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Discharge Destination as a Surrogate for Modified Rankin Scale Defined Outcomes at 3- and 12-Months Poststroke Among Stroke Survivors

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Abstract

Objective—To determine the predictive value of discharge destination as a surrogate for defining unfavorable outcome at 3- and 12-months poststroke.

Design—Analysis of the prospectively collected data from a randomized, placebo-controlled trial in patients with ischemic stroke presenting within 3 hours of symptom onset.

Setting—Post hoc analysis of patients recruited in a clinical trial.

Participants—Patients (N=530) discharged alive from the hospital after ischemic stroke.

Interventions—Not applicable.

Main Outcome Measures—Positive and negative predictive value and likelihood ratios of discharge destination for unfavorable outcome at 3- and 12-months poststroke defined by a Modified Rankin Scale (MRS) score of 2 to 6, 3 to 6, or 4 to 6. A likelihood ratio indicates how many times more (or less) likely a particular discharge destination is seen in patients with an unfavorable outcome compared with those without unfavorable outcome.

Results—The positive predictive value of nursing home and rehabilitation facility discharges was highest for unfavorable outcome defined by an MRS score of 2 to 6 (95%) and rehabilitation facility (89%) at 3-months poststroke, respectively. The positive predictive value of rehabilitation facility/nursing home (90%) was also highest for unfavorable outcomes defined by an MRS score of 2 to 6 compared with those defined by MRS scores of 3 to 6 (79%) and 4 to 6 (57%). The positive likelihood ratio was highest for nursing home discharges (13; 95% confidence interval [CI], 4.1– 41) followed by rehabilitation facility discharges for unfavorable outcome defined by an MRS score of 2 to 6 at 3-months poststroke (5.3; 95% CI, 3.5–7.9). The negative likelihood ratio was the highest for home discharge for unfavorable outcome defined by an MRS score of 2 to 6 (4.5; 95% CI, 3.4 – 6.1). A similar pattern was observed with unfavorable outcome defined using various thresholds at 12 months.

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Conclusions—Discharge destination can provide high predictive values and likelihood ratios for death and disability at 3-months poststroke, as defined by an MRS of score of 2 to 6.

Keywords

Nursing homes; Patient discharge; Rehabilitation; Stroke

Ascertainment of disability at 3-months poststroke is an essential component of outcome assessment in stroke patients. The Modified Rankin Scale (MRS) has become one of the most widely used assessment tools to determine the severity of disability, because of its high interobserver reliability, superiority to other indices (eg, Barthel Index),[1] and consistent use in trials and registries conducted in patients with stroke.[1–6] However, large studies using datasets such as the Nationwide Inpatient Sample,[7,8] National Hospital Discharge Survey,[9] University HealthSystems Consortium,[10] and Statewide Inpatient Sample[11] do not have outcomes ascertained at 3-months poststroke using the MRS and have used discharge destination as a surrogate for defining favorable and unfavorable outcomes. Given the value of studies conducted using data from large administrative datasets, a better understanding of the relationship between discharge destination and MRS score at 3-months poststroke will allow a more accurate interpretation of results. We evaluated the predictive values of using discharge destination as the surrogate marker for 3 and 12 month MRS score using data collected as part of the randomized National Institute of Neurological Disorders and Stroke (NINDS) recombinant tissue plasminogen activator (rt-PA) Stroke Trial.[12]

METHODS

We used the public access data files available from the National Technical Information Services (Springfield, Virginia) for the NINDS rt-PA stroke trial that was a double-blinded, placebo-controlled, randomized trial that recruited patients from January 1991 through October 1994. The details of the trial have been previously published.[12–14] The trial was conducted in 8 centers each of which developed a flowchart of acute stroke patient screening, assessment, and treatment and multidisciplinary teams that participated in treatment and hospital care in the preparatory phase of the trial.[15] The study was approved by the Data Safety Monitoring Board appointed by NINDS and the local institutional review board at each of the participating sites. Detailed information on inclusion and exclusion criteria has been published in a previous publication.[12] Briefly, eligible patients had an ischemic stroke with a clearly defined time of onset, a deficit measurable on the National Institutes of Health Stroke Scale score (NIHSS), and no evidence of intracranial hemorrhage on a prerandomization computed tomographic scan of the brain. After the neurologic deficits were quantified using the NIHSS, 624 patients were randomized to receive either placebo or rt-PA, 0.9mg/kg body weight within 3 hours of stroke onset.[15]

Disability and functional status was assessed using the Barthel Index, MRS, and Glasgow Outcome Scale and assessed at 3 and 12 months after randomization in all the randomized patients. The outcome was determined at 24 hours and 3-months poststroke by certified examiners who had not performed the baseline examination and was not present during the initial treatment and thus were unaware of the initial NIHSS.[12] Certified nurse coordinators

or study physicians determined the vital status and patient's ability to perform daily activities (measured with the Barthel Index) and degree of functional disability (measured with the MRS) at 12 months using a telephone interview.[13] The evaluators, patients, and their caregivers were unaware of the treatment assignments. The relatively homogenous cohort of ischemic stroke patients with well-defined and validated methods for outcome ascertainment up to 1 year provided adequate data for our analysis.

Statistical Analysis

We provided the data distribution (frequency for categorical and means for continuous variables) for baseline demographic and clinical variables according to discharge destination. The baseline variables assessed included age, sex, ethnicity/race, NIHSS strata (0 –9, 10 –19, or ≥20), hypertension, diabetes mellitus, angina pectoris, congestive heart failure, atrial fibrillation, hyperlipidemia, previous history of stroke or transient ischemic attack, and current cigarette smoking. The 4 discharge destinations (home, relative's/friend's home, rehabilitation facility, and nursing home) were analyzed individually. The outcome of interest was unfavorable outcomes defined by the MRS score at 3 and 12 months. The MRS score categorizes the magnitude of death or disability into 6 grades: 0 (no symptoms), 1 (no significant disability), 2 (slight disability), 3 (moderate disability), 4 (moderately severe disability), 5 (severe disability), and 6 (dead).[16] We focused on the MRS score to define unfavorable and favorable outcomes rather than the Barthel Index because of increasing use of the MRS in clinical trials related to stroke. The preferential use of the MRS in trials is related to high interobserver reliability,[16] smaller sample size requirement if the MRS score is used as a primary endpoint,[17] and lower variation in methodology of using the MRS score as a primary endpoint in previous stroke trials.[18]

We sought to evaluate the positive and negative predictive value of various discharge destinations for 3 different definitions of unfavorable outcome at 3 and 12 months, defined by an MRS score of 2 to 6, 3 to 6, or 4 to 6. These 3 thresholds for defining unfavorable outcome have been used in previous clinical studies depending on the magnitude of benefit sought with intervention. Unfavorable outcome has been defined by an MRS score of 2 to 6 in trials evaluating the benefit of intravenous rt-PA,[12,19] an MRS score of 3 to 6 in trials evaluating the benefit of endovascular treatment,[20,21] and an MRS score of 4 to 6 in trials evaluating the benefit of hemicraniectomy.[22] We evaluated the predictive value of discharge destination for all 3 definitions of unfavorable outcomes to provide a comprehensive analysis that can be used in a variety of settings for ischemic stroke patients. Unfavorable outcome (rather than favorable outcome) was chosen as the outcome of interest based on previous recommendations.[18]

The positive predictive value is the proportion of patients with a particular discharge destination who have experienced an unfavorable outcome. The negative predictive value is the proportion of patients discharged to a particular discharge destination who have experienced a favorable outcome. We also calculated the likelihood ratio, which provides a direct estimate of the odds of experiencing an unfavorable outcome based on discharge destination, either presence (positive) or absence (negative). A likelihood ratio indicates how many times more (or less) likely a particular discharge destination is seen in patients with an

unfavorable outcome compared with those with a favorable outcome.[23] A positive likelihood ratio is calculated as [sensitivity/(1–specificity)] and a negative likelihood ratio as [1–(sensitivity/specificity)].[23] Therefore, the likelihood ratios are more informative than sensitivity and specificity alone, because the posttest probabilities are calculated from both sensitivity and specificity. In addition, likelihood ratios are less influenced by variation in prevalence of particular outcomes compared with predictive values. We sought to evaluate the positive and negative predictive value and likelihood ratios of discharge destination for an unfavorable outcome at 3 and 12 months in 2 strata defined by age (<65y and ≥65y) to remain consistent with age strata used in previous studies using age strata derived from administrative datasets.[24] All multivariate analyses were performed using SAS version 9.0.[a]

RESULTS

Of the 624 patients recruited, 94 patients died during hospitalization and 530 patients were discharged from the hospital after ischemic stroke. Of these 530 patients, 242 were discharged home, 21 to a relative's/friend's home, 206 to a rehabilitation facility, and 61 to a nursing home. The mean time ±SD from recruitment to discharge was 12±11 days. The demographic and clinical characteristics of the patients according to discharge destination are provided in table 1. A higher proportion of patients aged ≥65 years and those with initial NIHSS ≥20 were seen in patients discharged to nursing homes. Table 1 also provides the rates of various categories of the MRS, and the proportions of patients with Barthel Index scores of 95 to 100 and Glasgow Outcome Scale scores of 0 to 1 in patients groups defined by discharge destination.

At 3-months poststroke, the rates of unfavorable outcome defined by the 3 MRS-based definitions were as follows: 2 to 6 (n=318), 3 to 6 (n=257), and 4 to 6 (n=178). There were 26 (4.2%) patients who were unavailable for the follow-up assessment at 12 months. Among the remaining 504 patients with 12-month follow-up, the rates of unfavorable outcome defined by the MRS definitions were as follows: 2 to 6 (n=295), 3 to 6 (n=237), and 4 to 6 (n=165). The positive and negative predictive value of discharge destination for unfavorable outcomes defined using the various MRS thresholds at 3 and 12 months is provided in table 2. The positive predictive value of discharge to nursing home or rehabilitation facility was the highest for unfavorable outcome defined by an MRS score of 2 to 6 (95% and 89%, respectively). The positive predictive value of rehabilitation facility/nursing home was also highest for unfavorable outcomes defined by an MRS score of 2 to 6 as compared with those defined by an MRS score of 3 to 6 (79%) and 4 to 6 (57%). The negative predictive value was the highest for unfavorable outcome defined by an MRS score of 4 to 6 (90%) compared with those defined by an MRS score of 3 to 6 (83%) and 2 to 6 (71%). A similar pattern was observed with unfavorable outcome, defined using various thresholds at 12 months.

The positive likelihood ratio was highest for nursing home discharges (13; 95% confidence interval [CI], 4.1– 41) followed by rehabilitation facility discharges for unfavorable outcome defined by an MRS score of 2 to 6 at 3-months poststroke (5.3; 95% CI, 3.5–7.9). A similar positive likelihood ratio was seen for unfavorable outcome defined by an MRS score of 3 to

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6. The negative likelihood ratio was the highest for home discharge for unfavorable outcome defined by an MRS score of 2 to 6 (4.5; 95% CI, 3.3– 6.1). A similar pattern was observed with unfavorable outcomes defined using various thresholds at 12 months.

When the results were analyzed in 2 strata defined by age, the positive likelihood ratio for all discharge destinations for unfavorable outcome (MRS score 2–6) were similar between those aged less than 65 years compared with those aged ≥65 years (data not shown) (see supplemental tables 1 and 2, available online at the Archives website: www.archives-pmr.org).

DISCUSSION

Salient Findings

We found that discharge destination after acute care hospitalization had the highest positive predictive value and likelihood ratios for unfavorable outcome defined by an MRS score of 2 to 6 at 3-months poststroke compared with unfavorable outcome defined by other MRS thresholds. Discharge to nursing home provided the best positive predictive value for unfavorable outcome, although combining both discharge to nursing home or rehabilitation facility yielded similar results. Any home discharge (home or relative's/friend's home) provided the lowest negative predictive value for unfavorable outcome followed by home discharge when unfavorable outcome was defined by an MRS score of 2 to 6. The discharge destination has certain unique attributes that allow generalization and widespread use. Such attributes include: (1) availability of the data at the time of discharge and with no impact of attrition because of loss to follow-up; (2) comprehensible for patients and family to understand; (3) data are readily available through multitude of sources; and (4) ascertainment is not subject to interrater variability.

Our goal is not to demonstrate discharge destination as a more effective predictor of outcome after acute stroke. Functional measures, such as the MRS, the Glasgow Outcome Scale, and the Barthel Index, have been used as the primary outcome measures in acute stroke treatment trials. There have also been studies showing the usefulness of the NIHSS in categorizing stroke outcomes.[25,26] On a comparative basis, an improvement to an NIHSS of 1 or less or by 11 or more points (prognosis adjusted) at 90 days turned out to be the most powerful outcome measure in a simulated study of 6000 acute stroke clinical trials.[27] The resources required for such ascertainment may not always be possible for assessment in real world scenarios. Discharge destination appears to be an optimal surrogate measure for such scenarios.

The issues regarding the clinical and research implications of the findings need to be discussed. The effect of any programmatic change or introduction of new therapeutic interventions in such settings is best ascertained by rate of unfavorable outcome (defined by MRS) at 3-months poststroke in the patient population under study. However, there are numerous scenarios where data regarding 3-month ascertainment using the MRS are not available because of the lack of standardized follow-up within medical systems, infrastructure to collect clinical data, and/or patient compliance. Discharge disposition is readily available through medical records and ascertained consistently in administrative

datasets.[7–11] Our results allow extrapolation of outcomes defined by discharge destination into outcomes defined by an MRS score of 2 to 6 at 3 and 12 months. Other definitions of unfavorable outcome, such as an MRS score of 3 to 6 and 4 to 6, although used in previous studies,[20–22] are less optimal for such extrapolation. Based on a positive predictive value of 95%, we can assume that 95 of 100 patients discharged to nursing home will have an MRS score of 2 to 6. But the negative predictive value is 45%, meaning that 55 of the 100 patients who were not discharged to a nursing home will also have an MRS score of 2 to 6. Therefore, if the researcher is interested in presence of unfavorable outcome in the study sample,[28] the selection of patients with nursing home discharges may be the best option. However, if the researcher is interested in absence of unfavorable outcome in the study sample, then the goal may be best achieved by choosing discharge to home with a negative predictive value of 13% as the selection variable; 87% of persons who were discharged home are not going to have an MRS score of 2 to 6 at 3-months poststroke. Measures, such as the likelihood ratio, can assist in providing easily comprehensible prognostic information regarding chances of disability and death at the time of discharge based on destination. For example, the odds are 6 times higher in patients discharged to a nursing home (positive likelihood ratio=6) to have an MRS score of 2 to 6 at 3-months poststroke compared with those who were not discharged to nursing homes. Similarly, the odds are 4 times higher for patients discharged to home (negative likelihood ratio=4) to not have an MRS score of 2 to 6 at 3-months poststroke.

Study Limitations

There are certain issues that need to be understood prior to interpretation of our results. The predictive values are highly dependent on the pretest probability, which is 60% (MRS score of 2 to 6 was seen in 318 of 530 patients) in this sample of ischemic stroke patients. If the pretest probability was higher in patients with a diagnosis such as intracerebral or subarachnoid hemorrhage, the posttest probability would be higher. The data of derivation is based on a clinical trial, which is likely to consist of patients with more favorable characteristics and thus a lower rate of death and disability.[29] The patients recruited in the NINDS rt-PA study were those who presented within 3 hours of symptom onset. In a population based study of 1590 patients with ischemic stroke,[30] patients who presented earlier after symptom onset had more severe neurologic deficits (higher NIHSS) and lower rates of favorable outcome. Depending on the influence of various factors that influence the rate of death and disability in patients treated outside clinical trials, discharge destination to a nursing home or rehabilitation facility may have a higher or lower probability of predicting an MRS score of 2 to 6 in unselected groups of ischemic stroke patients. Discharge destination is not always based on functional status and magnitude of disability. Other factors such as patient-related factors, including social support and fiscal status, and institutional factors, such as inpatient rehabilitation capabilities, determine discharge destination.[31] Discharge destination may underestimate the effect of posthospital improvement in functional status. Our analysis is derived from an aggregate sample of various ischemic stroke subtypes. The rate of death and disability varied substantially between patients with total anterior circulation infarcts and those with lacunar or partial anterior circulation infarcts in 1 study.[32] Thus our results may be more reflective of an

aggregate of stroke subtypes and may lose some of its validity in a patient population consisting of 1 stroke subtype.

CONCLUSIONS

Our results provide insight into the predictive value of discharge destination as a surrogate for defining favorable and unfavorable outcome at 3 and 12 months. These results are expected to allow better study design and interpretation for studies and clinical decisions that rely on discharge destination as an outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of Abbreviations

CI	confidence interval
MRS	Modified Rankin Scale
NINDS	National Institute of Neurological Disorders and Stroke
NIHSS	National Institutes of Health Stroke Scale score
rt-PA	recombinant tissue plasminogen activator

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Table 1

Demographic and Clinical Characteristics of Patients Discharged Alive After Ischemic Stroke According to a Discharge Destination

Variables	Discharged to Home (n=242) n (%)	Discharged to Relative's/Friends' Home (n=21) n (%)	Discharged to Rehabilitation Facility (n=206) n (%)	Discharged to Nursing Home (n=61) n (%)
Demographic characteristics				
Age strata (y)				
<65	116 (47.9)	3 (14.3)	75 (36.4)	10 (16.4)
≥65	126 (52.1)	18 (85.7)	131 (63.6)	51 (83.6)
Men	153 (63.2)	8 (38.1)	113 (54.8)	29 (47.5)
Race/ethnicity				
Black	76 (31.4)	5 (23.8)	53 (25.7)	7 (11.5)
White	146 (60.3)	15 (71.4)	136 (66.0)	47 (77.1)
Hispanic	12 (4.9)	0	14 (6.8)	5 (8.2)
Asian	6 (2.5)	1 (4.7)	0	1 (1.6)
Other	2 (0.83)	0	3 (1.5)	1 (1.6)
Clinical characteristics				
Baseline NIHSS strata				
0–9	118 (48.7)	8 (38.1)	41 (19.9)	6 (9.8)
10–19	101 (41.7)	9 (42.8)	115 (55.8)	27 (44.3)
≥20	23 (9.5)	4 (19.1)	50 (24.3)	28 (45.9)
Presumptive diagnosis				
Large vessel occlusion	46 (19.0)	3 (14.3)	24 (11.6)	3 (4.9)
Cardioembolic	98 (40.5)	10 (4.5)	88 (42.7)	27 (44.3)
Small vessel occlusion	90 (37.2)	8 (38.1)	88 (42.7)	30 (49.2)
Other	8 (3.3)	0	6 (2.9)	1 (1.6)
Prior stroke at baseline	35 (14.6)	5 (25.0)	20 (9.8)	11 (18.0)
No preexisting disability at baseline	42 (18.1)	4 (21.0)	29 (15.3)	9 (16.8)
Diabetes mellitus	46 (19.0)	1 (4.7)	40 (19.6)	20 (33.3)
Hypertension	148 (61.4)	17 (80.9)	138 (67.6)	36 (61.0)
Myocardial infarction	56 (24.0)	4 (21.0)	36 (18.5)	12 (20.6)
Atrial fibrillation	33 (13.8)	5 (23.8)	38 (18.5)	13 (21.3)
Angina	55 (23.2)	3 (15.0)	37 (18.8)	13 (22.0)
Congestive heart failure	31 (13.2)	6 (31.5)	29 (14.6)	12 (21.4)
Valvular heart disease	18 (7.6)	4 (21.0)	12 (6.1)	4 (7.0)
Cigarette smoking	105 (44.3)	5 (23.8)	60 (29.4)	14 (23.3)
Hyperlipidemia	57 (26.8)	6 (40.0)	45 (25.8)	10 (21.3)
Outcome measures				
Barthel Index at 3mo				
<95	45 (19.8)	9 (47.4)	131 (65.8)	51 (86.4)
≥95	182 (80.2)	10 (52.6)	68 (34.2)	8 (13.5)

Variables	Discharged to Home (n=242) n (%)	Discharged to Relative's/Friends' Home (n=21) n (%)	Discharged to Rehabilitation Facility (n=206) n (%)	Discharged to Nursing Home (n=61) n (%)
Glasgow Outcome Scale Score at 3mo				
≤1	175 (77.1)	10 (52.6)	42 (21.1)	4 (6.7)
>1	52 (22.9)	9 (47.3)	157 (78.8)	55 (93.2)
Outcome of patients at 3mo by the MRS				
0	82 (33.8)	5 (23.8)	2 (0.9)	0
1	93 (38.4)	6 (28.5)	21 (10.2)	3 (4.9)
2	30 (12.4)	1 (4.7)	28 (13.5)	2 (3.3)
3	14 (5.8)	5 (23.8)	55 (26.7)	5 (8.2)
4	8 (3.3)	2 (9.5)	70 (33.9)	20 (32.8)
5	7 (2.9)	1 (4.7)	15 (7.3)	13 (21.3)
6	8 (3.3)	1 (4.7)	15 (7.3)	18 (29.5)
Outcome of patients at 12mo by the MRS				
0	83 (36.5)	5 (26.3)	4 (2.0)	1 (1.7)
1	77 (33.9)	4 (21.1)	32 (16.1)	3 (5.1)
2	24 (10.5)	2 (10.5)	29 (14.5)	3 (5.1)
3	12 (5.3)	2 (10.5)	52 (26.1)	6 (10.2)
4	6 (2.6)	1 (5.3)	40 (20.1)	6 (10.2)
5	3 (1.3)	2 (10.5)	12 (6.0)	14 (23.7)
6	22 (9.7)	3 (15.8)	30 (15.1)	26 (44.1)

Table 2

Predictive Values and Likelihood Ratios for Categories of Discharge Destinations Alone or in Combination for (unfavorable) Outcome Defined by the MRS at 3 and 12 Months

	Positive Predictive Value (%)			Negative Predictive Value (%)			Positive Likelihood Ratio (95% CI)			Negative Likelihood Ratio (95% CI)		
Discharge Destinations	**MRS 2–6**	**MRS 3–6**	**MRS 4–6**	**MRS 2–6**	**MRS 3–6**	**MRS 4–6**	**MRS 2–6**	**MRS 3–6**	**MRS 4–6**	**MRS 2–6**	**MRS 3–6**	**MRS 4–6**
Unfavorable Outcome Defined by the MRS at 3mo												
Home	28	15	10	13	24	46	0.3 (0.2–0.3)	0.2 (0.1–0.3)	0.21 (0.1–0.3)	4.5 (3.3–6.1)	3.4 (2.7–4.2)	2.3 (1.9–2.7)
Relative's/friend's home	48	43	19	39	51	66	0.6 (0.3–1.4)	0.8 (0.3–1.9)	0.47 (0.2–1.4)	1.0 (0.9–1.1)	1.0 (0.9–1.0)	1.0 (0.9–1.0)
Rehabilitation facility	89	75	49	58	69	76	5.3 (3.5–7.9)	3.2 (2.4–4.2)	1.87 (1.5–2.3)	0.5 (0.4–0.5)	0.4 (0.4–0.5)	0.6 (0.5–0.7)
Nursing home	95	92	84	45	57	73	13 (4.1–41)	12 (4.8–29)	10 (5.3–19)	0.8 (0.7–0.8)	0.8 (0.7–0.8)	0.7 (0.7–0.8)
Rehabilitation facility/ nursing home discharge	90	79	57	71	83	90	6.2 (4.3–8.9)	4.0 (3.1–5.1)	2.6 (2.2–3.0)	0.3 (0.2–0.3)	0.2 (0.2–0.3)	0.2 (0.2–0.3)
Unfavorable Outcome Defined by the MRS at 12mo												
Home	23	18	19	18	30	52	0.3 (0.2–0.3)	0.2 (0.2–0.3)	0.3 (0.2–0.4)	3.3 (2.5–4.2)	2.6 (2.2–3.2)	1.9 (1.6–2.2)
Relative's/friend's home	53	42	32	41	53	67	0.8 (0.3–1.9)	0.8 (0.3–2.0)	0.9 (0.3–2.5)	1.0 (0.9–1.0)	1.0 (0.97–1.0)	1.0 (0.9–1.0)
Rehabilitation facility	82	67	41	57	66	73	3.2 (2.3–4.4)	2.3 (1.8–2.9)	1.4 (1.2–1.8)	0.5 (0.5–0.6)	0.5 (0.5–0.7)	0.7 (0.6–0.91)
Nursing home	93	88	78	46	58	73	9.7 (3.6–26)	8.3 (3.8–18)	7.2 (4.0–13)	0.8 (0.8–0.8)	0.8 (0.7–0.8)	0.7 (0.6–0.8)
Rehabilitation facility/ nursing home discharge	84	72	50	69	79	85	3.8 (2.9–5.1)	2.9 (2.4–3.5)	2.0 (1.7–2.3)	0.3 (0.3–0.4)	0.3 (0.2–0.4)	0.4 (0.2–0.5)