Healthy Vaccinee Bias

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[We should not be so easily fooled]

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Figure 1: COVID-19 vaccine coverage from Dec 14, 2020, to Sept 30, 2021 among adults in Ontario with a recent history of homelessness compared to the general adult population of Ontario, by dose.
Among 11 million people >12 in the US enrolled in Kaiser Permanente Healthcare

Unvaccinated almost 70% more likely to die of non-COVID-19 causes than those with two doses of mRNA vaccine
Potential “Healthy Vaccinee Bias” in a Study of BNT162b2 Vaccine against Covid-19

BNT162b2 Vaccine Booster and Mortality Due to Covid-19

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ABSTRACT

BACKGROUND

The emergence of the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 and the reduced effectiveness over time of the BNT162b2 vaccine (Pfizer-BioNTech) led to a resurgence of coronavirus disease 2019 (Covid-19) cases in populations that had been vaccinated early. On July 30, 2021, the Israeli Ministry of Health approved the use of a third dose of BNT162b2 (booster) to cope with this resurgence. Evidence regarding the effectiveness of the booster in lowering mortality due to Covid-19 is still needed.

METHODS

We obtained data for all members of Clalit Health Services who were 50 years of age or older at the start of the study and had received two doses of BNT162b2 at least 5 months earlier. The mortality due to Covid-19 among participants who received the booster during the study period (booster group) was compared with that among participants who did not receive the booster (nonbooster group). A Cox proportional-hazards regression model with time-dependent covariates was used to estimate the association of booster status with death due to Covid-19, with adjustment for sociodemographic factors and coexisting conditions.

RESULTS

A total of 843,208 participants met the eligibility criteria, of whom 758,118 (90%) received the booster during the 54-day study period. Death due to Covid-19 occurred in 65 participants in the booster group (0.16 per 100,000 persons per day) and in 137 participants in the nonbooster group (2.98 per 100,000 persons per day). The adjusted hazard ratio for death due to Covid-19 in the booster group, as compared with the nonbooster group, was 0.10 (95% confidence interval, 0.07 to 0.14; P<0.001).

CONCLUSIONS

Participants who received a booster at least 5 months after a second dose of BNT162b2 had 90% lower mortality due to Covid-19 than participants who did not receive a booster.

over a 6-month period between participants who had received the BNT162b2 vaccine (15 deaths) and those who had received placebo (14 deaths); there were more cardiovascular- and sepsis-related deaths in the BNT162b2 group (12 deaths) than in the placebo group (6 deaths). Another informative variable would be the number needed to vaccinate with a booster dose to prevent one Covid-19-related death. Such comprehensive analysis of real-world data may inform the risk-benefit assessment of boosters and better guide public health decisions.

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THE AUTHORS REPLY: In response to Rohban: during our study period, 506 deaths occurred in the booster group (441 deaths were not related to Covid-19 and 65 were Covid-19-related), as compared with 1100 deaths in the nonbooster group (963 deaths were not related to Covid-19 and 137 were Covid-19-related). These results are in line with those of a large-scale population study in the United States, which showed a 66% lower risk of non-Covid-19-related death among participants who received primary vaccination with two doses of the BNT162b2 vaccine than among unvaccinated participants. However, our reported figures regarding deaths not related to Covid-19 should be interpreted with caution, because they were not adjusted for the numerous factors that may affect All-cause mortality and are beyond the scope of our study.
All vaccine and booster studies of VE vs COVID mortality from Israel’s Clality Health, by Høeg TB, Duriseti R, Prasad V [unpublished]
Healthy Vaccinee Bias in Influenza Vaccine Studies
Healthy Vaccinee bias is a term originally applied to influenza vaccine research in 2009 by Jennifer Nelson.

Influenza Vaccine Effectiveness against mortality in ≥65 year olds

Figure 1

Relative risk (and 95% CI) of all cause mortality and pneumonia or influenza hospitalization in vaccinated seniors compared with unvaccinated seniors, during periods before, during, and after influenza seasons, September 1995 through August 2003.

Examples of Healthy Vaccinee Bias in many countries: influenza vaccine (all from the last 20 years)

Canada (Campitelli, et al; Hottes, et al)
Sweden (Örtqvist, et al)
USA (McGrath, et al; Jackson, et al)
Germany (Tessmer, et al)
Spain (Vila-Corcoles, et al)
40 country analysis (Johnstone et al)
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In 100% (4/4) that included a preseason all-cause mortality, HVB could explain the entire observed vaccine effectiveness.

Remschmidt et al, 2015
Recommendations

Prioritize Randomized trials which *should* eliminate healthy vaccinee bias
• why were randomized studies of the boosters looking at COVID-19 deaths not done?

Observational studies of vaccines should require data on all-cause mortality and hospitalization rate differences by **vaccine group**, preferably from the pre-study period

Do not assume test negative designs are unaffected by healthy vaccinee bias
"Healthy user bias" & the influenza vaccine


**FEATURE**

**INFLUENZA**

**Influenza: marketing vaccine by marketing disease**

The CDC pledges to "forsake all public health decisions on the highest quality scientific data, openly and objectively derived." But Peter Doshi argues that in the case of influenza vaccinations and their marketing, this is not so.

Peter Doshi postdoctoral fellow
Johns Hopkins University School of Medicine, Baltimore, Maryland

Promotion of influenza vaccines is one of the most visible and aggressive public health policies today. Twenty years ago, in 1990, 20 million doses of influenza vaccine were available in the United States. Today around 125 million doses of influenza vaccine annually enter the US market, with vaccinations administered in drug stores, supermarkets—even some drive-throughs. This enormous growth has not been fueled by popular demand but instead by a public health campaign that delivers a single message: we in our right mind could possibly disagree: influenza is a serious disease, we are all at risk of complications from influenza, the flu shot is virtually free, and vaccination covers everyone. Through this line, the lack of influenza vaccine availability for all 35 million US adults seems to be the only way to achieve high vaccination rates. Close examination of state and national policies shows that although proponents employ the rhetoric of science, the studies underlying the policy are often of low quality, and direct reimbursement-official claims. The vaccine might be less beneficial and less safe than has been claimed, and the threat of influenza appears overstated.

Now we are all "at risk" of serious complications

Influenza vaccine production has grown parallel to increases in the perceived threat for the vaccine. In the US, the first recommendation for annual influenza vaccination was made in 1990 (table 1). Through the 1990s, the key objectives of this policy were to reduce excess mortality. Because most of influenza deaths occurred in the older population, vaccines were directed to this age group. But since 2000, the concept of who is "at risk" has rapidly expanded, incrementally encompassing groups across the general population (table 1). As one US Centers for Disease Control and Prevention (CDC) press briefing put it:

"...young people vary. Even healthy people can get the flu, and it can be serious. ..." Today, national guidelines call for everyone 6 months of age and older to get vaccinated. Now we are all "at risk."

**Not to worry: officials say influenza vaccines save lives**

Risk of serious illness is a problem—but, according to the official narrative, a manageable problem, thanks to vaccines. As another CDC press briefing noted earlier in 2015, "In fact, the risk of getting a flu shot is quite low. In fact, the flu shot is safe. Another way to say that is that the risk of getting the flu from the flu shot is very, very, very low." That is, the relative risk of getting the flu from the flu shot is lower than the relative risk of getting the flu from influenza disease. This is a key point that the CDC's current risk assessment must address: the relative risk of getting the flu from the flu shot is lower than the relative risk of getting the flu from influenza disease.

"...they calculated a reduction of 25% to 35% for preventing deaths from all causes—that is, a 35% lower risk of dying from any cause, not just influenza. CDC also cites a recent study published in the New England Journal of Medicine, funded by the National Vaccine Program Office and the CDC, which found an even larger relative reduction in risk of death: 50%..."

However, these statistics do not indicate that influenza vaccines can save more lives than any other single licensed medicine on the planet. Perhaps this is a reason CDC does not publish this from the outset; it is not a good idea to overstate. Since at least 2015, some CDC researchers have pointed out the seeming impossibility that influenza vaccines could be preventing 90% of all deaths from all causes when influenza is estimated to only cause around 5% of all non-injury deaths. ..."
“Healthy user bias” & the influenza vaccine


...
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This: the purpose of the study was to demonstrate that the fantastic benefit they expected to and did find—and that others have found, such as the two studies that CDC cites—is simply implausible, and likely the product of the “healthy-user effect” (in this case, a propensity for healthier people to be more likely to get vaccinated than less healthy people). Others have gone on to demonstrate this bias to be present in other influenza vaccine studies.17 18 Healthy user bias threatens to render the observational studies, on which officials’ scientific case rests, not credible.