CME CREDIT

Ronan Factora, MD
Center for Geriatric Medicine, Cleveland Clinic, Cleveland, OH;
Associate Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH

Having the conversation: Individualizing RSV vaccination in older patients

ABSTRACT

The new vaccines against respiratory syncytial virus (RSV) reduce the risk of RSV illness, which is common in older people and carries the risk of hospitalization with its attendant risks such as delirium and physical decline leading to loss of function and independence. Individualized discussions regarding vaccination should weigh the risks of vaccination, which are minor, against the preventive benefits. Discussions incorporating these elements may lead to greater vaccine uptake, especially by those at high risk.

KEY POINTS

RSV illness is frequent in older persons, those with cardiovascular disease, and those who are immunosuppressed, and is associated with significant harms, particularly pneumonia and hospitalization.

Older people who are hospitalized are at risk for serious complications, including delirium, malnutrition, increased physical weakness, decreased function, advancing frailty, and loss of independence. These risks increase with age, comorbidity, and frailty.

The currently available RSV vaccines have shown effectiveness in reducing RSV illness-associated acute respiratory symptoms, and are more beneficial in recipients who are older, sicker, and more frail.

By discussing the risks and benefits of vaccination with the patient, the provider may be able to overcome vaccination hesitancy and convince them to get the shot.

doi:10.3949/ccjm.91.s1.05

Vaccination is an integral part of preventive care for older patients to protect against diseases such as bacterial pneumonia, tetanus, influenza, shingles, and now, COVID. Multiple vaccines have been clinically proven to reduce morbidity and mortality rates in this vulnerable population, and professional medical associations recommend them in older persons.[1–3] However, many people are passing up the opportunity to receive newer vaccines, likely because of misinformation.[4] This trend is particularly dangerous for older people, who are at risk of the severe outcomes of the diseases that these vaccines protect against.

A frank discussion with the patient can allay their hesitancy. Translating published evidence into understandable, practical, and individualized recommendations can prove extremely useful in these discussions, as can open communication about the pros and cons of vaccination and weighing the potential outcomes for that person if they do or do not get vaccinated.

The new vaccines against respiratory syncytial virus (RSV) provide an additional layer of protection to help preserve the health of older patients. According to the US Centers for Disease Control and Prevention, RSV vaccine is recommended "for everyone ages 75 and older and adults ages 60 to 74 at increased risk of severe RSV." Additionally, it should be considered in "adults 60 to 74 who are at increased risk including those with chronic heart or lung disease, certain other chronic medical conditions, and those who are residents of nursing homes or other long-term care facilities." (https://www.cdc.gov/vaccines/vpd/rsv/index.html).

This article reviews the risks of RSV illness, the characteristics of older people most at risk for poor outcomes from RSV illness, and how to apply available evidence on an individual basis. Sharing this information with the patient can help support the recommendation to proceed with vaccination, with the goal of preventing these RSV illness-associated complications.

RSV'S IMPACT ON OLDER PEOPLE AND OTHERS AT RISK

Though RSV infection is more common in children younger than age 5, older people and adults with underlying medical conditions such as cardiopulmonary disease and immunocompromising conditions also have a greater RSV burden.[5,6] In a meta-analysis, Nguyen-Van-Tam et al[7] estimated the seasonal incidence of RSV infection in older adults at 16.11 cases per 1,000 persons per year. In annual studies (as opposed to seasonal studies), RSV accounted for 4.66% of cases of respiratory infection in older adults, and 7.03% of cases in adults at high risk.

For people at high risk in the same analysis,[7] the estimated annual incidence of RSV infection was 36.88 cases per 1,000 persons per year. The incidence rose significantly during RSV season, to 260.89 cases per 1,000 persons per year. The annual incidence of RSV infection was higher among patients with cardiopulmonary disease than in those with immunodeficiency (9.68% vs 6.33%). During RSV season, an analysis of the same high-risk subgroups showed that RSV accounted for 7.69% of respiratory infections in people at high risk: by subgroup, 11.28% in immunodeficient individuals, 7.22% in persons with cardiopulmonary disease, and 5.20% in institutionalized individuals.

Age is also a risk factor for RSV illness-associated hospitalization. A meta-analysis[8] showed that hospitalization rates rose with age, increasing from 0.8 cases per 10,000 persons per year at ages 50 through 64 to 2.5 per 10,000 persons per year at ages 65 through 79 and then 5.0 per 10,000 persons per year at age 80 or older.

Older people with RSV are at risk for severe infection-related outcomes. In the meta-analysis by Nguyen-Van-Tam et al,[7] 27.44% of older people who contracted RSV developed pneumonia, 24.48% needed to be hospitalized, 5.01% needed to be admitted to an intensive care unit, and 8.18% died.

For RSV-positive patients at high risk, 32.82% required hospitalization and 26.74% were admitted to the intensive care unit.[7] In a subgroup analysis of immunodeficient individuals with RSV, 35.33% developed pneumonia, 20.62% had respiratory failure, 38.30% required hospitalization, 24.09% were admitted to the intensive care unit, and 13.65% required ventilatory support.

The case fatality proportion was 9.98% in high-risk adults, 10.80% in patients with cardiopulmonary disease, and 9.27% in immunodeficient adults,[7] further demonstrating the higher risk of RSV-associated infection in these subpopulations. Tseng et al[9] reported that the cumulative mortality rate 1 year after admission for RSV infection was 25.8% in adults age 60 and older.

In summary, published data clearly show that older people and those with cardiovascular disease or who are immunocompromised have a higher incidence of RSV-associated respiratory illness compared with the general population. The incidence in this group is higher during RSV season. These specific populations are also at higher risk for complications related to RSV acute respiratory illness, including hospitalization, intensive care unit admission, and death.

UNIQUE COMPLICATIONS IN OLDER PERSONS

Increasing age by itself is a risk factor for acute illness-related complications. But older people are a heterogeneous group: some remain physically and cognitively robust and independent, while others experience cognitive or physical decline or both and consequent loss of independence—a state often called clinical frailty.

Most older people want to preserve their function and prevent functional decline, and so would probably accept interventions to achieve this goal. Understanding the impact of age and clinical frailty on clinical outcomes helps clinicians appropriately counsel patients on steps to prevent complications of acute illness.

Hospitals are dangerous for older people

Compared with younger people, older people are more likely to be admitted to the hospital and stay longer.[10–12] Hospitalization-related complications are myriad, including delirium, functional decline, falls, pressure injuries, and urinary incontinence. Between 30% and 40% of people age 70 or older who are admitted to the hospital experience such complications,[13–15] and deficits can still be evident 1 year later.[14,16] These complications are often the consequences of prolonged bed rest, physiological stress, polypharmacy, and suboptimal nutrition.[15,17]

In the hospital, older adults spend most of their time in bed, with only 9% of their day spent walking or standing in one study,[18] with a mean of only 807 steps per day in another study.[19] This inactivity leads to loss of muscle strength (sarcopenia), potentially compounded by undernutrition, especially low protein intake.[20,21]

In an analysis of the relationship between hospitalization and cognitive decline in older adults, the

pooled odds ratio for dementia or severe cognitive impairment following hospitalization was calculated at 1.92 compared with those who were not hospitalized.[22] Risk factors for cognitive decline in various studies included increasing age,[23–28] poorer baseline cognition,[26,27] lower functional status,[29] and increased comorbidities.[23,26] Specific factors related to hospitalization have also been shown to be associated with worse cognitive decline. These include greater illness severity,[29,30] hospital length of stay,[26,27] and critical care admission.[31,32]

Cognitive domains that were affected the most were memory, processing speed, and executive function.[27,28,33–35] Impairments in these areas can potentially affect a person's ability to remain in the workforce and live independently following hospitalization.[36,37]

Older adults carry a significant burden of chronic illness, physical and cognitive impairment, functional impairment, impairments in sensation (hearing, vision), and mental health challenges such as depression and anxiety. The accumulation of these elements can produce increased vulnerability to additional health stressors. Recognizing these comorbidities in individual patients helps identify those at highest risk for complications from acute medical illness so that they can undergo individualized preventive measures to reduce their risk.

Frailty as a risk factor

Frailty is the cumulative impact of age and comorbidity on functional status.[38] Clinical frailty can be a manifestation of either physical or cognitive deficits.[39] Higher levels of frailty are associated with decreased function, lower levels of independence, and more reliance on others for physical and cognitive assistance. With accumulating comorbidities and age-related subcellular deficits, the prevalence of frailty increases with age.[40] **Table 1** shows how frailty can be evaluated clinically.[39]

Frailty is also a risk factor for poor clinical out-

TABLE 1
Assessing frailty severity: The Clinical Frailty Scale

Frailty severity rating	Description	Dementia severity
1. Very fit	Robust, active, energetic, and motivated; exercise regularly; "fittest for their age"	
2. Well	No active disease symptoms; less fit than category 1; often exercise or are very active occasionally (eg, seasonally)	
3. Managing well	Medical problems are well controlled; not regularly active beyond routine walking	
4. Vulnerable	Not dependent on others for daily help, but symptoms often limit activities (eg, "slowed up," tired during the day)	
5. Mildly frail	Need help in high-order instrumental activities of daily living (finances, transportation, heavy housework, medications) with progressive impairment in shopping, meal preparation, and housework.	Mild dementia
6. Moderately frail	Need help with all outside activities, keeping house and may have problems with stairs Basic activity of daily living impairment—may need help with bathing, dressing (cuing, standing by)	Moderate dementia
7. Severely frail	Completely dependent for personal care (physical or cognitive impairments); stable and not at high risk of dying within about 6 months	Severe dementia
8. Very severely frail	Completely dependent, approaching the end of life; difficulty recovering from a minor illness	Severe advanced dementia
9. Terminally ill	Approaching the end of life; life expectancy < 6 months who are not otherwise evidently frail	Severe end-stage dementia

Data from reference 39

comes. Frail older adults are more vulnerable to iatrogenic complications related to their disease or its treatment (eg, adverse drug events, hospitalization-associated complications). Hospitalization-associated complications become significantly more common as frailty severity increases.[13,41,42] Frail older people are also more susceptible to accelerated functional decline and adverse hospital events.[43]

For older people, and particularly those who are clinically frail, the consequence of hospitalization is a higher likelihood of serious decline following an acute illness, often coupled with slower (and at times incomplete) recovery to baseline,[43] or an acceleration of functional or cognitive decline that results in a new disability that was not present at admission.[44] As most older people wish to remain independent and cognitively intact, preventing and avoiding these complications would be aligned with these goals. Identifying an individual's specific risk factors for hospitalization-related complications aids in discussions meant to help prevent such consequences for that person (**Table 2**).

TABLE 2
Risk factors for functional decline following hospitalization in older persons

Increasing age
Baseline presence of cognitive impairment or dementia
Increasing functional impairment
Higher frailty status
Increasing comorbidities
Higher acute illness severity
Longer hospital length of stay
Intensive care unit admission
Bed rest during hospitalization
Dietary restrictions, malnutrition
Delirium

EFFICACY OF BIVALENT VACCINE

The RSV Vaccine Efficacy Study in Older Adults Immunized against RSV Disease (RENOIR)[45] examined the efficacy of a bivalent RSV prefusion F protein (RSVpreF) vaccine (Abrysvo; Pfizer, Rochester, MI). The 2 primary end points were the efficacy of this vaccine in preventing RSV-associated lower respiratory tract illness with either

- At least 2 signs or symptoms lasting more than 1 day, or
- At least 3 signs or symptoms also lasting more than 1 day.

For both primary end points, RSV infection was confirmed by reverse transcriptase polymerase chain reaction assay.

The only secondary end point of the trial was the first episode of RSV-associated acute respiratory illness (at least 1 symptom of an acute respiratory illness) with reverse transcriptase polymerase chain reaction-confirmed RSV infection within 7 days after symptom onset. Symptoms that were monitored included new or increased cough, wheezing, sputum production, shortness of breath, or tachypnea.

Patients

There were 34,284 participants (17,215 in the vaccine group, 17,069 in the placebo group) enrolled in 7 countries (Argentina, Canada, Finland, Japan, The Netherlands, South Africa, and the United States).[45] Participants were at least 60 years of age, with an average age of 68.3 ± 6.16 years.

Of the participants, 51.6% had 1 or more stable chronic high-risk condition (current tobacco use, diabetes, lung disease [including asthma], heart disease [including heart failure], liver disease) with 15.3% having 1 or more stable chronic cardiopulmonary condition (asthma, chronic obstructive pulmonary disease, and congestive heart failure).

Efficacy results

During the surveillance period of 7 months, a total of 44 cases of RSV-associated lower respiratory tract illness with at least 2 signs or symptoms (the first primary end point) occurred, with 11 cases in the vaccine group (1.19 cases per 1,000 person-years of observation) and 33 in the placebo group (3.58 cases per 1,000 person-years of observation).[45] From these numbers, we calculate the number needed to treat (NNT) to prevent 1 instance of the first primary end point in 1 year as 1 divided by the absolute risk reduction, or 418. This corresponds to a vaccine efficacy of 66.7% for this primary end point.

There were a total of 16 cases of RSV-associated lower respiratory tract illness with at least 3 signs or symptoms (the second primary end point): 2 in the vaccine group (correlating to 0.22 cases per 1,000 person-years of observation) and 14 in the placebo group (1.52 cases per 1,000 person-years of observation). From this, we calculate the NNT at 769. This corresponds to a vaccine efficacy of 85.7%.

For the secondary end point, 80 cases of RSV-associated acute respiratory illness were recorded (58 in the placebo group, 22 in the vaccine group) corresponding to a vaccine efficacy of 62.1% (NNT 255).

Vaccine efficacy was maintained throughout the end of the first RSV season, with efficacy in RSV A and RSV B subgroups generally similar to those of the primary end points.

Subgroup analysis of vaccine effectiveness for the 3 end points was conducted, and for the most part, the calculated effectiveness was higher with increasing age for all end points, but because of lower numbers of participants in the 70 through 79 and 80-and-older categories, most confidence intervals were very wide and not statistically significant. A similar conclusion could be drawn in the subgroup analysis of vaccine efficacy in higher-risk individuals for all end points. With the exception of the secondary end point of preventing RSV-associated acute respiratory illness, confidence intervals were also not statistically significant. Despite these observations, it is notable that the vaccine effectiveness was higher in preventing more severe illness (RSV-associated illness with 3 or more signs or symptoms).

Safety results

Side effects in this trial were generally mild, with more local reactions in the vaccine group (12% vs 7%), similar rates of systemic events (27% vs 26%), and with severe events occurring in 0.7% or less of the participants in each group.[45] One month after injection, adverse events had been reported in 9% of the vaccinated group vs 8.5% of the placebo group. Common events included infection and infestation (2.3% in the vaccine group vs 2.2% in the placebo group), respiratory, thoracic, and mediastinal disorders (2.2% in the vaccine vs 2.4% in placebo groups), and cough (0.6% in each group).

Severe or life-threatening adverse events were reported in 0.5% of vaccine recipients and 0.4% of placebo recipients. At the end of the data cutoff date, 2.3% vs 2.3% of the vaccine vs placebo recipients had reported serious adverse events, with 3 of these events identified as related to the trial intervention: a delayed allergic reaction 7 hours after injection of vaccine, a case of Miller-Fisher syndrome, and a myocardial infarction developing 6 days after injection in a patient later diagnosed with Guillain-Barré syndrome beginning 7 days after injection. There were no reported trial intervention-related deaths or adverse events leading to withdrawal from the trial.

EFFICACY OF ADJUVANTED VACCINE

Papi et al[46] tested an adjuvanted RSVpreF protein vaccine (Arexvy; GSK, Brentford, Middlesex, United Kingdom), which demonstrated similar efficacy. Their trial also looked into the vaccine's efficacy in preventing RSV-related lower respiratory tract disease in people age 60 and older during 1 RSV season. Secondary objectives included evaluation of efficacy against RSV-related acute respiratory infection, severe RSV-related lower respiratory tract disease, and RSV-related lower respiratory tract disease according to RSV subtype (A or B), age of participant, presence or absence of coexisting conditions at baseline, and frailty status.

In this trial, 26,664 participants were initially enrolled. Their mean age was 69.5 years, approximately 55.9% were age 60 through 69, 36% were age 70 through 79, and 8.2% were age 80 or older. They were predominantly white (with Blacks comprising 8.5% of the vaccine group and 8.8% of the placebo group, and 7.6% in both groups being Asian), and 92.2% lived in the Northern Hemisphere.

Using the gait speed test, participants were rated as fit (59.9% in the vaccine vs 60.2% in the placebo group), prefrail (38.4% in vaccine vs 38.3% in the placebo group), frail (1.5% in the vaccine vs 1.4% in the placebo group), or frailty status unknown (0.2%).

Using the Charlson Comorbidity Index, participants were rated as being at low or medium risk (66.1% in the vaccine group vs 66.9% in the placebo group) or high risk (33.9% vs 33.1%).

Coexisting conditions of interest (chronic obstructive pulmonary disease, asthma, any chronic respiratory or pulmonary disease, chronic heart failure [cardiorespiratory condition], type 1 or type 2 diabetes mellitus, and advanced liver or renal disease [endocrine or metabolic condition]) were identified in the trial population. Some 39.6% of the vaccine group had at least 1 preexisting condition vs 38.9% of the placebo group, 20% vs 19.4% had cardiorespiratory preexisting conditions, and 25.7% vs 25.9% had endocrine or metabolic preexisting conditions.

Efficacy results

Over a median follow-up of 6.7 months, vaccine efficacy for the primary end point was 82.6% (NNT 208).[46] Efficacy against RSV-related acute respiratory infection was 71.7% (27 cases in the vaccine group vs 95 in the placebo group, NNT 100). Efficacy against severe RSV-related lower respiratory tract disease was 94.1% (1 case in the vaccine group vs 17 in the

placebo group NNT 417). Four participants with RSV-related lower respiratory disease required supplemental oxygen. Two participants were hospitalized for RSV-related respiratory disease. No RSV-related deaths were reported.

In subgroup analysis, efficacy against RSV-related lower respiratory tract disease was more than 80% in participants age 60 through 69 as well as those age 70 through 79; there were too few cases in the age 80-and-older subgroup to draw a conclusion regarding efficacy. In individuals with coexisting conditions, vaccine efficacy was 94.6%, while in those who were prefrail, vaccine efficacy was 92.9%. Efficacy was inconclusive in the frail participants, as there were too few cases.

In summary, in this trial this vaccine achieved its desired end points and demonstrated even higher efficacy in those who were older, frailer, and those with more pre-existing conditions.

INDIVIDUALIZING DECISIONS: BALANCING RISKS AND BENEFIT

Despite these positive findings, there are limitations to the available data. Neither study addressed rates of hospitalization, intensive care unit admission, or need for ventilator use, nor did they measure important hospitalization-related outcomes such as delirium, loss of physical function, frailty, and loss of independence. These specific outcomes may be measured in future clinical trials of RSV vaccines, but in the interim, the known data regarding the potential clinical outcomes of RSV-associated illness in older and high-risk persons along with potential outcomes of hospitalization in this same population could be used to inform patients and their clinicians about the pros and cons of vaccination.

In discussions with patients about the benefits of vaccination, the following elements should be incorporated in the decision-making process:

- RSV illness is common in older persons, those with cardiovascular disease, and those who are immunosuppressed.
- RSV illness in these populations is associated with significant harms, particularly pneumonia and hospitalization.
- Older people who are hospitalized are at risk for serious complications, including delirium, malnutrition, increased physical weakness, decreased function, advancing frailty, and loss of independence. These risks are higher with increasing age, comorbidity, and frailty.
- Cognitive and physical decline occurring during the index hospitalization may persist after acute illness has passed and may result in a higher level of disability and functional impairment. This consequence is more likely in persons who are older, frailer, or have more severe illness.
- The currently available RSV vaccines have shown effectiveness in reducing RSV illness-associated acute respiratory symptoms, with vaccine efficacy shown to be greater with increasing age, comorbidity, and frailty status of the individual vaccinated.

The impact of RSV-related illness is similar to that of influenza, COVID, and bacterial pneumonia.[47] Vaccines have been developed and are available to help prevent these other respiratory illnesses. The RSV vaccines add another tool to that toolbox.

As preserving function and independence has been identified as more important than increasing lifespan in older persons,[48] assessing the impact that any illness or medical intervention on function and independence would be of value in medical decisions. Identifying people who are most at risk for these complications (based on factors such as age, comorbidity, cognitive or physical impairment, and clinical frailty) can aid in discussions regarding the appropriateness of RSV vaccination for a specific individual. Discussing goals beyond surviving acute illness (such as preventing delirium and loss of physical function and mobility—both of which are associated with loss of independence) may also be useful in understanding the practical goal of vaccination for each individual.

The new RSV vaccines are effective in reducing RSV-associated acute respiratory illness, and even more so in reducing severe illness. Preventing severe disease likely also reduces the probability of a person dying of the illness, being hospitalized for it, or experiencing hospitalization-related complications that could lead to cognitive decline, physical decline, and loss of independence.

DISCLOSURES

Dr. Factora has disclosed ownership interest (stock, stock options in a publicly owned company) in Pfizer.

REFERENCES

1. **American Geriatrics Society.** AGS older adults vaccine initiative. https://www.americangeriatrics.org/programs/ags-older-adults-vaccine-initiative. Accessed March 4, 2024.
2. **Infectious Diseases Society of America.** Immunization. https://www.idsociety.org/public-health/immunization/immunization/. Accessed March 4, 2024.
3. **Centers for Disease Control and Prevention.** Adult immunization schedule by age. Updated November 16, 2023. https://www.cdc.

gov/vaccines/schedules/hcp/imz/adult.html. Accessed March 4, 2024.
4. **Marks P, Califf R.** Is vaccination approaching a dangerous tipping point? JAMA 2024; 331(4):283–284. doi:10.1001/jama.2023.27685
5. **GBD 2016 Lower Respiratory Infections Collaborators.** Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis 2018; 18(11):1191–1210. doi:10.1016/S1473-3099(18)30310-4
6. **Jackson ML, Scott E, Kuypers J, Nalla AK, Roychoudury P, Chu HY.** Epidemiology of respiratory syncytial virus across five influenza seasons among adults and children one year of age and older—Washington State, 2011/2012–2015/2016. J Infect Dis 2021; 223(1):147–156. doi:10.1093/infdis/jiaa331
7. **Nguyen-Van-Tam JS, O'Leary M, Martin ET, et al.** Burden of respiratory syncytial virus infection in older and high-risk adults: a systematic review and meta-analysis of the evidence from developed countries. Eur Respir Rev 2022; 31(166):220105. doi:10.1183/16000617.0105-2022
8. **Shi T, Denouel A, Tietjen AK, et al.** Global disease burden estimates of respiratory syncytial virus-associated acute respiratory infection in older adults in 2015: a systematic review and meta-analysis. J Infect Dis 2020; 222(Suppl 7):S577–S583. doi:10.1093/infdis/jiz059
9. **Tseng HF, Sy LS, Ackerson B, et al.** Severe morbidity and short- and mid- to long-term mortality in older adults hospitalized with respiratory syncytial virus infection. J Infect Dis 2020; 222(8):1298–1310. doi:10.1093/infdis/jiaa361
10. **Boltz M, Resnick B, Capezuti E, Shuluk J, Secic M.** Functional decline in hospitalized older adults: can nursing make a difference? Geriatr Nurs 2012; 33(4):272–279. doi:10.1016/j.gerinurse.2012.01.008
11. **Lisk R, Uddin M, Parbhoo A, et al.** Predictive model of length of stay in hospital among older patients. Aging Clin Exp Res 2019; 31(7):993–999. doi:10.1007/s40520-018-1033-7
12. **Smyth B.**, Marsden P., Donohue F., et al. Planning for health: trends and priorities to inform health service planning 2017. Report from the Health Service Executive. https://www.lenus.ie/handle/10147/621262. Accessed March 4, 2024.
13. **Covinsky KE, Pierluissi E, Johnston CB.** Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure". JAMA 2011; 306(16):1782–1793. doi:10.1001/jama.2011.1556
14. **Hoogerduijn JG, Buurman BM, Korevaar JC, Grobbee DE, de Rooij SE, Schuurmans MJ.** The prediction of functional decline in older hospitalised patients. Age Ageing 2012; 41(3):381–387. doi:10.1093/ageing/afs015
15. **Zisberg A, Shadmi E, Sinoff G, Gur-Yaish N, Srulovici E, Admi H.** Low mobility during hospitalization and functional decline in older adults. J Am Geriatr Soc 2011; 59(2):266–273. doi:10.1111/j.1532-5415.2010.03276.x
16. **Boyd CM, Landefeld CS, Counsell SR, et al.** Recovery of activities of daily living in older adults after hospitalization for acute medical illness. J Am Geriatr Soc 2008; 56(12):2171–2179. doi:10.1111/j.1532-5415.2008.02023.x
17. **Falvey JR, Mangione KK, Stevens-Lapsley JE.** Rethinking hospital-associated deconditioning: proposed paradigm shift. Phys Ther 2015; 95(9):1307–1315. doi:10.2522/ptj.20140511
18. **Mudge AM, McRae P, McHugh K, et al.** Poor mobility in hospitalized adults of all ages. J Hosp Med 2016; 11(4):289–291. doi:10.1002/jhm.2536
19. **McCullagh R, Dillon C, Dahly D, Horgan NF, Timmons S.** Walking in hospital is associated with a shorter length of stay in older medical inpatients. Physiol Meas 2016; 37(10):1872–1884. doi:10.1088/0967-3334/37/10/1872
20. **Paddon-Jones D, Rasmussen BB.** Dietary protein recommendations and the prevention of sarcopenia. Curr Opin Clin Nutr Metab Care 2009; 12(1):86–90. doi:10.1097/MCO.0b013e32831cef8b
21. **Cederholm T, Barazzoni R, Austin P, et al.** ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017; 36(1):49–64. doi:10.1016/j.clnu.2016.09.004
22. **Chinnappa-Quinn L, Makkar SR, Bennett M, et al.** Is hospitalization a risk factor for cognitive decline in older age adults? Int Psychogeriatr 2022; 34(11):963–980. doi:10.1017/S1041610220001763
23. **Davydow DS, Hough CL, Levine DA, Langa KM, Iwashyna TJ.** Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. Am J Med 2013; 126(7):615–24.e5. doi:10.1016/j.amjmed.2012.12.006
24. **Garcez FB, Apolinario D, Campora F, Curiati JAE, Jacob-Filho W, Avelino-Silva TJ.** Delirium and post-discharge dementia: results from a cohort of older adults without baseline cognitive impairment. Age Ageing 2019; 48(6):845–851. doi:10.1093/ageing/afz107
25. **James BD, Wilson RS, Capuano AW, et al.** Hospitalization, Alzheimer's disease and related neuropathologies, and cognitive decline. Ann Neurol 2019; 86(6):844–852. doi:10.1002/ana.25621
26. **Mendes-Chiloff CL, Torres AR, Lima MC, Ramos-Cerqueira AT.** Prevalence and correlates of cognitive impairment among the elderly in a general hospital. Dement Geriatr Cogn Disord 2009; 28(5):442–448. doi:10.1159/000255512
27. **Wilson RS, Hebert LE, Scherr PA, Dong X, Leurgens SE, Evans DA.** Cognitive decline after hospitalization in a community population of older persons. Neurology 2012; 78(13):950–956. doi:10.1212/WNL.0b013e31824d5894
28. **Woods AJ, Mark VW, Pitts AC, Mennemeier M.** Pervasive cognitive impairment in acute rehabilitation inpatients without brain injury. PM R 2011; 3(5):426–432. doi:10.1016/j.pmrj.2011.02.018
29. **Inouye SK, Zhang Y, Han L, Leo-Summers L, Jones R, Marcantonio E.** Recoverable cognitive dysfunction at hospital admission in older persons during acute illness. J Gen Intern Med 2006; 21(12):1276–1281. doi:10.1111/j.1525-1497.2006.00613.x
30. **Cole MG, McCusker J, Ciampi A, Belzile E.** The 6- and 12-month outcomes of older medical inpatients who recover from subsyndromal delirium. J Am Geriatr Soc 2008; 56(11):2093–2099. doi:10.1111/j.1532-5415.2008.01963.x
31. **Ehlenbach WJ, Hough CL, Crane PK, et al.** Association between acute care and critical illness hospitalization and cognitive function in older adults. JAMA 2010; 303(8):763–770. doi:10.1001/jama.2010.167
32. **Eriksson LI, Lundholm C, Narasimhalu K, et al.** Hospitalization, surgery, and incident dementia. Alzheimers Dement 2019; 15(4):534–542. doi:10.1016/j.jalz.2018.12.005
33. **Brown CH 4th, Sharrett AR, Coresh J, et al.** Association of hospitalization with long-term cognitive and brain MRI changes in the ARIC cohort. Neurology 2015; 84(14):1443–1453. doi:10.1212/WNL.0000000000001439
34. **Hallgren J, Fransson EI, Reynolds CA, Finkel D, Pedersen NL, Dahl Aslan AK.** Cognitive trajectories in relation to hospitalization among older Swedish adults. Arch Gerontol Geriatr 2018; 74:9–14. doi:10.1016/j.archger.2017.09.002
35. **O'Brien H, O'Leary N, Scarlett S, O'Hare C, Kenny RA.** Hospitalisation and surgery: are there hidden cognitive consequences? Evidence from The Irish Longitudinal study on Ageing (TILDA). Age Ageing 2018; 47(3):408–415. doi:10.1093/ageing/afy020
36. **Albert SM, Tabert MH, Dienstag A, Pelton G, Devanand D.** The impact of mild cognitive impairment on functional abilities in the elderly. Curr Psychiatry Rep 2002; 4(1):64–68. doi:10.1007/s11920-002-0015-8
37. **Steinmetz J, Christensen KB, Lund T, Lohse N, Rasmussen LS; ISPOCD Group.** Long-term consequences of postoperative cognitive dysfunction. Anesthesiology 2009; 110(3):548–555. doi:10.1097/ALN.0b013e318195b569
38. **Fried LP, Tangen CM, Walston J, et al.** Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56(3):M146–M156. doi:10.1093/gerona/56.3.m146
39. **Rockwood K, Song X, MacKnight C, et al.** A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173(5):489–495. doi:10.1503/cmaj.050051
40. **Collard RM, Boter H, Schoevers RA, Oude Voshaar RC.** Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc 2012; 60(8):1487–1492. doi:10.1111/j.1532-5415.2012.04054.x

41. **Hubbard RE, Peel NM, Samanta M, Gray LC, Mitnitski A, Rockwood K.** Frailty status at admission to hospital predicts multiple adverse outcomes. Age Ageing 2017; 46(5):801–806. doi:10.1093/ageing/afx081
42. **Fimognari FL, Pierantozzi A, De Alfieri W, et al.** The severity of acute illness and functional trajectories in hospitalized older medical patients. J Gerontol A Biol Sci Med Sci 2017; 72(1):102–108. doi:10.1093/gerona/glw096
43. **Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K.** Frailty in elderly people [published correction appears in Lancet 2013; 382(9901):1328]. Lancet 2013; 381(9868):752–762. doi:10.1016/S0140-6736(12)62167-9
44. **Zisberg A, Shadmi E, Gur-Yaish N, Tonkikh O, Sinoff G.** Hospital-associated functional decline: the role of hospitalization processes beyond individual risk factors. J Am Geriatr Soc 2015; 63(1):55–62. doi:10.1111/jgs.13193
45. **Walsh EE, Pérez Marc G, Zareba AM, et al.** Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. N Engl J Med 2023; 388(16):1465–1477. doi:10.1056/NEJMoa2213836
46. **Papi A, Ison MG, Langley JM, et al.** Respiratory syncytial virus prefusion F protein vaccine in older adults. N Engl J Med 2023; 388(7):595–608. doi:10.1056/NEJMoa2209604
47. **Surie D, Yuengling KA, DeCuir J, et al.** Disease severity of respiratory syncytial virus compared with COVID-19 and influenza among hospitalized adults aged ≥ 60 years—IVY Network, 20 US States, February 2022–May 2023. MMWR Morb Mortal Wkly Rep 2023; 72(40):1083–1088. doi:10.15585/mmwr.mm7240a2
48. **Kuluski K, Gill A, Naganathan G, Upshur R, Jaakkimainen RL, Wodchis WP.** A qualitative descriptive study on the alignment of care goals between older persons with multi-morbidities, their family physicians and informal caregivers. BMC Fam Pract 2013; 14:133. doi:10.1186/1471-2296-14-133

Correspondence: *Ronan Factora, MD, Center for Geriatric Medicine, X10, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; factorr@ccf.org*