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1 **Screening and vaccination against COVID-19 to minimize school closure: a modeling study**

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18 **Background.** Schools were closed extensively in 2020-2021 to counter COVID-19 spread, impacting students'
19 education and well-being. With highly contagious variants expanding in Europe, safe options to maintain schools
20 open are urgently needed.

21 **Methods.** We developed an agent-based model of SARS-CoV-2 transmission in school. We used empirical contact
22 data in a primary and a secondary school, and data from pilot screenings in 683 schools during the 2021 spring
23 Alpha wave in France. We fitted the model to observed school prevalence to estimate the school-specific
24 reproductive number (R^{Alpha} , R^{Delta}) and performed a cost-benefit analysis examining different intervention
25 protocols.

26 **Findings.** We estimated $R^{\text{Alpha}}=1.40$ (95%CI 1.35-1.45) in the primary and $R^{\text{Alpha}}=1.46$ (1.41-1.51) in the secondary
27 school during the wave, higher than R_t estimated from community surveillance. Considering the Delta variant and
28 vaccination coverage in Europe, we estimated $R^{\text{Delta}}=1.66$ (1.60-1.71) and $R^{\text{Delta}}=1.10$ (1.06-1.14) in the two settings,
29 respectively. Under these conditions, weekly screening with 75% adherence would reduce cases by 34% (95%CI 32-
30 36%) in the primary and 36% (35-39%) in the secondary school compared to symptom-based testing. Insufficient
31 adherence was recorded in pilot screening (median $\leq 53\%$). Regular screening would also reduce student-days lost
32 up to 80% compared to reactive closure. Moderate vaccination coverage in students would still benefit from
33 regular screening for additional control (23% case reduction with 50% vaccinated children).

34 **Interpretation.** COVID-19 pandemic will likely continue to pose a risk to the safe and normal functioning of
35 schools. Extending vaccination coverage in students, complemented by regular testing largely incentivizing
36 adherence, are essential steps to keep schools open with highly transmissible variants.

37 **Funding.** EU Framework Programme for Research and Innovation Horizon 2020, Horizon Europe Framework
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41 INTRODUCTION

42 School closure has been extensively used worldwide against the COVID-19 pandemic. The first wave witnessed
43 many countries go into strict lockdowns closing schools for long periods of time¹, and their reopening has been
44 continuously challenged by successive waves and the need for social distancing restrictions. In Europe, depending
45 on the country, students lost from 10 to almost 50 weeks of school from March 2020 to October 2021 due to
46 partial or total school closure (Figure 1a). Strategies were affected by the limited understanding of viral circulation
47 in children and their contribution to transmission².

48 Outbreaks in schools are difficult to document, as infections in children are mostly asymptomatic or present mild
49 non-specific symptoms³. Despite the lower susceptibility to infections in children compared to adults⁴, viral
50 circulation can occur in school settings, especially in secondary schools². Accumulating evidence is consistent with
51 increased transmission in the community if schools are in session^{2,5}, and model-based findings suggest that school
52 closure may be used as an additional brake against the COVID-19 pandemic if other social distancing options are
53 exhausted or undesired^{6,7}.

54 Keeping schools safely open remains a primary objective that goes beyond educational needs, and affects the
55 social and mental development of children⁸, as well as the reduction of inequalities. Several countries
56 implemented safety protocols at school, including the use of masks, hand hygiene, staggered arrival and breaks.
57 Regular testing⁹⁻¹² was introduced in a few countries as an additional control measure. Vaccination was extended
58 to the 5+ population in Europe, yet it was reported to progress slowly in the majority of countries by January
59 2022¹³. School protocols were challenged by the rapid surge of cases due to the Delta and Omicron variants in the
60 winter 2021-2022 in Europe¹⁴, threatening classroom safety. Assessing vaccination and protocols in schools is
61 therefore key to maintaining schools open in light of a continuously evolving pandemic. Here, through an agent-
62 based transmission model parameterized on empirical contacts at schools and fitted to field screening data in
63 schools, we estimate the school-specific effective reproductive number. We then evaluate intervention protocols
64 combining closures and screening, under varying immunity profiles of the school population, and accounting for
65 age-specific differences in susceptibility to infection, contagiousness, contact patterns, and vaccine effectiveness.
66 Findings from this work informed the recommendations of the French National Immunisation Technical Advisory
67 Group (Haute Autorité de Santé) on children vaccination in December 2021.

68

69 METHODS

70 **Empirical patterns of contacts.** We used empirical data describing time-resolved face-to-face proximity contacts
71 between individuals in two educational settings, collected in France using wearable RFID sensors in a pre-
72 pandemic period. The *Primary school* dataset describes the contacts among 232 students (6-11 years old) and 10
73 teachers in a primary school in Lyon, composed of 5 grades, each of two classes¹⁵. The *Secondary school* dataset
74 describes the contacts between 325 students (17-18 years old) of 9 classes in a secondary school in Marseille¹⁶.
75 Classes belong to the second year of “classes préparatoires”, specific to the French schooling system for
76 preparation to University entry, and are divided in three groups, based on the specialization.

77 We built temporal contact networks, composed of nodes representing individuals (classified by class and
78 student/teacher), and links representing empirically measured proximity contacts occurring at a given time (Figure
79 1b,c). As each dataset covers only a few days, we developed an approach to temporally extend the datasets by
80 generating synthetic networks of contacts that reproduce the main features observed empirically (class structure,
81 within- vs. between-classes links, contact duration heterogeneity, and similarity across days; Appendix, pp.14-18).
82 The secondary school synthetic network was further extended to generate a synthetic first year (to consider the
83 full curriculum of the “classes préparatoires”) including teachers whose contacts were inferred from an additional
84 dataset for the same school. The resulting network for the secondary school was composed of 650 students and 18
85 teachers.

86 **Field screening data in schools during the spring 2021 wave in France.** In response to a rising third wave in France
87 in the spring 2021 due to the Alpha variant, local authorities in the Auvergne-Rhône-Alpes region proposed pilot
88 screenings at schools on a voluntary basis to detect cases. We used data on adherence to screening and test

89 results collected in 683 schools between March 8 and June 7, 2021 (weeks 10-23), in the Ain, Loire and Rhône
90 departments of the region. Screening was interrupted in April due to reactive school closure (week 14) and Easter
91 holidays (weeks 15-16) while the country underwent the third national lockdown; it was resumed in week 17 at
92 school reopening (week 18 for secondary schools; Figure 1i). Screenings involved 94 pre-schools, 427 primary
93 schools, 158 middle schools, and 4 high schools, for a total of 209,564 students and 18,019 personnel tested. PCR
94 tests from saliva samples were proposed in pre-schools and primary schools, and anterior nasal LFD (lateral flow
95 device) tests in middle and high schools. More details are provided in the Appendix, pp.19-22.

96 **Ethics statement.** Contact studies were approved by the Commission Nationale de l'Informatique et des Libertés
97 (CNIL, the French national body responsible for ethics and privacy) and school authorities. Informed consent was
98 obtained from participants or their parents if minors. No personal information of participants was associated with
99 the RFID identifier. Testing at school was part of surveillance activities approved by school authorities and
100 proposed with parental consent. Screening data were provided in aggregated and anonymized form.

101 **Transmission model in primary school and secondary school.** We developed a stochastic agent-based model of
102 SARS-CoV-2 transmission on the network of contacts. Infection progression includes prodromic transmission,
103 followed by clinical or subclinical disease stages, informed from empirical distributions. Transmission occurs with a
104 given transmissibility β per contact per unit time between an infectious individual and a susceptible one. β was
105 inferred by fitting the model to data from screening results during the 2021 spring wave. Individuals in the
106 asymptomatic compartments are considered to be less infectious and to remain undocumented unless tested¹⁷; a
107 sensitivity analysis was performed on the reduced transmissibility.

108 The model is parameterized with age-specific estimates of susceptibility, transmissibility, probability of developing
109 symptoms, and probability to detect a case based on symptoms (Appendix, pp.4-6). A systematic review indicates
110 that minors have lower susceptibility to SARS-CoV-2 compared to adults⁴, but building evidence suggests that high
111 school students may be as susceptible as adults¹⁸. Here we considered a relative susceptibility of 50% in children
112 and 75% in adolescents compared to adults, and tested 100% susceptibility in adolescents for sensitivity. The
113 probability to recognize a suspect COVID-19 infection from symptoms was set to 30% for children and 50% for
114 adolescents and adults, based on studies indicating that about two thirds of symptomatic children³ and half of
115 symptomatic adults¹⁹ have unrecognized symptoms before diagnosis. These values were varied for sensitivity. We
116 considered a lower transmissibility in children, as evidence suggests that transmission in children may be less
117 efficient²⁰, and we tested different values for sensitivity.

118 The model is further stratified to account for vaccination status and to include vaccine effectiveness against
119 infection, transmission, and clinical symptoms given infection²¹ (Appendix, pp.9-12). Higher and lower vaccine
120 effectiveness were also tested for sensitivity. Full details on the transmission model are reported in the Appendix,
121 pp.4-13.

122 **Closure and screening protocols.** *Symptom-based testing and case isolation (ST)* is considered as the basic
123 strategy, present in all protocols, and against which interventions are evaluated. It considers that clinical infections
124 are detected with the estimated probability and tested, and confirmed cases are isolated for 7 days. We
125 considered the following intervention protocols:

- 126 • *Reactive quarantine of the class (ST+Qc):* once a case is identified through ST, their class is put in quarantine
127 for 7 days. If quarantined individuals develop symptoms, they remain in isolation for an additional period of
128 7 days, before returning to school. This protocol was largely adopted in France before the Delta wave.
- 129 • *Reactive quarantine of the class level or specialization (ST+Ql):* as the previous protocol, but quarantine is
130 applied to the classes of the same level (2 classes in the primary school) or specialization (3 in the secondary
131 school) of the detected case. This option is considered as empirical data show a larger mixing between
132 students of the same level or specialization compared to the others.
- 133 • *Reactive screening of the class (+1d from detection) followed by a control screening (+nd) with α adherence*
134 *(ST+rT+cnT α):* once a case is identified through ST, their class is reactively screened at +1 day, and again at
135 +n days (n=4, or 7) for control of possible infections that went previously undetected. Only a percentage α
136 of the non-vaccinated school population adheres to the screening. This protocol was adopted in France
137 during the Delta wave.

- 138 • *Regular testing with α adherence ($ST+RT\alpha\%$):* in addition to ST, regular testing is performed at a certain
139 frequency (once every two weeks, once or twice per week). Adherence α was informed from field data, and
140 further explored in a range between 10% and 100%.
- 141 • *Regular testing with α adherence, and reactive quarantine of the class ($ST+RT\alpha\%+Qc$):* in addition to the
142 protocol above, the reactive closure of the class is triggered at every detected case.

143 Following protocols adopted in France, we considered PCR tests on saliva samples in the primary and anterior
144 nasal LFD tests in the secondary school, with time-varying test sensitivity specific to each test, and results available
145 after 24h and after 15', respectively (Appendix, pp.7-8). Teachers are required to show proof of a negative PCR test
146 when returning to school after infection.

147 **Inference framework.** We used data on test results collected in the pilot screenings during the 2021 spring wave in
148 the Ain, Loire and Rhône departments to estimate the transmissibility β^{Alpha} per contact per unit time of the
149 Alpha variant and the corresponding school-specific effective reproductive number R in that period. The model is
150 fitted to the observed prevalence of cases in students in the tested schools through a maximum likelihood
151 approach. We used data from screenings performed during the rise of the spring wave (March 8 to April 2, 2021),
152 involving at least 5 schools and 500 screened students per week per department per school type (primary or
153 secondary), and with reported adherence $\geq 50\%$ (reference inclusion criteria). For sensitivity, we relaxed the
154 constraint on adherence (sensitivity inclusion criteria). Simulations for the fit covered the period from week 8
155 (starting February 22, 2021, at school reopening after winter holidays) to week 13 (ending April 4) before the
156 reactive school closure, and they were initialized with age-specific seroprevalence estimates²². Weekly
157 introductions at school were modeled stochastically, inferred from age-specific community surveillance data, and
158 adjusted to account for detection rate and within-school transmission²³. We computed R in each school as the
159 ratio of the number of individuals infected at the 2nd generation to the number infected at the 1st generation for
160 each initial seed over 5,000 simulated outbreaks. The estimated R refers to the ST+Qc protocol with mask mandate
161 applied in that period. Full details on the procedure are reported in the Appendix, pp.23-29.

162 **Analysis of school protocols in a Delta winter wave scenario in Europe.** To evaluate the efficacy of intervention
163 protocols, we considered a 2021-2022 winter scenario due to the Delta variant initialized with 25% natural
164 immunity in the population, 60% of teachers vaccinated, and 40% of adolescents vaccinated, corresponding to the
165 median vaccination coverage registered in countries in Europe by mid-September 2021 (Appendix, p.31). The
166 transmissibility β^{Delta} per contact per unit time for Delta was estimated from the maximum likelihood estimate
167 $\beta_{MLE} = \beta^{Alpha}$, accounting for the transmissibility advantage of the Delta variant²⁴. The corresponding school-
168 specific R was estimated from simulated outbreaks under the above immunity conditions, and considering the
169 ST+Qc protocol with mask mandate. We additionally explored a range of R values to account for the uncertainty in
170 the estimate of Delta transmissibility²⁴, seasonal effects²⁵, and variations in β_{MLE} due to the inclusion criteria
171 considered in the inference. We considered low, moderate, sustained, and high weekly introductions modeled
172 stochastically and corresponding to community surveillance incidence in primary school students ranging in time
173 from 25 to >600 cases per 100,000 (low introductions), from 50 to 900 (moderate), from 100 to 1,300 (sustained),
174 and from 200 to 1,800 cases per 100,000 (high); values for the secondary school are reported in the Appendix,
175 p.33.

176 To assess the efficacy of screening protocols under different immunity conditions, we explored a full range of
177 vaccination coverage in children, adolescents, and teachers.

178 **Analysis of school protocols in an Omicron winter wave scenario in Europe.** We considered the circulation of the
179 highly transmissible and immune evasive Omicron variant that became dominant in Europe by the start of 2022¹⁴,
180 at the time the revision of this work was finalized. We tested the efficacy of school protocols under the high
181 incidence conditions registered in France by mid-January 2022 (5,500 cases in 6-10y children per 100,000). Details
182 are reported in the Appendix, p. 37.

183 **Simulation details and analysis.** Estimates for β and R were obtained from 5,000 simulated stochastic outbreaks
184 for each parameter set. Estimates for R were compared to age-specific R_t estimated from community surveillance
185 data with a one-sample t-test. We fitted the predicted offspring distribution to a negative-binomial to estimate the
186 overdispersion parameter k^{26} . In the protocols' analysis, we performed 1,000 stochastic runs for the primary and

187 2,000 for the secondary school for each parameter set, over the course of a trimester (90 days). We computed
188 medians and 95% bootstrap confidence intervals from simulation outputs to compare protocols with a Mood's
189 median test. Interquartile ranges (IQR) were used to describe observed adherence.

190 **Role of the funding source.** The funders had no role in study design, data collection, data analysis, data
191 interpretation, writing of the manuscript, and decision to submit. The first author, the second author, and the
192 corresponding author had full access to all the data in the study and had final responsibility for the decision to
193 submit for publication.

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195

196 RESULTS

197 Contact networks measured through wearable sensors displayed a strong community structure around the classes,
198 common to both the primary and secondary schools (Figure 1b,c). The patterns of interaction, however, varied
199 substantially between the two settings. On average, children had a larger number of distinct contacts during a day,
200 interacting with almost their entire class (83% of the class), compared to adolescents (33% of the class, Student
201 test $p < 10^{-15}$; Figure 1d). Approximately 50% more links occurred between classes than within classes in the primary
202 school (19 vs. 28 links, $p < 10^{-15}$), contrary to what observed for adolescents (12 vs. 3 links, 75% fewer links, $p < 10^{-15}$).
203 But accounting for duration, students in both settings spent on average more time interacting within the class than
204 outside the class ($p < 10^{-15}$), and established longer contacts (+64%, $p = 0.009$) compared to teachers (Figure 1e,f).

205 Using the empirical contact patterns, we inferred the school-specific transmissibility from screening data in
206 primary schools satisfying the inclusion criteria: 71 primary schools and 12,146 tested students with the reference
207 inclusion criteria; 103 primary schools and 15,916 tested students with the sensitivity inclusion criteria. Secondary
208 schools were excluded because of limited participation. We estimated a school-specific R^{Alpha} during the Alpha
209 2021 spring wave in France between 1.40 (1.35 -1.45) and 1.44 (1.40-1.48) in the primary school, and 1.46 (1.41 -
210 1.51) and 1.50 (1.46-1.54) in the secondary school (for the reference and sensitivity inclusion criteria, respectively),
211 with the reactive class closure protocol and mask mandate in place (Figure 2a). Estimates were higher compared to
212 the time-varying reproductive number R_t obtained from age-specific community surveillance in the same period
213 (one-sample t-test $p < 10^{-7}$ in the primary, $p < 0.0001$ in the secondary school; Figure 2c,d). We quantified a large
214 individual-level variation in SARS-CoV-2 transmission in both schools, corresponding to an overdispersion
215 parameter k estimated to be 0.56 (95% CI 0.49-0.63) in the primary and 0.52 (95% CI 0.46-0.58) in the secondary
216 school (Figure 2b). Accounting for the transmissibility advantage of the Delta variant and vaccination coverage in
217 Europe, we estimated a school-specific R^{Delta} between 1.66 (1.60 -1.71) and 1.70 (1.66-1.75) in the primary school,
218 and 1.10 (1.06 -1.14) and 1.13 (1.10-1.16) in the secondary school (for both inclusion criteria). In the protocols'
219 analysis, we considered the R^{Delta} estimate obtained with the reference inclusion criteria, and explored the ranges
220 1.46-2.00 and 0.97-1.34 in the primary and secondary schools, respectively, estimated accounting for the
221 uncertainty associated to Delta transmissibility, seasonal effects, and sensitivity inclusion criteria.

222 Under the estimated Delta transmissibility and sustained introductions, regular testing constitutes an efficient
223 protocol for preventing infections in a partially immunized school population (Figure 3a,b). If adherence is large
224 enough, regular testing can substantially outperform protocols based on simply identifying cases given
225 recognizable symptoms and additionally closing or screening the class of the detected case (even with a follow-up
226 control screening). However, screenings at schools during the 2021 spring wave in France were met with low or
227 moderate participation rates. Adherence was higher in lower school levels (39% (IQR 26-49%) in pre-school, 53%
228 (43-65%) in primary school) compared to secondary schools (10% (5-17%) in middle school, 6% (3-10%) in high
229 school; Mood's median test $p < 10^{-15}$; Figure 1h). We found that with 50% adherence, i.e. approximately the value
230 recorded in the French primary schools, weekly screening would reduce the number of cases by 21% (95%CI 19-
231 23%) in the primary and by 26% (25-28%) in the secondary school compared to symptom-based testing alone. Case
232 reduction would rise to 34% (32-36%) and 36% (35-39%) in the two schools, respectively, with 75% adherence.
233 Alternatively, similar reductions would be achieved with 50% adherence and twice-weekly testing. This shows how
234 infection prevention improves with both adherence and frequency of tests, and higher frequency is needed to
235 compensate for lower adherence. However, if adherence to regular testing is too low (10%), as recorded in the

236 French secondary schools, weekly testing would have little impact (<10% case reduction), similarly to reactive
237 screening and lower than reactive closure. While trends are similar across settings, partial vaccination coverage in
238 adolescents leads to smaller epidemic sizes in the secondary school compared to the primary (relative to the
239 school size; Figure 3c,d and Appendix, p.41).

240 Next to reducing the number of infections, regular testing is predicted to strongly limit the number of days of
241 absence of students. The quarantine of the class implies 17.7 (95% CI 17.4-17.9) and 33 (95% CI 32-34) times more
242 student-days lost in the primary and secondary schools, respectively, compared to symptom-based testing alone
243 (Figure 4a). Days lost inevitably increase when reactive closure is extended to classes of the same level or
244 specialization. Not being sufficiently targeted, reactive closure quarantines individuals while their risk of infection
245 may be low, and the virus may have spread to other classes (Figure 3e,f). Reducing mixing across classes through
246 cohorting improves control (Appendix, p.44). Despite detecting more cases, regular testing leads to a small
247 increase in student-days lost, <6.6 (6.4-6.8) times the number of days lost with the basic strategy and about 63-
248 80% less than reactive class closure, as isolation is only applied to detected cases. The cost-benefit analysis shows
249 that for all regular testing strategies, the cost expressed by person-days lost remains low, even when the benefit
250 becomes high, for a range of different epidemic conditions (Figure 4b,c). Strategies based on class closures do not
251 manage to reach a high benefit, even at large cost. Reactive screening limits days lost but with a negligible impact
252 on viral circulation. Closing the class at each case detected by regular testing improves case reduction but at the
253 cost of increased absence from school. Findings were robust against changes in detection rates and test sensitivity
254 (Appendix, pp.51-52).

255 Higher incidence in the community (increasing the expected introductions at school), and larger reproductive
256 numbers (increasing within-school transmission) reduce the benefit of weekly testing in primary schools, thus
257 requiring increased adherence or frequency (Figure 4d,e). The impact of introductions is milder in the secondary
258 school, due to vaccination (Figure 4f). Moreover, increasing R in this setting would increase the benefit of regular
259 testing, contrary to the primary school case. This is due to a bell-shaped dependence of the infection prevention
260 capacity of regular testing vs. R (Appendix, p.46): in low-transmission conditions, only few cases are present even
261 for ST, so that additional protocols yield marginal benefit; as transmission increases from small values (the
262 secondary school case, where R is small thanks to vaccination), efficiency increases; in high-transmission
263 conditions, instead, case prevention is hindered by too many infections generated between successive screenings,
264 and efficiency decreases as transmission increases (the primary school case, with high R because of unvaccinated
265 children). Changes in epidemiological parameters (transmissibility, susceptibility) yield changes in R and
266 consequently in protocols' efficiencies, but protocols' ranking according to their benefit remains robust (Appendix,
267 pp.48-50).

268 High incidence conditions due to immune evasion and higher transmissibility compatible with an Omicron scenario
269 confirm the value of screening with high frequency (Appendix, p.37).

270 Benefits and costs of regular testing remain stable when vaccination coverage of teachers increases from 60% to
271 100% (Figure 5a and Appendix, p.41, 53). Increasing vaccination coverage in students, both in primary and
272 secondary schools, is a strong protective factor against school outbreaks (Figure 5b,c,d), expected to reduce the
273 epidemic size by 38% with 20% coverage in children and by 75% with 50% coverage, without intervention (i.e. with
274 ST) and with respect to non-vaccination, for robust vaccine effectiveness (Figure 5d, Figure S32). Regular testing
275 would provide an important supplementary control, especially while rolling out vaccination campaigns in primary
276 schools: weekly screening 75% of the non-vaccinated students would additionally reduce cases by 36% (32-39%)
277 with 20% coverage in children, and by 23% (20-26%) with 50% coverage, without impacting class closure (Figure
278 5e). Similar results are obtained with lower vaccine effectiveness (Appendix, p. 54). The minimum vaccination
279 coverage to reduce the benefit of regular testing to 20% case reduction or below increases with R; for R between
280 1.6 and 2 the required coverage stabilizes around 55-60% (Figure 5f).

281 282 **DISCUSSION**

283 Strategies to safely maintaining schools open during the COVID-19 pandemic are a matter of controversial debate
284 and relatively limited knowledge from the field. Using screening data from schools during the 2021 spring wave in
285 France and empirical contact data, our study provides the first estimate of transmissibility in different school

286 settings, suggesting that contacts at school increase SARS-CoV-2 transmission potential compared to the
287 community. With countries in Europe experiencing record-high cases due to the Omicron variant¹⁴, protocols at
288 school remain a central issue as high community transmission leave schools vulnerable while children vaccination
289 progresses dramatically slow in several countries¹³. Our analysis indicates that regularly screening the school
290 population is efficient in preventing infections while reducing absence from school, especially in settings where the
291 school population is not yet vaccinated, coverage is low to moderate, or vaccine protection has largely waned.

292 We estimated a higher transmissibility in the school compared to the community during the Alpha 2021 spring
293 wave in France. This suggests that repeated contacts in dense classrooms, with mask mandate except during sport
294 and lunch, favor transmission in absence of screening protocols, with potentially high overdispersion^{26,27}. These
295 findings align with available evidence of increased transmission in the population if schools are open^{2,5}. In absence
296 of vaccination, secondary school students are predicted to infect on average a larger number of individuals
297 compared to primary school students, consistent with observations², due to age-specific epidemiological
298 properties and contact patterns. However, more contagious variants and limited vaccination coverage in children
299 currently put them at higher risk. A disproportionately higher Omicron circulation is observed in children
300 compared to the general population (5,500 cases per 100,000 in 6-10y children vs. 3,000 per 100,000 in all age
301 classes in France by mid-January 2022) that is further sustained by transmission at school, resulting in large school
302 disruption^{28,29}, a higher risk of infection for students' household members³⁰ and rapid transmission in the
303 community³¹. Even when conditions due to the circulating variant and vaccination coverage brings school-specific
304 R below 1 (as estimated e.g. under a Delta wave in secondary schools in France with 77% vaccinated adolescents
305 and high vaccine effectiveness; Appendix, pp.35-36), the predicted highly-overdispersed offspring distribution
306 suggests that –together with highly likely extinctions– chains of transmissions in schools are relatively rare but
307 possible.

308 Using the estimated school-specific transmission rate for Delta and a range of realistic epidemic conditions
309 (introductions, seasonality, vaccination coverage), we found that regular testing with large enough adherence
310 provides an optimal balance in controlling school outbreaks while maintaining schools open. This is consistent with
311 results showing that twice-weekly testing in England helped to control within-school transmission in secondary
312 schools¹². Adherence is however critical, suggesting that at least $\frac{3}{4}$ of non-vaccinated individuals should participate
313 to weekly testing to achieve a considerable case reduction. This was not achieved in the pilot screenings in the
314 2021 spring in France, despite schools mainly participated once. Implementing regular testing should consider
315 improving strategies for the communication and engagement of the school community to considerably boost
316 participation and maintain it over time.

317 Our findings corroborate previous numerical evidence on the value of regular testing in preventing infections⁹⁻¹¹.
318 In addition to prior work, our study estimated school-specific R in primary and secondary schools, also integrating
319 empirical face-to-face proximity data allowing us to quantify individual-level variation in SARS-CoV transmission. It
320 also provides a cost-benefit analysis considering successive variants, comparing multiple protocols, and evaluating
321 the key role of adherence in the context of partially vaccinated school populations.

322 Reactive class closure is highly costly in terms of student-days lost, despite detecting a case is rarer in younger
323 individuals. Countries adopting this strategy during the current Omicron wave registered record-high absenteeism
324 from school (20% of students in remote learning in Italy in January 2022²⁸). It also has a limited value in epidemic
325 control, as other classes may be already affected due to unobserved introductions from the community or silent
326 spreading within the school. This second effect becomes particularly important when between-classes mixing is
327 higher, as observed in the primary school. Cohorting that reduces contacts between classes remains therefore an
328 important component of school protocols, in support to screening. While regular testing is able to detect more
329 cases than symptom-based detection, it keeps days lost low for two main reasons. First, isolation is only applied to
330 cases during their infectious period, being therefore more targeted than class quarantine. Second, detecting cases
331 that otherwise go unnoticed helps control the epidemic, breaking the chains of transmission and preventing
332 further diffusion. As a consequence, the overall time spent in isolation is also reduced. Reactive screening, instead,
333 would leave many cases undetected even when retesting a few days after. The iterative nature of the regular
334 testing is key to ensure control over time.

335 Our analysis on the Omicron wave (Appendix, p.37) confirms the large benefit of regularly screening students
336 compared to reactive strategies, even when these strategies are strengthened, for example, by increasing the
337 number of reactive screenings following the index case. The reinforced reactive protocol adopted in France at the
338 reopening of schools in January 2022 required 3 screenings to be performed at day 0, 2, and 4 from detection. But
339 under the high Omicron incidence experienced at the start of 2022, this protocol led to an unprecedented demand
340 in tests, impacting logistics, available resources, and surveillance capacity²⁹. Our findings support instead
341 strengthening regular screening by increasing adherence and adjusting frequency to local incidence and policy
342 expectations, next to cohorting, mask use, and ventilation.

343 Increasing vaccination in teachers protects them from infection and symptomatic disease²¹, but yields limited
344 protection for the school population, even under full coverage. This results from the small number of teachers and
345 the observed lower rate of interaction they have with students, and it is confirmed even when community
346 incidence in adults is much higher than in the student age classes. Extending vaccination to students is needed to
347 achieve a collective benefit, reducing the likelihood and size of school outbreaks with active vaccination
348 protection. In these conditions, regular testing would bring a supplementary control whose application should be
349 evaluated in light of resources, logistics, adherence, epidemic conditions, and waning of vaccine effectiveness.
350 Regular testing remains however critical in moderate (or lower) coverage situations, or when protection against
351 infection has waned, as it would prevent a substantial portion of undetected infections, with a direct impact to the
352 school environment, reducing the number of infections and long-COVID in children³², and an indirect impact on the
353 community, protecting students' contacts³⁰.

354 This study has a set of limitations. First, it focuses on two school settings for which empirical contact data were
355 available, but contacts in other schools may be different, depending on the structure of curricula and the
356 organization of activities. Findings on the efficiency of regular testing and vaccination are however robust across a
357 range of epidemic conditions and synthetic contact patterns, and can thus inform on the choice of strategies to
358 safely keep schools open. Second, data availability for the inference was limited by the pilot screening. Further
359 work could also focus on the decreasing phase of the Alpha wave. Third, the study focuses on school outbreaks
360 and it does not assess the impact that these strategies will have on the viral circulation in the community. Fourth,
361 we did not model waning of vaccine effectiveness throughout the epidemic wave, but tested lower effectiveness
362 values that confirmed the efficiency of regular testing.

363 COVID-19 epidemic will likely continue to pose a risk to the safe and normal functioning of schools. Regular testing
364 remains a key strategy to epidemic control in school settings with moderate vaccination coverage or following
365 waned vaccine protection, all the while minimizing days lost.

366

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375 **AUTHORS' CONTRIBUTION**

376 V.C., A.B. conceived and designed the study. E.C., G.B., V.C. accessed and verified all the data. E.C., G.B., D.A.C.,
377 C.P. analysed the data. E.C., G.B., P.-Y.B., V.C. developed the inference framework. E.C., D.A.C. developed the code.
378 E.C., G.B. performed the numerical simulations, and analysed the results. E.C. G.B., D.A.C., C.P., P.-Y.B., S.C., Y.Y.,
379 B.L., A.F., A.B., V.C. interpreted the results. V.C. wrote the Article. All authors contributed to and approved the final
380 version of the Article.

381 **CONFLICT OF INTEREST**

382 We declare that we have no conflicts of interest.

383 **DATA SHARING**

384 De-identified individual data on contacts of the two schools under study are publicly available at the Sociopatterns
385 project website (<http://www.sociopatterns.org/datasets/>). De-identified aggregated COVID-19 community
386 surveillance data by age class are publicly available at Sante publique France Data Observatory platform
387 (<https://geodes.santepubliquefrance.fr/>). De-identified aggregated COVID-19 prevalence data of pilot screenings
388 during the Alpha wave used in this study are available in the tables reported in the Appendix.

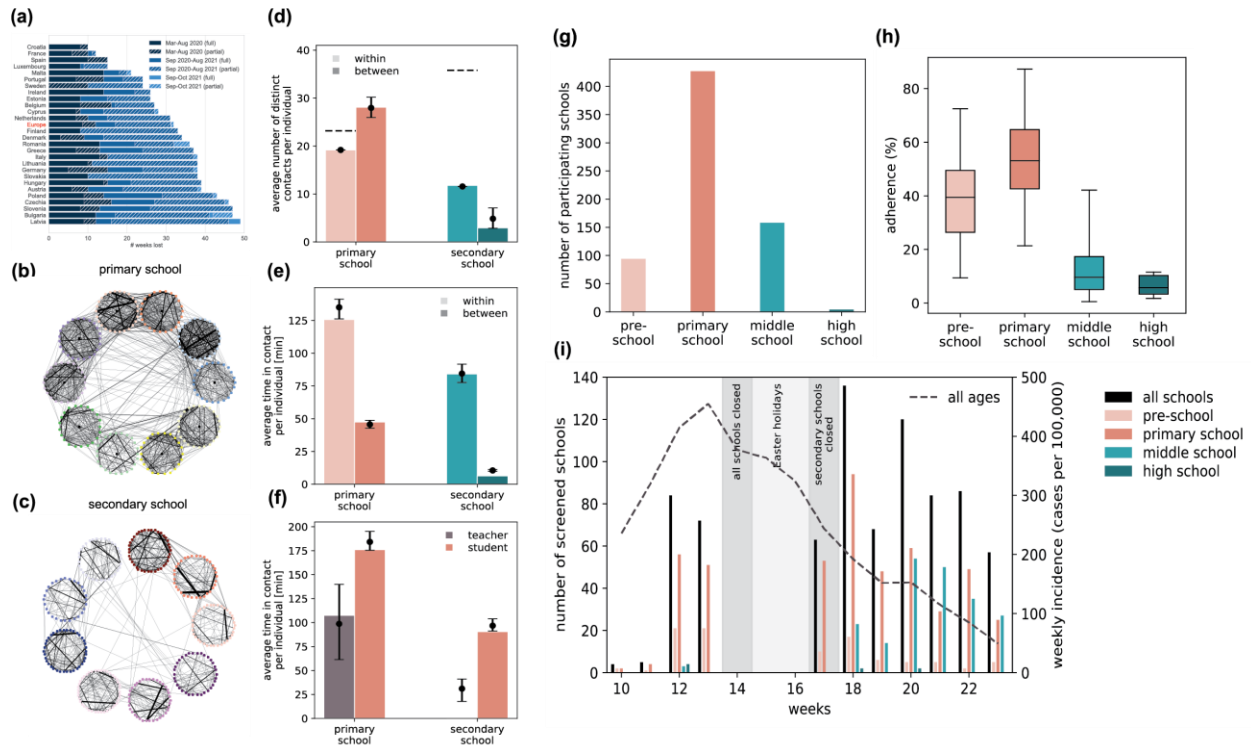
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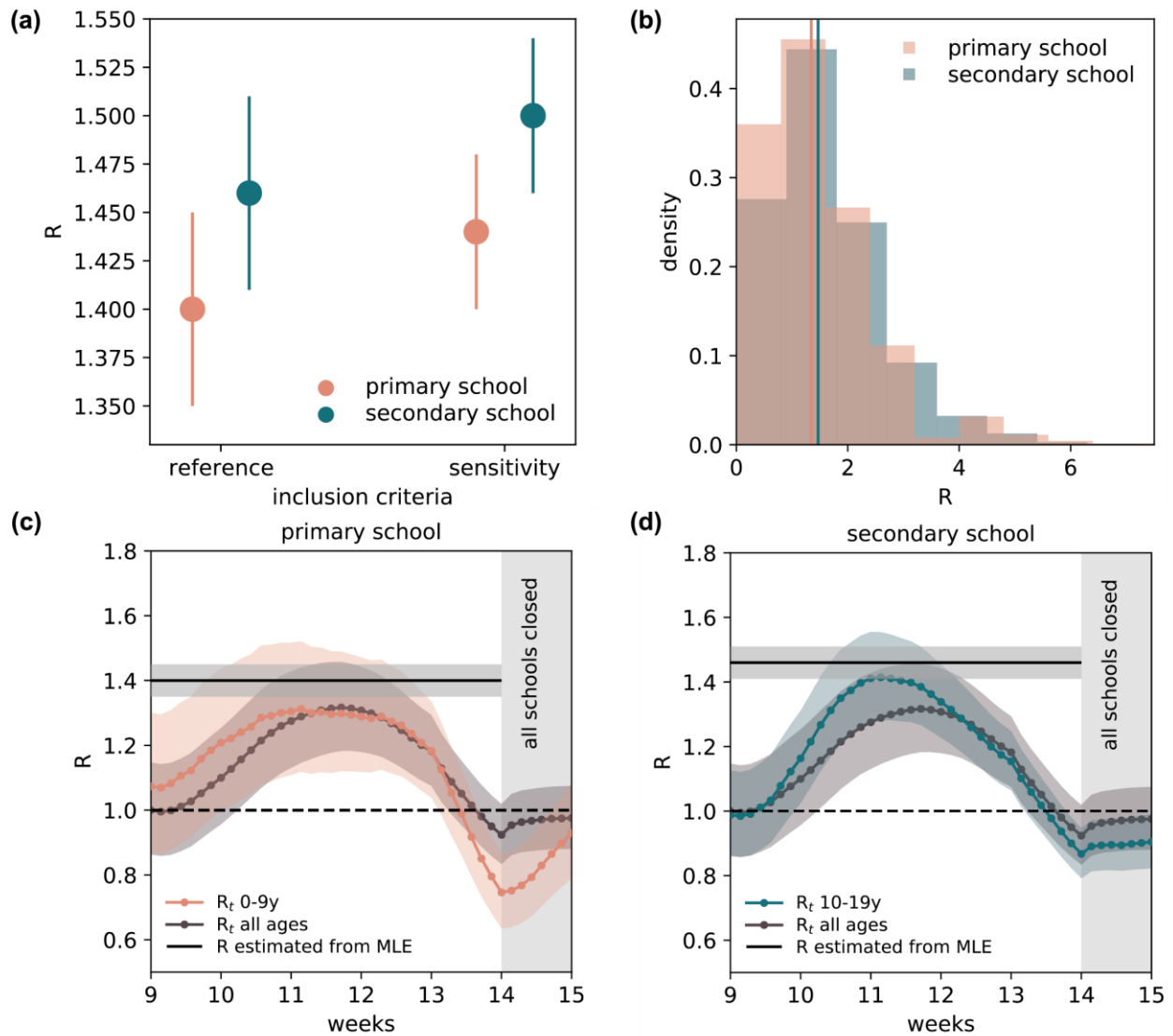
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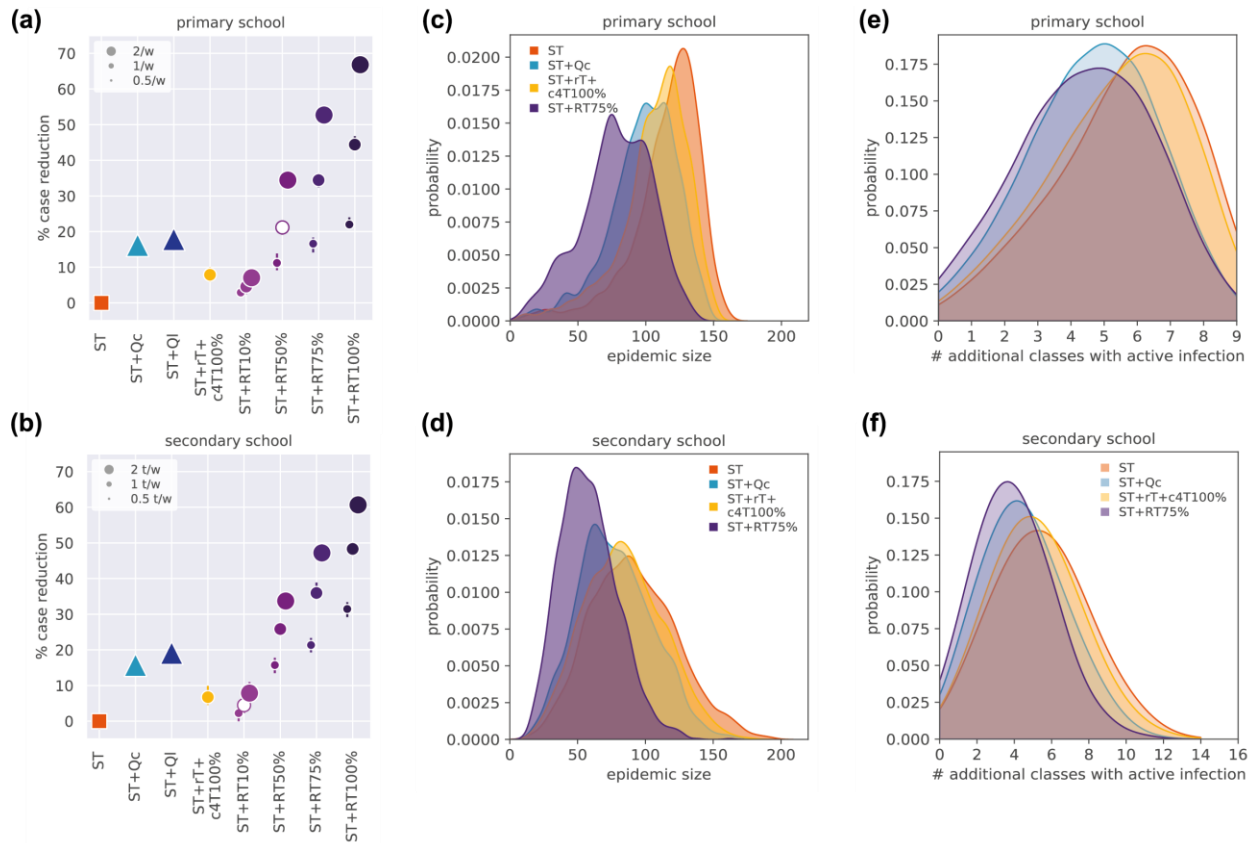


474
 475 **Figure 1. School closure in Europe, empirical contact networks in a primary and secondary school, and field**
 476 **screening data in schools in France.** (a) Number of in-presence weeks lost by students in Europe because of school
 477 closures due to the pandemic¹. (b), (c) Visualization of the empirical temporal contact data aggregated over two
 478 days, for the primary (panel b) and the secondary (panel c) school. Nodes represent teachers and students, circles
 479 represent classes, and links represent contacts (thickness proportional to contact duration). (d) Daily average
 480 number of distinct contacts per individual within the class or between classes. Horizontal dashed lines represent
 481 the average class size. (e) Daily average time that an individual spends in interaction within the class or between
 482 classes. (f) Daily average time that a teacher or student spends in interaction. In panels d-e-f, histogram bars refer
 483 to the empirical networks; points and error bars (95% bootstrap confidence intervals) refer to the synthetic
 484 networks. In panels d-e, the increase of average number of contacts and duration in the synthetic secondary
 485 school networks compared to their empirical counterparts is due to the *ad hoc* addition of contacts between
 486 school years. In panel f, no empirical data is shown for teachers, as they did not participate to the data collection,
 487 and their contact behavior was inferred from another dataset. (g) Number of schools participating to the pilot
 488 screenings during the spring 2021 wave in the Ain, Loire, and Rhône departments. (h) Observed adherence to
 489 screening. Boxplots represent the median (middle line), interquartile range (box limits) and 2.5th and 97.5th
 490 percentiles (whiskers). (i) Number of schools participating to the pilot screenings (left y axis) and weekly incidence
 491 over time from community surveillance in the 3 departments during the 2021 spring wave. The vertical shaded
 492 areas indicate the school closures.



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Figure 2. Estimates of the effective reproductive number in the school setting during the 2021 spring wave in France due to the Alpha variant. (a) Estimates of the effective reproductive number in the primary and secondary school obtained with the reference and the sensitivity inclusion criteria by fitting the model to pilot screening data. Estimates refer to the Alpha variant during the 2021 spring wave in France, when reactive closure of the class and mask mandates were in place. Errors indicate the 95% confidence intervals. (b) Predicted offspring distribution in the primary and secondary school. Vertical lines indicate the effective reproductive number (i.e. the average of the distribution) obtained with the reference inclusion criteria. (c) Comparison between the estimate R^{Alpha} (horizontal line; the shaded area corresponds to its 95% confidence interval) and R_t estimated from community surveillance incidence in the three departments during the rise of the 2021 spring wave. (d) As in panel c, for the secondary school.



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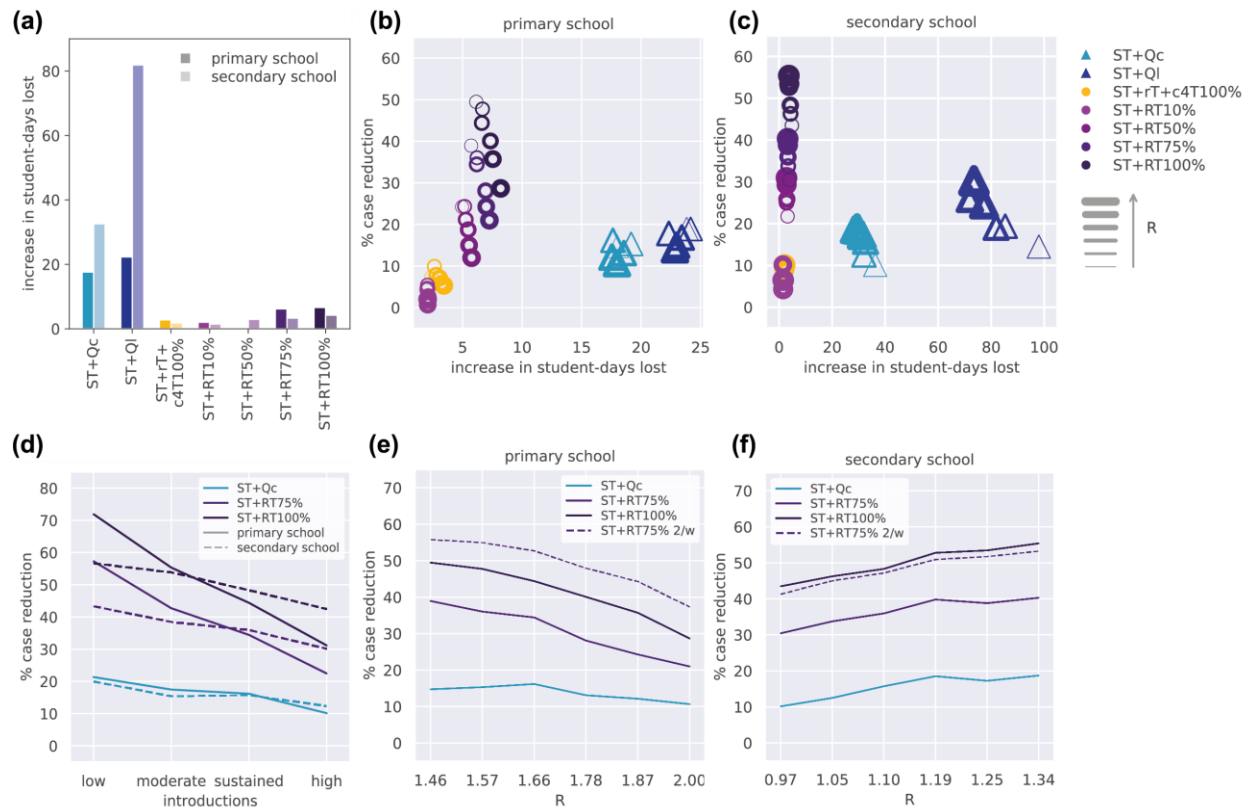
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Figure 3. Efficiency of regular testing in educational environments. (a) Predicted case reduction relatively to symptom-based testing (ST) in the primary school. The reduction is computed on the final size over 90 days. (b) As in panel a for the secondary school. (c) Probability distribution of the simulated epidemic size over 90 days in the primary school for selected protocols (regular testing is performed weekly). (d) As in panel c, for the secondary school. (e) Probability distribution of the additional number of classes in the primary school with at least one active infection when a case is confirmed, for selected protocols (regular testing is performed weekly). (f) As in panel e, for the secondary school. In all panels, simulations are parameterized with sustained introductions and estimated R^{Delta} corresponding to reactive class closure and mask mandate, and accounting for differences in vaccination coverage.



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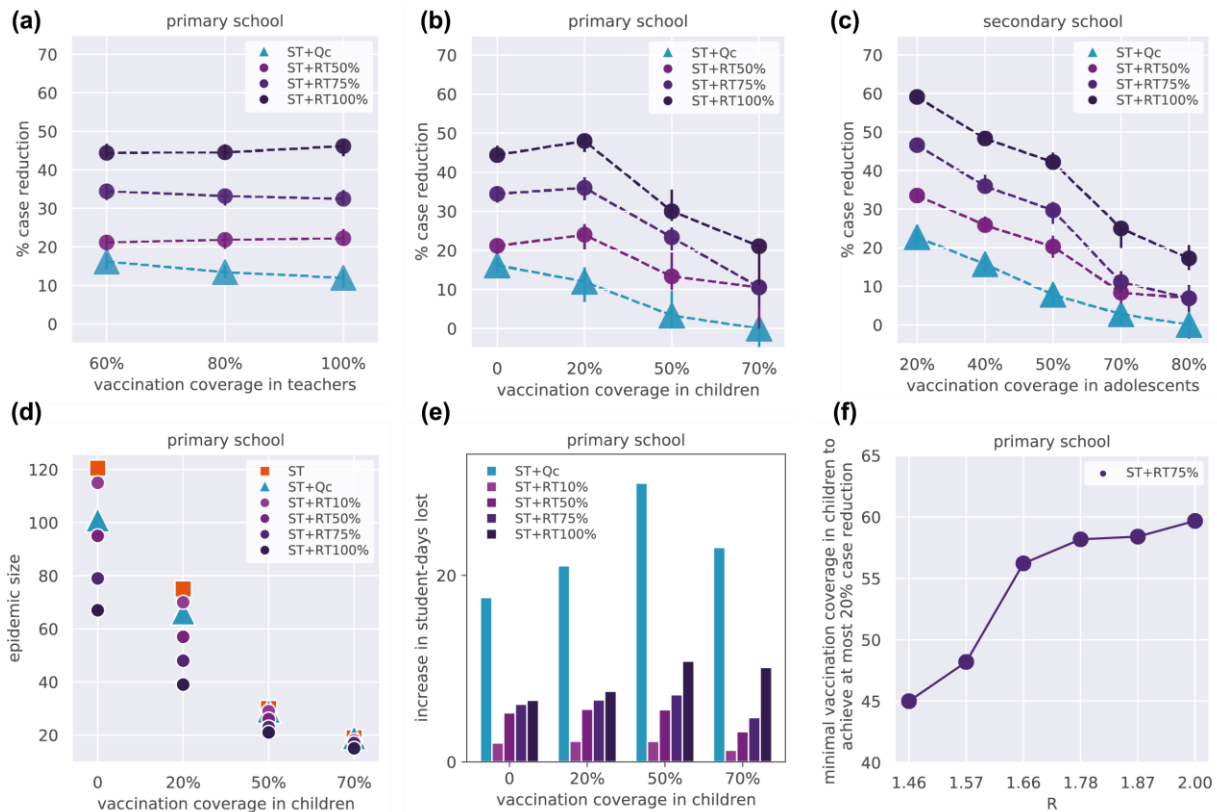
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Figure 4. Cost-benefit of regular testing in educational environments and impact of introductions and effective reproductive number. (a) Predicted increase in student-days lost relative to symptom-based testing for all protocols of Figure 3 (regular testing is performed weekly). Simulations are parameterized with sustained introductions and estimated R^{Delta} corresponding to reactive class closure and mask mandate, and accounting for differences in vaccination coverage. (b) Predicted case reduction vs. predicted increase in student-days lost in the primary school relative to symptom-based testing. Each point corresponds to a protocol (color-coded) and to a value of R (coded with the border thickness) in the range 1.46-2.00. Simulations are parameterized with sustained introductions. (c) As panel b, for the secondary school, with R in the range 0.97-1.34. (d) Predicted case reduction relative to symptom-based testing for selected protocols (regular testing is performed weekly) as a function of the introductions. Simulations are parameterized with the estimated R^{Delta} . (e) Predicted case reduction relative to symptom-based testing for selected protocols in the primary school as a function of R. Solid lines refer to weekly screening, dashed line to twice-weekly screening. Simulations are parameterized with sustained introductions. (f) As in panel e for the secondary school.



533
534 **Figure 5. Impact of vaccination coverage.** (a) Predicted case reduction relatively to symptom-based testing for
535 selected protocols (see legend in Figure 3) as a function of the vaccination coverage in teachers in the primary
536 school. (b) As in panel a, as a function of vaccination coverage in children. (c) As in panel a, for the secondary
537 school, as a function of vaccination coverage in adolescents. (d) Predicted final epidemic size over 90 days vs. the
538 vaccination coverage in children in the primary school for selected protocols. (e) Predicted increase in student-days
539 lost relatively to symptom-based testing for selected protocols as a function of the vaccination coverage in children
540 in the primary school. (f) Minimal vaccination coverage in children above which weekly testing with 75%
541 adherence (ST+RT75%) in the primary school has at most a benefit of 20% case reduction, as a function of R. In all
542 panels: simulations are parameterized with sustained introductions; regular testing is performed weekly.

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