The How Matters: Simulation-Based Assessment of the Potential Contributions of Lateral Flow Device Tests for Keeping Schools Open and COVID-Safe in England

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ABSTRACT

Environments where exact contact tracing is infeasible pose a challenge to ‘test and trace’ approaches for containing infectious diseases like COVID-19 that rely on following up on the close contacts of an index case. This is particularly problematic in primary schools and some workplaces. The additional benefit of using rapid screening tests over mere isolation restrictions of contacts has repeatedly been put forward for schools in the United Kingdom as potentially leading to improved containment and less absence from school for the pupils, but setting up randomized comparisons in primary schools is particularly challenging. Investigating this issue continues to be relevant as many countries take similar steps and more infectious mutations of the virus emerge while pupils, especially young ones, remain largely unvaccinated. We use a customized agent-based simulation to assess the impact of different test and isolation schemes on containment of outbreaks and school days missed in a primary school setting. The simulation links the screening test sensitivity and the infection risk to each individual’s latent viral load. Robustness with respect to a number of criticisms of previous models is assessed by extensive sensitivity analyses. We made the core functionality of our simulation tool available as an interactive web app allowing investigators to explore parameter ranges relevant to their scenario of interest. Reactive use of repeated lateral flow device (LFD) screening tests (‘test for release’) is less effective than regular whole school cross-sectional testing in primary schools and comparable settings and the influence of screening test sensitivity is secondary to that of other key parameters that impact transmission. Results are stable with respect to a wide range of previously debated additional factors like test-retest autocorrelation, imperfect test compliance, and assumptions on the dynamics of viral loads in infected individuals. Our findings support the adoption of regular (e.g. once- or twice-weekly) cross-sectional testing to contain COVID-19 in primary school settings.

Keywords: COVID-19, agent-based simulation, public health, policy

1. Introduction

Controlling infections in schools during the COVID-19 pandemic while allowing pupils as much in-person contact with teachers as possible is important. The challenge for decision makers lies in balancing the health risks from infection of children in schools and potential secondary infections in their families with the risks of loss of skills for the young and of increased inequality, the risks also to child and parental mental health, and the economic and social impact of parents not being able to return to work (DELVE Initiative, 2020). Since the start of the pandemic, many countries have incorporated periods of school closures as part of their nonpharmaceutical interventions (NPIs) implemented to control disease transmission (Hale et al., 2021).

Our work focuses on within-school transmission and addresses the public health issue of how to keep schools open during an ongoing wave of the COVID-19 pandemic, as articulated by the World Health Organization

(2021). The scenarios considered in this article are inspired by the situation in the United Kingdom prior to the reopening of schools on March 8, 2021, after a prolonged period of school closures since early January, closures that had been justified by accumulating evidence consistent with increased transmission occurring among school children (Children’s Task and Finish Group, 2020; Office for National Statistics, 2020). This raised intense discussion about which infection-control policies combining rapid testing and isolation would be both beneficial and feasible to implement in schools and how to evaluate their effectiveness (Bird et al., 2005; Wise, 2020). The scenario remains highly relevant in the light of concern about emerging mutations, such as Delta (Torjesen, 2021) and Omicron (European Centre for Disease Prevention and Control, 2021) and increasing infection rates among pupils reported in the United Kingdom (Steel & Haughton, 2021).

We compare a set of NPIs with respect to the dual goals of outbreak control and school days lost by means of an agent-based simulation tailored to the school setting and an interactive web application (Kunzmann & Lingjærde, 2021). We also conduct extensive sensitivity analyses with respect to aspects such as lateral flow device (LFD)-test compliance, additional within-subject autocorrelation of LFD-tests, and the population structure.

Leng and colleagues considered a similar setting (Leng, Hill, Holmes et al., 2021; Leng, Hill, Thompson et al., 2021) to ours. Our approach differs in three key aspects. First, we model both the test sensitivity and the probability to infect others as functions of the underlying viral load of each individual (here pupil) instead of considering these characteristics as independent functions of time since infection. This allows a realistic correlation between infectivity and test sensitivity driven by the underlying biology. Second, we focus on a primary school setting with a fine-grained population structure. We consider policies that act on the level of classes or subgroups of close contacts within classes instead of entire age groups. Third, the focus of our policy evaluation is on the additional benefit that LFD testing can provide while maintaining the principle of the test and trace symptom-based isolation instead of substituting it.

We base our model on the following assumptions:

1. The proportion of asymptomatic SARS-CoV-2 infections is higher in children than in adults (Hippich et al., 2021; Wald et al., 2020).
2. Transmission can occur from asymptomatic infections (Arons et al., 2020; Oran & Topol, 2020; Sutton et al., 2020).
3. Overall transmissibility is related to viral load (VL) (He et al., 2020) and is higher for symptomatic infections due to their generally longer clearance time (Larremore et al., 2021).
4. Delay from swab date to polymerase chain reaction (PCR) result date is seldom less than 24 hours (Fraser & Briggs, 2021; Larremore et al., 2021).
5. LFD tests have been used for screening purposes in nursing homes, workplaces, and primary schools (Department for Education, 2021b; Department of Health and Social Care, 2021a, 2021b), and give a nonquantitative test-result within 30 minutes (Mina et al., 2021).

6. PCR confirmation of any LFD-positive results is recommended (Department for Education, 2021a).

2. Methods

We adopt an agent-based approach where agents correspond to individual pupils. The overall model is composed of independent submodels for

1. the contact structure between individual pupils,
2. viral load and symptom status trajectories during an acute SARS-CoV-2 infection,
3. the infection probability depending on the latent viral load,
4. and the sensitivity of the tests (PCR or LFD) that might be required for a policy.

The time resolution of the overall model is daily, that is, daily symptom status and viral load are determined at 7:30 a.m. Pupils then either go to school on weekdays or isolate at home depending on their symptom status and the policy in place. We assume that any policy intervention (screening tests, isolation) is executed before individuals have a chance to meet in school. This is an optimistic assumption but consistent with, for example, Whittaker (2021). On school days, we continue by randomly sampling risk contacts for pupils not currently isolating according to the school contact structure. For each contact involving an infected and a noninfected individual, we then sample whether or not an infection occurs according to the disease submodel. No mixing and thus no school-internal infections can occur on the weekends, but individuals are still at risk of external infections (see following).

We consider a time horizon of 6 weeks, which roughly corresponds to the length of a half-term. For each day of the simulation (6 weeks, 42 days), we additionally sample new school-external infection events for each pupil. We use a fixed binomial probability for each pupil and day of $2/324/7$, which means that two external infections can be expected per week in a primary school of 324 pupils. This corresponds to an incidence of 617 new cases per 100,000 individuals per week. This value is relatively high as our focus is on situations where there is a need for controlling infections.

For each scenario, we reran the simulation 250 times to capture the variability of the outcome measures of interest. All plots in this article were generated using a combination of R and Julia (Bezanson et al., 2017; R Core Team, 2021). The source code is available online, allowing our results to be fully reproducible (Kunzmann et al., 2021a, 2021b). For exploration of further scenarios and policies, we refer to the Shiny app that accompanies this work (see Supplementary Material, A13 for details).

2.1. Population Model

The average size of an English primary school in the academic year 2019–2020 was 281 pupils with an average class size of 27 (GOV.UK, 2021b). We consider a typical primary school with 6 years, two classes per year-group and 27 pupils per class, that is, 324 pupils overall. We further assume that each class is subdivided

into three *bubbles* of nine pupils each. Here the term ‘bubble’ refers to a group of pupils that is isolated as best as possible from other members of the same class (Department for Education, 2021b). Although contact tracing is an effective tool to control an epidemic (Ferretti et al., 2020), social distancing and contact tracing within bubbles are deemed unrealistic for younger pupils. The degree of isolation between bubbles depends, among other factors, on the availability of large enough classrooms and sufficient staff. We model this as a three-level hierarchical population of individual pupils who can interact either on the bubble, the class, or the school level. Members of staff are not modeled explicitly. Details of the population structure are given in section A1 of the Supplementary Material.

2.2. Model for Viral Load and Symptoms

Data on the evolution of viral load (VL) in children during an acute infection with SARS-CoV-2 are rare but cross-sectional data suggest that there is no substantial difference between VL of symptomatic children and adults (Baggio et al., 2020; Jones et al., 2020). We thus build on available evidence for VL-trajectories over time in adults and the Larremore model proposed by Larremore et al. (2021). Here, each individual's VL-trajectory is determined by a set of pivot points with ordinates on the log-10-VL scale and subsequent linear interpolation of the pivot points (see Figure 1 below for example trajectories and section A2 of the Supplementary Material for details of the model). Furthermore, we assume a daily rate of 1% for COVID-like symptoms due to non-COVID-related causes.

Figure 1. Thirty randomly sampled viral load (VL)-trajectories under the Larremore model, assuming that 50% of children are asymptomatic. Horizontal solid black line corresponds to the default lower limit of infectivity of ; the infection probability is calibrated to a school-level reproduction number of 3 and the mean presymptomatic lateral flow device (LFD) sensitivity is assumed to be 60% (see 2.3, 2.4, and 4.1).

2.3. Infectivity Model

We assume that individuals who already went through an infection are no longer susceptible to infection. We model the probability to infect a susceptible individual during a risk-contact (‘infection probability’) as function $f(VL_t)$ of the infected individual's latent viral load on the day of the risk-contact t . Larremore et al. (2021) conduct sensitivity analyses for different functional forms of f and base their main results on a model where the infection probability is assumed to be proportional to $\log_{10}(VL_t)$ if a lower limit of infectivity, LLI, is exceeded:

$$f_{\text{Larremore}}(VL_t) := \min(1, \max(0, \gamma(\log_{10}(VL_t) - \log_{10}(LLI)))) \quad (1)$$

Whenever LLI is fixed externally, infectivity only depends on the choice of γ . We follow Larremore and colleagues to match γ to a target school-level reproduction number R_S (see Supplementary Material, A3). This reproduction number is defined as the expected number of infections from a given index case in a completely susceptible school population over the first 21 days.

2.4. Model for the Screening Test Characteristics

Sensitivity of LFD tests has been shown to depend on viral load (Lennard et al., 2021; University of Liverpool, 2020). This is crucial since a joint dependence of test sensitivity and infection probability on the latent viral load trajectories implies a positive correlation between the two. Following data presented by Lennard et al. (2021), we consider a logistic regression model for the functional form $g(VL_t)$ of the test sensitivity as function of VL

$$g(VL_t) := \text{logit}^{(-1)}(\beta_{\text{test}} \log_{10}(VL_t) + c_{\text{test}}) \quad (2)$$

where β_{test} is the VL slope on the log-10 scale and c_{test} the intercept. We calibrate the sensitivity curve such that the sensitivity in a simulated presymptomatic set of infected individuals matches the target value (see Supplementary Material, A4). We assume a fixed LFD test specificity of 0.998 (University of Liverpool, 2020).

3. Policies

We assume that the swab for a confirmatory PCR follow-up test is taken on the day of symptom onset or of testing positive with an LFD screening test (GOV.UK, 2021a). The turnaround time for PCR tests is assumed to be 2 days (Fraser & Briggs, 2021) and the isolation time for PCR-confirmed cases is 10 days starting with the PCR swab day (NHS Test & Trace, 2020). PCR tests are more sensitive than antigen-based screening tests and we assume a flat sensitivity of 97.5% above a limit of detection of 300 and a specificity of 100% (U.S. Food and Drug Administration, 2020). We further assume that any pupil who becomes symptomatic is immediately isolated at home before school and that a swab for a PCR test is taken on the same day. These pupils only return to school after isolating for either 10 days from their swab date (positive result) or 2 days during the PCR turnaround time (negative swab test).

3.1. Reference Policy

The reference policy does not use LFD tests and solely relies on symptom-driven isolation. If an index case shows symptoms and starts their self-isolation period, the remaining members of the bubble (and class) continue to attend school until the test result of the symptomatic index case becomes available. Only if the index case's PCR test turns out to be positive do the remaining individuals in the bubble isolate for the remaining 8 days. Newly symptomatic cases while in isolation are also checked with PCR tests and newly emerging PCR-positive results reset the isolation clock for the entire bubble.

3.2. Extended Weekend

We consider a variant of the reference policy where the entire school is closed on Thursdays and Fridays. Otherwise the same procedures as under the reference policy apply. This effectively constitutes a mini-lockdown of 4 days over the extended weekend, facilitating the identification of symptomatic cases before they can spread the virus in school.

3.3. Regular Screening

To assess the added benefit of regular screening tests, we consider the reference policy extended by regular rapid-LFD screening tests either on Mondays or Mondays and Wednesdays before going into class for every pupil (except those already isolating). Since LFD tests are considerably more specific than mere symptoms, we assume that a positive LFD test result for an index case leads to an immediate isolation and return home of the entire bubble of the index case. The bubble (and the index case) return to school either after 2 days if the index case's PCR test turns out negative (2 days isolation) or after the full 10 days of isolation if the test turns out positive.

3.4. Test for Release

Finally, we consider a policy that we refer to as 'test for release.' Such an approach was proposed in early 2021 in the United Kingdom to avoid preemptive bubble isolation in schools (Department for Education, 2021a, 2021b). Instead, under a test for release policy, members of the bubble around newly symptomatic index cases are followed up using daily LFD testing. Only newly symptomatic or LFD-positive individuals isolate, while the remainder of the bubble attends school. Symptomatic or LFD-positive cases are told to self-isolate immediately and are then followed up with PCR tests as under the default strategy. The bubble-wide LFD testing starts on the day of the index case's triggering event (either symptom onset or a positive LFD test) and continues for up to 7 school days. If a new LFD-positive case is found in the bubble, the clock for daily testing of the bubble is reset. Daily bubble-contact testing is terminated early if all outstanding PCR tests turn out to be negative.

4. Results

4.1. The Baseline Case

The baseline scenario considered is based on a fraction of 50% asymptomatic cases (Hippich et al., 2021), two expected weekly community infections, $R_S = 3$, and a mean LFD test sensitivity of 60%.

Figure 2. Results for the baseline scenario with , mean presymptomatic lateral flow device (LFD) test sensitivity of 0.6, and 50% asymptomatic cases over the 6-week horizon. A: Box-plots of the distribution of the proportion of infected pupils and the proportion of school days missed; B: Scatterplot of the proportion of missed school days against the proportion of infected pupils of individual simulation runs; black line indicates first bisector; C: Box-plots of the average number of polymerase chain reaction (PCR) and LFD tests per pupil.

Figure 2 shows the policies' tradeoff between school days missed and the effectiveness of the containment of new outbreaks. The percentage of school days missed is plotted against the percentage of ultimately infected

individuals in panel B, where policies concentrated above the first bisector tend to favor containment over attendance. Boxplots of the corresponding marginal distributions are shown in Panel A. The numbers of LFD and PCR tests per pupil are given in panel C.

Neither the reference policy nor the test-for-release policies fully succeed in containing outbreaks sufficiently. The reference policy still performs slightly better than the LFD-based test-for-release approach due to the earlier isolation of bubbles with symptomatic cases. Additional regular weekly asymptomatic testing on Mondays clearly improves outbreak control over the reference policy with a similar proportion of school days missed and a higher LFD test burden per child. A second regular screening on Wednesday further improves containment at a small additional cost in terms of school days missed but doubles the LFD test burden. The extended weekend scenario gives intermediate results in terms of containment while considerably increasing the number of school days lost.

Figure 3. Median (10% and 90% quantiles) number of infected, recovered, and susceptible individuals over time for the baseline scenario with , mean presymptomatic lateral flow device (LFD) test sensitivity of 0.6, and 50% asymptomatic cases over the 6-week horizon.

Looking at the dynamics over time (Figure 3), it is evident that only the two policies making use of regular screening tests can control the spread of the virus over the 6-week period. For the reference, test-for-release,

and Thursday-/Friday-off policies, a clear weekend effect is discernible where the spread slows down on weekends when pupils are assumed not to mix.

Since test for release is not able to control outbreaks effectively, a larger number of individuals eventually develop symptoms and get tested with PCR tests. This explains the relatively high number of PCR tests per pupil required under this policy (Figure 2C). The initially low number of symptomatic cases implies that the number of LFD tests remains low until the infection has already spread throughout the population. In the beginning, the test-for-release policy is thus mainly relying on PCR tests and symptoms, which are both assumed to be fairly specific to COVID. This specificity translates in a low number of days spent ‘unnecessarily’ in isolation, that is, without being infected, but on the other hand, the policy is not able to control the spread over a longer time span.

4.2. Infectivity, Symptoms, and LFD Test Sensitivity

Data on the actual LFD test sensitivity and on the fraction of asymptomatic children are scarce. Moreover, evidence on between-student infectivity (R_S) is difficult to map to the particular school structure considered here. We thus investigate the stability of the results with respect to these three key parameters over a range of values (see Figure 4).

Figure 4. Sensitivity of results to change in key parameters. A: Proportion of infected pupils by and the fraction of asymptomatic cases over a 6-week horizon for a mean lateral flow device (LFD) test sensitivity of 0.6; B: Proportion of infected pupils by mean LFD test sensitivity for (LFD-based policies only).

The differences between policies are most pronounced in the highest infectivity scenario ($R_S = 6$), but the relative performance of the different policies remains stable. As expected, an increased proportion of

asymptomatic cases leads to a deterioration of infection containment for all policies. The relative impact of LFD test sensitivity is higher for policies with regular screening due to the higher overall number of tests conducted but remains small compared to the between-policy differences (see Figure 4).

4.3. Further Scenarios

We explored further scenarios to assess how perturbations of some of the model assumptions affect results. We considered imperfect LFD test compliance in section A5 and the impact of additional test-retest autocorrelation in section A6 of the Supplementary Material. The impact of a lower LLI is explored in section A7 of the Supplementary Material. We then considered a scenario where additional variation of the VL trajectories was introduced by adding a temporally correlated student's t process to the sampled log-10 VL trajectories of the Larremore model (see Supplementary Material, A8). We also explored how increasing between-individual heterogeneity with respect to LFD-test sensitivity would affect outcome by adding a random effect to the LFD test sensitivity model (see Supplementary Material, A9). Finally, we consider different external infection rates (A10), a scenario where effective between-bubble isolation is infeasible (A11), which is more in line with secondary schools and a larger school size (A12). Under all perturbations the results and the relative performance of the respective policies remain stable.

5. Discussion

Vaccination against COVID-19 is still not widely recommended for young children. Thus, controlling school outbreaks with minimal effect on attendance remains an important goal in the middle term, in particular, in the face of emerging variants with increased transmission potential.

Other agent-based simulation tools are available and were used to simulate policy impact during COVID-19 outbreaks. However, these models tend to focus on larger-scale settings (Li & Giabbanelli, 2021; Silva et al., 2020), or local geospatial aspects of transmission (Vermeulen et al., 2020). The tool openABM allows the evaluation of very flexible NPIs and the setting up of agent-based simulations on a much larger scale than single schools (Hinch et al., 2020, 2021). For our context of application, openABM does not support the very fine-grained control required to implement the test-for-release approach and the detailed model for LFD-test sensitivity as a function of viral load. In contrast, the simulation setup that we created captures important features of the SARS-CoV-2 infection process and the LFD test sensitivity. We have focused our attention on policy implications and developed a tool for decision support for schools, but the results are transferable to other small-population environments where exact contact tracing cannot be implemented. Our conclusions are also relevant to workplace settings.

We have based our work on the model for viral load presented by Larremore et al. (2021), which has been criticized for being unrealistically light-tailed (Deeks et al., 2021). We addressed this criticism with extensive robustness analyses and all results are stable across a wide spectrum of parameter configurations. Despite a very different approach to modeling the relationship between infectivity and test sensitivity, we reach the same

conclusion as Leng and colleagues with respect to the shortcomings of a dynamic testing regime without preemptive isolation of close contacts: testing alone is not sufficient to contain new outbreaks (Leng et al., 2021a). Since our initial preprint was made available in March 2021 (Kunzmann et al., 2021c), other agent-based studies with similar objectives to our work have emerged, providing further numerical evidence on the value of regular testing in preventing infections (Colosi et al., 2021; Lasser et al., 2021; Liu et al., 2021). Our conclusion on the benefit of regular testing is consistent with that of Colosi and colleagues, which tailored their simulations to the French school context and considered joint impact of regular testing and vaccination (Colosi et al., 2021). A randomized trial in 201 secondary schools in the United Kingdom where twice-weekly screening was carried out found a central estimate for relative reduction in COVID-19 related absences of 0.8 (95% CI: 0.54 to 1.19) in favor of rapid daily testing of contacts versus self isolation (Young et al., 2021).

While some data are available, compliance patterns under repeated testing policies are still largely speculative. It will thus be important to track and characterize compliance, so that in the future, realistic modeling of compliance can be calibrated against data. We have not considered any potential behavioral impact of a false negative test on the contact pattern of pupils. There has been some discussion of this as a potential issue, but behavioral modeling is beyond the scope of our work.

Despite these limitations posed by a lack of detailed longitudinal data to fit more complex joint models of viral load, infectivity, and test sensitivity, we reach the following conclusions:

1. Policies cannot be judged solely on either their ability to contain outbreaks or the amount of face-to-face schooling that they enable. Performance can only be judged by considering these quantities jointly and by taking test burden into account.
2. Depending on the scenario, the distribution of the outcomes of interest may be heavy-tailed and simple mean comparison may fail to adequately capture the risks associated with a particular policy.
3. We found that the relative performance of different policies is qualitatively stable over a wide range of scenarios and sensitivity analyses. In particular, additional autocorrelation between repeated testing, lower LFD-test compliance, or a worse LLI profile for infectivity all impede outbreak control to some degree but do not change the relative merits and disadvantages of the policies considered.
4. Containment depends on the fraction of asymptomatic cases—it is harder to control outbreaks in scenarios wherein the proportion of symptomatic cases is lower, but policies incorporating regular asymptomatic screening tests are more robust toward the proportion of asymptomatic cases. Test for release, however, still needs a symptomatic index case to trigger dynamic testing within a bubble and thus struggles to contain outbreaks.
5. If no effective between-bubble isolation is possible (one bubble per class), containment is impeded since the higher number of contacts offsets the wider scope of isolation and testing. Nevertheless, regular cross-sectional testing is still effective.

6. An extended weekend strategy can only be recommended as a last resort if no screening tests are available whatsoever, since a once-weekly regular screening test already dominates it clearly.
7. A once-weekly screening test in addition to symptomatic bubble isolation is already effective. A second test per week increases robustness in high-infectivity scenarios.
8. A test-for-release policy consistently achieves slightly worse containment than the reference policy at a smaller loss in school days. Both fare badly in terms of their absolute ability to contain outbreaks.
9. Overall, we conclude that LFD tests are not fit to replace symptomatic isolation of close contacts, but that the addition of asymptomatic testing to a policy incorporating some form of preemptive isolation of close contacts consistently shows benefit across all scenarios considered. This finding remains valid even if the test sensitivity is fairly low, but the degree of additional benefit scales with the LFD test quality.

We believe that our results have delivered new quantitative understanding of school policy effectiveness for controlling transmission of SARS-CoV-2 and should be used by policymakers to guide the choice of effective policies to be trialed and evaluated, both locally or nationally, so that schools can stay open for the benefit of our children. The Shiny app that accompanies this work allows all parameters in the model to be adjusted and is designed to help public health analysts to tailor simulations easily to their own scenarios and carry out sensitivity analyses of interest (Kunzmann & Lingjærde, 2021).

Interactive Shiny app [□](#)

Visit the web version of this article to view interactive content.

Kunzmann & Lingjærde, 2021

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Author Contributions

The manuscript was conceptualized by Sylvia Richardson, Kevin Kunzmann, and Sheila Bird. All authors contributed to the formal analysis, investigation, methodology, validation, visualization, and writing of the manuscript. Sylvia Richardson also contributed by funding acquisition, project administration, resources, and supervision. Kevin Kunzmann and Camilla Lingjærde have also contributed by developing the necessary software and validating the data presented in the manuscript.

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Sheila Bird: member of Royal Statistical Society (RSS) COVID-19 Taskforce; proposer and member of RSS Working Group on Diagnostic Tests; chairs RSS Panel on Test & Trace; member of Testing Initiatives Evaluation Board (since January 2021).

Sylvia Richardson: President of the Royal Statistical Society, co-chair of RSS COVID-19 Taskforce; member of the International Best Practice Advisory Group; member of the United Kingdom Health Security Agency Data Science Advisory Board, Technical Director of the Turing-RSS Statistics and Machine Learning lab within the United Kingdom Health Security Agency.

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Supplementary File

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