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# Interventions to control nosocomial transmission of SARS-CoV-2: a modelling study

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## Abstract

**Background:** Emergence of more transmissible SARS-CoV-2 variants requires more efficient control measures to limit nosocomial transmission and maintain healthcare capacities during pandemic waves. Yet the relative importance of different strategies is unknown.

**Methods:** We developed an agent-based model and compared the impact of personal protective equipment (PPE), screening of healthcare workers (HCWs), contact tracing of symptomatic HCWs and restricting HCWs from working in multiple units (HCW cohorting) on nosocomial SARS-CoV-2 transmission. The model was fit on hospital data from the first wave in the Netherlands (February until August 2020) and assumed that HCWs used 90% effective PPE in COVID-19 wards and self-isolated at home for 7 days immediately upon symptom onset. Intervention effects on the effective reproduction number ( $R_E$ ), HCW absenteeism and the proportion of infected individuals among tested individuals (positivity rate) were estimated for a more transmissible variant.

**Results:** Introduction of a variant with 56% higher transmissibility increased — all other variables kept constant —  $R_E$  from 0.4 to 0.65 (+ 63%) and nosocomial transmissions by 303%, mainly because of more transmissions caused by pre-symptomatic patients and HCWs. Compared to baseline, PPE use in all hospital wards (assuming 90% effectiveness) reduced  $R_E$  by 85% and absenteeism by 57%. Screening HCWs every 3 days with perfect test sensitivity reduced  $R_E$  by 67%, yielding a maximum test positivity rate of 5%. Screening HCWs every 3 or 7 days assuming time-varying test sensitivities reduced  $R_E$  by 9% and 3%, respectively. Contact tracing reduced  $R_E$  by at least 32% and achieved higher test positivity rates than screening interventions. HCW cohorting reduced  $R_E$  by 5%. Sensitivity analyses show that our findings do not change significantly for 70% PPE effectiveness. For low PPE effectiveness of 50%, PPE use in all wards is less effective than screening every 3 days with perfect sensitivity but still more effective than all other interventions.

**Conclusions:** In response to the emergence of more transmissible SARS-CoV-2 variants, PPE use in all hospital wards might still be most effective in preventing nosocomial transmission. Regular screening and contact tracing of HCWs are also effective interventions but critically depend on the sensitivity of the diagnostic test used.

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## Background

Effective interventions to limit nosocomial transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are pivotal to maintain healthcare capacities during pandemic waves [1, 2]. During the first epidemic wave many hospitals around the world restricted visits and cancelled non-essential medical procedures in order to maintain adequate staffing levels for patients with COVID-19. In the Netherlands, specific infection control measures were implemented but nosocomial transmission may have been facilitated by temporary shortness of supplies of personal protective equipment (PPE), including gloves, goggles, face shields, gowns and (N95) masks, at the onset of the pandemic.

Indeed, healthcare workers (HCWs) experienced a higher incidence of SARS-CoV-2 infections, compared to other professions, during the first pandemic wave [3–5]. Front-line HCWs in the UK and USA tested three times more frequently positive during the first epidemic wave than the general population after accounting for the frequency of testing [3]. Other studies from the UK and the Netherlands found higher SARS-CoV-2 incidences after the first epidemic wave among staff working in COVID-19 wards than staff working elsewhere in the hospital [5, 6]. In addition to direct contact with infectious patients, HCW-to-HCW transmission most likely also contributed to these elevated incidence rates.

Only a few studies incorporated modelling of SARS-CoV-2 transmission in healthcare settings [7–11]. In a stochastic within-hospital model, combined with a deterministic model reflecting SARS-CoV-2 transmission in the community, PPE use by HCWs and patients in the entire hospital substantially reduced nosocomial infections, while random weekly testing of asymptomatic HCWs and patients was less effective [9]. Moreover, strict cohorting of undiagnosed patients and HCWs in small units reduced the probability that SARS-CoV-2 introduction would lead to a large outbreak. In a deterministic within-hospital susceptible-exposed-infectious-recovered (SEIR) model isolating COVID-19 patients in single rooms or bays reduced infection acquisition in patients by up to 80% [8]. The model predicted that periodic testing of HCWs would have a smaller effect on the COVID-19 patient-burden than isolating patients but could reduce HCW infections by up to 64% and lead to a reduction of staff absenteeism. Both aforementioned models assumed a time-invariant SARS-CoV-2 infectiousness and diagnostic PCR test with 100% sensitivity. An individual-based modelling study assessed the impact of different interventions for SARS-CoV-2 transmission in a non-COVID-19 hospital unit [11]. The model was calibrated to COVID-19 outbreak data in a neurosurgery hospital unit in Wuhan (January until February 2020). High-efficacy face-masks were shown to be most

effective for reducing infection cases and workday loss. Reduction of contact rates had only a marginal effect on mitigating the outbreak in the long run. Another model (stochastic, individual-based, aimed at patients and HCWs in long-term care facilities (LTCF)) did incorporate a test sensitivity that varies with time since infection [7]. This model concluded that pooled testing (combining clinical specimens from multiple individuals into a single biological sample for a single RT-PCR test) was the most effective and efficient surveillance strategy for resource-limited LTCFs.

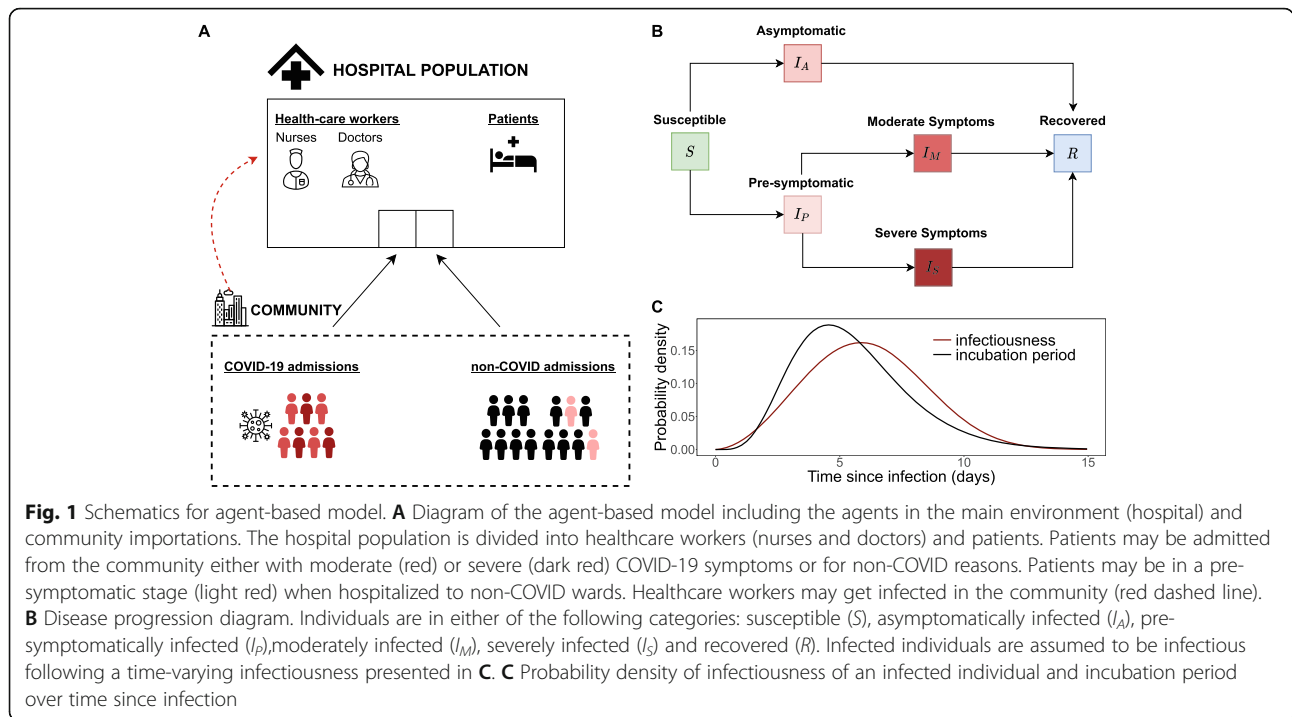
While these previous studies investigated interventions such as the PPE use, physical distancing among HCWs, various testing strategies and cohorting of patients and HCWs, the impact of contact tracing within-hospital settings has not been modelled yet. Observational evidence from 5700 HCWs in two large hospitals and 40 out-patient units in Milan, Italy, suggested that random testing (positivity rate of 2.6%) was less efficient than contact tracing (10%) [12].

In Dutch hospitals, patients and HCWs were cohorted in COVID wards, where HCWs used PPE during patient care, in addition to the basic infection control measures applied. With these measures, nosocomial transmission was considered well-controlled during the first wave of the pandemic, although outbreaks have been reported sporadically [13]. Yet, with the emergence of more transmissible variants, current infection control measures may become less effective. While COVID-19 vaccine rollout is underway, it is still unclear how they affect transmission and how their efficacy is affected by the new SARS-CoV-2 variants. We, therefore, explored the relative effectiveness of different infection prevention strategies for HCWs in hospitals in the absence of vaccination using an agent-based model of nosocomial SARS-CoV-2 transmission. First, we fitted the model to real-life data from the University Medical Center Utrecht (UMCU) during the period February–August 2020. Next, we evaluated the impact of various interventions on transmission, HCW absenteeism and test positivity as a marker of intervention efficiency for a more transmissible variant (e.g., B.1.1.7) and draw general conclusions for infection control in hospitals with a similar structure.

## Methods

### Agent-based model

We developed an agent-based model that describes the dynamics of SARS-CoV-2 transmission in a hospital allowing for importations of infections from the community (Fig. 1A). We modelled a hospital comprising four ward types: (1) general COVID wards, (2) general non-COVID wards, (3) COVID intensive-care units (ICUs) and (4) non-COVID ICUs. Within the hospital, we



distinguish patients, nurses and doctors. Patients are assumed to occupy a hospital bed in a single room. HCWs (nurses and doctors) work in duty shifts. HCWs meet patients in a number of rounds per shift (Additional file 1: Table S1), and HCWs meet other HCWs in the common staff room of each ward.

Individuals may be in one of the disease states: susceptible ( $S$ ), asymptotically infected ( $I_A$ ), pre-symptomatically infected ( $I_P$ ), infected with moderate symptoms ( $I_M$ ), infected with severe symptoms ( $I_S$ ) and recovered ( $I_R$ ). We did not explicitly model other respiratory tract infections with similar symptoms. Hence, all symptomatic individuals are necessarily infected with SARS-CoV-2. We did not model death in our simulations.

All infected individuals are assumed to be infectious following a time-varying infectiousness curve. We denote infectiousness over time since infection  $\tau$  by  $\beta(\tau)$ , i.e., it is the mean rate at which an individual infects others at time  $\tau$  after its time of infection. The reproduction number  $R$  (average number of secondary cases caused by an infected individual) is given by integrating  $\beta(\tau)$  over time since infection  $R = \int_0^\infty \beta(\tau) d\tau$ . Assuming the mean generation time  $\omega(\tau)$  to be equivalent with the observed mean serial interval, we calculated the infectiousness profile by  $\beta(\tau) = \omega(\tau)R$ . Based on this, the individual's infectiousness follows a Weibull distribution with a mean of 6 days (Fig. 1C) [14] and the reproduction number is a scaling factor of the

infectiousness profile. We assumed the infectiousness to differ between asymptomatic and symptomatic infected individuals, defined by  $\beta_A(\tau)$  and  $\beta_S(\tau)$ , respectively. Then,  $\beta(\tau)$  can be decomposed into

$$\beta(\tau) = P_A \beta_A(\tau) + (1 - P_A) \beta_S(\tau)$$

where  $P_A$  represents the proportion of asymptomatic infections. Asymptomatic individuals are assumed to have an infectiousness proportional to that of symptomatic individuals, i.e.,  $\beta_A = x_A \cdot \beta_S$ ,  $x_A \leq 1$ . Integrating over each of the two terms leads to the respective contribution to the overall reproduction number:

$$R = R_A + R_S = \int_0^\infty P_A \cdot x_A \cdot \beta_S(\tau) d\tau + \int_0^\infty (1 - P_A) \beta_S(\tau) d\tau.$$

Transmission events can occur between patients and HCWs and among HCWs. We assumed no patient-to-patient transmission as patients are assumed to occupy single-bed rooms. Only HCWs in their asymptomatic or pre-symptomatic phase contribute to transmission. We assumed that the incubation period has a Gamma distribution with mean 5.5 days [15].

Patients may be admitted to the hospital for non-COVID reasons or with moderate or severe COVID-19 symptoms. In the first case, they may be susceptible, pre-symptomatically or asymptotically infected. Symptomatically infected patients are admitted to

**Table 1** Parameter values for the agent-based model

Symbol	Description	Distribution/value <sup>a</sup>	Source
$s(t)$	Time between infection and symptom onset	Gamma distribution Shape = 5.807 Scale = 0.948 Mean = 5.510 SD = 2.284	Lauer et al. [15]
$\omega(t)$	Time between becoming infected and subsequent onward transmission events	Weibull distribution Shape = 2.826 Scale = 6.839 Mean = 6	Grassly et al. [14]
$P_A^p$	Proportion of asymptomatic infections among infected patients	20%	Buitraga-Garcia et al. [20]
$P_A^h$	Proportion of asymptomatic infections among infected HCWs	31%	Buitraga-Garcia et al. [20]
$P_s$	Proportion of severe symptomatic individuals	20%	Wu et al. [21]
$R_A^w$	Reproduction number of asymptomatic infectees for wild-type variant	0.5	Calibrated to UMCU data
$R_S^w$	Reproduction number of symptomatic infectees for wild-type variant	1.25	Calibrated to UMCU data
$R_A$	Reproduction number of asymptomatic infectees for new virus variant	0.8 (1.95)	Based on $R_A^w$ with 56% higher transmissibility, varied in sensitivity analysis
$R_S$	Reproduction number of symptomatic infectees for new virus variant	1.95	Based on $R_S^w$ with 56% higher transmissibility
	Maximum sensitivity of diagnostic PCR test	93.1% (79%)	Grassly et al. [14], varied in sensitivity analysis
	Proportion of HCWs that work in the same ward as during their previous shift	95% (baseline) 100% (intervention)	Assumed
	PPE effectiveness	90% (50%, 70%)	Suzuki et al. [22], Qian et al. [23] and Besbesen et al. [24], varied in sensitivity analysis
	Isolation period for HCWs	7 days	Assumed
$\gamma_A$	Recovery time for asymptomatic infection	14 days Sensitivity analysis: Unif(9, 19)	Assumed
$\gamma_S$	Recovery time for symptomatic (moderate, severe) infection	14 days (moderate) 35 days (severe) Sensitivity analysis: Unif(9, 19) Unif(30, 40)	Liu et al. [16]

**Table 1** Parameter values for the agent-based model (Continued)

	Symbol	Description	Distribution/value <sup>a</sup>	Source
LoS of non-COVID patients in ICU			Lognormal meanlog = 0.37 sdlog = 0.82 Mean = 1.45 days sd = 2.27	Fitted distributions to UMCU data from 2014-2017
LoS of non-COVID patients in normal ward			Weibull Shape = 0.92 Scale = 4.18 Mean = 4.35 days	Fitted distributions to UMCU data from 2014-2017
LoS of moderately infected patients			Gamma Shape = 1.88 Rate = 0.25 Mean = 31.8 days sd = 30.08	Fitted distributions to UMCU data from 2020
LoS of severely infected patients			Gamma Shape = 1.59 Rate = 0.05 Mean = 7.52 days sd = 636	Fitted distributions to UMCU data from 2020

<sup>a</sup>Values given are fixed in the simulations. Values in brackets were used in sensitivity analyses

COVID wards (moderate symptoms) or COVID ICUs (severe symptoms). Patients in non-COVID wards that develop symptoms during their stay are immediately transferred to COVID wards. We assumed that moderately and severely infected patients recover after 14 and 35 days, respectively [16].

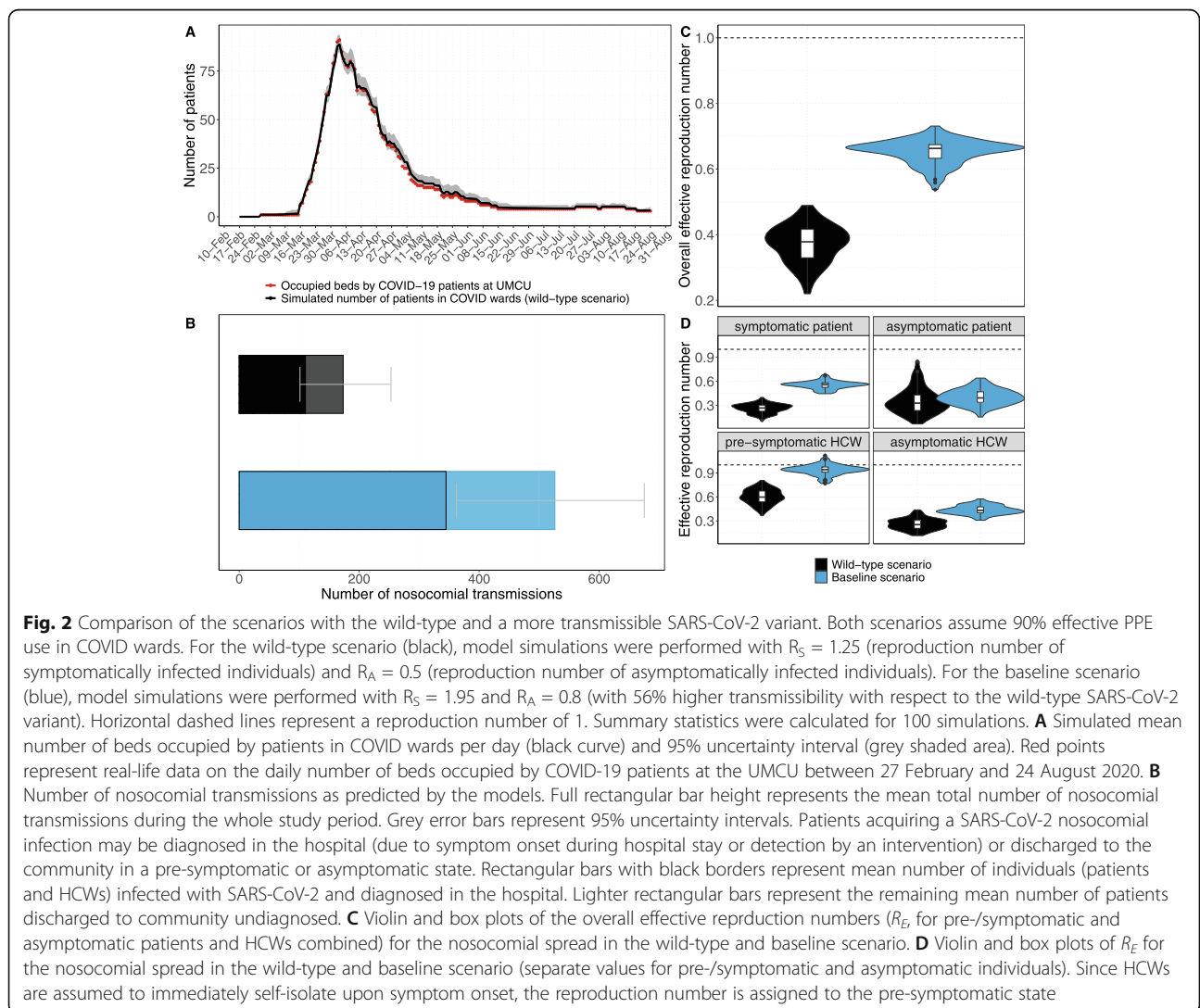
**Data and parametrization**

We used data from the UMCU to parametrize the number of wards and beds per ward (Additional file 1 pp. 2). We used the number of patients admitted to the UMCU for non-COVID reasons and their length of stay for the time period 2014–2017 and assumed a 50% decrease in admissions during the study period (Additional file 1: Table S1). The daily number of COVID-19 hospitalizations and their length of stay distribution was based on UMCU data from 27 February until 24 August 2020 (Additional file 1: Figure S1-S2). The simulations started

on 30 December 2019 with a hospital at 100% occupancy without any SARS-CoV-2-infected individuals.

The first COVID-19 admissions occurred on 27 February 2020. To account for admissions of patients that are infected but not (yet) symptomatic and HCWs who were (unknowingly) infected in the community, we used daily national numbers of SARS-CoV2 infectious individuals estimated by the Dutch National Institute for Public Health and the Environment (RIVM) from 17 February until 24 August 2020 (Additional file 1 pp. 2) [17]. We additionally used publicly available age-specific hospitalization rates in the Netherlands in 2012 and age-specific SARS-CoV-2 infection incidence rates in Utrecht province to scale the daily probability of being infected in the community for non-COVID patients and HCWs arriving in the hospital [18, 19].

Based on a published meta-analysis, we assumed that a fixed percentage of 20% and 31% of SARS-CoV-2





infections in patients and HCWs, respectively, were asymptomatic (see also Table 1) [20].

First, we chose the basic reproduction numbers  $R_S$  and  $R_A$  such that the numbers of occupied beds by COVID-19 patients predicted by our model were in good agreement with real-life UMCU data on the number of COVID-19 patients at UMCU during the first epidemic wave by visual inspection (Table 1 and Fig. 2A). During this calibration, a change in the basic reproduction numbers  $R_S$  and  $R_A$  resulted in a change of the individual’s infectiousness per time unit and thus the probability of transmission per contact. The remaining parameters did not change. These reproduction numbers incorporated the effects of typical (but not COVID-specific) infection prevention measures in the hospital. We will refer to the model parameterized with these reproduction numbers as the *wild-type scenario*. This scenario also assumed that HCWs use 90% effective PPE (i.e., 90% reduction in infectiousness) in COVID wards and isolate at home immediately upon symptom onset for 7 days, after which they return recovered to work. Next, we introduced a more transmissible SARS-CoV-2 variant into the hospital, keeping all other parameters — including PPE use in COVID wards and self-isolation after symptom onset — the same. Based on recent results for B.1.1.7, we assumed a 56% increase in transmissibility [25]. We will refer to the model parameterized with these higher reproduction numbers as our *baseline scenario*. Various intervention scenarios were compared to this baseline scenario.

**Diagnostic performance of the PCR test**

We assumed a PCR test specificity of 100% and distinguished two scenarios for the test sensitivity: (1) a time-invariant perfect sensitivity of 100% and (2) a sensitivity increasing with time since infection with a maximum sensitivity of 93.1% close to symptom onset and declining afterward (time-varying sensitivity) [14]. We considered two sensitivity analyses to test the impact of PCR test sensitivity assumptions on our results (Additional file 1 pp.3 and Fig S1). Hospital staff typically self-quarantine from symptom onset, get tested and receive their test results within hours (based on UMCU data). We, therefore, assumed no delay between testing and receiving test results and that HCWs do not contribute to virus transmission after symptom onset.







**Infection control interventions**

*Baseline scenario*

In the baseline scenario, HCWs were assumed to use PPE in COVID wards when attending to patients, but not during breaks or in other parts of the hospital. The baseline reduction factor (PPE effectiveness) was assumed to be 90%, which includes both perfect-use PPE efficacy and expected PPE use adherence level. We assumed that 95% of the HCWs work in the same ward as during their previous shift.

All interventions described below were in addition to the baseline scenario. An overview of all scenarios is given in Table 2.

**Table 2** Overview of all simulated scenarios. The main characteristics of the scenarios simulated in our agent-based model are presented

Scenarios	Virus type 	PPE use (90% effectiveness) 	HCW cohorting 	HCW screening 	HCW contact tracing 	PCR test sensitivity 
Wild-type scenario	Wild-type	COVID wards	X	X	X	—
Baseline scenario	more transmissible variant	COVID wards	X	X	X	—
No HCW ward change	more transmissible variant	COVID wards	✓	X	X	—
PPE in all wards	more transmissible variant	COVID wards non-COVID wards	X	X	X	—
Screening 3 days perfect sens	more transmissible variant	COVID wards	X	✓	X	time-invariant, perfect (100%)
Screening 3 days	more transmissible variant	COVID wards	X	✓	X	time-varying, imperfect
Screening 7 days	more transmissible variant	COVID wards	X	✓	X	time-varying, imperfect
7-day Contact tracing perfect sens	more transmissible variant	COVID wards	X	X	✓	time-invariant, perfect (100%)
7-day Contact tracing	more transmissible variant	COVID wards	X	X	✓	time-varying, imperfect
2-day Contact tracing	more transmissible variant	COVID wards	X	X	✓	time-varying, imperfect

**Intervention: PPE in all wards**

In this scenario, all HCWs used 90% effective PPE in all (non-COVID and COVID) wards. However, no PPE was used when HCWs meet each other off-ward. We performed sensitivity analyses assuming PPE effectiveness of 50% and 70%.

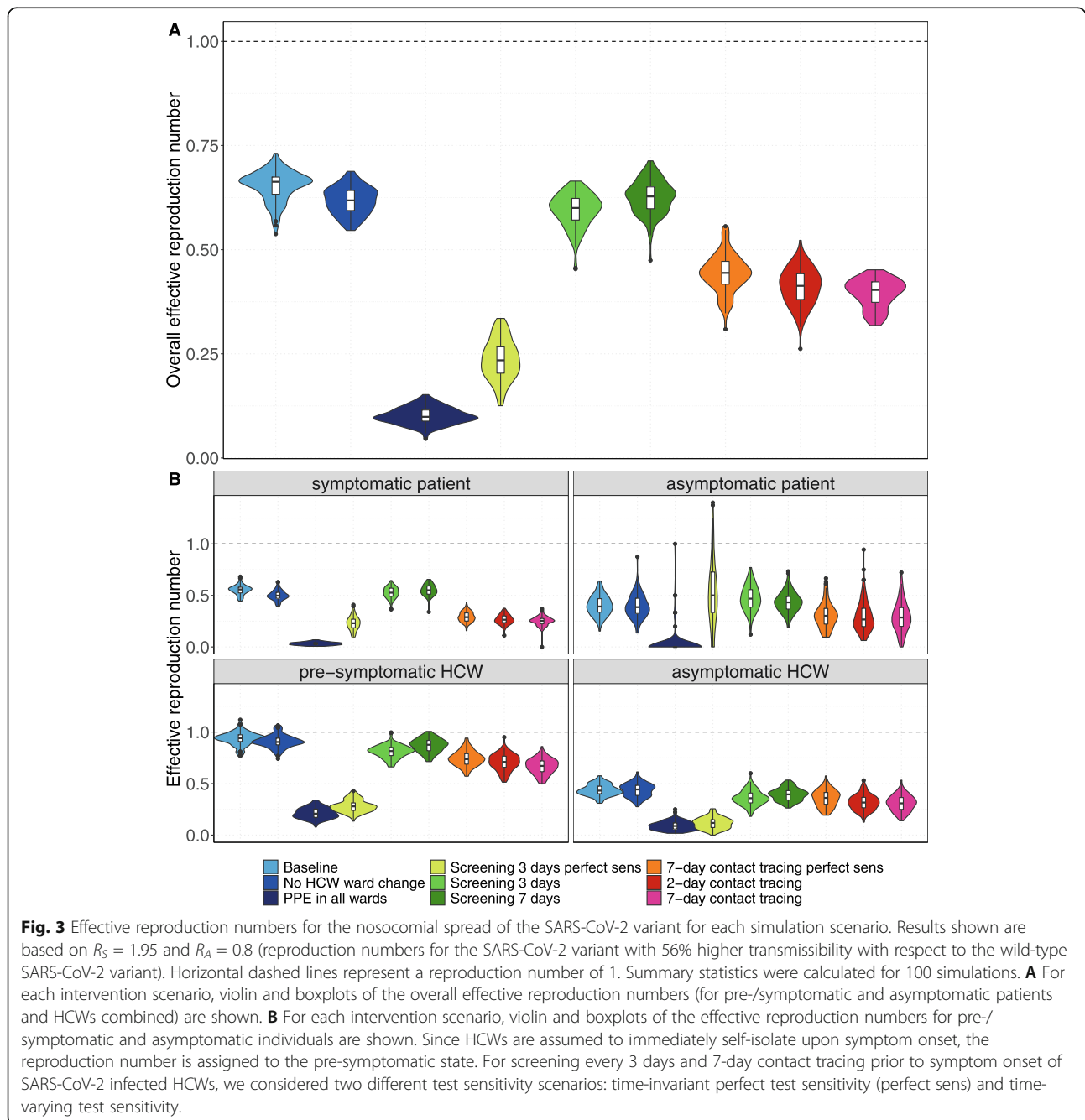
**Intervention: HCW cohorting (no ward change)**

This scenario restricted HCWs to work only in specific wards and did not allow any ward changes. This scenario

represents the most optimistic scenario where both nurses as well as physicians are assumed to be eligible for cohorting to the same degree.

**Intervention: regular HCW screening**

All HCWs were tested for SARS-CoV-2 either with (a) a test with perfect sensitivity every 3 days or a test with time-varying sensitivity, (b) every 3 days or (c) every 7 days. If tested positive, HCWs were assumed to immediately self-isolate at home for 7 days.





### Intervention: HCW contact tracing

If a HCW developed symptomatic SARS-CoV-2 infection, all contacts in the hospital during a time window of either two or 7 days before symptom onset were traced and tested. We will refer to these scenarios as *2-day contact tracing* and *7-day contact tracing*. For *2-day contact tracing*, contacts were always tested assuming a time-varying test sensitivity. For *7-day contact tracing*, we distinguished between perfect and time-varying sensitivity sub-scenarios. In the perfect sensitivity sub-scenario, contacts were instantaneously tested on the day of symptom onset of the index (the HCW). In the time-varying test sensitivity sub-scenario, the test was performed on the day of symptom onset if the contact with the index was more than 5 days ago. Otherwise, it was performed on day five after the contact. Exposed HCWs awaiting tests were assumed to wear PPE during contact with any patient and with other HCWs. In case of a positive test, patients were moved to a COVID ward while infected HCWs were sent home for self-isolation for 7 days and replaced by susceptible HCW. We did not model any absences of HCWs with disease symptoms caused by other respiratory pathogens.

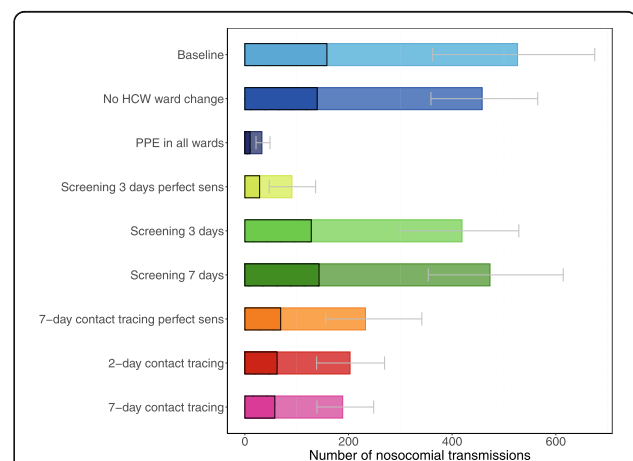
### Outcome measures

We computed the effective reproduction number  $R_E$  (average number of secondary cases caused by an infected individual) to evaluate an intervention's effectiveness. We calculated an overall  $R_E$  for an average individual (patients and HCWs combined) but also stratified  $R_E$  by patients, HCWs and symptom status. The reproduction numbers of patients were calculated for those who eventually developed symptoms ( $R_S^{pat}$ ) and those who remained without symptoms ( $R_A^{pat}$ ). Since HCWs were assumed to immediately self-isolate upon symptom onset, we calculated  $R$  during pre-symptomatic ( $R_S^{hcw}$ ) and asymptomatic states ( $R_A^{hcw}$ ). To evaluate the maximum demand on hospital capacity, we considered the total number of nosocomial infections among patients and HCWs over time. In addition, we computed the percentage of absent HCWs due to self-isolation (because of symptom onset or detection via screening or contact tracing) over time. We assessed the efficiency of screening and contact tracing interventions by their positivity rates (percentage of detected infected individuals among tested individuals). We did not include individuals that developed symptoms prior to being tested in the positivity rate calculations since those were already detected and isolated in our model. For every scenario and outcome measure, we calculated the mean and 95% percentiles over 100 simulation runs (95% uncertainty interval). We calculated positivity rates over time merging data from all simulation runs and computed 95% Bayesian beta-binomial credibility intervals.

A detailed description of the full model and the parameters can be found in the appendix (Additional file 1, [26–33]). We performed sensitivity analyses to test the robustness of our results (Table 1) and the respective results are shown in the appendix (Additional File 2, [26–33]). The data and full code are available from [https://github.com/htahir2/covid\\_intra-hospital\\_model.git](https://github.com/htahir2/covid_intra-hospital_model.git).

### Results

We observed good agreement between the number of patients in COVID wards predicted by our wild-type scenario and the real-life UMCU data during the first wave for  $R_S = 1.25$  and  $R_A = 0.5$ . However, the model slightly overestimates hospitalizations for the second half of the first wave (Fig. 2A). We subsequently assumed the introduction of a SARS-CoV-2 variant with a 56% increase in transmissibility (based on B.1.1.7 data), resulting in  $R_S = 1.95$  and  $R_A = 0.8$ . Keeping all other parameters the same, including HCWs using PPE in COVID wards and self-isolating at symptom onset, the total number of nosocomial transmissions increased by



**Fig. 4** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario. Results shown are based on  $R_S = 1.95$  and  $R_A = 0.8$  (reproduction numbers for the SARS-CoV-2 variant with 56% higher transmissibility with respect to the wild-type SARS-CoV-2 variant). Summary statistics were calculated for 100 simulations. The full rectangular bar height represents the mean total number of nosocomial transmissions during the whole study period. The grey error bars represent the corresponding 95% uncertainty intervals. Patients that acquire a SARS-CoV-2 nosocomial infection may be diagnosed in the hospital (due to symptom onset during hospital stay or due to detection by an intervention) or discharged to the community in a pre-symptomatic or asymptomatic state. The rectangular bars with the black border represent the mean number of individuals (patients and HCWs) infected with SARS-CoV-2 and diagnosed in the hospital. The lighter rectangular bars represent the remaining mean number of patients discharged to community undiagnosed. For screening every 3 days and 7-day contact tracing, we considered two different test sensitivity scenarios: time-invariant perfect test sensitivity (perfect sens) and time-varying imperfect test sensitivity.

303% (Fig. 2B) and the overall effective reproduction number increased by 62.5% (Fig. 2C).  $R_S^{hcw}$  and  $R_S^{pat}$  increased the most to 0.94 and 0.6, respectively (Fig. 2D), indicating that pre-symptomatic individuals pose the highest risk for onward transmissions.

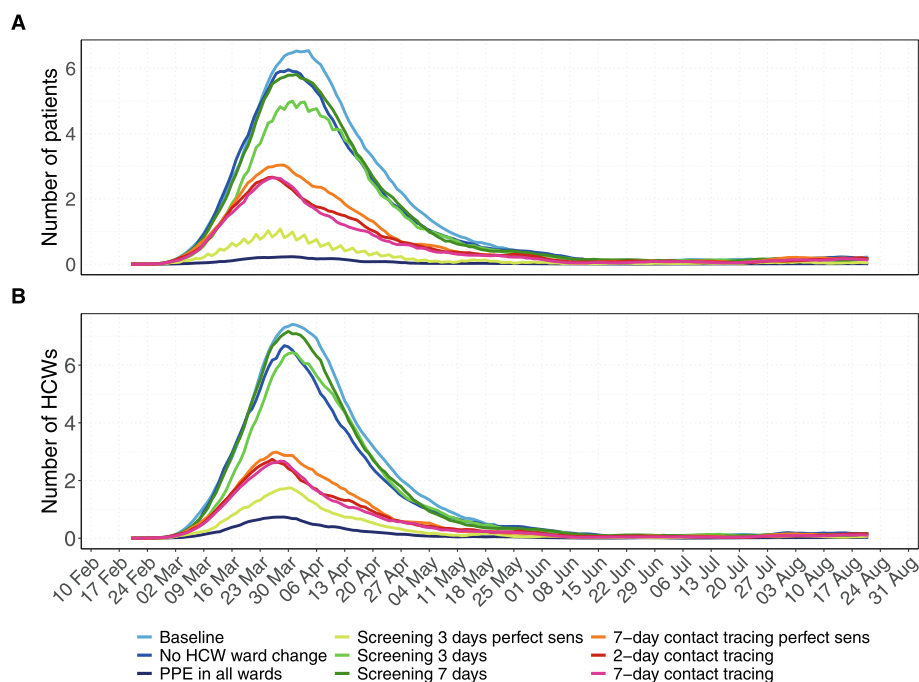
### Intervention effects on reproduction numbers

In the context of this SARS-CoV-2 variant with higher transmissibility, the baseline scenario of 90% effective PPE use in COVID wards yielded an overall  $R_E$  of 0.65 (Fig. 3A). Extending PPE use to non-COVID wards reduced  $R_E$  by an additional 85%, to 0.1. Restricting HCWs to work only in specific wards yielded a reduction in  $R_E$  of 5% (to 0.62). The effect of HCW screening on  $R_E$  highly depended on the test sensitivity. With time-varying test sensitivity, screening every 3 or 7 days reduced  $R_E$  to 0.59 and 0.63 (reductions of 9% and 3%), respectively. When perfect sensitivity was assumed, screening every 3 days reduced  $R_E$  by 63%, to 0.24. The impact of contact tracing also depended on the test sensitivity assumptions, but to a lesser extent. For perfect test sensitivity, 7-day contact tracing reduced  $R_E$  by 32%, to 0.44. For time-varying test sensitivity, the 2-day

and 7-day contact tracing scenarios reduced  $R_E$  to 0.41 and 0.39 (reductions of 37% and 40%), respectively. The additional reductions of  $R_E$  by the intervention scenarios over and above the baseline scenario were most prominent for pre-symptomatic HCWs (Fig. 3B).

### Intervention effects on numbers of nosocomial infections

PPE use in all wards or HCW screening every 3 days with perfect test sensitivity would prevent 93.7% and 82.7% of all transmissions, respectively (Fig. 4), and both interventions would also prevent outbreaks among patients and HCWs (Fig. 5). Reductions in nosocomial infections were much smaller for regular screening interventions with time-varying test sensitivity: screening every 3 days would lead to a 20.4% reduction and screening once a week to a 10.1% reduction. Testing with perfect test sensitivity followed by 7-day contact tracing was more effective (55.8% reduction of transmissions) than regular screening every 3 or 7 days. Testing with time-varying sensitivity followed by 2-day or 7-day contact tracing was similarly effective as testing with perfect sensitivity followed by 7-day contact tracing (reductions of 61.4% and 64.1%, respectively). HCW cohorting would decrease the total number of



**Fig. 5** Number of nosocomial infections among patients and HCWs over time for all simulation scenarios with the SARS-CoV-2 variant. Results shown are based on  $R_S = 1.95$  and  $R_A = 0.8$  (reproduction numbers for the SARS-CoV-2 variant with 56% higher transmissibility with respect to the wild-type SARS-CoV-2 variant). For each scenario, the 7-day moving average of the mean prevalence (over 100 simulation runs) is shown. **A** Number of hospital-acquired infections among patients. **B** Number of hospital-acquired infections among HCWs. For screening every 3 days and contact tracing 7 days prior to symptom onset of SARS-CoV-2 infected HCWs, we considered two different test sensitivity scenarios: time-invariant perfect test sensitivity (perfect sens) and time-varying imperfect test sensitivity

nosocomial infections by 13%. Note that our model predicted that approximately 30% of patients that either got admitted with SARS-CoV-2 or acquired the infection in the hospital were detected either due to testing at symptom onset or testing as part of an intervention (Additional file 2: Fig. S1). The remaining 70% of infected patients were discharged undiagnosed and without symptoms.

**Intervention effects on HCW absenteeism**

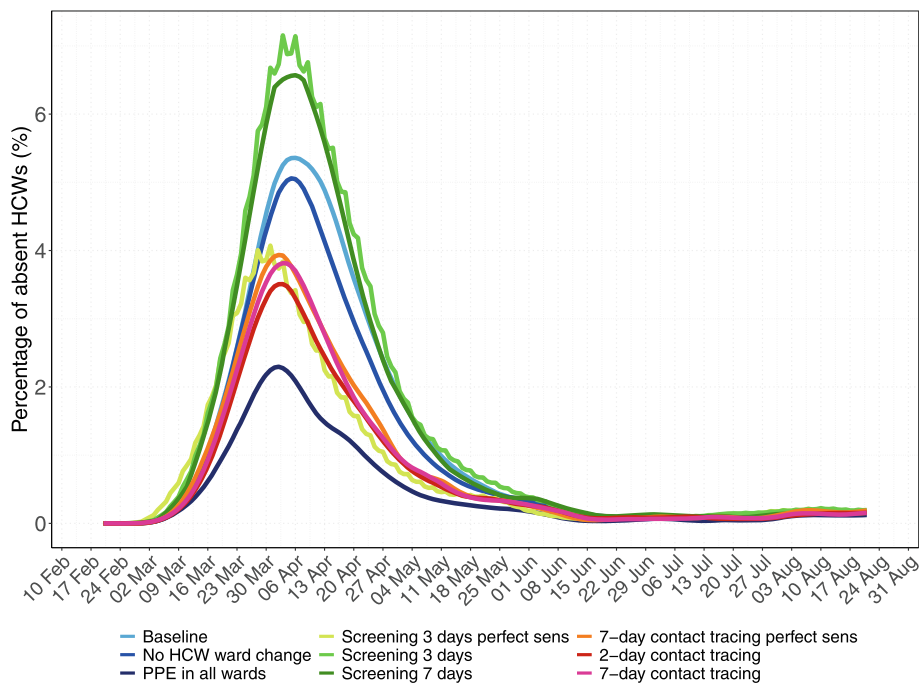
Our baseline scenario predicted a maximum HCW absenteeism of 5.4%, including absenteeism due to symptoms or home isolation (Fig. 6). When comparing intervention scenarios to the baseline scenario, HCW absenteeism is lowest for PPE use in all wards (a maximum of 2.3%). The maximum absenteeism percentages were 5.2% for HCW cohorting, 5.1% for regular screening with perfect test sensitivity, 8.6% for regular screening with time-varying test sensitivity every 7 days and 6.6% every 3 days, 4.0% for 7-day contact tracing with testing assuming perfect sensitivity, 3.6% for 2-day contact tracing with testing assuming time-varying sensitivity and 3.9% for 7-day contact tracing with testing assuming time-varying sensitivity.

**Efficiency of screening and contact tracing interventions**

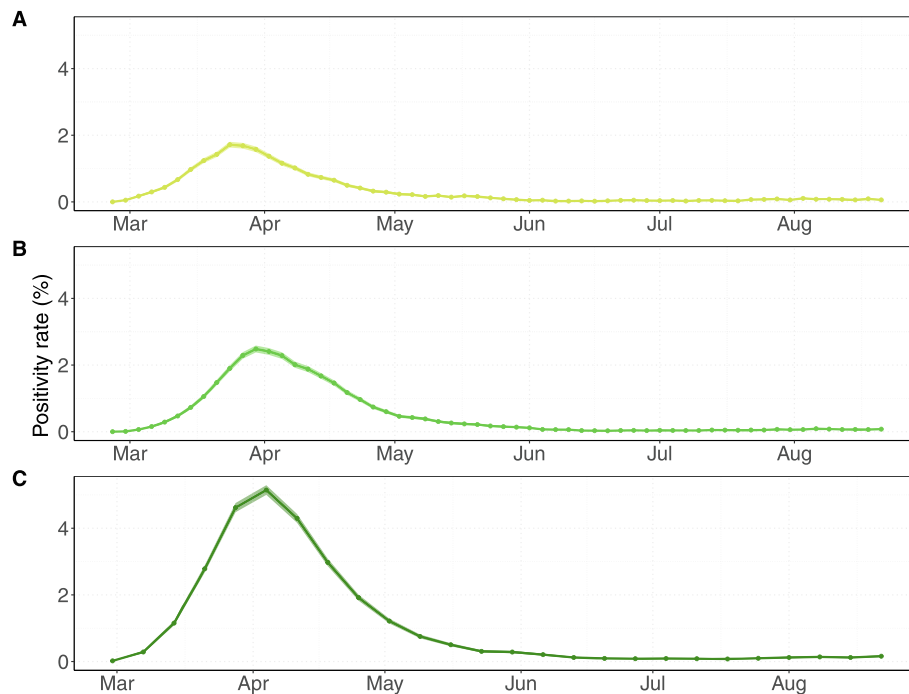
HCW screening every 3 days with a perfect test would lead to the lowest test positivity rate of all testing-based interventions (Fig. 7A). Screening of HCWs every week compared to every 3 days yields higher positivity rates with its mean reaching a maximum value of 5.1%. The positivity rate of screening interventions linearly increases with increasing prevalence (Additional file 2: Figure S1).

Positivity rates for contact tracing interventions are much higher than for screening interventions, reaching as high as 15.1% when a perfect test sensitivity is assumed (Fig. 8A). The maximum positivity rates for 2-day and 7-day contact tracing with time-varying test sensitivities are only slightly lower at 11.3% and 10.4%, respectively (Fig. 8B, C). Positivity rates of contact tracing interventions are stable across prevalence values (Additional file 1: Figure S2).

Sensitivity analyses show that our findings do not change significantly when the assumed PPE effectiveness is reduced to 70%. When PPE effectiveness is assumed to be as low as 50%, screening every 3 days with perfect sensitivity becomes more effective than PPE use in all wards. However, PPE use in all wards is still more effective than all other interventions (Additional file 2 p. 2).



**Fig. 6** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario. Results shown are based on  $R_S = 1.95$  and  $R_A = 0.8$  (reproduction numbers for the SARS-CoV-2 variant with 56% higher transmissibility with respect to the wild-type SARS-CoV-2 variant). The 7-day moving average of the mean percentage (over 100 simulation runs) of HCWs absent from work due to symptom onset or a detected SARS-CoV-2 infection screening or contact tracing is shown. For screening every 3 days and contact tracing 7 days prior to symptom onset of SARS-CoV-2 infected HCWs, we considered two different test sensitivity scenarios: time-invariant perfect test sensitivity (perfect sens) and time-varying imperfect test sensitivity



**Fig. 7** Positivity rates over time for screening interventions. Results shown are based on  $R_S = 1.95$  and  $R_A = 0.8$  (reproduction numbers for the SARS-CoV-2 variant with 56% higher transmissibility with respect to the wild-type SARS-CoV-2 variant). Positivity rates were calculated by the number of positive detected HCWs among the number of tested HCWs using data of all simulation runs combined (points). The shaded regions represent the 95% Bayesian beta-binomial credibility intervals. HCWs who developed symptoms prior to the day of testing were not included in the positivity rate as we assume that they were already correctly identified. **A** Screening every 3 days with time-invariant perfect test sensitivity. **B** Screening every 3 days with time-varying imperfect test sensitivity. **C** Screening every 7 days with time-varying test sensitivity

## Discussion

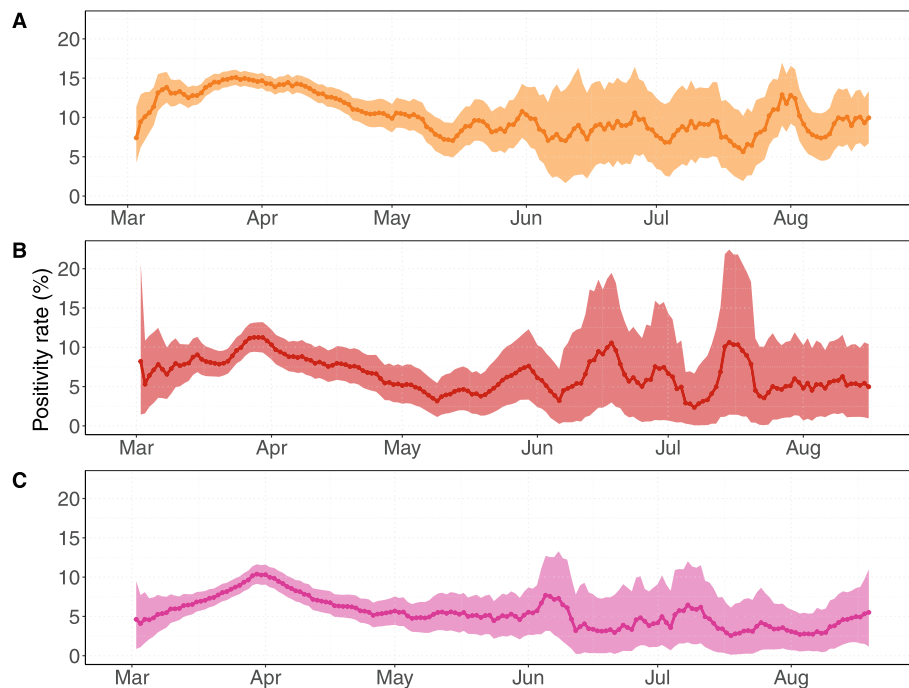
During the first epidemic wave of the wild-type SARS-CoV-2 in the Netherlands, nosocomial transmission was considered to be of relative minor importance. Our results suggest that a more transmissible virus variant could significantly increase the total number of nosocomial transmissions if hospital prevention measures would not be expanded beyond those implemented during the first wave (HCWs using PPE with assumed 90% effectiveness in COVID-19 wards and self-isolating at home after symptom onset). Our findings suggest that universal PPE use in all hospital wards is the most effective intervention to reduce the reproduction number and absenteeism. These results are consistent with a previous modelling study and previous findings on significant reductions of nosocomial-acquired SARS-CoV-2 infections after implementation of universal masking policies [1, 11, 13, 34–37].

In our model, HCW cohorting only had a small impact on nosocomial transmissions, which is due to the fact that we assumed 90% effective PPE use in the COVID wards in all scenarios. Several studies have reported elevated risks for HCWs working in COVID-19 patient care [5, 6]. Our results suggest that maintaining sufficient PPE supplies in hospital settings may reduce the

need for implementing additional HCW cohorting strategies.

Our model also suggested that regular screening of HCWs could have a strong impact, but only if the test sensitivity is high throughout the infectious period. Tests with imperfect time-varying sensitivity miss many infections during the pre-symptomatic phase. Indeed, our model identified pre-symptomatically infected HCWs as drivers of transmission both to patients and to other staff. This is consistent with a descriptive study on HCWs in France where contacts causing the transmissions took place in the pre-symptomatic phase of the index case in 30% of all cases and in almost 50% of HCW-HCW transmissions [33]. Our results also agree with previous modelling studies suggesting that regular screening of HCWs was less effective than effective PPE use.

Contact tracing was highly effective in limiting nosocomial transmissions in our model, especially when traced contacts are tested at least 5 days after their exposure and precautionary measures are undertaken in the meantime. If traced HCWs are immediately tested, self-isolated and replaced by susceptible HCWs, this can lead to increased transmission, a phenomenon that was also observed by Scarpino et al. [38]. The authors used a



**Fig. 8** Positivity rates over time for contact tracing interventions. Results shown are based on  $R_S = 1.95$  and  $R_A = 0.8$  (reproduction numbers for the SARS-CoV-2 variant with 56% higher transmissibility with respect to the wild-type SARS-CoV-2 variant). The positivity rate is computed by the percentage of positive tested contacts among all traced contacts using data of all 100 simulation runs merged. Positivity rates are assigned to the day of symptom onset of the index case, i.e., HCW that developed symptoms due to a SARS-CoV-2 infection. Traced contacts who developed symptoms due to a SARS-CoV-2 infection are excluded from contact tracing as we assume that they are always correctly identified. The plot shows the 7-day moving average (coloured line) and the 95% Bayesian beta-binomial confidence interval (shaded area). **A** Tracing contacts of symptomatically infected HCWs of the last 2 days before symptom onset using a diagnostic test with perfect test sensitivity. **B** Tracing contacts of symptomatically infected HCWs of the last 2 days before symptom onset with testing 5 days after contact with the index case assuming time-varying test sensitivity. **C** Tracing contacts of symptomatically infected HCWs of the last 7 days before symptom onset with testing 5 days after contact with the index case assuming time-varying test sensitivity

network model and evidence from data on influenza and dengue outbreaks to show that replacing infected individuals in essential societal roles with susceptibles may lead to accelerated transmission. Our results indicate that allowing traced HCWs to work with PPE in all hospital wards is more effective in limiting transmission. Finally, our model suggests that contact tracing yields higher positivity rates than screening interventions, not only at high prevalence but also during periods of low infection rates, making this also a potentially successful and cost-effective infection control strategy in hospital settings. Our findings reinforce the recommendation by Paltansing et al to test all close contacts of a SARS-CoV-2-positive case immediately and subsequently on day 3 and 7 regardless of symptoms and to allow HCWs to work with surgical masks while awaiting their test results [13].

Our study has several limitations. First, we assumed that transmission occurs solely via HCWs in the absence of a direct patient-to-patient contact pathway, as has been used before in an individual-based model of nosocomial influenza transmission [39]. Assuming similar

transmission modes for SARS-CoV-2, we consider this assumption reasonable for hospital settings in Western countries where direct patient-to-patient contact is rare. When this assumption is violated, our estimated impact of HCW-based interventions is likely to be overestimated. Second, we considered SARS-CoV-2 as a cause of symptoms and neglected other respiratory tract infections. Thus, real-life positivity rates of contact tracing may be lower than presented in this study. Third, while we have included age-specific hospitalization rates for patients admitted with SARS-CoV-2 and different proportions of asymptomatic infections for HCWs and patients, we have neglected age-structure in our transmission model. A possible extension of our model would be the inclusion of age-dependent susceptibility and infectiousness parameters. However, since the considered interventions in our model are not differential with respect to age, we do not expect any impact on the relative effect of the interventions. Further, our HCW cohorting intervention scenarios assume the same degree of cohorting both for nurses and physicians. In reality, cohorting strategies are only feasible for nurses. As



such, the estimated effect of this intervention is likely to be overestimated. Since the estimated effect of HCW cohorting was estimated to be small, we expect it to be even smaller when implemented in the real world. Moreover, the duration of contacts, SARS-CoV-2 reinfections, visitors or other ancillary staff, delays between symptom onset and isolation or delays between test application and test result were not included. Finally, while we identified one parameter set for which our model results fitted the available data well, it is possible that other parameter sets exist that would produce a comparable fit. We have not used formal fitting procedures to match our model results to the data given the large number of parameters. However, qualitatively, our conclusions were robust in sensitivity analyses to variation of the most important model parameters. While our model was developed using data of a large Dutch teaching hospital and of the first wave of the COVID-19 epidemic in the Netherlands, our results can be generalized to other hospitals with a similar structure and may be relevant for subsequent waves and future infectious disease outbreaks.

## Conclusions

In conclusion, our model demonstrates that PPE use in all wards is the most effective measure to substantially reduce nosocomial spread of SARS-CoV-2 variants with higher transmissibility. However, contact tracing and regular screening using high-sensitivity tests are also effective interventions, which might be preferred in some settings.

## Abbreviations

COVID-19: Coronavirus disease 2019; HCW: Healthcare worker; ICU: Intensive-care unit; LTCF: Long-term care facilities; PPE: Personal protective equipment;  $R_E$ : Effective reproduction number; RIVM: Rijksinstituut voor Volksgezondheid en Milieu (Dutch National Institute for Public Health and the Environment); RT-PCR: Reverse transcriptase polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SEIR: Susceptible-exposed-infectious-recovered; UMCU: University Medical Center Utrecht

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12916-021-02060-y>.

### Additional file 1: Supplementary Material. (1) Data: Figure S1.

Number of patients admitted to UMCU with a SARS-CoV-2 infection between 27 February and 2 August 2020. **Figure S2.** Length of stay data of UMCU and fitted distributions for non-COVID and COVID patients in the hospital. (2) Model: **Figure S3.** PCR test sensitivity over time since infection. (3) Calibration of parameters to data: **Table S1.** Model parameters. (4) Infection control interventions. (5) Implementation of the model: **Figure S4.** Overview of processes in the agent-based model. **Figure S5.** Flowchart for patient arrival and patient discharge in the agent-based model. **Figure S6.** Flowchart for HCW community transmission in the agent-based model. **Figure S7.** Flowchart for HCW ward change in the agent-based model. **Figure S8.** Flowchart for HCWs meeting in common room in the agent-based model. **Figure S9.** Flowchart for transition of disease states in agent-based model. **Figure S10.** Flowchart for HCWs

visiting patients in the agent-based model. **Figure S11.** Flowchart for contact tracing in the agent-based model. **Figure S12.** Flowchart for HCW screening in the agent-based model.

**Additional file 2: Supplementary results.** (1) Additional results for the main analysis: **Table S1.** Outcome measures for baseline and intervention scenarios. **Figure S1.** Positivity rate of screening interventions for different prevalence ranges. **Figure S2.** Positivity rate of contact tracing interventions for different prevalence ranges. **Figure S3.** Proportion of detected nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario. **Figure S4.** Transmission route contributions for nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario. **Figure S5.** Proportion of transmissions from HCWs and from patients for each simulation scenario. **Figure S6.** Proportion of nosocomial transmissions in COVID- and non-COVID wards for each simulation scenario. **Figure S7.** Proportion of transmissions during different infection states for each simulation scenario. (2) Results of sensitivity analyses: **Figure S8.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for each simulation scenario assuming 50% effective PPE. **Figure S9.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario assuming 50% effective PPE. **Figure S10.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario assuming 50% effective PPE. **Figure S11.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for each simulation scenario assuming 70% effective PPE. **Figure S12.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario assuming 70% effective PPE. **Figure S13.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario assuming 70% effective PPE. **Figure S14.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for each simulation scenario assuming equal reproduction numbers for symptomatically and asymptotically infected individuals  $R_{S}=1.95$  and  $R_{A}=1.95$ . **Figure S15.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario assuming equal reproduction numbers for symptomatically and asymptotically infected individuals  $R_{S}=1.95$  and  $R_{A}=1.95$ . **Figure S16.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario assuming equal reproduction numbers for symptomatic and asymptomatic individuals  $R_{S}=1.95$  and  $R_{A}=1.95$ . **Figure S17.** Effective reproduction numbers for the nosocomial spread of the wild-type SARS-CoV-2 variant. **Figure S18.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario assuming reproduction numbers of the wild-type SARS-CoV-2 variant. **Figure S19.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario assuming reproduction numbers of the wild-type SARS-CoV-2 variant. **Figure S20.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for each simulation scenario assuming higher contact rates between HCWs. **Figure S21.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario assuming higher contact rates between HCWs. **Figure S22.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario assuming higher contact rates between HCWs. **Figure S23.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for the high test sensitivity scenario. **Figure S24.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario for the high test sensitivity scenario. **Figure S25.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario for the high test sensitivity scenario. **Figure S26.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for the low test sensitivity scenario. **Figure S27.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario for the low test sensitivity scenario. **Figure S28.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario for the low test sensitivity scenario. **Figure S29.** Effective reproduction numbers for the nosocomial spread of the SARS-CoV-2 variant for the recovery time sensitivity scenario. **Figure S30.** Number of nosocomial transmissions of the SARS-CoV-2 variant for each simulation scenario for the recovery time sensitivity scenario. **Figure S31.** Daily percentage of absent HCWs during the hospital epidemic for each simulation scenario for the recovery time sensitivity scenario.



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### Authors' contributions

TMP and HT have contributed equally to this work. TMP, HT, MK, MCJB and JHHMvdW developed the conceptual framework of the study. TMP, HT, MK and MCJB developed the model. HT programmed the model and produced the output. HT and TMP produced the results of the model. TMP produced the visualization for the main text and the appendix. TMP, MK, BvdR and JHHMvdW conducted the literature research. PE and BvdR collected the data. TMP and HT have verified the underlying data. MK, MCJB, MB, JHHMvdW and PE contributed to interpretation of the results. TMP wrote the original draft of the main text. TMP and HT wrote the appendix. All authors provided critical review of the manuscript and approved its final version for submission.

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### Availability of data and materials

The datasets used and/or analysed as well as the full code reproducing the results in the current study are available from [https://github.com/htahir2/covid\\_intra-hospital\\_model.git](https://github.com/htahir2/covid_intra-hospital_model.git).

### Declarations

#### Ethics approval and consent to participate

Not applicable (only unlinked aggregated data is used).

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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