Effect of Deintensifying Diabetes Medications on Negative Events in Older Veteran Nursing Home Residents

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OBJECTIVE

Guidelines advocate against tight glycemic control in older nursing home (NH) residents with advanced dementia (AD) or limited life expectancy (LLE). We evaluated the effect of deintensifying diabetes medications with regard to all-cause emergency department (ED) visits, hospitalizations, and death in NH residents with LLE/AD and tight glycemic control.

RESEARCH DESIGN AND METHODS

We conducted a national retrospective cohort study of 2,082 newly admitted nonhospice veteran NH residents with LLE/AD potentially overtreated for diabetes (HbA$_{1c}$ ≤7.5% and one or more diabetes medications) in fiscal years 2009–2015. Diabetes treatment deintensification (dose decrease or discontinuation of a noninsulin agent or stopping insulin sustained ≥7 days) was identified within 30 days after HbA$_{1c}$ measurement. To adjust for confounding, we used entropy weights to balance covariates between NH residents who deintensified versus continued medications. We used the Aalen-Johansen estimator to calculate the 60-day cumulative incidence and risk ratios (RRs) for ED or hospital visits and deaths.

RESULTS

Diabetes medications were deintensified for 27% of residents. In the subsequent 60 days, 28.5% of all residents were transferred to the ED or acute hospital setting for any cause and 3.9% died. After entropy weighting, deintensifying was not associated with 60-day all-cause ED visits or hospitalizations (RR 0.99 [95% CI 0.84, 1.18]) or 60-day mortality (1.52 [0.89, 2.81]).

CONCLUSIONS

Among NH residents with LLE/AD who may be inappropriately overtreated with tight glycemic control, deintensification of diabetes medications was not associated with increased risk of 60-day all-cause ED visits, hospitalization, or death.

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Potential overuse of medications (1) is well-documented among older nursing home (NH) residents with limited life expectancy (LLE) and those with dementia, with as many as 50% being exposed to at least one medication with uncertain benefit near end of life (2). Specifically, investigators of recent observational studies have identified a high prevalence of possible overuse of aspirin (3), statins (4),

antihypertensives (5), and diabetes medications (6) in NH residents with advanced dementia (AD) or LLE. Efforts are needed to reduce the risk for adverse effects through deprescribing and deintensifying medications (i.e., reducing the dose or number of drugs).

The benefits of aggressive treatment are less certain in frail, older adults with medically complex conditions who are unlikely to live long enough to receive those benefits (7). Older adults may also be more susceptible to the adverse effects associated with diabetes medication due to changes in appetite and swallowing difficulty, as well as altered drug metabolism and distribution that accompany increasing age. The American Geriatrics Society (8), the U.S. Department of Veterans Affairs (VA) (9), and the American Diabetes Association (10) all advocate for less aggressive treatment targets (e.g., 8.0–9.0%) and against the use of medications other than metformin to manage diabetes in those with reduced life expectancy or high comorbidity burden.

The use of medications to manage diabetes in older adults requires complex decision-making to appropriately balance potential benefits and harms (8,9). In a recent study across the VA national health system, we identified that >40% of veteran NH residents with LLE/AD, who were being actively treated and monitored for diabetes, were potentially overtreated to HbA$_{1c}$ values <7.5% (6). Yet less than one-half of these potentially overtreated NH residents had their diabetes regimens deintensified within 90 days after HbA$_{1c}$ measurement.

A recent guideline by Farrell et al. (11) recommends deintensifying diabetes medications for individuals receiving medications known to contribute to hypoglycemia (e.g., insulin, short-acting sulfonylureas), those at heightened risk for hypoglycemia, and those for whom the benefits are uncertain due to frailty, dementia, or LLE. However, the authors noted only low-quality evidence from two before-and-after studies with examination of outcomes associated with deintensifying diabetes medications. A limited number of studies have included examination of outcomes associated with deintensifying diabetes medications in older adults, and only one small prospective study has included examination of deintensification of diabetes medications

in the NH setting (12). No studies have focused on NH residents with the least potential for benefit, such as those with LLE/AD.

For NH residents with life-limiting conditions, the goal of treatment deintensification is to reduce medication burden without increasing burdensome transitions (i.e., transfer from the NH setting to an emergency department [ED] or acute hospital setting) for disease-related complications. Thus, the objective of this study was to evaluate the impact of deintensifying diabetes medications with regard to all-cause 60-day ED visits and hospitalizations in a population of VA NH residents with LLE/AD. This study contributes new knowledge regarding the safety of deintensifying diabetes treatment as an approach to aligning medication use with goals of care and life expectancy in NH residents approaching end of life.

RESEARCH DESIGN AND METHODS

This study was approved under expedited review by the VA Pittsburgh Healthcare System institutional review board.

Study Design

This was a retrospective analysis of administrative and clinical data for a national cohort of VA NH residents from fiscal years 2009–2015 (Fig. 1). Briefly, we identified veterans who were potentially overtreated for diabetes at admission, on the basis of an HbA$_{1c}$ ≤7.5% measured within the first 90 days of the NH stay with concurrent use of diabetes medications. We then assessed exposure status (having diabetes medications deintensified vs. not) in the subsequent 30 days. Residents were followed for outcomes for 60 days beyond deintensification (or up to a date randomly assigned from the distribution of deintensification dates, if not deintensified, i.e., time-distribution matching [13]).

Data Sources

We merged administrative and clinical data from several sources including the VA Residential History File (RHF) (14), VA Minimum Data Set (MDS) version 2.0 and 3.0 assessments (15), the VA Corporate Data Warehouse (CDW), Medicare claims for veterans dually enrolled in Medicare (16), VA Vital Status

File (17), and the VA Support Service Center (16).

The VA RHF (14), which relies on linked data from VA, Medicare, and MDS records, was used to identify NH episodes of care for veterans during fiscal years 2009–2015. The MDS is a standardized set of health care assessments for NH residents that is required at admission and quarterly thereafter (15). The MDS was used to identify veterans with LLE/AD at admission and to capture detailed resident characteristics not available in claims. The CDW provided VA inpatient and outpatient use data to identify diabetes patients, develop covariates, and capture transfers to VA EDs and hospital settings, laboratory records for HbA$_{1c}$ values and other vital signs, and medications administered through the Bar Code Medication Administration (BCMA) system. BCMA records contain the name and dose as well as a date and time stamp for each medication administered in VA NHs and other inpatient settings. Fee-basis CDW files provided data on non-VA health care encounters billed to VA. Medicare claims for veterans dually enrolled in Medicare provided additional information on non-VA health care use. The VA Vital Status File provided date of death, the National Death Index (NDI) provided cause of death, and the VA Support Service Center provided NH facility characteristics.

Sample

The study sample was identified among all veterans who were newly admitted to one of the 133 VA NHs (i.e., Community Living Centers) across the U.S. In fiscal years 2009–2015, we identified 200,333 new NH admissions.

Eligible veterans had LLE/AD and were potentially overtreated for diabetes (6) (Fig. 2). Residents had to meet at least one of three criteria for LLE/AD: 1) MDS Mortality Risk Index-Revised (MMRI) based on MDS version 3.0 assessment items (MMRI-v3) (18) score ≥36 (>50% likelihood of 6-month mortality), 2) <6 months life expectancy endorsed in the MDS (item J5c in MDS version 2.0 and J1400 in MDS version 3.0), 3) evidence of AD with a score ≤7 on the Brief Interview for Mental Status (BIMS), or ≥4 on the Cognitive Performance Scale (CPS) (19). We excluded residents <65 years old and those
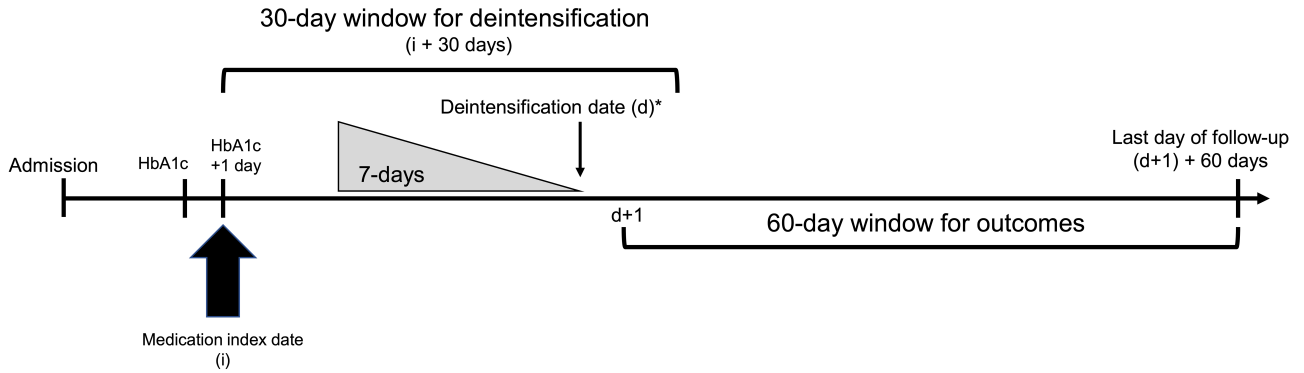
Figure 1—Study design. Note: residents were eligible for inclusion if they had an HbA_{1c} measurement with a value ≤7.5% within the first 90 days of the NH stay, with concurrent use of diabetes medications on or 1 day after the HbA_{1c} measurement (i.e., medication index date [i]). *Start date for window of follow-up for outcomes (d) randomly assigned if patient treatment not deintensified.

staying in the NH <7 days because of insufficient time to observe deintensification of medications. We identified residents with diabetes using a validated algorithm for ICD-9, Clinical Modification (ICD-9-CM), codes associated with inpatient and outpatient encounters in VA and/or Medicare records 2 years prior to admission (20). Residents
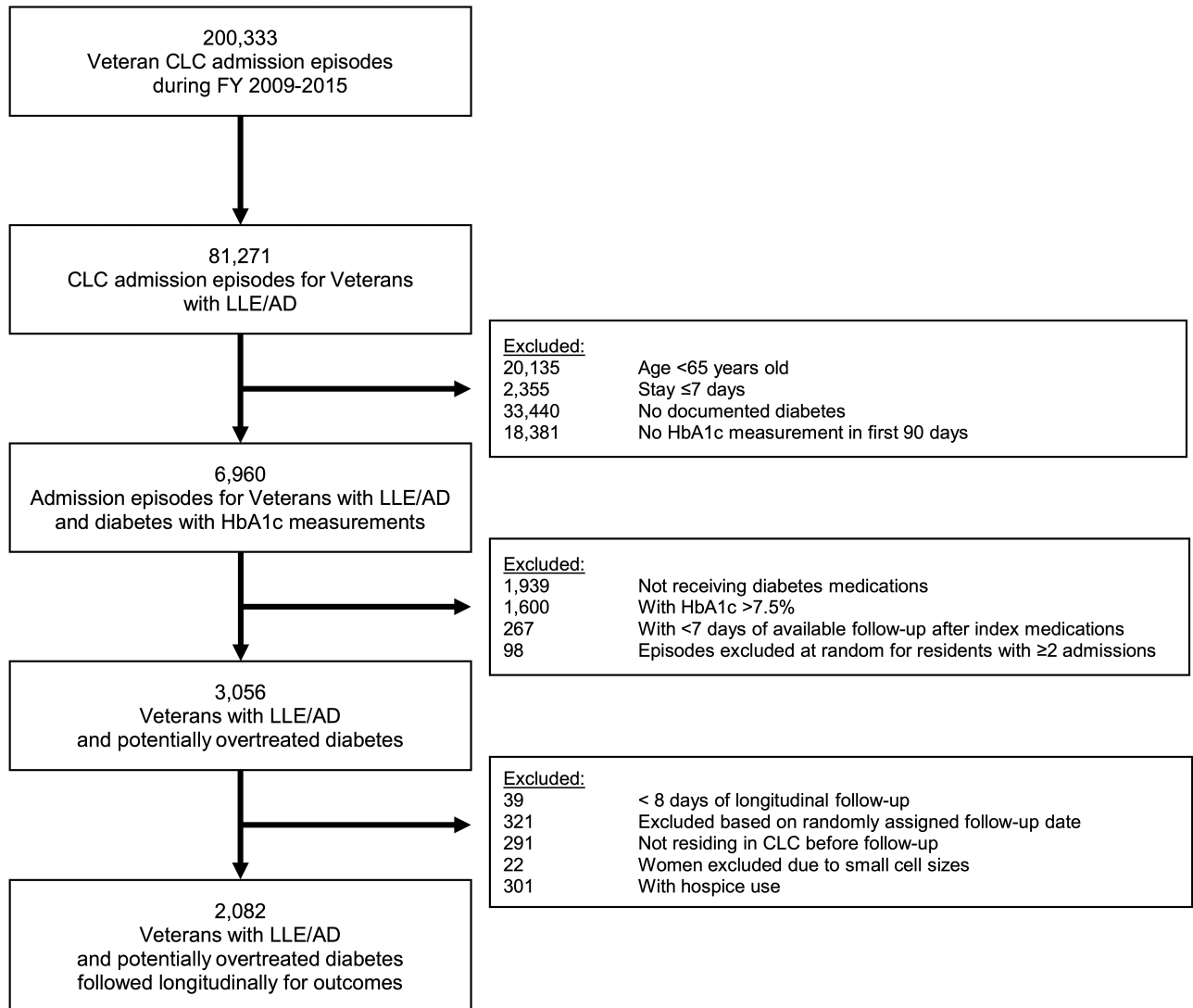

Figure 2—Sample construction for veteran NH residents potentially overtreated for diabetes. CLC, Community Living Center; FY, fiscal years.

with diabetes indicated on the MDS were also included. Residents without HbA$_{1c}$ measurements to evaluate treatment intensity were excluded.

Potential overtreatment was defined on the basis of HbA$_{1c}$ ≤7.5% observed within the first 90 days of a resident's stay and receipt of one or more diabetes medications on the day of or the day after HbA$_{1c}$ measurement (6), which constituted the baseline treatment regimen (Fig. 1). This threshold was selected based on modified treatment goals for NH residents and older adults with medically complex conditions from consensus guidelines (7,10).

Diabetes medications were grouped into the following categories: short-acting insulin, basal insulin, sulfonylureas, and other diabetes agents (biguanides, meglitinides, glucagon-like peptide 1 receptor agonists, α-glucosidase inhibitors, dipeptidyl peptidase 4 inhibitors, and sodium–glucose cotransporter 2 inhibitors). The day after HbA$_{1c}$ measurement was the medication index date. We required all residents to have at least 7 days of follow-up after the medication index date to identify deintensification (n = 3,056).

To conduct longitudinal analyses following deintensification, we required each resident to have at least one additional day of follow-up after deintensification (n = 39 excluded from the deintensification group). For residents with medication treatment that was deintensified within 30 days of the medication index date, the beginning of follow-up for outcomes was the day after deintensification. Residents whose diabetes medication treatment was not deintensified were randomly assigned a follow-up date based on the distribution of days among those whose medication treatment was deintensified (i.e., time distribution matching) (13). Residents whose treatment was not deintensified were excluded if the randomly assigned follow-up date occurred following death or NH discharge (n = 321 excluded from the nondeintensified group). We required that residents were residing in a VA NH bed section (rather than temporarily residing in another VA inpatient ward) at the date of entry into our analysis (n = 291 excluded). Due to small numbers, we excluded women (n = 22 excluded). Finally, we excluded residents who received hospice care at or before

the start of follow-up (n = 301 excluded), based on the admission treating specialty or a treatment indicator from the MDS (3,4). We excluded hospice residents due to the high overall mortality rate, proximal inevitability of death, and small sample size, which reduced our ability to conduct stratified analyses. This resulted in a final analytic sample of 2,082 nonhospice VA NH residents with LLE/AD who were potentially overtreated for diabetes.

Treatment Deintensification
The primary independent variable was whether residents had diabetes treatments deintensified. We looked for deintensification within the 30 days following the medication index date to allow sufficient time for HbA$_{1c}$ results to be reviewed by the prescriber and subsequently acted on, if needed (Fig. 1).

As described in our prior work (6), deintensification was defined as decreasing the dose of or discontinuing a noninsulin agent and/or discontinuing a type of insulin with no addition of new agents or dose increases. We did not measure incremental changes in insulin, as we were not able to distinguish transient changes in response to dietary changes or finger-stick blood glucose measurements from sustained treatment deintensification. Deintensification had to begin within the 30 days following the medication index date and be sustained for seven consecutive days. The seventh day served as the date of deintensification. The comparison group was NH residents who did not have diabetes medication treatment deintensified within this 30-day window.

Outcomes
The primary outcome for our analysis was occurrence of an ED or hospital visit for any cause, with death as a secondary outcome. We used a 60-day window to evaluate outcomes, given that most NH stays in the VA setting are for short stays (21) (i.e., <90 days) and that many residents in our sample had a life expectancy of <6 months. We chose to examine ED visits and hospitalizations separately from death, given that death is a proximal inevitability for many individuals in this population and burdensome transfers to the acute setting may

be a more clinically relevant outcome. We included any outcomes occurring on the last day of the NH stay or the following day.

Transfers to a VA acute hospital setting were captured with the bed section information from VA MedSAS inpatient files. We identified transfers to a non-VA acute hospital setting using CDW fee-basis files (which capture non-VA hospitalizations billed to VA) and short-stay hospitalizations documented in the CMS Medicare Provider Analysis and Review (MEDPAR) (which captures non-VA hospitalizations billed to Medicare). Emergency visits were captured with VA MedSAS inpatient and outpatient files, CDW fee-basis files, and Medicare claims (inpatient, outpatient, and carrier) (22,23). Deaths were identified with the VA Vital Status File, which provides death dates from multiple sources of mortality data including VA inpatient data, the Veterans Benefits Administration, Medicare, the Social Security Administration, and the NDI (17).

Residents were followed until the earliest of the following events: occurrence of a negative outcome, NH discharge, administrative censoring (i.e., end of available data) or end of 60-day follow-up. The earliest observed outcome was coded as the event date. For outcomes occurring on the same date, death took priority. We described the specific causes of hospitalizations or ED visits using diagnosis codes linked to the Agency for Healthcare Research and Quality Clinical Classifications Software (CCS) (24) categories. We reported the three most frequent broad categories of codes (level 1 codes), overall and stratified by deintensification status, as well as the corresponding specific diagnoses (level 2 and level 3 codes). The most frequent causes of death were reported in a similar fashion, with cause of death codes from the NDI linked to the Centers for Disease Control and Prevention list of 39 causes of death (25).

Covariates
We included covariates that may serve as confounders in the association of deintensification and outcomes from five main categories (6): demographics, environment of care, diabetes-related factors, cardiovascular risk factors, and markers of poor prognosis.

Demographics included age at admission and race/ethnicity. Sex was not included, as all residents in our sample were male. Diabetes-related factors included baseline HbA$_{1c}$ (<6.0%, 6.0 to <6.5%, 6.5 to <7.0%, 7.0–7.5%), classes of diabetes medications administered grouped according to risk for hypoglycemia (short-acting insulin, basal insulin, sulfonylureas, all other diabetes agents including metformin), and 1-year history of peripheral vascular disease, diabetic eye disease, lower-extremity ulcers, and serious hypoglycemic events (26,27). Cardiovascular factors included a count of the number of conditions that contribute directly to cardiovascular risk (coronary artery disease, stroke, or diabetes, range 1–3) as well as other cardiovascular risk factors (heart failure, hypertension, hyperlipidemia, venous thromboembolism, recent stroke, tobacco use, and BMI). Markers of poor prognosis included AD, MMRI score (18), documentation of <6 months prognosis in the MDS, Elixhauser Comorbidity Index conditions (28) (0–1, 2–3, 4–5, >5), and MDS measures capturing cancer, end-stage renal disease, loss of appetite, swallowing difficulty, mechanically altered diet, intravenous or parenteral nutrition, shortness of breath, pain, infection, acute change in mental status, activities of daily living (independent, requires assistance, dependent, or totally dependent) (29), and behavioral problems (none, moderate, severe) (30). We characterized polypharmacy based on the total number of nondiabetes drug classes administered in the 7 days prior to the beginning of follow-up (0–5, 6–10, >10 classes). Recent fall or fracture was identified with the MDS indicator for falls in the prior 180 days and/or VA or Medicare claims (31,32). We included several clinical indicators and vital signs shown in prior literature to predict shorter-term mortality (i.e., days to weeks) (33). These included supplemental oxygen, minimum systolic blood pressure, maximum heart rate, and maximum respiratory rate in the 2 days leading up to the 7-day window of deintensification (34). We also adjusted for whether residents had a hospitalization in the 30 days prior to follow-up.

Finally, analysis of environment of care included the admission source (acute/hospital, home/assisted living, NH, other), relationship to next of kin listed in the medical record, U.S. census region (Northeast, Midwest, South, West), Community Living Center bed size, and urban influence code (large metropolitan, small metropolitan, micropolitan, noncore rural) (35). We also included an indicator for the fiscal year of admission (2009–2012 or 2013–2015), which represents the periods before and after the publication of the American Geriatrics Society Choosing Wisely recommendations (7) for diabetes management in older adults and implementation of the VA Hypoglycemic Safety Initiative (HSI).

Statistical Analysis

Baseline characteristics were summarized overall and by deintensification status, with standardized differences to compare across groups. We addressed missing data (<5% on any given variable) with single imputation using chained equations (36).

Confounding by indication or severity is a major concern in this population, as many of the life-limiting conditions that lead prescribers to consider deprescribing also contribute to increased mortality risk (1). For addressing this concern, we used an entropy balancing approach in our sample to balance covariates between residents who were deintensified and those who were not. Entropy balancing (37) is a reweighting scheme similar to propensity score weighting but directly incorporates the desired level of covariate balance into the weighting scheme. It ensures that covariate distributions match exactly across treatment and control groups, reducing model dependence to a greater degree than with propensity methods in estimating treatment effects. In our analysis, a weight of 1 was assigned to the deintensified group, while the rest of the sample was weighted to match the distribution of covariates in the deintensified group. Entropy weights were applied to the sample to calculate the cumulative incidence for ED visits or hospitalizations, as well as death, and the corresponding risk differences (RDs) and risk ratios (RRs) associated with deintensification, which provided an estimate of the average treatment effect on those treated.

We estimated the cumulative incidence of ED visits and hospitalizations using the Aalen-Johansen estimator, which treats competing events like death as secondary outcomes (38). Thus, we were able to obtain estimates of risk for our primary outcome (ED visits and hospitalizations) as well as death. We used these estimates to calculate risk differences and RRs to evaluate the association of treatment deintensification with outcomes at 15, 30, 45, and 60 days. Bootstrapping with 2,000 iterations was used to generate 95% CIs for cumulative incidence, risk differences, and RRs. We also conducted sensitivity analyses to determine the impact of our definition for deintensification, using a longer sustained period of 14 days (6). Analyses were conducted with SAS, version 9.4, and Stata, version 15.0.

RESULTS

Sample Characteristics

Select characteristics of our sample (n = 2,082) are presented in Table 1. The full set of characteristics is presented in Supplementary Table 1. Most residents were age >75 years (61.8%) and White (75.7%), and 28.7% had AD. Approximately 27% of residents had diabetes medication treatment deintensified within 30 days of the index date. Prior to weighting, residents who had medication treatment deintensified were more likely to have HbA$_{1c}$ <6.0% (35.7% vs. 23.2%) and more likely to be receiving short-acting insulin (67.7% vs. 52.4%) or sulfonylureas (37.0% vs. 23.4%) at baseline. In the entropy-weighted sample, all characteristics were sufficiently balanced across groups with standardized differences <0.01.

Association of Deintensification With All-Cause Negative Events

Overall, 32.4% of residents experienced at least one all-cause negative event. Among the earliest events observed, the most common were hospitalizations (19.3%), followed by ED visits (9.3%) and death (3.9%). The most frequent causes of ED visits or hospitalizations are presented overall and by deintensification status in Supplementary Table 2. Overall, ED visits or hospitalizations were most often due to diseases of the circulatory system (e.g., congestive heart failure, dysrhythmias, peripheral atherosclerosis, acute cerebrovascular disease), diseases of the respiratory system (e.g., pneumonia, respiratory failure, aspiration pneumonia),

Table 1—Selectt baseline characteristics for veteran NH residents potentially overtreated for diabetes

	Full sample (n = 2,082)	Unweighted			Weighted		
		Treatment not deintensified (n = 1,528)	Treatment deintensified (n = 554)	Standardized difference	Treatment not deintensified (n = 554)	Treatment deintensified (n = 554)	Standardized difference
Demographics							
Age at admission, years				0.05			<0.01
65–74	797 (38.3)	585 (38.3)	212 (38.3)		212 (38.3)	212 (38.3)	
75–84	855 (41.1)	620 (40.6)	235 (42.4)		235 (42.4)	235 (42.4)	
≥85	430 (20.7)	323 (21.1)	107 (19.3)		107 (19.3)	107 (19.3)	
Race/ethnicity				0.08			<0.01
White	1,560 (75.7)	1,165 (76.2)	408 (73.6)		408 (73.6)	408 (73.6)	
Black	356 (17.3)	260 (17.0)	101 (18.2)		101 (18.2)	101 (18.2)	
Hispanic	109 (5.3)	79 (5.2)	32 (5.8)		32 (5.8)	32 (5.8)	
Other	37 (1.8)	24 (1.6)	13 (2.3)		13 (2.3)	13 (2.3)	
Diabetes-related factors							
Baseline HbA$_{1c}$, %				0.34*			<0.01
<6.0	553 (26.6)	355 (23.2)	198 (35.7)		198 (35.7)	198 (35.7)	
6.0 to <6.5	550 (26.4)	397 (26.0)	153 (27.6)		153 (27.6)	153 (27.6)	
6.5 to <7.0	555 (26.6)	427 (27.9)	128 (23.1)		128 (23.1)	128 (23.1)	
7.0–7.5	424 (20.4)	349 (22.8)	75 (13.5)		75 (13.5)	75 (13.5)	
Short-acting insulin	1,175 (56.4)	800 (52.4)	375 (67.7)	0.32*	375 (67.7)	375 (67.7)	<0.01
Basal insulin	1,017 (48.9)	800 (52.4)	217 (39.2)	0.27*	217 (39.2)	217 (39.2)	<0.01
Sulfonylureas	563 (27.0)	358 (23.4)	205 (37.0)	0.30*	205 (37.0)	205 (37.0)	<0.01
Other diabetes agents	426 (20.5)	308 (20.2)	118 (21.3)	0.03	118 (21.3)	118 (21.3)	<0.01
Peripheral vascular disease	670 (32.2)	505 (33.0)	165 (29.8)	0.07	165 (29.8)	165 (29.8)	<0.01
Diabetic eye disease	376 (18.1)	281 (18.4)	95 (17.1)	0.03	95 (17.1)	95 (17.1)	<0.01
Lower-extremity ulcer	487 (23.4)	363 (23.8)	124 (22.4)	0.03	124 (22.4)	124 (22.4)	<0.01
Serious hypoglycemic event	178 (8.6)	137 (9.0)	41 (7.4)	0.06	41 (7.4)	41 (7.4)	<0.01
Indicators of poor prognosis							
AD	598 (28.7)	459 (30.0)	139 (25.1)	0.11*	139 (25.1)	139 (25.1)	<0.01
MMRI	39 [34–44]	39 [34–44]	39 [36–44]	0.13*	39 [36–45]	39 [36–44]	<0.01
<6 months prognosis	76 (3.7)	54 (3.5)	22 (4.0)	0.02	22 (4.0)	22 (4.0)	<0.01

Data are n (%) or median [interquartile range]. *Standardized difference ≥0.10. †Full set of sample characteristics is presented in Supplementary Table 1.
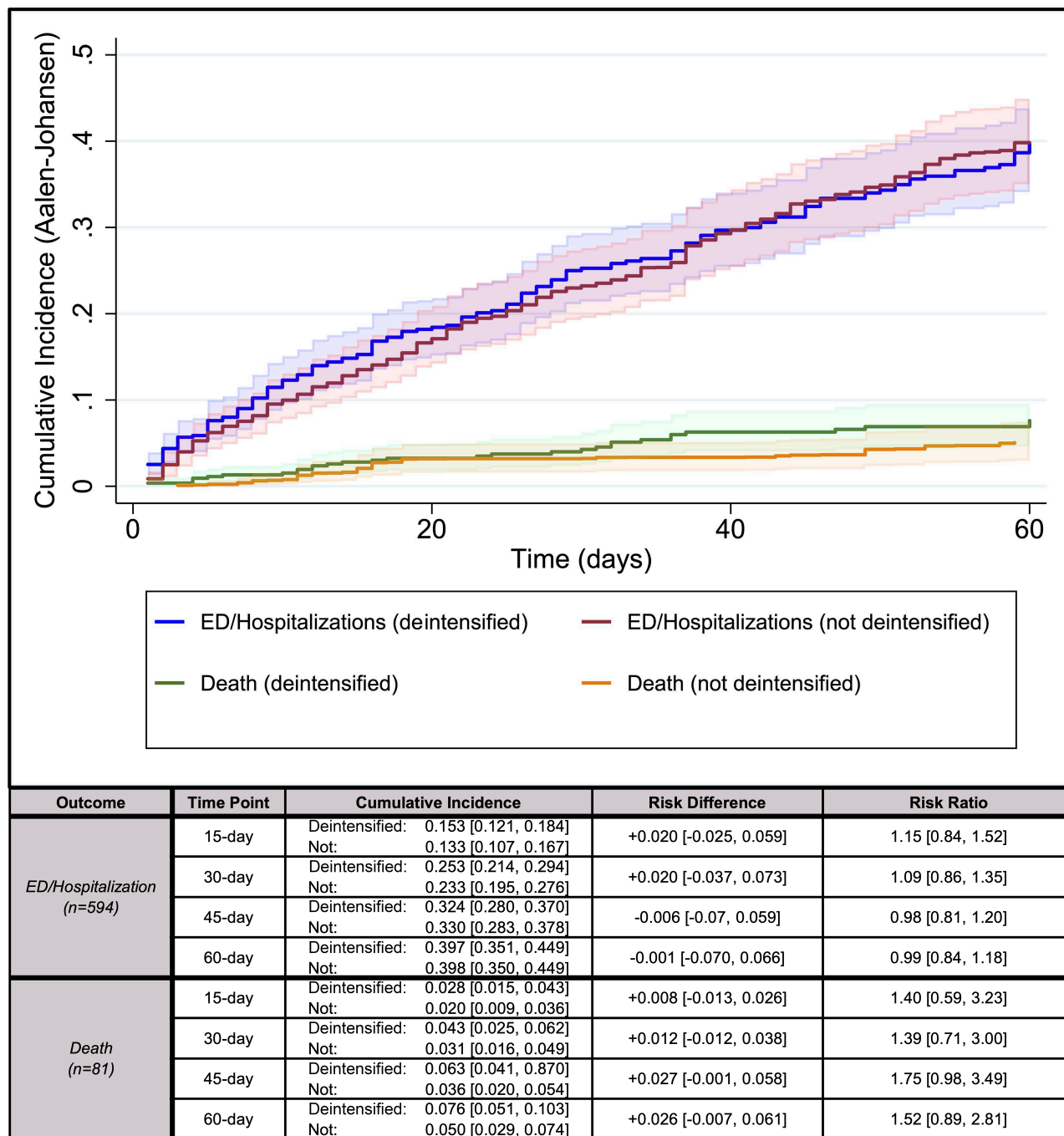
Outcome	Time Point	Cumulative Incidence	Risk Difference	Risk Ratio
ED/Hospitalization (n=594)	15-day	Deintensified: 0.153 [0.121, 0.184] Not: 0.133 [0.107, 0.167]	+0.020 [−0.025, 0.059]	1.15 [0.84, 1.52]
	30-day	Deintensified: 0.253 [0.214, 0.294] Not: 0.233 [0.195, 0.276]	+0.020 [−0.037, 0.073]	1.09 [0.86, 1.35]
	45-day	Deintensified: 0.324 [0.280, 0.370] Not: 0.330 [0.283, 0.378]	−0.006 [−0.07, 0.059]	0.98 [0.81, 1.20]
	60-day	Deintensified: 0.397 [0.351, 0.449] Not: 0.398 [0.350, 0.449]	−0.001 [−0.070, 0.066]	0.99 [0.84, 1.18]
Death (n=81)	15-day	Deintensified: 0.028 [0.015, 0.043] Not: 0.020 [0.009, 0.036]	+0.008 [−0.013, 0.026]	1.40 [0.59, 3.23]
	30-day	Deintensified: 0.043 [0.025, 0.062] Not: 0.031 [0.016, 0.049]	+0.012 [−0.012, 0.038]	1.39 [0.71, 3.00]
	45-day	Deintensified: 0.063 [0.041, 0.870] Not: 0.036 [0.020, 0.054]	+0.027 [−0.001, 0.058]	1.75 [0.98, 3.49]
	60-day	Deintensified: 0.076 [0.051, 0.103] Not: 0.050 [0.029, 0.074]	+0.026 [−0.007, 0.061]	1.52 [0.89, 2.81]

Figure 3—Entropy-weighted association of deintensifying diabetes medications with all-cause events (*n* = 2,082 residents). In the lower panel, cumulative incidence, RD, and RR data are presented with 95% CIs.

and diseases of the genitourinary system (e.g., urinary tract infections, renal failure). The top causes of ED visits and hospitalizations were relatively consistent across deintensification status. The only exception was that the category of injury and poisoning (e.g., complications of surgical procedures, fractures) was the third most common among those who had medication treatment deintensified. The most frequent causes of death in the sample were major cardiovascular disease (37.5% of deaths) and cancers (22.2% of deaths). We are unable to present frequencies of causes of death by deintensification because of small cell sizes.

Entropy-weighted Aalen-Johansen cumulative incidence functions for ED visits and hospitalizations as well as death are shown in Fig. 3 by whether residents had diabetes regimens deintensified. Point estimates for cumulative incidence of negative events, risk differences, and RRs are displayed in the bottom half of the figure. After application of entropy weights to the sample, treatment deintensification was not associated with increased risk of ED visits or hospitalizations by 60 days (RD −0.001 [95% CI −0.070, 0.066], RR 0.99 [0.84,

1.18]) or death (RD 0.026 [−0.007, 0.061], RR 1.52 [0.89, 2.81]). Unweighted analyses are presented in Supplementary Fig. 1.

Sensitivity Analyses

Results from sensitivity analyses are presented in Supplementary Material. When applying an alternate definition for sustained deintensification of 14 days (Supplementary Figs. 2 and 3), we noted no substantive differences. Treatment deintensification was not associated with 60-day ED visits and hospitalizations or death in the entropy-weighted sample.

CONCLUSIONS

To our knowledge, this is the first national study examining outcomes of deintensifying diabetes medications in a sample of NH residents near end of life, addressing a major gap in evidence regarding optimal diabetes treatment for this population with medically complex conditions. We found that deintensifying medication regimens for NH residents who were potentially overtreated for diabetes and near end of life was not associated with increased short-term risk of ED visits, hospitalizations, or death. Our findings support recommendations (7,9) advocating for less aggressive HbA$_{1c}$ goals in adults with reduced life expectancy and suggest that deintensifying medications is an appropriate strategy to achieve these goals in this population.

Potential overtreatment of diabetes in the NH setting has been reported in several prior studies (6,39) and underscores the need for targeted efforts to reconcile medication use with goals of care and life expectancy for the NH population generally but especially for those near end of life. However, no large observational studies have included examination of the impact of deintensifying diabetes treatments on outcomes in the NH setting, until now. In a recent systematic review, investigators identified several investigations of deintensifying diabetes medications in older adults with diabetes (12). However, in few instances were there reports on clinical outcomes beyond glycemic control, such as deaths and hospitalizations. Only one small prospective study included examination of deintensification of diabetes medications in the NH setting specifically, and no increase in mortality was reported among

those who had diabetes medications withdrawn (40). In another study, investigators examined the impact of discontinuing diabetes medications with regard to hospital admissions and mortality but in older adults hospitalized for myocardial infarction (41). They found that discontinuation was not associated with increased readmissions but was associated with increased mortality. Although these studies provide insight into the implications of deintensification, the findings should be interpreted with caution due to the respective limitations in design (40) and generalizability (41). Additionally, neither study specifically addressed the population of NH residents near end of life, who are most likely to be targeted for deintensification.

In the current study, approximately one-third of residents with LLE/AD experienced a negative event during 60 days of follow-up. For NH residents near end of life, the goal of treatment deintensification is to reduce medication burden without increasing the risk for disease-related complications. We observed no significant associations between treatment deintensification and ED visits or hospitalizations, suggesting that deintensification does not increase the risk for burdensome transitions in this population. Given the degree of comorbidity burden among NH residents with LLE/AD and the time to benefit for diabetes medications, it is highly unlikely that deintensifying diabetes medications would contribute directly to increased rates of serious negative outcomes in the short-term. This is supported by the findings that the most common causes of ED visits or hospitalizations were similar and diabetes-related negative events such as hyperglycemia, hypoglycemia, and falls were very infrequently observed, regardless of whether residents had diabetes medications deintensified. Additionally, from a clinical perspective, the specific causes of ED visits, hospitalizations, and death were just as likely to be related to LLE/AD status or other comorbidities.

Our study has several strengths, including a large, national sample of veteran NH residents for whom detailed information on HbA$_{1c}$ and diabetes medications was available. We focused on a clinically relevant subgroup that is most likely to be targeted for deintensification or deprescribing, NH residents

near end of life. We used detailed data from VA electronic health records, including laboratory values and BCMA data, to identify potential overtreatment of diabetes and deintensification of medications. We were also able to report causes of negative events to determine whether they may have resulted from deintensification. Finally, we used state-of-the-art methods to balance potential confounding between residents who had medications deintensified and those who did not.

There are a few limitations that should be acknowledged. First, our findings may not be generalizable to all NH residents. Due to the makeup of the veteran population and small cell sizes, we were also unable to include women in our sample. We acknowledge the potential for misclassification by virtue of using an HbA$_{1c}$ measurement from a single point in time and also using gaps in medication administration data to define treatment deintensification without the opportunity for adjudication through chart review. We did not measure changes in insulin doses as part of deintensification. However, we believe that our definitions for deintensification were quite conservative, and sensitivity analyses with a longer definition for deintensification resulted in no substantive changes. It should be noted that prescribing patterns may have changed in the time since these data were collected, particularly for newer medications such as sodium–glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists that have lower risk of hypoglycemia and additional cardiovascular benefits. We were also unable to identify veterans with type 1 versus type 2 diabetes, as we cannot accurately distinguish between the two using claims and MDS data. It is possible that we underestimated the number of adverse outcomes, as we only measured events that resulted in a transition of care or death. We also observed a relatively small number of deaths, which may have resulted in unstable effect estimates and wide CIs, so our results should be interpreted cautiously. Finally, although we included a very comprehensive list of potential confounders, we recognize the potential for unmeasured confounding by factors not measurable in our data sources.

The present study sets the stage for future research. To our knowledge, no large randomized studies of diabetes deintensification are currently underway or planned. Additional observational or randomized studies could provide insight as to whether our findings are translatable to other NH populations who are at risk for hypoglycemic adverse events due to potential overtreatment. In future studies investigators should also evaluate whether deintensifying diabetes treatment regimens can improve quality of life or reduce health care costs due to avoidable treatment-related adverse events. Finally, studies are needed to determine the most effective strategies to increase adoption of deintensification practices in the NH setting.

Conclusion

Deintensification of diabetes treatment regimens was not associated with increased risk for 60-day ED visits, hospitalizations, or death among NH residents with AD/LLE. Treatment deintensification may be a reasonable strategy to reduce medication burden among those who may be overtreated for diabetes, in considering prognosis and goals of care. Additional observational and randomized studies are needed to determine whether these findings are generalizable to other populations.

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