A cluster-randomised trial of the impact of a policy of daily testing for contacts of COVID-19 cases on attendance and COVID-19 transmission in English secondary schools and colleges

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44 Summary

46 **Background**
47 School-based COVID-19 contacts in England are asked to self-isolate at home, missing key
48 educational opportunities. We trialled daily testing of contacts as an alternative to test if
49 this resulted in similar control of transmission, while allowing more school attendance.

51 **Methods**
52 We performed an open-label cluster-randomised controlled trial in secondary schools and
53 further education colleges in England (ISRCTN18100261). Schools were randomised to self-
54 isolation of school-based COVID-19 contacts for 10 days (control) or to voluntary daily
55 lateral flow device (LFD) testing with LFD-negative contacts remaining at school
56 (intervention).

58 Co-primary outcomes in all students and staff were symptomatic PCR-confirmed COVID-19,
59 adjusted for community case rates, to estimate within-school transmission (non-inferiority
60 margin: <50% relative increase), and COVID-19-related school absence. Analyses were
61 performed on an intention to treat (ITT) basis using quasi-Poisson regression, also
62 estimating complier average causal effects (CACE). Secondary outcomes included
63 participation rates, PCR results in contacts and performance characteristics of LFDs vs. PCR.

65 **Findings**
66 Of 99 control and 102 intervention schools, 76 and 86 actively participated (19-April-2021 to
67 27-June-2021); additional national data allowed most non-participating schools to be
68 included in co-primary outcomes. 2432/5763(42.4%) intervention arm contacts participated.
69 There were 657 symptomatic PCR-confirmed infections during 7,782,537 days-at-risk
70 (59.1/100k/week) and 740 during 8,379,749 days-at-risk (61.8/100k/week) in the control
71 and intervention arms respectively (ITT-adjusted incidence rate ratio, aIRR=0.96[95%CI 0.75-
72 1.22;p=0.72]) (CACE-aIRR=0.86[0.55-1.34]). There were 55,718 COVID-related absences
73 during 3,092,515 person-school-days(1.8%) and 48,609 during 3,305,403 person-school-
74 days(1.5%) in the control and intervention arms (ITT-aIRR=0.80[95%CI 0.53-1.21;p=0.29])
75 (CACE-aIRR 0.61[0.30-1.23]). 14/886(1.6%) control contacts providing an asymptomatic PCR
76 sample tested positive compared to 44/2981(1.5%) intervention contacts (adjusted odds
77 ratio, aOR=0.73[95%CI 0.33-1.61;p=0.44]); rates of symptomatic infection in contacts were
78 44/4665(0.9%) and 79/5955(1.3%), respectively (aOR=1.21[0.82-1.79;p=0.34]).

80 **Interpretation**
81 Daily contact testing of school-based contacts was non-inferior to self-isolation for control
82 of COVID-19 transmission, with similar rates of student and staff symptomatic infections
83 with both approaches. Infection rates in school-based contacts were only around 2%. Daily
84 contact testing should be considered for implementation as a safe alternative to home
85 isolation following school-based exposures.

87 **Funding**
88 UK Government.

Introduction

In the COVID-19 pandemic, disease control in schools has ranged from no controls at one extreme, to school closure at another, the latter largely based on evidence regarding transmission of influenza.[1] Between these poles, different degrees of control have been applied, including isolation of suspected or confirmed cases, to isolation of close contacts of cases.[2] With widespread availability of SARS-CoV-2 point-of-care testing, daily contact testing (DCT) has been modelled and piloted as an alternative to compulsory unsupervised isolation of contacts.[3,4,5] DCT allows contacts to attend school provided a daily SARS-CoV-2 test is negative. Daily testing with antigen lateral flow devices (LFDs) is feasible,[6] with rapid turnaround times, relatively low cost and good detection of virus.[7,8,9] In addition to allowing students and staff to remain at school, DCT may make regular asymptomatic testing more popular and improve contact reporting, by removing the social penalty of positive cases triggering isolation in contacts.[10] This in turn may improve case detection and therefore may even reduce transmission.[3] However, concerns about LFD performance, especially outside of healthcare and expert settings, have left uncertainty about whether DCT is appropriate for schools or more widely.[11]

A policy of self-isolation of contacts assumes this reduces the risk of onward transmission in schools. In practice, its impact is unknown: adherence to isolation is incomplete,[12] and the number of isolation-days required to prevent one onward transmission has not been calculated. Evidence is lacking that the benefit of the policy outweighs the clear social[13,14] and educational[15,16,17] disadvantages. Contact-tracing data from England suggests that transmission following contact in secondary schools is infrequent, and occurs in <3% of contacts of infected teenagers.[18] Observational reports from England found educational outbreaks are uncommon, and strongly associated with community incidence.[19]

We undertook a cluster-randomised controlled trial of DCT in students and staff at secondary schools and colleges in England to determine if DCT increases school attendance and to assess the impact of DCT on SARS-CoV-2 transmission within the school.

Methods

Study design and participants

We conducted an open-label, cluster-randomised controlled trial to assess the effectiveness of offering daily testing to contacts of COVID-19 cases (ISRCTN18100261). The study took place in secondary schools and further education colleges in England. Secondary schools were studied as students at these schools were already participating in asymptomatic screening with LFDs, and so the trial built upon existing infrastructure which was not present in primary schools (students ≤11 years). Schools and colleges (hereafter collectively referred to as schools) were eligible to participate if willing to follow the trial procedures and able to operate assisted testing on site. A representative of the institution provided consent electronically. Participation by individual student and staff contacts was voluntary and followed written or electronic completion of a consent form. After randomisation, parents or guardians provided consent for participants <16 years old and for those otherwise unable to give consent. The study protocol was reviewed, and ethical approval granted, by Public Health England's Research Ethics and Governance Group (ref R&D 434).

134   The study was done in accordance with the Declaration of Helsinki and national legislation.
135   A nested qualitative process study of acceptability and feasibility for students, parents and
136   staff is reported separately.[20] The study protocol and analysis plan are provided as
137   supplementary material.
138

139   ## Randomisation
140   Schools were randomly assigned 1:1 to either a policy of offering contacts daily testing over
141   7 days to allow continued school attendance (intervention arm) or to follow usual policy of
142   isolation of contacts for 10 days (control arm). Stratification was used to ensure schools
143   representative of those in England were balanced between study arms (Table 1, details in
144   supplement).
145

146   ## Procedures
147   All control and intervention arm schools followed the national policy of offering twice
148   weekly asymptomatic testing with LFDs. Individuals with positive LFD results were required
149   to self-isolate immediately and requested to obtain a confirmatory PCR test within 2
150   days.[21] Those with indicator symptoms of possible COVID-19 (new cough, fever, loss or
151   change in taste or smell) were required to self-isolate along with their household and obtain
152   an urgent PCR test.
153

154   If a student or staff member tested positive by LFD or PCR, close contacts ("contacts") were
155   identified by schools using national guidelines (see supplement). Those in close contact with
156   a case <48h prior to symptom onset (or a positive test if asymptomatic) were required to
157   self-isolate for 10 days.[22]
158

159   At intervention arm schools, contacts were offered DCT as an alternative to self-isolation,
160   provided the contact was school-based (i.e. with a staff member or student), the contact did
161   not have indicator symptoms of COVID-19, and contacts were able to attend for on-site
162   testing at school. Contacts were excluded from DCT if they had a household member who
163   was isolating following a positive COVID-19 test. Contacts who did not consent to DCT were
164   required to self-isolate for 10 days.[22]
165

166   Participants who agreed to DCT swabbed their own anterior nose; swabs were tested by
167   school staff using a SARS-CoV-2 antigen LFD (Orient Gene).[23] Participants who tested
168   negative were informed and released from isolation that day to attend education, but were
169   asked to self-isolate after school and on non-testing days (weekends/holidays). Those with 5
170   negative tests over ≥7 days were released from self-isolation, allowing for no testing at
171   weekends. Where a school-based close contact tested positive, they were instructed to self-
172   isolate along with their household, their school-based contacts were identified, and the
173   process repeated for these contacts.
174

175   ## Data collection
176   A study worker was funded at each participating school. Schools provided a list of all
177   students and staff, including personal identifiers and demographics. For consented
178   randomised schools that stopped active participation, where available, a list of students was
179   provided by UK Government Department for Education (DfE).

180

181 Schools reported the numbers of staff and students present on each school day, absent for
182 COVID-19-related reasons and absent for other reasons. Data from schools who stopped
183 participating, where available, were obtained from DfE.

184

185 Schools recorded each SARS-CoV-2 infection ("index case") brought to their attention,
186 including PCR-positive cases and LFD-positive cases without a subsequent PCR test. LFD-
187 positive-PCR-negative individuals were not considered cases. The school-based contacts of
188 each index case, whether the contact consented to study procedures, and LFD results were
189 recorded. During the trial, the trial management team were blinded to the combined data.

190

191 ## PCR testing
192 Results of routine SARS-CoV-2 tests performed outside of the study in staff and students
193 were obtained from national public health data ("NHS Test and Trace"). Dedicated study
194 PCR testing was also undertaken in consenting contacts in both study arms on day 2 and 7
195 of the testing/isolation period. In addition, study PCRs were obtained from consenting
196 LFD/PCR-positive individuals for later analysis (see supplement).

197

198 ## Outcomes
199 The co-primary outcomes, across all students and staff, were (i) the number COVID-19-
200 related school absences amongst those otherwise eligible to be in school and (ii) the extent
201 of in-school COVID-19 transmission. Non-inferiority in transmission was considered
202 appropriate, as the intervention was hypothesised to produce beneficial increases in
203 attendance. Transmission was estimated from rates of symptomatic PCR-positive infections
204 recorded by NHS Test and Trace, after controlling for community case rates. Both these
205 endpoints were assessed using study data for actively participating schools and using
206 national administrative data on student attendance and student and staff lists for non-
207 participating randomised schools. Rates of symptomatic PCR-positive community tests were
208 compared as the incidence of these tests was not expected to be impacted by the study
209 intervention, whereas more intensive sampling of asymptomatic contacts in intervention
210 schools may have detected more asymptomatic infection. Twice weekly asymptomatic LFD
211 testing was not reliably reported, so results were not compared between arms.

212

213 Secondary outcomes reported include DCT participation rates in the intervention arm, the
214 proportion of contacts testing positive on asymptomatic study PCR tests and symptomatic
215 routine PCR tests, and the performance characteristics of LFD vs. PCR testing.

216

217 ## Statistical analysis
218 Rates of COVID-related absences and symptomatic PCR-positive SARS-CoV-2 infections were
219 compared on an intention to treat (ITT) basis using quasi-Poisson regression to account for
220 over-dispersion, considering each school as the unit of analysis. We adjusted for
221 randomisation strata groups and participant type (student/staff) and accounted for
222 repeated measurements from the same school over time (see supplement for details and
223 for following analyses). Infection incidence models were also adjusted for community SARS-
224 CoV-2 case counts at the lower tier local authority level (LTLA) in the prior week. To account
225 for incomplete participation in DCT, we present complier average causal effects (CACE)

226 estimates for both primary outcomes, which estimate the impact of the intervention
227 amongst those actively participating.
228
229 We report DCT uptake in intervention arm participants, on a per day and per participant
230 basis. We used Poisson regression to investigate factors associated with per individual
231 participation rates, including the randomisation stratification groups, participant type, age,
232 sex, and ethnicity.
233
234 The proportion of close contacts testing positive on an asymptomatic study PCR test or
235 symptomatic community PCR test was compared between study arms using logistic
236 regression. Given there were relatively few PCR-positive contacts, adjustment was made
237 only for randomisation strata groups and local case counts in the previous week.
238
239 We compared the performance of LFD to PCR testing in participants tested by both methods
240 on the same day, or up to 2 days later for those testing LFD-positive, regarding PCR testing
241 as the reference standard.
242

Sample size and power
244 The challenge with setting a non-inferiority margin for transmission events is that the
245 margin's meaning is highly dependent on the control group event rate. It was not possible
246 to determine the transmission event rate in the control group prior to the trial start, and it is
247 subject to on-going change. However, it was considered at the time of writing the study
248 protocol that with an example infection rate in contacts of 20%, an upper bound of the
249 confidence interval of an absolute increase of 10%, i.e., relative increase in transmission of
250 up to 50% would be acceptable. Given the uncertainties in the absolute rates of
251 transmission events in each arm, we powered the trial to detect a difference in school
252 attendance (details in supplement).
253

Role of the funding source
255 The UK Government Department of Health and Social Care sponsored the trial and was
256 involved in study design, matching of NHS Test and Trace data with study records, data
257 curation and interim monitoring. Otherwise, the study sponsor had no role in data analysis
258 and interpretation or writing and submission of the report.
259

Results
261 201 schools were randomised (Table S1;Figure S1) and started participating in the 10-week
262 study between 19-April-2021 and 10-May-2021 and continued until the pre-appointed stop
263 date 27-June-2021; 76/99(77%) control and 86/102(84%) intervention schools actively
264 participated, returning student/staff lists and attendance data (Figure 1).
265

Baseline characteristics
267 Schools were randomised using 9 school-type strata (Table 1). Schools in the control and
268 intervention arms had a median(IQR) 1014(529-1376) and 1025(682-1359) students and
269 142(91-189) and 125(91-173) staff respectively. Ages, sex and ethnic groups in students and
270 staff were similar between the study arms, most students were aged 11-18y (Table 2).

271

Index cases and contacts

273 The 76 and 86 actively participating control and intervention schools reported 338 and 450
274 index cases (students or staff) respectively, resulting in 5097 and 6721 recorded school-
275 based contact events in 4400 and 5797 individuals. A total of 247 and 343 control and
276 intervention arm index cases had ≥1 contact, where the 10 days following the contact event
277 included ≥1 study school day. The remaining index cases had no reported close contacts,
278 e.g. having tested positive during a weekend/holiday. These 4463 and 5763 contacts in 47
279 and 59 control and intervention schools involved a total of 22,466 and 27,973 school days
280 where without the intervention students and staff would have been asked to isolate at
281 home. In the intervention arm, this represented a theoretical maximum of
282 27,973/4,105,826(0.68%) school days where DCT could potentially prevent COVID-related
283 absences. On 13,846/27,973(49.5%) days an LFD result was recorded (or the contact had
284 already completed follow-up, i.e., recorded ≥5 tests or a positive test). In 1241 contact
285 episodes, the contact declined to participate in DCT (5598 person-school-days;19.9%) and
286 on 2600(9.2%) person-school-days a participating contact was unavailable testing (i.e. did
287 not attend school or declined testing). Testing on 4457(15.8%) person-school-days did not
288 occur after the whole cohort of contacts or school was sent home to isolate, following
289 either school or public health agency intervention (Figure 2A). These participation pauses
290 occurred at 14 schools, 5 due to school capacity issues, 6 following school or public health
291 agency concern about the Delta variant, and 3 after public health concern about cases in the
292 school arising from community transmission. No pause was instituted because of excess
293 transmission attributed to the intervention.

294

295 Per day DCT participation was highest at the start of the study and lowest in the week prior
296 to the "half-term" holiday (31-May-2021 to 04-June-2021) when participation fell,
297 predominately due to school-wide participation pauses (Figure 2A,2B).

298

299 Using reporting of ≥3 LFD results or an LFD-positive result to summarise participation per
300 contact rather than per day, 2432/5763(42.4%) contacts participated, with differing rates by
301 school (Figure 2C). The median(IQR) participation across the 59 schools was 63%(40-79%).
302 Staff were more likely to participate than students (adjusted rate ratio=1.40;95%CI 1.09-
303 1.80;p=0.009). Amongst schools with ≤17% of students receiving free school meals,
304 participation rates were higher in schools with students aged 11-16 years compared to 11-
305 18 years (Table 3).

306

COVID-related absences

308 Rates of student and staff COVID-related absence, due to known or suspected COVID or as a
309 contact, were compared. Student attendance data were available for part or all of the study
310 from 91(92%) of control and 99(97%) intervention schools; with data for 3551/4146(86%)
311 and 3836/4261(90%) of possible school-school day combinations (Figure S2). Similarly, staff
312 attendance was available from 94(95%) control and 100(98%) intervention arm schools, for
313 3767/4146(91%) and 3925/4261(92%) days. 95,545 and 102,134 students and 14,687 and
314 14,811 staff were reported in control and intervention arm attendance data. (Total numbers
315 of students and staff in aggregate attendance data differ to totals from student/staff
316 identifier lists used to identify symptomatic cases [Table 2], reflecting different underlying
317 data sources and different schools with available data).

318

Students had 55,718 COVID-related absences during 3,092,515 person-school-days in the control arm (1.80%), and 48,609 during 3,305,403 person-school-days in the intervention arm (1.47%, Figure 3). Rates of staff COVID-related absences were 3704/566,502(0.65%) in control schools and 2932/539,805(0.54%) in intervention schools.

On an ITT basis, adjusting for the randomisation strata group and participant type, the adjusted incidence rate ratio, aIRR, for COVID-related absence in the intervention arm was 0.80 (95%CI 0.54-1.19;p=0.27) (Table 4;Table S2). Overall, staff were less likely to be absent for COVID-related reasons than students (aIRR=0.39;95%CI 0.31-0.48;p<0.001), but there was no evidence a difference in the effect of the intervention between students and staff (heterogeneity p=0.98). As no covariate changed with time, the originally proposed approach has a more conservative confidence interval than required. We repeated the analysis aggregating the data per school and participant type, yielding an aIRR of 0.80 (95%CI 0.62-1.03;p=0.085;Table S3).

As per day participation in the intervention arm was 49.5%, we estimated the impact of the intervention among those participating; the point estimate showed a greater reduction in absences (CACE aIRR=0.61 (95%CI 0.30-1.23;Table S2). Applying this point estimate (with the caveat the range of uncertainty is wide) to COVID-related absence in control arm students (1.80%), would equate to a 39% relative and 0.70% absolute reduction in school days missed due to COVID. CACE estimates were relatively unaffected by the choice of imputation strategy for schools with no contacts and therefore no participation data (Table S4). See Tables S5-S6 for separate ITT and CACE results for students and staff.

There was no evidence of an impact on all-cause absence rates (ITT aIRR=0.97, 95%CI 0.82-1.16, p=0.77), with non-COVID-related reasons responsible for most absences (Table S7).

Symptomatic PCR-confirmed SARS-CoV-2 infection

PCR results from symptomatic SARS-CoV-2 infections in students were available for 96/99(97%) control schools and 101/102(99%) intervention schools and staff results for 76(76%) and 85(83%) respectively.

614 and 683 students at control and intervention schools tested PCR-positive and reported symptoms during 6,966,653 and 7,541,525 days-at-risk (61.7 and 63.4 cases/100,000 population/week). Rates in staff were 43/790,219 (38.1/100,000/week) and 57/819,487 (48.7/100,000/week). Incidence rose during the study, as the Delta variant spread nationally,[24] similarly in each arm (Figure 4A). Incidence was higher than the number of index cases reported by schools, partly because not all randomised schools actively reported cases and in active schools not all community-diagnosed infections were reported or recorded (Table S8).

Adjusting for the randomisation strata, participant type, and the community rate of SARS-CoV-2 infection in the previous week, there was no evidence of difference between study arms in symptomatic PCR-confirmed infection (ITT aIRR=0.96;95%CI 0.75-1.22;p=0.72) (Table 4;Table S9). Overall rates of infection were lower in staff than students (aIRR=0.75;95%CI 0.61-0.92;p=0.006), but there was no evidence that the effect of the

365   intervention differed in staff and students (heterogeneity p=0.41). Infection rates in
366   students were approximately linearly related to local case counts, plateauing as community
367   incidence rose (Figure S3); estimates were similar with varying plausible lags between
368   community case counts and student and staff infections (Table S10).
369
370   A CACE analysis allowing the impact of the intervention to be estimated given theoretical
371   full participation, also showed no evidence of difference between study arms in
372   symptomatic PCR-confirmed infection (aIRR=0.86;95%CI 0.55-1.34). CACE estimates were
373   relatively unaffected by the choice of imputation strategy for schools with missing
374   participation data (Table S11).
375
376   Similar results were obtained in a secondary analysis of any positive PCR-result from routine
377   community-based testing (Figure 5B) (ITT aIRR=0.96;95%CI 0.76-1.20;p=0.71 and CACE
378   aIRR=0.88;95%CI 0.57-1.41) (Table S12). There was no evidence of a difference in the effect
379   of the intervention for students and staff (ITT model, heterogeneity p=0.21). Separate
380   analyses for students and staff for symptomatic and any PCR-positive infection are
381   presented in Tables S13-S16.
382

Incidence of PCR-confirmed infection in contacts

384   PCR testing of asymptomatic contacts was undertaken in 886 non-overlapping contact
385   episodes in the control arm, 14(1.6%) tested PCR-positive, 1(0.1%) indeterminate and
386   871(98%) negative. In 2981 intervention arm contacts, 44(1.5%) tested positive, 14(0.5%)
387   indeterminate and 2923(98%) negative. Adjusting for randomisation stratification group and
388   community case counts in the prior week, there was no evidence that the proportion of
389   contacts testing positive varied between study arms (adjusted OR, aOR=0.73;95%CI 0.33-
390   1.61;p=0.44) (Table S17). Of control and intervention arm contacts testing
391   positive/indeterminate, 4/15(27%) and 19/58(33%) went on to have a positive symptomatic
392   test (exact p=0.76).
393
394   We also compared the proportion of contacts with a symptomatic PCR-positive test, which
395   included those initially testing positive while asymptomatic above who went on to have a
396   symptomatic test. This analysis is contingent on schools reporting contacts, with several
397   control arm schools with higher incidence not actively participating and reporting contacts
398   (Figure S4). In the control arm 44/4665(0.9%) contacts tested PCR-positive within 10 days,
399   compared to 79/5955(1.3%) in the intervention arm. Adjusting for randomisation strata
400   groups and community case counts, there was no evidence that the proportion of contacts
401   testing positive differed between arms (aOR=1.21;95%CI 0.82-1.79;p=0.34) (Table S18).
402

Performance characteristics of LFDs vs. PCR

404   Across the study, and the non-randomised pilot phase, 4757 contacts completed at least
405   one LFD during DCT generating 20,289 LFD results overall. For 3226 a paired PCR test was
406   available from the same day, or up to 2 days later for those testing LFD-positive. 3166 were
407   PCR-negative and 60 PCR-positive. Specificity was 3164/3166 (99.93%, exact binomial 95%CI
408   99.77-99.99%) and sensitivity 32/60 (53%, 40-66%) (Table S19). These results largely reflect
409   performance in students (Table S20,S21), as 3003/3226(93.1%) of participants with paired
410   tests were students. PCR-positive cycle threshold (Ct) values were lower in those testing

411 LFD-positive (median 18.5, IQR 16.3-22) than LFD-negative (median 25.3, IQR 21.6-28.5)
412 (Kruskal-Wallis p<0.001;Figure S5).

Discussion

414 Daily LFD testing of school-based COVID-19 contacts was trialled as a voluntary alternative
415 to 10 days of self-isolation. Although DCT avoids students and staff missing school while
416 isolating, at the conception of the trial there was uncertainty whether it would substantially
417 increase SARS-CoV-2 transmission, e.g. via infections missed by LFD testing.[3] The trial
418 provides evidence this was not the case.

420 We investigated the incidence of symptomatic infection as an unbiased outcome measure
421 that could be ascertained across nearly all schools, as national public health policy was that
422 all symptomatic children and adults, whether or not they had a LFD test, should obtain a
423 PCR test for SARS-CoV-2. As the intervention was not expected to impact the relative
424 incidence of asymptomatic versus symptomatic infection this measure should also indicate
425 the impact on all infections. Based on a non-inferiority margin of ensuring any relative
426 increase in symptomatic infection, as a proxy for transmission, did not exceed >50%, we
427 show allowing student and staff contacts to remain in school after a negative lateral flow
428 test was non-inferior to routine isolation. On an ITT basis, i.e. implementing DCT at
429 participation rates seen in the trial, using data for students from 197/201 schools and staff
430 data from 161/201 schools, we can be 97.5% confident that any increase in the rate of
431 symptomatic infection did not exceed 22% more than seen in the control arm. If all those
432 eligible to participate did so, then, based on a CACE model, we can be 97.5% confident that
433 any increase does not exceed 34%. In both analyses the point estimate favours a slight to
434 modest reduction in incidence with the intervention.

436 The range of absolute changes in symptomatic infection rates potentially seen with the
437 intervention, depends on prevailing incidence. At the average incidence in the control arm
438 during the study (0.06% students/week), the range of uncertainty in the impact of the
439 intervention is equivalent to 1.2 fewer to 0.9 more infections/1000-student-school/month,
440 or 3.6 fewer to 2.7 more at the highest weekly rate seen (0.18% students/week).
441 Throughout the study, cases in both arms remained well below the >1% level seen in 2020
442 when schools remained open.[25] Staff had lower rates of infection than students. There
443 was no evidence of a difference in the effect of the intervention for students and staff.

445 Asymptomatic and symptomatic infections were uncommon in school-based contacts in
446 both study arms: 1.6% and 1.5% of students and staff participating in study PCRs tested
447 positive while asymptomatic, and 0.9% and 1.3% tested positive in symptomatic testing in
448 the control and intervention arms respectively. These figures are comparable to the
449 estimates for school-age children from national contact-tracing data.[18] Therefore, given
450 precautions in place in schools during the trial (routine mask use was discontinued during
451 the trial on 17-May-2021, but other precautions were maintained), the overall risks to
452 students and staff following exposure to a contact at school are low. Indeed, whether the
453 extent of transmission and performance of LFDs (discussed below) is sufficient to make
454 contact testing necessary and cost-effective will require careful discussion and may vary
455 with changes in incidence, virus transmissibility or the prevalence of any vaccine evasive
456 strains. Participation in study PCR testing in control schools was lower than in the

457 intervention schools, in part because participation in DCT facilitated intervention arm PCR-
458 testing and because the greater awareness of the study in intervention schools. It is unclear
459 whether this introduced bias in the results for the study PCR tests, however we also found
460 no evidence of difference in symptomatic infection rates in contacts.
461
462 We did not clearly demonstrate superiority of the intervention for avoiding student and
463 staff COVID-related school absences. This possibly reflects that the trial was relatively
464 underpowered given the large extent of variation in absence rates over time and between
465 schools, requiring overdispersion to be accounted for in regression models fitted. Pooling
466 data on a per school basis, in an ITT analysis, our point estimate showed a 20% decrease in
467 COVID-related absences, but with a broad range of uncertainty (95%CI 0.62-1.03), similarly
468 in the CACE analysis amongst those who participated the point estimate was a 38%
469 reduction, but with broader uncertainty (95%CI 0.29-1.33).
470
471 Reductions in COVID-related absences were not greater because not all those eligible
472 participated, and not all absences were amenable to the intervention, e.g. household
473 contacts were ineligible. However, despite the lack of statistical evidence from the trial, in
474 the absence of increased transmission, it is reasonable to assume that a policy allowing
475 students and staff to remain in school would lead to increased attendance, but this may be
476 more limited than initially anticipated.
477
478 DCT participation rates in intervention arm contacts were 42% on a per-person basis with
479 marked variation between schools (range 0-100%). Staff were more likely to participate
480 than students. Although contacts at government-funded schools with students 11-16 years
481 old with a low percentage of free school meals were most likely to participate, other school
482 types were similar, such that differences in participation related to factors other than school
483 type. A qualitative analysis of interviews with participants to understand why some
484 participated and others did not will be presented separately.[20] Additionally, at some
485 stages, schools paused the intervention because of capacity limitations or public health
486 officials' concerns about the Delta lineage or rising transmission in the community. No local
487 public health teams reported concern that transmission increased because of this study. We
488 did not formally assess compliance with isolation in the control arm, although it was school
489 policy that known cases and contacts did not attend school. However, it is still possible that
490 in both study arms there was incomplete compliance with isolation at home outside of
491 school hours and during school hours in the control arm, particularly as lockdown
492 restrictions eased.
493
494 Previous estimates for the performance of antigen LFDs compared to PCR testing have
495 varied markedly.[7,9,26] Here we estimate the overall sensitivity of school-based LFD
496 testing in largely asymptomatic individuals as 53%, i.e., within the range of previously
497 reported rates. It is worth noting our findings on transmission in this study are in the
498 context of this level of performance. Specificity was 99.93%. As LFD performance varies by
499 viral load[27] performance can change as the population viral load distribution changes.
500 Consistent with previous reports[7] we find higher viral loads, i.e. lower PCR cycle threshold
501 values, are associated with increased sensitivity, and therefore LFDs are more likely to
502 detect those who are most infectious.[18]
503

504 The study has several limitations. Schools and colleges, despite provision of dedicated
505 resources, were not always able to participate due to competing pressures. It is also likely as
506 a result that data capture was imperfect, e.g. it is possible that not all PCR-positive cases
507 were reported to schools, and not all contacts were documented for all index cases.
508 However, our primary outcomes are robust to this. We used the incidence of
509 symptomatically driven testing as a primary endpoint as this was least likely to be affected
510 by the two testing strategies; in fact, there was little difference in the incidence of all
511 community PCR tests between the study arms. Relying on linkage to Test and Trace data is a
512 potential weakness, as it depended on imperfectly recorded identifiers, however this would
513 not be expected to differ between study arms. Furthermore, using incidence data means we
514 do not directly measure within-school transmission, rather we estimate it by controlling for
515 the rate of community infections, as a proxy for the extent of introductions into the school.
516 The trial was conducted during periods of low to moderate COVID-19 incidence. We
517 therefore did not estimate the impact of DCT in high incidence settings; monitoring of the
518 impact of DCT may be needed if it is deployed when incidence is high. Changes in incidence
519 may relate to new variants, which may impact LFD performance, and so on-going
520 assessment of LFD performance would be needed as well. High incidence may also pose
521 logistical challenges, in the last two weeks of the study, community incidence rose making
522 the DCT protocol unwieldy for some schools, given the space and staff required to perform
523 testing. We did not have sufficient power to study if the intervention had different impacts
524 across different school types and settings.
525
526 Future work includes whole-genome sequencing of positive samples from school members
527 and from the community, which may help analyse transmission networks in schools,
528 including during periods of higher incidence in a manner successfully achieved for SARS-
529 CoV-2[28,29] and a number of healthcare-associated pathogens.[30,31] This study includes
530 staff and students from secondary schools and colleges of further education but most of the
531 participants were students aged 11-18 years. Therefore, it is unclear the extent to which it
532 can be generalised to other settings, and other context-specific studies are required.
533
534 Our findings have implications for policy makers seeking to balance control of COVID-19
535 with student well-being, education and avoiding social inequalities. We show DCT is a safe
536 alternative to home isolation for school-based contacts, which has potential to facilitate
537 increased school attendance and therefore to reduce the wider long-term negative
538 consequences of the pandemic.
539
540 Overall, this study shows that in secondary school and college of further education, student
541 and staff infection of following contact with a COVID-19 case at school occurs in only around
542 2%. We found switching from isolation at home to DCT, at least in the settings of the schools
543 studied, kept rates of symptomatic COVID in students and staff at similar levels. DCT is a
544 safe alternative to home isolation in school-based contacts and should be considered an
545 alternative to routine isolation of close contacts following school-based exposures.
546

Evidence in context

Evidence before this study

We searched PubMed for research articles for any date up until 26th June 2021. We used the terms "SARS-CoV-2" and "school" and "transmission", as well as "COVID-19" and "school" and "transmission". No clinical trials have been reported on interventions to impact SARS-CoV-2 transmission in schools or other educational settings.

Evidence synthesis on COVID-19 transmission has found the evidence for school closure relies on extrapolating from studies of influenza transmission. Further data from schools has accrued from observational data and modelling. Public health data after school opening in England in summer 2020 showed that school related outbreaks were uncommon, and strongly associated with community incidence of infection. A review of all case-contact pairs in the UK Test and Trace system estimated a low chance of transmission following educational contact with COVID-19 in young people. Modelling studies have suggested that implementing daily contact testing in place of contact isolation may be neutral or advantageous with regard control of transmission.

Added value of this study

We report the first randomised-controlled trial of a public health intervention on COVID-19 transmission in secondary schools and colleges of further education, during a period of low to moderate community incidence, predominantly with the Delta variant. Infection in close contacts in these educational settings was uncommon and around 2%. Supervised daily testing with lateral flow devices as an alternative to self-isolation for close contacts was non-inferior for control of COVID-19 transmission. School absence was reduced where testing was available, but did not demonstrate statistically significant reduction.

Implications of all available evidence

Safe alternatives to mass isolation for young people in education are crucial to reducing the impact of the COVID-19 pandemic. With low transmission to contacts, in the context of other mitigations, the results here show daily testing of contacts is an acceptable alternative. Further randomised controlled trials of public health policy interventions can ensure an evidence-based response to the pandemic.

Data availability

Data from the trial will be available within the Office for National Statistics Secure Research Service. Applications for access can be made by Accredited Researchers. For more details please see -

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742

Tables

Characteristic	Control n = 99[1]	Intervention n = 102[1]
Strata		
Government-funded, 11-18y, free school meals ≤17%	32 (32%)	34 (33%)
Government-funded, 11-16y, free school meals ≤17%	8 (8.1%)	8 (7.8%)
Government-funded, 11-18y, free school meals >17%	22 (22%)	24 (24%)
Government-funded, 11-16y, free school meals >17%	19 (19%)	18 (18%)
Any residential school	5 (5.1%)	6 (5.9%)
Special needs or alternate provision	5 (5.1%)	5 (4.9%)
Further education college, 16-18y	3 (3.0%)	2 (2.0%)
Independent day school ≥500 pupils	3 (3.0%)	3 (2.9%)
Independent day school <500 pupils	2 (2.0%)	2 (2.0%)
Students attending school	1,014 (529, 1,376)	1,025 (682, 1,359)
Missing data	3	1
School staff	142 (91, 189)	125 (91, 173)
Missing data	23	17

Table 1. School level baseline characteristics by study arm. The number of students and staff at each school are based on participant lists provided as part of the study and for students from the UK Government Department for Education (DfE) for schools not actively participating after randomisation. [1]n (%); Median (IQR). Four schools had missing student lists as schools stopped participating before this was provided and the school had not submitted student lists to DfE previously. Forty schools had missing staff lists as schools stopped participating before this was provided and only student data were available from DfE.

755

	Students		Staff	
Characteristic	Control, n = 102,859[1]	Intervention n = 111,693[1]	Control, n = 11,798[1]	Intervention, n = 12,229[1]
Ethnicity				
Asian	14,735 (14%)	12,885 (12%)	562 (4.8%)	522 (4.3%)
Black	6,240 (6.1%)	5,772 (5.2%)	239 (2.0%)	204 (1.7%)
Chinese	491 (0.5%)	703 (0.6%)	12 (0.1%)	20 (0.2%)
Mixed	4,975 (4.8%)	4,565 (4.1%)	120 (1.0%)	96 (0.8%)
Other	2,137 (2.1%)	2,123 (1.9%)	65 (0.6%)	57 (0.5%)
Prefer not to say	8,709 (8.5%)	9,948 (8.9%)	3,411 (29%)	3,502 (29%)
White	65,339 (64%)	75,470 (68%)	7,389 (63%)	7,828 (64%)
Missing data	233	227	0	0
Age group				
11 to 14	48,396 (47%)	50,400 (45%)		
15 to 18	49,461 (48%)	52,185 (47%)	16 (0.1%)	5 (<0.1%)
19 to 34	3,602 (3.5%)	6,974 (6.2%)	3,453 (29%)	3,411 (28%)
35 to 44	744 (0.7%)	1,232 (1.1%)	2,807 (24%)	3,015 (25%)
45 to 54	418 (0.4%)	672 (0.6%)	2,865 (24%)	3,145 (26%)
55 to 64	143 (0.1%)	209 (0.2%)	2,215 (19%)	2,193 (18%)
65+	95 (<0.1%)	21 (<0.1%)	442 (3.7%)	460 (3.8%)
Sex				
Female	49,502 (48%)	58,148 (52%)	8,092 (69%)	8,395 (69%)
Male	53,356 (52%)	53,545 (48%)	3,706 (31%)	3,834 (31%)
Missing data	1	0	0	0

756
757 **Table 2. Student and staff level baseline characteristics by study arm**. Note students aged
758 ≥19 years attended further education colleges providing courses for students at any age.
759 Data based on 96 control schools and 101 intervention arm schools with data on student
760 demographics and 76 and 86 schools respectively with data on staff. [1]n (%).

	Descriptive		Univariable			Multivariable		
Characteristic	Did not participate, n = 3,331[1]	Participated, n = 2,432[1]	RR[2]	95% CI[2]	p-value	RR[2]	95% CI[2]	p-value
Study week of first contact test								
1	7 (17%)	34 (83%)	1.10	0.77, 1.58	0.60	1.45	0.92, 2.27	0.11
2	70 (25%)	213 (75%)	—	—		—	—	
3	147 (43%)	195 (57%)	0.76	0.58, 0.99	0.041	0.81	0.60, 1.09	0.17
4	138 (41%)	200 (59%)	0.79	0.60, 1.02	0.075	0.96	0.68, 1.36	0.82
5	306 (72%)	118 (28%)	0.37	0.14, 0.95	0.038	0.43	0.20, 0.95	0.036
6	412 (93%)	30 (6.8%)	0.09	0.02, 0.43	0.003	0.12	0.03, 0.49	0.003
8	206 (42%)	280 (58%)	0.77	0.59, 0.99	0.041	0.82	0.62, 1.09	0.17
9	332 (31%)	755 (69%)	0.92	0.79, 1.08	0.32	1.03	0.84, 1.28	0.75
10	1,713 (74%)	607 (26%)	0.35	0.24, 0.50	<0.001	0.39	0.25, 0.60	<0.001
Strata group								
Government-funded, 11-18y free school meals ≤17%	1,018 (51%)	979 (49%)	—	—		—	—	
Government-funded, 11-16y free school meals ≤17%	70 (22%)	252 (78%)	1.60	1.17, 2.19	0.003	1.44	1.06, 1.95	0.020
Government-funded, 11-18y free school meals >17%	987 (66%)	501 (34%)	0.69	0.39, 1.22	0.20	0.71	0.45, 1.11	0.13
Government-funded, 11-16y free school meals >17%	904 (67%)	439 (33%)	0.67	0.31, 1.44	0.30	0.76	0.47, 1.23	0.26
Other	209 (58%)	154 (42%)	0.87	0.51, 1.47	0.59	0.82	0.49, 1.36	0.45
Independent day school	143 (57%)	107 (43%)	0.87	0.64, 1.19	0.39	1.00	0.68, 1.47	>0.99
Ethnicity								
White	2,320 (57%)	1,764 (43%)	—	—		—	—	
Asian	394 (63%)	236 (37%)	0.87	0.49, 1.53	0.62	1.06	0.85, 1.31	0.61
Black	167 (61%)	106 (39%)	0.90	0.62, 1.30	0.57	1.03	0.82, 1.30	0.82
Chinese	12 (23%)	40 (77%)	1.78	1.18, 2.69	0.006	1.72	1.15, 2.55	0.008
Mixed	134 (64%)	75 (36%)	0.83	0.61, 1.13	0.24	0.93	0.79, 1.10	0.39

			RR[2]	CI	p	RR[2]	CI	p
Other	76 (77%)	23 (23%)	0.54	0.31, 0.92	0.024	0.69	0.48, 0.98	0.037
Prefer not to say	228 (55%)	188 (45%)	1.05	0.70, 1.57	0.83	0.94	0.70, 1.28	0.71
Age group								
11 to 14	1,840 (65%)	984 (35%)	—	—		—	—	
15 to 18	1,400 (53%)	1,258 (47%)	1.36	0.91, 2.03	0.14			
Over 18	91 (32%)	190 (68%)	1.94	1.26, 2.99	0.003			
Sex								
Female	1,619 (54%)	1,390 (46%)	—	—		—	—	
Male	1,712 (62%)	1,042 (38%)	0.82	0.72, 0.93	0.002	0.92	0.82, 1.03	0.14
Participant type								
Student	3,257 (59%)	2,253 (41%)	—	—		—	—	
Staff	74 (29%)	179 (71%)	1.73	1.33, 2.25	<0.001	1.40	1.09, 1.80	0.009
School size, students and staff, RR per 100	1,274 (958, 1,410)	1,070 (801, 1,506)	0.99	0.97, 1.01	0.35	0.99	0.98, 1.00	0.18

761

762 **Table 3. Associations with participation in lateral flow testing in 5763 contacts in intervention arm schools where the 10 days following the**
763 **positive test in the index case included ≥1 school day**. Participant age is omitted from the multivariable model due to collinearity with
764 participant type. Results from Poisson regression, with robust variance estimation, adjusting variance to account for repeated measurements
765 from the same school (for univariable and multivariable models). [1]n (%); Median (IQR); [2]RR = Rate Ratio, CI = Confidence Interval. Note week 7
766 is the school "half-term" holiday, when school-based lateral flow testing was not undertaken. Note participation in the final week of the study
767 appears lower than in Figure 2, as participation is summarised as completion of ≥3 LFDs, and contacts in the final week may not have
768 completed testing before the end of the study.

	End point	Intention to treat			Complier average causal effect	
		aIRR / aOR	95% CI	p value	Effect	95% CI
Primary end points	Rate of COVID-related absence	0.80	0.54, 1.19	0.27	0.61	0.30, 1.23
	Rate of COVID-related absence (aggregated dataset)	0.80	0.62, 1.03	0.085	0.62	0.29, 1.33
	Rate of symptomatic PCR-confirmed infection	0.96	0.75, 1.22	0.72	0.86	0.55, 1.34
Secondary end points	Rate of any absence	0.97	0.82, 1.16	0.77	0.89	0.71, 1.18
	Rate of any community testing PCR-confirmed infection	0.96	0.76, 1.20	0.71	0.88	0.57, 1.41
	Proportion of asymptomatic contacts testing PCR positive on a research PCR test	0.73	0.33, 1.61	0.44	-	-
	Proportion of contacts testing PCR-positive while symptomatic on a routine community test	1.21	0.82, 1.79	0.34	-	-

769
770
771 **Table 4. Co-primary and secondary end points.** aIRR, adjusted incidence rate ratio for rates;
772 aOR, adjusted odds ratio for proportions; CI, confidence interval.

773

Figure legends

Figure 1. Consort diagram of participating schools for two co-primary outcomes: COVID related school absence (panel A) and symptomatic PCR-positive infection (panel B). The former depends on availability of daily school attendance data for students and staff aggregated at school level. The latter depends on provision of student and staff lists to enable matching of identifiers with NHS Test and Trace national community testing data. DfE, UK Government Department for Education. School participation was defined based on submission of student/staff lists and attendance data for at least part of the study. A total of 2000 schools were notified of the study by email, 226 attended webinars to learn more about the study, within this group 204 schools were taken through the consent process, during which 3 decided not to participate further. Of the 39 schools that stopped active participation between randomisation and the study starting, 26 provided reasons: 20 stated resource constraints, 3 intervention schools cited concerns about the protocol, 2 control schools did not wish to be in the control arm, 1 intervention school on local authority public health advice.

Figure 2. Study participation during 27,973 potential isolation school days in 5763 intervention arm contacts. Panel A shows the number of contacts in the intervention arm by study day, by participation or reason for non-participation. Note the school "half-term" holiday (31-May-2021 to 04-June-2021). Panel B shows the percentage of contacts in the intervention arm participating, by study day; the bars are coloured according to the number of contacts under follow up on a given day. Panel C shows the percentage of contacts participating in LFDs in 59 intervention arm schools reporting ≥1 contact affecting school days. For each contact event return of ≥3 LFD results or a positive LFD result is used to summarise participation in the intervention. The bars are coloured by strata group, which summarises the 9 strata used for randomisation. LFDs, lateral flow tests. Schools with no contacts participating are shown with a small negative value on the y-axis to aid visualisation.

Figure 3. Co-primary outcome: Percentage of students (panel A) and staff (panel B) absent for COVID-related reasons as a proportion of all those not absent for other reasons by study day. Note the school "half-term" holiday (31-May-2021 to 04-June-2021).

Figure 4. Co-primary outcome: incidence of symptomatic PCR positive results in students and staff by study arm (panel A), and secondary outcome: all PCR positive results (panel B). Weekly incidence is shown per 100,000 at risk. The shaded area is the mean rate ± 1 standard deviation using a negative binomial model to account for over-dispersion (theta=0.28).