

Guidelines. *Circulation*. 2019;140(11):e563-e595. doi:10.1161/CIR.0000000000000678

3. Centers for Disease Control and Prevention. About the National Health and Nutrition Examination Survey. Updated May 21, 2023. Accessed December 3, 2024. https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

4. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(25 Pt B)(25, pt B):2935-2959. doi:10.1016/j.jacc.2013.11.005

5. Gupta M, Gulati S, Nasir K, Sarraju A. Aspirin use prevalence for cardiovascular disease prevention among US adults from 2012 to 2021. *Ann Intern Med*. 2024;177(8):1139-1141. doi:10.7326/M24-0427

6. Davidson KW, Barry MJ, Mangione CM, et al; US Preventive Services Task Force. Aspirin use to prevent cardiovascular disease: US Preventive Services Task Force recommendation statement. *JAMA*. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983

COMMENT & RESPONSE

Electronic Nudges for Influenza Vaccination

To the Editor In a recent study,¹ electronically delivered nudges directed at patients with chronic diseases significantly improved influenza vaccination uptake, although the magnitude of improvement was limited. This result may have reflected the selection characteristics of the study population, which included patients with chronic diseases who likely had high baseline awareness of the benefits of influenza vaccination. Consequently, high baseline intent may have attenuated the intervention's effect. The "repeated letter" group achieved the greatest increase, improving by 13.5%, while other messaging frames, such as "cardiovascular benefits" and "respiratory benefits," yielded gains of approximately 11.0% to 11.9%. These increases were modest relative to the control group, suggesting a ceiling effect in populations with preexisting intent to be vaccinated.

Several factors potentially influencing outcomes were not considered in this study.¹ The timing of intervention letters may have affected vaccination behavior, as health risk perceptions can vary at different points in the influenza season. Stratified analyses by timing could provide insight into timing-specific effects on vaccine uptake. Additionally, risk perception may differ across disease groups; for example, patients with cardiovascular disease might respond more to risk-focused messages. Evaluating risk perceptions across subgroups could clarify differential behavioral responses.²

Geographic accessibility to vaccination sites may also have influenced uptake. While Denmark's electronic letter system ensures broad information dissemination, physical proximity to vaccination sites could directly affect patient behavior. Future research could incorporate geographic accessibility as a variable to better understand its role in vaccine decisions. Furthermore, previous experiences with COVID-19 vaccines, such as adverse reactions or vaccination fatigue, may shape attitudes toward influenza vaccination. Including COVID-19 vaccination history as a confounder may have provided greater insight into the pandemic's long-term impact on vaccination behavior.³

Recent trials have similarly shown that behavioral nudges have limited impact on COVID-19 vaccine uptake in populations with high baseline intent. Mehta et al⁴ noted that phy-

sician recommendations and scarcity framing had limited effect among individuals already inclined to get vaccinated, while Patel et al⁵ found that "reserved for you" prompts minimally influenced patients to go to primary care appointments. Behavioral nudges grounded in behavioral economics can increase vaccine uptake, yet randomization may inadequately capture intent variation. Stratified analyses across population subgroups may better assess the utility of these nudges.

Enhanced randomization designs—via stratification or adjusted allocation—could better boost vaccination rates across diverse populations, thereby advancing public health goals.

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1. Johansen ND, Vaduganathan M, Bhatt AS, et al. Electronic nudges to increase influenza vaccination in patients with chronic diseases: a randomized clinical trial. *JAMA*. 2024;332(22):1900-1911. doi:10.1001/jama.2024.21060

2. Bussink-Voorend D, Hautvast JLA, Vandeberg L, Visser O, Hulscher MEJL. A systematic literature review to clarify the concept of vaccine hesitancy. *Nat Hum Behav*. 2022;6(12):1634-1648. doi:10.1038/s41562-022-01431-6

3. Daly M, Robinson E. Willingness to vaccinate against COVID-19 in the US: representative longitudinal evidence from April to October 2020. *Am J Prev Med*. 2021;60(6):766-773. doi:10.1016/j.amepre.2021.01.008

4. Mehta SJ, Mallozzi C, Shaw PA, et al. Effect of text messaging and behavioral interventions on COVID-19 vaccination uptake: a randomized clinical trial. *JAMA Netw Open*. 2022;5(6):e2216649. doi:10.1001/jamanetworkopen.2022.16649

5. Patel MS, Milkman KL, Gandhi L, et al. A randomized trial of behavioral nudges delivered through text messages to increase influenza vaccination among patients with an upcoming primary care visit. *Am J Health Promot*. 2023;37(3):324-332. doi:10.1177/08901171221131021

In Reply We appreciate the Letter from Ms Wu and colleagues about our trial.¹ Vaccination behavior is known to be influenced by multiple factors, and we completely agree that invitation timing, geographical accessibility to vaccination sites, and prior vaccination beliefs and experiences may be significant determinants. These factors were not directly incorporated into the interventions in our trial as we primarily focused on testing the delivery method and varying letter content across groups; however, owing to the randomized design, we would expect potential confounders such as geographical location and prior vaccination beliefs and experiences to be evenly distributed across groups. In addition, because all intervention letters in the trial were delivered on the same date (September 24, 2023), further analyses of the effects of differential invitation timing were not possible but should be investigated in future efforts. While Danish registries contain data across numerous domains, they do not contain detailed information about prior vaccination

experiences or individual risk perception. We were therefore unable to include these data in our analyses. Interestingly, in another recent trial, offering free round-trip Lyft rides to vaccination sites in an attempt to decrease geographical barriers to vaccination did not result in increased vaccination rates.²

We disagree with the perception by Wu and colleagues about that the effect sizes were “limited” and “modest.” The absolute increases in vaccination in our trial of approximately 11 to 14 percentage points are, to our knowledge, the largest observed with letter-based interventions to increase influenza vaccination. Prior trials have typically yielded effect sizes of 1 to 2 percentage points in US populations with similar background vaccination rates.³ We are unable to discern whether the greater effect sizes observed in our trial can be attributed to using an official governmental electronic letter system for delivery, the specific behavioral concepts incorporated in the letters, or another factor inherent in the Danish system. Ongoing validation efforts are currently testing whether similar letter content can be effective in a US setting.

Wu and colleagues emphasize the importance of stratified analyses to identify subgroups with differential responses to the interventions for which further tailored strategies may be needed to encourage influenza vaccination. Throughout the NUDGE-FLU trial program, we have conducted several such analyses. In the first NUDGE-FLU trial, we found no significant effect modification according to whether participants had received COVID-19 vaccination during the previous season.⁴ Across both the first NUDGE-FLU trial and a recent secondary analysis of the present trial, we found evidence of an attenuated effect of our letter interventions in individuals with diabetes.⁵ In a recently published analysis of more than 2 million participants in the NUDGE-FLU trial program, we found that patients with a history of myocardial infarction were more likely to obtain vaccination when receiving cardiovascular-focused messaging compared with the other participants.⁶ Further subgroup analyses are planned, and we hope to be able to share the results in the near future.

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1. Johansen ND, Vaduganathan M, Bhatt AS, et al. Electronic nudges to increase influenza vaccination in patients with chronic diseases: a randomized clinical trial. *JAMA*. 2024;332(22):1900-1911. doi:10.1001/jama.2024.21060

2. Milkman KL, Ellis SF, Gromet DM, et al. Megastudy shows that reminders boost vaccination but adding free rides does not. *Nature*. 2024;631(8019):179-188. doi:10.1038/s41586-024-07591-x

3. Milkman KL, Gandhi L, Patel MS, et al. A 680,000-person megastudy of nudges to encourage vaccination in pharmacies. *Proc Natl Acad Sci U S A*. 2022; 119(6):e2115126119. doi:10.1073/pnas.2115126119

4. Johansen ND, Vaduganathan M, Bhatt AS, et al. Electronic nudges to increase influenza vaccination uptake in Denmark: a nationwide, pragmatic, registry-based, randomised implementation trial. *Lancet*. 2023;401(10382):1103-1114. doi:10.1016/S0140-6736(23)00349-5

5. Lassen MCH, Johansen ND, Vaduganathan M, et al. Electronic nudge letters to increase influenza vaccination uptake in younger and middle-aged individuals with diabetes. *JACC Adv*. 2024;3(12):101391. doi:10.1016/j.jacadv.2024.101391

6. Bhatt AS, Johansen ND, Vaduganathan M, et al. Electronic nudges and influenza vaccination among patients with a history of myocardial infarction: insights from 3 nationwide randomized clinical trials. *JAMA Cardiol*. Published online November 17, 2024. doi:10.1001/jamacardio.2024.4648

Statins for Primary Prevention of Cardiovascular Disease

To the Editor A recent study reported that utilizing the Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations, developed by the American Heart Association (AHA) and American College of Cardiology (ACC), for calculating cardiovascular risk, would lead to millions fewer US residents at low risk of heart disease being recommended statins.¹

Dr Diao and colleagues¹ reported that the PREVENT equations would reclassify 53% of US residents to a lower category of cardiovascular risk, estimating that 14 million fewer adults would be recommended statins, resulting in 77 000 additional cases of myocardial infarctions and strokes over the next decade.

This finding spurred calls to lower the current predictive risk threshold for initiating statin therapy. Currently, the 2013 AHA/ACC guidelines recommend statins for adults with a greater than 7.5% 10-year risk, which was lowered from 10% in the previous guidelines. Now, Drs Khan and Lloyd-Jones have suggested the risk threshold should be lowered again: “3% to 5% may now be reasonable.”² However, we disagree.

There is no evidence that lowering the threshold to 3% or 5% would be beneficial. The calculation of 77 000 additional cases of myocardial infarctions and strokes over the next decade by Diao and colleagues¹ relied on meta-analyses, including the Cholesterol Treatment Trialists’ (CTT) 2012 analysis. However, a recalculation of the CTT 2012 analysis reported “statin therapy prevents one serious cardiovascular event per 140 low-risk people (five-year risk <10%) treated for five years,”³ and statins for people with less than 10% 10-year risk resulted in neither a statistical nor numerical reduction in all-cause mortality (relative risk [RR], 1.05 [95% CI, 0.86-1.28]). Furthermore, “statin therapy in low-risk people does not reduce all-cause mortality or serious illness.”³

We are concerned that lowering the risk threshold will only lead to millions more healthy people being recommended for statin therapy, but it may not help them feel better or live longer.

There also may be unintended consequences of widespread statin use in healthy people. For example, a 2014 study reported that people taking statins were more likely to have increased caloric and fat intake and body mass index over time than people who do not use statins.⁴