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Modeling COVID-19 in school settings to evaluate prevention and control protocols

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The first wave of COVID-19 pandemic has led many countries to trigger global lockdowns as an emergency brake on an exponentially increasing number of contaminations. Such broad, nationwide measures have been efficient in reducing the mobility and number of contacts between individuals [1–4], however with large societal costs. In the successive waves, less restrictive lockdowns or curfews have been implemented [5]. Most importantly, more targeted strategies have been used, such as telework, mandatory masks in transports and closed settings, and others.

In parallel, school closures have been widely used in the pandemic's first year, with 10 to almost 40 weeks of school lost in EU countries from March 2020 to March 2021 [6]. While infections in children are mostly asymptomatic or present mild symptoms [7], accumulating scientific evidence points to a non-negligible role of schools in contributing to transmission in the community [7,8]. Closure of schools and remote teaching represent thus one of the several possible brakes on the epidemic spread [9]. However, given the dire consequences in terms of educational needs and increase of inequalities, keeping schools open while limiting contagion has become an important objective. In addition to mask wearing and hand hygiene, various protocols have been used in various countries, including: staggered arrivals and limitation of the mixing between classes, reactive class closure upon the appearance of one or several symptomatic cases, reactive testing of the class, regular testing and isolation of positive cases. These protocols have been designed and sometimes abruptly changed in a mostly ad hoc fashion and without any evaluation nor anticipation of their respective advantages and limitations.

Experimentally comparing protocols by implementing different measures in different schools is generally difficult to achieve because of many confounders, possibly problematic if measures need to be applied nationwide, and it would require long periods of application, often hardly compatible with the timescales of evolution of a pandemic wave. Infectious disease modelling can instead anticipate the impact of such measures, integrating data on the behaviour and interactions of individuals, on the progression of SARS-CoV-2 infection and its transmission, with the advantage of exploring potential outbreaks under different conditions (e.g. epidemic conditions, but also a variety of protocols). In addition, we can compare simulated outbreaks along several dimensions, such as the reduction of the number of cases and of the days of school lost by quarantined individuals. Being able to create "what if" scenarios through mathematical modelling offers elements to elucidate mechanisms at play (e.g. is it better to reactively close a class or proactively screen students?) and to provide the expected impact of different measures to inform decisions.

To this aim, we developed a stochastic agent-based model of SARS-CoV-2 within-school propagation [10], parameterized with age-specific estimates of susceptibility [11], transmissibility [12], probability of developing symptoms [13], and probability to detect a case based on symptoms [7], and considering external introduction of infected individuals in the school [10]. Using this data-driven model, we evaluated the benefit and cost of a wide range of scenarios in terms of epidemic conditions and protocols.

We considered symptom-based testing and case isolation (ST) as the basic strategy, and the following intervention protocols: reactive quarantine of the class (ST+Qc: once a case is identified through ST, their class is put in quarantine); reactive quarantine of the class level (ST+Ql: as ST+Qc, but quarantine is applied to the classes of the same level); reactive screening of the class (+1d from detection) followed by a control screening (+nd) with α adherence (ST+rT+cnTα%: once a case is identified through ST, a percentage α of the non-vaccinated school population in their class is reactively screened at +1 and +4 days); regular testing with α adherence (ST+RTα%: in addition to ST, regular testing is performed at a certain frequency).

The empirical contact data involved 232 students (6-11 years old) and 10 teachers in a primary school in Lyon composed of 5 levels, each of two classes [14]. We used it to build a network of contacts, synthetically extending the empirical data to 90 days (Figure 1a). It displays a strong community structure around the classes, students spent more time interacting within their class than outside the class ($p<10^{-15}$), and established longer contacts (+64%, p=0.009) compared to teachers (Figure 1b).

We tested the performance of different protocols under the estimated Delta transmissibility and moderate introductions (community surveillance incidence in primary school students from 50 to 900 cases per 100,000) (Figure 2a). We find that reactive class closure performs better than reactive screening, but only reduces by 17% (95% CI 14-21%) the number of cases compared to symptom-based testing. With reactive strategies, many cases remain undetected while other classes may already be affected due to the silent spreading within school or to unobserved introductions from the community (Figure 2b). Instead, if adherence is large enough, regular testing substantially outperforms reactive protocols. With 50% adherence, weekly screening would reduce the number of cases by 30% (95%CI 26-33%) compared to symptom-based testing, and by 43% (39-46%) with 75% adherence. Alternatively, similar reductions would be achieved with 50% adherence and twice-weekly testing.

Despite detecting many cases, regular testing leads to a very limited increase in student-days lost, <5.6 (5.2-5.9) times the number of days lost with the basic strategy and about 68-91% less than reactive class closure (Figure 3a). With regular testing indeed, isolation is targeted, only applied to cases during their infectious period, and it detects cases that otherwise go unnoticed, preventing further diffusion. Reactive class closure implies 17.4 (95% CI 17.0-17.8) times more student-days lost than symptom-based testing. Not being sufficiently targeted, reactive closure quarantines individuals while their risk of infection may be low, and the virus may have spread to other classes (Figure 2a). We have also considered cohorting, i.e., limiting the mixing between classes, which would substantially improve control (Figure 3b).

Higher incidence in the community and larger reproductive numbers reduce the benefit of weekly testing, thus requiring increased adherence or frequency [10]. Our results are robust against changes in detection rates, test sensitivity and relative transmissibility of children [10].

Finally, we tested the effect of vaccination coverage. We find that a high vaccination coverage in teachers does not achieve a collective benefit for the school population, mainly because of the small number of teachers and their low rate of interaction with students. Instead, extending vaccination to students grants a protective effect, reducing the likelihood and size of school outbreaks. When vaccination coverage is low or moderate, regular testing remains a key strategy to prevent a substantial portion of undetected infections, and its direct impact in the school environment is reflected in the community [15].

Studies such as ours show the huge potential of modelling for the evaluation of detailed scenarios and protocols, and thus for public health decision making tailored to specific contexts such as schools [10,16–18]. Models can be built at different levels of realism, including different levels of details on human behaviour and interaction, depending on the available data. Crucially, while the precise numbers, concerning e.g. the reduction of cases for a specific protocol, might depend on the specific epidemic conditions and on some specificities of the context considered (e.g., number of classes in a school, precise schedule), the main findings remain robust. In particular, the ranking of protocols according to efficiency or cost criteria is preserved across a range of epidemic conditions.

These considerations can be put in a broader perspective. During the Covid-19 pandemic, most public health measures, including lockdowns, have been taken reactively in situations of explosive numbers of cases [2,3,5]. On the contrary, anticipation is key, and, in a context of exponentially increasing contagions, timely implementations of measures can have a huge benefit, leading to a much smaller epidemic peak and to an earlier exit from these measures [5].
In the context of schools as well, reactive protocols are not able to make significant impacts because waiting for symptomatic cases to be detected corresponds to a lack of anticipation of the spread dynamics. Moreover, at high incidence, reactive testing imposes a large number of tests but in an unanticipated way, thus causing shortages and delays [19].
Iterative screening protocols instead detect both presymptomatic and asymptomatic cases, can be planned efficiently and would constitute moreover an epidemic surveillance tool allowing to detect the beginning of a new wave in a timely fashion.
Iterative screening comes clearly also at a cost, in terms of equipment (testing kits, reagents etc), personnel and organisation. This shows the crucial interest of preparedness of an infrastructure that could be activated rapidly when needed: a network of relationships between academic authorities, public health authorities, individual schools, suppliers, analysis laboratories, funding pipelines. Creating such networks at local and national levels would not only help in the current pandemic but represent an invaluable tool allowing rapid deployment of better containment strategies in future crises.

Competing interests
The authors declare that they have no competing interest.

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Figures

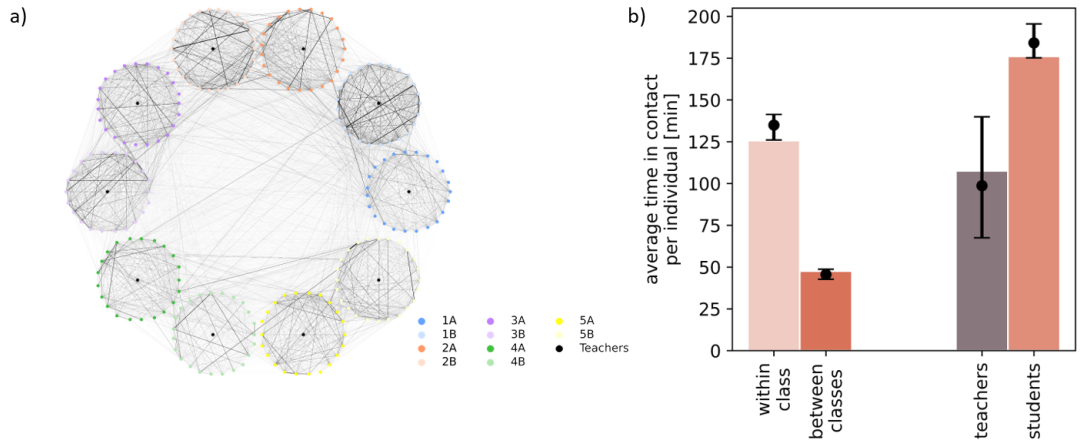

Figure 1. Empirical contact networks. a) Empirical temporal contact data aggregated over two days. Nodes represent teachers and students, circles classes (different colors), and links contacts (thickness coding duration). b) Daily average time that an individual spends in interaction within the same class or in different classes (left), and daily average contact time of teachers and students (right). Bars refer to empirical networks, points and errors (95% bootstrap confidence intervals) to synthetic networks.

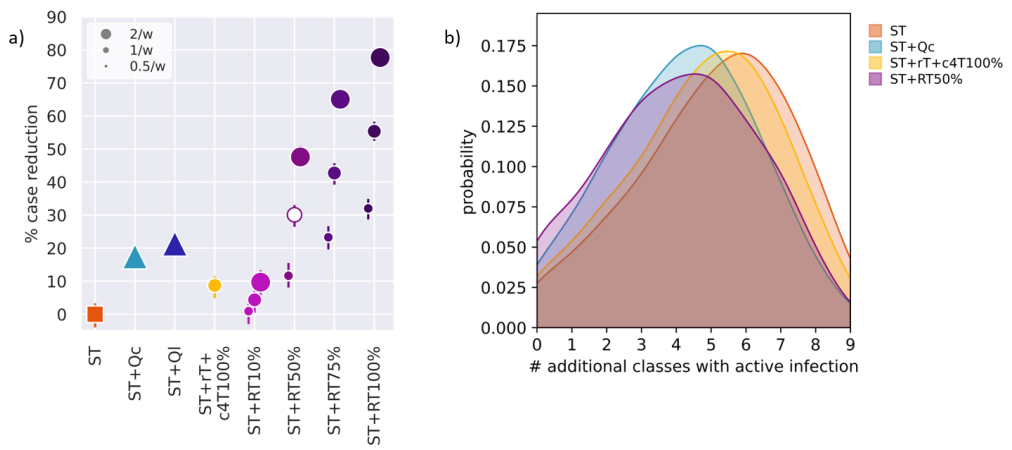

Figure 2. Efficiency of regular testing. a) Predicted percentage of reduction in the number of cases achieved by each intervention protocol with respect to the symptom-based testing (ST), computed on the epidemic final size over 90 days of simulation. Intervention protocols are: symptom-based testing with reactive quarantine of the class (ST+Qc); symptom-based testing with reactive quarantine of the class level (ST+Ql); symptom-based testing and reactive screening of the class, followed by a control screening with full adherence (ST+rT+c4T100%); symptom-based testing coupled with regular testing (ST+RTα%) with adherence α=10%, 50%, 75%, 100%, and frequencies: one test every two weeks, weekly test, two tests per week. Error bars correspond to 95% bootstrap confidence intervals. The empty marker corresponds to the adherence estimated from empirical data. b) Probability

distribution of the additional number of classes with at least one active infection when a case is confirmed. Four selected protocols are shown, regular testing is done with weekly frequency. Simulation results are obtained under the immunity profile of the Delta wave scenario, with moderate introductions.

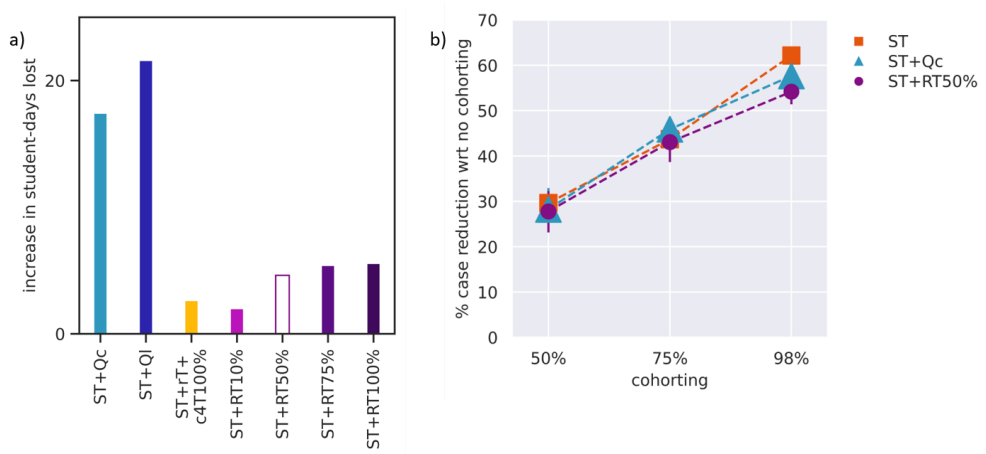

Figure 3. Cost-benefit of regular testing. a) Predicted increase in student-days lost with respect to symptom-based testing (ST), computed over 90 days. Intervention protocols are: symptom-based testing with reactive quarantine of the class (ST+Qc); symptom-based testing with reactive quarantine of the class level (ST+Ql); symptom-based testing and reactive screening of the class, followed by a control screening with full adherence (ST+rT+c4T100%); symptom-based testing coupled with weekly regular testing (ST+RTα%) with adherence α=10%, 50%, 75%, 100%. The empty bar corresponds to the adherence estimated from empirical data. b) Predicted percentage of reduction in the number of cases achieved by selected protocols when the duration of contacts between cohorts is reduced by p_cohorting=50%, 75%, 98%. Quantities are computed relatively to the same strategy when no cohorting is in place. Error bars correspond to 95% confidence intervals. Simulation results are obtained under the immunity profile of the Delta wave scenario, with moderate introductions.