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

Ben Warne (✉ bw252@cam.ac.uk)

University of Cambridge <https://orcid.org/0000-0003-1326-0373>

Jessica Enright

University of Glasgow <https://orcid.org/0000-0002-0266-3292>

Marina Metaxaki

University of Cambridge, Department of Medicine, Cambridge, UK

Stewart Fuller

University of Cambridge, Department of Medicine, Cambridge, UK

Richard J. Samworth

Statistical Laboratory, Centre for Mathematical Sciences, University of Cambridge

Gillian Weale

Health, Safety & Regulated Facilities Division, University of Cambridge, Cambridge, UK

Jon Holgate

University Information Services, University of Cambridge, Cambridge, UK

Vijay Samtani

University of Cambridge <https://orcid.org/0000-0002-4246-6453>

Craig Brierley

Office of External Affairs and Communications, University of Cambridge

Dinesh Aggarwal

University of Cambridge <https://orcid.org/0000-0002-5938-8172>

Sarah Hilborne

University of Cambridge

Mahin Bagheri Kahkeshi

University of Cambridge

Sarah Berry

University of Cambridge

Julie A. Douthwaite

Biopharma RD, AstraZeneca

Alexandra L. Orton

<https://orcid.org/0000-0002-5440-6802>

Rebecca Clarke

Institute for Manufacturing, Department of Engineering, University of Cambridge

Darius Danaei

Institute for Manufacturing, Department of Engineering, University of Cambridge

Rory Dyer

Institute for Manufacturing, Department of Engineering, University of Cambridge

Rob Glew

Institute for Manufacturing, Department of Engineering, University of Cambridge

Oliver Lambson

Institute for Manufacturing, Department of Engineering, University of Cambridge

Aastha Dahal

Cambridge Students' Union

Ben Margolis

Cambridge Students' Union

Edna Murphy

Office of Intercollegiate Services Ltd., Cambridge

Matthew Russell

Office of Intercollegiate Services Ltd., Cambridge

Vickie S. Braithwaite

Public Health Directorate, Cambridgeshire County Council and Peterborough City Council

Kathryn Faulkner

Public Health Directorate, Cambridgeshire County Council and Peterborough City Council

Elizabeth Wright

Public Health Directorate, Cambridgeshire County Council and Peterborough City Council, UK

Afzal Chaudhry

Cambridge Institute for Medical Research <https://orcid.org/0000-0001-6156-9194>

Lenette Mactavous

Cambridge University Hospitals NHS Foundation Trust

Maharshi Dhada

Institute for Manufacturing, Department of Engineering

Ajith Parlikad

Institute for Manufacturing, Department of Engineering

University of Cambridge Asymptomatic COVID-19 Screening Programme Consortium

University of Cambridge (see Supplementary File for full list of authors)

Jane Greated

Lucy Cavendish College, University of Cambridge

Ian Leslie

University Information Services, University of Cambridge

Andy Neely

Vice Chancellor's Office, University of Cambridge

Steve Rees

Biopharma RD, AstraZeneca

Ashley Shaw

Cambridge University Hospitals NHS Foundation Trust

Martin Vinnell

Occupational Health and Safety Services, University of Cambridge

Linda Sheridan

Public Health Directorate, Cambridgeshire County Council and Peterborough City Council

Emmeline Watkins

Public Health Directorate, Cambridgeshire County Council and Peterborough City Council, UK

Stephen Baker

University of Cambridge <https://orcid.org/0000-0003-1308-5755>

Ian G. Goodfellow

University of Cambridge

Paul J. Lehner

University of Cambridge <https://orcid.org/0000-0001-9383-1054>

Kathleen Liddell

Faculty of Law, University of Cambridge

Roger Clark

Charles River Laboratories <https://orcid.org/0000-0003-4167-6317>

Rob Howes

Cambridge Covid-19 Testing Centre, Discovery Sciences, R&D, AstraZeneca, Cambridge, UK

Michael P. Weekes

University of Cambridge <https://orcid.org/0000-0003-3196-5545>

Duncan McFarlane

Institute for Manufacturing, Department of Engineering, University of Cambridge

Patrick H. Maxwell

University of Cambridge

Nicholas J. Matheson

University of Cambridge <https://orcid.org/0000-0002-3318-1851>

Article**Keywords:**

Posted Date: May 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-520626/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

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

Ben Warne^{1,2,3,*}, Jessica Enright⁴, Marina Metaxaki¹, Stewart Fuller¹, Richard J Samworth⁵, Gillian Weale⁶, Jon Holgate⁷, Vijay Samtani⁷, Craig Brierley⁸, Dinesh Aggarwal^{1,3,9,10}, Sarah Hilborne¹, Mahin Bagheri Kahkeshi¹, Sarah Berry¹, Julie A. Douthwaite¹¹, Alexandra L. Orton¹¹, Rebecca Clarke¹², Darius Danaei¹², Rory Dyer¹², Rob Glew¹², Oliver Lambson¹², Aastha Dahal¹³, Ben Margolis¹³, Edna Murphy¹⁴, Matthew Russell¹⁴, Vickie S. Braithwaite^{15,16}, Kathryn Faulkner¹⁵, Elizabeth Wright¹⁵, Afzal Chaudhry^{1,3}, Lenette Mactavous³, Maharshi Dhada¹², Ajith Parlikad¹², University of Cambridge Asymptomatic COVID-19 Screening Programme Consortium[#], Jane Greated¹⁷, Ian Leslie⁷, Andy Neely¹⁸, Steve Rees¹¹, Ashley Shaw³, Martin Vinnell¹⁹, Linda Sheridan¹⁵, Emmeline Watkins¹⁵, Stephen Baker^{1,2}, Ian G. Goodfellow²⁰, Paul J. Lehner^{1,2,3}, Kathleen Liddell²¹, Roger Clark²², Rob Howes^{11,†}, Michael P. Weekes^{1,3,23,†}, Duncan McFarlane^{12,24†}, Patrick H. Maxwell^{23,25,†}, Nicholas J. Matheson^{1,2,3,26,†*}

1. Department of Medicine, University of Cambridge, UK
2. Cambridge Institute of Therapeutic Immunology and Infectious Disease (CITIID), Jeffrey Cheah Biomedical Centre, University of Cambridge, UK
3. Cambridge University Hospitals NHS Foundation Trust, UK
4. School of Computing Science, University of Glasgow, UK
5. Statistical Laboratory, Centre for Mathematical Sciences, University of Cambridge, UK
6. COVID-19 Operations Centre, University of Cambridge, UK
7. University Information Services, University of Cambridge, UK
8. Office of External Affairs and Communications, University of Cambridge, UK
9. Public Health England, London, UK.
10. Wellcome Sanger Institute, Hinxton, Cambridge, UK.

11. Biopharma RD, AstraZeneca, Cambridge, UK
12. Institute for Manufacturing, Department of Engineering, University of Cambridge, UK
13. Cambridge Students' Union, Cambridge, UK
14. Office of Intercollegiate Services Ltd., Cambridge, UK
15. Public Health Directorate, Cambridgeshire County Council and Peterborough City Council, UK
16. MRC Epidemiology Unit, University of Cambridge, UK
17. Lucy Cavendish College, University of Cambridge, UK
18. Vice Chancellor's Office, University of Cambridge, UK
19. Occupational Health and Safety Services, University of Cambridge, UK
20. Division of Virology, Department of Pathology, University of Cambridge, UK
21. Centre for Law, Medicine and Life Sciences, Faculty of Law, University of Cambridge, UK
22. Charles River Laboratories, Chesterford Research Park, Saffron Walden, UK
23. Cambridge Institute for Medical Research (CIMR), University of Cambridge, UK
24. St John's College, University of Cambridge, UK
25. School of Clinical Medicine, University of Cambridge, UK
26. NHS Blood and Transplant, Cambridge, UK

Full list of consortium members and affiliations is provided in the supplementary materials

†Joint senior authors

*Correspondence: bw252@cam.ac.uk; njm25@cam.ac.uk

52 **Abstract**

53 Transmission of SARS-CoV-2 without symptoms is well described, and may be mitigated by
54 mass testing. Nonetheless, the optimal implementation and quantitative real-world impact of
55 this approach remain unclear. During a period of rising SARS-CoV-2 prevalence, students at
56 the University of Cambridge were enrolled in a voluntary programme of weekly PCR-based
57 asymptomatic screening. Swab pooling by household reduced the total testing capacity
58 required by five-fold, without affecting laboratory workflows or compromising test sensitivity.
59 Participation remained >75% throughout the study period. 299/671 (45%) of students
60 diagnosed with SARS-CoV-2 were either identified or pre-emptively quarantined because of
61 the screening programme. After a negative screening test, the risk of developing COVID-19
62 over the following 7 days was decreased by 51%. Modelling transmission using parameters
63 from our study suggests a reduction in R_0 of up to 31% attributable to weekly screening. We
64 therefore demonstrate the feasibility and efficacy of regular, voluntary mass testing for
65 COVID-19.

Main

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 cases¹⁻³. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the absence of symptoms is well documented⁴⁻⁶, 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)^{7,8}. 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 transmission⁹⁻¹¹. 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 care¹²⁻¹⁵. It has also been trialled in other settings with high risk of transmission such as prisons and professional sport^{16,17}. In England, regular mass testing has recently been extended to schools¹⁸, and offered to all adults in the community¹⁹. Nonetheless, clear empiric evidence of efficacy is limited, and the approach remains controversial^{20,21}.

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 transmission²²⁻²⁴. Amongst university students (typically, healthy young adults), the rate of asymptomatic infection is expected to be higher than in the general population^{25,26}. 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^{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^{29,30} or demonstrated enhanced case ascertainment³¹⁻³³, but provided limited epidemiological metadata or direct evidence for a reduction in transmission on campus or in the community. Despite several modelling studies^{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)^{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)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)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

119 university, identifying risk factors for infection and linking secondary attack rates amongst
120 household contacts with the characteristics of index cases. By combining these data, we
121 provide evidence for the efficacy of asymptomatic screening which goes beyond simple
122 numerical case ascertainment. We demonstrate how regular screening is able to identify
123 many students with presymptomatic as well as asymptomatic SARS-CoV-2 infection,
124 quantify the reduction in risk of COVID-19 associated with a negative screening test, and
125 use model-based analysis parameterised from our study to quantify the ability of mass
126 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, 2020⁴⁹. 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 split 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 studies⁴⁶⁻⁴⁸, 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 report⁵¹.

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)⁵². 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^{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 populations⁸. 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 infectious⁵⁵. 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 households 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 (R_0) 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 R_0 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 R_0 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 students⁵³. 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 study⁶², 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 community⁵¹.

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

378 testing pools correspond with units of household quarantine e.g. universities, long-term care
379 facilities, prisons, workers housed in dormitories, or private households. Nonetheless, it may
380 also be applied in other settings where individuals are grouped together, such as schools or
381 workplaces⁶³.

382 Our data suggest that voluntary participation and the use of nose and throat swabs (rather
383 than less invasive sampling, such as saliva) are not *per se* barriers to widespread uptake
384 amongst students, and likely other populations. Other factors which may have enhanced
385 participation in our programme include: ease of access and convenience of home testing, a
386 proactive communication strategy, engagement with student representatives, the collegiate
387 university structure, the use of household-based pooled screening, and careful attention to
388 ethical and legal issues (e.g. personal data governance). Many of the approaches taken in
389 the development, operation and evaluation of our programme have been supported by a
390 recent ethical review of asymptomatic COVID-19 screening programmes in higher education
391 settings⁶⁴.

392 Criticisms of mass testing for COVID-19 typically have typically focussed on the potential for
393 false positives (leading to unnecessary periods of quarantine) and false negatives (leading to
394 missed cases)^{20,21}. Our two-step testing strategy (including individual confirmatory PCR
395 tests) mitigates the chance of false positive tests leading to prolonged periods of
396 unnecessary individual or household quarantine. Moreover, swab pooling effectively
397 increases the prevalence of true positive samples. In theory, the high sensitivity of PCR tests
398 could result in the detection of individuals with low levels of viral RNA late in their course of
399 infection, even when they are no longer infectious⁶⁵. Whilst this is a valid concern for one-off
400 mass testing, it is not relevant for programmes based on regular, frequent screening.
401 Conversely, the high sensitivity of PCR tests ensures that the risk of false negatives is
402 minimised. This may be particularly important for the detection of breakthrough infections
403 following vaccination, when viral loads may be reduced⁶⁶. 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 studies⁵¹.

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^{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 testing³⁶. When LFTs are conducted by trained staff and volunteers, however, sensitivity for SARS-CoV-2 detection is roughly 50% compared with PCR tests^{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 infectious⁶⁵. 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^{53,70}, laboratory data on recovery of infectious virus⁵⁵, and analysis of contact tracing data⁷¹. 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 screening⁵⁴.

The development of SARS-CoV-2 variants with mutations enhancing transmissibility and enabling at least partial escape from vaccine-induced and natural immunity⁷²⁻⁷⁴, together with the limited availability of vaccination on a global scale⁷⁵, 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 viruses⁷⁶. 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

431 consequences of mass testing are much less severe. Taken together, our data strongly
432 support the role of regular asymptomatic screening as an effective means to control SARS-
433 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

485 households to ensure testing pools of 6-10 students. Household and testing pool
486 membership were determined by each college prior to the start of term (based on guidance
487 provided by the university and the screening programme) and recorded in a central database
488 that could be updated at any time. This database provided a single reference point used for
489 test kit production and result notification (see below).

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

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

509 All samples were tested by PCR in the established University of Cambridge/AstraZeneca
510 Cambridge COVID-19 Testing Centre (see below). Pseudonymised results were transferred
511 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 report⁵¹.

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 test⁷⁷ and the more recent Generalised Residual Prediction (GRP) test⁷⁸. 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 Programme⁷⁹. 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.

Acknowledgements

NJM is supported by the MRC (CSF MR/P008801/1) and NHSBT (WPA15-02). RJS is supported by the EPSRC (EP/P031447/1 and EP/N031938/1). MPW was funded by the Wellcome Trust through a Senior Clinical Research Fellowship (108070/Z/15/Z), Addenbrooke's Charitable Trust and the NIHR Cambridge Biomedical Research Centre. BW and AC receive funding from the National Institute for Health Research Cambridge

Biomedical Research Centre at the Cambridge University Hospitals NHS Foundation Trust. DA is a Wellcome Clinical PhD Fellow and gratefully supported by the Wellcome Trust (222903/Z/21/Z). VSB receives funding from the National Institute for Health Research at the University of Cambridge. PJJ was funded by the Wellcome Trust through a Principal Research Fellowship (210688/Z/18/Z), the MRC (MR/V011561/1), the Addenbrooke's Charitable Trust and the NIHR Cambridge Biomedical Research Centre. SB was funded by the Wellcome Trust through a Senior Research Fellowship (215515/Z/19/Z). IG is a Wellcome Senior Fellow and supported by funding from the Wellcome Trust (207498/Z/17/Z and 206298/B/17/Z). We thank members of NHS Test and Trace and the Public Health England contact tracing data team for their contributions to this study. We are grateful to all staff members of the Cambridge COVID-19 Testing Centre for generating qPCR data. We thank all students at the University of Cambridge who participated in screening, as well as the College and University staff who have supported the programme.

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.

767 **Competing interests**

768 RH and SR are employees of AstraZeneca AB. RC is an employee of Charles River
769 Laboratories. All other authors declare no competing interests relevant to the submitted
770 work.

Figures

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.

Fig. 2: Schematic overview of asymptomatic screening programme.

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).

793 Some eligible students were excluded from screening each week because of a recent
794 positive test for SARS-CoV-2, symptoms of possible COVID-19, or a requirement to self-
795 isolate. **e**, Predicted total number of pooled screening and individual confirmatory tests
796 required to screen 1,000 students in the presence of different testing pool sizes and SARS-
797 CoV-2 prevalences (grey lines, 0.1-10%). Crosses indicate the actual mean pool sizes and
798 tests utilised at the indicated time points. In the absence of swab pooling (equivalent to a
799 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

821 anosmia/ageusia) experienced at some time during infection; blue, no symptoms or minor
822 symptoms only (no cardinal symptoms). *Cases where potential for onward transmission
823 was interrupted by asymptomatic screening are indicated by patterned areas. †Estimated
824 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.

834 Extended Data Figures

835

836 Extended Data Fig. 1: Impact of communications on study participation.

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

838 Key communications are highlighted. Where students consented more than once, only their

839 first consent is included.

840

841 **Extended Data Fig. 2: Technical validation of swab pooling.**

842 Detection of SARS CoV-2 standards in reconstituted individual (1 swab) or pooled (5-8
 843 swabs) samples. Experiment conducted in triplicate, with individual data points, mean and
 844 standard deviation shown for each SARS-CoV-2 concentration. dC/mL, digital copies/mL.
 845 CT value, cycle threshold. Solid lines, non-linear regression lines; shaded areas, 95%
 846 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).

a: Number of non-household activity groups

e: Mean presymptomatic infectious period

b: Proportion symptomatic

f: Mean infectious period after symptoms develop

c: Probability of transmission for a household contact per day

g: Ratio of infectiousness of asymptomatics (compared to symptomatics)

d: Ratio of probability of transmission for a non-household contact per day to probability of transmission for a household contact per day

900

901 **Extended Data Fig. 6: Sensitivity analyses.**

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

907 **References**

- 908 1 Ferretti, L. *et al.* Quantifying SARS-CoV-2 transmission suggests epidemic control
909 with digital contact tracing. *Science* **368**, doi:10.1126/science.abb6936 (2020).
- 910 2 Hellewell, J. *et al.* Feasibility of controlling COVID-19 outbreaks by isolation of cases
911 and contacts. *Lancet Glob Health* **8**, e488-e496, doi:10.1016/S2214-109X(20)30074-
912 7 (2020).
- 913 3 Kretzschmar, M. E. *et al.* Impact of delays on effectiveness of contact tracing
914 strategies for COVID-19: a modelling study. *The Lancet Public Health* **5**, e452-e459
915 (2020).
- 916 4 Oran, D. P. & Topol, E. J. The proportion of SARS-CoV-2 infections that are
917 asymptomatic: a systematic review. *Ann Intern Med*, doi: 10.7326/M7320-6976
918 (2021).
- 919 5 Tabata, S. *et al.* Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2
920 infection on the Diamond Princess cruise ship: a retrospective analysis. *Lancet Infect*
921 *Dis* **20**, 1043-1050, doi:10.1016/S1473-3099(20)30482-5 (2020).
- 922 6 Wang, Y. *et al.* Clinical Outcomes in 55 Patients With Severe Acute Respiratory
923 Syndrome Coronavirus 2 Who Were Asymptomatic at Hospital Admission in
924 Shenzhen, China. *J Infect Dis* **221**, 1770-1774, doi:10.1093/infdis/jiaa119 (2020).
- 925 7 Johansson, M. A. *et al.* SARS-CoV-2 Transmission From People Without COVID-19
926 Symptoms. *JAMA Network Open* **4**, e2035057-e2035057,
927 doi:10.1001/jamanetworkopen.2020.35057 (2021).
- 928 8 Buitrago-Garcia, D. *et al.* Occurrence and transmission potential of asymptomatic
929 and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-
930 analysis. *PLoS Med* **17**, e1003346, doi:10.1371/journal.pmed.1003346 (2020).
- 931 9 Paltiel, A. D., Zheng, A. & Walensky, R. P. Assessment of SARS-CoV-2 Screening
932 Strategies to Permit the Safe Reopening of College Campuses in the United States.
933 *JAMA Netw Open* **3**, e2016818, doi:10.1001/jamanetworkopen.2020.16818 (2020).
- 934 10 Peto, J. *et al.* Weekly COVID-19 testing with household quarantine and contact
935 tracing is feasible and would probably end the epidemic. *Royal Society Open*
936 *Science* **7**, 200915 (2020).
- 937 11 Grassly, N. C. *et al.* Comparison of molecular testing strategies for COVID-19
938 control: a mathematical modelling study. *Lancet Infect Dis* **20**, 1381-1389,
939 doi:10.1016/S1473-3099(20)30630-7 (2020).
- 940 12 Rivett, L. *et al.* Screening of healthcare workers for SARS-CoV-2 highlights the role
941 of asymptomatic carriage in COVID-19 transmission. *Elife* **9**, doi:10.7554/eLife.58728
942 (2020).
- 943 13 World Health Organization. *Infection prevention and control guidance for long-term*
944 *care facilities in the context of COVID-19: interim guidance*, 21 March 2020,
945 <<https://apps.who.int/iris/handle/10665/331508>> (2020).

946 14 Centers for Disease Control and Prevention. *Interim infection prevention and control*
947 *recommendations for healthcare personnel during the coronavirus disease 2019*
948 *(COVID-19) pandemic*, <[https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html)
949 [control.html](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html)> (2020).

950 15 Jones, N. K. *et al.* Effective control of SARS-CoV-2 transmission between healthcare
951 workers during a period of diminished community prevalence of COVID-19. *Elife* **9**,
952 doi:10.7554/eLife.59391 (2020).

953 16 Hagan, L. M. *et al.* Mass Testing for SARS-CoV-2 in 16 Prisons and Jails - Six
954 Jurisdictions, United States, April-May 2020. *MMWR Morb Mortal Wkly Rep* **69**,
955 1139-1143, doi:10.15585/mmwr.mm6933a3 (2020).

956 17 Kissler, S. M. *et al.* *Viral dynamics of SARS-CoV-2 infection and the predictive value*
957 *of repeat testing.* , <Preprint at
958 [https://www.medrxiv.org/content/medrxiv/early/2020/10/23/2020.10.21.20217042.full.](https://www.medrxiv.org/content/medrxiv/early/2020/10/23/2020.10.21.20217042.full.pdf)
959 [pdf](https://www.medrxiv.org/content/medrxiv/early/2020/10/23/2020.10.21.20217042.full.pdf)> (2020).

960 18 Torjesen, I. What do we know about lateral flow tests and mass testing in schools?
961 *BMJ* **372**:n706 (2021).

962 19 Iacobucci, G. Covid-19: Government rolls out twice weekly rapid testing to all in
963 England. *BMJ* doi: **10.1136/bmj.n902** (2021).

964 20 Raffle, A. E., Pollock, A. M. & Harding-Edgar, L. Covid-19 mass testing programmes.
965 *BMJ* **370**, m3262, doi:10.1136/bmj.m3262 (2020).

966 21 Gill, M. & Gray, M. Mass testing for covid-19 in the UK. *BMJ* **371**, m4436,
967 doi:10.1136/bmj.m4436 (2020).

968 22 Wilson, E. *et al.* Multiple COVID-19 Clusters on a University Campus - North
969 Carolina, August 2020. *MMWR Morb Mortal Wkly Rep* **69**, 1416-1418,
970 doi:10.15585/mmwr.mm6939e3 (2020).

971 23 Fox, M. D., Bailey, D. C., Seamon, M. D. & Miranda, M. L. Response to a COVID-19
972 Outbreak on a University Campus - Indiana, August 2020. *MMWR Morb Mortal Wkly*
973 *Rep* **70**, 118-122, doi:10.15585/mmwr.mm7004a3 (2021).

974 24 Vang, K. E. *et al.* Participation in Fraternity and Sorority Activities and the Spread of
975 COVID-19 Among Residential University Communities - Arkansas, August 21-
976 September 5, 2020. *MMWR Morb Mortal Wkly Rep* **70**, 20-23,
977 doi:10.15585/mmwr.mm7001a5 (2021).

978 25 Davies, N. G. *et al.* Age-dependent effects in the transmission and control of COVID-
979 19 epidemics. *Nature Medicine* **26**, 1205-1211, doi:10.1038/s41591-020-0962-9
980 (2020).

981 26 Poletti, P. *et al.* Association of Age With Likelihood of Developing Symptoms and
982 Critical Disease Among Close Contacts Exposed to Patients With Confirmed SARS-
983 CoV-2 Infection in Italy. *JAMA Netw Open* **4**, e211085,
984 doi:10.1001/jamanetworkopen.2021.1085 (2021).

985 27 Benneyan, J., Gehrke, C., Ilies, I. & Nehls, N. Community and Campus COVID-19
986 Risk Uncertainty Under University Reopening Scenarios: Model-Based Analysis.
987 *JMIR Public Health Surveill* **7**, e24292, doi:10.2196/24292 (2021).

988 28 Yamey, G. & Walensky, R. P. Covid-19: re-opening universities is high risk. *BMJ* **370**,
989 m3365, doi:10.1136/bmj.m3365 (2020).

990 29 Gillam, T. B. *et al.* Norwich COVID-19 testing initiative pilot: evaluating the feasibility
991 of asymptomatic testing on a university campus. *J Public Health (Oxf)* **43**, 82-88,
992 doi:10.1093/pubmed/fdaa194 (2021).

993 30 Blake, H. *et al.* Perceptions and Experiences of the University of Nottingham Pilot
994 SARS-CoV-2 Asymptomatic Testing Service: A Mixed-Methods Study. *Int J Environ*
995 *Res Public Health* **18**, doi:10.3390/ijerph18010188 (2020).

996 31 Denny, T. N. *et al.* Implementation of a Pooled Surveillance Testing Program for
997 Asymptomatic SARS-CoV-2 Infections on a College Campus - Duke University,
998 Durham, North Carolina, August 2-October 11, 2020. *MMWR Morb Mortal Wkly Rep*
999 **69**, 1743-1747, doi:10.15585/mmwr.mm6946e1 (2020).

1000 32 Hamer, D. H. *et al.* Control of COVID-19 transmission on an urban university campus
1001 during a second wave of the pandemic. *medRxiv*, 2021.2002.2023.21252319,
1002 doi:10.1101/2021.02.23.21252319 (2021).

1003 33 Rennert, L. *et al.* Surveillance-based informative testing for detection and
1004 containment of SARS-CoV-2 outbreaks on a public university campus: an
1005 observational and modelling study. *Lancet Child Adolesc Health*, doi:10.1016/S2352-
1006 4642(21)00060-2 (2021).

1007 34 Hemani, G. *et al.* Modelling pooling strategies for SARS-CoV-2 testing in a university
1008 setting [version 1; peer review: awaiting peer review]. *Wellcome Open Research* **6**,
1009 doi:10.12688/wellcomeopenres.16639.1 (2021).

1010 35 Hill, E. M., Atkins, B. D., Keeling, M. J., Tildesley, M. J. & Dyson, L. Modelling SARS-
1011 CoV-2 transmission in a UK university setting. *medRxiv*, 2020.2010.2015.20208454,
1012 doi:10.1101/2020.10.15.20208454 (2021).

1013 36 Pray, I. W. *et al.* Performance of an Antigen-Based Test for Asymptomatic and
1014 Symptomatic SARS-CoV-2 Testing at Two University Campuses - Wisconsin,
1015 September-October 2020. *MMWR Morb Mortal Wkly Rep* **69**, 1642-1647,
1016 doi:10.15585/mmwr.mm695152a3 (2021).

1017 37 Ford, L. *et al.* Epidemiologic characteristics associated with SARS-CoV-2 antigen-
1018 based test results, rRT-PCR cycle threshold values, subgenomic RNA, and viral
1019 culture results from university testing. *Clin Infect Dis*, doi:10.1093/cid/ciab303 (2021).

1020 38 Barak, N. *et al.* Lessons from applied large-scale pooling of 133,816 SARS-CoV-2
1021 RT-PCR tests. *Sci Transl Med* **13**, doi:10.1126/scitranslmed.abf2823 (2021).

1022 39 Ben-Ami, R. *et al.* Large-scale implementation of pooled RNA extraction and RT-
1023 PCR for SARS-CoV-2 detection. *Clinical Microbiology and Infection* **26**, 1248-1253
1024 (2020).

1025 40 Gupta, E. *et al.* Pooled RNA sample reverse transcriptase real time PCR assay for
1026 SARS CoV-2 infection: A reliable, faster and economical method. *PLoS One* **15**,
1027 e0236859, doi:10.1371/journal.pone.0236859 (2020).

1028 41 Hogan, C. A., Sahoo, M. K. & Pinsky, B. A. Sample Pooling as a Strategy to Detect
1029 Community Transmission of SARS-CoV-2. *JAMA* **323**, 1967-1969,
1030 doi:10.1001/jama.2020.5445 (2020).

1031 42 Lohse, S. *et al.* Pooling of samples for testing for SARS-CoV-2 in asymptomatic
1032 people. *Lancet Infect Dis* **20**, 1231-1232, doi:10.1016/S1473-3099(20)30362-5
1033 (2020).

1034 43 Perchetti, G. A. *et al.* Pooling of SARS-CoV-2 samples to increase molecular testing
1035 throughput. *J Clin Virol* **131**, 104570, doi:10.1016/j.jcv.2020.104570 (2020).

1036 44 Torres, I., Albert, E. & Navarro, D. Pooling of nasopharyngeal swab specimens for
1037 SARS-CoV-2 detection by RT-PCR. *J Med Virol* **92**, 2306-2307,
1038 doi:10.1002/jmv.25971 (2020).

1039 45 Yelin, I. *et al.* Evaluation of COVID-19 RT-qPCR Test in Multi sample Pools. *Clin*
1040 *Infect Dis* **71**, 2073-2078, doi:10.1093/cid/ciaa531 (2020).

1041 46 Christoff, A. P. *et al.* Swab pooling: A new method for large-scale RT-qPCR
1042 screening of SARS-CoV-2 avoiding sample dilution. *PLoS One* **16**, e0246544,
1043 doi:10.1371/journal.pone.0246544 (2021).

1044 47 Thanh, T. T. *et al.* The Application of Sample Pooling for Mass Screening of SARS-
1045 CoV-2 in an Outbreak of COVID-19 in Vietnam. *Am J Trop Med Hyg*,
1046 doi:10.4269/ajtmh.20-1583 (2021).

1047 48 Chen, F. *et al.* Comparing two sample pooling strategies for SARS-CoV-2 RNA
1048 detection for efficient screening of COVID-19. *J Med Virol* **93**, 2805-2809,
1049 doi:10.1002/jmv.26632 (2021).

1050 49 Steel, K. & Fordham, E. *Coronavirus (COVID-19) Infection Survey pilot: England,*
1051 *Wales and Northern Ireland, 9 October 2020, Office for National Statistics,*
1052 *<[https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditi](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveyspilot/englandwalesandnorthernireland9october2020)*
1053 *[onsanddiseases/bulletins/coronaviruscovid19infectionsurveyspilot/englandwalesandno](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveyspilot/englandwalesandnorthernireland9october2020)*
1054 *[rthernireland9october2020](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveyspilot/englandwalesandnorthernireland9october2020)> (2020).*

1055 50 Medicines & Healthcare products Regulatory Authority. *Target Product Profile:*
1056 *Laboratory-Based SARS-CoV-2 Viral Detection tests,*
1057 *<[https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-](https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-laboratory-based-sars-cov-2-viral-detection-tests)*
1058 *[coronavirus-covid-19-work/target-product-profile-laboratory-based-sars-cov-2-viral-](https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-laboratory-based-sars-cov-2-viral-detection-tests)*
1059 *[detection-tests](https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-laboratory-based-sars-cov-2-viral-detection-tests)> (2021).*

1060 51 Aggarwal, D. *et al.* Genomic epidemiology of SARS-CoV-2 in the University of
1061 Cambridge identifies dynamics of transmission. (2021).

1062 52 Byrne, A. W. *et al.* Inferred duration of infectious period of SARS-CoV-2: rapid
1063 scoping review and analysis of available evidence for asymptomatic and
1064 symptomatic COVID-19 cases. *BMJ Open* **10**, e039856, doi:10.1136/bmjopen-2020-
1065 039856 (2020).

1066 53 Wolfel, R. *et al.* Virological assessment of hospitalized patients with COVID-2019.
1067 *Nature* **581**, 465-469, doi:10.1038/s41586-020-2196-x (2020).

1068 54 Hellewell, J. *et al.* Estimating the effectiveness of routine asymptomatic PCR testing
1069 at different frequencies for the detection of SARS-CoV-2 infections. *BMC Med* **19**,
1070 106, doi:10.1186/s12916-021-01982-x (2021).

1071 55 Singanayagam, A. *et al.* Duration of infectiousness and correlation with RT-PCR
1072 cycle threshold values in cases of COVID-19, England, January to May 2020. *Euro*
1073 *Surveill* **25**, doi:10.2807/1560-7917.ES.2020.25.32.2001483 (2020).

1074 56 He, X. *et al.* Temporal dynamics in viral shedding and transmissibility of COVID-19.
1075 *Nat Med* **26**, 672-675, doi:10.1038/s41591-020-0869-5 (2020).

1076 57 Long, Q. X. *et al.* Clinical and immunological assessment of asymptomatic SARS-
1077 CoV-2 infections. *Nat Med* **26**, 1200-1204, doi:10.1038/s41591-020-0965-6 (2020).

1078 58 Wolf, A., Hulmes, J. & Hopkins, S. *Lateral flow device specificity in phase 4 (post*
1079 *marketing) surveillance*, <[https://www.gov.uk/government/publications/lateral-flow-](https://www.gov.uk/government/publications/lateral-flow-device-specificity-in-phase-4-post-marketing-surveillance)
1080 [device-specificity-in-phase-4-post-marketing-surveillance](https://www.gov.uk/government/publications/lateral-flow-device-specificity-in-phase-4-post-marketing-surveillance)> (2021).

1081 59 Woloshin, S., Patel, N. & Kesselheim, A. S. False Negative Tests for SARS-CoV-2
1082 Infection - Challenges and Implications. *N Engl J Med* **383**, e38,
1083 doi:10.1056/NEJMp2015897 (2020).

1084 60 Sehanobish, E. *et al.* COVID-19-Induced Anosmia and Ageusia Are Associated With
1085 Younger Age and Lower Blood Eosinophil Counts. *Am J Rhinol Allergy*,
1086 19458924211004800, doi:10.1177/19458924211004800 (2021).

1087 61 von Bartheld, C. S., Hagen, M. M. & Butowt, R. Prevalence of Chemosensory
1088 Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis Reveals
1089 Significant Ethnic Differences. *ACS Chem Neurosci* **11**, 2944-2961,
1090 doi:10.1021/acscchemneuro.0c00460 (2020).

1091 62 Li, F. *et al.* Household transmission of SARS-CoV-2 and risk factors for susceptibility
1092 and infectivity in Wuhan: a retrospective observational study. *Lancet Infect Dis* **21**,
1093 617-628, doi:10.1016/S1473-3099(20)30981-6 (2021).

1094 63 Berke, E. M. *et al.* Pooling-in-a-pod: A Strategy for COVID-19 Testing to Facilitate
1095 Safe Return to School. *medRxiv*, 2021.2003.2024.21254230,
1096 doi:10.1101/2021.03.24.21254230 (2021).

1097 64 Cox C *et al.* Developing an ethical framework for asymptomatic COVID-19 testing
1098 programmes in higher education institutions [version 1; peer review: awaiting peer
1099 review]. *Wellcome Open Res* **6** (2021).

1100 65 Mina, M. J., Peto, T. E., Garcia-Finana, M., Semple, M. G. & Buchan, I. E. Clarifying
1101 the evidence on SARS-CoV-2 antigen rapid tests in public health responses to
1102 COVID-19. *Lancet* **397**, 1425-1427, doi:10.1016/S0140-6736(21)00425-6 (2021).

1103 66 Levine-Tiefenbrun, M. *et al.* Initial report of decreased SARS-CoV-2 viral load after
1104 inoculation with the BNT162b2 vaccine. *Nat Med*, doi:10.1038/s41591-021-01316-7
1105 (2021).

1106 67 Pavelka, M. *et al.* The impact of population-wide rapid antigen testing on SARS-CoV-
1107 2 prevalence in Slovakia. *Science*, doi:10.1126/science.abf9648 (2021).

1108 68 Scientific Advisory Group for Emergencies. *Innova Lateral Flow SARS-CoV-2*
1109 *Antigen test accuracy in Liverpool Pilot: Preliminary Data*, 26 November 2020,
1110 <[https://www.gov.uk/government/publications/innova-lateral-flow-sars-cov-2-antigen-](https://www.gov.uk/government/publications/innova-lateral-flow-sars-cov-2-antigen-test-accuracy-in-liverpool-pilot-preliminary-data-26-november-2020)
1111 [test-accuracy-in-liverpool-pilot-preliminary-data-26-november-2020](https://www.gov.uk/government/publications/innova-lateral-flow-sars-cov-2-antigen-test-accuracy-in-liverpool-pilot-preliminary-data-26-november-2020)> (2020).

1112 69 Peto, T. COVID-19: Rapid Antigen detection for SARS-CoV-2 by lateral flow assay: a
1113 national systematic evaluation for mass-testing. *medRxiv*,
1114 2021.2001.2013.21249563, doi:10.1101/2021.01.13.21249563 (2021).

1115 70 Tu, Y. P. *et al.* Swabs Collected by Patients or Health Care Workers for SARS-CoV-2
1116 Testing. *N Engl J Med* **383**, 494-496, doi:10.1056/NEJMc2016321 (2020).

1117 71 Lennard, Y. *et al.* An observational study of SARS-CoV-2 infectivity by viral load and
1118 demographic factors and the utility lateral flow devices to prevent transmission. URL
1119 [http://modmedmicro.nsms.ox.ac.uk/wp-](http://modmedmicro.nsms.ox.ac.uk/wp-content/uploads/2021/01/infectivity_manuscript_20210119_merged.pdf)
1120 [content/uploads/2021/01/infectivity_manuscript_20210119_merged.pdf](http://modmedmicro.nsms.ox.ac.uk/wp-content/uploads/2021/01/infectivity_manuscript_20210119_merged.pdf) (2021).

1121 72 Sabino, E. C. *et al.* Resurgence of COVID-19 in Manaus, Brazil, despite high
1122 seroprevalence. *Lancet* **397**, 452-455, doi:10.1016/S0140-6736(21)00183-5 (2021).

1123 73 Madhi, S. A. *et al.* Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the
1124 B.1.351 Variant. *N Engl J Med*, doi:10.1056/NEJMoa2102214 (2021).

1125 74 Shinde, V. *et al.* Preliminary Efficacy of the NVX-CoV2373 Covid-19 Vaccine Against
1126 the B.1.351 Variant. *medRxiv*, 2021.2002.2025.21252477,
1127 doi:10.1101/2021.02.25.21252477 (2021).

1128 75 Irwin, A. What it will take to vaccinate the world against COVID-19. *Nature* **592**, 176-
1129 178 (2021).

1130 76 Davies, N. G. *et al.* Estimated transmissibility and impact of SARS-CoV-2 lineage
1131 B.1.1.7 in England. *Science* **372**, doi:10.1126/science.abg3055 (2021).

1132 77 Hosmer, D. W. & Lemeshow, S. Goodness of fit tests for the multiple logistic
1133 regression model. *Communs Statist* **9**, 1043-1069 (1980).

1134 78 Janková, J., Shah, R. D., Bühlmann, P. & Samworth, R. J. Goodness-of-fit testing in
1135 high dimensional generalized linear models. *J. Roy. Statist. Soc., Ser. B* **82**, 773-795
1136 (2020).

1137 79 Enright, J. *et al.* SARS-CoV-2 infection in UK university students: Lessons from
1138 September-December 2020 and modelling insights for future student return. *INI*
1139 *Preprint Series* (2021). <<https://www.newton.ac.uk/files/preprints/ni20004.pdf>>.
1140
1141

Supplementary tables

Supplementary Table 1. Characteristics of study population.

		Eligible	Participating	Not-participating	P value
N		15,561	12,781	2,780	
Sex	Male	8,060 (51.8%)	6,504 (50.9%)	1,556 (56.0%)	<0.001
	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)		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)	<0.001
Ethnicity	White	9,453 (60.7%)	8,168 (63.9%)	1,285 (46.2%)	<0.001
	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	UK	9,870 (63.4%)	8,504 (66.5%)	1,366 (49.1%)	<0.001
	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	1 st	3,788 (24.3%)	3,336 (26.1%)	452 (5.5%)	<0.001
	2 nd	3,239 (20.8%)	2,673 (20.9%)	566 (20.4%)	
	3 rd	2,832 (18.2%)	2,434 (19.0%)	398 (14.3%)	
	4 th (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	Undergraduate	10,857 (69.8%)	9,288 (72.7%)	1,569 (56.4%)	<0.001
	Postgraduate	4,369 (28.1%)	3,368 (26.3%)	1,001 (36.0%)	
	Missing	335 (2.2%)	125 (1.0%)	210 (7.5%)	
Course*	Undergraduate arts and humanities	5,490 (35.3%)	4,553 (35.6%)	937 (33.7%)	<0.001
	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	1 person	472 (3.0%)	299 (2.3%)	173 (6.2%)	<0.001
	2 to 5 people	4,535 (29.1%)	3,703 (29.0%)	832 (29.9%)	
	6 to 10 people	9,228 (59.3%)	7,688 (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).

1158 **Supplementary Table 2. Tests conducted.**

1159

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

1160

1161 *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
1162 3 (weeks 8-9): whole testing pool screened each week.

1163

1164

1165 **Supplementary Table 3. Case ascertainment.**

1166

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	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	8	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	5 Oct – 18 Oct	47	38	47	1.2	1 to 2	1.2	1 to 2	85	10	142	33.1%
Weeks 3-7	19 Oct – 22 Nov	188	164	206	1.3	1 to 4	1.3	1 to 4	245	68	519	39.7%
Weeks 8-9	23 Nov – 6 Dec	17	3	3	1.0	1	1.0	1	5	2	10	30.0%
All weeks	5 Oct – 6 Dec	252	205	256	1.3	1 to 4	1.3	1 to 4	335	80	671	38.2%

1167

1168

1169

1170

1171

1172

*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.

1173 **Supplementary Table 4. Technical validation: number of replicates detected for each**
 1174 **target concentration of SARS-CoV-2 virus.**
 1175

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

1176

1177 **Supplementary Table 5. Distribution of CT values for individual confirmatory tests.**
 1178

	CT value					
	<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 programme	23 (9%)	85 (33%)	68 (27%)	43 (17%)	37 (14%)	256 (100%)
Presymptomatic with cardinal symptoms	6 (9%)	30 (44%)	21 (31%)	7 (10%)	6 (9%)	68 (100%)
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%)

1179

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			
	Male	346	6,158	1.00	0.86-1.17	0.97
	Other/unknown	5	147	0.61	0.21-1.34	0.28
Ethnicity	White	509	7,659			
	Other	153	3,944	0.58	0.48-0.70	<0.001
	Unknown	14	502	0.42	0.23-0.69	0.002
Residency	UK	570	7,934			
	International	103	4,102	0.35	0.28-0.43	<0.001
	Unknown	3	69	0.61	0.15-1.63	0.40
Year of study	1 st	367	5,195			
	2 nd	166	2,999	0.78	0.65-0.95	0.01
	3 rd 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
	25 th centile	6	5			
	Median	7	7			
	75 th 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			
	Male	1.21	1.03-1.42	0.02
	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	1 st			
	2 nd	0.63	0.52-0.76	<0.001
	3 rd 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

1188
1189

Supplementary Table 8: Model settings, parameters, and assumptions.

Parameter or setting	Value or assumption	Source	Change from HE-INI model ¹
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} This notation means: Size_of_household:fraction_of_households_t hat_size	From data: household structure of eligible students	Yes – {10: 0.5, 5: 0.5} used in preprint, arbitrary choice
Sizes of other activity groups	Full specification: {50:0.01, 10:0.5, 5:0.49} Notation as above	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) Note that this parameter has a relationship to the sizes and number of other activity groups: an increase in the number of other activity groups or their sizes gives similar results to an increase in this parameter For computational reasons it is more efficient to increase this parameter than the total number of non-household contacts	Yes – 0.2 used in preprint, chosen for plausibility
Mean non-infectious latent period	2.9 days	Alene <i>et al.</i> (2021) ²	Yes (small change) – 3 days in preprint, chosen for plausibility

Mean presymptomatic infectious period	3.6 days	From data: observed presymptomatic infectious period	Yes – 2 days in preprint, chosen for plausibility
Proportion asymptomatic	19.7%	From data: observed proportion of asymptomatic students	Yes – 50%, chosen for plausibility
Infectiousness of presymptomatics relative to symptomatics	Equal	By assumption	No change
Infectiousness of asymptomatics relative to symptomatics	18%	From data: observed ratio of secondary household attack rates for asymptomatic and symptomatic index cases	Yes – equal infectiousness used in preprint, chosen for plausibility
Mean infectious period after symptoms develop	4 days	Singanayagam, A. <i>et al.</i> (2020) ³	Yes – 10 days used in preprint, chosen for plausibility
Total mean period of infectiousness of an asymptomatic individual	Equal to symptomatic individual (mean 7.6 days)	By assumption	No change
Testing and isolation			
Probability and speed of symptomatic tests	Symptomatic individuals immediately seek tests with no false positives or false negatives. Positive tests result in household isolation from the following day	By assumption	No change
Participation in asymptomatic screening	100%	By assumption	No change
Performance of asymptomatic tests	Asymptomatic testing is perfect with no false negatives or false positives. Positive tests result in household isolation from the following day	By assumption	No change
Isolation	Entire household isolates upon any positive test within the household	By assumption	No change
Expected isolation period	14 days	By assumption	No change
Isolation implications for contact	When a household isolates, all contacts between members of the household and non-members cease, but all contacts within the household continue as before including with the index case.	By assumption	No change
Tracing	50% probability of each non-household contact of a test-positive being contacted and isolating from the day after the positive test.	By assumption	No change

1. Enright, J. *et al.* SARS-CoV-2 infection in UK university students: Lessons from September-December 2020 and modelling insights for future student return. *INI Preprint Series* (2021). Available in preprint at: <https://www.newton.ac.uk/files/preprints/ni20004.pdf>.
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).

1197 **Supplementary notes**

1198 **University of Cambridge Asymptomatic COVID-19 Screening Programme Consortium**

1199 **Rapid Response Working Group to Test, Trace and Isolate**

1200 Patrick Maxwell, Nicholas Matheson, Chris Abell, Vickie Braithwaite, Craig Brierley, Jon Crowcroft,
1201 Aastha Dahal, Kathryn Faulkner, Michael Glover, Ian Goodfellow, Jane Greated, Jon Holgate, Rob
1202 Howes, Laura James, Paul Lehner, Ian Leslie, Kathleen Liddell, Ben Margolis, Duncan McFarlane,
1203 Sally Morgan, Linda Sheridan, Sally Valletta, Anna Vignoles, Martin Vinnell, Ben Warne, Michael
1204 Weekes, Mark Wills

1205

1206 **Clinical Research Nurse Team**

1207 Stewart Fuller, Marina Metaxaki, Sarah Hilborne, Sarah Berry, Mahin Bagheri Kahkeshi, Dawn
1208 Hancock, Jennifer Winster

1209

1210 **Biopharma RD, AstraZeneca, Cambridge**

1211 Rob Howes, Alexandra Orton, Julie Douthwaite, Steve Rees

1212

1213 **Charles River Laboratories, Chesterford Research Park, Saffron Walden, UK**

1214 Christopher Brown, Daniel R Jones, Fred Kuenzi, Jennifer Rankin, Ian Waddell

1215

1216 **Statistics/modelling**

1217 Jessica Enright, Richard Samworth

1218

1219 **University Information Services**

1220 Jon Holgate, Vijay Samtani, Gabriela Ahmadi-Assalemi, Tom Feather, Robin Goodall, Steve
1221 Hoensch, Dean Johnson, Martin Hunt, Nick Mathieson, Katya Nikitina, Zara Sheldrake

1222

1223 **Clinical School Computing Service**

1224 Martin Keen, Aris Sato, David Connor, Jonathan Tolhurst, Jack Williman

1225

1226 **Clinical School Information Governance Office**

1227 Victoria Hollamby

1228

1229 **COVID-19 Operations Centre, University of Cambridge**

1230 Gillian Weale, Sinead Jordan, Tania Fatseas, Peter Taylor, Christine Georgiou, Michelle Caspersz,
1231 Claire McNulty, Richard Davies

1232

1233 **Institute for Manufacturing, University of Cambridge**

1234 Duncan McFarlane, Rebecca Clarke, Darius Danaei, Rory Dyer, Rob Glew, Oliver Lambson

1235

1236 **Testing Kit Packing Team**

1237 Karen Gibbs, Barbara Mozdzen, Gabor Raub, Asako Radecki, Phil White, Robert Hughes, Lucie
1238 Gransden, Matt Ceaser

1239

1240 **Administrative Support**

1241 Robert Sing, Karl Wilson

1242

1243 **Operational Systems Support**

1244 Ajith Parlikad, Maharshi Dhada, Tom Ridgman

1245

1246	University Messenger Service
1247	Diane Mungovan, Steve Matthews, Paul Searle, John Mills
1248	
1249	Collegiate University
1250	Andy Neely, Robert Henderson, Edna Murphy, Matthew Russell, Anthony Freeling, Steve Poppitt, Jo
1251	Tynan
1252	
1253	Data Protection and Information Compliance
1254	James Knapton, Filippo Marchetti
1255	
1256	COG-UK Cambridge
1257	Sharon Peacock, Ian Goodfellow, Ewan Harrison, Dinesh Aggarwal, Thomas Fieldman, Beth Blane,
1258	Yasmin Chaudhry, Daniela De Angelis, Theresa Feltwell, Iliana Georgana, Nazreen F. Hadjirin, Grant
1259	Hall, William Hamilton, Myra Hosmillo , Chris Illingworth, Aminu Jahun, Danielle Leek, Catherine
1260	Ludden, Malte Pinckert
1261	
1262	Cambridge University Hospitals NHS Foundation Trust
1263	Ashley Shaw, Afzal Chaudhry, Nicholas M Brown, Lenette Mactavous, Sophie Hannan, Aleksandra
1264	Hosaja, Clare Leong
1265	
1266	Occupational Health and Wellbeing (Cambridge University Hospitals NHS Foundation Trust) Jo
1267	Wright, Natalie Quinnell, Chris Workman, Mark Ferris, Giles Wright
1268	
1269	Public Health Directorate, Cambridgeshire County Council and Peterborough City Council, UK
1270	Emmeline Watkins, Elizabeth Wright, Linda Sheridan, Kathryn Faulkner, Vickie Braithwaite

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryInformationWarneetal.pdf](#)
- [ExtendedFiguresHighResWarneetal.pdf](#)
- [MainFiguresHighResWarneetal.pdf](#)