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Accessibility
Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia: retrospective cohort study

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ABSTRACT

OBJECTIVE
To characterize the absolute risks for older patients of readmission to hospital and death in the year after hospitalization for heart failure, acute myocardial infarction, or pneumonia.

DESIGN
Retrospective cohort study.

SETTING

PARTICIPANTS
More than 3 million Medicare fee for service beneficiaries, aged 65 years or more, surviving hospitalization for heart failure, acute myocardial infarction, or pneumonia.

MAIN OUTCOME MEASURES
Daily absolute risks of first readmission to hospital and death for one year after discharge. To illustrate risk trajectories, we identified the time required for risks of readmission to hospital and death to decline 50% from maximum values after discharge; the time required for risks to approach plateau periods of minimal daily to day change, defined as 95% reductions in daily changes in risk from maximum daily declines after discharge; and the extent to which risks are higher among patients recently discharged from hospital compared with the general elderly population.

RESULTS
Within one year of hospital discharge, readmission to hospital and death, respectively, occurred following 67.4% and 35.8% of hospitalizations for heart failure, 49.9% and 25.1% for acute myocardial infarction, and 55.6% and 31.1% for pneumonia. Risk of first readmission had declined 50% by day 38 after hospitalization for heart failure, day 13 after hospitalization for acute myocardial infarction, and day 25 after hospitalization for pneumonia; risk of death declined 50% by day 11, 6, and 10, respectively. Daily change in risk of first readmission to hospital declined 95% by day 45, 38, and 45; daily change in risk of death declined 95% by day 21, 19, and 21. After hospitalization for heart failure, acute myocardial infarction, or pneumonia, the magnitude of the relative risk for hospital admission over the first 90 days was 8, 6, and 6 times greater than that of the general older population; the relative risk of death was 11, 8, and 10 times greater.

CONCLUSIONS
Risk declines slowly for older patients after hospitalization for heart failure, acute myocardial infarction, or pneumonia and is increased for months. Specific risk trajectories vary by discharge diagnosis and outcome. Patients should remain vigilant for deterioration in health for an extended time after discharge. Health providers can use knowledge of absolute risks and their changes over time to better align interventions designed to reduce adverse outcomes after discharge with the highest risk periods for patients.

Introduction
Patients are vulnerable to major adverse outcomes after hospital stay. Readmissions are common: nearly one in five adults aged more than 65 is readmitted to hospital within 30 days of discharge.2 Death is also common in this first month, during which rates of post-discharge mortality may exceed initial inpatient mortality.2 The range of illnesses to which patients are susceptible is extremely broad.4 This period of heightened and generalized vulnerability to a broad spectrum of conditions has been called the post-hospital syndrome.5 Yet risk after discharge from hospital remains incompletely characterized. Previous research has largely focused on calculating rates of readmission and death within the first month after discharge (for example, 30 day readmission rates).2–6 In contrast, a few studies have compared relative differences in risk after hospital stay among different patient groups admitted with the same condition.9–11 Yet none of these studies have characterized patients’ absolute risks of readmission and death or the extent to which these risks change with time over the full year after hospital discharge. We therefore do not know when these risks are highest after discharge or the extent to which these risks change with time over the full year after hospital discharge.
discharge; when they become stable over time, with minimal day to day change; and the extent to which they are increased compared with a general elderly population. We also do not know if risk varies by admitting condition or outcome. This knowledge of absolute risks and their changes over time is critical to defining the period in which post-hospital syndrome persists and can help inform patients and their healthcare professionals about the timing of vulnerability after hospital discharge. This information is needed to set realistic expectations and goals for recovery after discharge. These data can also help hospitals to more efficiently align interventions designed to reduce adverse outcomes after hospital stay to the highest risk periods for patients.

Several specific questions need to be addressed. Firstly, are the absolute risks of hospital readmission and death increased beyond 30 days after discharge, indicating that patients and providers should maintain high vigilance for deterioration in health beyond the initial month after hospitalization? Secondly, do the risks of readmission to hospital and death decline at different rates over time, suggesting that these outcomes result from different factors and therefore require different interventions to be most effectively reduced? Thirdly, does the period of increased risk differ by the initial condition triggering admission to hospital, implying a potential benefit of tailoring the duration and intensity of follow-up to the index diagnosis? Fourthly, do risks of readmission to hospital and death eventually approach plateau periods of relative stability, suggesting that patients may have entered a new phase of recovery with reduced vulnerability? Finally, is the risk of hospital admission and death after discharge noticeably higher than among the general elderly population for the full year after discharge from hospital, indicating that acute illness and hospital stay have longstanding affects on major adverse outcomes?

Accordingly, we define absolute risks of first readmission to hospital and death and their changes in the year after discharge among a national cohort of Medicare fee for service beneficiaries surviving hospitalization for heart failure, acute myocardial infarction, or pneumonia. These three conditions are common reasons for hospital admission among older adults and have been the focus of public reporting. Knowledge of explicit risk trajectories can help patients and physicians set realistic goals and can help hospitals to more efficiently align the duration and intensity of follow-up care with each patient’s condition specific risk for readmission to hospital and death.

Methods

Study sample

We used Medicare standard analytic and denominator files to identify all admissions to acute care hospitals from 2008–10 with a principal discharge diagnosis of heart failure, acute myocardial infarction, or pneumonia. Cohorts were defined using international classification of diseases, ninth revision, clinical modification (ICD-9-CM) codes identical to those used in the publicly reported readmission and mortality measures from the Centers for Medicare & Medicaid Services (see supplementary table 1). We included admissions to hospital among patients aged 65 years or older. We excluded patients with in-hospital death, less than one year post-discharge enrollment in Medicare fee for service in the absence of death, transfer to another acute care facility, discharge against medical advice, and uncertain vital status. As with the federal readmission measures, we used all index hospital hospitalizations across three years of study for analyses of readmissions to hospital. We restricted analyses of death to one random hospitalization per patient over the three year period to avoid repeated measurement of patients who died within one year of multiple admissions for heart failure, acute myocardial infarction, or pneumonia.

Study endpoints

For the year after hospitalization, we identified the occurrence of first readmission to hospital and death on each day after discharge. As with the federal readmission measures, we only included readmissions to short term acute care hospitals and excluded all planned readmission to hospitals based on the presence of specific ICD-9-CM procedure and principal diagnosis codes. We did not consider transfers to other hospitals on the day of discharge or the next day after discharge to be readmission to hospitals.

Comparator population

To compare the risks of readmission and death after hospitalization for heart failure, acute myocardial infarction, or pneumonia with the risks of hospital admission and death in the general elderly population, we constructed a comparator population using the 2009 Medicare denominator and provider analysis and review files. The Medicare denominator file contains information on beneficiaries’ enrolment status in Medicare fee for service, date of birth, and date of death. The Medicare provider analysis and review file contains information on inpatient hospital admissions for enrolled Medicare fee for service beneficiaries, including the principal discharge diagnosis, date of admission, and date of discharge. Our comparator population included all Medicare fee for service beneficiaries aged 65 years or older on 1 January 2009 with at least 12 months of enrolment in fee for service Medicare in the absence of death.

Outcomes

Daily risks of readmission and death

We estimated the daily risks of first readmission to hospital and death by day (1–365) after hospitalization for heart failure, acute myocardial infarction, or pneumonia. To illustrate risk trajectories, we identified the length of time required for daily risks of first readmission to hospital and death to each decline 50% from its maximum value after discharge. We also characterized the length of time required for daily risks of first readmission to hospital and death to approach plateau periods of minimal day to day change by calculating the
number of days required for the daily change in risk of each to decline 95% from its maximum daily decline after discharge.

Relative risks of admission and death
We characterized the extent to which the risks of hospital admission and death are higher among patients recently discharged from hospital compared with the general elderly population. This was done by calculating the cumulative incidence of readmission to hospital and death after hospitalization for heart failure, acute myocardial infarction, or pneumonia and comparing these results with the cumulative incidence of hospital admission and death among all beneficiaries in the Medicare fee for service comparator population.

Statistical analyses
Daily risks of readmission and death
We fit separate survival models for the risk of first readmission to hospital and death after hospitalization for heart failure, acute myocardial infarction, or pneumonia. The analytic approach differed based on the presence or absence of competing risk. In models that estimated the daily risk of first readmission to hospital, we considered death before first readmission to hospital as a competing risk and therefore calculated the subdistribution hazard—an unconditional hazard—that was derived from the cumulative incidence function by Fine and Gray and corrects for competing risk.20 This approach allows the estimation of unconditional risk after consideration of competing risks. We censored data at planned readmission20 or at one year after the index hospitalization, whichever occurred first. In models that estimated the daily risk of death, there was no competing risk and we censored data at one year after the index hospitalization. In the absence of competing risk, we calculated hazard estimates for death using the life table method.

We used Gray’s test to compare the cumulative incidence of first readmission to hospital and its corresponding hazard across cohorts with heart failure, acute myocardial infarction, and pneumonia.21 To compare the cumulative incidence of death and its corresponding hazard across the cohorts, we used the log rank test. We used the bootstrap method with 2000 iterations to construct 95% confidence intervals for the number of days required for the daily change in risk to decline 95% from its maximum daily decline after discharge.

Relative risks of admission and death
We calculated the one year cumulative incidence of hospital admission and one year cumulative incidence of death among all beneficiaries in the Medicare fee for service comparator population in 2009. We prorated these results by day and compared them with the cumulative incidence of hospital readmission and cumulative incidence of death by day (1–365) after discharge from index hospitalization for heart failure, acute myocardial infarction, or pneumonia. We did this by calculating the relative risk of hospital admission and death between study cohorts and the Medicare fee for service comparator population over the first 30, 60, 90, 180, and 365 days after discharge.

To make study and comparator populations more similar, we directly standardized cumulative incidence by age, sex, and race. We used three age categories (65–74, 75–84, ≥ 85), two sex categories, and three race categories (white, black, other). We used the Fine and Gray method to derive the cumulative incidence function of first readmission to hospital for each age-sex-race stratum in the heart failure, acute myocardial infarction, and pneumonia cohorts.20 We derived the cumulative incidence of death for each age-sex-race stratum using the life table method. We directly standardized the study populations to the Medicare fee for service comparator population to calculate the age-sex-race standardized cumulative incidence of hospital admission and death.

AFH, ZL, and HL conducted analyses using SAS 9.3 (SAS Institute, Cary, NC).

Results
For readmission analyses, we included 1462453 hospitalizations for heart failure (4735 hospitals), 561926 for acute myocardial infarction (4423 hospitals), and 1125234 for pneumonia (4767 hospitals). Supplementary figure 1 shows the reasons for excluding hospitalizations. The cohorts were comprised, respectively, of 972339, 516380, and 951084 unique patients who were used in mortality analyses. The comparator population of Medicare fee for service beneficiaries included 27764699 people. Table 1 lists the characteristics of the cohorts.

Within one year of discharge, readmission to hospital and death, respectively, occurred following 67.4% and 35.8% of hospitalizations for heart failure by age, sex, and race. We used three age categories (65–74, 75–84, ≥ 85), two sex categories, and three race categories (white, black, other). We used the Fine and Gray method to derive the cumulative incidence function of first readmission to hospital for each age-sex-race stratum in the heart failure, acute myocardial infarction, and pneumonia cohorts.20 We derived the cumulative incidence of death for each age-sex-race stratum using the life table method. We directly standardized the study populations to the Medicare fee for service comparator population to calculate the age-sex-race standardized cumulative incidence of hospital admission and death.
heart failure, acute myocardial infarction, or pneumonia, risk of first readmission to hospital was highest on day 3, day 2, and day 2 after discharge, respectively, and declined 50% after day 38, day 13, and day 25 (Table 3). Risk of death was highest on day 1 for patients with all three conditions and declined 50% after day 11, day 6, and day 10 after hospitalization for heart failure, acute myocardial infarction, or pneumonia, respectively.

Daily risks of first readmission to hospital and death were different across the three index conditions (P < 0.001) and declined most quickly for acute myocardial infarction and most slowly for heart failure (see supplementary figure 2). Supplementary figure 3 presents the cumulative incidence function of first readmission to hospital and its competing risk of death.

Daily risks of first readmission to hospital and death approached plateau periods of minimal day to day change by seven weeks after hospitalization for all three conditions (table 3). After hospitalization for heart failure, acute myocardial infarction, or pneumonia, the number of days required for the daily change in risk of first readmission to decline 95% from its maximum daily decline after discharge was 45, 38, and 45, respectively (table 3). The number of days required for the daily change in risk of death to decline 95% was 21, 19, and 21, respectively.

Risk after hospitalization was noticeably higher than among the comparator population of Medicare fee for service beneficiaries throughout the year after hospital discharge (fig 2). For example, after hospitalization for heart failure, the age-sex-race standardized relative risk of hospital admission was greater by a factor of 16, 12, and 9, respectively (table 3). The number of days required for the daily change in risk of first readmission to decline 95% from its maximum daily decline after discharge was 45, 38, and 45, respectively.

Through study of a national cohort of Medicare beneficiaries initially hospitalized with heart failure, acute myocardial infarction, or pneumonia, we have defined explicit trajectories of risk for the full year after hospital discharge. Unlike rates of readmission and mortality, these trajectories convey how absolute risks change over time. Our major finding is that patients remain at increased risk of acute health events necessitating readmission to hospital for an extended time after hospital discharge that is longer than the period in which they are at increased risk of death. We also found that risk trajectories vary by admitting diagnosis. For example, risk of first readmission to hospital takes 38 days to decline by 50% after hospitalization for heart failure and 13 days to decline by 50% after hospitalization for acute myocardial infarction. Yet within seven weeks of hospitalization, the risks of both first readmission to hospital and death were significantly lower than at discharge and were no longer rapidly changing for all three conditions, suggesting that patients surviving to this time while avoiding readmission to hospital may have progressed to a new phase of recovery with reduced vulnerability. As the US health system increasingly focuses on improving long term health12-22 and personalizing interventions, explicit descriptions of the time dependent nature of risk after hospitalization can enhance patients’ understanding of recovery from acute illness and better align interventions designed to reduce adverse outcomes with the periods of greatest risk for patients.

**Table 1 | Personal characteristics of study cohorts and comparator population. Values are percentages unless stated otherwise**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Heart failure</th>
<th>Acute myocardial infarction</th>
<th>Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age (years)</td>
<td>80.5 (8.2)</td>
<td>80.7 (8.2)</td>
<td>78.7 (8.4)</td>
</tr>
<tr>
<td>Race:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>55.9 (n = 817 059)</td>
<td>56.2 (n = 545 923)</td>
<td>50.0 (n = 280 986)</td>
</tr>
<tr>
<td>White</td>
<td>83.0 (n = 1 213 963)</td>
<td>84.9 (n = 825 341)</td>
<td>88.0 (n = 494 226)</td>
</tr>
<tr>
<td>Black</td>
<td>12.5 (n = 182 593)</td>
<td>10.8 (n = 105 173)</td>
<td>7.7 (n = 43 013)</td>
</tr>
<tr>
<td>Other</td>
<td>4.5 (n = 65 897)</td>
<td>4.3 (n = 41 825)</td>
<td>4.4 (n = 24 667)</td>
</tr>
</tbody>
</table>

**Table 2 | Daily risk of first readmission to hospital and death after hospitalization for heart failure, acute myocardial infarction, or pneumonia**

<table>
<thead>
<tr>
<th>Discharge diagnosis and outcome</th>
<th>% Experiencing outcome on specific day after hospital discharge (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 7</td>
</tr>
<tr>
<td><strong>Heart failure:</strong></td>
<td></td>
</tr>
<tr>
<td>First readmission</td>
<td>1.17 (1.16 to 1.18)</td>
</tr>
<tr>
<td>Death</td>
<td>0.34 (0.34 to 0.35)</td>
</tr>
<tr>
<td><strong>Acute myocardial infarction:</strong></td>
<td></td>
</tr>
<tr>
<td>First readmission</td>
<td>0.97 (0.95 to 0.99)</td>
</tr>
<tr>
<td>Death</td>
<td>0.33 (0.32 to 0.34)</td>
</tr>
<tr>
<td><strong>Pneumonia:</strong></td>
<td></td>
</tr>
<tr>
<td>First readmission</td>
<td>0.86 (0.84 to 0.87)</td>
</tr>
<tr>
<td>Death</td>
<td>0.34 (0.33 to 0.35)</td>
</tr>
</tbody>
</table>

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Our findings suggest that the risks of readmission to hospital and death are increased well beyond the initial month after hospital discharge. For example, after hospitalization for heart failure, the absolute risk of first readmission to hospital on day 30 after hospital discharge is 0.7%. For perspective, the daily risk of stroke among patients with atrial fibrillation and a CHADS2 score of 2, a group traditionally thought to benefit from oral anticoagulation, is only 0.01%. Moreover, the relative risks of hospital admission and death were considerably higher after hospital discharge than among the general elderly population for the full year after hospitalization, likely due to the combined effects of chronic disease, acute illness, the hospital environment, and the social and environmental settings to which patients return. These findings suggest that patients should remain vigilant for deterioration in health well beyond the first month after hospital discharge and should expeditiously report any concerns to their healthcare providers. Findings also suggest that physicians and hospitals should provide follow-up care that is timely, longitudinal, and comprehensive, with special attention to the completion of advanced care directives, rates of which are low even among patients admitted to hospital.

Our findings may also illuminate different stages of recovery after hospitalization for patients who neither die nor are readmitted. The initial period of extended risk may relate to a post-hospital syndrome derived from the synergistic effects of acute illness, comorbidities, and potential toxicities of hospitalization, such as immobility, sleep deprivation, poor nutrition, pain, secondary illnesses, and iatrogenic events. This first phase of recovery may last up to seven weeks, after which the risks of first readmission to hospital and death have significantly declined and are no longer rapidly changing. Patients surviving to this time without a major adverse event may have therefore progressed to a new stage of recovery with improved physiologic function and reduced vulnerability to deterioration. The serial assessment after hospitalization of specific biomarkers, physiologic variables, and physical performance measures may further explain empiric trajectories of risk.

Our demonstration that the daily risks of readmission to hospital and death decline at different rates over time additionally suggests that these adverse outcomes result from different factors and may require different interventions to be most effectively reduced. Depending on diagnosis, we found that risk of readmission to hospital declined 50% within 13–39 days after hospital discharge, whereas the risk of death required only 6–12 days for a similar relative decline. These differences may explain why models predicting short term mortality among patients admitted to hospital have generally been more successful than models predicting short term readmission. As death is more likely to occur relatively soon after discharge, models that include markers for illness severity at the time of hospital presentation have shown excellent ability to predict short term mortality. In contrast, models for predicting short term readmission to hospital, when restricted to similar markers of illness acuity, have performed substantially worse. This may not be surprising in light of our findings, as the relatively prolonged period of increased risk of readmission to hospital may be more sensitive to factors with effects beyond the acute period of illness, such as cognitive impairment, medication compliance, social factors, and follow-up care. In contrast, the relatively short period of increased mortality risk may relate...
primarily to the effects of acute illness as well as to available interventions provided in the inpatient setting. The particularly high mortality risk immediately after acute myocardial infarction may specifically relate to its pathophysiologic association with sudden cardiac death from arrhythmia and acute structural complications of the heart muscle. ⁴⁷

Ultimately, our findings can help align post-discharge interventions with the periods of greatest risk for patients. Absolute risks may be used to guide the intensity of post-discharge care, whereas the rate of decline in risk with time may be used to guide the duration of follow-up. Organizations with scarce resources for preventing adverse events after hospital admission, such as accountable care organizations, may therefore dynamically alter the duration and intensity of follow-up to match each patient’s condition-specific risk for death and readmission to hospital by using data derived from the electronic health record. Predicted risk trajectories can be fine-tuned as additional data are generated during outpatient follow-up. This more nuanced approach to post-discharge care may grow in importance as health providers seek efficient strategies that minimize patient risk for extended periods after hospitalization. Future models with more granular clinical information can show if risk trajectories are modified by particular patient characteristics.

Strengths of this study

Our study is the first to characterize risk as it dynamically changes on a day by day basis in the year after hospitalization. Although previous work has accurately characterized rates of adverse outcomes in the year after hospital discharge, ¹¹ the calculation of rates obscures how absolute risk changes in dynamic ways for different conditions and outcomes over time. In addition, we calculated and compared trajectories of risk for both readmission to hospital and death using a competing risk methodology. In contrast, previous work has largely been restricted to analyzing only one of these outcomes, ¹¹ thereby precluding their comparison. Finally, we provide patients, providers, and policy makers with an alternative way to comprehend the magnitude and duration of risk after hospitalization by comparing risk among patients recently discharged from hospital with people in the general elderly population matched for age, sex, and race. The results from these analyses can help patients, clinicians, and health systems set realistic goals and plan for appropriate care.

Additional factors need to be considered when interpreting this study. Firstly, data were limited to Medicare fee for service beneficiaries, so findings may not apply to other populations. Nevertheless, our study includes most elderly patients in the United States, who are the focus of current federal policies. ¹³ Secondly, we relied on administrative data and were unable to incorporate clinical variables into our models. However, our goal was to identify general trends in risk, and claims data are ideal for this purpose. Thirdly, we used administrative codes to identify index hospital admissions. However, claims data have been shown to be accurate for cardiovascular and pulmonary diagnoses. ⁴⁶ ⁴⁹ Fourthly, we could have chosen an alternate threshold other than a 95% reduction in rate to define the period after which risk exhibits minimal day to day change. However, as
our goal was to identify the time after which risk is largely invariant from a clinical perspective, we believe that a 95% reduction in rate of decline would reasonably meet this standard. In addition, we were not certain a priori that risk would ever become totally invariant, with a slope of zero in the risk trajectory curve. Fifthly, we did not define risk trajectories separately for patients receiving or not receiving hospice care. As our aim was to generate generalizable estimates of risk among patients recently discharged from hospital, the exclusion of patients expected to have the worst outcomes would bias results towards inappropriately low overall estimates of population risk.

Conclusions

We defined trajectories of risk for the full year after hospitalization for heart failure, acute myocardial infarction, or pneumonia and found that absolute risk is noticeably increased after hospitalization and variably declines over time by discharge diagnosis and outcome. Risk of death declines relatively rapidly, whereas the risk of readmission to hospital remains increased for longer. Although prolongation of risk trajectory among patients admitted with any of the three conditions are at considerably higher risk of adverse outcomes than the general elderly population for the full year after hospital discharge. Yet risk ultimately plateaus by seven weeks after discharge, suggesting that patients reaching this point without having been readmitted may have entered a new and less vulnerable stage of recovery. Patients should therefore remain vigilant for deterioration in health well beyond the first month after hospitalization and maintain extended ties with their healthcare providers. Physicians and hospitals should use knowledge of absolute risk to align interventions designed to reduce adverse outcomes after hospital discharge with the highest risk periods for patients.

Contributors: KD and HKM devised the study concept and design, analyzed and interpreted the data, and drafted the paper; they are the guarantors. AFH performed all statistical analyses. AFH, VTK, ZL, JSR, LIH, and S-LTN analyzed and interpreted the data and critically revised the manuscript for important intellectual content. HMK obtained funding, acquired the data, and supervised the study. KD and HKM had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: support from the National Heart, Lung, and Blood Institute for the submitted work; VTK and HL have no financial relationships in the previous three years with any organizations that might have an interest in the submitted work; KD, AFH, VTK, ZL, JSR, LIH, NK, LGS, S-LTN, and HMK work under contract with the Centers for Medicare & Medicaid Services in the United States to develop and maintain performance measures; JSR is a member of a scientific advisory board for FairHealth; HMK is chair of a cardiac scientific advisory board for UnitedHealth; JSR and HKM are the recipients of research grants from Medtronic and Johnson & Johnson through Yale University.

Ethical approval: This study was approved by the Human Investigation Committee (institutional review board) at Yale University.

Data sharing: No additional data available owing to data use agreement with the Centers for Medicare & Medicaid Policy. Transparency: The lead authors (KD and HKM) affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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