Feasibility and efficacy of mass testing for SARS-CoV-2 in a UK university using swab pooling and PCR

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Abstract

Transmission of SARS-CoV-2 without symptoms is well described, and may be mitigated by mass testing. Nonetheless, the optimal implementation and quantitative real-world impact of this approach remain unclear. During a period of rising SARS-CoV-2 prevalence, students at the University of Cambridge were enrolled in a voluntary programme of weekly PCR-based asymptomatic screening. Swab pooling by household reduced the total testing capacity required by five-fold, without affecting laboratory workflows or compromising test sensitivity. Participation remained >75% throughout the study period. 299/671 (45%) of students diagnosed with SARS-CoV-2 were either identified or pre-emptively quarantined because of the screening programme. After a negative screening test, the risk of developing COVID-19 over the following 7 days was decreased by 51%. Modelling transmission using parameters from our study suggests a reduction in $R_0$ of up to 31% attributable to weekly screening. We therefore demonstrate the feasibility and efficacy of regular, voluntary mass testing for COVID-19.
Effective control of coronavirus disease 2019 (COVID-19) through a combination of case isolation, household quarantine, and contact tracing/quarantine requires near-complete ascertainment of infectious cases\(^1\text{-}^3\). Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the absence of symptoms is well documented\(^4\text{-}^6\), however, and a substantial proportion of onward transmission has been associated with presymptomatic individuals (before they develop symptoms) and/or asymptomatic individuals (who never develop symptoms at all)\(^7\text{-}^8\). Strategies focussed on the identification and isolation of symptomatic cases have therefore been ineffective in controlling the COVID-19 pandemic.

Mass testing (large-scale screening of populations in the absence of symptoms) has the potential to identify presymptomatic and asymptomatic individuals with SARS-CoV-2 infection. Modelling studies suggest that weekly or twice-weekly screening, together with quarantine of cases and their contacts, will substantially reduce transmission\(^9\text{-}^{11}\). Regular asymptomatic screening has therefore been routinely deployed in specific settings associated with a high risk or high consequence of infection, such as health and social care\(^12\text{-}^{15}\). It has also been trialled in other settings with high risk of transmission such as prisons and professional sport\(^16\text{-}^{17}\). In England, regular mass testing has recently been extended to schools\(^18\), and offered to all adults in the community\(^19\). Nonetheless, clear empiric evidence of efficacy is limited, and the approach remains controversial\(^20\text{-}^{21}\).

Multiple outbreaks of COVID-19 have occurred in higher education institutions, often associated with large social gatherings and student accommodation, in spite of infection control measures introduced to prevent viral transmission\(^22\text{-}^{24}\). Amongst university students (typically, healthy young adults), the rate of asymptomatic infection is expected to be higher than in the general population\(^25\text{-}^{26}\). In principle, mass testing is therefore particularly suited to preventing transmission between university students. Controlling transmission in the student
population also has the potential to reduce viral spread to university staff and members of
the local community, who may be at higher risk of developing severe disease\textsuperscript{27,28}. Lessons
learnt from mass testing in universities should be broadly applicable to asymptomatic
screening for COVID-19 in other settings.

Variable levels of information on asymptomatic screening programmes at European and
North American universities are available from institutional websites, but outcomes of these
programmes have generally not been formally evaluated. Existing reports have focussed on
the practicability and acceptability of asymptomatic screening\textsuperscript{29,30} or demonstrated enhanced
case ascertainment\textsuperscript{31-33}, but provided limited epidemiological metadata or direct evidence for
a reduction in transmission on campus or in the community. Despite several modelling
studies\textsuperscript{34,35}, the quantitative real-world impact of mass testing on SARS-CoV-2 transmission
in higher education settings therefore remains unclear.

Regular screening of student populations requires large numbers of tests. One option is to
bypass the need for fixed laboratory capacity by utilising community testing with lateral flow
tests (LFTs)\textsuperscript{36,37}. Another option is to use laboratory polymerase chain reaction (PCR) tests,
but screen individuals in pools. Pooling approaches have the potential to increase greatly the
efficiency of resource utilisation where testing capacity is limited. Most studies have relied on
combining samples from multiple individuals in the laboratory (sample pooling)\textsuperscript{38-45}. This
method requires additional sample manipulation, and results in dilution of viral RNA present
in individual samples. Alternatively, tests may be pooled at the time swabs (samples) are
taken, by combining multiple swabs from individuals in the same sample tube (swab pooling,
also known as cohort pooling, or pooling at source)\textsuperscript{46-48}. This approach avoids reductions in
test sensitivity caused by sample dilution, and disruption of existing laboratory workflows.

In this study, we describe the implementation and validation of swab pooling and PCR
testing in a UK university, and demonstrate how this approach can be used for weekly
asymptomatic screening of student households. At the same time, we present a detailed
epidemiological description of the characteristics and spread of COVID-19 within the
university, identifying risk factors for infection and linking secondary attack rates amongst household contacts with the characteristics of index cases. By combining these data, we provide evidence for the efficacy of asymptomatic screening which goes beyond simple numerical case ascertainment. We demonstrate how regular screening is able to identify many students with presymptomatic as well as asymptomatic SARS-CoV-2 infection, quantify the reduction in risk of COVID-19 associated with a negative screening test, and use model-based analysis parameterised from our study to quantify the ability of mass testing to reduce transmission.
Results

Implementation of asymptomatic screening programme and characteristics of study participants

The prevalence of COVID-19 amongst older teenagers and young adults in the UK rose steeply in autumn 2020, reaching approximately 1.5% by October 1, 2020 \(^49\). Against this backdrop, 12,781 students living in University of Cambridge accommodation participated in a weekly asymptomatic COVID-19 screening programme during the autumn term, spanning 9 weeks between October 5, 2020 and December 6, 2020 (Fig. 1). In addition to asymptomatic screening, the University of Cambridge also provided a dedicated, PCR-based testing service for all students and staff with cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia). Amongst study participants, 1,031 undertook at least 1 of these symptomatic tests during the study period (Fig. 1).

A detailed description of the asymptomatic screening programme is provided in the Methods, and further information is available from the University of Cambridge website (https://www.cam.ac.uk/coronavirus/stay-safe-cambridge-uni/asymptomatic-covid-19-screening-programme). In brief, students were screened using swab pooling and two-step confirmatory PCR testing (Fig. 2). Combined nose and throat swabs were obtained by self-administration in the students’ own accommodation. Swabs from up to 10 students were then immediately pooled in the same tube of viral transport medium. In general, testing pools corresponded with student households. In the event of a positive pooled screening test, students in the pool were instructed to self-isolate, and invited for same-day individual PCR confirmatory testing. Students with positive individual confirmatory tests were treated in the same way as students with positive results from symptomatic testing, including self-isolation, household quarantine and contact tracing. If all individual confirmatory tests were negative, students were released from self-isolation, typically after 1-2 days (depending on whether 1 or 2 rounds of individual tests were required) (Fig. 2).
University accommodation was divided into 3,094 households (mean 5.0 household members, range 1-20) (Fig. 3a). For pooled sample collection, students were organised into 2,275 testing pools (mean 6.8 students, range 1-10) (Fig. 3b). To minimise the number of screening tests required, 1,476 (47.7%) smaller households were combined in merged testing pools. To ensure a maximum of ten swabs per sample tube, 151 (4.9%) larger households were spilt between multiple testing pools. Overall, 65% of testing pools corresponded exactly with households, 21% of pools included more than one household, 10% of pools included a part of one household, and 4% of pools included students from more than one household and part of one household. Participation was higher by household than by individual student, increasing from 91.3% (week 1) to 92.9% (week 9) of all households with eligible students (Fig. 3c).

Compared with the overall population of eligible students, the characteristics of participating students were similar (Supplementary Table 1). Undergraduates (particularly first year students and those studying science and technology courses) were somewhat better represented, with small but significant differences in sex, age, ethnicity and UK/international residency. The proportion of students consenting to participate increased over the course of the term, from 75.2% (week 1) to 81.9% (week 9) of all eligible students (Fig. 3d and Supplementary Table 2). Spikes in recruitment were observed after email communications to students providing information about the programme (Extended Data Fig. 1).

In theory, the total testing capacity required each week (including both pooled screening and individual confirmatory tests) was expected to vary according to testing pool size and the prevalence of infection amongst screened students (Fig. 3e). In practice, the programme was scaled up in stages over the course of the university term, by increasing the number of students invited to participate in pooled sample collection each week (weeks 1-2, 2 students from each testing pool; weeks 3-7, half the students from each testing pool, alternating week by week; weeks 8-9, all the students from each testing pool, every week) (Fig. 3c,d). At full
scale (weeks 8-9), utilisation of testing capacity was almost 5x more efficient than screening with individual tests alone (Fig. 3e and Supplementary Table 2).

Clinical performance of pooled screening tests

In total, 16,945 pooled screening tests were analysed between October 5, 2020 and December 6, 2020 (weeks 1-9), of which 252 were positive (Supplementary Table 3). 205/252 (81.3%) of these tests were followed by at least one positive individual confirmatory test (Fig. 4a and Supplementary Table 3), increasing to 183/189 (96.8%) for pooled screening tests with cycle threshold (CT) values ≤36. Amongst all pooled screening tests, approximately 1/360 were characterised pragmatically as “operational false positives” (a positive pooled screening test, followed by negative individual confirmatory tests from all students in the testing pool). Because pooled screening and individual confirmatory tests were conducted on separate samples obtained on sequential days, these operational false positives likely reflect some true negative individual confirmatory tests from students with declining viral loads, false negative individual confirmatory tests from students with borderline viral loads, as well as technical false positive screening test results. Amongst positive pooled screening tests, the proportion of operational false positives was lowest in weeks 2 (1/28, 3.6%), 3 (2/38, 5.3%) and 6 (8/67, 11.9%) when the prevalence of infection amongst screened students was highest. Conversely, the fraction characterised as false positives was highest in weeks 8-9 (14/17, 82.4%), when the prevalence of infection amongst screened students was lowest (Supplementary Table 3).

Because students contributing swabs to negative pooled screening tests did not undergo paired individual tests, it was not possible to calculate an operational false negative rate for pooled screening tests. Nonetheless, we did not observe any loss in analytical sensitivity for pooled samples containing ≥5 swabs tested using spike-in standards (Extended data Fig. 2), and the limit of detection of the assay ≤125 SARS-CoV-2 digital copies/mL viral transport
media remained well within the UK Medicines and Healthcare Products Regulatory Agency (MHRA) performance specification for laboratory-based SARS-CoV-2 PCR tests (Supplementary Table 4)\(^50\). There was a good correlation between CT values from pooled screening tests and paired individual confirmatory tests (Fig. 4b), and no differences in the distributions of CT values were observed between paired tests stratified by number of swabs (Fig 4c). Taken together, and in agreement with previous studies\(^46-48\), these data strongly argue that swab pooling does not result in any significant loss of PCR test sensitivity.

**Characteristics of students with SARS-CoV-2 infection**

Over the entire term, 5.2% (671/12,781) of participating students were diagnosed with SARS-CoV-2 infection across all testing routes (Supplementary Table 3). After an initial increase in week 2, the incidence of infection fell gradually during weeks 3-5 (Fig. 5a). A second increase in week 6 followed Halloween and the announcement of the second UK national lockdown, with a dramatic decline in cases over weeks 7-9 with lockdown measures in place. Compared with the overall population of participating students, students diagnosed with SARS-CoV-2 were more likely to be male, of white ethnicity and resident in the UK out of term time, according to both single variable and multivariable models (Supplementary Table 5, 6). There were also significant associations with the first year of study at the university, studying arts and humanities subjects at undergraduate level and living in a larger household. Other determinants of transmission within the university, and the impact of lockdown measures, were analysed using genomic epidemiology and contact tracing data in a separate report\(^51\).

In total, 39.2% (256/671) of all participating students with SARS-CoV-2 infection were identified by the asymptomatic screening programme (range 0-75%, week by week) (Supplementary Table 3). To determine how many of these students experienced symptoms at any time during their infection, we conducted a retrospective telephone survey,
and obtained 140/256 (54.7%) responses. Amongst respondents, 68/140 (48.6%) reported cardinal symptoms of COVID-19 (fever, cough and/or anosmia/ageusia) at some point in their infection (Extended Data Fig. 3a,b). The distribution of time intervals between positive pooled screening tests and symptom onset for these students implies a variable presymptomatic infectious period, with a mean of 3.6 days (Extended Data Fig. 3c). This is consistent with estimates from other populations, but slightly longer than most (typically 1-4 days)\(^2\). This may reflect methodological differences, or the particular demographic characteristics of our study population.

Of the respondents to the survey, 29/140 (20.7%) remained entirely asymptomatic. An additional 43/140 (30.7%) students detected by the asymptomatic screening programme reported minor symptoms, excluding fever, cough and anosmia/ageusia. Since these students did not meet criteria for self-isolation or symptomatic testing, they were classified pragmatically with asymptomatic students.

**Viral RNA shedding and transmission of SARS-CoV-2 in student households**

Compared with students with SARS-CoV-2 infection identified by symptomatic testing, CT values from students identified by asymptomatic screening were somewhat higher (mean CT values 24.8 vs 27.2, \(P<0.0001\); 59% vs 42% CT values <25, \(P<0.0001\)), suggesting lower viral loads (Extended Data Fig. 4a and Supplementary Table 5). We therefore stratified CT values from students sampled by our telephone survey, according to the presence (presymptomatic students) or absence (asymptomatic students) of cardinal symptoms of COVID-19 at some point in their infection. CT values were lower for presymptomatic students (mean CT value 25.5; 53% CT values <25), similar to students identified by symptomatic testing (Extended Data Fig. 4b and Supplementary Table 5). These results are consistent with the known peak in RNA shedding early in SARS-CoV-2 infection, typically on or just before symptom onset, and coinciding with symptomatic testing or
identification of presymptomatic students\textsuperscript{53,54}. Conversely, within the limit of the screening interval, asymptomatic students may be sampled at any point in their infection.

Next, we assessed the number of secondary infections amongst household contacts of students with SARS-CoV-2 infection (index cases). Compared with index cases identified by symptomatic testing, the secondary attack rate for index cases identified by asymptomatic screening was lower (6.9\% vs 12.0\% of household contacts, \(P=0.0003\)) (Extended Data Fig. 5a). Similar to CT values, we therefore stratified secondary attack rates for index cases sampled by our telephone survey, according to the presence (presymptomatic students) or absence (asymptomatic students) of cardinal symptoms of COVID-19 at some point in their infection. Remarkably, the secondary attack rate was much higher for presymptomatic students (15.2\%), similar to index cases identified by symptomatic testing (Extended Data Fig. 5b). Conversely, the secondary attack rate for asymptomatic students was much lower (2.3\%), consistent with the differences observed in CT values, and suggesting a lower infectiousness (transmission potential) of students who never develop symptoms (relative risk 0.17 compared with symptomatic students, 95\% C.I. 0.08-0.38). This is consistent with estimates from other populations\textsuperscript{8}. Whilst some infections amongst household contacts may have been acquired outside the home, that would tend to bias towards the null (smaller relative risk reduction for asymptomatic students).

Infectious virus is more readily recovered in the laboratory from patient samples with low CT values (higher viral loads), and individuals with low CT values are therefore presumed to be more infectious\textsuperscript{55}. To test this hypothesis, we examined the relationship between the secondary attack rate amongst household contacts and the CT value of the index case. As predicted, there was an inverse correlation between the CT value and the secondary attack rate (Extended Data Fig. 5c). Nonetheless, the magnitude of the effect was relatively modest, ranging from 10.3\% (CT<20, highest viral loads) to 5.5\% (CT>30, lowest viral loads) (Extended Data Fig. 5d).
Efficacy of asymptomatic screening

Combining our data on case ascertainment with the results of our telephone survey (and assuming that sampling was random), we estimate that 20% (95% C.I. 16.4-22.9%) of all students with confirmed COVID-19 were asymptomatic (no cardinal symptoms) (Fig. 5b). Of the remaining students with confirmed COVID-19 who developed symptomatic disease, 23% (95% C.I. 19.0-27.1%), were detected by the asymptomatic screening programme. A further 8% of these students were detected by symptomatic testing, but were already quarantined at the time of symptom onset because of detection of a household contact by the asymptomatic screening programme. Taken together, the asymptomatic screening programme may therefore have contributed to the interruption of onward transmission from 45% of all students with confirmed SARS-CoV-2 infection.

To measure directly the efficacy of asymptomatic screening for the detection of students with presymptomatic infection using an orthogonal approach, we focussed on weeks 3-7 of the programme. During this period, half the students from each testing pool were screened each week, with a screening interval of 14 days for individual participating students. The risk of a positive symptomatic test was smallest immediately following a negative screening test (Fig. 6a), and the likelihood of a positive symptomatic test 1-7 days after a negative screening test was reduced by approximately 51% (52 vs 106 students) compared with days 8-14. This reduction corresponds to the successful detection of presymptomatic cases. It further suggests that weekly asymptomatic screening will detect approximately half of all students who ultimately develop cardinal symptoms of COVID-19 whilst still presymptomatic, in agreement with the presymptomatic infectious period observed in our study (mean 3.6 days).

Finally, to quantify the potential of different screening strategies to reduce SARS-CoV-2 transmission, we parameterised a discrete-timestep forward-simulation SEAIR network model using key real-world metadata derived from our study (Supplementary Table 8). These metadata included: distribution of household sizes (Fig. 3a); within and between household secondary attack rates (Extended Data Fig. 5); proportion of asymptomatic
infections (Fig. 5b); and duration of presymptomatic infectious period (Extended Data Fig. 3c). In all simulations, we assumed that symptomatic individuals self-isolate with their household from the day of symptom onset. We projected new cases over time (Fig. 6b,c), and compared the effect of each screening strategies on the basic reproduction number (R0) and the number of students quarantined (Fig. 6c,d).

Weekly screening of all students (as implemented during weeks 8-9 of the programme) resulted in a 31% reduction in R0 from a median of 1.78 (95% CIs 1.37-2.23) to a median of 1.22 (95% CIs 0.82-1.62), with screening of half the students from each testing pool each week (as implemented during weeks 3-7 of the programme) intermediate in effect (median R0 1.45, 95% CIs – 1.02-1.88). Similar effects on transmission were observed in all sensitivity analyses (Extended Data Fig. 6), and the number of students quarantined was reduced, rather than increased, by more frequent screening (Fig. 6c,d). These simulations therefore support the efficacy of the asymptomatic screening programme for the control SARS-CoV-2 transmission in the university.
**Discussion**

To our knowledge, this is the most comprehensive epidemiological evaluation to date of regular, large-scale asymptomatic screening for COVID-19 in a university or any other defined residential setting. The duration of SARS-CoV-2 RNA shedding from the upper respiratory tract is typically 2-3 weeks\(^{56,57}\). Even allowing for the possibility of false negative PCR tests\(^{58,59}\), the combination of regular asymptomatic screening with readily accessible symptomatic testing is therefore likely to have detected almost all cases of SARS-CoV-2 infection in our study population, which could then be mapped to the known household structure.

Amongst all students with confirmed SARS-CoV-2 infection, the proportion of asymptomatic students (20%) was comparable with overall estimates from other studies\(^7,8\), but lower than predicted given the age range of study participants. This may reflect the retrospective ascertainment of symptoms, including subjective loss or change to the sense of smell or taste (which may be more frequent in young adults, and mild disease)\(^{60,61}\). Conversely, the proportion of infected individuals who ultimately developed symptoms identified by asymptomatic screening (25%) was greater than predicted, given that weekly screening of all participating students was only achieved by week 8. Nonetheless, this proportion is in keeping with the observed reduction in likelihood of symptomatic disease in the week after a negative screening test (51%), as well as the observed presymptomatic infectious period (3.6 days).

Consistent with the known peak in SARS-CoV-2 viral load early in infection (on or just before symptom onset), CT values in presymptomatic students were low, and comparable to CT values in symptomatic students\(^{53}\). In agreement with this, the observed secondary attack rate amongst household contacts was significantly greater for presymptomatic and symptomatic index cases, than index cases who never developed symptoms. Taken together, these observations support our classification of presymptomatic and asymptomatic
students, and imply that the infectiousness of students who never develop symptoms is significantly reduced. They are consistent with data from another recent study\textsuperscript{62}, and suggest that screening programmes should be designed to target individuals with presymptomatic infection, for example by maximising testing frequency.

Quantifying the efficacy of our screening programme by comparison with different universities is not possible, because of the variable and multi-faceted infection prevention and control measures deployed by different institutions. Nonetheless, we are able to present direct evidence for the efficacy of regular asymptomatic screening: first, enhanced case ascertainment, including students with presymptomatic as well as asymptomatic infection (39\% of all cases); second, the pre-emptive quarantine of students with symptomatic COVID-19 infection, because of a positive household contact detected by the screening programme (7\% of all cases); and third, the reduction in risk of symptomatic COVID-19 in the period following a negative screening test result (corresponding to the successful detection of presymptomatic cases). This direct evidence is strongly supported by indirect evidence from our model-based analysis, parameterised empirically using data from our study. Genomic epidemiology and contact tracing data from our student cohort are presented in a separate report, and confirm the impact of asymptomatic screening and other infection control policies in limiting introductions of SARS-CoV-2 to the university, containing viral spread within student accommodation, and restricting transmission between the university and the surrounding community\textsuperscript{51}.

Our screening programme was deployed within 8 weeks of inception without pre-existing clinical, information technology or logistics infrastructure. Swab pooling from up to 10 students is compatible with standard nasopharyngeal swabs and sample tubes, and ensures that samples can be analysed without significant changes to laboratory workflow. Taking into account variation in household size and the requirement for individual confirmatory testing, this approach increases effective PCR testing capacity roughly three- to five-fold for SARS-CoV-2 prevalences up to 2\%. It is particularly well-suited to residential settings, where
testing pools correspond with units of household quarantine e.g. universities, long-term care facilities, prisons, workers housed in dormitories, or private households. Nonetheless, it may also be applied in other settings where individuals are grouped together, such as schools or workplaces\textsuperscript{63}.

Our data suggest that voluntary participation and the use of nose and throat swabs (rather than less invasive sampling, such as saliva) are not \textit{per se} barriers to widespread uptake amongst students, and likely other populations. Other factors which may have enhanced participation in our programme include: ease of access and convenience of home testing, a proactive communication strategy, engagement with student representatives, the collegiate university structure, the use of household-based pooled screening, and careful attention to ethical and legal issues (e.g. personal data governance). Many of the approaches taken in the development, operation and evaluation of our programme have been supported by a recent ethical review of asymptomatic COVID-19 screening programmes in higher education settings\textsuperscript{64}.

Criticisms of mass testing for COVID-19 typically have typically focussed on the potential for false positives (leading to unnecessary periods of quarantine) and false negatives (leading to missed cases)\textsuperscript{20,21}. Our two-step testing strategy (including individual confirmatory PCR tests) mitigates the chance of false positive tests leading to prolonged periods of unnecessary individual or household quarantine. Moreover, swab pooling effectively increases the prevalence of true positive samples. In theory, the high sensitivity of PCR tests could result in the detection of individuals with low levels of viral RNA late in their course of infection, even when they are no longer infectious\textsuperscript{65}. Whilst this is a valid concern for one-off mass testing, it is not relevant for programmes based on regular, frequent screening. Conversely, the high sensitivity of PCR tests ensures that the risk of false negatives is minimised. This may be particularly important for the detection of breakthrough infections following vaccination, when viral loads may be reduced\textsuperscript{66}. At the same time, PCR testing
facilitates the reliable reporting of cases from laboratories to public health systems, and the provision of samples for viral sequencing to support surveillance and transmission studies\textsuperscript{51}. LFTs offer a relatively cheap alternative to laboratory-based testing, typically return results in only 30 minutes, and can be deployed rapidly at scale with minimal fixed infrastructure. They have therefore been used in the UK and elsewhere for regular and one-off mass testing in different settings\textsuperscript{19,67}. The false positive rate of these tests is comparable to the operational false positive rate observed in our programme, and may be mitigated by confirmatory PCR testing\textsuperscript{36}. When LFTs are conducted by trained staff and volunteers, however, sensitivity for SARS-CoV-2 detection is roughly 50\% compared with PCR tests\textsuperscript{58,68,69}, and their performance when used for home testing is not well documented. In general, the false negative rate is lower for individuals with high viral loads, who are likely to be most infectious\textsuperscript{65}. Nonetheless, the difference in secondary attack rates amongst household contacts of index cases with high or low CT values observed in our study suggests that this gradient in infectiousness may be modest, consistent with variability in serial sampling\textsuperscript{53,70}, laboratory data on recovery of infectious virus\textsuperscript{55}, and analysis of contact tracing data\textsuperscript{71}. Notwithstanding the rapid turnaround of LFTs, and asymmetric profile of SARS-CoV-2 viral shedding, it is therefore likely that adherence to twice weekly mass testing using home LFTs will be required to match or even exceed the benefits of weekly PCR-based screening\textsuperscript{54}. The development of SARS-CoV-2 variants with mutations enhancing transmissibility and enabling at least partial escape from vaccine-induced and natural immunity\textsuperscript{72-74}, together with the limited availability of vaccination on a global scale\textsuperscript{75}, suggest that non-pharmaceutical interventions to control the transmission of SARS-CoV-2 will be required for some time yet. Our study was conducted in the UK before the widespread circulation of B.1.1.7 lineage viruses\textsuperscript{76}. Although the relative efficacy of mass testing will likely be retained for different lineages, the precise impact may be subject to changes in transmission dynamics associated with different variants, such as the presymptomatic infectious period. Compared with social distancing and lockdown measures, the social and economic
consequences of mass testing are much less severe. Taken together, our data strongly support the role of regular asymptomatic screening as an effective means to control SARS-CoV-2 transmission, in universities as well as other settings.
Methods

Ethics statement

Ethical approval for this study was granted by the University of Cambridge Human Biology Research Ethics Committee (HBREC.2020.35). Participation was voluntary, with no coercion or incentives. Informed consent was obtained from all participants, who were free to withdraw from the programme at any time. All data was processed fairly, lawfully and transparently, in accordance with the EU General Data Protection Regulation (GDPR) 2016/679 and the UK Data Protection Act 2018. The student information sheet, privacy notice, consent form, protocols for sample collection, additional information and answers to frequently asked questions are available on the programme website (https://www.cam.ac.uk/coronavirus/stay-safe-cambridge-uni/asymptomatic-covid-19-screening-programme).

Study design and participants

The Asymptomatic COVID-19 Screening Programme is a weekly screening programme for SARS-CoV-2 infection for students at the University of Cambridge. During autumn (Michaelmas) term 2020, screening took place over 9 weeks from October 5, 2020 to December 6, 2020. Students were screened using swab pooling and two-step confirmatory PCR testing (Fig. 1). Additional tests were provided by the university for all students and staff with symptoms of possible COVID-19.

The University of Cambridge comprises 31 colleges. All undergraduate and postgraduate students resident in university (college) accommodation were eligible for participation in the programme, along with resident students of the Cambridge Theological Federation (weeks 1-9). To accord with UK government guidance on student testing prior to the Christmas vacation 2020, eligibility was extended to include students resident in private
accommodation on November 30, 2020 (week 9). Results from these students will be described in a separate report.

Eligible students were invited to participate by email. The programme was initially announced to students on September 9, 2020 by email communication. Formal email invitations were sent to all eligible students on September 26, 2020 and weekly thereafter. Each email contained links to the programme website, which included the consent form, student information sheet and privacy notice. Additional communications were sent via email from individual colleges and promoted on social media by student representatives.

The screening programme was introduced in phases, to ensure that all aspects of the system operated effectively and had capacity to manage greater numbers. Initially, two students from each testing pool were randomly selected to contribute swabs for pooled sample collection each week (weeks 1-2). Then, half of the students in each testing pool were asked to contribute swabs each week (weeks 3-7, ensuring every student was tested every two weeks). Then, all students in each testing pool were asked to contribute swabs each week (weeks 8-9, ensuring every student was tested weekly).

At any point in the term, students were excluded from pooled sample collection if: 1) they had tested positive for SARS-CoV-2 within the preceding 8 weeks; 2) they had symptoms of possible COVID-19 or were awaiting an individual symptomatic test result; 3) they were self-isolating for any other reason, for example due to contact with a confirmed or suspected COVID-19 case or international travel from a high prevalence area; or 4) for weeks 1-7 only, they had not been selected to participate (see above).

Asymptomatic screening programme

Students living in university accommodation with high-contact shared facilities such as a bathroom, toilet or kitchen area are considered to share the same household. For the purposes of screening, some households were split or merged with neighbouring
households to ensure testing pools of 6-10 students. Household and testing pool membership were determined by each college prior to the start of term (based on guidance provided by the university and the screening programme) and recorded in a central database that could be updated at any time. This database provided a single reference point used for test kit production and result notification (see below).

Bespoke screening kits were prepared within the university. Each kit was labelled with the names of students belonging to a particular testing pool, and contained packaging and cleaning materials, a number of nasopharyngeal flocked swabs (A04-96000P, Trafalgar Scientific, or MSC-96000, Sterilab) corresponding to the number of students within that pool, and one tube of viral transport medium (HiViral Transport Medium, Trafalgar Scientific) labelled only with a pseudonymised code associated with that testing pool. Screening kits were delivered to each college weekly for distribution to testing pools. Each college was assigned a testing day, with all students from that college invited to participate on the same day. Drop-off points were allocated in every college, with same-day sample collection and delivery to the testing facility ensuring the availability of results within 24 hours. Screening took place Mon-Thurs, with individual confirmatory tests (see below) Tues-Fri.

A detailed swabbing protocol is available from the programme website. In brief, combined nose (anterior nasal) and throat swabs were obtained by self-administration in the students’ own accommodation. Swabs from all students in a testing pool were immediately pooled in the same tube of viral transport medium. Each tube had capacity for up to 10 swabs, which therefore determined the maximum number of students in a testing pool. To confirm the number of students participating each week, one member of each testing pool was asked to complete a simple electronic form at the time of pooled sample collection, indicating the number of swabs present in the sample tube (“swab count”).

All samples were tested by PCR in the established University of Cambridge/AstraZeneca Cambridge COVID-19 Testing Centre (see below). Pseudonymised results were transferred to the secure data hosting service (SDHS) provided by the University of Cambridge (School
of Clinical Medicine), where they were associated with members of each testing pool.

Results were typically communicated to students by text message, and shared with colleges and the university COVID-19 Operations Centre via the SDHS. In addition, results of individual confirmatory tests (see below) were reported to Public Health England using the Second Generation Surveillance System (SGSS).

Students contributing swabs to positive pooled screening tests were instructed to self-isolate, and either invited for same-day individual confirmatory tests at a University of Cambridge/Cambridge University Hospitals NHS Foundation Trust (CUHNFT) testing facility in the city centre (weeks 1-6, see below) or provided with a test kit for individual self-swabbing in their own accommodation (weeks 7-9). Students with positive individual confirmatory tests were treated in the same manner as students with positive results from existing University of Cambridge or NHS pathways for symptomatic testing. In all cases, isolation of cases and contacts was in accordance with UK national guidance, instructions from NHS Test and Trace and the local public health teams.

In brief, cases were required to self-isolate for 10 days from their date of symptom onset (or test date, if asymptomatic). Households of confirmed cases were quarantined for 14 days. If a positive student could not be identified by individual testing, the CT value of the positive pooled screening test was reviewed (Fig. 2): if >36, the pooled screening test was considered to be an operational false positive; if ≤36, a further round of individual tests was performed, to minimise the risk of a false negative individual test result. If all individual confirmatory tests were negative, students were released from self-isolation/household quarantine. This approach is concordant with NHS guidelines for individual PCR tests which are positive at the limit of detection.
**Symptomatic testing**

In addition to asymptomatic screening, the University of Cambridge (in partnership with CUHNFT) also provided a dedicated testing service for all students and staff with cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia). Combined nose and throat swabs were obtained by self-administration at a university testing facility in the city centre, Mon-Fri during the study period. Alternative testing via NHS pathways was also available to all students.

Individual results from the university’s symptomatic testing pathway were reported via the electronic medical record at CUHNFT (Epic Systems, Verona, WI, USA). Ascertainment of students testing positive by NHS pathways was derived from self-reporting to the university COVID-19 Operations Centre, completion of the university’s COVID-19 monitoring form, or information provided by the Local Authority or Public Health England as part of investigations into transmission networks during the study period.

**Other control measures**

A detailed description of additional COVID-19 reduction measures implemented by the University of Cambridge, including social distancing and the use of face coverings, is provided in a separate report.

**Telephone survey**

To investigate the presence, nature and timing of symptoms experienced by students with SARS-CoV-2 infection identified by asymptomatic screening, we conducted a retrospective telephone survey of all students with positive individual confirmatory tests. Students were contacted between November 24, 2020 and December 17, 2020 by clinical research nurses or members of the university COVID-19 Operations Centre (contact tracing team), and
assessed using an adapted pro forma employed for screening symptomatic staff members at CUHNFT. In brief, students were asked if they developed cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia) or other minor symptoms (such as sore throat, headache, myalgia, fatigue, breathlessness or gastrointestinal symptoms) before their positive test result, or during their period of self-isolation.

To estimate the proportions of all students identified by asymptomatic screening who experienced symptoms, the sample of students responding to the telephone survey was assumed to be representative and independent of the manifestation of symptoms. Binomial confidence intervals were calculated using the Clopper-Pearson interval.

**Laboratory procedures and validation of swab pooling**

All samples were tested by PCR in the University of Cambridge/AstraZeneca COVID-19 Testing Centre (Anne McLaren Building, Cambridge Biomedical Campus), part of the UK Lighthouse Labs Network, in accordance with existing procedures for clinical samples. In brief, RNA was extracted from heat-inactivated samples using the Beckman RNA Advance Viral Kit, then tested by RT-qPCR for the presence of the orf1ab gene of SARS-CoV-2 using the Genesig Real Time PCR COVID-19 High Throughput (HT) Assay Kit.

To investigate the impact of swab pooling on SARS-CoV-2 detection, swabs and residual viral transport medium (VTM) from negative samples were used to reconstitute mock samples containing known concentrations of SARS-CoV-2, in the presence of either a single swab (individual samples) or 5-8 swabs (pooled samples). VTM volumes were normalised to 1 mL, spiked with serial dilutions of SARS CoV-2 (250,000 to 125 digital copies/mL) using the Qnostics SARS Cov-2 Analytical Q Panel (whole, inactivated SARS-CoV-2 virus), then incubated for 1.5 h and tested using existing procedures for clinical samples.
Where indicated, distributions of CT values of pooled or individual tests were compared using paired or unpaired 2 sample 2-tailed $t$-tests (comparison of 2 distributions) or ordinary one-way ANOVA (comparison of 3 or more distributions), as specified in the figure legends.

**Other statistical analyses**

All pooled screening, individual confirmatory and symptomatic test results were linked with participating students, households and testing pools in a single pseudonymised database. Participation rates were estimated by comparing the number of samples received and reported by the testing facility with the mean number of students participating per testing pool, as determined by “swab counts” (see above). Student characteristics associated with programme participation were assessed using unpaired 2 sample 2-tailed $t$-tests (continuous variables) or chi-square tests (categorical variables), as specified in the table legend.

To evaluate the secondary attack rate amongst household contacts, we first identified all index cases (the first case diagnosed in each household). For each index case, we then compared the number of household contacts testing positive within 14 days of the index, compared with the total number of household contacts. Results were stratified according to the characteristics of the index case (testing route, symptoms and CT values of their individual sample). Where multiple index cases were identified in the same household on the same day, they were either reported as a separate “mixed” category or the household was excluded from analysis. Secondary attack rates were compared using Fisher’s exact test. Confidence intervals for the relative risk estimates were calculated using the Koopman asymptotic score method. To assess the relationship between the CT value of each index case and the probability of household contacts testing positive within 14 days, fitted probabilities were obtained from a logistic regression model.

To calculate the presymptomatic infectious period in our study population, a positive PCR test was taken as proxy for infectiousness. Data were analysed from 68 students identified
by asymptomatic screening, who reported cardinal symptoms of COVID-19 at some time during their infection (presymptomatic students). Provided the screening interval is longer than the presymptomatic infectious period, presymptomatic students will be sampled at random during this period, and (on average) halfway through. We therefore calculated the mean presymptomatic infectious period as twice the mean observed time interval between a positive pooled screening test and symptom onset.

To estimate the number of students with presymptomatic SARS-CoV-2 infection detected by asymptomatic screening, we reasoned that successful identification of these cases should correspondingly reduce the number of students identified by symptomatic testing in the period after a negative screening test, in accordance with the duration of the presymptomatic infectious period. We therefore analysed data from 158 students with SARS-CoV-2 infection identified by symptomatic testing during weeks 3-7 of the programme. Over this period, half the students from each testing pool were screened each week, corresponding to a screening interval of 14 days for individual participating students. For each student, we assessed the time interval between their positive symptomatic test and their most recent negative screening test. We then compared the number of students testing positive 1-7 days or 8-14 days after a negative screening test. We selected these periods because: 1) we observed a mean presymptomatic infectious period ≤7 days in most students (mean 3.6 days); 2) we wished to estimate the proportion of students who ultimately develop cardinal symptoms of COVID-19 likely to be detected whilst still presymptomatic in the presence of weekly asymptomatic screening (that is, every 7 days); and 3) the screening interval of 14 days sets an upper bound.

To predict the total number of pooled screening and individual confirmatory tests (testing capacity) required to screen every 1,000 participating students in the presence of different testing pool sizes and prevalences of SARS-CoV-2 infection, we assumed that: 1) 1/360 pooled screening tests are false positives (equal to the observed rate of operational false positives); 2) test sensitivity is 100%; 3) testing pool sizes are homogenous; and 4) positive
students are evenly distributed throughout the population screened. For each week of screening, predicted testing capacity was compared with the observed mean testing pool size (swab count) and numbers of pooled screening and individual confirmatory tests conducted.

Associations between testing positive for SARS-CoV-2 (by any testing route at any time during the study) and individual risk factors were examined by logistic regression and expressed as odds ratios with 95% confidence intervals and associated $P$ values. All variables were treated as categorical, with the exception of household size, which was treated as continuous.

A multivariable logistic regression analysis was fitted with six covariates, namely gender, ethnicity, residence (out of term time), year group, course and household size. All variables were significant, so were retained in the final model. Pairwise interaction terms were also considered, but did not lead to an improved model. To assess the goodness-of-fit, we applied two tests: the classical Hosmer-Lemeshow test and the more recent Generalised Residual Prediction (GRP) test. The $P$ value from the Hosmer-Lemeshow test was 0.44, while the GRP test $P$ value was 0.002. While the latter suggests that there is potentially some scope for improved predictions using nonparametric techniques such as random forests, the much simpler logistic regression model has great advantages in terms of interpretability and was therefore our preferred model.

Data were initially compiled in Azure (Microsoft) and Excel 2013 (Microsoft) and analysed in STATA 14.2 (College Station, TX, USA) and GraphPad Prism version 9.0.0 (GraphPad Software, CA, USA). Single variable and multivariable analyses were performed in R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) using the glm command. The Hosmer-Lemeshow test is available in the package 'generalhoslem', while the Generalised Residual Prediction test is available in the package 'GRPtests'.
Model-based analysis

To further evaluate the impact of different testing strategies on SARS-CoV-2 cases and numbers of students in isolation over the term, we developed a model parameterised primarily from findings in our study (Supplementary Table 8). This is based on an existing model specifically created to provide insights into the impact of SARS-CoV-2 in UK higher education settings, and developed by a working group from multiple institutions following meetings as part of the Isaac Newton Institute Infectious Dynamics of Pandemics Research Programme. It is an adaptation of the layered network model of student contacts, with one layer for household contacts and another for non-household contacts, and is ultimately based on code produced by Sara Jakubiak available at https://github.com/SaraJakubiak/covid19-caribbean-educational-model. The code used for this manuscript can be found at: https://github.com/magicicada/covid19-caribbean-educational-model/tree/manuscript_cambs_testing_scheme.

Students are allocated to households according to a specified distribution of household sizes, and allocated out-of-household contacts in groups according to another specified distribution of activity groups intended to simulate group teaching and social activities. Both household and non-household contacts are produced in groups, and all individuals within the group are pairwise in contact within the network. The disease model is a stochastic SEAIR simple compartmental model in which infectious (I compartment) individuals may be symptomatic or asymptomatic, and presymptomatic (A compartment) individuals are also infectious. Compartments for isolating individuals are also included. Movement between model compartments is by fixed daily probability for each individual. No severe illness or hospitalisation are modelled. For the main results, 2500 simulations were run for each testing regime: 50 different network instantiations with 50 separate simulations on each. We model several asymptomatic testing regimes structured at the household level; in all testing regimes symptomatic individuals are assumed to immediately seek testing. When a positive case is detected, the entire household of the case isolates, as well as a parameter-
specified proportion of the test-positive’s out-of-household contacts. When a household is isolating, infection can occur within the household, but not outside of the household.

While a full analysis of the sensitivity of this model to all parameters is not feasible here, given the large number of variables, we report a basic univariate sensitivity analysis on parameters: 1) to which we judge the model likely to be most sensitive; 2) about which we are most uncertain; and 3) for which the structure of the model allows us to straightforwardly adjust. For each of these, we show results of a model run with the parameter decreased by 15% and increased by 15%. For each parameter setting and testing regime combination, we ran a total of 600 model runs: 20 different network instantiations with 30 separate simulations on each.

While a multivariate analysis would add certainty, this would require a very large number of additional experiments and is beyond the scope of this work. We caution that a number of assumptions that are not straightforwardly adjusted within this model framework are also likely to have an important quantitative (though not qualitative) impact on the outcome of the model, in particular assumptions about perfect adherence to testing and isolation procedures. Evaluating the impact of varying adherence is beyond the scope of this particular investigation.

Role of the funding source

The programme is primarily funded, overseen and implemented by the University of Cambridge, its associated Colleges and the Cambridge Theological Federation. The Cambridge COVID-19 testing facility represents a collaboration between the University of Cambridge, AstraZeneca and Charles River Laboratories, funded by the Department of Health and Social Care. AstraZeneca and Charles River Laboratories reviewed the data from the study and the final manuscript before submission, but the academic authors retained editorial control. Other funders had no role in the study design, data collection, data
analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data availability

Weekly reports are available from the programme website (https://www.cam.ac.uk/coronavirus/stay-safe-cambridge-uni/asymptomatic-covid-19-screening-programme), together with data from the University of Cambridge symptomatic testing programme (https://www.cam.ac.uk/coronavirus/stay-safe-cambridge-uni/data-from-covid-19-testing-service). Reasonable requests for additional de-identified data will be facilitated by the authors, provided they are in accordance with the terms of consent and ethical approval, and relevant legal and regulatory requirements (such as, relating to data protection and privacy).

Code availability

The code used for the model-based analysis included in this manuscript can be found at: https://github.com/magicicada/covid19-caribbean-educational-model/tree/manuscript_cambs_testing_scheme.

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Author contributions

NM designed the screening programme, with input from PL, MW, BW, PM, DM, RH, KL, VS and JH. NM is lead PI for the screening programme. BW is clinical lead for the screening programme. PM chairs the oversight committee for the screening programme. DM is logistics lead for the screening programme. MW is lead PI for the symptomatic testing programme. SF is nursing lead for the screening programme. RH led the COVID-19 testing facility. KL advised on legal and regulatory compliance. VS and JH developed IT systems. MM led the telephone symptoms survey. All authors assisted with programme implementation and data collection. BW cleaned the data. BW, NM and JE analysed the data. JE performed modelling. RS advised on statistical analysis. NM and BW drafted the manuscript, with input from JE and editing and approval from all authors.
Competing interests

RH and SR are employees of AstraZeneca AB. RC is an employee of Charles River Laboratories. All other authors declare no competing interests relevant to the submitted work.
Fig. 1: Study cohort.

Participation in University of Cambridge SARS-CoV-2 asymptomatic screening programme and symptomatic testing by students living in university accommodation from October 5, 2020 to December 5, 2020. *Includes 19 repeat individual confirmatory tests. †Excludes symptomatic tests conducted by NHS pathways.
Pools of students, generally corresponding with student households, were screened weekly. In the event of a positive pooled screening test, follow-up individual confirmatory tests were used to identify the infected student or students. If all individual confirmatory tests were negative, students were released from self-isolation. CT, cycle threshold. Operational false positive, a positive pooled screening test followed by negative individual confirmatory tests from all students in the testing pool.
**Fig. 3: Student participation and implementation of swab pooling.**

- **a-b**, Distribution of (a) household size and (b) testing pool size for eligible students in university accommodation.  
- **c-d**, Weekly participation rates during autumn term by household (c) and individual student (d). The number of eligible (red circles), enrolled (blue squares) and screened (black triangles) students and households is shown during the phased implementation of the screening programme (indicated by the shaded areas in each plot).
Some eligible students were excluded from screening each week because of a recent positive test for SARS-CoV-2, symptoms of possible COVID-19, or a requirement to self-isolate. Predicted total number of pooled screening and individual confirmatory tests required to screen 1,000 students in the presence of different testing pool sizes and SARS-CoV-2 prevalences (grey lines, 0.1-10%). Crosses indicate the actual mean pool sizes and tests utilised at the indicated time points. In the absence of swab pooling (equivalent to a mean pool size of 1), 1,000 tests would be required.
**Fig. 4:** Clinical validation of swab pooling.

**a,** SARS-CoV-2 cycle threshold (CT) values for pooled screening tests, comparing 203 pooled samples resulting in positive individual confirmatory tests with 47 operational false positives (no positive individual confirmatory tests). Centre line indicates median, boxes indicate interquartile range, whiskers indicate range. Distributions were compared using an unpaired 2-tailed \( t \)-test. **b,** Comparison of CT values between positive paired pooled screening and individual confirmatory tests. Where a positive pooled screening test resulted in \( >1 \) positive individual confirmatory test, the lowest individual CT value is plotted. **c,** Comparison of CT values between positive paired pooled screening and individual confirmatory tests, stratified by number of swabs in the pooled sample. Distributions were compared using paired 2-tailed \( t \)-tests. ns, not significant, \( P > 0.05 \).
**Fig. 5.** Case ascertainment by asymptomatic screening and symptomatic testing.

**a,** Epidemic curve of weekly SARS-CoV-2 cases amongst participating students identified by asymptomatic screening (blue), symptomatic testing (red) or other testing routes (grey). The steep decline in cases coinciding with the second UK national lockdown is indicated by the shaded area.

**b,** Classification of SARS-CoV-2 cases amongst participating students according to testing pathway (inner doughnut) and symptoms (outer doughnut). Inner doughnut: same colours as (a). Outer doughnut: red, cardinal symptoms of SARS-CoV-2 (fever, cough and/or...
anosmia/ageusia) experienced at some time during infection; blue, no symptoms or minor symptoms only (no cardinal symptoms). *Cases where potential for onward transmission was interrupted by asymptomatic screening are indicated by patterned areas. †Estimated numbers based on retrospective telephone survey (sampling 140/256 students).
Fig. 6. Efficacy of asymptomatic screening.

a, Time between positive symptomatic test and most recent negative screening test for 158 students with symptomatic SARS-CoV-2 infection identified during weeks 3 to 7. Half of each testing pool was screened on alternating weeks over this period, corresponding to a screening interval of 14 days for individual students. b-d, Model outputs indicating numbers of new SARS-CoV-2 cases (a), cumulative SARS-CoV-2 cases (b) and students in household isolation (c) under different testing regimens. Solid lines, median values; shaded areas, 95% confidence intervals.
Extended Data Fig. 1: Impact of communications on study participation.

Daily number of students consenting to participate in asymptomatic screening programme.

Key communications are highlighted. Where students consented more than once, only their first consent is included.
Extended Data Fig. 2: Technical validation of swab pooling.

Detection of SARS CoV-2 standards in reconstituted individual (1 swab) or pooled (5-8 swabs) samples. Experiment conducted in triplicate, with individual data points, mean and standard deviation shown for each SARS-CoV-2 concentration. dC/mL, digital copies/mL. CT value, cycle threshold. Solid lines, non-linear regression lines; shaded areas, 95% confidence intervals.
Extended Data Fig. 3: Symptoms identified by telephone survey.

a, Proportion of students identified by asymptomatic screening who went on to develop cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia) at some time during infection (presymptomatic, red), those who experienced no symptoms at all (asymptomatic, pale blue), and those who reported only minor symptoms (minor symptoms, dark blue). Data are shown for 140 students who responded to the retrospective telephone survey. b, Frequency of individual symptoms reported by 68 presymptomatic students from (a). c, Time interval between positive screening test and onset of cardinal symptoms of COVID-19 for 68 presymptomatic students from (a). Since presymptomatic students may be sampled at any time during their presymptomatic infectious period, and (on average) halfway through, the mean presymptomatic infectious period is expected to be twice the mean observed time interval.
Extended Data Fig. 4: Comparison of CT values by testing pathway and symptoms.

a, SARS-CoV-2 cycle threshold (CT) values for positive university symptomatic tests, compared with positive individual confirmatory tests from the asymptomatic screening programme. b, Comparison of CT values for students identified by asymptomatic screening who went on to develop cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia) at some time during infection (presymptomatic, red), those who experienced no symptoms at all (asymptomatic, dark blue), and those who reported only minor symptoms (minor symptoms, pale blue). Data are shown for 140 students who responded to the retrospective telephone survey. Centre line indicates median, boxes indicate interquartile range, whiskers indicate range. P values were calculated for pairwise comparisons using unpaired two-tailed t-tests (a) and ordinary one-way ANOVA (b).
Extended Data Fig. 5: Secondary household attack rates.

a, Total number (left panel) and proportion (right panel) of household contacts of students with confirmed SARS-CoV-2 infection who tested positive for SARS-CoV-2 within 2 weeks of the index case (any testing pathway). Total household contacts (orange plus blue bars) and household contacts testing positive for SARS-CoV-2 (orange bars) are shown. Data are
stratified by testing pathway of the index cases. Other, students identified from notifications
to Public Health England. Mixed, multiple students from same household identified on the
same index day, using different testing pathways. The proportion of household contacts who
tested positive was significantly different for asymptomatic (6.9%) versus symptomatic
(12.0%) index cases ($P = 0.0003$, Fisher’s exact test). b, As for (a), but results are shown for
140 index cases identified by asymptomatic screening who responded to the retrospective
telephone survey. Data are stratified according to whether index cases went on to develop
cardinal symptoms of COVID-19 (fever, cough, and/or anosmia/ageusia) at some time
during infection (presymptomatic), or remained asymptomatic/reported only minor symptoms
(asymptomatic or minor symptoms). The proportion of household contacts who tested
positive was significantly different for contacts of presymptomatic index cases (15.2%)
versus contacts of index cases who remained asymptomatic/reported only minor symptoms
(2.3%) ($P < 0.0001$, Fisher’s exact test). c, Fitted probability of a household contact testing
positive within 14 days of an index case testing positive, as a function of the cycle threshold
(CT) value of the index case (solid line). The estimated regression coefficient corresponding
to the index case CT value was -0.06239. Testing whether this coefficient was zero yielded
a $P < 0.001$. Positive and negative household contacts are plotted as crosses at the top and
bottom of the plot, respectively. Data are shown for 1,595 household contacts, excluding
households where multiple students were identified on the same index day. d, As for (a), but
data are stratified according to CT value of the index case. Where multiple students from the
same household were identified on the same index day, data are shown separately (multiple
index cases).
Extended Data Fig. 6: Sensitivity analyses.

Sensitivity analyses for model outputs indicating numbers of cumulative SARS-CoV-2 cases under different testing regimens. In each case, the indicated parameter is decreased or increased by 15%. No asymptomatic testing, no asymptomatic screening; weekly half-household testing, half of each testing pool screened on alternating weeks; weekly household testing, whole testing pool screened each week.
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### Supplementary Table 1. Characteristics of study population.

| Characteristic                        | Eligible | Participating | Not-participating | P value |
|---------------------------------------|----------|---------------|-------------------|---------|
| N                                     | 15,561   | 12,781        | 2,780             |         |
| **Sex**                               |          |               |                   | <0.001  |
| Male                                  | 8,060 (51.8%) | 6,504 (50.9%) | 1,556 (56.0%)     |         |
| Female                                | 7,213 (46.4%) | 6,125 (47.9%) | 1,088 (39.1%)     |         |
| Other/unknown                         | 288 (1.9%) | 152 (1.2%)    | 136 (4.9%)        |         |
| **Age, years, median (IQR, range)**   |          |               |                   | <0.001  |
| Eligible                              | 20.6 (19.4-22.6, 16.4-71.7) | 20.5 (19.3-22.3, 16.4-58.1) | 21.3 (19.8-24.3, 17.4-71.7) |         |
| Participating                         |          |               |                   |         |
| Not-participating                     |          |               |                   |         |
| **Ethnicity**                         |          |               |                   | <0.001  |
| White                                 | 9,453 (60.7%) | 8,168 (63.9%) | 1,285 (46.2%)     |         |
| Black, Asian and minority ethnic      | 5,302 (34.1%) | 4,097 (32.1%) | 1,205 (43.3%)     |         |
| Refused/unknown                       | 806 (5.2%) | 516 (4.0%)    | 290 (10.4%)       |         |
| **Residency**                         |          |               |                   | <0.001  |
| UK                                    | 9,870 (63.4%) | 8,504 (66.5%) | 1,366 (49.1%)     |         |
| International                         | 5,496 (35.3%) | 4,205 (32.9%) | 1,291 (46.4%)     |         |
| Unknown                               | 195 (1.3%) | 72 (0.6%)     | 123 (4.4%)        |         |
| **Year of study**                     |          |               |                   | <0.001  |
| 1st                                   | 3,788 (24.3%) | 3,336 (26.1%) | 452 (5.5%)        |         |
| 2nd                                   | 3,239 (20.8%) | 2,673 (20.9%) | 566 (20.4%)       |         |
| 3rd                                   | 2,832 (18.2%) | 2,434 (19.0%) | 398 (14.3%)       |         |
| 4th (or above)                        | 997 (6.4%)  | 844 (6.6%)    | 153 (5.5%)        |         |
| Postgraduate                          | 4,369 (28.1%) | 3,366 (26.3%) | 1,003 (36.0%)     |         |
| Missing                               | 336 (2.2%)  | 126 (1.0%)    | 210 (7.5%)        |         |
| **Stage**                             |          |               |                   | <0.001  |
| Undergraduate                         | 10,857 (69.8%) | 9,288 (72.7%) | 1,569 (56.4%)     |         |
| Postgraduate                          | 4,369 (28.1%) | 3,366 (26.3%) | 1,001 (36.0%)     |         |
| Missing                               | 335 (2.2%)  | 125 (1.0%)    | 210 (7.5%)        |         |
| **Course***                           |          |               |                   | <0.001  |
| Undergraduate arts and humanities     | 5,490 (35.3%) | 4,553 (35.6%) | 937 (33.7%)       |         |
| Undergraduate science and technology  | 5,454 (35.1%) | 4,806 (37.6%) | 648 (23.3%)       |         |
| Postgraduate vocational               | 466 (3.0%)  | 343 (2.7%)    | 123 (4.4%)        |         |
| Postgraduate (other)                  | 3,815 (24.5%) | 2,953 (23.1%) | 862 (31.0%)       |         |
| Unknown                               | 336 (2.2%)  | 126 (1.0%)    | 210 (7.6%)        |         |
| **Household size**                    |          |               |                   | <0.001  |
| 1 person                              | 472 (3.0%)  | 290 (2.3%)    | 172 (6.2%)        |         |
| 2 to 5 people                         | 4,536 (29.1%) | 3,703 (29.0%) | 832 (29.9%)       |         |
| 6 to 10 people                        | 9,228 (59.3%) | 7,686 (60.2%) | 1,540 (55.4%)     |         |
| >10 people                            | 1,326 (8.5%) | 1,091 (8.5%)  | 235 (8.5%)        |         |

Student characteristics associated with programme participation were assessed by comparing participating and non-participating students using unpaired 2 sample 2 tailed t-tests (continuous variables) or chi-square tests (categorical variables).

*Courses are grouped as: undergraduate arts and humanities (undergraduate students in the School of Arts and Humanities and the School of Humanities and Social Sciences); undergraduate science and technology (undergraduate students in the School of Biological Sciences, the School of Physical Sciences and the School of Technology); postgraduate vocational courses (students in clinical medicine, clinical veterinary medicine and postgraduate certificates in education); and other postgraduate courses (all other postgraduate students, including those in doctoral and masters programmes).
### Supplementary Table 2. Tests conducted.

| Week | Dates       | Eligible students | Participating students | Asymptomatic screening programme | University symptomatic testing |
|------|-------------|-------------------|------------------------|----------------------------------|-------------------------------|
|      |             |                   |                        | Screening tests | Valid results | Scale* | Mean swab count per pool | Students screened (estimated) | Individual confirmatory tests | Valid results | Students screened per total tests | Individual tests | Valid results |
| 1    | 5 Oct – 11 Oct | 15,479            | 11,638                 | 1,867              | 1,837         | 2 students per pool | 1.87   | 3,435                    | 36                     | 34             | 1.81                       | 102             | 96           |
| 2    | 12 Oct – 18 Oct | 15,511            | 12,100                 | 1,890              | 1,866         | 2 students per pool | 1.92   | 3,583                    | 56                     | 56             | 1.84                       | 221             | 219          |
| 3    | 19 Oct – 25 Oct | 15,488            | 12,195                 | 1,913              | 1,886         | Half-pool          | 2.47   | 4,658                    | 105                    | 104            | 2.31                       | 195             | 194          |
| 4    | 26 Oct – 1 Nov | 15,440            | 12,383                 | 1,923              | 1,900         | Half-pool          | 2.92   | 5,548                    | 109                    | 109            | 2.73                       | 109             | 109          |
| 5    | 2 Nov – 8 Nov | 15,385            | 12,372                 | 1,873              | 1,865         | Half-pool          | 2.49   | 4,644                    | 79                     | 77             | 2.38                       | 112             | 110          |
| 6    | 9 Nov – 15 Nov | 15,323            | 12,350                 | 1,864              | 1,851         | Half-pool          | 2.89   | 5,349                    | 228                    | 226            | 2.56                       | 265             | 263          |
| 7    | 16 Nov – 22 Nov | 15,307           | 12,424                 | 1,743              | 1,727         | Half-pool          | 2.42   | 4,179                    | 102                    | 102            | 2.27                       | 87              | 87           |
| 8    | 23 Nov – 29 Nov | 15,309           | 12,498                 | 1,919              | 1,889         | Whole pool         | 5.02   | 9,483                    | 45                     | 44             | 4.83                       | 28              | 28           |
| 9    | 30 Nov – 6 Dec | 15,310           | 12,544                 | 1,953              | 1,938         | Whole pool         | 4.90   | 9,496                    | 52                     | 52             | 4.74                       | 27              | 27           |
| Weeks 1-2 | 5 Oct – 18 Oct | 3,757             | 3,703                  | 2 students per pool | 7,018         | 92                 | 90     | 1.82                     | 323                    | 315            |
| Weeks 3-7 | 19 Oct – 22 Nov | 9,316             | 9,229                  | Half-pool        | 24,379        | 623                | 618    | 2.45                     | 768                    | 763            |
| Weeks 8-9 | 23 Nov – 6 Dec | 3,872             | 3,827                  | Whole pool       | 18,979        | 97                 | 96     | 4.78                     | 55                     | 55             |
| All weeks | 5 Oct – 6 Dec | 15,561            | 12,979                 | 16,945            | 16,759        |                  | 50,376 | 812                      | 804                    | 2.84           | 1,146                      | 1,133           |              |

*Phase 1 (weeks 1-2): two students per testing pool screened each week; phase 2 (weeks 3-7): half of each testing pool screened on alternating week; phase 3 (weeks 8-9): whole testing pool screened each week.
Supplementary Table 3. Case ascertainment.

| Week | Dates          | Asymptomatic screening programme | University symptomatic testing | Other* | Total positive individual tests | % ascertained through screening |
|------|----------------|---------------------------------|-------------------------------|--------|--------------------------------|--------------------------------|
|      |                | Positive pooled screening tests | Confirmed positive pools (at least one positive individual test) | Positive individual tests per positive pool (mean, range) | Positive individual tests per positive household (mean, range) | Positive tests |
| 1    | 5 Oct – 11 Oct | 19                              | 11                            | 12     | 1.1                            | 1 to 2                          | 1.1                        | 1 to 2                           | 6                                  | 2                                  | 20                                 | 60.0%                             |
| 2    | 12 Oct – 18 Oct| 28                              | 27                            | 35     | 1.3                            | 1 to 2                          | 1.2                        | 1 to 2                           | 79                                 | 9                                  | 122                                | 28.7%                             |
| 3    | 19 Oct – 25 Oct| 38                              | 36                            | 38     | 1.1                            | 1 to 2                          | 1.2                        | 1 to 3                           | 50                                 | 12                                 | 100                                | 38.0%                             |
| 4    | 26 Oct – 1 Nov | 35                              | 30                            | 38     | 1.3                            | 1 to 3                          | 1.3                        | 1 to 3                           | 21                                 | 7                                  | 66                                 | 57.6%                             |
| 5    | 2 Nov – 8 Nov  | 26                              | 22                            | 23     | 1.1                            | 1 to 2                          | 1.1                        | 1 to 2                           | 37                                 | 17                                 | 76                                 | 28.9%                             |
| 6    | 9 Nov – 15 Nov | 67                              | 59                            | 80     | 1.4                            | 1 to 4                          | 1.4                        | 1 to 4                           | 122                                | 26                                 | 228                                | 35.1%                             |
| 7    | 16 Nov – 22 Nov| 22                              | 17                            | 27     | 1.6                            | 1 to 4                          | 1.6                        | 1 to 4                           | 15                                 | 6                                  | 48                                 | 56.3%                             |
| 8    | 23 Nov – 29 Nov| 7                               | 3                             | 3      | 1.0                            | 1                               | 1.0                        | 1                               | 1                                  | 0                                  | 4                                  | 75.0%                             |
| 9    | 30 Nov – 6 Dec | 10                              | 0                             | 0      | -                              | -                               | -                          | -                               | 4                                  | 2                                  | 6                                  | 0.0%                              |
| Weeks 1-2 |           | 47                              | 38                            | 47     | 1.2                            | 1 to 2                          | 1.2                        | 1 to 2                           | 85                                 | 10                                 | 142                                | 33.1%                             |
| Weeks 3-7 |           | 188                             | 164                           | 206    | 1.3                            | 1 to 4                          | 1.3                        | 1 to 4                           | 245                                | 68                                 | 519                                | 39.7%                             |
| Weeks 8-9 |           | 17                              | 3                             | 3      | 1.0                            | 1                               | 1.0                        | 1                               | 5                                  | 2                                  | 10                                 | 30.0%                             |
| All weeks |           | 252                             | 205                           | 256    | 1.3                            | 1 to 4                          | 1.3                        | 1 to 4                           | 335                                | 80                                 | 671                                | 38.2%                             |

*Other includes: positive results obtained through other testing pathways, such as NHS testing facilities, and reported to the university by Public Health England; and 7 asymptomatic positive cases identified through a distinct programme of screening undertaken by the university in conjunction with local public health teams during an outbreak investigation in a single accommodation block during term week 3. An additional 2 cases reported to the university by Public Health England during the study period were excluded, because their test dates could not be confirmed.
### Supplementary Table 4. Technical validation: number of replicates detected for each target concentration of SARS-CoV-2 virus.

| Target concentration of SARS CoV-2 (dC/mL) | Calculated SARS CoV-2 copies per RT-PCR reaction | Number of swabs | Replicates detected | Number of swabs | Replicates detected |
|--------------------------------------------|----------------------------------------------------|----------------|---------------------|----------------|---------------------|
| 250,000                                    | 4,444                                              | 1              | 3/3                 | 5-6            | 3/3                 |
| 100,000                                    | 1,778                                              | 1              | 3/3                 | 5-7            | 3/3                 |
| 25,000                                     | 444                                                | 1              | 2/2                 | 5-6            | 3/3                 |
| 10,000                                     | 178                                                | 1              | 3/3                 | 5-6            | 3/3                 |
| 2,500                                      | 44                                                 | 1              | 3/3                 | 5-6            | 3/3                 |
| 1,000                                      | 18                                                 | 1              | 3/3                 | 5-7            | 3/3                 |
| 500                                        | 9                                                  | 1              | 3/3                 | 5-6            | 3/3                 |
| 250                                        | 4                                                  | 1              | 3/3                 | 5-8            | 3/3                 |
| 125                                        | 2                                                  | 1              | 3/3                 | 5-7            | 3/3                 |
Supplementary Table 5. Distribution of CT values for individual confirmatory tests.

|                              | CT value | <20 | 20-25 | 25-30 | 30-35 | ≥35 | All  |
|------------------------------|----------|-----|-------|-------|-------|-----|------|
| Symptomatic testing          |          |     |       |       |       |     |      |
| Asymptomatic screening       |          |     |       |       |       |     |      |
| programme                    |          |     |       |       |       |     |      |
| Presymptomatic with          |          |     |       |       |       |     |      |
| cardinal symptoms            |          |     |       |       |       |     |      |
| Minor symptoms               |          |     |       |       |       |     |      |
| Asymptomatic                 |          |     |       |       |       |     |      |

|    | <20 | 20-25 | 25-30 | 30-35 | ≥35 | All  |
|----|-----|-------|-------|-------|-----|------|
| Symptomatic testing          | 60 (18%) | 137 (41%) | 83 (25%) | 41 (12%) | 14 (4%) | 335 (100%) |
| Asymptomatic screening       | 23 (9%) | 85 (33%) | 68 (27%) | 43 (17%) | 37 (14%) | 256 (100%) |
| programme                    |          |       |       |       |     |      |
| Presymptomatic with          | 6 (9%) | 30 (44%) | 21 (31%) | 7 (10%) | 6 (9%) | 68 (100%) |
| cardinal symptoms            |          |       |       |       |     |      |
| Minor symptoms               | 4 (9%) | 14 (33%) | 17 (40%) | 3 (7%) | 5 (12%) | 43 (100%) |
| Asymptomatic                 | 2 (7%) | 6 (21%) | 4 (14%) | 7 (24%) | 10 (34%) | 29 (100%) |
Supplementary Table 6. Single variable logistic regression analysis of student characteristics associated with a positive SARS-CoV-2 result, n=12,781.

| Variable     | Category                      | Positive | Not positive | OR       | (95% CI)   | P value |
|--------------|-------------------------------|----------|--------------|----------|------------|---------|
| Sex          | Female                        | 325      | 5,800        | 1.00     | 0.86-1.17  | 0.97    |
|              | Male                          | 346      | 6,158        | 0.61     | 0.21-1.34  | 0.28    |
|              | Other/unknown                 | 5        | 147          |          |            |         |
| Ethnicity    | White                         | 509      | 7,659        | 0.58     | 0.48-0.70  | <0.001  |
|              | Other                         | 153      | 3,944        | 0.42     | 0.23-0.69  | 0.002   |
|              | Unknown                       | 14       | 502          |          |            |         |
| Residency    | UK                            | 570      | 7,934        | 0.35     | 0.28-0.43  | <0.001  |
|              | International                 | 103      | 4,102        | 0.61     | 0.15-1.63  | 0.40    |
|              | Unknown                       | 3        | 69           |          |            |         |
| Year of study| 1st                           | 367      | 5,195        |          |            |         |
|              | 2nd                           | 166      | 2,999        | 0.78     | 0.65-0.95  | 0.01    |
|              | 3rd or higher                 | 142      | 3,786        | 0.53     | 0.43-0.65  | <0.001  |
|              | Unknown                       | 1        | 125          | 0.11     | 0.006-0.51 | 0.03    |
| Course       | Undergraduate arts and humanities | 348  | 4,205        |          |            |         |
|              | Undergraduate science and technology | 246  | 4,560        | 0.65     | 0.55-0.77  | <0.001  |
|              | Postgraduate vocational       | 22       | 321          | 0.83     | 0.52-1.26  | 0.41    |
|              | Postgraduate (other)          | 59       | 2,894        | 0.25     | 0.18-0.32  | <0.001  |
|              | Unknown                       | 1        | 125          | 0.10     | 0.0055-0.43| 0.02    |
| Household size| Minimum                      | 1        | 1            | 1.08     | 1.05-1.11  | <0.001  |
|              | 25th centile                  | 6        | 5            |          |            |         |
|              | Median                        | 7        | 7            |          |            |         |
|              | 75th centile                  | 8        | 8            |          |            |         |
|              | Maximum                       | 20       | 20           |          |            |         |
Supplementary Table 7. Multivariable logistic regression analysis of student characteristics associated with a positive SARS-CoV-2 result, n=12,781.

| Variable        | Category                | OR    | 95% CI         | P value |
|-----------------|-------------------------|-------|----------------|---------|
| Sex             | Female                  | 1.21  | 1.03-1.42      | 0.02    |
|                 | Male                    |       |                |         |
|                 | Other/unknown           | 0.44  | 0.07-1.42      | 0.26    |
| Ethnicity       | White                   |       |                |         |
|                 | Other                   | 0.69  | 0.57-0.84      | <0.001  |
|                 | Unknown                 | 0.46  | 0.23-0.81      | 0.01    |
| Residency       | UK                      |       |                |         |
|                 | International           | 0.53  | 0.42-0.67      | <0.01   |
|                 | Unknown                 | 12.4  | 1.63-113       | 0.01    |
| Year of study   | 1st                     |       |                |         |
|                 | 2nd                     | 0.63  | 0.52-0.76      | <0.001  |
|                 | 3rd or higher           | 0.44  | 0.36-0.54      | <0.001  |
|                 | Unknown                 | 0.04  | 0.002-0.24     | 0.004   |
| Course          | Undergraduate arts and humanities |       |                |         |
|                 | Undergraduate science and technology | 0.74 | 0.62-0.88      | 0.001   |
|                 | Postgraduate vocational | 0.73  | 0.45-1.11      | 0.16    |
|                 | Postgraduate (other)    | 0.28  | 0.21-0.38      | <0.001  |
|                 | Unknown                 | NA    | -              |         |
| Household size  |                         | 1.06  | 1.03-1.09      | <0.001  |
| Parameter or setting | Value or assumption | Source | Change from HE-INI model¹ |
|---------------------|---------------------|--------|--------------------------|
| **Network settings** |                     |        |                          |
| Number of individuals | 12,781              | From data: number of study participants | Yes – generic 15,000 used in preprint |
| Household structure | Full specification: {1: 0.151, 2: 0.105, 3: 0.074, 4: 0.114, 5: 0.115, 6: 0.130, 7: 0.094, 8: 0.117, 9: 0.036, 10: 0.029, 11: 0.014, 12: 0.012, 13: 0.003, 14: 0.003, 15: 0.001, 16: 0.001, 18: 0.001} | From data: household structure of eligible students | Yes – {10: 0.5, 5: 0.5} used in preprint, arbitrary choice |
|                     | This notation means: Size of household: fraction of households that size | | |
| Sizes of other activity groups | Full specification: {50: 0.01, 10: 0.5, 5: 0.49} | By assumption: to model a majority of small groups, with a small number of larger events | Yes - {40: 0.05, 10: 0.3, 5: 0.5, 3: 0.15} used in preprint, arbitrary choice |
| Number of other activity groups | 4,000 | By assumption: note relationship to probability of transmission for a non-household contact below | Yes – 3,000 used in preprint, arbitrary choice |
| **Disease progression and transmission** |                     |        |                          |
| Probability of transmission for a household contact per day | 0.017 | From data: calibrated to produce the observed within-household attack rate, accounting for symptomatic and asymptomatic infections | Yes – 0.025 used in preprint, chosen for plausibility |
| Ratio of probability of transmission for a non-household contact per day to probability of transmission for a household contact per day | 1.0 | From data: calibrated to produce a between-household attack rate roughly consistent with the observed rate to week 7 (before the UK national lockdown) | Yes – 0.2 used in preprint, chosen for plausibility |
| Mean non-infectious latent period | 2.9 days | Atene et al. (2021)² | Yes (small change) – 3 days in preprint, chosen for plausibility |
| Description                                                                 | Value             | Notes                                                                 |
|----------------------------------------------------------------------------|-------------------|----------------------------------------------------------------------|
| Mean pre-symptomatic infectious period                                      | 3.6 days          | From data: observed pre-symptomatic infectious period                 |
| Proportion asymptomatic                                                     | 19.7%             | From data: observed proportion of asymptomatic students              |
| Infectiousness of presymptomatic relative to symptomatics                   | Equal             | By assumption                                                        |
| Infectiousness of asymptomatic relative to symptomatics                     | 18%               | From data: observed ratio of secondary household attack rates         |
| Mean infectious period after symptoms develop                               | 4 days            | Singanayagam, A. et al. (2020)*                                      |
| Total mean period of infectiousness of an asymptomatic individual           | Equal to symptomatic individual (mean 7.6 days) | By assumption                                                        |

### Testing and Isolation

| Description                                                                 | Value             | Notes                                                                 |
|----------------------------------------------------------------------------|-------------------|----------------------------------------------------------------------|
| Probability and speed of symptomatic tests                                 | Symptomatic       | By assumption                                                        |
| Participation in asymptomatic screening                                    | 100%              | By assumption                                                        |
| Performance of asymptomatic tests                                         | Asymptomatic       | By assumption                                                        |
| Isolation                                                                  | Entire household  | By assumption                                                        |
| Expected isolation period                                                  | 14 days           | By assumption                                                        |
| Isolation implications for contact                                         | When a household  | By assumption                                                        |
| Tracing                                                                    | 50% probability   | By assumption                                                        |

### References

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2. Alene, M. *et al.* Serial interval and incubation period of COVID-19: a systematic review and meta-analysis. *BMC Infect Dis* **21**, 257, doi:10.1186/s12879-021-05950-x (2021).
3. Singanayagam, A. *et al.* Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. *Euro Surveill* **25**, doi:10.2807/1560-7917.ES.2020.25.32.2001483 (2020).
Supplementary notes

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