



REVIEW

REVISED Rapid evidence review to inform safe return to campus in the context of coronavirus disease 2019 (COVID-19) [version 2; peer review: 3 approved]

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted predominantly through the air in crowded and unventilated indoor spaces, especially among unvaccinated people. Universities and colleges are potential settings for its spread.

Methods: An interdisciplinary team from public health, virology, and biology used narrative methods to summarise and synthesise evidence on key control measures, taking account of mode of transmission.

Results: Evidence from a wide range of primary studies supports six measures. **Vaccinate** (aim for > 90% coverage and make it easy to get a jab). **Require masks indoors**, especially in crowded settings. If everyone wears well-fitting cloth masks, source control will be high, but for maximum self-protection, respirator masks should be worn. Masks should not be removed for speaking or singing. **Space people out** by physical distancing (but there is no “safe” distance because transmission risk varies with factors such as ventilation, activity levels and crowding), reducing class size (including offering blended learning), and cohorting (students remain in small groups with no cross-mixing). **Clean indoor air** using engineering controls—ventilation (while monitoring CO₂ levels), inbuilt filtration systems, or portable air cleaners fitted with high efficiency particulate air [HEPA] filters). **Test asymptomatic staff and students** using lateral flow tests, with tracing and isolating infectious cases when incidence of coronavirus disease 2019 (COVID-19) is high. **Support clinically vulnerable people** to work remotely. There is no direct evidence to support hand sanitising, fomite controls or temperature-taking. There was no evidence that freestanding plastic screens, face visors and electronic air-cleaning systems are effective.

Open Peer Review

Reviewer Status

	Invited Reviewers		
	1	2	3
version 2 (revision) 05 Jan 2022	 report		
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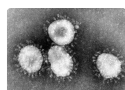
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Any reports and responses or comments on the article can be found at the end of the article.

Conclusions: The above evidence-based measures should be combined into a multi-faceted strategy to maximise both student safety and the continuation of in-person and online education provision. Those seeking to provide a safe working and learning environment should collect data (e.g. CO₂ levels, room occupancy) to inform their efforts.

Keywords

SARS-CoV-2, aerosol transmission, hierarchy of controls, higher education policy, infection prevention and control



This article is included in the [Coronavirus \(COVID-19\)](#) collection.

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REVISED Amendments from Version 1

In response to three helpful reviews, we have made the following major changes as well as minor changes of emphasis and nuance:

We've lengthened the methods section and included a more extensive search. This turned up additional papers which are now included in the findings section and referenced.

We've better distinguished where we're basing our statements on evidence and where we are expressing our own opinions. A much higher proportion of statements are now backed up by a reference to an empirical study.

We've changed the covid risk chart to a colour blind friendly version.

We've included a more nuanced discussion of the pros and cons of mass PCR testing in asymptomatic staff and students. We've also added detail to the section on lateral flow tests.

We've said more about hybrid learning as a partial solution.

Any further responses from the reviewers can be found at the end of the article

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and university life

The United Kingdom (UK) is currently (Winter 2021) experiencing high and rising levels of coronavirus disease 2019 (COVID-19)¹. Cases spread fastest among the 17–24 year age group in June and July 2021², likely due to a combination of low vaccination rates in this age group and suboptimal mitigation strategies in schools and colleges. Whilst young people are much less likely to develop severe acute disease from COVID-19 than older people, some will be hospitalised and a minority will die³. The precise incidence of persistent symptoms beyond the acute illness (post-acute or “long” Covid⁴) is disputed, but a secondary analysis of Office of National Statistics data (published as a preprint) suggests that 4.7% of the 18–24 year age group have some symptoms persisting beyond 12 weeks and 1.1% have symptoms which

interfere “a lot” with their daily activities⁵. University staff and graduate students include older age groups, minority ethnic groups and those with medical conditions, all of which increase the risk of developing serious complications from COVID-19.

For all these reasons, measures to reduce transmission of the virus are needed. Most universities and colleges in the UK now have the infrastructure to implement rapid and frequent testing and support students to isolate when necessary. Since most courses were delivered online in 2020–21, they have also learnt a great deal about how to deliver effective learning online. There is, however, a considerable appetite to return to face-to-face modes of teaching as well as return to traditional levels of socialising, arts and sport.

The science of SARS-CoV-2 transmission

There is strong and consistent evidence that the main—and perhaps the most significant—mode of transmission of SARS-CoV-2 is through the air^{6,7}. Indeed, super-spreader events (in which one or a few people infect large numbers of others)—including choir practices, funerals, conferences, gym sessions and other mass indoor events—are likely to be the main drivers of the pandemic⁸. Higher education includes many preconditions for such super-spreader events, including living and eating communally, lectures and seminars, sports training and competition, arts and singing performances, and socialising.

Some indoor events show no COVID-19 transmission, even when infected people are present, while others are shown in retrospect to have been super-spreader events; this phenomenon is known as heterogeneity or *overdispersion* of transmission dynamics, and is highly relevant to our efforts to control the virus in schools and universities⁹. Whilst the highest risk of airborne viral transmission occurs with coughing and sneezing, speaking and singing are also high-risk activities^{10,11}.

A landmark paper on minimising risk of airborne transmission (written before effective vaccines had been discovered) used their own adaptation of the US Centers for Disease Control and Prevention’s “hierarchy of controls” (Figure 1)¹². In the sections which follow, we consider all the measures

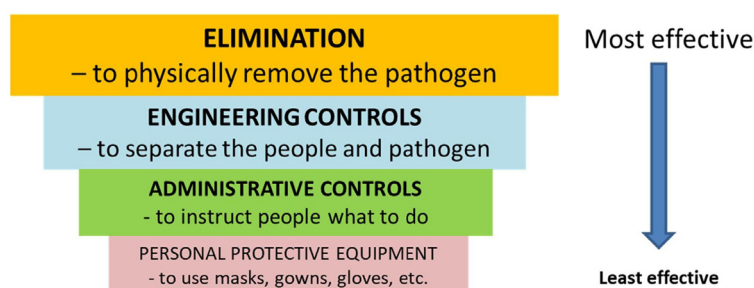


Figure 1. The hierarchy of controls for an infectious pathogen (reproduced under Creative Commons license from 12).

in the hierarchy of controls plus vaccination. We begin with vaccination, masking and administrative controls as these are things which individual university employees may be able to influence. We then discuss engineering controls (ventilation and air filtration).

Methods

This review, which aimed to produce a synthesis rapidly in time for the new university term, was undertaken in September 2021 and updated in early November 2021. The literature on COVID-19 is known to be vast and of variable quality. We did not have the resources to undertake a comprehensive search of that literature with formal critical appraisal of every potentially relevant article (nor, to our knowledge, had any other research team). We took the view that in the absence of any published review on this topic, a more limited search and assessment informed by professional judgement and interdisciplinary expertise would still address a considerable knowledge gap. We also rejected the option of following Cochrane rapid review methodology¹³ since this technique (which we have used successfully in other studies) is geared to answering a single, focused question (e.g. about the efficacy of mask-wearing in classrooms on incidence of positive cases) rather than the much broader question of what should be done to reduce on-campus transmission. The purpose of this preliminary review, then, was to scope the breadth of the literature and identify areas that might be further explored in more focused reviews.

We began with sources known to the authors, including a rapid review by Independent SAGE¹, and a search of the PubMed database using the terms “SARS-CoV-2”, “COVID-19”, “transmission”, “mitigation”, “school[s]” and “university/ies” (initially restricted to review articles but then, when few studies were identified, extended to include empirical studies). Using a method previously shown to be highly efficient for identifying key studies from complex and heterogeneous datasets¹⁴, we identified seminal papers (highly-cited for their age and judged by others within the discipline as influential) and used snowball searching (tracking the article in Google Scholar and pursuing relevant sources from its reference lists) to identify further key studies from these. For specialist subsections that were beyond our own expertise, we undertook further key word searches (e.g. HEPA filters) and consulted with experts in the field. In producing our narrative synthesis of these sources, we prioritised findings that would be useful to inform actual policies in universities.

Main findings

Most of the 60 papers which contributed to this findings section were sourced from seminal sources known to the authors (including the Independent SAGE report) and citation-tracking from those. Our original PubMed search was insufficiently sensitive (e.g. it turned up only 18 papers but did not identify key papers known to our team) but modifying the search terms (e.g. by omitting the term ‘university’ from title or abstract) and Boolean operators (e.g. changing ‘and’ to ‘or’) made it insufficiently specific (it turned up tens of thousands of papers). Despite these limitations, which mean that we may well have

missed some key papers, we were able to identify several reviews and empirical studies which were either directly or indirectly relevant to our research question, which we describe below.

It is noteworthy that direct empirical evidence on mitigation strategies specifically for universities was sparse, but there was much relevant evidence on mitigation measures more generally. Our review suggested that six key measures, which we consider in turn below, are likely to be effective at reducing on-campus spread: vaccination, masking, spacing people out (physical distancing, reducing class size and cohorting), engineering controls (ventilation or filtration of air), a test/trace/isolate policy when COVID-19 incidence is high, and supporting clinically vulnerable people to work remotely. Other widely-promoted measures including sanitising hands, taking temperatures, plastic screens and face visors, were not supported by evidence.

Encourage vaccination—and make it easy

Vaccines have been a game-changer for COVID-19; they dramatically reduce the incidence of symptomatic disease and risk of transmission of the virus to others; breakthrough infections in vaccinated persons are rare and generally mild¹⁵. Some countries—notably US and Australia—have mandated vaccination in some university settings^{16–18}.

A recent BMJ review concluded that the most important single intervention for preventing on-campus transmission is vaccination¹⁹. These authors suggest (based on a modeling study²⁰) that if 90% of staff and students are fully vaccinated with a vaccine that is 85% effective, campuses may be able to reopen safely without other measures.

The evidence, while sparse, supports strenuous efforts to increase the proportion of staff and students who are fully vaccinated. Most universities are a long way from meeting a 90% target. As of end September 2021, for example, only 58% of 18–24 year olds in England were fully vaccinated²¹. This is partly because younger age groups were the last to be invited, but also because of relatively high levels of vaccine hesitancy among student age groups, due to a combination of perceived low vulnerability and the “inconvenience” of attending for a jab¹⁹.

One key measure for improving safety is to make it very easy for people to get a vaccination on campus—for example by locating vaccination hubs close to settings frequented by target groups (e.g. outside lecture theatres or dining halls) and not requiring paperwork that people are unlikely to be carrying, though we were unable to identify empirical studies evaluating such measures. A reviewer of an earlier draft of this paper commented that in some parts of Australia, as a result of state legislation or local mandates, students and staff must show evidence of vaccination before returning to campus. We could find no empirical studies of the impact of such mandates (and as the reviewer points out, mandating vaccination raises questions about industrial relations and individual freedoms).

Vaccination, however, is unlikely to be the sole measure to protect students and staff. Another preprint modelling study, which used the delta variant, found that even at 100% coverage, vaccination was insufficient to eliminate SARS-CoV-2 transmission in a university dormitory setting²². Some vulnerable groups are unable to receive the vaccine or mount an effective immune response to it²³. An individual interacting with another group of people in a university setting has no way of knowing what proportion of them are vaccinated. For all these reasons, other measures are needed to mitigate the risk of infection.

Everyone should wear masks

Masking has two main effects: reducing emission of the virus by the wearer (“source control”), and protecting the wearer from virus emitted by others^{24–26}. It also has a third potential effect—reminding us that we are still in a pandemic and signalling to others that we are taking *their* safety seriously²⁷.

Reviews of a wide range of evidence (including laboratory studies and natural experiments) have shown that, broadly speaking, masks are effective—but by no means perfect—for source control^{24–26}. Masks reduce the amount of virus-laden particles that get into the air, and hence the probability that someone else in the room will be infected²⁶. Wearing a mask reduces viral emissions from coughing and sneezing approximately 20-fold²⁸, but around half of all people who transmit the virus have no symptoms at the time (i.e. they are not coughing or sneezing but simply *exhaling* the virus as aerosols)²⁹. Different materials for cloth masks have very different filtration properties³⁰; a well-fitting mask with no leaks round the side is crucial³¹. A double-layer neck gaiter (bandana) and a medical mask both reduce emission of aerosols by around 60%, but respirator (FFP2 or FFP3, N95) masks are much more effective, blocking up to 99% of aerosols³². Note that face visors reduced aerosol emission by only 5%—i.e. they are ineffective³².

There have been claims that randomised controlled trial (RCT) evidence is the only “robust” way to test the impact of masks. This is incorrect, because most such RCTs are designed only to test the hypothesis that the mask protects the wearer over a short period³³. Actually, masks work *mainly* by protecting other people, and even a non-statistically significant effect on transmission dynamics (e.g. in lectures) can lead to very large effects over time (for example, if instead of doubling every 9 days, new cases increased by only 1.9-fold (i.e. almost but not quite doubling), after 180 days cases would be down by 60%).

The above findings support mandating (rather than merely encouraging) masking in shared spaces. If everyone is wearing a mask, source control will be high and double-layer cloth masks will be adequate for most healthy people. In one recent Centers for Disease Control and Prevention (CDC) report, US schools without mask mandates in July–August 2021 were 3.5 times more likely to have COVID-19 outbreaks than schools with mandates³⁴. To *protect the wearer* effectively from airborne virus when others in the room are unmasked,

a higher grade of filtration is needed, hence in the absence of near-universal use of source control masks, individuals may be left with little choice but to consider respirators²⁴. Those who are clinically vulnerable (hence requiring masks for self-protection) should use respirators in any case.

Perhaps the most persuasive argument for masks in the university context is that if everyone wears one, there is a much lower risk that teaching will need to return to online as a result of rising case numbers, though this reasoning is based on indirect evidence²⁵.

Since speaking and singing increase emission of aerosols^{10,11}, masks should be worn continuously indoors and not removed for these activities. The suggestion in some universities that masks should be worn only until people are seated but may be removed thereafter makes no scientific sense. Indeed, because of the airborne nature of the disease, masking is *more* important when in a classroom learning setting (indoors, with others, and with some people talking) than when moving between classrooms (especially if walking alone, outdoors and in silence). Likewise, rules in gyms that masks should be worn when walking between equipment but not when exercising *on* the equipment are nonsensical, since heavy breathing during exercise will increase emission of viral particles^{35,36}.

Whilst the odds of becoming infected increases with the number of people in any indoor space, there is no occupancy threshold below which those odds reach zero. Transmission may occur after an infected person has left a room^{37,38}. Since asymptomatic transmission is common in this disease, groups of any size should wear masks to maximise protection of everyone.

A major risk setting for transmission of COVID-19 is lunch and tea/coffee breaks, since masks must be removed for eating and drinking, and because people often sit at close quarters and talk. To reduce transmission, refreshment breaks should ideally be taken out of doors. If this is not possible, physical distancing should be increased and vocalisation discouraged while unavoidably unmasked (i.e. when eating or drinking). Chatting during breaks could occur, for example, during the walk to the café (while masked) but not while eating—though this is likely to prove difficult to implement in most campus settings. Ventilation is particularly important in settings such as eating areas where people will be unmasked.

A minority of people have a medical reason not to mask (e.g. neurodiverse or anxious)³⁹; in some universities they may obtain a lanyard to indicate they are exempt.

Space people out (physical distancing, joining remotely, cohorting)

Physical distancing (sometimes called social distancing) is effective at reducing droplet transmission, since droplets fall to the ground within a few feet due to gravity⁴⁰. Physical distancing also protects against airborne transmission, since most

airborne particles are spread via close contact, especially when a person is in the direct stream of someone else's exhaled breath (think of smelling the garlic on someone's breath—you might be able to smell it across the room but it is much stronger at close range)⁷.

Many university guidelines stipulate a specific physical distance such as 1 or 1.5 metres to space desks apart. Whilst this is a useful rule of thumb, a “safe” distance cannot be calculated precisely, since a) airborne particles spread throughout a room within about 30 minutes (and can remain even after the room has been vacated), hence time spent indoors must also be factored in; b) if nobody is wearing a mask, viral emission is considerably greater (hence, close contact is more risky—and conversely if everyone is masked, it is less risky); c) singing or loud talking increases viral transmission (hence, again, close contact is more risky); d) even wide separation will not protect fully against the turbulent jets emitted when a symptomatic person coughs or sneezes⁴⁰.

Figure 2 summarises this information in a semi-quantitative way⁴⁰; a paper offering a quantified version of this diagram is available as a preprint⁴¹.

In reality, however, university staff are often given a rigid separation distance to impose. It is important not to be overly reassured by such measures but instead take account of the multiple influences on transmission risk. Separating desks is a good idea since most transmission occurs at close quarters, but since a key determinant of transmission is likely to be the extent to which air is shared, there are benefits to using large spaces (e.g. lecture theatres) even for small group teaching⁴² and taking steps to reduce congregating when entering and leaving lecture theatres and in “attraction areas” (e.g. café queues)⁴³. In addition, those responsible for local policy should encourage people to get fully vaccinated, keep masks on, and speak quietly rather than loudly (and perhaps keep talking to a minimum while indoors).

Distancing guidelines will tend to reduce room occupancy. The fewer people who are physically present in the room, the lower the risk of transmitting the virus. This is partly because desks can be more spread out, but it is also because fewer breathing humans will be exhaling virus into the air. We could find no direct empirical evidence that cohorting (that is, keeping students in fixed groups and not allowing mixing between groups) reduces transmission in university settings, though there is evidence that social events held soon after students' arrival (“freshers' week” activities) are associated with high transmission risk⁴⁴ and that first-year students (who are more likely to be in shared on-campus accommodation) drive transmission more than other year groups⁴⁵. The airborne nature of the virus and the documented value of cohorting (‘bubbles’) in school settings⁴⁶ suggests that such measures may be worthwhile in higher education settings too. However, the practicalities of cohorting (e.g. preventing students from switching class mid-term, asking staff to only attend campus on particular days) may prove logistically problematic. Staff should be discouraged from teaching at multiple institutions—a

measure that will probably require institutional-level policies to reduce casualisation of the teaching workforce.

Moving teaching online dramatically reduces transmission⁴⁷, but is not popular as a long-term strategy. While the virus is still circulating, there is an argument for offering a blended learning option in which those who wish to join the class remotely are supported to do so (especially if they or a household member are clinically vulnerable). Staggering the start dates of students has been recommended⁴⁸ but in a recent UK study it did not appear to reduce on-campus transmission⁴⁹.

There is no evidence that introducing freestanding plastic screens (or other barriers between desks) reduces the risk of transmission or alters the benefit that is conferred by spacing desks, and such barriers may interfere with the effective circulation of clean air¹². Hence, universities should not attempt to install screens as a substitute for distancing or engineering controls.

Deliver clean air by ventilation, filtration or ultraviolet (UV) inactivation

Heating, ventilation and air conditioning (HVAC) technologies and standards are designed to deliver clean air and thermal comfort to indoor spaces. The literature on HVAC uses the key concept of *air changes per hour* (ACH), and generally recommends 4 to 6 per hour equivalent for an average teaching room, achieved through natural or mechanical ventilation, air filtration or sterilisation (note that higher ACH rates are needed for some activities such as singing or gym⁵⁰). Another key metric for air quality when portable filtration units are used is the *clean air delivery rate* (CADR); these and other standards are explained in a recent review paper⁵¹.

Ventilation in this context is defined as the intentional delivery of the outside air to a building's indoor space. The obvious way to do this is to open windows (preferably on opposite sides of a room, or with a door open, to get a through draught). Because of temperature differentials, the effectiveness of opening windows depends on the design of the window and also on the weather. In one modelling study (currently a preprint⁵²), the most effective single intervention for reducing aerosols was natural ventilation through the full opening of six windows all day during the winter—a measure which led to a 14-fold decrease in cumulative dose of aerosol. This was more effective than universal use of surgical masks (which led to an 8-fold decrease). In the spring and summer, natural ventilation with windows fully open all day was less effective (2-fold decrease in cumulative dose), because the effectiveness of natural ventilation depends on the difference between indoor and outdoor temperature (which is less in spring and summer). In the winter, partly opening two windows all day or fully opening six windows at the end of each class produced an approximately 2-fold decrease in cumulative dose of aerosols. In that study, opening windows during breaks only had minimal effect (≤ 1.2 -fold decrease). The conclusion from this study is that if it is not possible to open windows more than a crack, a different way of cleaning the air is likely needed.

Wearing face coverings, contact for a short time						
	Low occupancy			High occupancy		
	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated
Silent	L	L	L	L	L	M
Speaking	L	L	L	L	L	M
Shouting, singing	L	L	M	M	M	H

Wearing face coverings, contact for a prolonged time						
	Low occupancy			High occupancy		
	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated
Silent	L	L	M	L	M	H
Speaking	L	L	M	M	M	H
Shouting, singing	L	M	H	M	H	H

No face coverings, contact for a short time						
	Low occupancy			High occupancy		
	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated
Silent	L	L	M	M	M	H
Speaking	L	M	M	M	H	H
Shouting, singing	M	M	H	H	H	H

No face coverings, contact for a prolonged time						
	Low occupancy			High occupancy		
	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated	Outdoors, well ventilated	Indoors, well ventilated	Poorly ventilated
Silent	L	M	H	M	H	H
Speaking	M	M	H	H	H	H
Shouting, singing	M	H	H	H	H	H

Risk of transmission low L medium M high H

From Jones N et al BMJ 2020;370:m3223

Figure 2. Risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in different settings, assuming people are asymptomatic (adapted from 40 under Creative Commons licence).

Whereas mechanical ventilation in domestic settings tends to occur through extractor fans (such as those in kitchens and bathrooms) or ceiling fans (often used as an alternative to air conditioning in hot climates), most mechanical ventilation in universities and colleges is through large systems which take in air through air handling units and supply and extract through a system of ducts and diffuser grilles. Lecture theatres and laboratories are generally mechanically ventilated via centralised HVAC systems. Hence it should not be assumed that if a space has no opening windows, it must be inadequately ventilated.

If indoor spaces are fitted with air conditioning systems, it is important to ensure that air which is removed is not recycled unfiltered (or inadequately filtered) back into that space¹². Air conditioning is not mechanical ventilation, though it may be linked to mechanical ventilation via large, central HVAC systems which both filter and heat (or cool) the air as needed. More problematic are isolated rooms fitted with their own local air conditioning systems, which are less likely to include any significant filtration and may give a false sense that the room is being ventilated.

The level of ventilation and occupancy in ventilated spaces can be approximated by measuring carbon dioxide (CO₂) levels, since this is present in higher concentrations in exhaled air than in outdoor air. The higher the CO₂ level in a room, the more exhaled air (and hence, potentially, the more virus) there is. Before the pandemic, indoor air quality standards were generally set around the goal of avoiding “sick building syndrome” (with symptoms such as headaches a sense of stuffiness, due to accumulation of multiple contaminants in the air) and clearing body odours and other smells.

Whilst CO₂ levels can be used to approximate the risk of COVID-19 transmission⁵³, they are only a proxy for this risk. With that caveat, some authors have suggested that CO₂ levels might be used strategically in negotiations with employers⁵⁴. Figure 3 shows some suggested cut-off levels, based on a publication, by Di Gilio *et al.*, for denoting “low risk” (below 700 ppm), “medium risk” (700–800 ppm), “high risk” (800–1000 ppm) and “very high risk” (>1000 ppm), though other publications recommend different cut-offs for these categories⁵⁴. These authors suggest that measures to address moderate risk include opening classroom doors and windows, opening windows between classes, and reducing the number of students in the classroom. If levels indicate “high risk” despite these measures, infrastructure changes (such as mechanical or portable air filters) are needed.

Note that the cut-off values for unacceptable CO₂ levels in Figure 3 are substantially lower than those in many official documents (e.g. from UK Health and Safety Executive, who recommend 1500 ppm⁵⁵). The narrow bands proposed by Di Gilio *et al* may be difficult to operationalise because levels can fluctuate (depending on where the sensor is placed in the room for example), and CO₂ levels are only a proxy for risk of transmission. The priority should be to address settings where levels are significantly and consistently above 1500 ppm in the absence of filtration systems, since these reflect the kind of setting where super-spreader cases have been most consistently observed⁵⁶.

When it is not possible or desirable to use ventilation (e.g. for energy efficiency reasons) to maintain clean air, other kinds of control are needed. There are two main kinds: an inbuilt mechanical filter (for which standards are expressed as the

	RISK LEVEL			
	LOW	MODERATE	HIGH	VERY HIGH
CO2 peak concentration or class time average concentration	< 700 ppm	700-800 ppm	800-1000 ppm	> 1000 ppm
Recommended action	No action needed	A If A active, do B If B active, do C If C active, do D	A and B If both active, do C then D If all active, do E	A and C If both active, do D If all active, do E

A: door always open

B: windows open for 10 min at lunch break

C: windows open for 10 min at end of each teaching hour

D: change setting (e.g. windows open longer, reduce number of students per class)

E: infrastructure changes needed (e.g. inbuilt or portable filtration system)

Figure 3. Risk classification scheme for carbon dioxide (CO₂) levels in indoor air (adapted under Creative Commons licence from 54).

minimum efficiency reporting value (MERV) in the USA⁵¹ or ISO 16890 in Europe) or a portable air cleaner fitted with a HEPA (high-efficiency particulate air) filter. Such filtration systems have been designed to remove particles of many different kinds and sizes (e.g. dust, pollen, smoke, bacteria, viruses).

The SARS-CoV-2 virus is approximately 100 nanometres (0.1 μm) in diameter (though it is unlikely to travel naked so the size of particle to be filtered will be larger than this). The system installed should be efficient in the 0.1 to 1 μm range. Of note to those in charge of supplying clean air to old-fashioned university or school buildings is this warning: *“most central mechanical systems were not designed for HEPA filters. Instead, these systems use filters on a different rating scale, minimum efficiency reporting value, or MERV, and typically use a low-grade filter (eg, MERV 8) that captures only approximately 15% of 0.3- to 1- μm particles, 50% of 1- to 3- μm particles, and 74% of 3- to 10- μm particles. For infection control, buildings should upgrade to MERV 13 filters when possible, which could capture approximately 66%, 92%, and 98%, of these sized particles, respectively”*⁵¹.

Upgrading from MERV8 to MERV13 filters (or the ISO equivalent) is potentially a rapid, affordable and effective intervention for universities and colleges in some settings, but higher-grade filters may induce a bigger pressure drop so unless the fan speeds can be increased, the ventilation rate may be inadequate.

Portable air filtration units fitted with HEPA filters are highly effective at removing aerosols in the 0.1 to 1 μm range^{57–60}. In the Villiers study described above, one HEPA filter was as effective as two windows partly open all day during the winter (2.5-fold decrease in cumulative dose of aerosols) while two HEPA filters were more effective (4-fold decrease)⁵². A combination of interventions (masks along with natural ventilation and HEPA filtration) were the most effective, producing a 30-fold decrease in cumulative aerosol dose⁵². Aerosol scientists have begun to develop and test home-made, low-cost box fans fitted with HEPA filters as a quick and effective solution for improving mechanical ventilation in poorly-ventilated spaces⁶¹.

Ultraviolet (UV) light in the UV-C region of the spectrum (200–280 nm) has been shown to destroy SARS-CoV-2 in numerous studies⁶², though if this method is used it is important to select appropriate units that do not generate ozone. UV-C inactivation holds potential for enhancing safety in indoor spaces where risk of transmission is particularly high (e.g. hospitals, gyms). In a small before-and-after study published as a preprint, a combination of HEPA filtration and UV-C lamps was highly effective at removing bioaerosols (including but not limited to SARS-CoV-2) in a COVID-19 surge ward and intensive care unit in one hospital, though the contribution of the UV-C component to the result is unknown⁵⁸.

Electronic air cleaning systems, for example those which use ozone, lack any proven efficacy in reducing COVID-19

transmission⁶³; they currently have no place in preventing transmission of SARS-CoV-2. Air filtration does not remove CO₂, so CO₂ monitors cannot be used to monitor the quality of filtered air.

In the longer term, universities should consider the need for a *paradigm shift* in the design and ventilation of buildings, to improve air quality standards and ensure that all indoor spaces meet these through adequate ventilation, filtration or sterilisation⁵⁰.

Test, trace and isolate while COVID-19 incidence is high
In the context of high incidence of COVID-19 and an unvaccinated or partially-vaccinated student population, frequent testing of asymptomatic staff and students along with contact tracing and support to isolate has been shown to be acceptable to students and staff and to reduce on-campus transmission substantially^{49,64}. Universities should ensure clear and consistent communication on this matter as confusion still abounds.

While lateral flow device (LFD) tests can detect asymptomatic cases and break chains of transmission, this measure depends on the efficacy of efforts to track and trace contacts and maintain and support the isolation of infected individuals. Anyone with symptoms, even if they are perceived to be “just a cold”, should isolate immediately and take a gold-standard polymerase chain reaction (PCR) test, irrespective of the status of their LFD test. The provision of hybrid learning options would allow students who are mildly symptomatic and/or awaiting test results to participate in learning, and remove pressure to attend and increase risk to others. Note that the most common symptoms of Covid-19 infection (in order: headache, runny nose, sneezing, sore throat, loss of smell, fatigue) are different from the standard triad of cough, fever and shortness of breath which are still widely used to prompt PCR testing in the UK⁶⁵; the US Centers for Disease Control and Prevention has a more extensive list⁶⁶. Students and staff who are unwell should not be expected to participate in online classes.

Hybrid teaching options greatly facilitate immediate isolation, and students and staff with symptoms that may be due to COVID-19 should be supported to engage remotely if they are well enough to do so. A staff member who tests positive must observe the full recommended isolation period and should be paid while doing so (whether on the regular or ‘casual’ payroll) to maximise compliance.

Track and trace efforts are constrained by the specifics of the system. Universities may have additional information that can be harnessed to provide a further layer of safety. In the UK for example, individuals sharing a confined space for extended periods of time, for example, may not be contacted by the official Track and Trace system but could be identified via attendance lists.

Some authors have questioned the validity and expense of mass asymptomatic testing in populations where incidence of

COVID-19 is low, due to the very large number of tests required to detect small numbers of positive cases⁶⁷. A recent modelling study suggests that as vaccination rates rise and the incidence of COVID-19 falls, the cost-benefit balance of frequent testing becomes less favourable²⁰. However, at the time of writing, the UK is a long way from a low-incidence state and we strongly recommend maintaining asymptomatic testing. The optimal frequency of mass testing will depend on both transmission rates and the size of the population; it is (by convention) often done twice weekly—an interval which appears to have been selected to balance the cost and inconvenience of testing (and the risk of poor compliance if the interval was reduced) with the need to detect and isolate new cases⁶⁴. In addition to regular testing, tests could be made available and encouraged in order to attend particular events. Many UK universities, for example, request attendees to take lateral flow tests on the day of social events, or larger meetings.

Below, we explain some of the science behind the tests.

LFDs detect the presence of virus antigen in the nose and throat using a swab sample tested in a flow device (like a pregnancy test)⁶⁸. Multiple types of LFD test are available with differing accuracy⁶⁹, they are designed to test people (perhaps repeatedly) who are not displaying overt COVID symptoms. LFD tests are all highly specific i.e. they are very unlikely to give a positive result if the person is not infected. But LFD tests are not particularly sensitive (i.e. less able to detect very small quantities of the virus) compared with the gold standard PCR (polymerase chain reaction) tests. This means that testing negative on an LFD is not a “green light” i.e. it does NOT guarantee that the individual is not infected with SARS-CoV-2, so they should continue to practice mitigations as advised. On the other hand, testing *positive* on an LFD means it is highly likely the person *is* infected (it is a “red light”, indicating that they are potentially infectious). Such individuals should self-isolate immediately, report the positive test, and order a confirmatory PCR test as soon as possible. A positive LFD test should trigger a call from the Track and Trace service.

Whilst LFD tests are used mainly in people without symptoms, they are actually more likely to be positive if the infected person is symptomatic (probably because such people have higher levels of the virus)⁶⁹. However, people with a positive LFD may well be infectious despite lack of symptoms—hence the value of these tests in identifying infectious cases (who should then isolate) and reducing the chance of a super-spreader event on campus. LFD tests also tend to reflect past infection (they are more likely to be positive 2 weeks after the onset of symptoms than on the day symptoms appear)⁶⁹.

Some authors have suggested that mass PCR testing of undergraduates may be a viable option^{20,64}. While we agree that on purely technical grounds this could be a gold-standard means of conducting mass testing, there are disadvantages in terms of costs and logistics.

First, costs and effort to establish testing facilities on a large scale for routine mass PCR testing would be considerable in terms of required equipment, reagents and laboratory safety; sample processing for CL3 materials will require additional staff training, appropriate PPE and microbial safety cabinets. In contrast, LFD tests, including swabbing and disposal, are self-administered in adults, generate few processing costs and detect the majority of cases (especially highly infectious individuals with high viral load).

Second, whereas a LFD test gives an immediate result, results of PCR tests are delayed by at least a day (and must be sent confidentially). Infected individuals are likely to attend classes or other interactions during the interim (especially if asymptomatic), increasing transmission risk. Furthermore, pooled individuals will require re-testing and, depending upon the timescale in which this is achieved, could mean that peak virus load has passed, especially for vaccinated individuals in which the kinetics of declining virus titre in the upper respiratory tract are more rapid. Whilst LFDs lack the fine sensitivity of PCR, they retain impressive specificity and are particularly suited to detecting the higher end of virus loads present within more infectious individuals.

Finally, the convenience and immediacy of LFD testing is likely to appeal to students and staff.

In sum, the on-site LFD testing established at many UK university sites appears to be evidence-based (though not scientifically perfect) and its regular, frequent use is recommended while the incidence of COVID-19 remains high. Those with symptoms also need a PCR test.

Clinically vulnerable staff and students

Universities and colleges have a duty of care to their staff and students. They must provide a safe environment for learning, teaching, and working. If a person has a condition or risk state which makes them vulnerable to COVID-19 and its complications, the institution must take account of this. Increased vulnerability to COVID-19 occurs in people who are immunosuppressed (including those on medication which suppresses the immune system, and pregnant women), those with certain long-term conditions, older age groups, some minority ethnic groups and those who are overweight. These risk groups were considered in detail in the Independent SAGE report¹.

The evidence supports a policy of vulnerable groups (whether staff or students) being supported to work from home if possible while the incidence of COVID-19 is high. If they must enter indoor spaces they should be advised to wear a respirator mask for self-protection, and it is particularly important for others in the room to wear a mask to maximise source control. If clinically vulnerable people are required to enter indoor spaces, those spaces should be adequately ventilated (confirmed using CO₂ levels) or have high-quality air filtration systems (MERV13 or HEPA) installed.

Interventions for which there is no evidence (“hygiene theatre”)

We found no direct scientific evidence to support taking temperatures, sanitising hands before entering the classroom (though washing hands when they are dirty and after going to the lavatory is of course a general hygiene measure), restricting the sharing or exchange of fomites (i.e. potentially contaminated objects such as pens, paper, books or other study materials), wearing face visors, or separating desks with plastic screens. Such measures are based on a discredited hypothesis that the virus is spread mainly or exclusively by droplets⁷⁰, and if over-emphasised could potentially distract staff and students from measures for which there is firm evidence of effectiveness.

In relation to sanitising, hand hygiene is recognised good practice for the prevention of many infectious diseases, so it should not be dismissed or discouraged (but equally, should not be used as the sole mitigation measure). In relation to fomite transmission, a large Brazilian study detected no SARS-CoV-2 virus on over 400 samples of mask fronts, cell phones, paper money or card machines during a wave of the pandemic⁷¹. However, the Brazilian study was undertaken before the more contagious delta variant was widespread in that country. And since the mode of transmission remains contested, it would seem sensible to discourage widespread sharing of pencils, books and other objects among students.

Conclusion

The key to effective prevention of COVID-19 is acknowledgement of its predominantly airborne mode of transmission. Many widely-promoted measures—hand sanitising, strict 1- or 2-metre distancing, fomite precautions—wrongly assume an exclusively droplet mode of transmission assume and are therefore ineffective in the absence of provision against airborne

transmission. Such thinking also dominates the thinking of senior management and many staff and students.

Acknowledging the importance of airborne transmission should lead to policies such as: a) masking at all times while indoors, with encouragement to wear higher-grade respirators for best protection (especially if clinically vulnerable); b) continuing attention to physical distancing but in a way that does not assume that a particular interval between desks makes the space “safe”, and using additional measures (joining remotely, cohorting, frequent breaks) to reduce crowding and time spent indoors; c) a greater focus on engineering controls (ventilation and/or filtration of air). In addition, university and college staff should encourage and facilitate vaccination, attend to testing and tracing, and be ready to instigate tighter controls (e.g. return to online teaching) if case numbers rise.

These measures should be implemented and evaluated. Monitoring of metrics such as CO₂ levels and room occupancy rates may provide staff with hard data with which to negotiate with management, yet we strongly recommend that higher education settings should lead by example and implement safety measures following appropriate risk assessments accounting for the major contribution of airborne transmission underpinning the spread of SARS-CoV2 infections.

Data availability

No primary data are associated with this article.

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The points I raised during my previous review have been addressed well. I have no further comments.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

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Excellent and timely review with no major concerns. The following are suggestions that may enhance the manuscript:

- Worth including a statement on mandating vaccination which some universities in the US (Yale I think) and Australia have done. This intervention has greatly increased uptake of

vaccination in younger people and staff.

- Please further clarify page 4 para 2 "new cases increased by only 1.9 fold... 60%". It is difficult to understand, please revise.
- To remain silent while unmasked is not pragmatic nor feasible in a University setting. The credibility of the paper could be called into question if the measures proposed are not implementable. Consider making this a suggestion or placing a higher emphasis on HVAC improvements.
- Please elaborate as to why natural ventilation with the windows fully open in spring and summer was less effective accounting for a 2 fold decrease only. What is the likely basis for this result?
- A CO₂ ppm upper limit of 1500 ppm was set for another purpose, please mention this other purpose because it may be a barrier otherwise to the adoption of a lower threshold.
- Re LFD testing in asymptomatic people: how often should this be done and would it vary depending on community transmission rates.
- Consider a box summarising key interventions.

Is the topic of the review discussed comprehensively in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: health services research, artificial intelligence, clinical leadership

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 08 Dec 2021

Trish Greenhalgh, University of Oxford, Oxford, UK

REVIEWER 3

Excellent and timely review with no major concerns. The following are suggestions that may enhance the manuscript:

- Worth including a statement on mandating vaccination which some universities in the US (Yale I think) and Australia have done. This intervention has greatly increased uptake of vaccination in younger people and staff.

Yes, this is an important point. New text and reference(s) added:

WHITE HOUSE REPORT: Vaccination Requirements Are Helping Vaccinate More People, Protect Americans from COVID-19, and Strengthen the Economy OCTOBER 7, 2021.

Accessed 3 November 2021 at

<https://www.whitehouse.gov/wp-content/uploads/2021/10/Vaccination-Requirements-Report.pdf>

Redden, E. (2021) *Climbing Toward Vaccine Compliance, Inside Higher Ed*. Available at:

<https://www.insidehighered.com/news/2021/09/21/colleges-mandating-vaccines-see-progress-toward-compliance> (Accessed: 3 November 2021).

Patty A. Mandatory jabs for students and staff to return to universities. Sydney Morning Herald October 13 2021. Accessed 12 November 2021 at

<https://www.smh.com.au/national/mandatory-jabs-for-students-and-staff-to-return-to-universities-20211013-p58znl.html>

- Please further clarify page 4 para 2 "new cases increased by only 1.9 fold... 60%". It is difficult to understand, please revise.

We have changed this text to "(for example, if instead of doubling every 9 days, new cases increased by only 1.9-fold (i.e. almost but not quite doubling), after 180 days cases would be down by 60%)"

- To remain silent while unmasked is not pragmatic nor feasible in a University setting. The credibility of the paper could be called into question if the measures proposed are not implementable. Consider making this a suggestion or placing a higher emphasis on HVAC improvements.

Point taken. We've adapted the paragraph to read as follows:

"A major risk setting for transmission of COVID-19 is lunch and tea breaks, since masks must be removed for eating and drinking, and because people often sit at close quarters and talk. To reduce transmission, refreshment breaks should ideally be taken out of doors. If this is not possible, physical distancing should be increased and silence maintained while unavoidably unmasked (i.e. when eating or drinking). Chatting during breaks could occur, for example, during the walk to the café (while masked) but not while eating - though this is likely to prove unimplementable in most campus settings."

- Please elaborate as to why natural ventilation with the windows fully open in spring

and summer was less effective accounting for a 2 fold decrease only. What is the likely basis for this result?

Added:

), because the effectiveness of natural ventilation depends on the difference between indoor and outdoor temperature (which is less in spring and summer 38)

- A CO2 ppm upper limit of 1500 ppm was set for another purpose, please mention this other purpose because it may be a barrier otherwise to the adoption of a lower threshold.

We have softened this recommendation since SAGE have recommended 1500 as the cutoff for Covid controls and we don't want to lock horns over it. We've now made clear that the levels recommended by Di Gilio et al are a counsel of perfection but the priority is to address settings where levels are above 1500.

- Re LFD testing in asymptomatic people: how often should this be done and would it vary depending on community transmission rates.

We have acknowledged that there is uncertainty about this and said that optimum interval will depend on transmission rates and size of population. We have also given a recommended interval of twice weekly from a recent BMJ editorial and said this appears based on convention and an attempt to balance costs/hassle (and possible attrition of compliance) with detecting new cases.

-
- Consider a box summarising key interventions.
- Don't we sort of do this at the beginning? Why does it need to be in a box?

We do this in the abstract - happy to take an editorial steer on this (we can do a box if you want).

Competing Interests: no coi

Reviewer Report 01 November 2021

<https://doi.org/10.21956/wellcomeopenres.19088.r46604>

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Stephen Duckett 

¹ Health Program, Grattan Institute, Carlton, Vic, Australia

²

The University of Melbourne, Melbourne, Vic, Australia

This is an excellent and comprehensive review of the evidence relevant to improve the safety of return of students to universities and schools in the context of the continuing transmission of SARS-CoV-2. The review should be augmented to consider more explicitly a number of issues:

Vaccination:

- The review is written specifically for a United Kingdom audience, and it is perhaps for that reason that it does not mention universities or schools requiring vaccination of students or staff. In Australia, for example, in some states, government regulations effectively require that only vaccinated people are able to return to campus. A number of universities have also introduced mandatory vaccination of the staff and students who are to be on campus. This obviously requires consultation with industrial organisations, but some reference to this issue would be useful to ensure a comprehensive review of options.

Physical distancing:

- The review appropriately refers to the droplet induced theories about physical distancing. This section should be broadened to include stronger consideration of issues relating to remote and hybrid working, cohorting, and workplace bubbles. There may be limited published evidence on these strategies, and for this reason they may have been excluded, but these are strategies that universities and schools are considering and have a logical basis.
- Separation of cohorts is an effective way of reducing the likelihood of spread from one group to another. For example, if a university or school has multiple offerings of the same subject, it may introduce rules to require students not to swap between offerings in a term/semester. Similarly, it might encourage staff work on campus only on designated days to minimise overlap between staff cohorts.
- Risk of transmission is maximised when people are congregating in small areas such as waiting to use lifts/elevators. In administrative workplaces, it may be useful to consider encouraging staggered start times to minimise congregation in lift/elevator waiting areas. Similarly, consideration should be given to dispersal strategies for students leaving large lecture theatres, including encouraging use of stairs. The emphasis on masks is appropriate but could be augmented by other strategies.

Testing:

- The paper discusses the importance of rapid testing but does not discuss how to encourage people to respond if they test positive. This includes for staff, ensuring that they are paid while isolating. Special provisions may be required for casual and temporary contract staff.
- Some staff will be able to continue to work remotely, and that should be encouraged, and arrangements should already be in place for that to occur.
- The review does not discuss the frequency of testing — whether people should be tested every day before attending school/university, every second day, etc. There may be evidence on optimal testing frequency that should be included. On a related matter, there is no mention of managing the risk of staff who are employed in multiple organisations because

of casualisation of the workplace. Multiple employment increases the risk of transmission from one workplace to another and universities and schools may wish to attempt to limit the number of separate workplaces that casual staff physically attend.

Is the topic of the review discussed comprehensively in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Health policy, including policies about SARS-CoV-2

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 08 Dec 2021

Trish Greenhalgh, University of Oxford, Oxford, UK

REVIEWER 2

This is an excellent and comprehensive review of the evidence relevant to improve the safety of return of students to universities and schools in the context of the continuing transmission of SARS-CoV-2. The review should be augmented to consider more explicitly a number of issues:

Vaccination:

- The review is written specifically for a United Kingdom audience, and it is perhaps for that reason that it does not mention universities or schools requiring vaccination of students or staff. In Australia, for example, in some states, government regulations effectively require that only vaccinated people are able to return to campus. A number of universities have also introduced mandatory vaccination of the staff and students who are to be on campus. This obviously requires consultation with industrial organisations, but some reference to this issue would be useful to ensure a comprehensive review of options.

Yes, this is an important point. New text and reference(s) added:

WHITE HOUSE REPORT: Vaccination Requirements Are Helping Vaccinate More People, Protect Americans from COVID-19, and Strengthen the Economy OCTOBER 7, 2021.

Accessed 3 November 2021 at

<https://www.whitehouse.gov/wp-content/uploads/2021/10/Vaccination-Requirements-Report.pdf>

Redden, E. (2021) *Climbing Toward Vaccine Compliance, Inside Higher Ed*. Available at: <https://www.insidehighered.com/news/2021/09/21/colleges-mandating-vaccines-see-progress-toward-compliance> (Accessed: 3 November 2021).

Patty A. Mandatory jabs for students and staff to return to universities. Sydney Morning Herald October 13 2021. Accessed 12 November 2021 at

<https://www.smh.com.au/national/mandatory-jabs-for-students-and-staff-to-return-to-universities-20211013-p58znl.html>

Physical distancing:

- The review appropriately refers to the droplet induced theories about physical distancing. This section should be broadened to include stronger consideration of issues relating to remote and hybrid working, cohorting, and workplace bubbles. There may be limited published evidence on these strategies, and for this reason they may have been excluded, but these are strategies that universities and schools are considering and have a logical basis.

Agree, we have added some text to address all these points. In relation to 'bubbles', we've included a new reference (Thompson DA, Abbasizanjani H, Fry R, et al Staff-pupil SARS-CoV-2 infection pathways in schools in Wales: a population-level linked data approach. *BMJ Paediatrics Open* 2021;5:e001049. doi: 10.1136/bmjpo-2021-001049) which provides statistically significant evidence that year-level bubbles have a positive impact, since cases are correlated within year cohorts but not between years.

Separation of cohorts is an effective way of reducing the likelihood of spread from one group to another. For example, if a university or school has multiple offerings of the same subject, it may introduce rules to require students not to swap between offerings in a term/semester. Similarly, it might encourage staff work on campus only on designated days to minimise overlap between staff cohorts.

Added - thanks. We've emphasised the important contribution of hybrid learning (with some people learning remotely).

- Risk of transmission is maximised when people are congregating in small areas such as waiting to use lifts/elevators. In administrative workplaces, it may be useful to consider encouraging staggered start times to minimise congregation in lift/elevator waiting areas. Similarly, consideration should be given to dispersal strategies for students leaving large lecture theatres, including encouraging use of stairs. The emphasis on masks is appropriate but could be augmented by other strategies.

Added - thanks

Testing:

- The paper discusses the importance of rapid testing but does not discuss how to encourage people to respond if they test positive. This includes for staff, ensuring that they are paid while isolating. Special provisions may be required for casual and temporary contract staff.

-
- Thanks - we've added some text on this.
 - Some staff will be able to continue to work remotely, and that should be encouraged, and arrangements should already be in place for that to occur.
 -
- We completely agree. Staff should be enabled to work from home wherever possible to do so.
 - The review does not discuss the frequency of testing — whether people should be tested every day before attending school/university, every second day, etc. There may be evidence on optimal testing frequency that should be included. On a related matter, there is no mention of managing the risk of staff who are employed in multiple organisations because of casualisation of the workplace. Multiple employment increases the risk of transmission from one workplace to another and universities and schools may wish to attempt to limit the number of separate workplaces that casual staff physically attend.
- We've added some comments about this. The only published recommendations we could find are based on convention (twice weekly). We've added that this interval appears to seek to balance cost, the potential reduction in compliance if the interval is very short, and the need to pick up new cases quickly.
- Competing Interests:** no coi

Reviewer Report 25 October 2021

<https://doi.org/10.21956/wellcomeopenres.19088.r46568>

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Stefan J. Marciniak 

Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK

This review aims to provide a timely synthesis of the literature relevant to SARS-CoV-2 transmission in an educational setting and of the available mitigation strategies that might be employed to facilitate a return of in-person university teaching.

This is an ambitious piece and will be of value to those involved in delivering higher education during the pandemic. Helpfully, the authors critically evaluate a wide variety of potential mitigation strategies, highlighting those supported by published evidence, while importantly identifying those for which the evidence does not support continuation. In the former “effective” category, the authors include vaccination, mask wearing, physical distancing, engineering solutions (room ventilation and air filtration), test/trace/isolation, and blended learning. Approaches that the authors conclude to be “ineffective” include strict hand hygiene, restricting spread via fomites, the wearing of face shields, and the separation of individuals by plastic

screens.

The article is clear, well-written, and makes useful evidence-based recommendations. The authors may wish to consider the following critical comments, which might help to improve the article further. In particular, in their effort to provide a useful synthesis of the evidence, at times the distinction between published literature and their interpretation becomes unclear. It might be helpful, and would strengthen the review, if this distinction were to be made more obvious.

Methods section:

- The methods section describes a search of PubMed in September 2021 for the terms “SARS-CoV-2”, “COVID-19”, “transmission”, “mitigation”, “school[s]” and “university/ies”, restricted initially to reviews. These were examined for relevant papers by “snowball searching”. It would be helpful to know the total number of articles assessed and to be provided with more detail about the processes and metrics used to evaluate their quality. Would a PRISMA diagram be valuable in this regard? The authors refer to the screening of articles, in part, by considering the impact factor of the journals in which they were published. While impact factors have some value as a heuristic for quality, this approach also has limitations. It would be reassuring to learn how the threshold for impact factor was set and whether this was corrected for journal type, for example, clinical vs non-clinical journals. It would also be valuable to provide more detail on the methodologies employed to avoid the introduction of any bias. This might be provided in the Methods section or in a dedicated “limitations” section.

Main findings section:

General comments:

- This section provides a narrative synthesis of the above search. It is clearly written and generally well-referenced. In places, however, the referencing is less extensive and it is not always clear if this reflects a deficiency in the published literature. More clarity on this would be helpful in allowing readers to evaluate the validity of the recommendations. It might also be helpful to provide a quantification of the strength of the recommendations, perhaps along the lines of the GRADE (Grades of Recommendation Assessment, Development and Evaluation) approach used in clinical guidelines.¹

Specific comments:

- It is stated that “.. this 90% cut-off is based on a single preprint modelling study [16] that has yet to be peer-reviewed.” Would the authors double check that this statement is true? The article appears to have been published on 31 August 2021 in *Annals of Internal Medicine*, although at the time of writing (24/10/2021), its status has not been updated on medRxiv.
- It is stated, “One key measure for improving safety is to make it very easy for people to get a vaccination on campus—for example by locating vaccination hubs close to settings frequented by target groups (e.g. outside lecture theatres or dining halls) and not requiring paperwork that people are unlikely to be carrying.” This is an important point, but is this an opinion of the authors or are there empirical studies to support it? Is it possible to make clearer the distinction between available data, knowledge gaps, and opinion?
- It is stated, “There have been claims that randomised controlled trial (RCT) evidence is the only “robust” way to test the impact of masks. This is incorrect, because most such RCTs are designed

only to test the hypothesis that the mask protects the wearer over a short period." Again, this is very important. Is it possible to provide citations for the relevant articles? Similarly, elsewhere in this section, comments are made such as *"Perhaps the most persuasive argument for masks in the university context is that if everyone wears one, there is a much lower risk that teaching will need to return to online as a result of rising case numbers"*. These comments are important and would be strengthened if published evidence could be cited. However, if this is interpretation, would it be valuable to separate the literature review from the interpretation?

- It is stated, *"The benefit of mask wearing by all is not dependent on the size of a group, so suggestions that masking is needed only above a certain occupancy threshold means that unmasked smaller groups would carry a preventable risk (and also provide a false sense of security)." Are there published studies available to support this?*
- Figure 2 encodes "risk of transmission" graphically by using a red/amber/green colour scheme. Would it be possible to amend the figure to be more accessible for those with deficiencies in colour vision? I suspect that in its current form it would be challenging for readers with deuteranopia or protanopia.
- In the section on testing, the authors might wish to consider a discussion of mass asymptomatic PCR testing of undergraduates, which has been shown both to be possible and effective in the university setting, for example, through the testing of pooled screening-samples from groups of 10 to 12 students followed by individual testing of positive groups. This has recently been reviewed.²
- I do not feel able to comment usefully on the engineering solutions section, which falls outside my areas of knowledge.

References

1. Atkins D, Best D, Briss PA, Eccles M, et al.: Grading quality of evidence and strength of recommendations. *BMJ*. 2004; **328** (7454): 1490 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Paltiel AD, Schwartz JL: Assessing COVID-19 Prevention Strategies to Permit the Safe Opening of Residential Colleges in Fall 2021. *Ann Intern Med*. 2021. [PubMed Abstract](#) | [Publisher Full Text](#)

Is the topic of the review discussed comprehensively in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Partly

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory medicine, including COVID-19; cell biology, ER stress

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 08 Dec 2021

Trish Greenhalgh, University of Oxford, Oxford, UK

Reviewer Report 1

25 Oct 2021 | for Version 1

Stefan J. Marciniak, Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK

APPROVED WITH RESERVATIONS

This review aims to provide a timely synthesis of the literature relevant to SARS-CoV-2 transmission in an educational setting and of the available mitigation strategies that might be employed to facilitate a return of in-person university teaching.

This is an ambitious piece and will be of value to those involved in delivering higher education during the pandemic. Helpfully, the authors critically evaluate a wide variety of potential mitigation strategies, highlighting those supported by published evidence, while importantly identifying those for which the evidence does not support continuation. In the former “effective” category, the authors include vaccination, mask wearing, physical distancing, engineering solutions (room ventilation and air filtration), test/trace/isolation, and blended learning. Approaches that the authors conclude to be “ineffective” include strict hand hygiene, restricting spread via fomites, the wearing of face shields, and the separation of individuals by plastic screens.

The article is clear, well-written, and makes useful evidence-based recommendations. The authors may wish to consider the following critical comments, which might help to improve the article further. In particular, in their effort to provide a useful synthesis of the evidence, at times the distinction between published literature and their interpretation becomes unclear. It might be helpful, and would strengthen the review, if this distinction were to be made more obvious.

Methods section:

- The methods section describes a search of PubMed in September 2021 for the terms “SARS-CoV-2”, “COVID-19”, “transmission”, “mitigation”, “school[s]” and “university/ies”, restricted initially to reviews. These were examined for relevant papers by “snowball searching”. It would be helpful to know the total number of articles assessed and to be provided with more detail about the processes and metrics used to evaluate their quality. Would a PRISMA diagram be valuable in this regard? The authors refer to the screening of articles, in part, by considering the impact factor of the journals in which

they were published. While impact factors have some value as a heuristic for quality, this approach also has limitations. It would be reassuring to learn how the threshold for impact factor was set and whether this was corrected for journal type, for example, clinical vs non-clinical journals. It would also be valuable to provide more detail on the methodologies employed to avoid the introduction of any bias. This might be provided in the Methods section or in a dedicated “limitations” section.

- [response]

We agree the methods section was too short and didn’t sufficiently describe the search strategy or its rationale. We’ve now included a longer methods section and also a new paragraph at the start of the findings section describing the dataset. Note however that we deliberately did not use a ‘technocratic’ approach to searching and critical appraisal for reasons set out in the revised paper. In short, we weren’t resourced to do so and the sheer breadth of the review (along with the trade-off against time pressures) precluded anything approaching a Cochrane-style approach or formal application of GRADE criteria. There is also the argument that GRADE was designed for clinical epidemiology type studies and is less useful for assessing studies from the engineering literature for example. We’ve flagged that this is a preliminary review and that the literature would benefit from others undertaking more focused reviews with formal critical appraisal of studies in all the topic areas covered.

We have removed the phrase “impact factor of the journal”. Agree it’s a red herring, and whilst MOST seminal sources were published in high-impact factor journals, that’s not what makes them seminal. What makes them seminal is the fact that others in the same sub-field judge them to be authoritative. We’ve amended the text accordingly. The use of seminal sources is discussed in more detail in the Greenhalgh and Peacock 2004 paper we reference.

Main findings section:

General comments:

- This section provides a narrative synthesis of the above search. It is clearly written and generally well-referenced. In places, however, the referencing is less extensive and it is not always clear if this reflects a deficiency in the published literature. More clarity on this would be helpful in allowing readers to evaluate the validity of the recommendations. It might also be helpful to provide a quantification of the strength of the recommendations, perhaps along the lines of the GRADE (Grades of Recommendation Assessment, Development and Evaluation) approach used in clinical guidelines.¹

See above. We’re concerned that GRADE isn’t the right approach here. The lead author has just written the following paragraph for a different paper: “Evidence hierarchies such as GRADE (Grading of Recommendations, Assessment, Development and Evaluations) have a respectable provenance within clinical epidemiology (Guyatt et al., 2008) but in recent years they have come to be used excessively, naïvely and in increasingly politicized ways. Such hierarchies are used by journal editors, reviewers and grant-giving panels—usually in well-intentioned efforts to maintain scientific quality—as a technocratic substitute for deeper engagement with quality of scholarship. The effect of such hierarchies is to vastly restrict the range and diversity of evidence that is generated, published, acknowledged as good research, and fed into policy deliberations.”

We do agree that ideally, this entire study would be repeated with each section subjected to a more exhaustive literature search AND a formal assessment of the evidence base using quality criteria appropriate to the sub-discipline (e.g. modelling studies assessed according to what good looks like in modelling science etc). However, the present paper is not that more exhaustive output (which would take an order of magnitude more hours). We've amended the paper to make it very clear that we agree this piece of work needs doing and we invite others to contribute to the collective effort.

Specific comments:

- It is stated that "*.. this 90% cut-off is based on a single preprint modelling study [16] that has yet to be peer-reviewed.*" Would the authors double check that this statement is true? The article appears to have been published on 31 August 2021 in *Annals of Internal Medicine*, although at the time of writing (24/10/2021), its status has not been updated on medRxiv.

We have updated the reference to the peer-reviewed published paper: Paltiel, A. D and Schwartz, J. L. (2021) Assessing covid-19 prevention strategies to permit the safe opening of residential colleges in fall 2021, *Annals of Internal Medicine* doi:10.7326/M21-2965 <https://www.acpjournals.org/doi/full/10.7326/M21-2965?journalCode=aim>]

- It is stated, "*One key measure for improving safety is to make it very easy for people to get a vaccination on campus—for example by locating vaccination hubs close to settings frequented by target groups (e.g. outside lecture theatres or dining halls) and not requiring paperwork that people are unlikely to be carrying.*" This is an important point, but is this an opinion of the authors or are there empirical studies to support it? Is it possible to make clearer the distinction between available data, knowledge gaps, and opinion?

We agree this was a comment rather than an empirical finding and have now flagged it as such.

- It is stated, "*There have been claims that randomised controlled trial (RCT) evidence is the only "robust" way to test the impact of masks. This is incorrect, because most such RCTs are designed only to test the hypothesis that the mask protects the wearer over a short period.*" Again, this is very important. Is it possible to provide citations for the relevant articles?

We've added a reference: Frieden, T. R., & Cash-Goldwasser, S. (2021). Of masks and methods. *Annals of Internal Medicine*, 174(3), 421-422.

- Similarly, elsewhere in this section, comments are made such as "*Perhaps the most persuasive argument for masks in the university context is that if everyone wears one, there is a much lower risk that teaching will need to return to online as a result of rising case numbers*". These comments are important and would be strengthened if published evidence could be cited. However, if this is interpretation, would it be valuable to separate the literature review from the interpretation?

We understand that this request reflects how conventional medical reviews are presented. However, this review is constructed with a view to being a very quick reference guide (it's likely to be skim-read by busy academics and administrators). In the social sciences, it is standard practice for the 'findings' from a review to be presented alongside an interpretation of those findings. Indeed, one can think of a continuum with 'pure findings' at one end and 'pure interpretation' at the other end but quite a bit in between. If this were a RCT with an effect size and a confidence interval that directly addressed the research question, we'd be operating at the poles of the continuum--with a clear 'results' section and then a 'discussion' section. But what we have here is a bunch of marginally-relevant studies with findings that don't stand independently and it's impossible to present them without also adding a rider about how relevant or useful they are. This means that SOME of the interpretation is inevitably going to be in the findings section. We don't want to double-handle the studies so would prefer to keep the interpretation where it is.

- It is stated, "*The benefit of mask wearing by all is not dependent on the size of a group, so suggestions that masking is needed only above a certain occupancy threshold means that unmasked smaller groups would carry a preventable risk (and also provide a false sense of security).*" Are there published studies available to support this?

We agree this was a misleading sentence. We've changed it to "whilst the odds of becoming infected increases with the number of people in any indoor space, there is no occupancy threshold below which those odds reach zero. Since asymptomatic transmission is common in this disease, groups of any size should wear masks to maximise protection of everyone."

- Figure 2 encodes "risk of transmission" graphically by using a red/amber/green colour scheme. Would it be possible to amend the figure to be more accessible for those with deficiencies in colour vision? I suspect that in its current form it would be challenging for readers with deuteranopia or protanopia.

This is an important point (one of the authors has colourblindness and another is a carrier of the condition and has brothers and a son with it). We have replaced Fig 2 with a colourblind friendly version for which we thank the charity Colourblind Awareness for the revised graphic which has been tested on three commonest forms of colourblindness (deut, trit and prot).

- In the section on testing, the authors might wish to consider a discussion of mass asymptomatic PCR testing of undergraduates, which has been shown both to be possible and effective in the university setting, for example, thought the testing of pooled screening-samples from groups of 10 to 12 students followed by individual testing of positive groups. This has recently been reviewed.[2](#)

We have amended the text to acknowledge that this is a potential option (and included the helpful reference suggested by the reviewer). However, there are also some counter-arguments which we have set out in the revised paper. We summarised those below:

We agree that PCR could represent a gold-standard means of conducting mass testing, and sample pooling is an eminently sensible strategy for the University setting. However, there may also be disadvantages compared with the use of lateral flow devices (LFDs) and a cost/benefit analysis may be pertinent.

First, the costs and work necessary to establish testing facilities on a large scale will be substantially increased in terms of required equipment, reagents and laboratory safety; sample processing for CL3 materials will require additional staff training, appropriate PPE and microbial safety cabinets. This compares to a self-administered LFD, where both swabbing and disposal are conducted primarily at the individual level in adults.

Second, the speed with which results are delivered by PCR will clearly be slower than LFD, and the information will require a form of confidential electronic dissemination; presumably relevant apps exist, but will further increase cost. This could potentially mean that infected individuals attend classes or other interactions during the interim (unless symptomatic), increasing transmission risk. Furthermore, pooled individuals will require re-testing and, depending upon the timescale in which this is achieved, could mean that peak virus load has passed, especially for vaccinated individuals in which the kinetics of declining virus titre in the upper respiratory tract are more rapid. Whilst LFDs lack the fine sensitivity of PCR, they retain impressive specificity and are particularly suited to detecting the higher end of virus loads present within more infectious individuals.

Lastly, convenience and immediacy are likely to appeal to students and staff alike as, whilst LFDs ought not to be used as a green light test, regular asymptomatic testing amongst fixed populations is likely to detect the majority of cases and, combined with other mitigations, limit transmission. However, the value of asymptomatic LFD tests is likely to be reduced where SARS-CoV2 prevalence is low amongst populations.

- I do not feel able to comment usefully on the engineering solutions section, which falls outside my areas of knowledge.
- **Is the topic of the review discussed comprehensively in the context of the current literature?**
Yes
- **Are all factual statements correct and adequately supported by citations?**
Partly
- **Is the review written in accessible language?**
Yes
- **Are the conclusions drawn appropriate in the context of the current research literature?**
Yes

References

1. Atkins D, Best D, Briss PA, Eccles M, et al.: Grading quality of evidence and strength of

recommendations.*BMJ*. 2004; **328** (7454): 1490 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Paltiel AD, Schwartz JL: Assessing COVID-19 Prevention Strategies to Permit the Safe Opening of Residential Colleges in Fall 2021.*Ann Intern Med*. 2021. [PubMed Abstract](#) | [Publisher Full Text](#)

Competing Interests

No competing interests were disclosed.

Reviewer Expertise

Respiratory medicine, including COVID-19; cell biology, ER stress

Competing Interests: none