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Vaccines in Long-Term Care Settings: A Narrative Review

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Abstract
Background: Older people living in long-term care facilities represent a particularly vulnerable segment of the population, who disproportionately bear the burden of infectious diseases, as recently highlighted by the COVID-19 pandemic. ***Summary:*** Older long-term care residents typically cumulate several risk factors for infection and experience serious life-threatening outcomes once infected. These common infections are often compounded by the collective living environment, where it is more difficult to contain the spread of infection. Moreover, the staff may represent an additional reservoir of potential infection and mode of transmission. In this paper, we review the burden of infectious respiratory diseases in residents in long-term care and discuss the potential gains from higher vaccine coverage in this older and most vulnerable population but also from higher vaccine coverage among the facility staff. We highlight the compelling need to integrate specific vaccine recommendations for residents of long-term care into national vaccination schedules, as well as the need to include vaccination campaigns in routine protocols for infection control. Surveillance, reporting, hygiene, and individual protective measures remain key aspects in basic infection control, both in ordinary times and during epidemics. ***Key Message:*** Vaccination of residents in long-term care facilities against respiratory diseases including influenza, pneumococcal disease, pertussis, and COVID is a simple, inexpensive, and effective means to reduce the burden of infection in this segment of the population.

Introduction

According to the World Health Organization (WHO), more than 80% of all deaths related to the COVID-19 pandemic occurred in persons aged over 60 years [1]. More specifically, 50% of those deaths occurred in long-term care facilities, such as nursing homes [2]. Typically, these residents are older adults who are the most vulnerable, as they cumulate several individual risk factors, amplified by a collective living environment, in establishments where the quality of care may be variable [3–5]. Statistics have shone a light on the rate of vaccine coverage against SARS-CoV-2 in long-term care residents, which was around 76% on average, albeit with substantial variations between high-income and low- and middle-income countries [1]. Nevertheless, we are still learning

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lessons from this human catastrophe, especially regarding residents in long-term care. To illustrate this, no current guidelines focus on the need for improved vaccine uptake against the main vaccine-preventable diseases, other than COVID-19, among older people living in long-term care [6].

This situation greatly alarmed the International Federation of Ageing, which recently published a report stating that among 19 countries around the world, none had vaccine recommendations specifically for residents in long-term care facilities as part of the national vaccination schedules.

This absence has alarmed the International Federation of Ageing, which has just published a study attesting that in 19 countries of the world (AR, BR, CA, MX, US, AU, KR, GR, IT, UK, BT, IN, TH, LB, UAE, QT, KE, and ZA), no specific vaccination recommendations for older people residing in long-stay institutions exist in national plans.

In the European Union alone, 2.9 million individuals live in one of the 43,000 long-term care facilities [7]. Is it possible to overlook such a large segment of the population, the oldest and some of the most vulnerable segment, and to leave them without the right of vaccines that could prevent infectious diseases other than COVID-19?

In this mini-review, we propose to assess the burden of infectious respiratory diseases in residents in long-term care and discuss the potential return on investment from higher vaccine coverage in this population, as well as that among the healthcare workers. Both these populations (residents and healthcare workers) warrant inclusion in national infection control strategies. Then, we propose recommendations for vaccination among residents in long-term care, in the hope that national policymakers worldwide will issue specific official guidelines.

Burden of Infectious Respiratory Diseases in Long-Term Care Facilities

Some studies have investigated the prevalence or incidence of infectious respiratory diseases in long-term care facilities. A 1-day study in 9 geriatric hospitals in France and Switzerland in December 1987, totalling 1,919 patients, 44% aged more than 85 years and 74% being female, found a high rate of infections (18.7% in males and 15.4% in females) [8]. In a systematic review of 108 studies, Zhang showed a SARS-CoV-2 infection rate of 32.63% for residents [9]. In a prospective, longitudinal study, Aronow et al. [10] investigated the major clinical cause of death among all residents aged 60 years older in a large nursing home. During the 15-year study, 2,372 (75%) residents died (766 males, 1,606 females, mean age 81 ± 8 years). The main causes of death were cardiovascular diseases (63%) and infectious diseases (21%) (respiratory disease in 15%, urinary infection in 4%, and septicaemia in 2%), with 16% of deaths related to various other causes [10]. The COVID-19 pandemic has confirmed the susceptibility of residents in long-term care facilities, with an estimated 50% of all deaths despite vaccine efficacy against SARS-CoV-2 being estimated to be 63% [2, 11]. The excess deaths observed were predominantly among residents suffering from dementia, hypertension, diabetes, or asthma [12]. The rate of pneumonia among residents is estimated to be six- to tenfold higher than in the general population [13, 14]. In a study of 1,311 hospital patients in Norway over a 12-month period, pneumonia was the cause for one-half of all infection-related admissions of residents from long-term care facilities [15]. This burden of disease is disproportionately borne by older adults in long-term residential care, where it is estimated that reported rates of infectious disease are around tenfold higher than those observed in community-dwelling adults [16, 17].

Before the onset of the pandemic, the risk factors for respiratory infection among residents were well identified and profiled as male with swallowing disorders, inability to take oral medication, multimorbidity, and functional disability [18], to which of course we must add the lack of vaccination against influenza, pneumococcal disease, and pertussis. Indeed, it must be remembered that in addition to the severity of the respiratory infection itself, influenza infection may also aggravate underlying pathologies in older people, such as diabetes, cardiovascular, renal, or neurological disease [19]. Influenza infection may therefore have a particularly debilitating impact on functional capacity, by triggering new-onset dependency, or by compounding a pre-existing loss of autonomy [20]. Similarly, pneumococcal disease accounts for half of all cases of pneumonia and is estimated to be 4 times as frequent in residents in long-term care facilities as in community-dwelling older people [21, 22]. Considering pertussis clusters are rarely observed in long-term care facilities, but pertussis-related chronic cough is a concern in residents and more importantly, among the healthcare workers in the facilities [23], who may be parents of small children [24]. Finally, an independent prospective study conducted during the 2004–2005 respiratory syncytial virus (RSV) seasons to assess RSV acute respiratory illnesses (ARI) and lower respiratory tract infections in long-term care residents aged ≥65 years and older in the

Czech Republic reported that among 1,280 participants, RSV-positive ARI and lower respiratory tract infections episode incidence rates were 45.82 and 30.40 per 1,000 person-years, respectively [25]. In another prospective cohort study, RSV-ARIs were identified among adults aged ≥65 years living in long-term care in Europe and the USA [26]. In the RSV seasons from October 2019–March 2020, the authors observed an overall incidence rate for confirmed RSV-related ARIs of 47.85 cases per 1,000 person-years (95% confidence interval [CI]: 22.58–101.4) and an attack rate of 2.26% among adults in LTCFs [26].

Another major cause of acute respiratory distress among young children is the respiratory syncytial virus, which also has ravaging effects in older persons, especially those with cardiovascular disease. In this at-risk population, symptoms are like those of influenza. Only molecular testing can distinguish the virus responsible for infection. Regarding prevention of RSV-related infections, the future is bright, with over 30 candidate vaccines under development, and one extended half-life monoclonal antibody for all infants nearing regulatory approval [27]. More importantly, Falsey et al. [28] recently reported that an adenovirus serotype 26 RSV vector, encoding a prefusion F (preF) protein (Ad26.RSV.preF) in combination with RSV preF protein, was immunogenic and prevented RSV-mediated lower respiratory tract disease in 5,782 adults aged 65 years and older enrolled in the randomized, double-blind, placebo-controlled, phase 2b CYPRESS trial. These promising results pave the way for inclusion of RSV vaccines in the standard vaccination schedule for older adults, especially residents in long-term care facilities.

Available Vaccines for Preventing Respiratory Infection in Residents in Long-Term Care Facilities

Influenza Vaccination for Residents in Long-Term Care Settings

A study using data from the Services and Health for Elderly in Long-TERm (SHELTER) project collected prospective follow-up for 3,510 residents from 57 nursing homes in eight countries (Czech Republic, England, Finland, France, Germany, Italy, The Netherlands, and Israel) [29]. The residents' mean age was 84.6 ± 7.7 years, and 81.7% received influenza vaccination, while 27.0% received pneumococcal vaccination. Over the follow-up period of 1 year, there were 727 deaths (20.7%). By multivariable analysis, after adjustment for age, sex, comorbidities, cognitive and functional status, the authors found that influenza vaccination (hazard ratio 0.80; 95% CI: 0.66–0.97) and a combination of both influenza and pneumococcal vaccination (hazard ratio = 0.72; 95% CI: 0.57–0.91), but not pneumococcal vaccination alone, were associated with a statistically significant reduction in mortality compared to no vaccination [29]. In a single-blind, pragmatic, comparative effectiveness, cluster-randomised trial, 823 nursing homes in the USA were recruited to participate, of which 409 facilities were randomised for residents to receive high-dose vaccine and 414 facilities for residents to receive standard-dose vaccine, for a total of 75,917 participants aged 65 years or older [30]. The authors reported that the incidence of respiratory-related hospital admissions was significantly lower in facilities where residents received high-dose influenza vaccines compared to those that received standard-dose (adjusted relative risk 0.873, 95% CI: 0.776–0.982, $p = 0.023$) [30]. Staff vaccination rates did not differ between groups in the study. Post hoc analysis of Gravenstein's study found no statistically significant differences in hospitalization for major adverse cardiac events, acute coronary syndromes, stroke, or heart failure between the high-dose and standard-dose arms [31].

Importance of Vaccine Uptake Rates among Staff Working in Long-Term Care Facilities

In a retrospective study of a chain of for-profit nursing homes in the USA, it was shown that although staff and resident immunization rates did not independently predict the likelihood of an influenza outbreak alone, they were strong predictors when considered jointly, underlining the need for high uptake of vaccination among both staff and residents to achieve a meaningful impact against outbreaks [32]. In that study, facilities that had more than 55% of staff and more than 89% of residents vaccinated were almost 60% less likely to have a cluster of influenza-like illness (odds ratio 0.41; 95% CI: 0.19, 0.89) [32].

These findings underline the importance of achieving high vaccine uptakes among staff, as well as residents in nursing homes. Indeed, in addition to national influenza vaccination campaigns targeting older people (from age 55, 60, or 65 upwards, depending on the country), many countries also recommend influenza vaccination for healthcare workers. Nevertheless, reported uptake rates among healthcare workers are alarmingly low. In a nationwide cross-sectional survey of nursing home staff during the 2018–2019 season in France, Vaux et al. reported among 589 healthcare workers that the overall influenza vaccination coverage rate was only 31.9% [95% CI: 29.7–34.1] and varied according to occupational

category, at 75.5% [69.3–81.7] for physicians, 42.9% [39.4–46.4] for nurses, 26.7% [24.5–29.0] for nurses' aides, and 34.0% [30.1–38.0] among other paramedical staff [33]. Of note, this study took place before the current COVID pandemic. Of note, in that study, was that influenza vaccination uptake rates were higher in private residential facilities, smaller facilities, in those where vaccination was provided free of charge, and when promotional activities to publicise vaccination were implemented [33].

The importance of communication surrounding influenza vaccination has often been overlooked as an instrument to improve vaccine coverage. In a cluster-randomized controlled from the Paris region in France, including 3,600 residents in long-term care, 40 residential homes matched in pairs were randomly allocated to a "vaccination" (intervention) arm or a "no vaccination" (control) arm [34]. In the intervention arm, volunteer staff were vaccinated against influenza after a face-to-face interview. Staff influenza vaccination rates were 69.9% in the vaccination arm versus 31.8% in the control arm. Using multivariable analysis, there was significantly lower all-cause mortality among residents in the intervention arm homes during the primary study period (odds ratio 0.80, 95% CI: 0.66–0.96) [34]. More recently, a study performed during the COVID-19 pandemic highlighted once again that staff are a major reservoir of disease in residential facilities, justifying the mandates issued in numerous countries for staff to be vaccinated against SARS-CoV-2 [35]. In their study, McGarry et al. classified 12,364 facilities (81% of all homes in the USA) into quartiles of staff COVID-19 vaccination coverage as of June 13, 2021, and compared outcomes between facilities with low versus high staff vaccine coverage. After accounting for the COVID-19 prevalence in the geographical area, facilities in the lowest quartile of staff vaccination coverage had 1.56 (95% CI: 1.05 to 2.07) additional COVID-19 cases per 100 beds among residents, 1.50 (95% CI: 1.06 to 1.94) additional cases per 100 beds among staff, and 0.19 (95% CI: 0.08 to 0.30) additional COVID-19-related deaths of residents per 100 beds, compared to facilities in the highest quartile of staff vaccination [35]. In areas with high COVID-19 prevalence, models estimated that if all residential facilities had been in the highest quartile of vaccine coverage (82.7% on average), then 4,775 cases among residents (29% of the total during the study window), 7,501 cases among staff (29% of the total), and 703 COVID-19-related deaths among residents (48% of the total) might have been prevented [35]. This again highlights the extraordinary benefits that can be gained from a simple and inexpensive preventive measure.

Vaccine Campaigns and Other Measures for the Prevention of Infectious Disease among Residents of Long-Term Care Facilities

The frequency and severity of acute respiratory infection in older people, and especially among the more vulnerable such as those in long-term care facilities no longer need to be demonstrated, as the evidence is unequivocal. The range of reported estimates for the incidence and prevalence of respiratory infections, especially among non-vaccinated older long-term care residents, is wide, reaching 85.2% and 55.8%, respectively, according to studies [36]. There are substantial benefits to be yielded from vaccination programmes among long-term care residents, while the additional gains from high vaccination rates among staff have also been proven [36, 37].

There are numerous obstacles to the efficient application of vaccine recommendations in long-term care facilities. These include low medical coverage, as many facilities do not have physicians on site. Atypical presentation of infection in the elderly (including lack of fever) and the lack of access to imaging and biological testing can make diagnosis challenging [37]. Finally, year-round admissions and the large volume of information to be collected for each new incoming resident also represent a challenge, notably regarding accurate notation of vaccine status. Possible strategies to address these particular obstacles include systematic recording of flu, pneumococcal, and COVID vaccination status at admission, associated with standing orders, or systematic administration of these vaccines to eligible residents. Adapted vaccination campaigns can be systematically implemented before every winter season, when virus circulation peaks. Pneumococcal vaccines with their long-lasting efficacy must be offered repeatedly after assessment, for example, at fixed dates during the year. The same approach could be adopted with the new RSV vaccines. A recent review of 108 studies from 19 countries, totalling 1,902,044 residents and 255,498 staff from 81,572 LTCFs, found significantly lower COVID-19 infection rates among both residents and staff when vaccination was available during the study period, indicating that vaccination is an effective means to reduce the spread of infection in congregate living facilities [9].

In addition to vaccination in residential care facilities, be it for residents, staff, or both, population density in the

facility also has to be considered. It has been shown that crowding in the facility is significantly associated with rates of respiratory infection and mortality, and the association was consistent across various respiratory pathogens (i.e., not just for COVID-19) [38]. In that study, Leece et al. calculated a "crowding index," whereby one resident for one bedroom with a single private bathroom corresponded to a crowding index of 1, while a four-bed room with one shared bathroom corresponded to a crowding index of 4. Compared with residences with a low crowding index, those with a high crowding index had higher numbers of outbreak-associated infections and deaths per 100 residents per year and a higher average outbreak size, despite similar frequency of outbreaks. Crowding effects were consistent across pathogen subgroups, which included COVID-19, rhinovirus, enterovirus, and influenza A [38]. Similarly, during the COVID-19 pandemic, Brown et al. [39] reported that more crowded nursing homes experienced larger and deadlier outbreaks. These findings suggest that reducing crowding in facilities is a valuable strategy to containing the spread of respiratory disease pathogens [39].

Other measures can also be recommended to mitigate infectious risk in long-term care facilities, such as those proposed by the Hong Kong government in 2007 in response to an outbreak of severe acute respiratory syndrome [40]. These measures include appointing an infection control officer, maintaining adequate indoor ventilation (e.g., open windows or mechanical solutions such as extractor fans), early detection of outbreaks by close monitoring of health status among both residents and staff. Once an infected person is identified, mask-wearing should be mandatory until symptoms resolve. Infected residents could be isolated in an individual room or separated by partitions from non-infected residents [40]. These measures, among others, can be used to mitigate infectious risk, and many of these behaviours were implemented successfully during the COVID pandemic.

Many of these measures are integral parts of infection control programmes within long-term care facilities. The existence of such programmes prior to the onset of the COVID-19 pandemic made it possible to scale-up measures that have since become ubiquitous, namely, hand-washing, isolation, as well as education and antibiotic stewardship [37, 41]. Indeed, it is well established that inappropriate use of antibiotics in long-term care can promote an increase in infections caused by multi-resistant strains [42]. Unfortunately, the absence of systematic infection control plans was most marked in for-profit facilities, especially during the pandemic [43]. Long-term care facilities should have a formal written protocol for infection control, which should include systematic vaccination against leading infectious diseases (flu, pneumococcal infection, RSV, shingles).

The specific profiles of the residents, particularly high-risk populations (e.g., functional status, comorbidities, etc.) may also prompt modulated preventive measures with programmes tailored to the risk of mortality among the resident population [4, 5, 44].

A final consideration is the overall number of staff working in the facility, from the top-level management through to medical and paramedical staff, reception staff, housekeeping, and catering staff. Notably, there is consistent chronic understaffing and low profit margins as a surrogate for low resources, which all constitute impediments to the implementation of adequate quality control initiatives aimed at containing spread of infections [45]. Educating nursing home staff to enhance their critical thinking skills has also been shown to have a positive impact on the prevention and control of infection [46].

Taken together, these findings, viewpoints, knowledge, and experience will shape the perceptions and attitudes of healthcare workers towards vaccination and its advantages, opening important perspectives to be leveraged with a view to enhancing vaccine uptake among healthcare workers in long-term care facilities [47]. This in turn will also affect how healthcare workers communicate with residents and colleagues about vaccination [47].

Conclusion

This short review of the importance of vaccination for both residents and staff in long-term care facilities draws three main conclusions. Firstly, the absence of specific vaccine recommendations for older, multimorbid, dependent older people residing in nursing homes urgently needs to be remedied across all countries. Indeed, it has been clearly demonstrated that high vaccine uptake, especially against routine respiratory diseases (influenza, pneumococcal disease, pertussis, and COVID), has a major beneficial impact. Secondly, the value of high vaccine coverage among healthcare workers in residential care facilities must not be overlooked. It has also been well established for respiratory diseases such as influenza and COVID-19 and is therefore legitimate to consider mandatory vaccination for all categories of staff in these facilities. Thirdly, vaccine recommendations made in isolation cannot be effective but rather must be an integral part of a broader infection control programme. Surveillance, reporting, hygiene, and individual protective

measures always play a key role in basic infection control, both in ordinary times and during epidemics. We urge policymakers and decision-makers worldwide to include specific vaccine recommendations for residents in their national vaccination programmes.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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