Emerging evidence on effectiveness of COVID-19 vaccines among residents of long-term care facilities

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To the Editor:

The development and deployment of several COVID-19 vaccines within a little over a year after the pandemic started is seen as a success story in high-income countries. However, evidence on the effectiveness of the various vaccine candidates among users of long-term care (LTC) services was missing at the time of market entry. Given the disproportionate mortality burden carried by this population throughout the pandemic, it is important to understand whether vaccines protect the often frail and vulnerable users of LTC from infection and severe outcomes. We aimed to monitor and summarise emerging evidence on the effects of COVID-19 vaccines in LTC users.

Methods

We conducted weekly searches of one academic literature database (MEDLINE via PubMed) between 22 February and 11 May 2021 to identify any original research articles reporting on the effect of COVID-19 vaccines in users of LTC. Eligible studies either focused solely on LTC or reported data separately for LTC users. We also searched two additional databases on 11 May 2021 (Web of Science; CINAHL Plus). We extracted key findings from included studies and summarised them narratively. This was a pragmatic and rapid review to monitor emerging evidence. We did not register a protocol for this work.

Results

We identified 17 studies reporting on effects of COVID-19 vaccines in LTC users (including five pre-prints). All studies were conducted in institutional care facilities and none reported on community or home-based care.

Studies reporting estimates of vaccine effectiveness are summarised in the Table. Large cohort studies from England and Denmark (not yet peer-reviewed) estimated vaccine effectiveness against infection at 60% or higher four weeks or more after the first dose,[1] or one week after the second dose.[2] These results are not directly comparable due to different intervals between first and second doses in the two countries. Two smaller studies found similar levels of protection against infection, and one also showed protection from severe outcomes (Table).[3,4]

The impact of vaccination campaigns was assessed in four ecological studies (three from the US, one from Spain). Exploiting natural variation in vaccine rollout, two studies found statistically significant lower rates of new infections among residents of LTC facilities in the weeks following the start of vaccination drives compared to what would be expected without vaccinations, although evidence of the impact on death rates was less consistent.[5,6] Another study found decreased risk of infections once 50% of residents in a facility had received their first dose, although the effect varied over time.[7] A Spanish study estimated COVID infections and deaths were reduced by three-quarters once 70% of LTC residents were fully vaccinated.[8]

Four studies documented breakthrough infections among vaccinated LTC residents. Three studies from Germany, Northern Ireland, and the US reported substantial outbreaks despite high first-dose vaccination rates of residents, with attack rates between 18% and 34% in affected facilities.[3,9] Potential for breakthrough infections in fully vaccinated residents (i.e., infection occurred more than two weeks after administration of the second dose) was reported in studies from the US and Northern Ireland.[4,10,11] Viral load in vaccinated, infected residents may be smaller compared to unvaccinated residents.[12]

Five studies investigated immune response among LTC users, consistently showing higher antibody levels in residents with prior infections. In residents without prior infections, immune

response may be insufficient for approximately half of residents after the first dose,[13–15] and for some even after the second dose.[16] Those with prior infection also had higher antibody levels after the second dose, but other characteristics (including frailty and cognitive impairment) were not associated with different antibody levels.[17]

Table: Studies of vaccine effectiveness in LTC users

Study (country)	**Vaccine studied**	**Study overview**	**Vaccine effectiveness (VE) estimates**
Britton et al.[3] (United States)	BioNTech / Pfizer	Outbreak report after breakthrough infections; 2 facilities (463 residents, 81% had at least 1 dose).	VE against infection after 1st dose: 63% (95% CI = 33-79).
Cavanaugh et al.[4] (United States)	BioNTech / Pfizer	Outbreak report after breakthrough infections; 1 facility (83 residents, 90% had 2 doses).	VE among fully vaccinated residents (>14 days after 2nd dose): against infection 66% (95% CI 41–81); against symptomatic illness 87% (95% CI 66–95); against death 94 (95% CI 45–99)
Rask-Moustsen Helms et al.[1] (Denmark)	BioNTech / Pfizer	Cohort study; 39,040 residents at LTC facilities (95% vaccinated with at least 1 dose).	No protective effect against infection after 1st dose. VE against infection after 2nd dose: 52% (95% CI 27-69) after 0-7 days, and 64%

			(95% CI 14-84) beyond 7 days.
Shrotri et al.[2] (England)	Oxford/ AstraZeneca and Pfizer/ BioNTech	Cohort study; 10,412 residents at LTC facilities (88% vaccinated with at least 1 dose)	VE against infection after 1st dose: 56% (95% CI 19-76) at 28-34 days; 62% (95% CI 23-81) at 35-48 days.

Discussion

Following the widespread rollout of vaccinations in LTC facilities, there is now a growing body of evidence on the effectiveness of COVID-19 vaccinations in these populations. Studies range from providing evidence of vaccine effectiveness at the individual level, facility level and documenting immune response.

These studies fill a gap that was left by the large registration trials of COVID-19 vaccines, which systematically excluded older and frail people.[18] While narrow inclusion criteria may have helped speed up the completion of trials, the fact that evidence on vaccine effectiveness in the population most severely hit by the pandemic only emerges now highlights the issue of continued underrepresentation of vulnerable populations in pharmaceutical trials.

A key issue in achieving high levels of protection is the take-up of vaccines among LTC staff. While not covered in this evidence summary, we are aware of quantitative and qualitative work in this area that aims to better understand willingness to be vaccinated and barriers to achieve high levels of uptake.

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