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Estimating the early impact of the US COVID-19 vaccination programme on COVID-19 cases, emergency department visits, hospital admissions, and deaths among adults aged 65 years and older: an ecological analysis of national surveillance data

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Summary

Background In the USA, COVID-19 vaccines became available in mid-December, 2020, with adults aged 65 years and older among the first groups prioritised for vaccination. We estimated the national-level impact of the initial phases of the US COVID-19 vaccination programme on COVID-19 cases, emergency department visits, hospital admissions, and deaths among adults aged 65 years and older.

Methods We analysed population-based data reported to US federal agencies on COVID-19 cases, emergency department visits, hospital admissions, and deaths among adults aged 50 years and older during the period Nov 1, 2020, to April 10, 2021. We calculated the relative change in incidence among older age groups compared with a younger reference group for pre-vaccination and post-vaccination periods, defined by the week when vaccination coverage in a given age group first exceeded coverage in the reference age group by at least 1%; time lags for immune response and time to outcome were incorporated. We assessed whether the ratio of these relative changes differed when comparing the pre-vaccination and post-vaccination periods.

Findings The ratio of relative changes comparing the change in the COVID-19 case incidence ratio over the post-vaccine versus pre-vaccine periods showed relative decreases of 53% (95% CI 50 to 55) and 62% (59 to 64) among adults aged 65 to 74 years and 75 years and older, respectively, compared with those aged 50 to 64 years. We found similar results for emergency department visits with relative decreases of 61% (52 to 68) for adults aged 65 to 74 years and 77% (71 to 78) for those aged 75 years and older compared with adults aged 50 to 64 years. Hospital admissions declined by 39% (29 to 48) among those aged 60 to 69 years, 60% (54 to 66) among those aged 70 to 79 years, and 68% (62 to 73), among those aged 80 years and older, compared with adults aged 50 to 59 years. COVID-19 deaths also declined (by 41%, 95% CI –14 to 69 among adults aged 65–74 years and by 30%, –47 to 66 among those aged ≥75 years, compared with adults aged 50 to 64 years), but the magnitude of the impact of vaccination roll-out on deaths was unclear.

Interpretation The initial roll-out of the US COVID-19 vaccination programme was associated with reductions in COVID-19 cases, emergency department visits, and hospital admissions among older adults.

Funding None.

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Introduction

In the USA, COVID-19 vaccines first became available under Emergency Use Authorizations in mid-December, 2020, with rapid implementation after authorisation. Because older adults are at an increased risk of severe COVID-19 outcomes,[1] including hospitalisation and death, this population was among those prioritised for early vaccination. The US Advisory Committee on Immunization Practices recommended that health-care personnel and residents of long-term care facilities be prioritised for vaccination during the earliest weeks of vaccine availability,[2] followed by adults aged 75 years and older, then adults aged 65–74 years and people aged 16–64 years with medical conditions associated with an increased risk of severe outcomes from COVID-19.[3] Although vaccine roll-out varied by state, by April 19, 2021, all people aged 16 years or older were eligible for vaccination nationally. As of June 8, 2021, 52% of the total US population had received one or more doses of COVID-19 vaccine, and 42% were fully vaccinated; among adults aged 65 years and older, 86% had received at least one dose, and 76% were fully vaccinated.[4]

Evaluating the effect of COVID-19 vaccination on the trajectory of the pandemic is important to verify that

Research in context

Evidence before this study

COVID-19 vaccines first became available in the USA under Emergency Use Authorizations in mid-December, 2020, with rapid implementation among the highest risk populations, including people aged 65 years and older, immediately after authorisation. Although safety, efficacy, and effectiveness studies showed that COVID-19 vaccines can prevent morbidity and mortality, the national-level effect of the COVID-19 vaccination programme among older adults in the USA had not been fully examined. We searched PubMed and medRxiv for studies published in English up to May 7, 2021, that assessed the impact of COVID-19 vaccination at the population level, using the following terms ((COVID* OR SARS-CoV-2)) AND ((effectiv* OR impact)) AND (vaccin*) AND (English[Language]), and restricted to papers in English. Published studies from Israel reported an age-specific population-level impact of their vaccination programme. Studies among health-care workers, another population prioritised for vaccination, also showed that case incidence declined more rapidly among health-care workers than among the surrounding community.

Added value of this study

Using population-representative data, our study shows that the initial phases of the US COVID-19 vaccination programme were associated with reductions in COVID-19 cases, emergency department visits, and hospital admissions among US adults aged 65 years and older. COVID-19 deaths also declined, but the contribution of vaccination to population-level mortality trends remains unclear. State-specific reductions in outcomes are also reported.

Implications of all the available evidence

A third of all US adults are not fully vaccinated against COVID-19. Our findings add to the growing body of evidence that COVID-19 vaccines are working at the population level and could reinforce the importance of vaccination and increase public confidence in the vaccination programme.

vaccines are working as expected at the population level and might increase public confidence in the vaccination programme. Several reports have estimated the impact of COVID-19 vaccination among groups prioritised for vaccination in Israel,[5,6] in selected US states,[7] and in hospitals.[8,9] However, the national-level impact of the COVID-19 vaccination programme among older adults in the USA has not been fully examined. We did an ecological analysis to assess the impact of the initial phases of the US COVID-19 vaccination programme on COVID-19 cases, emergency department visits, hospitalisations, and deaths among adults aged 65 years and older.

Methods

Study design

For this ecological analysis, the analytical period was defined as Nov 1, 2020, to April 10, 2021, to capture a pre-vaccination period during which both reporting and treatment trends were relatively stable (appendix p 2), as well as an early post-roll-out period during which coverage differences between older (age ≥65 years) and younger (age 50–64 years) US adults were greatest.

This activity was reviewed by the US Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy. Because this project was determined to be public health surveillance and not human subject research, neither consent nor ethical approval were required.

Data sources

Jurisdictional health departments voluntarily submit individual-level data on probable and laboratory-confirmed COVID-19 cases to the CDC through the COVID-19 Case Report Form and the National Notifiable Diseases Surveillance System.[10,11] The present analysis was limited to 31 states where individual-level data reporting was consistent and reasonably complete (≥60%) compared with required jurisdiction-reported aggregate case totals during the analytic period (appendix pp 2–3).

Emergency department visits with a COVID-19 discharge diagnosis were obtained from the National Syndromic Surveillance Program.[12] Emergency department visits for COVID-19 were defined as those with International Classification of Diseases, tenth revision (ICD-10) codes U07.1 or J12.82 or Systematized Nomenclature of Medicine codes 840539006, 840544004, or 840533007. 17 states and the District of Columbia had sufficient data quality and reporting during the analytic period to allow use of population-based denominators and were included in the analysis (appendix p 3).

Hospital admissions for laboratory-confirmed COVID-19 were obtained from the Unified Hospital Dataset,[13] which contains daily hospital-level data from all US hospitals registered with the Centers for Medicare & Medicaid Services (CMS) as of June 1, 2020, and data from hospitals not registered with CMS but reporting since July 15, 2020. Psychiatric, rehabilitation, and religious non-medical facilities were excluded from the analytic dataset. Data include all 50 states and the District of Columbia and were both consistent and complete during the analytic period (at least 5146 [98%] of 5251 hospitals reporting COVID-19 admissions data on any given day between Nov 1, 2020, and April 10, 2021).

Death data are from death certificates reported to the National Vital Statistics System. COVID-19 deaths are those with confirmed or presumed COVID-19 reported

See Online for appendix

on the death certificate as a contributing or underlying cause of death and assigned the ICD-10 code U07.1.[14] Provisional data available as of May 18, 2021, from all 50 states and the District of Columbia were included in the analysis, aggregated by week, age group, and jurisdiction.[15] To protect patient privacy, data are suppressed in any stratum with 1–9 deaths, such that the exact number of deaths was unavailable for analysis.

Individual-level COVID-19 vaccine administration data were submitted to the CDC through jurisdiction immunisation information systems, the Vaccine Administration Management System, or direct data submission to the CDC Data Clearinghouse.[16] A cloud-hosted data repository received, deduplicated, and deidentified vaccination data; quality checks were done on data before release for analysis.[17] All vaccinations administered to people aged 18 years or older by May 8, 2021, in 49 states and the District of Columbia were included in the analysis. Texas was excluded from national vaccination coverage calculations because data on the number of individuals vaccinated by age group were not available.

Denominators for incidence and cumulative vaccine coverage were calculated using age group-specific and county-specific or state-specific population denominators from the US Census Bureau 2019 Population Estimates Program.

For the **US Census Bureau 2019 Population Estimates Program** see https://www2.census.gov/programs-surveys/popest/datasets/2010-2019/counties/

Statistical analysis

To assess the potential impact of COVID-19 vaccination on COVID-19 outcomes, we applied a difference-in-differences framework to evaluate whether outcomes declined more rapidly after vaccination roll-out in age groups with earlier vaccine eligibility (ie, people aged ≥65 years) relative to age groups who became eligible for vaccination only later, but who might be expected to have similar behaviours and risks (eg, people aged 50–64 years). Cases, emergency department visits, hospital admissions, deaths, and vaccine recipients were stratified and aggregated into age groups based on reported patient age or date of birth and date of event. For cases, emergency department visits, and deaths, the age groups were 50–64 years (reference group), 65–74 years, and 75 years and older. For hospital admissions, the age groups were 50–59 years (reference group), 60–69 years, 70–79 years, and 80 years and older, since these were the age groups reported by hospitals.

To define the post-vaccination period for assessing vaccine impact, we assessed cumulative vaccination coverage (≥1 dose and complete series) over time. The initial cutpoint was defined as the week in which vaccination coverage in a given age group first exceeded coverage in the reference age group (50–64 years or 50–59 years, depending on outcome) by at least 1%. We then defined the analytical cutpoint by adding 2 weeks to account for the time needed for recipients to generate an immune response to the vaccine. An additional lag time of 1 week for hospital admissions and 2 weeks for deaths was incorporated to account for time needed for progression from infection to more severe outcomes.[18] Outcomes occurring before these analytical cutpoints were defined as pre-vaccine roll-out, and outcomes occurring on or after analytical cutpoints were defined as post-vaccine roll-out. Cutpoints were assigned at the national level for use in the primary, national-level analysis; jurisdiction-specific (state or District of Columbia) cutpoints were used for all jurisdiction-specific analyses, with the exception of Texas, where national cutpoints were used. For California, a single coverage cutpoint was calculated for ages 70 years and older because of inconsistencies in reporting of birthdate. Sensitivity analyses using cutpoints of other magnitudes (5%, 10%, and 20% coverage differences) are shown in the appendix (pp 6–7, 38–42). As even a single dose of the two-dose vaccines has been shown to have moderate efficacy and effectiveness against symptomatic infection and severe outcomes,[19–23] we used one-dose coverage for the primary analysis and complete-series coverage as a sensitivity analysis. Use of one-dose coverage also maximises the differences between the two time periods by allocating the initial roll-out period (during which people received their first dose of the two-dose vaccines) to the post-vaccine period as opposed to the pre-vaccine period.

The difference-in-differences framework was applied as follows. Within each period (before and after vaccination roll-out) and separately for each age group, we calculated the relative change over time in incidence, and then calculated the ratio of these relative changes. We compared this ratio of these relative changes in the period after the designated vaccine coverage cutpoints to the ratio of these relative changes for the period before these cutpoints, with the null hypothesis of no change in the ratio of these relative changes between the post-vaccination versus pre-vaccination roll-out periods. Results are reported as the percentage reduction, calculated as 1 minus the ratio of these relative changes. The analysis for cases, emergency department visits, and hospital admissions was done using a regression model[24] on data aggregated by week, county, and age group. Because of suppression in county-level data, the model for deaths included data aggregated by week, jurisdiction, and age group. For a full description of the methods, the form of the model, sensitivity analyses using people aged 18–49 years as the reference group, and aforementioned sensitivity analyses of the cutpoint see the appendix (pp 3–7, 34–42).

All analyses were done in R version 4.0.3 with models fit using the nlme package.[25]

Role of the funding source

This work was supported by the CDC's regular operating funds. The CDC was involved in the study design, data analysis, data interpretation, and writing and submission of the report.

Results

Nationwide vaccination coverage among people aged 50–64 years remained substantially lower than coverage among older age groups throughout the period included in this analysis (figure 1). Reported COVID-19 cases among all analysed age groups began to decline by mid-January, 2021 (figure 2A). However, after acceleration of COVID-19 vaccination among people aged 65 years and older, the ratio of incidence among people aged 65–74 years or 75 years and older compared with people aged 50–64 years declined sharply (figure 2B). The ratio of these relative changes when comparing the change in ratio over the post-vaccine period to that over the pre-vaccine period showed a relative decrease of 53% (95% CI 50–55) for the 65–74 years age group and 62% (59–64) for the 75 years and older age group, compared with the 50–64 years age group (table). State-level analyses showed similar patterns, with vaccine impact observed in 25 (81%) of 31 states for both the 65–74 years and the 75 years and older age groups (appendix pp 15–33; incidence ratios are shown in the appendix p 9) for the five most populous states. Our findings were similar when using vaccination cutpoints based on complete-series COVID-19 vaccination coverage, and when using vaccination cutpoints of other magnitudes; the estimated impact tended to be larger when using people aged 18–49 years as the reference group and when more restrictive pre-vaccine and post-vaccine roll-out periods were used (appendix pp 13–14, 34–42).

Our findings were similar for emergency department visits and hospital admissions (table; figure 2C–F; appendix pp 10–11, 13–42). For both emergency department visits and hospital admissions, an age-based gradient was observed wherein the ratio of relative changes furthest from the null was in the oldest age group, corresponding to a 77% (95% CI 71–81) relative decline in emergency department visits among those aged 75 years and older compared with those aged 50–64 years, and a 68% (62–73) relative decline in hospital admissions among those aged 80 years and older compared with those aged 50–59 years. At the jurisdiction level, the ratio of relative changes for emergency department visits suggested meaningful vaccine impact in 10 (56%) of 18 jurisdictions for the 65–74 years age group, and in 17 (94%) of 18 jurisdictions for those aged 75 years and older (appendix pp 15–33). Ratios of relative changes indicated larger reductions in hospital admissions for both the 70–79 years and 80 years and older age groups, compared with those aged 50–59 years, in 21 states (appendix pp 15–33). Findings were similar across sensitivity analyses (appendix pp 13–14, 34–42).

Although the ratios of deaths among people aged 75 years and older or 65–74 years versus people aged 50–64 years decreased substantially over the analytical period, this decline began before the period of potential vaccine effect, with no obvious change in trajectory after the vaccination coverage cutpoints (figure 2G, H).

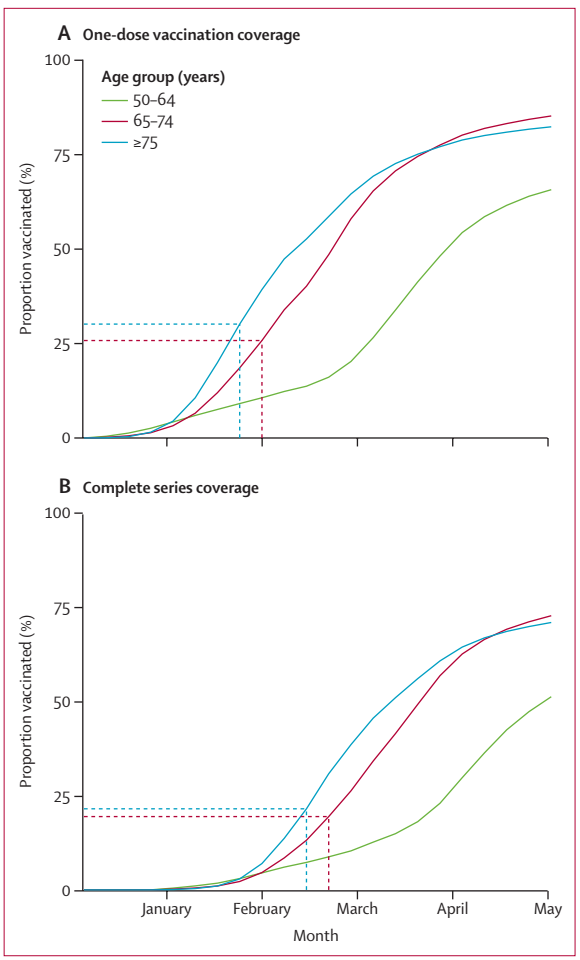

Figure 1: **Vaccination coverage cutpoints for analysis of COVID-19 cases—one-dose vaccine coverage (A) and complete series coverage (B) with any COVID-19 vaccine—in the USA during the period Dec 14, 2020, to May 8, 2021**

Cutpoints for the 65–74 years and 75 years and older age groups were 14 days after the coverage reached at least 1% higher than the reference age group (50–64 years) to allow the time needed to generate an immune response. Cutpoints were defined based on coverage data from 31 jurisdictions: Alaska, Alabama, Arkansas, Arizona, California, Colorado, Delaware, Georgia, Iowa, Idaho, Illinois, Kansas, Massachusetts, Maine, Minnesota, Montana, North Carolina, New Hampshire, New Jersey, Nevada, New York, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Utah, Vermont, Washington, and Wisconsin. Dashed lines indicate the cutpoints.

Patterns at the state level varied, and a high degree of uncertainty was observed, but state-level patterns were similar to national patterns in four (80%) of five of the most populous states (appendix pp 15–33). Nationally, the ratios comparing change in deaths among people aged 75 years and older or 60–74 years to that among people aged 50–64 years were similar in the post-vaccination versus pre-vaccination periods (table). Findings were similar when using vaccination cutpoints based on complete-series vaccination coverage and across other sensitivity analyses, although the estimated impact was higher when using people aged 18–49 years as the

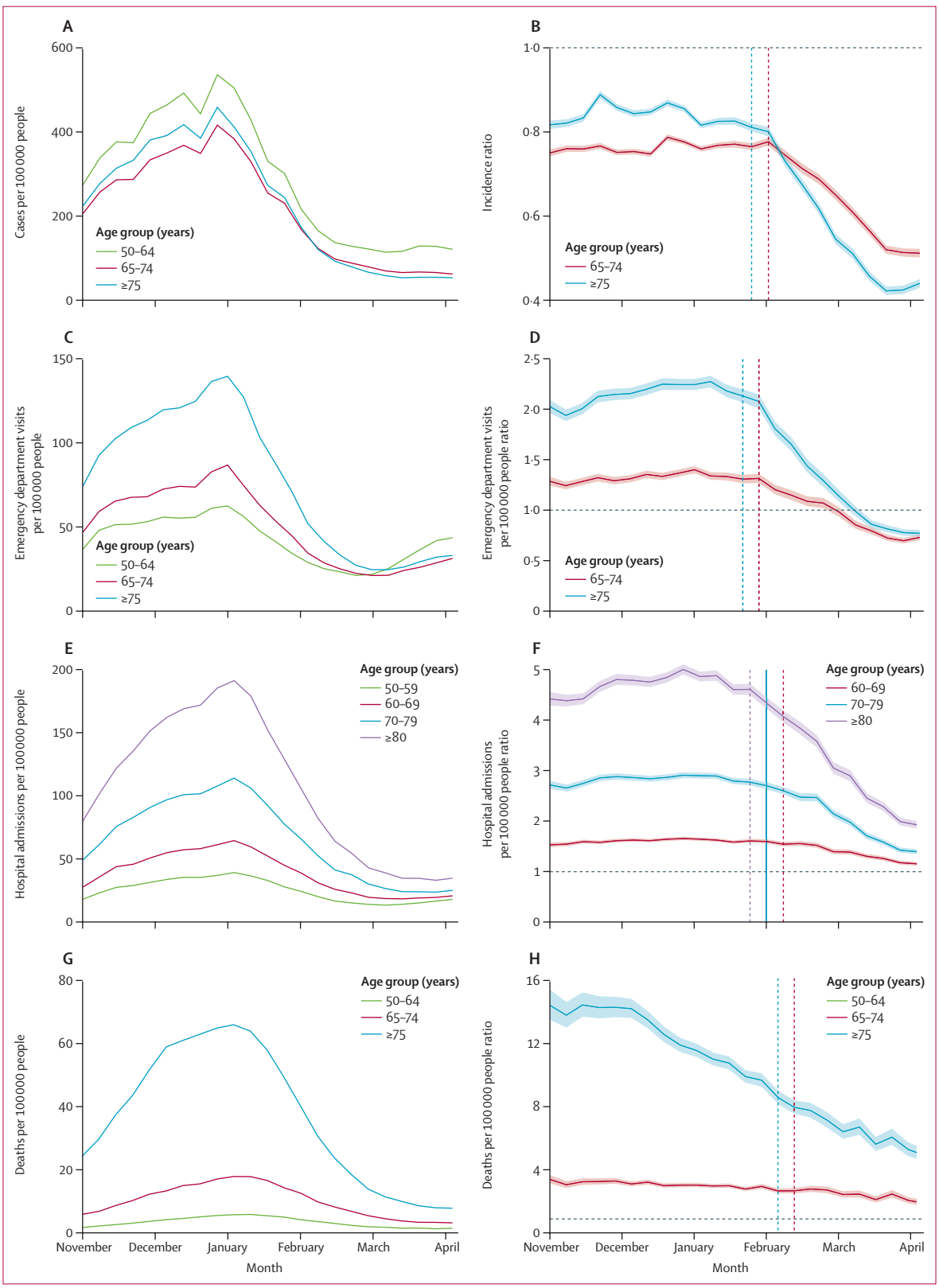

Figure 2: **Incidence rates (A, C, E, G) and rate ratios (B, D, F, H) for COVID-19 cases, emergency department visits, hospital admissions, and deaths by age group in the USA during the period Nov 1, 2020, to April 10, 2021**

Incidence rate ratios are relative to the younger referent age group (B, D, H: 50–64 years; F: 50–59 years). Shaded areas represent mid-p exact 95% CIs. Dashed vertical lines represent cutpoints defining the pre-vaccination and post-vaccination periods based on coverage with at least one dose of COVID-19 vaccine in the corresponding age group, with lag times added for time to generate immune response (14 days) and time to outcome (cases and emergency department visits: 0 days; hospital admissions: 7 days; deaths: 14 days). Case data include the following jurisdictions: Alaska, Alabama, Arkansas, Arizona, California, Colorado, Delaware, Georgia, Iowa, Idaho, Illinois, Kansas, Massachusetts, Maine, Minnesota, Montana, North Carolina, New Hampshire, New Jersey, Nevada, New York, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Utah, Vermont, Washington, and Wisconsin. Emergency department visits include the following jurisdictions: Connecticut, District of Columbia, Florida, Illinois, Maine, Maryland, Massachusetts, Michigan, Nevada, New Mexico, North Carolina, Oregon, Tennessee, Utah, Vermont, Virginia, Washington, and Wisconsin. Hospital admission and death data include all 50 states and the District of Columbia.

	Mean (range) coverage before the date that 1% difference occurred	Mean (range) coverage beginning at the date that 1% difference occurred	Date of vaccination cutpoint*	Relative percentage reduction in incidence over the pre-vaccine rollout period (95% CI)	Relative percentage reduction in incidence over the post-vaccine rollout period (95% CI)	Relative percentage reduction accounting for pre-vaccine differences (95% CI)
Cases (1762 counties)†						
1% difference between age groups first reached on 17/01/2021						
50–64 years	1·3 (0·0–6·0)	24·6 (7·6–54·6)	31/01/2021	Ref	Ref	Ref
65–74 years	1·1 (0·0–6·6)	50·6 (12·0–80·4)	31/01/2021	–16 (–19 to –12)	45 (44 to 47)	53 (50 to 55)
1% difference between age groups first reached on 10/01/2021						
50–64 years	0·9 (0·0–4·3)	23·1 (6·0–54·6)	24/01/2021	Ref	Ref	Ref
≥75 years	0·6 (0·0–4·5)	53·7 (10·7–79·1)	24/01/2021	–4 (–7 to 0)	60 (59 to 62)	62 (59 to 64)
Emergency department visits (883 counties)						
1% difference between age groups first reached on 17/01/2021						
50–64 years	1·3 (0·0–6·0)	24·6 (7·6–54·6)	31/01/2021	Ref	Ref	Ref
65–74 years	1·1 (0·0–6·6)	50·6 (12·0–80·4)	31/01/2021	–13 (–27 to –1)	56 (50 to 61)	61 (52 to 68)
1% difference between age groups first reached on 10/01/2021						
50–64 years	0·9 (0·0–4·3)	23·1 (6·0–54·6)	24/01/2021	Ref	Ref	Ref
≥75 years	0·6 (0·0–4·5)	53·7 (10·7–79·1)	24/01/2021	–14 (–28 to –1)	74 (70 to 77)	77 (71 to 81)
Hospital admissions (2451 counties)						
1% difference between age groups first reached on 17/01/2021						
50–59 years	1·4 (0·0–6·1)	22·5 (7·6–49·5)	07/02/2021	Ref	Ref	Ref
60–69 years	1·2 (0·0–6·2)	36·4 (9·1–68·7)	07/02/2021	–4 (–13 to 4)	37 (31 to 43)	39 (29 to 48)
1% difference between age groups first reached on 10/01/2021						
50–59 years	0·9 (0·0–4·4)	21·3 (6·1–49·5)	31/01/2021	Ref	Ref	Ref
70–79 years	0·5 (0·0–3·5)	52·1 (8·4–82·7)	31/01/2021	0 (–9 to 8)	60 (56 to 64)	60 (54 to 66)
1% difference between age groups first reached on 03/01/2021						
50–59 years	0·5 (0·0–2·7)	20·1 (4·4–49·5)	24/01/2021	Ref	Ref	Ref
≥80 years	0·3 (0·0–1·9)	49·2 (5·5–76·3)	24/01/2021	4 (–5 to 12)	69 (66 to 72)	68 (62 to 73)
Deaths (51 jurisdictions)						
1% difference between age groups first reached on 17/01/2021						
50–64 years	1·3 (0·0–6·0)	24·6 (7·6–54·6)	14/02/2021	Ref	Ref	Ref
65–74 years	1·1 (0·0–6·6)	50·6 (12·0–80·4)	14/02/2021	8 (–38 to 38)	45 (19 to 63)	41 (–14 to 69)
1% difference between age groups first reached on 10/01/2021						
50–64 years	0·9 (0·0–4·3)	23·1 (6·0–54·6)	07/02/2021	Ref	Ref	Ref
≥75 years	0·6 (0·0–4·5)	53·7 (10·7–79·1)	07/02/2021	43 (8 to 64)	60 (38 to 74)	30 (–47 to 66)

*Defined as the Saturday ending the week in which vaccination coverage in a given age group first exceeded coverage in the reference age group by ≥1%, plus 2 (cases and emergency department visits), 3 (hospital admissions), or 4 (deaths) weeks to account for the time needed to generate an immune response and additional lag time between symptom onset and hospitalisation or death.[18] †Case data include the following jurisdictions: Alaska, Alabama, Arkansas, Arizona, California, Colorado, Delaware, Georgia, Iowa, Idaho, Illinois, Kansas, Massachusetts, Maine, Minnesota, Montana, North Carolina, New Hampshire, New Jersey, Nevada, New York, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Utah, Vermont, Washington, and Wisconsin. Emergency department visits include the following jurisdictions: Connecticut, District of Columbia, Florida, Illinois, Maine, Maryland, Massachusetts, Michigan, Nevada, New Mexico, North Carolina, Oregon, Tennessee, Utah, Vermont, Virginia, Washington, and Wisconsin. Hospital admission and death data include all 50 states and the District of Columbia.

Table: **Relative percentage reduction in incidence in the pre-vaccine and post-vaccine rollout periods using vaccination cutpoints based on one-dose vaccine coverage in the USA, Nov 1, 2020, to April 10, 2021**

reference group; none of the ratios of relative changes in state-specific models indicated meaningful differences before versus after vaccine roll-out (appendix pp 15–33).

Discussion

After acceleration of COVID-19 vaccine administration among older US adults, COVID-19 cases, emergency department visits, and hospital admissions declined faster among people aged 65 years and older compared with a younger reference group. Although it is not possible to conclusively attribute these declines solely to vaccination given the ecological design of this analysis, these results suggest that the initial phases of the US COVID-19 vaccination programme led to a meaningful reduction in COVID-19 burden among US people aged 65 years and older, a group at high risk of severe outcomes from COVID-19.[1]

Results from this comprehensive analysis of the population impact of COVID-19 vaccines in the USA are consistent with expectations given the demonstrated high efficacy and effectiveness of the available vaccines[6,20,22,23,26–29] and are also in alignment with previously published research. Ecological analysis of data from Israel showed the age-specific population-level impact of their

vaccination programme.[5,6,30,31] Similarly, analyses of health-care workers in Boston and Dallas (USA) showed that incidence in these populations, among the first people prioritised for vaccination, declined more rapidly than did incidence in the surrounding communities.[8,9]

Although COVID-19 deaths declined more steeply over the post-vaccine period among older age groups than among the younger age group, these decreases began before vaccines were approved in the USA, and no obvious change in the slope of the decrease was observed during the post-vaccination period. The pre-vaccine timing of the observed declines in age-group mortality ratios might have been affected by trends in long-term care facilities, specifically the earlier declines in cases and deaths in long-term care facilities relative to overall US trends.[32,33] Although long-term care facility residents and staff were among the first group to be prioritised for vaccination, these declines occurred before vaccines would be expected to have a biologically plausible impact on mortality, even accounting for the higher risk of severe outcomes among this population. Non-pharmaceutical interventions in long-term care facilities, such as limiting visitors during periods of high incidence in surrounding counties, strict adherence to masking, and physical distancing,[34,35] might have helped decrease deaths in this population before vaccine was widely available, leading to observed patterns and thus limiting our ability to identify the effect of vaccines. We acknowledge that the power to detect differences in our mortality analysis was limited by suppression of small cell counts at the state and county levels, which prevented inclusion of county information in our models. However, state-level models from states without data suppression, as well as a national-level analysis using unsuppressed data (but not including a state-level random effect), are also consistent with the null hypothesis of no change. Our null findings for mortality contrast with a previous US publication,[36] which used a pre-post design comparing two snapshots in time, one before vaccine implementation, and one after implementation was well underway. Our analysis applied regression models to compare trends in rate ratios by age group over the post-vaccination period with those in the pre-vaccination period, while accounting for trends that had already begun in the pre-vaccine period; we also incorporated lag times to account for biological response to vaccination. Additionally, we chose a comparator age group of 50–64 years, close in age to the age group of interest, instead of people aged 18–49 years, who might be notably different in risks, behaviours, and outcomes. Although our analyses did not show a clear impact of vaccine roll-out on COVID-19 mortality, the efficacy and effectiveness of available COVID-19 vaccines against death has previously been shown.[6,19,21,22]

The present analysis benefits from large datasets that cover a substantial proportion of the US population (cases and emergency department visits) or are national in scope (hospital admissions and deaths). Our analytical design, in which we included county in our regression models (with the exception of the mortality analysis), also controls for possible confounding by geographically associated variables, such as differences in COVID-19 transmission patterns, mitigation measures, or adherence to COVID-19 prevention guidelines. Jurisdiction-level models also incorporate jurisdiction-specific coverage cutpoints to account for differences in roll-out at the jurisdiction level versus the national level.

This analysis had several limitations. First, it is possible that vaccinated people might be less likely to be tested for SARS-CoV-2, which could deflate estimates of COVID-19 incidence among age groups with higher vaccination coverage and thus possibly bias results away from the null. However, compared with reported cases, this phenomenon would be less likely to affect severe outcomes (such as emergency department visits, hospital admissions, and deaths), and we observed a similar or greater impact of vaccination on emergency department visits and hospital admissions, as compared with cases. Furthermore, although testing did decline among people aged 65 years and older during the analysis period (Hall CJ, CDC, personal communication), percentage positivity also declined overall and relative to the 45–64 years age group, suggesting that testing volume remained sufficient to capture disease occurrence in the older population. Second, because this was an ecological analysis, we could not assess individual behaviours that might have varied over time, differed among age groups, and had the potential to affect the likelihood of COVID-19 infection. For instance, it is possible that adherence to mitigation measures (eg, masking, physical distancing) could have decreased with the availability of vaccines, and that this decrease could have been even greater among younger people because of a perception that they are at lower risk of severe disease, even in the absence of vaccination. We attempted to mitigate such an effect by choosing a comparator age group close in age to the 65 years and older vaccine-eligible population, hypothesising that people aged 50–64 years might behave more similarly, and have more similar COVID-19 risks, to people aged 65 years and older. Confounding by other variables, such as measures of social deprivation, is also possible; however, as these factors are geographically associated, the inclusion of county in the regression models helps to reduce this confounding. Third, the age groups available for analysis of hospitalisation data (50–59 years, 60–69 years, 70–79 years, and 80 years and older) do not directly align with the age groups prioritised for vaccination, potentially leading to underestimation of vaccine impact in people aged 60–69 years and 70–79 years, since these age groups have a mix of vaccine-eligible and non-vaccine-eligible people over time. Nonetheless, we observed relative declines in hospital admissions in all three age groups we investigated after acceleration of vaccine roll-out in the older population, with the strongest impact in the 80 years and older age group, in which all people would be vaccine

eligible. Fourth, vaccination coverage data were not available for Texas. If uptake patterns in Texas were meaningfully different from national patterns, then exclusion of Texas data could have affected the cutpoints used for national and Texas-specific analysis of hospital admissions and deaths. Fifth, although hospitalisation and death data are national in scope, cases and emergency department visits were not. Thus, observed results for cases and emergency department visits cannot be considered nationally generalisable. If overall trends in cases and emergency department visits were different in included states compared with full national trends, this could have biased our results. However, consistency in results across outcomes lends credibility to our findings. Sixth, COVID-19 hospital admissions and deaths might include a higher proportion of people with high-risk conditions, who might have become vaccine eligible earlier than they would have based on age; if a high proportion of vaccinated people are included in the reference group, then this might have decreased estimates of impact for these severe outcomes. Finally, any indirect protective effect of the vaccine (ie, if vaccination reduced incidence not only among the vaccinated population but also among those not yet eligible for vaccination) would also probably have decreased our estimates of vaccine impact relative to the true effect.

In conclusion, we found that the initial phases of the US COVID-19 vaccination programme were associated with reductions in COVID-19 cases, emergency department visits, and hospital admissions among older adults, a group prioritised for vaccination and at higher risk of severe outcomes from COVID-19. Our findings, which are consistent with the established high effectiveness of available vaccines,[6,20,22,23,26–29] reinforce the importance of increasing vaccination coverage among all eligible people and support continued investment in COVID-19 vaccination. Nationally, as of June 8, 2021, more than 86% of people aged 65 years and older had received at least one dose of a COVID-19 vaccine, but this figure varied widely by state. Among all US people aged 12 years and older, 61% had received at least one dose of COVID-19 vaccine, and 50% were fully vaccinated. Continued monitoring will be important to further evaluate the impact of the COVID-19 vaccination programme on outcomes in younger adults and children, in addition to the impact of booster doses. The present methodology, with some modifications, might provide important insight into these new situations as they unfold.

Contributors

LAM, REW, RMB, and AJS wrote the manuscript. REW and MS did the primary analyses and drafted the tables and figures with input from LAM, RMB, AJS, MM, JRV, and SJS. JA, FBA, RNA, KEB, AMB, SD, DLD, ESJ, JLK, BCL, HER, LER, and DW curated the data. All authors were involved in data interpretation. JA, FBA, RNA, KEB, AMB, SD, DLD, ESJ, JLK, BCL, HER, LER, DW, LAM, REW, RMB, and AJS verified the underlying data. MM, DCP, JRV, and SJS contributed overall leadership and, with LAM and REW, conceptualised the analysis framework. All authors reviewed the manuscript and revised it critically.

Declaration of interests

We declare no competing interests.

Data sharing

Mortality data are publicly available. Aggregated or redacted data are publicly available for hospitalisations and cases. Data on emergency department visits are not publicly available at this time.

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