Covid-19 vaccine boosters for young adults: A risk-benefit assessment and five ethical arguments against mandates at universities

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Abstract
Students at North American universities risk disenrollment due to third dose Covid-19 vaccine mandates. We present a risk-benefit assessment of boosters in this age group and provide five ethical arguments against mandates. We estimate that 22,000 - 30,000 previously uninfected adults aged 18-29 must be boosted with an mRNA vaccine to prevent one Covid-19 hospitalisation. Using CDC and sponsor-reported adverse event data, we find that booster mandates may cause a net expected harm: per Covid-19 hospitalisation prevented in previously uninfected young adults, we anticipate 18 to 98 serious adverse events, including 1.7 to 3.0 booster-associated myocarditis cases in males, and 1,373 to 3,234 cases of grade ≥3 reactogenicity which interferes with daily activities. Given the high prevalence of post-infection immunity, this risk-benefit profile is even less favourable. University booster mandates are unethical because: 1) no formal risk-benefit assessment exists for this age group; 2) vaccine mandates may result in a net expected harm to young people; 3) mandates are not proportionate: expected harms are not outweighed by public health benefits given the modest and transient effectiveness of vaccines against transmission; 4) US mandates violate the reciprocity principle because rare serious vaccine-related harms will not be reliably compensated due to gaps in current vaccine injury schemes; and 5) mandates create wider social harms. We consider counter-arguments such as a desire for socialisation and safety and show that such arguments lack scientific and/or ethical support. Finally, we discuss the relevance of our analysis for current 2-dose Covid-19 vaccine mandates in North America.

1. Introduction

Covid-19 vaccine booster mandates have been controversial, especially in younger age groups. Two main factors are driving scientific controversy: a lack of evidence that booster doses provide meaningful reduction in hospitalisation risk among young people and mounting evidence that (widespread) prior infection confers significant protection against hospitalisation due to (re-)infection. Further, mandates have deleterious societal consequences and are eroding trust in scientific and government institutions.[1] In North America, as of May 2022 at least 1,000 colleges and university campuses required Covid-19 vaccination, and over 300 required boosters.[2] More than fifty petitions have been written opposing these vaccine mandates[3], raising specific legal and ethical complaints.[4] In many cases, young people, parents, and faculty have been ignored by administrators and mandate proponents.

Policymakers, public health scholars and bioethicists have argued both for and against Covid-19 vaccine mandates. The strongest argument made by mandate proponents is based on the harm principle: insofar as vaccines prevent transmission and thereby reduce harm to others, restrictions on individual freedom are viewed as more ethically justifiable.[5] Of course, a reduction in risk to others (especially if this is a small or temporary effect) might not alone be sufficient to justify a booster mandate in young people. Savulescu[6] and colleagues[7] have argued that, to be ethical, mandates require four conditions: that the disease be a grave public health threat; that there is a safe and effective vaccine; that mandatory vaccination has a superior cost/benefit profile in comparison to other alternatives; and that the level of coercion is proportionate.

Proportionality is a key principle in public health ethics.[1] To be proportionate, a policy must be expected to produce public health benefits that outweigh relevant harms, including harms related to coercion, undue pressure, and other forms of liberty restriction. Williams[8] has argued that Covid-19 vaccine mandates may be justified for older but not younger people, among whom such policies are not proportionate given a lack of clarity that benefits outweighs harms. Such ethical assessments should rely on empirical data: thorough risk-benefit assessment requires quantification (where possible) of relevant risks and benefits *for the group affected by the policy*. With respect to poor outcomes due to Covid-19, the most consistent predictors are age[9] and comorbidities.[10] Similarly, age and sex are prominent risk factors for vaccine-associated reactogenicity[11] and serious adverse events such as myocarditis, which is more common in males.[12] Vaccine requirements must therefore be predicated on an age- and sex-stratified risk-benefit analysis and consider the protective effects of prior infection.

In this paper, we provide (to our knowledge) the first risk-benefit assessment of SARS-CoV-2 boosters for young previously *uninfected* adults under 40 years old. Our estimate suggests an expected net *harm* from boosters in this young adult age group, whereby the negative outcomes of all severe adverse events and hospitalizations may on average outweigh the expected benefits in terms of Covid-19 hospitalizations averted. We also examine the specific harms to males from myo/pericarditis. Our analysis is conservative given the fact that we did not account for the protective effects of prior infection, which is estimated to be substantive.[13] We then outline a five-part ethical argument against booster mandates for young people informed by our empirical assessment. First, we argue that there has been a lack of transparent risk-benefit assessment; second, that vaccine mandates may result in a net expected harm to individual young adults; third, that vaccine mandates are not proportionate; fourth, that US mandates violate the reciprocity principle because of current gaps in vaccine injury compensation schemes; fifth, that mandates are even less proportionate than the foregoing analyses suggest because current high levels of coercion or pressure create wider societal harms. We consider possible counterarguments including potential rationales for mandates based on a desire for social cohesion or safety and summarise why such arguments cannot justify current Covid-19 vaccine mandates. We suggest that general mandates for young people ignore key data, entail wider social harms and/or abuses of power, and are arguably undermining rather than contributing to social trust and solidarity.

2. Background

To provide background for our risk-benefit assessment and ethical arguments, we outline recent controversies among experts regarding vaccine boosters and summarise current data on Covid-19 vaccines, specifically: vaccine effectiveness against transmission, effectiveness in those with prior infection, and the age-stratified risk of severe COVID-19.

2.1. Controversy Among Experts

The rapidly shifting policy response to the pandemic has exacerbated a crisis in the *trustworthiness* of scientific institutions, health agencies and regulatory bodies. Transparency in policy making has been threatened in part by political expediency, sometimes even to the point of government agencies over-ruling appointed scientific expert groups without clear explanation of the reasons for such reversals. For example, in July 2021, the CDC released a joint statement with the FDA[14] reassuring the public that boosters were not necessary. Just two months later, in September 2021, a US FDA advisory committee overwhelmingly voted 16-2 against boosting healthy young adults.[15] Yet, this recommendation was overruled by the White House and CDC leading to the resignation of two high-level FDA vaccine experts. These experts wrote in *The Lancet* about the "…need to identify specific circumstances in which the direct and indirect benefits of doing so are, on balance, clearly beneficial."[16] To date, no such favourable risk-benefit assessment has been made public.[17]

Because the mRNA vaccine 3rd dose booster trials were too small to measure important clinical endpoints, additional doses have been granted Emergency Use Authorisation (EUA) based on observational data suggesting benefits in older populations.[18] Prior to the emergence of the Omicron variant, the US CDC estimated[18] that administering a booster dose to 9,000 (Pfizer) or 12,000 (Moderna) 18–29-year-olds would prevent one Covid-19 hospitalisation over six months. As of August 2022, this estimate has not been updated to reflect increasing natural immunity or waning vaccine effectiveness. Data on vaccine effectiveness specific to young adults is scarce, but reports from the UK[19] and Israel[20] failed to identify additional protective effects of boosters against severe disease for people younger than 40. In a recent CDC publication, which stratified for ages 18-49, a booster dose increased effectiveness against emergency department encounters and hospitalizations among immunocompetent adults during the Omicron wave, but the analysis did not adjust for comorbidities and excluded those with a history of prior infection "to reduce the influence of protection from previous infection."[21]

Risk-benefit calculations for the primary series among younger children and adolescents are similarly scant. A cohort study conducted in Hong Kong estimated the number needed to harm (NNH) from myo/pericarditis for dose two of BNT162b2 was 2563 among adolescent males[22] yet the CDC never published a U.S.-specific NNH, nor recommended shifting to a one-dose policy for adolescents as did the UK, Norway, Taiwan and Hong Kong.[22] The most recent Covid-19 number needed to vaccinate (NNV) calculation conducted by the CDC in June 2022 estimated that 1660 to 3320 children ages 6 months to 4 years would need to be vaccinated to prevent one hospitalisation; no NNH was offered for comparison.[23] Moreover, the CDC's outdated risk-benefit analysis for adolescents and young adults does not distinguish important subgroups such as or those who have recovered from previous infection or healthy young people (as opposed to those with comorbidities or immunocompromised status). Finally, many countries have not required or mandated booster doses for young healthy adults at universities[24], suggesting that, at a minimum, there is a diversity of expert views on whether the expected benefits of such policies outweigh their potential harms.

2.2. Current Data Regarding Covid-19 vaccines

A thorough *ethical* evaluation of risks and benefits requires relevant *empirical* data, especially where risks and benefits can be quantified to a reasonable degree of certainty. Relevant data include not only those regarding average individual vaccine safety and effectiveness but also age-stratification of these data as well as the protective effect of prior infection and the effectiveness of vaccines against transmission.

Proponents of mandates have argued that current vaccines "prevent transmission," which would support a standard ethical reason in favour of mandates: the protection of others. Yet it is increasingly clear that current vaccines provide, at most, partial and transient protection against infection, which decreases precipitously after a few months[25,26], with secondary transmission largely unaffected (in other words: an infected vaccinated person poses similar risks to others as an infected unvaccinated person).[27,28] The CDC states: "anyone with Omicron infection, regardless of vaccination status or whether or not they have symptoms, can spread the virus to others."[29] It is therefore inaccurate to infer a sustained or long-term reduction in transmission from a short-term reduction in infection.[30]

A second limitation is ignoring the protective effects of prior infection. In February 2022, the CDC estimated that 67% of adults 18-49 had infection-induced SARS-CoV-2 antibodies, up from 30% in September 2021.[13] By now (August 2022), the majority of young adults, both vaccinated and unvaccinated, have most likely already been infected with Covid-19. Evidence increasingly shows that prior SARS-CoV-2 infection provides at least similar clinical protection to current vaccines[31-33], something that is not acknowledged in current university policies. It is not clear whether vaccination of previously infected individuals provides any meaningful benefits with respect to severe disease, especially for healthy young people.[34]

Mass vaccination had been proposed as a way to “end the pandemic.”[35] However, elimination or eradication of the virus is not a tenable goal with vaccines that provide only temporary and incomplete reduction in infection risk, and the presence of multiple animal reservoirs. Because of this, nearly all human beings will eventually be infected with SARS-CoV-2, as with other endemic coronaviruses (and every pandemic influenza virus on record), many times in their lifetime.[36] Denmark has, for example, acknowledged vaccinating children was not effective at curbing spread of the virus and is thus no longer recommending vaccination against Covid-19 for most children.[37,38]

A final point relates to the burden of Covid-19 in young adults under 40. Using pre-vaccine era mortality data from 190 countries, an adjusted infection fatality ratio (IFR) for 18 to 29 year-olds ranges from 100 per million (18 year-olds) to 500 per million (29 year-olds) with significant variation by country within each age stratum.[39] During the Omicron surge, and stratified by vaccination status, the CDC’s maximum reported crude mortality incidence rate (IR) for 18-29 year-olds was 1 per million among the vaccinated and 5 per million among the unvaccinated.[40] Taking population immunity into account with variant severity and projected coincident surges of influenza, SARS-CoV-2, and respiratory syncytial virus in the winter of 2022-2023, the UK’s Joint Committee on Vaccination and Immunisation (JCVI) currently recommends for its fall booster campaign that the following groups at high risk for severe outcomes be *offered* a booster: residents and staff in care homes for older adults; frontline healthcare and social care workers; adults over 50 years; people aged 5 to 49 years in a clinical risk group or living with someone who has immunosuppression; and persons age 16 to 49 who are care givers. [41] Both vaccination and prior infection can substantially reduce the likelihood of mortality[32,33,41] but the protection against hospitalisation afforded by a booster wanes at 15 weeks to an estimated 80% during BA.1 and 56.5% during for BA.2.[42] Using a national population-wide dataset in Qatar, both previous infection alone and vaccination alone were found to provide >70% protection against severe, critical or fatal Omicron (BA.1 or BA.2).[43] Prior infection alone was 91% effective whereas protection from two or three doses of vaccine alone was 66% and 83%, respectively. Covid-19 does cause acute illness, and may have long-term effects for some, particularly those who develop critical illness, but vaccination appears to confer at best modest protection against longer-term sequelae[44] and the existing data are non-randomized, from variants that predate Omicron and with unclear relevance for current adults under age 40. The existence of effective treatments for clinical management[45] is also an argument against vaccine mandates, especially for groups not considered at risk for severe illness.

3. Risk-Benefit Assessment

In a recent editorial, vaccine developer and paediatrician Paul Offit[34] argued that "because boosters are not risk-free, we need to clarify which groups most benefit….It is now incumbent on the CDC to determine who most benefits from booster dosing and to educate the public about the limits of mucosal vaccines."[1] Below, we provide an Omicron-specific risk-benefit assessment of booster vaccination for young adults ages 18 to 29 years for both Pfizer

[1] Offit recommended that his own son not receive a booster dose due to concerns that benefits would not outweigh risks [https://www.theatlantic.com/health/archive/2022/01/should-teens-get-booster-omicron/621222/].

(BNT162b2) and Moderna (mRNA-1273) vaccines. This analysis builds on the first stratified risk-benefit analysis of vaccination among adolescents 12-17 years of age which considered age, sex, health status, virulence of the dominant variant, and population prevalence of post-infection immunity.[46] For the booster among young adults ages 18-29, the calculations leverage the CDC's pre-Omicron number needed to vaccinate, the estimated reduction in severity of Omicron vs Delta[47], and current estimated seroprevalence.[13] While harms from Covid-19 vaccines are rare[48] they should be factored into policy recommendations. This risk-benefit analysis considers the overall rate of reported SAEs and grade ≥3 reactogenicity (Figure 1) and myo/pericarditis among males (Figure 2). Rates and definitions are consolidated in Table 1.

Serious adverse events are defined by the FDA and the National Institutes of Health[49] as an adverse event that results in any of the following conditions: death; life-threatening at the time of the event; inpatient hospitalisation or prolongation of existing hospitalisation; persistent or significant disability/incapacity; a congenital anomaly/birth defect; or a medically important event, based on medical judgement. Grade 3 or 4 reactogenicity is defined as local/systemic events that prevent daily routine activity or require use of a pain reliever (grade 3) or requiring an emergency room visit or hospitalisation (grade 4).[49,50]

To estimate the expected harms (SAEs including myocarditis and grade ≥3 reactogenicity) and benefits (Covid hospitalizations prevented) specific to boosting 18–29-year-old young adults, we used data reported by CDC from phase 2/3 clinical trials[18,50-52], peer-reviewed observational data from large integrated health systems[53-57], post-marketing surveillance collected via V-Safe by the CDC[58], and an international estimate in a young adult population.[54]

3.1. Serious adverse event (SAE) rates reported from manufacturer-provided data

Of the 12 SAEs reported by Pfizer in the booster trial (n=5055), three were found by blinded investigators to be attributable to the vaccine, providing a rate of 1 in 1685 (3/5055)[18] as the lower bound while the upper bound is drawn from the CDC's Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) review which reported a rate of 1 in 306.[50] For a campus of 30,000 boosted with the Pfizer product, the expected SAE rate is therefore 18 (3/5055*30,000) to 98 (1/306*30,000). Surprisingly, Moderna found that none of the 5 SAEs experienced by 4 out of 344 participants[50] in its open-label booster trial (4/344=1.2%)[2] were attributable to the vaccine, thus our SAE estimates are for Pfizer only.

3.2. Reactogenicity rates

According to self-report data, side effects from the booster dose prevent up to a third of recipients from being able to carry out normal daily activities in the days following vaccination.[55] Sponsor-reported rates for grade ≥3 reactogenicity are 1 in 22 (14/306)[50] for the Pfizer booster to 1 in 9 (18/167)[50] for the Moderna booster. For a campus of 30,000 boosted previously uninfected young adults, the expected number of grade ≥3 reactogenicity cases is therefore 1373 (14/306*30,000) to 3234 (18/167*30,000), respectively. In those with a prior SARS-CoV-2 infection, post-vaccination symptoms causing missed work or daily activities are reported two- to three-fold more often than those without a history of infection[56,57], a major concern given that seroprevalence among adults aged 18-49 is now well above the February 2022 estimate of 67%.[13] Conservatively assuming 67% as the proportion with a history of

[2] Table 3e footnote h: Overall, 4/344 (1.2%) participants experienced 5 SAEs during a median follow-up of 5.7 months after booster dose (administered at least 6 months after a 50 mcg (n=173) or 100 mcg (n=171) 2-dose primary series); the sponsor deemed these unrelated to mRNA-1273. Data on an equivalent primary series comparison group was not available at the time of the GRADE assessment.

Covid-19 infection, and a two- to threefold increased likelihood of systemic effects, expected grade ≥3 reactogenicity cases would be at least 1839 to 4333 for Pfizer and Moderna boosters, respectively. Even without taking into account prior infection, the proportion reporting to V-Safe being "unable to perform daily activities" was between 20-40% depending on booster product, and higher among those receiving a heterologous booster.[58]

3.3. Booster vaccine-associated myocarditis rates in university-age males 18-29 years

The CDC estimated the rate of post-booster myocarditis during days 0 to 7 following BNT162b2 vaccine administration in 16–17 year-old males to be 1 in 41,500[51] using passive surveillance through the Vaccine Adverse Event Reporting System (VAERS), and 1 in 5000[51] using active surveillance with the Vaccine Safety Datalink (VSD). In 18–29 year-old males, the post-booster myocarditis rate for both products combined using VAERS was reported to be 1 in 101,000[52] (ages 18–24) to 1 in 208,000[52] (ages 25–29) while the VSD rate was much higher at 1 in 14,200[52] (mRNA-1273) to 1 in 21,000[52] (BNT162b2). Two other population-based studies from the US and Israel in 18–24-year-old males found the rate to be 1 in 7000[53] to 9000.[54] In both of these studies, BNT162b2 was the vaccine administered prior to diagnosis. For our estimates, and assuming a precautionary stance, we have used active surveillance rates or population-based rates. For 16–17 year old males we use the VSD rate of 1 in 5000[51]; for 18–29 year olds we consider the rate 1 in 7000[53] to be the most reliable because the same method was used to estimate the dose-two myocarditis rate for adolescents ages 12–17[59], based on CDC definitions and databases, and was consistent with international estimates for this age group.[46] We provide a 16–17 year-old rate given that academic acceleration allows younger adults to attend college along with the freshman cohort. In our figures, we provide a range of myopericarditis estimates for consideration.

3.4. Hospitalizations prevented

To estimate the benefits of hospitalizations prevented by boosters, we updated the CDC's estimated number needed to vaccinate (NNV)[18] for a strain such as Omicron which was found to be approximately 59% less virulent[47] than Delta. Scaling the CDC's NNV estimates of 9,000 for BNT162b2 and 12,000 for mRNA-1273 by this reduced severity, we estimate that 22,000 (9000/0.41) to 30,000 (12,000/0.41) young adults would need to be boosted with BNT162b2 or mRNA-1273, respectively, to prevent one Covid-19 hospitalisation over six months.

3.5. Risk-benefit estimates

At this scale, and as shown in Figure 1, a hypothetical campus with 30,000 young adults receiving the BNT162b2 booster could expect *more* SAEs (18 to 98) than Covid-19 hospitalizations averted (1.0-1.4). Our hypothetical campus may also expect 1373 to 3234 young adults (rate of 1 in 9-22[50]) to experience Grade ≥3 reactogenicity disrupting daily activities or requiring medical care when vaccinated with BNT162b2 or mRNA-1273, respectively. Given that prior SARS-CoV-2 infection increases the rate of systemic reactions by two- to three-fold[56,57], the number of young adults expected to experience disruptions in their school and daily activities is likely to exceed 1839 with BNT162b2 and 4333 with mRNA-1273.

If the 15,000 males and 15,000 females ages 18-29 years on the hypothetical campus were all boosted under a universal mandate, we estimate between 1.7 to 3.0 occurrences of myocarditis (rates of 1 in 7,000[53] to 1 in 5000[51]) among males and 0.7 cases among females.[51] Boosting the entire campus could thus cause approximately 3-4 myo/pericarditis cases, among males predominantly, per single hospitalisation averted. (Figure 2)

Most media reports, as well as a recent systematic review[60] and expert opinion from the American College of Cardiology[61] present vaccination-associated myo/pericarditis as rare, (typically) "mild" and followed by rapid recovery with anti-inflammatory treatment. The reviews have not framed vaccine-associated risks versus infection-associated risks using compatible denominators based on exposure (vaccination) and infection (seroprevalence), thus the infection-associated risks may have been overstated by at least a factor of four according to CDC estimates of the burden of Covid-19 illness.[62] However, it has been found to occur in as many as 1 in 2652 males aged 12–17 years old and 1 in 1862 males aged 18–24 years old after the second dose[59] (and as high as 1/1300 after the second dose in a Pfizer-Moderna combination).[63] An Israeli study described 1 in 5 cases among 16–29 year-olds to be of intermediate severity, meaning these cases had persistent new/worsening abnormalities in left ventricular (LV) function, or persistent ECG anomalies, or frequent non-sustained ventricular arrhythmias without syncope.[64] The CDC reported that 1200 of the 1314 verified myocarditis cases with known hospitalisation status following primary series or booster had been hospitalized.[65] Among adolescents, 69%[66]-80%[67] of those diagnosed with vaccine associated myopericarditis had findings consistent with cardiac scarring on MRI testing three to eight months after the second dose. The potential long-term impact of scar tissue on heart conduction remains unknown.[66,67] Post-vaccination myocarditis has been found to be equivalent to or exceed the risk of post-Covid myocarditis in males less than 40 years old despite the lack of seroprevalence-based estimates of Covid-associated myocarditis.[68] Rare incidences of death in young males attributed to mRNA vaccine induced myocarditis have also been reported.[69,70]

Table 1. Risk-benefit analysis inputs: definitions and rates for serious adverse events (SAEs), reactogenicity, and myo/pericarditis

<table>
<tr><th>Rate</th><th colspan="2">Definition</th><th colspan="2">Numerator/Denominator</th><th>Risk</th></tr>
<tr><td>Serious Adverse Events (SAEs)</td><td colspan="2">An adverse event that results in any of the following conditions: death; life-threatening at the time of the event; inpatient hospitalisation or prolongation of existing hospitalisation; persistent or significant disability/incapacity; a congenital anomaly/birth defect; or a medically important event, based on medical judgement.</td><td colspan="2">Pfizer: 3 / 5055[18]
Slide 26

Pfizer: 1 / 306[50]
Table 4a

Moderna: 0 / 171*[50]
Table 4b</td><td>1 in 1685

1 in 306</td></tr>
<tr><td>Reactogenicity</td><td colspan="2">Grade 3 or 4 reactogenicity is defined as local/systemic events that prevent daily routine activity or require use of a pain reliever (grade 3) or requiring an emergency room visit or hospitalisation (grade 4).</td><td colspan="2">Pfizer: 14 / 306[50]
Table 3f

Pfizer: 19 / 289[50]
Table 4a

Moderna: 18 / 167[50]
Table 3f, 4b</td><td>1 in 22

1 in 15

1 in 9</td></tr>
<tr><td>Myo/pericarditis</td><td>CDC case definitions[17]
Myocarditis
Probable
1. Presence of ≥1 new or worsening of the following clinical symptoms:*
-Chest pain/pressure/discomfort
-Dyspnea/shortness of breath
-Palpitations
2. Abnormal testing
-Elevated troponin
-ECG or EKG findings</td><td>

Confirmed
1. Symptoms
-Chest pain/pressure/discomfort
-Dyspnea/shortness of breath
-Palpitations
2. Abnormal testing
-Biopsy</td><td>Males Booster Ages 18-29

147/mill[53]
Sharff et al
112.5/mill[54]
Friedensohn et al (IDF)

Pfizer (VAERS):
18-24 9.9/mill[52]
25-29 4.8/mill[52]</td><td>Females Booster Ages 18-29

n/a

n/a

Pfizer (VAERS):
18-24 0.6/mill[52]
25-29 2.0/mill[52]</td><td>

Male: 1 in 6800

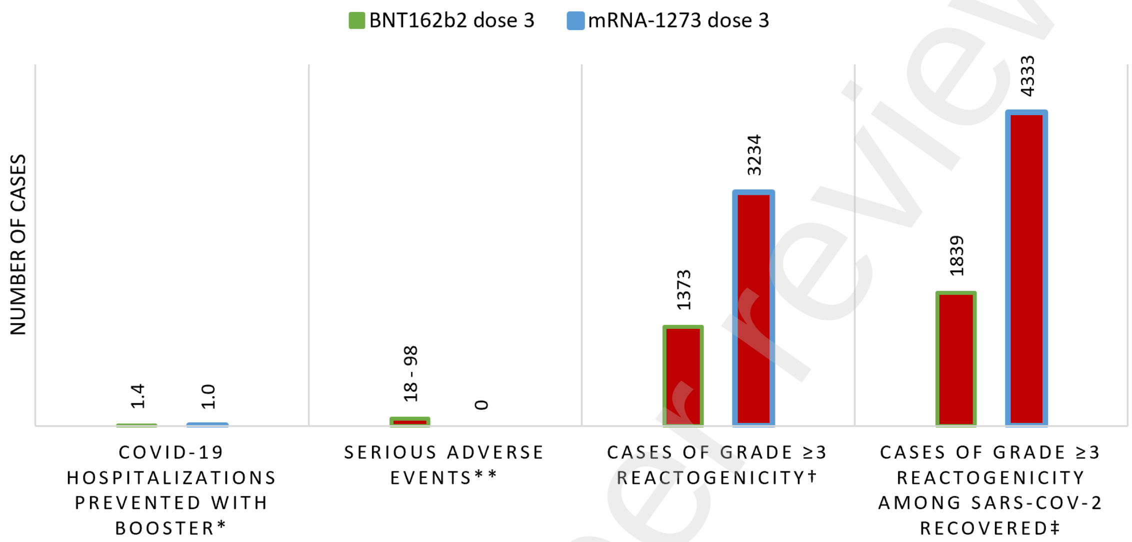
Male: 1 in 8900

Male: 1 in 101k
Female: 1 in 1.7 mill
Male: 1 in 208k</td></tr>
</table>

Rate	Definition		Numerator/Denominator		Risk
	-Decreased function on ECHO or MRI -cMRI findings consistent with myocarditis 3. No other identified cause **Pericarditis** Presence of ≥2 new or worsening of the following clinical features: -acute chest pain -pericardial rub on exam -new ST-elevation or PR-depression on EKG -new or worsening pericardial effusion on ECHO or cMRI	-Elevated troponin AND MRI findings consistent with myocarditis 3. No other identified cause	slide 11 Pfizer (VSD): 47.6/mill[52] slide 23 Moderna (VSD): 70.3/mill[52] slide 23 **Ages 16-17** Pfizer (VAERS): 24.1/mill[51] slide 10 Pfizer (VSD): 200.3/mill[51] slide 25	slide 11 Pfizer (VSD): 4.7/mill[52] slide 23 Moderna (VSD): 13.9/mill[52] slide 23 **Ages 16-17** Pfizer (VAERS): 0.0/mill[51] slide 10 Pfizer (VSD): 44.0/mill[51] slide 25	Female: 1 in 500k Male: 1 in 21k Female: 1 in 213k Male: 1 in 14k Female: 1 in 72k Male: 1 in 41.5k Female: 0 Male: 1 in 5000 Female: 1 in 23k

*Footnote from GRADE: Overall, 4/344 (1.2%) participants experienced 5 SAEs during a median follow-up of 5.7 months after booster dose (administered at least 6 months after a 50 mcg (n=173) or 100 mcg (n=171) 2-dose primary series); the sponsor deemed these unrelated to mRNA-1273. Data on an equivalent primary series comparison group was not available at the time of the GRADE assessment.

Fig 1: Expected Serious Adverse Events (SAEs) and Grade ≥3 Reactogenicity Per Single Hospitalisation Prevented with Universal Booster Vaccination on a Large University Campus of 30,000 Students



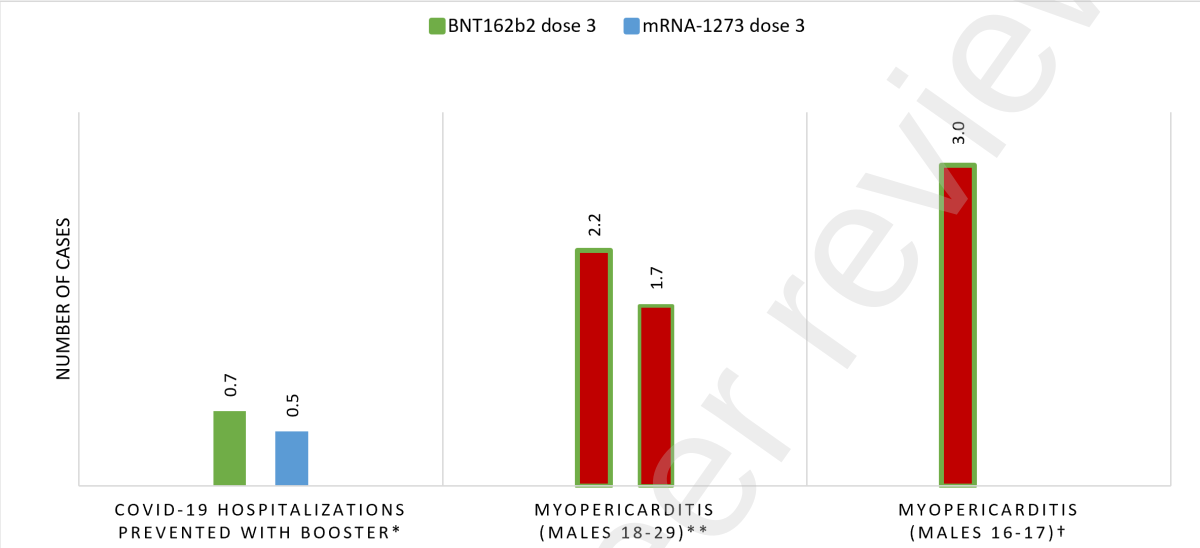
*CDC-estimated number needed to vaccinate (NNV) with a booster to prevent 1 hospitalization in 18–29-year-olds[18] was adjusted for reduced Omicron severity (aHR=0.41)[47] as follows: BNT162b2 (8,738/0.41=21,312) and mRNA-1273 (11,994/0.41=29,254). These rates were scaled to a hypothetical campus of 30,000 students.

**SAEs: CDC reports 3/5055 for BNT162b2 while sponsor's reported rate is 1/306.[50] Expected SAEs on a campus of 30,000 universally boosted students) is 18 (3/5055*30,000) to 98 (1/306*30,000=98). Sponsor reported SAE for mRNA-1273 was 0/344; 4 people had 5 SAEs, none of which sponsor found to be attributable to the booster.[18,50]

† Reactogenicity rates are BNT162b2 (14/306*30,000=1,373) and mRNA-1273 (18/167*30,000=3,234).[50]

‡ Estimated reactogenicity rates computed assuming 67% seroprevalence[13] and at least 2x reactogenicity among those with prior SARS-CoV-2 infection.[56,57] BNT162b2 (14/306*0.67*2*30,000=1,839) and mRNA-1273 (18/167*0.67*2*30,000=4,333).

Fig 2: Expected Myopericarditis Cases per Single Hospitalisation Prevented with Universal Booster Vaccination on a Large University Campus with 30,000 Students (15,000 Males)



*CDC-estimated number needed to vaccinate (NNV) with a booster to prevent 1 hospitalization in 18–29-year-olds[18] was adjusted for reduced Omicron severity (HR=0.41)[47] as follows: BNT162b2 (8,738/0.41=21,312) and mRNA-1273 (11,994/0.41=29,254).
**Sex-specific myocarditis rates assume boosting 15,000 18-29 year old males on campus. Estimated rates computed as follows: Sharff, et al. (14.7/100,000*15,000=2.2)[53]; Friedensohn, et al. (11.25/100,000*15,000=1.7)[54]; CDC VSD[51,52] rates for BNT162b2 (47.6/1 mill*15,000=0.7) and mRNA-1273 (70.3/1 mil*15,000=1.1).
† Boosting 16-17 year old males on campus: CDC VSD (200.3/1 mill*15,000=3.0).[51]

3.6. Limitations of analysis

These estimates have a number of limitations. First, our estimates rely on sponsor-reported and CDC summaries of adverse events; we cannot account for failures to report or loss to follow-up during the clinical trials. Second, we do not distinguish between specific types or clinical significance of SAEs because of scarce data, including the small sample size of the original booster clinical trials and the inability to verify reasons for participant loss to follow-up, which may have been due to unreported SAEs. The Pfizer trial, for example, included only 78 individuals 16–17 years of age randomised to receive booster or placebo.[71] Nevertheless one male in this age group was diagnosed with myocarditis. It is also possible that multiple severe side-effects were reported by the same participant and that the number of people impacted by such reactions is lower than our estimate. We are extrapolating SAE data to young adults (18–29 years old) that were originally generated in clinical trials involving all age groups. However, studies have shown that younger people have a greater likelihood of vaccine-related adverse events.[72] The three vaccine-associated SAEs reported by Pfizer were moderate persistent tachycardia, moderate transient elevated hepatic enzymes, and mild elevated hepatic enzymes.[18] Hence, the causal relationship between our estimated SAEs and the Covid-19 vaccines needs to be approached with caution. Haas et al.[73] suggested that many systemic AEs in the RCTs (76% of systemic and 24% of local reactogenicity) may have been due to a nocebo effect—anxiety, expectations and background symptoms. It is very likely, however, that real-world severe or serious AEs may be greater than those reported in the RCT data because standard trials are underpowered to detect rare AEs and there may also be selection bias: those with greater expectation of harmful side effects are less likely to enrol in a trial. In fact, these data are usually collected after a drug has been approved and is on the market (phase IV clinical trial data). Such limitations show the need for more robust post-marketing data and ideally large, controlled trials to determine costs and benefits for any future booster doses, especially in younger age groups. Universities have not recorded cumulative adverse event rates on their Covid-19 dashboards, thus there is no way to validate our estimates with real-world data. Even with the residual uncertainties, our risk-benefit assessment shows that it is at least plausible that expected individual harms outweigh benefits for young healthy people (i.e., most young adults), and it is implausible that individual benefits significantly outweigh risks. Pfizer's public data supports this inference.[72] In requesting the EUA for boosting adolescent males, the Pfizer's risk-benefit analysis estimated 23-69 cases of myocarditis per one million booster doses administered and 29-69 hospitalizations averted, yet this estimate of 23-69 cases of myocarditis per million third doses administered is now known to be an order of magnitude below the 200.3 per million reported by the US CDC among adolescents aged 16–17 years.[51]

4. Five ethical arguments against university booster mandates

Below, we present five ethical arguments against university booster mandates informed by our risk-benefit assessment and ethical analysis of mandatory policies to date. These arguments relate to (1) the importance of transparency in policy (which has been lacking), (2) the potential for net individual harm, (3) the lack of a proportionate public health benefit, (4) the lack of reciprocity in terms of compensation for vaccine-related harms, and (5) the wider social harms of vaccine mandates.

4.1. Transparency

Risk-benefit assessment is essential to the ethical acceptability of public health policy, and transparent assessments help maintain trust in public health, especially in the context of controversial policies. There is an even stronger rationale for thorough and transparent risk-benefit assessment when interventions are mandated or when (given uncertainty or relevant population differences) some people might face harms not outweighed by individual benefits. In such cases, risk-benefit assessments should be stratified by demographic factors and updated as new data become available to reduce uncertainty. At a minimum, if an intervention is implemented despite significant uncertainty (especially if it is mandated), there is a strong ethical rationale to collect (controlled) data to resolve relevant uncertainties.

It is arguably negligent that key institutions such as the CDC and FDA have not conducted a risk-benefit assessment either before or after recommending that all adults *should* receive a booster dose. Without such a formal analysis, professional associations (such as the American College of Cardiology (ACC) expert panel[61]) have been forced to infer from the literature and CDC's own analyses. For example, the ACC expert panel produced a graphic displaying a favourable harms vs. benefits ratio for young adults ages 12-29.[61] The ACC's widely promoted graphic is tied to data presented by the CDC[74] and relies on four key assumptions which necessarily bias the findings in favour of vaccination: 1) vaccine effectiveness of 95% over 120 days to prevent Covid-19 cases and hospitalizations; 2) myocarditis rates were derived from passive surveillance in VAERS instead of active surveillance available to the CDC (VSD) resulting in harms being underestimated by a factor of 10[51,52]; 3) harms and benefits were averaged across ages 12–29 when the risk may be highest among those aged 16–19[51,52]; and 4) hospitalisation rates were tied to May 2021 data, more than a year prior to the ACC's review and pre-Omicron. Nevertheless, for adolescent males ages 12–17, the CDC estimated 56-69 myocarditis cases would be expected while 71 ICU admissions could be averted.[74]

It was foreseeable that the decision to approve boosters (against the advice of the FDA panel) would be followed by booster mandates since pandemic vaccine mandates were already in place in many universities and colleges throughout the United States at the time.[13] Universities rely upon public health agencies such as the CDC for guidance. Thus, we maintain that if mandates remain then there is an ethical obligation for the agency (and independent scientists) to update public NNV estimates for boosters among adults younger than 40, stratified by sex, comorbidity status and history of infection to provide evidence that the intervention confers an expected net benefit to individuals younger than 40 years in the context of the prevailing SARS-CoV-2 variants and pre-existing immunity. Without this, it is problematic to simply claim that Covid-19 vaccines are "safe and effective" without specific risk-benefit analyses for different age categories and with consideration for individual health status, including evidence of prior infection, because risks of both disease and vaccination are highly variable according to these factors.[9,10]

Since there has not been any RCT specific to evaluating boosters in young adults, the CDC relied on data from an older cohort with a median age of 51.7[71,75] and perhaps assumed that the benefits would also outweigh risks for younger age groups. As we have shown, it is likely that this assumption is incorrect. Under such uncertainties, ethical vaccine policymaking arguably requires radical transparency about scientific knowledge and uncertainties regarding vaccine risks and benefits (i.e., even more transparency than where certainty is high).

Transparent policymaking can encounter a "trust paradox" in providing information about vaccine risks to the public. As noted by Petersen, et al.[76] governments have a perverse incentive to withhold negative information about vaccines since they are actively promoting such products and negative information about vaccines reduces vaccination uptake. And yet transparent disclosure about negative information (e.g., side effects) helps to sustain trust in health officials and reduces the politicisation of vaccines.[77] Transparency may reduce the uptake of vaccination in the short-term but will uphold trust in health authorities and vaccines in the longer-term—just as open disclosure regarding clinical harms promotes trust in medicine.[78] Conversely, efforts by the FDA to prevent the release of internal documents and communications with Pfizer when requested by a civil society group (https://phmpt.org) through a Freedom of Information Act (FOIA) reinforce the view that regulatory agencies are not being transparent with the public. To address the "trust paradox" in regulatory politics, and to maintain trust in government and scientific institutions, greater data accountability (in this case, a risk-benefit analysis) should precede mandates. Given concerns about pharmaceutical influence on the political process[78,79] this should be facilitated by new mechanisms for independent scrutiny of regulatory science during emergencies.[79]

4.2. Potential Net Expected Individual Harm

The reasonable possibility of a net harm to individuals (as presented in our risk-benefit assessment) should provide a strong basis to argue for the ethical case against booster mandates for young adults. Mandates at institutions of higher education serve the age group with one of the lowest public health burdens from Covid-19. Hence boosters provide a low impact on hospitalisation and a low impact on transmission for an age group with a low prospect of benefit. Arguably, this has been considered by most universities and colleges and is the reason why most do *not* have booster mandates for the fall of 2022. In fact, this is likely why European countries, including the UK, France, Germany and Norway, Sweden and Denmark (to our knowledge) never had university-implemented mandates.[24] When the European Centre for Disease Control and Prevention (ECDC) recommended boosters for all adults in November 2021, priority was focused on those over age 40.[80] Taking a different view of the data, the US CDC recommended boosters for all adults and currently recommends a *second* booster for all Americans aged 50 years or more.[81] The ECDC, in contrast, recommended that first boosters be "offered" with prioritisation for those over 40 years, and second boosters only for those over age 60 and those with an immunocompromised status or high risk medical conditions.[82]

The UK's *Joint Committee on Vaccination and Immunisation* (JCVI) provides an interesting example of using the potential for net harm to advise *against* the primary vaccination series for 12–15-year-olds.[83] The JCVI argued that the potential benefit of vaccination in this age group was only "marginally greater than the potential known harms," since healthy 12–15-year-olds are at very low risk of serious outcomes from Covid-19. Although it may (or may not) be the case that the JCVI adopted worst-case estimates[84], such an approach reinforces the need to act judiciously under conditions of uncertainty where the clear benefits of an intervention are not confidently above the potential harms. Note also that they mention "potential known harms" without taking into consideration potential long-term effects. The UK Health Ministers subsequently voted to offer a single dose of vaccination to adolescents ages 12-15 in consideration of: "…the health and wider social benefits to this cohort."[85] A second dose was offered to those with underlying health conditions. There are important parallels between the JCVI decision and the outcome of the FDA panel that recommended against universal booster recommendations for adults in the US in the fall of 2021: in both cases, the US and UK governments went against these recommendations. A key ethical difference is that the UK has not implemented any Covid-19 vaccine mandates at schools or universities, and the mandate proposed for care home and healthcare workers was withdrawn.[86]

As noted above, blanket mandates ignore critical data, such as the benefits of prior infection and data on adverse effects. These factors make an expected net harm now even more likely than when mandates began and make it even more urgent to update Covid-19 vaccine policy. Policies for other vaccines have been updated following the accumulation of new data. For example, adult boosters for tetanus and diphtheria vaccines (though previously widely administered) have been shown to provide no benefit.[87] Vaccines for influenza, dengue, and rotavirus have been withdrawn or had strict limitations placed on their use in children due to unexpected harms.[88] Adenovirus-vectored Covid-19 vaccines have been limited in their use due to thrombosis (especially in younger women).[89] Uncertainties remain regarding mRNA vaccines, for example related to their effects on menstruation[90], shingles[91], or the overall safety of current formulations in younger adults and children as well as evidence in support of booster vaccination.[92]

There are two other theoretical problems that could be factored into mandatory programs from a precautionary standpoint: original antigenic sin and the non-specific effects of vaccines. Original antigenic sin refers to the decreased ability of an individual to respond to a new viral variant because the immune system has been "locked" onto the original immunogen.[93] While data has not shown this to be true with certainty for Covid-19 it cannot yet be ruled out as an important side effect of repeat vaccination including with the new bivalent booster. Non-specific effects of vaccination refers to the effects of a vaccine on overall health and all-cause mortality, which have been shown to differ based on the type of vaccine (live vs. non-live) and age/sex.[94,95] Both of these theoretical issues are at the frontiers of our current knowledge of vaccinology and are rarely considered in the media and by the lay public. We cite these examples to prove our main point: proportionality of mandates should account for the precautionary principle in the context of uncertain evidence that benefits outweigh risks and harms. The net effect of these uncertainties, combined with other factors such as the rising prevalence of post-infection immunity[13], is that future risk-benefit assessments of mRNA vaccines may be even less favourable. Further, with vaccination mandates, young males in particular are being coerced into assuming a documented, albeit very small, risk of death related to vaccination[69,70] for, in most cases of booster vaccination, an uncertain individual and societal benefit.

4.3. Lack of proportionate public health benefit

Proportionality, a key principle in public health ethics, requires that the benefits of a public health policy must be expected to outweigh harms, including harms arising from the restriction of individual liberty.[1,5-8,86] Where mass vaccination involves harm to a minority of individuals or coercion or undue inducements are used to increase vaccine uptake, proportionality requires that these considerations be outweighed by public health benefits, typically in the form of reduced transmission from vaccinated individuals to others.[96]

Covid-19 booster mandates often involve a degree of coercion, including the threat of loss of access to education and free choice of occupation.[96] Contrary to those who restrict the concept of coercion to situations of a direct threat to something people should have access to as a matter of right[97], we endorse here a broader concept of coercion that includes situations of structural pressure that deprive people of reasonable options.[98] To be ethically acceptable, such severe restrictions of individual liberty need to be justified not only by an individual benefit but by the expectation that vaccination reduces harm to others. Booster doses of Covid-19 vaccines provide no lasting reduction in the probability of infection or transmission[27-29] and extremely low expected benefits to young healthy individuals, especially those who have already been infected.[31-33,100-102] The net expected harms to individuals and the harms of coercive mandates themselves are not counterbalanced by a large public health benefit; such harms and restrictions of liberty are therefore disproportionate and ethically unjustifiable.

4.4. Failure of Reciprocity

The use of booster mandates raises an additional ethical problem of *reciprocity* for institutions of higher education and public health authorities.[103,104] Most vaccines are covered in the US[105], the Canadian province of Quebec[106], and 18 other countries[106] by an injury compensation program based on fair (reciprocal) compensation for those who experience a vaccine-related harm. Mandatory vaccines arguably require even stronger protections for individuals who experience harmful consequences that lead to permanent harm[107] because their free choice regarding vaccination has been limited. While institutions of higher education are mandating boosters, the US and Canadian compensation programs have failed to uphold their social justice responsibility to injured individuals. In the US, Covid-19 vaccines and therapeutics are processed by the Countermeasures Injury Compensation Program (CICP) which is designed to cover epidemics, pandemics and security threats as designated by the Secretary of Health and Human Services and as authorised by the PREP Act.[105] As of August 1, 2022, 37 claims have been denied compensation because "the standard of proof for causation was not met" or "a covered injury was not sustained."[108] No claims have been paid out by the US CICP but one claim for anaphylaxis has been approved for compensation and pay-out is currently pending assessment of eligible expenses.[108]

It is highly problematic that young adults are being mandated to take a third dose—especially given the risk-benefit assessment—while the federal US vaccine injury program has failed to compensate but one Covid-19 vaccine-injured individual.[108] It is also important to note that boosters have been granted an EUA by the FDA, but are still not fully approved.[109] Universities and colleges that mandate Covid-19 boosters are pressuring young adults to receive a vaccine that, in case of injury, has no transparent legal route to adequate compensation. In sum, one core precondition for vaccine mandates is a functioning and fair compensation program, which has not been achieved for Covid-19 vaccines.

4.5. Wider Social Harms

Strong coercion creates significant social harms. Covid-19 vaccine mandates have often involved a high degree of coercion, effectively ostracising unvaccinated individuals from society. University mandates involve significant coercion in that they exclude unvaccinated people from the benefits of university education (or employment) and thereby entail major infringements to free choice of occupation and freedom of association. When such mandates are not supported by a *compelling* public health justification and where exemptions are not easily available, the likelihood of reactance and negative social effects are increased.[1] The social harms of university Covid-19 mandates have not been formally studied, but there is reason to think that they may be significant.[1] Policies can have wide-ranging consequences for non-compliance, such as loss of employment, loss of internet use, restriction to off-campus vs. on-campus housing, delays or refusal to process student housing requests, loss of enrolment, a hold placed on grades, inability to use recreational facilities to train for competitive sports or register for class, and delays in ability to repay student loans post-graduation. A number of young adults and professors affected by mandates have outlined publicly their perspectives and the social harms of these policies, such as loss of access to schooling and social services[110], psychosocial stress, reputational damage and lost income, and threats of being disenrolled or deported.[111] This punitive public health approach may also provoke reactance in young adults[1], with long-term negative consequences on trust in society and institutions and vaccine confidence in general, including vaccine hesitancy for routine paediatric and adult vaccines, a problem which predated the pandemic and is considered one of the World Health Organization's top ten "threats to global health."[112]

5. Objections: possible rationales for mandates

Despite the considerations above, proponents of university Covid-19 booster mandates might argue that such policies are justified (even if some individuals experience uncompensated harms) because they: (i) help *normalize* compliance with vaccination as a social duty (thereby promoting solidarity or pro-vaccine attitudes that undermine anti-vaccination sentiment) and/or (ii) help to increase the safety of the university environment or wider society. Mandates may help some people "feel better," knowing that everyone in a crowd, dorm, or classroom is vaccinated, that they are among peers that have "done the right thing" and "care about the safety of others." For instance, some faculty and staff may "feel protected" by the new booster mandate introduced at Western University in Ontario, Canada, on August 22, 2022.[113] From this perspective, if a majority of university policymakers (whether clinical advisory group members, administrators and/or professors) or students *believe* that vaccination should be socialised to promote solidarity, counteract anti-vaccination sentiment, or create a safe environment, then such beliefs (and values) should guide policy.

However, even if many people hold such beliefs and even if such goals are valuable, policy must be responsive to facts. Risk-benefit assessments should remain objective and avoid the use of some people feeling better or safer to justify behavioural rules with sanctions for non-compliance in the absence of rational justification. While many vaccines do improve group safety by reducing transmission, the current generation of Covid-19 vaccines do not provide significant lasting effects of this kind, and repeated doses appear to provide diminishing benefits (in terms of reduced infection) per dose, especially among young adults.[114] It therefore makes little sense to claim that Covid-19 vaccination is a pro-social act (or that the unvaccinated are a disproportionate threat to others). Moreover, it is unclear whether *mandating* Covid-19 boosters will produce a net positive effect on pro-vaccine sentiment in society—in fact, booster mandates appear to be associated with an increase in anti-vaccination beliefs and reduced uptake of other (non-coronavirus) vaccines.[1,86,96] As highlighted above, there are also wider social harms of policies that purport to reduce transmission of a ubiquitous virus: such policies may create a fear of infection among young healthy people (out of proportion to the actual risks) and contribute to worsening mental health which predated the pandemic.[115]

Moreover, the claim that the *socialisation* of compliance with public health measures can justify those measures is problematic for three other reasons. First, such an argument is circular:

compliance is not an end itself; policy must be justified by the expectation of public health benefit. Second, people may have different attitudes to compliance depending on their values (e.g., the views regarding the importance of individual liberty) and experiences (e.g., those with low baseline levels of trust in public health due to negative experiences of health professionals or government agencies). Policies that require people to comply against their values and preferences require ethical justification, especially where voluntary compliance is likely to be lower among those who are disempowered (e.g., students) or marginalised for other reasons[5,116], for example those from social groups which have been mistreated by government agencies or by the medical system in the past, including in the context of research.[117] Third, the socialisation argument is based, in part, on concepts of civic duty and responsibility to others. Pushing for boosters even when these will not contribute to overall risk reduction runs counter to the responsible use of public resources. Policies that encourage waste of valuable health care resources, to make some feel better, are sending a distorted message about important societal obligations.

The proclivity for university vaccine mandates may also reflect harmful trends toward intolerance in university bureaucracies that value compliance over individual freedoms. Mandates, by their nature, encourage conformity and acquiescence to authority, and exclude those with different views or values. Though universities might take pride in being places that permit the free exchange of ideas, mandates reduce the scope for reasoned debate regarding scientific uncertainties or conflicts of ethical values.[118] For example, how many universities have held public debates about mandatory Covid-19 vaccination? To our knowledge, very few such debates have taken place in North American institutions. We are aware of only one academic event[119] which some of us organised, in which booster mandates were critically debated. Sanctions for lack of full vaccination imposed on university professors who publicly voiced their opposition against mandates could arguably also have been intended to suppress public debate or be interpreted as such.

6. Implications for Broader Covid-19 Vaccine Mandates for Youth in Schools, and Other Institutions

The arguments presented above are relevant not only to 3rd, 4th, or 5th dose booster mandates but also to university or school policies that maintain primary two-dose Covid-19 vaccine mandates in 2022 in the face of high rates of previous SARS-CoV-2 infection. Two dose mandates are being upheld in at least 1000 universities and colleges across the United States, far more than the 300 or so maintaining booster mandates[2], and also some primary and secondary schools[120] which instituted mandates then extended the deadline when it was apparent that serious inequities in access to education would result.[121] It is even harder to justify a two-dose primary vaccine mandate in late 2022 than when such policies began in mid-2021.[46] Consistent with our argument above, the now high prevalence of prior infection, data regarding the lack of sustained transmission reduction by current vaccines, and the age at peak risk for myo/pericarditis being college-bound students ages 17–19 all undermine the case for two-dose vaccine mandates. We would therefore urge universities and schools to rescind all Covid-19 vaccine mandates. Strong statements in support of mandates made in 2021 by organisations such as the Association of Bioethics Program Directors in North America[122], the American Civil Liberties Union[123], and the Ontario Human Rights Commission[124] should be updated. Such organisations have an ethical obligation to revise these public statements and consider whether they are valid in light of current data.

The continued policy of two-dose mandates may represent status quo bias: when a rule is normalised it remains even when it has no (current) rational basis. The more rules, the more paperwork and cumbersome "busy work" that administrators and young students and professionals need to jump through. Yet rules come with consequences: how much are universities, corporations, consulting firms and the military paying in staff time to monitor and maintain vaccine mandates? How much time and energy are young adults using to comply with these policies? How much frustration and psychosocial stress is this causing? What about attrition from institutions and the military at times when the labour market and recruitment is difficult? When vaccine mandates are unethical, individuals may have an ethical duty to oppose them, in part to promote tolerance and prevent further bureaucratic encroachment and disenfranchisement of individuals with reasoned arguments against such mandates. Finally, we argue that institutions have an ethical duty to evaluate the effectiveness of such programs if the status quo is to be maintained.

7. Conclusion

Based on public data provided by the CDC[18], we estimate that approximately 22,000 to 30,000 previous *uninfected* young adults ages 18–29 years must be boosted with an mRNA vaccine to prevent one Covid-19 hospitalisation. Given the fact that this estimate does not take into account the protection conferred by prior infection nor a risk-adjustment for comorbidity status, this should be considered a conservative and optimistic assessment of benefit. Our estimate shows that university Covid-19 vaccine mandates are likely to cause net expected harms to young healthy adults—between 18 and 98 serious adverse events requiring hospitalisation and 1373 to 3234 disruptions of daily activities—that is not outweighed by a proportionate public health benefit. Serious Covid-19 vaccine-associated harms are not adequately compensated for by current US vaccine injury systems. As such, these severe infringements of individual liberty are ethically unjustifiable.

Worse still, mandates are associated with wider social harms. The fact that such policies were implemented despite controversy among experts and without updating the sole publicly available risk-benefit analysis to the current Omicron variants suggests a profound lack of transparency in scientific and regulatory policy making. These findings have implications for mandates in other settings such as schools, corporations, healthcare systems and the military. Policymakers should repeal booster mandates for young adults immediately, ensure pathways to compensation to those who have suffered negative consequences from these policies, provide open access to participant-level clinical trial data to allow risk- and age-stratified harm-benefit analyses of any new vaccines prior to issuing recommendations[125], and begin what will be a long process of rebuilding trust in public health.

Conflicts of Interest

We have no interests to declare.

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