay, UVSQ, Inserm, CESP, Anti-infective evasion and pharmacoepidemiology team, Montigny-Le-Bretonneux, France
3. Modélisation, épidémiologie et surveillance des risques sanitaires (MESuRS), Conservatoire national des arts et métiers, Paris, France
4. IAME, UMR 1137, Université Paris 13, Sorbonne Paris Cité, France
5. Service de Microbiologie Clinique et Unité de Contrôle et de Prévention du Risque Infectieux, Groupe Hospitalier Paris Seine Saint-Denis, AP-HP, Bobigny, France
6. PACRI unit, Institut Pasteur, Conservatoire national des arts et métiers, Paris, France

Abstract

Background: Surges in community SARS-CoV-2 incidence increase risk of importation and subsequent transmission in healthcare facilities. Antigen rapid diagnostic testing (Ag-RDT) is widely used for population screening, but its health and economic benefits as a reactive intervention in healthcare settings are unclear.

Methods: We used stochastic, individual-based modelling to simulate SARS-CoV-2 transmission in a long-term care facility with varying COVID-19 containment measures in place (social distancing, face masks, vaccination). In contrast to routine symptomatic testing using reverse-transcriptase polymerase chain reaction (RT-PCR), we evaluated the efficacy and health-economic efficiency of single or repeated population-wide Ag-RDT screening interventions implemented in response to surges in nosocomial outbreak risk.

Results: Depending on the baseline containment measures in place, nosocomial SARS-CoV-2 incidence was reduced by up to 40-47% (range of means) with routine RT-PCR testing, 59-63% with the addition of a timely round of Ag-RDT screening, and 69-75% with well-timed two-round screening. For the latter, a delay of 4 to 5 days between the first and second rounds was optimal for transmission prevention. Efficacy varied depending on test sensitivity, subpopulations targeted, and SARS-CoV-2 incidence in the community. Efficiency, however, varied primarily depending on the other containment measures in place: surveillance costs for a combined strategy of routine RT-PCR testing and reactive Ag-RDT screening ranged from a mean €420-€10,260/infection averted across scenarios (default unit costs: €5/Ag-RDT test, €50/RT-PCR test).

Interpretation: Reactive Ag-RDT screening complements routine RT-PCR testing, and systematic two-round screening helps overcome limited, time-varying diagnostic sensitivity. Health-economic gains scale significantly with underlying nosocomial outbreak risk.

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Introduction

A range of vaccines have proven safe and effective for prevention of SARS-CoV-2 infection, offering hope towards an end to the COVID-19 pandemic.[1] Yet hospitals and long-term care facilities (LTCFs) remain vulnerable to nosocomial outbreaks despite high vaccination rates.[2] LTCFs globally report instances of breakthrough infection and ensuing transmission among immunized staff and residents, notably due to variants of concern like B.1.1.7 (Alpha) and B.1.351 (Beta), which may partly escape vaccine-induced immunity relative to wild type.[3–5] This suggests that testing and screening interventions will remain important tools for detecting and isolating SARS-CoV-2 infections in healthcare facilities, even in settings with high vaccine coverage.

However, while repeated screening may be an effective tool for nosocomial transmission prevention,[6,7] it also imposes substantial economic cost and occupational burden on healthcare staff.[8,9] For potentially vulnerable, resource-limited facilities, a key challenge is knowing if, when and how to implement SARS-CoV-2 surveillance interventions.[10] When outbreak risk is low – perhaps in a highly immunized LTCF around low community incidence and few variants of concern – screening at frequent intervals is probably an inefficient use of limited health-economic resources. Yet outbreak risk is in constant flux, and is sometimes predictable. Festive holidays, for instance, draw individuals from distant places into close contact for prolonged periods, and have been associated with surges in SARS-CoV-2 epidemic risk in China, Israel, and elsewhere.[11,12] Into autumn 2021, widespread post-holiday, inter-generational population movement in the context of variants like B.1.617.2 (Delta) and C.37 (Lambda) may pose similar concerns. In such a context where local knowledge or epidemiological data indicate a suspected spike in epidemic risk, or where identification of a new case or exposed contact within a healthcare facility indicates potential for a nosocomial outbreak, reactive use of antigen rapid diagnostic testing (Ag-RDT) may be an efficient public health response.

Here, to help determine the best surveillance strategies for control of SARS-CoV-2 transmission in healthcare facilities, we adapt a simulation model to assess the epidemiological efficacy and health-economic efficiency of single or repeated Ag-RDT screening conducted in response to surges in nosocomial outbreak risk in the long-term care setting.

Methods

Simulating SARS-CoV-2 outbreaks in the long-term care hospital setting

We simulated SARS-CoV-2 outbreaks using CTCmodeler, a previously developed stochastic, individual-based transmission model in the LTCF setting.[13,14] Using high-resolution close-proximity interaction data from a 170-bed rehabilitation hospital in northern France, this model simulates (i) detailed inter-individual contacts among patients and staff, (ii) transmission of SARS-CoV-2 along simulated contact networks, and (iii) clinical progression of COVID-19 among infected individuals. A range of *COVID-19 containment measures* were built into the model. These include: (i) a patient social distancing intervention (cancellation of social activities; see Supplementary figure S1), (ii) mandatory face masks among patients and staff (80% reduction in transmission rates), and (iii) partial vaccination of patients and staff (50% immunizing seroprevalence at simulation outset). Three distinct combinations of containment measures were applied to the baseline LTCF to represent variable degrees of investment in COVID-19 prevention (Figure 1A). These are presented as: (i) *low-control LTCF 1*, with no explicit measures in place, (ii) *moderate-control LTCF 2,* with patient social distancing, and (iii) *high-control LTCF 3,* with patient social distancing, face masks and vaccination. Further modelling details are provided in Supplementary appendix section I.

Simulation initialization

Simulations were initialized to include a surge in SARS-CoV-2 introductions from the community. We assumed that 50% of patients and 100% of staff were exposed to contacts outside the LTCF in the week prior to simulation, conceptualized as representing family gatherings over a festive period. Calibrated to French epidemic data from January 2021, this translated to one patient and three staff infections, with a mean 1.4 symptomatic infections upon simulation initialization (Figure 1B). Detection of symptomatic infection at simulation outset was interpreted as coinciding with initial SARS-CoV-2 outbreak detection within the LTCF, triggering implementation of surveillance interventions (see below). We further assumed a low baseline rate of subsequent SARS-CoV-2 introductions from the community, again calibrated to French data and depicting a situation of ongoing localized risk. See Supplementary appendix section I for more initialization details. Outbreaks were simulated over two weeks to evaluate short-term outbreak risk and immediate health-economic benefits to surveillance interventions.

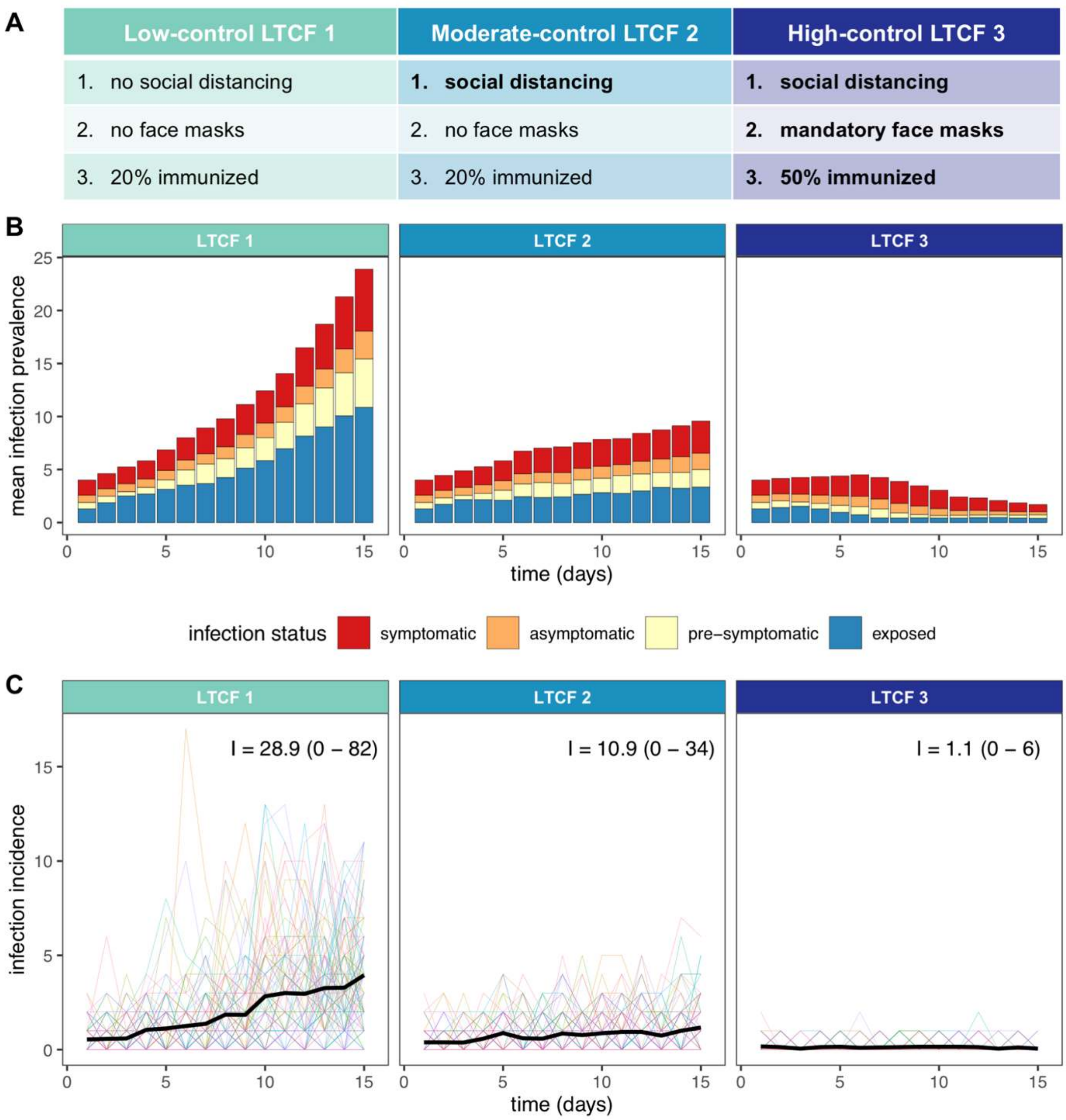

Figure 1. Modelling context: simulating SARS-CoV-2 outbreaks in a long-term care facility (LTCF) with three different levels of COVID-19 control. **(A)** A list of the COVID-19 containment measures in place across low-control LTCF 1, moderate-control LTCF 2, and high-control LTCF 3 (see Supplementary appendix section I for details). **(B)** Daily infection prevalence, the mean number of individuals in each infection stage (colours) over time. Pre-symptomatic infection combines pre-symptomatic and pre-asymptomatic infection, and symptomatic infection combines mild symptomatic and severe symptomatic infection. **(C)** Daily nosocomial infection incidence, the number of new SARS-CoV-2 infections acquired within the LTCF each day. Thin coloured lines are individual simulations; the thick black line is the mean across 100 simulations. In text, the mean (range) cumulative nosocomial incidence, I, over two weeks.

Surveillance interventions

Surveillance interventions were implemented in response to the identified surge in nosocomial outbreak risk at simulation outset. We distinguish between *routine testing*, the targeted use of RT-PCR upon onset of COVID-19-like symptoms or admission of new patients into the LTCF, and *population screening*, the mass testing of entire populations (e.g. patients, staff) on selected dates. We assessed 27 surveillance interventions grouped into four categories: (i) routine testing, (ii) 1-

round screening, (iii) routine testing + 1-round screening, and (iv) routine testing + 2-round screening (see list of interventions in Supplementary table S2). The latter two categories are defined as *multi-level surveillance interventions* that combine both screening and testing. Based on published estimates, diagnostic sensitivities of RT-PCR $s_{PCR}(t)$ and Ag-RDT $s_{RDT}(t)$ were assumed to vary with time since SARS-CoV-2 exposure t.[15,16] Ag-RDT was on average 73.5% as sensitive as RT-PCR, with greater sensitivity (87.5%) up to 7-days post-symptom onset and lower sensitivity (64.1%) thereafter (see sensitivity curves in Supplementary figure S4 and further methodological detail in Supplementary appendix section III).

Simulating counterfactual scenarios

Surveillance interventions were applied retrospectively to daily outbreak data for precise estimation of intervention effects, using methods adapted from single-world counterfactual analysis (see Kaminsky *et al*.).[17] Counterfactual scenarios were simulated by: (i) retrospectively isolating individuals who tested positive for SARS-CoV-2 (assuming immediate isolation for Ag-RDT but a 24-hour lag for RT-PCR, reflecting a delay between sample and result), and (ii) pruning transmission chains, i.e. removing all transmission events originating from isolated individuals. Single-world matching facilitated estimation of marginal benefits of multi-level surveillance interventions, i.e. additional benefits of screening relative to a baseline routine testing intervention already in place (illustrated in Figure 3). Simulation of counterfactual scenarios is described further in Supplementary appendix section III. We simulated 100 counterfactual scenarios per intervention per outbreak, across all factors resulting in a total 43.7 million simulations for estimation of surveillance efficacy, efficiency and cost-effectiveness.

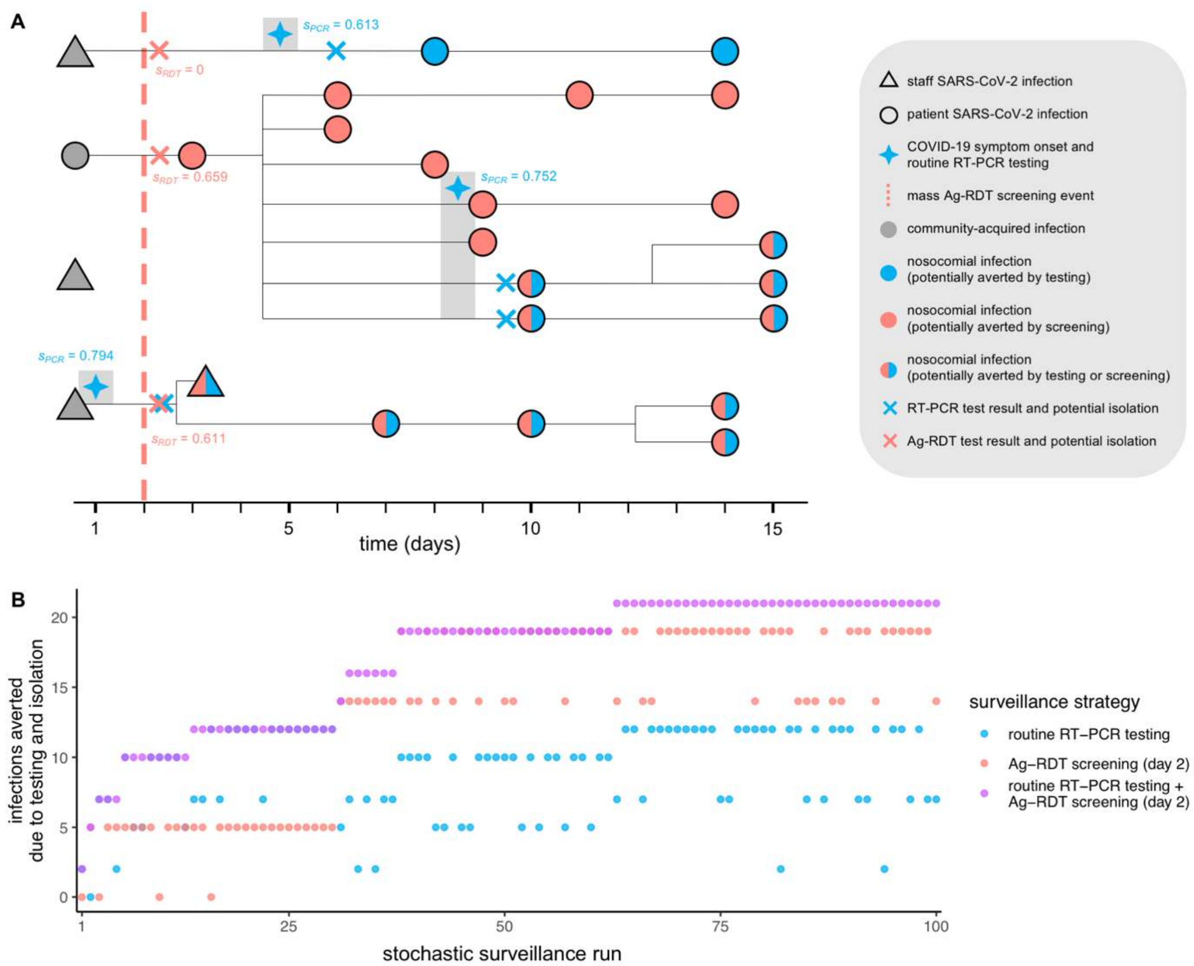

Figure 2. Surveillance interventions were applied retrospectively to simulated SARS-CoV-2 outbreaks, illustrated here using data from outbreak simulation #22 from LTCF 1. **(A)** The SARS-CoV-2 transmission chain, with infections (shapes) transmitted from left to right following black lines. Of four community-onset infections (grey shapes) at simulation outset, three transmitted to other individuals in the LTCF, triggering a nosocomial outbreak. Routine RT-PCR testing was conducted upon COVID-19 symptom onset (blue four-pointed stars), with results and case isolation 24-hours later (blue crosses). A population-wide Ag-RDT screening event was conducted on day 2 (red dashed line) with immediate results and isolation (red crosses). Test sensitivity – the probability of a positive test result and subsequent isolation – is given by *s* adjacent to each test, as determined by infection age *t* at the time of each test (see Supplementary figure S4). Nosocomial infections are coloured blue if potentially averted by routine testing, red if by screening, or both if by either. **(B)** Corresponding surveillance results from three selected surveillance interventions evaluated over 100 stochastic surveillance runs. The multi-level testing + screening intervention always averted at least as many infections as either individual intervention in the same run, demonstrating matching of "controlled" and "uncontrolled" epidemics across interventions, and its relevance for calculation of marginal benefits of multi-level interventions.

Surveillance outcomes

For each outbreak simulation, cumulative nosocomial incidence I was re-calculated for each surveillance simulation after transmission chain pruning. Surveillance efficacy was reported as reduction in I, given by

$$efficacy = 1 - \frac{(I|surveillance)}{(I|no\ surveillance)}$$

We calculated three measures of efficiency. First, *apparent efficiency* was defined as perceived operational efficiency, calculated using the per-test number of detected infections *D* as

$$apparent\ efficiency = \frac{(D|surveillance)}{n} \times 1{,}000$$

where *n* is the number of tests used.

Second, *real efficiency* was defined as the relative health benefit resulting from intervention, calculated using the per-test number of infections averted as

$$real\ efficiency = \frac{(I|no\ surveillance) - (I|surveillance)}{n} \times 1{,}000$$

For multi-level interventions combining routine testing and screening, marginal real efficiency of screening was calculated by excluding infections already averted and tests already used due to routine testing ("testing"), given by

$$marginal\ real\ efficiency_{screening} = \frac{(I|testing) - (I|testing + screening)}{n_{screening}} \times 1{,}000$$

Third, *cost-effectiveness* was defined as total surveillance costs per case averted, accounting for unit costs *c* of routine testing ($c_{testing}$) and screening ($c_{screening}$),

$$cost\ effectiveness = \frac{n_{testing} \times c_{testing} + n_{screening} \times c_{screening}}{(I|no\ surveillance) - (I|surveillance)}$$

where we assumed use of RT-PCR for routine testing at a baseline €50/test, and Ag-RDT for screening at a baseline €5/test, similar to previous cost estimates for France and the UK.[18,19] Other outcomes evaluated to assess performance of testing and screening interventions were true-positive rate (TPR), true-negative rate (TNR), negative predictive value (NPV) and positive predictive value (PPV). All surveillance outcomes are reported as means across 10,000 simulations (100 outbreaks × 100 surveillance runs) and were calculated in R software v3.6.0. Confidence intervals were calculated using bootstrap resampling with 100 replicates and normal approximation (R package *boot*).

Results

SARS-CoV-2 outbreak risk depends on the COVID-19 prevention measures in place

Following the simulated surge in SARS-CoV-2 importations, nosocomial incidence varied across LTCFs depending on the COVID-19 containment measures in place (Figure 1, Supplementary figure S2). The low-control LTCF 1 experienced exponential epidemic growth driven by patient-dominated clusters. With patient social distancing in the moderate-control LTCF 2, epidemic growth was linear, and nosocomial incidence was reduced by a mean 62.2%, more evenly split among patients and staff. Finally, with 50% immunization, mandatory face masks and social distancing combined in the high-control LTCF 3, outbreaks tended towards extinction, with a mean 96.2% reduction in incidence relative to LTCF 1. In this latter LTCF, staff members infected in the community represented the majority of cases, and rarely transmitted. Super-spreaders drove high incidence in LTCF 1, representing a mean 5.5% of infected individuals but responsible for a mean 47.3% of nosocomial infections, versus just 0.2% of infected individuals and 1.1% of nosocomial infections in LTCF 3 (Supplementary figure S3).

Reactive Ag-RDT screening complements, but does not replace routine RT-PCR testing

Routine RT-PCR testing significantly reduced incidence of hospital-acquired SARS-CoV-2 infection, by a mean 39.8% in LTCF 1, 41.2% in LTCF 2, and 46.6% in LTCF 3 (Figure 3, Supplementary figure S6). This corresponded to a mean 11.9 infections averted in LTCF 1, 4.8 in LTCF 2, and 0.51 in LTCF 3 (Supplementary figure S7). Greater relative efficacy in higher-control LTCFs was consistent with a higher average probability of positive test results, a consequence of fewer new, as-yet undetectable infections (Supplementary figure S5). On its own, 1-round Ag-RDT screening was less effective than routine testing, reducing incidence of hospital-acquired SARS-CoV-2 infection by up to 31.2-37.5% (range of means across LTCFs). For 1-round Ag-RDT screening in combination with routine testing, nosocomial incidence was reduced by 58.4-63.5%. Among infections not prevented by routine testing, this represents a 30.5-32.4% reduction in remaining incidence due to screening. Whether paired with routine testing or conducted independently, 1-round Ag-RDT screening was most effective if conducted immediately upon outbreak detection (Figure 3).

Two-round Ag-RDT screening improves screening efficacy, but is time-sensitive

Two-round screening – conducting a first round of screening immediately upon outbreak detection, and an additional second round over the following days – increased overall surveillance efficacy. Nosocomial incidence was reduced by up to 69.4%-75.0% across LTCFs with well-timed 2-round screening (Figure 3). This represents a reduction of 48.1%-52.8% among remaining infections not averted by routine testing alone. Optimal timing for the second round of screening was on days 5-6 (4-5 days after the first round). In an alternative scenario of higher community incidence and more frequent introductions of SARS-CoV-2 into the LTCF, screening was overall less effective for transmission prevention than in the baseline scenario, and optimal timing for second round screening was delayed further in LTCFs 2 and 3 (Supplementary figure S8).

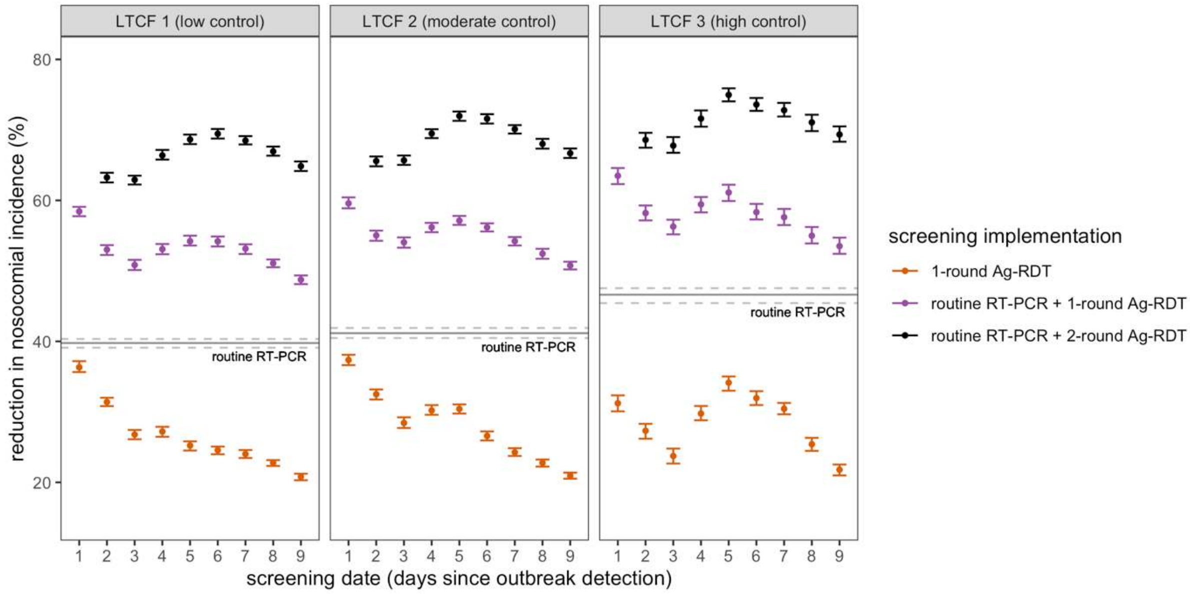

Figure 3. Efficacy of Ag-RDT screening interventions for reducing nosocomial SARS-CoV-2 incidence. Points represent mean efficacy (across 10,000 simulations) for each of 26 screening interventions, arranged by timing of the screening intervention (days since initial outbreak detection, x-axis) and coloured by screening implementation (either as 1-round screening with no other testing, orange; as 1-round screening in combination with routine RT-PCR testing, purple; or as 2-round screening with routine RT-PCR testing, black). For 2-round screening, the first round was conducted on day 1, with points arranged according to the date of the second round (days 2 to 9). The solid horizontal line represents mean efficacy of routine RT-PCR testing in absence of screening, which is conducted continuously over time and does not correspond to a specific date. Relative reductions in incidence were similar across LTCFs, but there was significant variation in the number of infections averted (Supplementary figure S7). Error bars (dashed lines for routine testing) represent 95% confidence intervals estimated by bootstrap resampling. Baseline assumptions underlying simulations include: "low" community SARS-CoV-2 incidence; time-varying Ag-RDT sensitivity relative to RT-PCR (Ag-RDT A); and screening interventions that target all patients and staff in the LTCF.

Screening efficacy depends on screening targets and test type

Targeting both patients and staff for screening was always more effective than only targeting one or the other (Supplementary figure S8A). Targeting only patients was substantially more effective than staff for LTCF 1, consistent with its large patient-led outbreaks. This difference was less pronounced in LTCF 2, while in LTCF 3 screening efficacy was nearly identical whether targeting patients or staff. We also evaluated use of RT-PCR instead of Ag-RDT for screening, maintaining its higher diagnostic sensitivity and longer turnaround time (24h). For all types of screening considered (1-round, 1-round with routine testing, 2-round with routine testing), Ag-RDT screening led to greater reductions in incidence than RT-PCR screening, suggesting that faster turn-around time for Ag-RDT outweighs its reduced sensitivity. This finding was robust to a sensitivity analysis considering an alternative curve for diagnostic sensitivity of Ag-RDT relative to RT-PCR (Supplementary figure S8B).

Screening efficiency and cost-effectiveness scale with underlying outbreak risk

Routine RT-PCR testing was more efficient per test than Ag-RDT screening: across LTCFs, mean apparent efficiency ranged from 28-65 infections detected/1,000 RT-PCR tests, while mean real efficiency ranged from 5-105 infections averted/1,000 RT-PCR tests (Supplementary figure S9). Relative to RT-PCR, the apparent efficiency of different Ag-RDT screening interventions was similar across LTCFs. This reflects that these interventions detected similar numbers of infections in each LTCF relative to the large number of tests used when screening. However, LTCFs varied greatly in terms of marginal real efficiency, with a well-timed patient screening intervention averting approximately 20 cases/1,000 Ag-RDT tests in LTCF 1, 5 cases/1,000 Ag-RDT tests in LTCF 2, and 0.5 cases/1,000 Ag-RDT tests in LTCF 3 (Figure 4). For two-round screening, efficiency and other measures of performance (TPV, NPV, PPV, NPV) varied substantially over time, depending on which populations were included for screening (Supplementary figure S10).

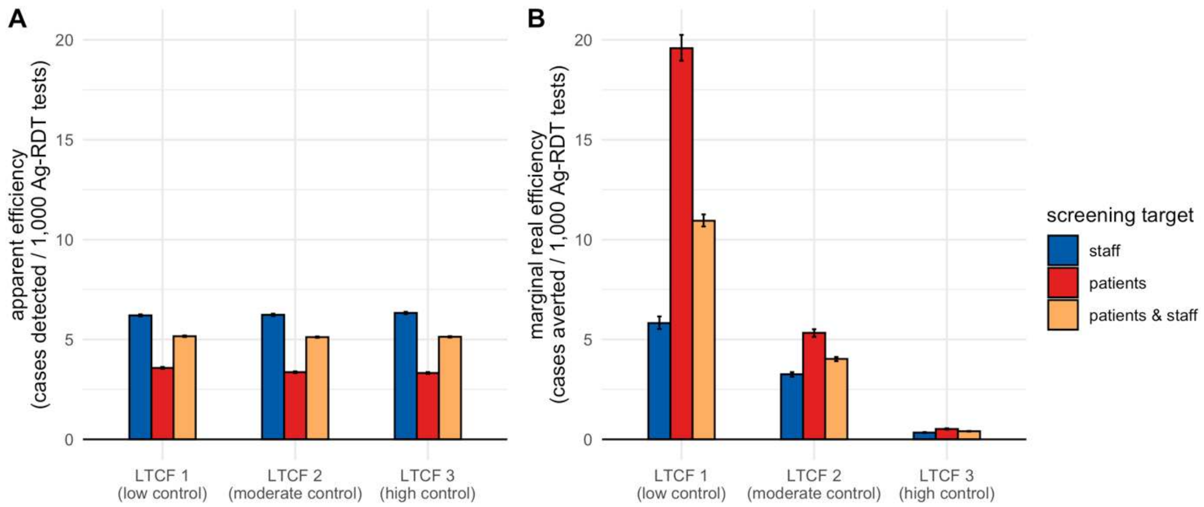

Figure 4. Efficiency of 2-round Ag-RDT screening in the context of a highly effective surveillance intervention (routine RT-PCR + 2-round Ag-RDT screening on days 1 and 5), comparing (**A**) apparent screening efficiency with (**B**) marginal real screening efficiency. Marginal real screening efficiency describes efficiency of Ag-RDT screening for prevention of remaining nosocomial SARS-CoV-2 infections not already averted by routine RT-PCR testing. Screening interventions targeted either all members of staff (blue), all patients (red), or all individuals in the LTCF (orange). Baseline assumptions underlying simulations include: "low" community SARS-CoV-2 incidence and time-varying Ag-RDT sensitivity relative to RT-PCR (Ag-RDT A).

Cost-effectiveness of different surveillance interventions varied by orders of magnitude across LTCFs (Figure 5). In LTCF 1, assuming baseline costs of €50/RT-PCR test and €5/Ag-RDT test, routine RT-PCR testing + 1-round Ag-RDT screening cost €422 (€413-€431)/case averted, with similar estimates for 2-round screening. In LTCF 2, the same intervention cost €1,070 (€1,051-€1,088)/case averted, and in LTCF 3 €10,263 (€9,963-€10,583)/case averted. Cost-effectiveness estimates were highly sensitive to testing unit costs. Above €50/RT-PCR test, routine testing was overall more cost-effective when coupled with Ag-RDT screening. Conversely, above €5/Ag-RDT test, routine testing was overall less cost-effective when coupled with Ag-RDT screening. Although combined testing and screening strategies were much more epidemiologically effective than screening on its own (Figure 3), they were generally less cost-effective (Figure 5).

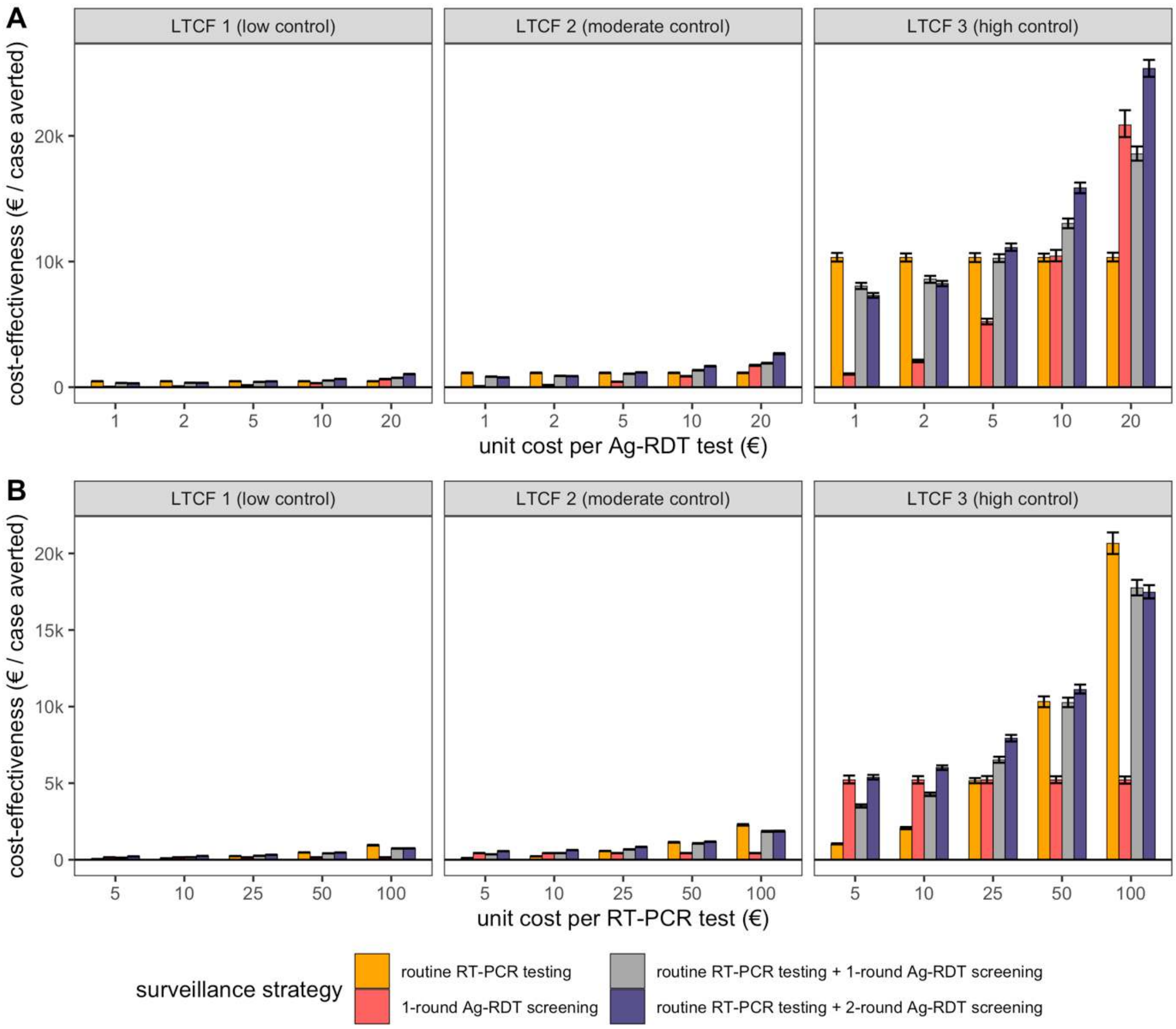

Figure 5. Cost-effectiveness of four surveillance interventions (colours), estimated as surveillance unit costs per case averted. Cost-effectiveness was estimated while varying either (**A**) the unit cost per Ag-RDT test (at a fixed €50/RT-PCR test), or (**B**) the unit cost per RT-PCR test (at a fixed €5/Ag-RDT test). One-round screening was conducted on day 1 (strategies 2 and 11 in Supplementary table S2), and 2-round screening on days 1 and 5 (strategy 23). Baseline assumptions underlying simulations include: “low” community SARS-CoV-2 incidence; time-varying Ag-RDT sensitivity relative to RT-PCR (Ag-RDT A); and screening interventions that target all patients and staff in the LTCF.

Discussion

Surges in nosocomial SARS-CoV-2 outbreak risk are often predictable, resulting from phenomena like local emergence of a highly transmissible variant, seasonal or festive gatherings that increase population mixing, and the identification of index cases or exposed contacts within a healthcare facility. When such risks are known, implementing reactive surveillance may help to identify and isolate asymptomatic and pre-symptomatic infections, limiting onward nosocomial transmission. Using simulation modelling, we demonstrate how reactive Ag-RDT screening complements routine RT-PCR testing in reducing nosocomial SARS-CoV-2 incidence following a known surge in outbreak risk. With two rounds of well-timed Ag-RDT screening, up to 75% of infections were prevented, compared to 47% with routine RT-PCR testing alone. Underlying outbreak risk was the greatest driver of screening efficiency, more important than screening timing (immediate vs. delayed), test type (Ag-RDT vs. RT-PCR) or target (patients vs. staff). We estimated that a vulnerable LTCF gains between one and two orders of magnitude more health-economic benefit (>10 infections averted/1,000 Ag-RDT tests used) than a resilient LTCF with alternative COVID-19 control measures already in place (<1 infection averted/1,000 Ag-RDT tests).

Ag-RDT screening is widely used in healthcare settings, but there is limited empirical evidence demonstrating efficacy for SARS-CoV-2 transmission prevention.[20] Despite a range of studies reporting efficacy for case identification,[21–23] interventional trials are needed to understand impacts on nosocomial spread. Our comparison of apparent and real screening efficiency demonstrates why case identification may be a poor proxy measure for actual health and economic benefit. In the absence of empirical data, mathematical models have been useful tools to evaluate performance of SARS-CoV-2 screening interventions in healthcare settings. Most studies have simulated use of routine screening at regular intervals (e.g. weekly, biweekly), finding that more frequent screening reduces outbreak probability, that targeting patients versus staff can significantly impact effectiveness, and that faster diagnostic turn-around time of Ag-RDT tends to outweigh reduced sensitivity relative to RT-PCR.[6,7,24–31] These conclusions were recapitulated in our findings.

Despite potential to reduce transmission, routine screening is an economic and occupational burden with uncertain suitability for low-risk healthcare settings.[8,9] These considerations have generally been neglected in previous work. A few modelling studies have estimated cost-effectiveness of nosocomial screening interventions in specific use cases, including for hospital patients admitted with respiratory symptoms,[32] patients admitted to German emergency rooms,[33] and routine staff and resident testing in English nursing homes.[34] However, key impacts of stochastic transmission dynamics, screening heterogeneity, and other concomitant COVID-19 containment measures have rarely been accounted for. Further, to our knowledge no studies have evaluated efficacy and efficiency of reactive, as opposed to routine screening, although findings from See *et al*. suggest greater efficiency of testing in outbreak versus non-outbreak settings.[35] Overall, our use of high-resolution, stochastic, individual-based modelling complements previous studies in demonstrating how epidemiological and health-economic benefits of reactive screening scale with test sensitivity, screening timing, test type, population targets, and – most critically – underlying nosocomial outbreak risk.

Our findings should be interpreted in the context of several methodological limitations. First, some results may reflect specificities of the rehabilitation hospital contact network underlying our model. We estimated greater efficiency for screening patients relative to staff, but the opposite result may be expected in settings where staff have higher rates of contact than patients. Second, our use of retrospective counterfactual analysis facilitated precise estimation of intervention efficacy, but precluded consideration of how surveillance interventions might impact human behaviour. For instance, healthcare workers that conduct screening inevitably come into contact with many individuals, potentially creating new opportunities for transmission. This limitation does not hold if our results are interpreted in the context of self-administered auto-tests, which may be a cost-effective intervention in the context of at-home testing in the community.[36] However, auto-testing may be less feasible for patients or residents than staff, particularly in certain high-risk settings.[37] Third, our cost-effectiveness estimates only considered testing unit costs, but decision-makers must consider a range of other implementation costs, from human resources, to logistical coordination, to opportunity costs of false-positive isolation. Finally, we limited our analysis to the two weeks following intervention implementation, under the assumption that LTCFs came to control nosocomial transmission at the same time. We thus do not capture potential downstream exponential benefits of preventing infections, including those that go on to seed transmission in the community.

Since its widespread uptake as a SARS-CoV-2 surveillance intervention, there has been substantial debate about whether the potential health-economic efficiency of Ag-RDT justifies an elevated risk of false-negative diagnosis.[38,39] Our findings are consistent with the view that Ag-RDT is on its own insufficient to eliminate nosocomial SARS-CoV-2 outbreak risk, but that it is nonetheless an effective component of multi-modal infection prevention strategies.[40] We demonstrate that reactive Ag-RDT screening is a potentially efficient public health response to surges in outbreak risk in the LTCF setting, but that its health and economic benefits scale by orders of magnitude depending on other epidemiological risk factors, including the facility's inter-individual contact patterns, infection prevention measures, and vaccine coverage. This suggests that healthcare institutions should carefully evaluate their vulnerability to COVID-19 – and hence potential returns on investment – before implementation of Ag-RDT screening interventions.

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