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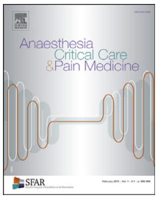

Editorial

Modelling 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 a rapidly 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 or 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], parameterised 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 benefits and costs 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 (Fig. 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 (Fig. 1b).

We tested the performance of different protocols under a Delta wave scenario with moderate introductions (community surveillance incidence in primary school students from 50 to 900 cases

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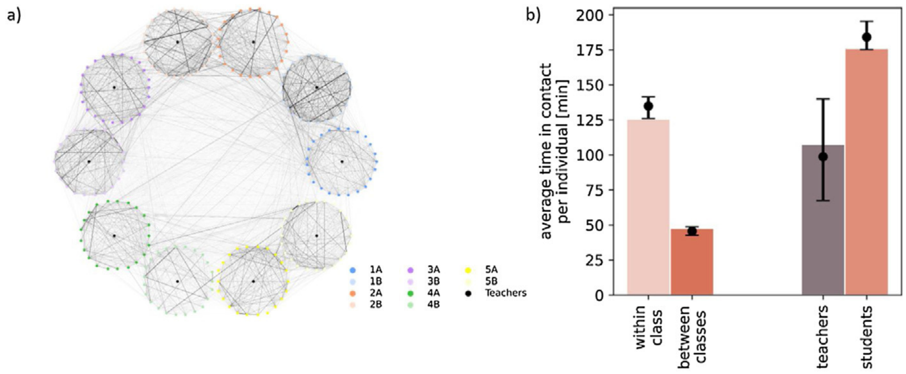

Fig. 1. Empirical contact networks.

(a) Empirical temporal contact data aggregated over two days. Nodes represent teachers and students, circles classes (different colours), 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.

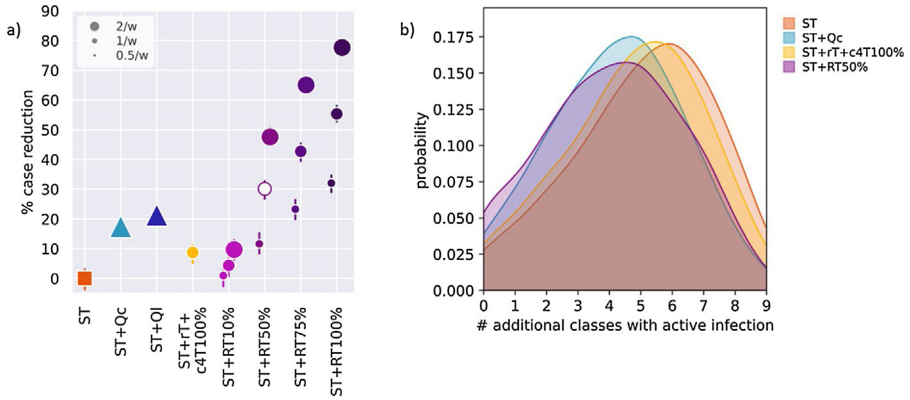

Fig. 2. Efficiency of regular testing.

(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 [10]. (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.

per 100,000) (Fig. 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 (Fig. 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 (Fig. 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 (Fig. 2a). We have also considered cohorting, *i.e.*, limiting the mixing between classes, which would substantially improve control (Fig. 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 high vaccination coverage in teachers does not provide a strong 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

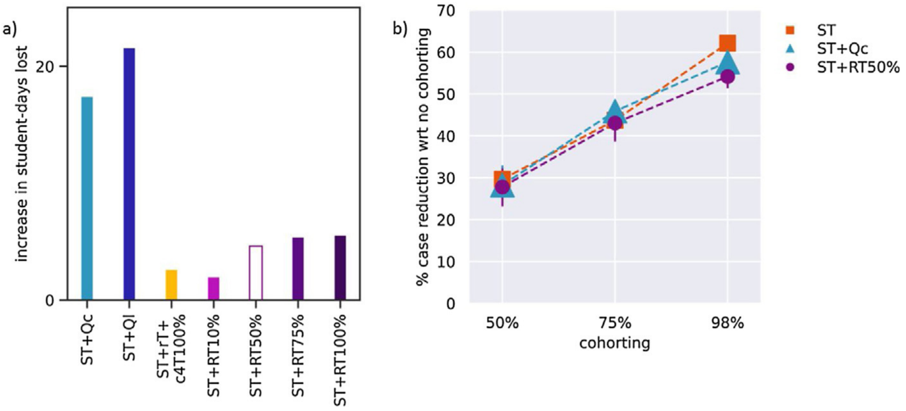

Fig. 3. Cost-benefit of regular testing.

(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 [10]. (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.

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 for example 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 that allows detecting 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 represents an invaluable tool allowing rapid deployment of better containment strategies in future crises.

Data availability

De-identified individual data on contacts at school are publicly available at the SocioPatterns project website (http://www.sociopatterns.org/datasets/).

Competing interests

The authors declare that they have no competing interest.

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References

[1] Pullano G, Valdano E, Scarpa N, Rubrichi S, Colizza V. Evaluating the effect of demographic factors, socioeconomic factors, and risk aversion on mobility during the COVID-19 epidemic in France under lockdown: a population-based study. Lancet Digit Health 2020;2(December (12)):e638–49. http://dx.doi.org/10.1016/S2589-7500(20)30243-0.
[2] Kraemer MUG, Yang C-H, Gutierrez B, Wu C-H, Klein B, Pigott DM, et al. The effect of human mobility and control measures on the COVID-19 epidemic in China. Science)2020;(May). http://dx.doi.org/10.1126/science.abb4218.
[3] Di Domenico L, Pullano G, Sabbatini CE, Boëlle P-Y, Colizza V. Impact of lockdown on COVID-19 epidemic in Île-de-France and possible exit strategies. BMC Med 2020;18(July (1)):240. http://dx.doi.org/10.1186/s12916-020-01698-4.
[4] Jarvis CI, Van Zandvoort K, Gimma A, Prem K, Auzenbergs M, O'Reilly K, et al. Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK. BMC Med 2020;18(May (1)):124. http://dx.doi.org/10.1186/s12916-020-01597-8.
[5] Di Domenico L, Sabbatini CE, Boëlle P-Y, Poletto C, Crépey P, Paireau J, et al. Adherence and sustainability of interventions informing optimal control against the COVID-19 pandemic. Commun Med 2021;1(December (1)):1–13. http://dx.doi.org/10.1038/s43856-021-00057-5.

[6] UNESCO. "Education: From disruption to recovery," *UNESCO Building peace in the minds of men and women*, Mar. 04, 2020. https://en.unesco.org/covid19/educationresponse [Accessed 20 May 2021].

[7] Goldstein E, Lipsitch M, Cevik M. On the effect of age on the transmission of SARS-CoV-2 in households, schools, and the community. J Infect Dis 2021;223(February (3)):362–9. http://dx.doi.org/10.1093/infdis/jiaa691.

[8] Li Y, Campbell H, Kulkarni D, Harpur A, Nundy M, Wang X, et al. The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries. Lancet Infect Dis 2021;21(February (2)):193–202. http://dx.doi.org/10.1016/S1473-3099(20)30785-4.

[9] Di Domenico L, Pullano G, Sabbatini CE, Boëlle P-Y, Colizza V. Modelling safe protocols for reopening schools during the COVID-19 pandemic in France. Nat Commun 2021;12(February (1)):1073. http://dx.doi.org/10.1038/s41467-021-21249-6.

[10] Colosi E, Bassignana G, Contreras DA, Poirier C, Boëlle P-Y, Cauchemez S, et al. Screening and vaccination against COVID-19 to minimize school closure: a modeling study. Lancet Infect Dis 2022. In press. Available at https://www.medrxiv.org/content/10.1101/2021.08.15.21261243v2.

[11] Viner RM, Mytton OT, Bonell C, Melendez-Torres GJ, Ward J, Hudson L, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. JAMA Pediatr 2021;175(February (2)):143. http://dx.doi.org/10.1001/jamapediatrics.2020.4573.

[12] Dattner I, Goldberg Y, Katriel G, Yaari R, Gal N, Miron Y, et al. The role of children in the spread of COVID-19: using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children. PLoS Comput Biol 2021;17(February (2)). http://dx.doi.org/10.1371/journal.pcbi.1008559.

[13] Davies NG, Klepac P, Liu Y, Prem K, Jit M, Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. Nat Med 2020;26(August (8)). http://dx.doi.org/10.1038/s41591-020-0962-9. Art. no. 8.

[14] Gemmetto V, Barrat A, Cattuto C. Mitigation of infectious disease at school: targeted class closure vs school closure. BMC Infect Dis 2014;14(December (1)):695. http://dx.doi.org/10.1186/s12879-014-0695-9.

[15] Grant R, Charmet T, Schaeffer L, Galmiche S, Madec Y, Platen CV, et al. Impact of SARS-CoV-2 Delta variant on incubation, transmission settings and vaccine effectiveness: results from a nationwide case-control study in France. Lancet Reg Health Eur)2021;(November). http://dx.doi.org/10.1016/j.lanepe.2021.100278.

[16] McGee RS, Homburger JR, Williams HE, Bergstrom CT, Zhou AY. Model-driven mitigation measures for reopening schools during the COVID-19 pandemic. PNAS 2021;118(September (39)). http://dx.doi.org/10.1073/pnas.2108909118.

[17] Paltiel AD, Zheng A, Walensky RP. Assessment of SARS-CoV-2 screening strategies to permit the safe reopening of college campuses in the United States. JAMA Netw Open 2020;3(July (7)):e2016818. http://dx.doi.org/10.1001/jamanetworkopen.2020.16818.

[18] Lasser J, Sorger J, Richter L, Thurner S, Schmid D, Klimek P. Assessing the impact of SARS-CoV-2 prevention measures in schools by means of agent-based simulations calibrated to cluster tracing data. medRxiv)2021;(April). http://dx.doi.org/10.1101/2021.04.13.21255320. p. 2021.04.13.21255320.

[19] Morin V, et al. "Covid-19: dans les écoles, la semaine de toutes les tensions," *Le Monde.fr*, Jan. 08, 2022. Accessed: 20 January 2022. [Online]. Available: https://www.lemonde.fr/education/article/2022/01/08/covid-19-dans-les-ecoles-la-semaine-de-toutes-les-tensions_6108656_1473685.html.

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