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Use and Discontinuation of Insulin Treatment Among Adults Aged 75 to 79 Years With Type 2 Diabetes

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IMPORTANCE Among older individuals with type 2 diabetes, those with poor health have greater risk and derive less benefit from tight glycemic control with insulin.

OBJECTIVE To examine whether insulin treatment is used less frequently and discontinued more often among older individuals with poor health compared with those in good health.

DESIGN, SETTING, AND PARTICIPANTS This longitudinal cohort study included 21 531 individuals with type 2 diabetes followed for up to 4 years starting at age 75 years. Electronic health record data from the Kaiser Permanente Northern California Diabetes Registry was collected to characterize insulin treatment and glycemic control over time. Data were collected from January 1, 2009, through December 31, 2017, and analyzed from February 2, 2018, through June 30, 2019.

EXPOSURES Health status was defined as good (<2 comorbid conditions or 2 comorbidities but physically active), intermediate (>2 comorbidities or 2 comorbidities and no self-reported weekly exercise), or poor (having end-stage pulmonary, cardiac, or renal disease; diagnosis of dementia; or metastatic cancer).

MAIN OUTCOMES AND MEASURES Insulin use prevalence at age 75 years and discontinuation among insulin users over the next 4 years (or 6 months prior to death if <4 years).

RESULTS Of 21 531 patients, 10 396 (48.3%) were women, and the mean (SD) age was 75 (0) years. Nearly one-fifth of 75-year-olds (4076 [18.9%]) used insulin. Prevalence and adjusted risk ratios (aRRs) of insulin use at age 75 years were higher in individuals with poor health (29.4%; aRR, 2.03; 95% CI, 1.87-2.20; $P < .01$) and intermediate health (27.5%; aRR, 1.85; 95% CI, 1.74-1.97; $P < .01$) relative to good health (10.5% [reference]). One-third (1335 of 4076 [32.7%]) of insulin users at age 75 years discontinued insulin within 4 years of cohort entry (and at least 6 months prior to death). Likelihood of continued insulin use was higher among individuals in poor health (aRR, 1.47; 95% CI, 1.27-1.67; $P < .01$) and intermediate health (aRR, 1.16; 95% CI, 1.05-1.30; $P < .01$) compared with good health (reference). These same prevalence and discontinuation patterns were present in the subset with tight glycemic control (hemoglobin A_{1c} <7.0%).

CONCLUSIONS AND RELEVANCE In older individuals with type 2 diabetes, insulin use was most prevalent among those in poor health, whereas subsequent insulin discontinuation after age 75 years was most likely in healthier patients. Changes are needed in current practice to better align with guidelines that recommend reducing treatment intensity as health status declines.

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In the United States, type 2 diabetes affects more than 20% of adults older than 75 years,[1] yet there is little evidence to guide treatment decisions in older patients. Many of the landmark randomized clinical trials that established glycemic control targets for reducing the risk of microvascular and macrovascular complications excluded patients older than 75 years.[2,3] Subsequent follow-up of trial participants and observational studies have demonstrated that the benefits conferred by tight glycemic control may not be realized for 5 to 9 years,[4,5] a time period that may exceed many older adults' life expectancies. Moreover, adults older than 75 years are at the greatest risk of hypoglycemia, particularly when insulin is used.[6,7]

Professional societies have published guidelines based on clinical expertise and interpolation of the existing evidence. The American Diabetes Association (ADA), American Geriatrics Society, and the US Department of Veterans Affairs all recommend that healthier adults with longer life expectancies be treated to lower glycemic targets, whereas patients with poor health and shorter life expectancy to higher glycemic targets.[8-10] The American College of Physicians' newest guidelines[11] do not specify hemoglobin A_{1c} (HbA_{1c}) targets for adults with limited life expectancy; however, the organization recommends that treatment intensity be limited by symptoms of hyperglycemia with general goals of reducing burden of treatment. The unifying theme across these disparate guidelines is the recommendation to individualize treatment in older adults to balance risks and benefits of treatment.

None of these existing guidelines specifically address the use of insulin in older adults. While insulin may be necessary to achieve glycemic targets, it is also associated with dramatic increases in the risk of hypoglycemia in older adults—especially for those with multiple comorbidities.[12,13] Prior studies have raised concern for potential insulin overtreatment in older adults with poor health status and suggest medication deprescribing may be warranted.[14-19] However, these cross-sectional or short-term (follow-up, <1 year) analyses do not capture how insulin treatment may change over time.

Studying the longitudinal relationship between health status and insulin therapy in a real-world context can help inform future interventions, practice guidelines, and policy recommendations to reduce overtreatment of older adults with type 2 diabetes. We investigated the prevalence and predictors of insulin use in a large cohort of 75-year-old patients and assessed insulin discontinuation during the subsequent 4 years. We tested the hypothesis that adults with poor health would be more likely to discontinue insulin over a 4-year follow-up period after age 75 years.

Key Points

Question Is insulin treatment used less frequently and discontinued more often among older individuals with poor health compared with those in good health?

Findings In this cohort study of 21 531 adults, it was demonstrated that patients in poorer health were most likely to use insulin at age 75 years and that subsequent discontinuation of insulin use over a 4-year follow-up period was more common in healthier patients even after accounting for level of glycemic control.

Meaning Persistent insulin use among older adults with poor health is associated with increased risk for hypoglycemia and limited future health benefit; these results suggest a need to better align current practice with guidelines that support reducing treatment intensity as health status declines.

Methods

Study Design and Setting

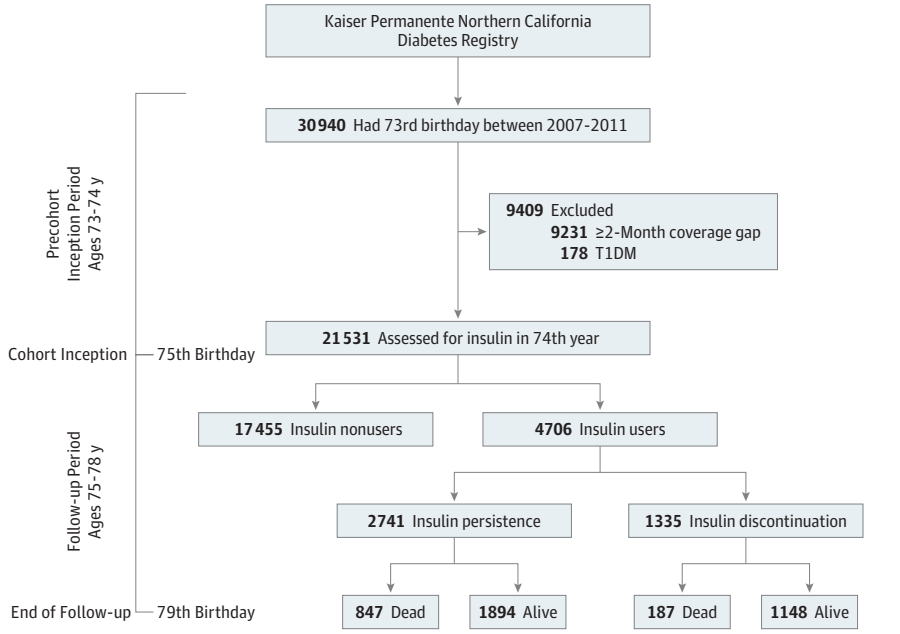
We conducted a longitudinal cohort study of individuals older than 75 years with type 2 diabetes who were members of Kaiser Permanente Northern California (KPNC), a large integrated health care delivery system that serves 4.2 million members. In this care system, members with type 2 diabetes older than 75 years are primarily managed by their primary care physicians. Individuals included in the study cohort were in the KPNC Diabetes Registry, turned 75 years of age between January 1, 2009, and December 31, 2013, and had no gaps 2 months or longer in health insurance coverage during the period from their 73rd birthday until their 79th birthday or death. The KPNC Diabetes Registry uses a validated algorithm that has been shown to be 99% sensitive and 99% specific in identifying members with diabetes.[20] Individuals with type 1 diabetes were excluded based on *International Classification of Diseases, Ninth Revision (ICD-9)* codes. We evaluated clinical characteristics of each member in the 2 years prior to cohort entry (ie, ages 73 and 74 years) and assessed outcomes for each member up to 4 years (through December 31, 2017) following cohort entry (ie, ages 75 to 79 years) or until death (**Figure 1**).

We compared individuals by insulin use at age 75 years (baseline cohort). In the subset of individuals who used insulin at baseline, we compared individuals who continued insulin vs those who discontinued insulin during the 4-year follow-up period (follow-up cohort). The KPNC Institutional Review Board approved the study and granted permission for a waiver of consent for study participants.

Clinical Measures

We collected standard demographic, diagnostic, medication, hospital use, and test result data directly from the electronic health record (EHR). Race and ethnicity information were collected by participant self-report and documented in the EHR. Because KPNC is an integrated health care delivery system with a single EHR, virtually all clinically relevant data (>98%) were available within the electronic record. Neighborhood deprivation index was computed using the American Community Survey data.[21,22] Baseline HbA_{1c}; body mass index, calculated as weight in kilograms divided by height in meters squared; and estimated glomerular filtration rate (eGFR) values were taken from the most recent results at the time of cohort entry. We categorized weight using body mass index categories based on Centers for Disease Control and Prevention definitions.[23] Chronic kidney disease stage was calculated based on the estimated glomerular filtration rate using a validated approach.[24,25] For the follow-up period, we report the

Figure 1. Flowchart of Cohort Formation and Outcome Assessment



T1DM indicates type 1 diabetes mellitus.

Figure 2. Cohort Health Status Definition Compared With American Diabetes Association (ADA) Guideline Definition

Status	Cohort Health Status Definition	ADA Guideline Health Status Definition
Good Health	0-1 Comorbidities 2 Comorbidities + any reported weekly exercise (comorbidities include CVD, stroke, retinopathy, CKD stage II-IV, COPD, and CHF)	0-2 Comorbidities with intact functional status (comorbidities include arthritis, cancer, CHF, depression, COPD, falls, HTN, urinary incontinence, CKD stage ≥3, MI, and stroke)
Intermediate Health	2 Comorbidities + reported no weekly exercise >2 Comorbidities Use of a walker	≥2 IADL impairments >2 Comorbidities Mild to moderate cognitive impairment
Poor Health	Any indicator of end-stage disease, including home oxygen use, metastatic cancer, and CKD stage V, including patients on hemodialysis Dementia	Any end-stage disease, including CHF stage III-IV, oxygen dependent, CKD with HD, and metastatic cancer Moderate to severe cognitive impairment or ≥2 ADL dependencies

ADL indicates activity of daily living; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; HTN, hypertension; IADL, instrumental activity of daily living; MI, myocardial infarction.

HbA_{1c} result preceding the last insulin prescription dispensed (ie, the last-measured HbA_{1c}). Because the ADA-recommended individualized HbA_{1c} targets for different populations based on health status do not have lower limits, we specified HbA_{1c} categories of less than 7.0% (53 mmol/mol), 7.0% to 8.4% (53-68 mmol/mol), and 8.5% or greater (69 mmol/mol) to define 3 mutually exclusive ranges. We defined baseline use of noninsulin medications as those medications dispensed from an outpatient pharmacy within 6 months of age 75 years. We gathered 2 functional status measures from the EHR: self-reported prior-week exercise (dichotomized as none vs any and collected at KPNC in a standardized intake form as part of routine clinical care), and prescription for a walker.

Health Status Category Definition

We defined health status corresponding to categories proposed by the ADA as a treatment framework,[8] which classifies older adults as having poor, intermediate, or relatively good health based on medical comorbidities, functional status measures, and cognitive impairment. A previous study applied this framework to categorize a sample of older adults from the National Health and Nutrition Examination Survey.[16] For this investigation, we adapted a modified version of the ADA health status categories to a large, real-world patient population using available data from the EHR (**Figure 2**).

We defined baseline health status categories at age 75 years using comorbidities (cardiovascular disease, stroke, diabetic retinopathy, chronic kidney disease, chronic obstructive pulmonary disease, and congestive heart failure), functional status (self-reported prior-week exercise and walker prescription), and indicators of end-stage disease (home oxygen use, metastatic cancer, diagnosis of dementia, or end-stage renal disease). We created 3 mutually exclusive health status groups that corresponded to ADA guidelines for individualizing HbA_{1c}

targets in older adults: good health (<2 comorbidities or 2 comorbidities with evidence of physical activity), intermediate health (>2 comorbidities or 2 comorbidities and no self-reported physical activity in the prior week or use of a walker), and poor health (any end-stage disease, regardless of number of comorbidities). In a validation analysis, we found that these categories aligned well with mortality rates (7.4% for good health, 21.4% for intermediate health, and 52.4% for poor health; $P < .01$) and hospitalization (31.7%, 55.0%, and 69.0%, respectively; $P < .01$) during the follow-up period.

Insulin Use and Discontinuation

We assessed insulin use at the time of cohort entry and for each 6-month period during the 4-year follow-up period. Prevalent insulin use at age 75 years was defined as having insulin dispensed from an outpatient pharmacy in both the first half and the second half of the 74th year of age. Among insulin users, the duration of insulin use at baseline was defined as the time between the first insulin prescription and 75th birthday. For our longitudinal analyses, we investigated insulin discontinuation over 4 years among the subset of 75-year-olds at cohort entry who were prevalent insulin users. Individuals were followed until the end of the cohort period (ie, age 79 years), insulin discontinuation, or death. Insulin discontinuation was defined as no insulin dispensed over 6 months. We chose a 6-month gap to allow for a grace period of roughly 3 months after the 3-month insulin supply ended (>95% of prescriptions were written for 100 days) based on a previously validated approach for detecting medication discontinuation using KPNC pharmacy data.[26] There is a closed pharmacy system at KPNC, ensuring that nearly all prescriptions are detected.[27]

We defined insulin persistence as no gaps greater than 6 months between insulin dispensings during the 4 years of cohort follow-up. Individuals who died within 6 months of their last insulin prescription were classified as insulin persistent, whereas those who died more than 6 months after their last insulin dispensing were classified as insulin discontinuers. In a sensitivity analysis using a 3-month gap in insulin dispensing instead of 6 months, the relationship between health status and insulin discontinuation was unchanged. Among insulin-persistent participants on both short-acting and long-acting insulin at baseline, we defined insulin regimen simplification as discontinuing short-acting insulin (eg, at least 6 months with no short-acting insulin dispensed) while maintaining the long-acting basal regimen.

Statistical Methods

In bivariate analyses, we used χ^2 tests, *t* tests, or nonparametric tests as appropriate. We assessed insulin use by the 3 mutually exclusive health status categories stratified by baseline HbA_{1c} category. To examine the independent association of health status with prevalent insulin use at age 75 years, we created a multivariate log-binomial regression that adjusted for demographic variables (including gender, race, and neighborhood deprivation index) and measures of diabetes status (baseline HbA_{1c} and diabetes duration).

In the longitudinal analysis in the subset of individuals taking insulin at age 75 years, we examined insulin discontinuation by the 3 mutually exclusive health status categories with a multivariate log-binomial model. We included the same baseline variables used in the prevalent insulin use model, with the exception of updating HbA_{1c} and health status categories to last measured values prior to censoring (ie, insulin discontinuation, death, or end of the follow-up period) and adding history of hypoglycemia defined as an inpatient or emergency department encounter with the primary diagnosis of hypoglycemia. In a sensitivity analysis excluding individuals with stage 4 or higher chronic kidney disease (who may have contraindications to alternative therapies such as metformin), the results did not notably change. All analyses were performed using SAS, 9.3 version (SAS Institute, Inc).

Results

Study Cohort

Our final analytic cohort included 21 531 individuals. Mean (SD) follow-up time was 3.7 (0.9) years. The cohort was demographically diverse, including 10 396 (48.3%) women. Mean (SD) diabetes duration was 9.4 (6.0) years (**Table 1**). At baseline, 11 041 patients, roughly half of the cohort (51.3%) were classified as having good health, 8632 (40.1%) as having intermediate health, and 1858 (8.6%) as having poor health.

Insulin Use at Age 75 Years

Nearly 1 in 5 patients (4076; 18.9%) used insulin in the year prior to turning 75 years old, and the mean (SD) duration of insulin use was 7.9 (5.5) years. Insulin use was associated with ethnicity/race, longer diabetes duration, higher baseline HbA_{1c}, and the presence of diabetes-related comorbidities (Table 1). Diagnosed dementia prevalence was not statistically significantly different between insulin users and nonusers. Insulin use was most common among those with poor health (547; 29.4%) compared with those in the intermediate health (2370; 27.5%) and good health groups (1159;10.5%) ($P < .01$). Differences in insulin use by health status persisted after stratifying by HbA_{1c} category (**Figure 3**A), with smaller proportions of patients with good health prescribed insulin at each of the 3 HbA_{1c} strata. In a multivariate model, patients with worse overall health status had increasingly greater likelihood of insulin use: intermediate health group adjusted risk ratio (aRR), 1.85 (95% CI, 1.74-1.97; $P < .01$) and poor health group aRR, 2.03 (95% CI, 1.87-2.20; $P < .01$), with good health as the reference (eTable 1 in the Supplement).

Insulin Use Discontinuation After Age 75 Years

One-third of patients (1335 of 4076 [32.7%]) using insulin at age 75 years discontinued insulin during the 4-year follow-up period, and insulin regimens were simplified in only 7.9% (321 of 4076) of patients. The mean (SD) time to discontinuation was 1.6 (1.2) years. In contrast with insulin use at age 75 years, prevalent microvascular and macrovascular diabetes-related complications were not associated with likelihood of insulin discontinuation after age 75 years. Insulin discontinuation was significantly more prevalent among patients with a last-measured HbA_{1c} 7.0% or less (**Table 2**). Depression was asso-

Table 1. Individual Characteristics by Insulin Use at Age 75 Years[a]

Characteristic	No (%)			P Value
	Total (N = 21 531)	Insulin Users (n = 4076)	Insulin Nonusers (n = 17 455)	
Women	10 396 (48.3)	2022 (49.6)	8374 (48.0)	.12
Race				
White	10 628 (49.4)	2064 (50.7)	8564 (49.2)	<.01
Latino	3850 (17.9)	829 (20.4)	3021 (17.3)	
Asian	3091 (14.4)	403 (9.9)	2688 (15.4)	
Black	2035 (9.5)	491 (9.8)	1634 (9.4)	
Other	1886 (8.8)	376 (9.2)	1510 (8.7)	
Neighborhood Deprivation Index quartile[b]				
Q3 or Q4 (most deprived)	10 051 (47.3)	1963 (48.9)	8088 (47.0)	.03
BMI ≥ 30 kg/m^2	9453 (44.9)	2316 (57.0)	7137 (41.3)	<.01
Diabetes duration, mean (SD), y	9.4 (6.0)	14.5 (5.4)	8.2 (5.5)	<.01
Diabetes duration <10 y	11871 (55.1)	858 (21.1)	11 013 (63.1)	<.01
HbA_{1c} at age 75 y, mean (SD)	7.0 (1.1)	7.6 (1.3)	6.8 (1.0)	<.01
HbA_{1c} strata at age 75 y				
<7.0%	12 522 (59.4)	1330 (32.9)	11 192 (65.8)	<.01
7.0%-8.4%	6855 (32.6)	1957 (48.2)	4898 (28.8)	
≥8.5%	1687 (8.0)	766 (18.9)	921 (5.4)	
Diabetic retinopathy	4884 (22.7)	2121 (52.0)	2763 (15.8)	<.01
Diabetic neuropathy	6811 (31.6)	2196 (53.9)	4615 (26.4)	<.01
Chronic kidney disease				
Stage 0-2	14 810 (69.4)	2078 (51.1)	12 732 (73.7)	<.01
Stage 3a-3b	5712 (26.8)	1612 (39.5)	4100 (23.8)	
Stage 4-5 (including ESRD)	826 (3.9)	381 (9.4)	445 (2.5)	
Cardiovascular disease	10 714 (49.8)	2662 (65.3)	8052 (46.1)	<.01
Stroke	1463 (6.8)	420 (10.3)	1043 (6.0)	<.01
Congestive heart failure	3199 (14.9)	1080 (26.5)	2119 (12.1)	<.01
COPD	2758 (12.8)	642 (15.8)	2116 (12.1)	<.01
Depression	3094 (14.4)	802 (19.7)	2292 (13.1)	<.01
Dementia	662 (3.1)	129 (3.2)	533 (3.1)	.71
Medication use				
Insulin use	4076 (18.9)	4076 (100)	0	<.01
Long acting and short acting	2205 (10.0)	2205 (54.1)	0	
Long acting	1702 (7.9)	1702 (41.8)	0	
Short acting	169 (0.9)	169 (4.1)	0	
Metformin	9619 (44.7)	1413 (34.7)	8206 (47.0)	<.01
Sulfonylurea	8499 (34.5)	1487 (36.5)	7012 (40.2)	<.01
ACE inhibitors	8831 (41.0)	1776 (43.6)	7055 (40.4)	<.01
Statins	17 302 (80.0)	3490 (85.6)	13 812 (79.1)	<.01
Functional status				
Prescription for a walker	1658 (7.7)	464 (11.1)	1194 (6.8)	<.01
Self-reported weekly exercise	9439 (49.9)	1468 (41.9)	7971 (51.1)	<.01

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; COPD, chronic obstructive pulmonary disease; ESRD, end stage renal disease; HbA_{1c}, hemoglobin A_{1c}.

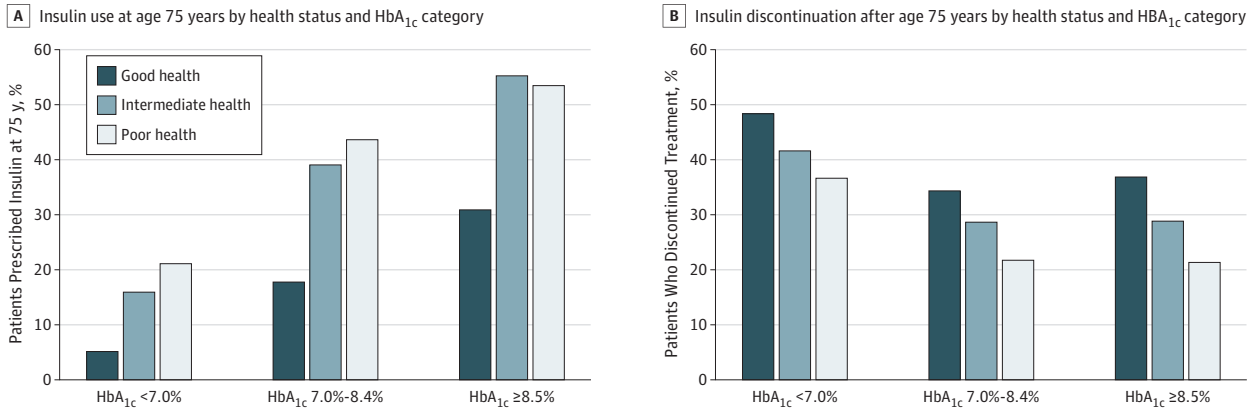
[a] Numbers are column percentages except where noted to be means (SD). Column percentages add up to less than 100% for some variables owing to missing data (<2%).

[b] Neighborhood Deprivation Index is defined using data from the US Census Bureau's American Community Survey from 2006 through 2010 with 5-year estimates divided into quartiles.

ciated with increased insulin discontinuation (288 of 1335 [21.6%] vs 514 of 2741 [18.8%]; $P = .03$).

Insulin discontinuation during the follow-up period was greatest among patients with good health (306 of 787 [38.9%]), followed by intermediate health (778 of 2380 [32.7%]), and poor health (251 of 909 [27.6%]) ($P < .01$). By contrast, insulin regimen simplification was most common among those with poor health (99 of 909 [10.9%] vs 185 of 2380 [7.8%] for intermediate health and 37 of 787 [4.7%] for good health; $P<.01$). In a multivariate model, likelihood of continued insulin use was higher among individuals in poor health (aRR, 1.47; 95% CI, 1.27-1.67; $P < .01$) and intermediate health (aRR, 1.16; 1.05-1.30; $P < .01$) compared with good health (reference). These same prevalence and discontinuation patterns were present in the subset with tight glycemic control (HbA_{1c} <7.0%) (Figure 3B). Diabetes duration less than 10 years, HbA_{1c} less than 7.0%, and use of long-acting insulin (reference, combination) were independently associated with insulin discontinuation (eTable 2 in the Supplement).

Figure 3. Insulin Use at Baseline and Insulin Use Discontinuation After Age 75 Years by Health Status and Hemoglobin A_{1c} Category



A, Bars are grouped into sets of 3 based on hemoglobin A_{1C} (HbA_{1c}) level measured at baseline. B, Bars are grouped into sets of 3 based on HbA_{1c} level measured prior to most recent insulin dispensing. Health status was measured prior to censorship (ie, end of cohort, discontinuation, or death).

Discussion

Existing guidelines recommend individualizing glycemic targets based on health status but do not make specific recommendations about insulin use. We studied the prevalence of insulin use and discontinuation among a cohort of 75-year-olds with type 2 diabetes to test the hypothesis that older adults with poor health would be less likely to use insulin and be more likely to discontinue insulin over time. We found that nearly 1 in 5 individuals were receiving insulin therapy at age 75 years. Insulin use was most prevalent among those in poor health, whereas subsequent insulin discontinuation after age 75 years was most likely in healthier patients, even after accounting for level of glycemic control.

The results of this study suggest that neither prevalent insulin use nor subsequent insulin discontinuation among older patients is closely aligned with current recommendations to incorporate health status (in conjunction with life expectancy and patient preferences) when making treatment decisions. These patterns remained evident even when accounting for level of glycemic control. For example, we would expect to find less insulin discontinuation among relatively healthy patients with poor glycemic control (HbA_{1c} ≥8.5%) relative to less healthy patients because these healthier patients are more likely to realize long-term clinical benefit with the tighter control that would be expected from continuing insulin therapy. However, Figure 3B demonstrates that discontinuation follows the opposite pattern: patients with poor health are least likely to discontinue insulin.

Also shown in Figure 3B is the higher prevalence of insulin discontinuation among patients with good health and tight glycemic control (HbA_{1c} <7.0%) relative to patients in intermediate or poor health. Here, the clinical question relates to insulin discontinuation, sometimes described as deprescribing in the recent literature.[28-30] Deprescribing potentially harmful medicines, such as insulin, when the risks outweigh the benefits represents a novel and potentially robust strategy for reducing adverse events and improving quality of individualized care in older patients. The observed pattern of insulin discontinuation in the present study runs contrary to what we would expect to find based on ADA and other guideline recommendations that suggest relaxed glycemic control in adults with poor health status.

Clinicians have reported barriers to deprescribing related to the lack of evidence to guide decisions, lack of time for informed shared decision-making conversations, and concerns that patients may feel like their care is being diminished.[31-33] Recent nationally weighted survey data of Medicare beneficiaries, in contrast, indicate that two-thirds of older patients wanted to reduce the total number of medicines they were taking, and most (92%) would be willing to stop a medicine if recommended by their provider.[34] Although this survey was not specific to insulin, the results indicate that the opportunity for safe deprescribing exists. Given the well-documented and severe clinical consequences of iatrogenic hypoglycemia in older patients on insulin, the results of the present study suggest that efforts to define and implement insulin deprescribing guidelines in high-risk patients will likely be applicable to a substantial proportion of older patients with tight glycemic control despite poor health status and limited life expectancy.

Existing medication deprescribing guidelines provide frameworks for prescribers to contemplate deintensification but do not necessarily provide practical recommendations to implement this process into everyday practice. A recent review of medication deintensification tools noted that only 4 of 15 published guidelines were medication specific, 1 of 15 pertained to antihyperglycemic medicines, and none had high or moderate quality evidence supporting them.[35] To date a small, single-arm trial of 65 patients testing the efficacy of an insulin deintensification algorithm has been performed,[36] and more trials are needed to provide clinicians with practical tools and protocols to reduce the use of high-risk, low-benefit medications.

In contrast with insulin discontinuation, we found that insulin regimen simplification (eg, from long-acting and

Table 2. Individual Characteristics by Insulin Use Discontinuation After Age 75 Years[a]

Characteristic	No (%)			*P* Value
	Total (N = 4076)	Insulin Persistent (n = 2741)	Insulin Discontinued (n = 1335)	
Women	2022 (49.6)	1320 (48.2)	702 (52.6)	<.01
Race				
White	2064 (50.6)	1453 (53.0)	611 (45.8)	<.01
Latino	829 (20.3)	538 (19.6)	291 (21.8)	
Asian	403 (9.9)	269 (9.8)	134 (10.0)	
Black	401 (9.8)	248 (9.1)	153 (11.5)	
Other	376 (9.2)	231 (8.4)	145 (10.9)	
Neighborhood Deprivation Index quartile[b]				
Q3 or Q4 (most deprived)	1963 (48.9)	1298 (47.9)	665 (50.8)	.09
BMI ≥30 kg/m^2	2316 (57.0)	1596 (58.4)	720 (54.3)	.09
Diabetes duration, mean (SD), y	14.5 (5.4)	14.8 (5.3)	14.1 (5.6)	<.01
Diabetes duration <10 y	858 (21.1)	534 (19.5)	324 (24.3)	<.01
Insulin duration <10 y	2665 (65.4)	1736 (63.3)	929 (69.6)	<.01
Last measured HbA_{1c} %, mean (SD)	7.7 (1.4)	7.8 (1.3)	7.5 (1.4)	<.01
Last-measured HbA_{1c} strata				
<7.0%	1249 (30.6)	729 (26.6)	520 (38.9)	<.01
7.0%-8.4%	1904 (46.7)	1358 (49.5)	546 (40.9)	
≥8.5%	923 (22.6)	654 (23.9)	269 (20.2)	
Diabetic retinopathy	2121 (52.0)	1436 (52.4)	685 (51.3)	.52
Diabetic neuropathy	2196 (53.9)	1483 (54.1)	713 (53.4)	.68
Chronic kidney disease				
Stage 0-2	2078 (51.0)	1378 (50.3)	700 (52.6)	.10
Stage 3a-3b	1612 (39.6)	1110 (40.6)	502 (37.7)	
Stage 4-5 (including ESRD)	381 (9.4)	250 (9.1)	131 (9.8)	
Cardiovascular disease	2662 (65.3)	1782 (65.0)	880 (65.9)	.57
Stroke	420 (10.3)	269 (9.8)	151 (11.3)	.14
Congestive heart failure	1080 (26.5)	740 (27.0)	340 (25.5)	.30
COPD	642 (15.8)	454 (16.6)	188 (14.1)	.04
Depression	802 (19.7)	514 (18.8)	288 (21.6)	.03
Dementia	129 (3.2)	82 (3.0)	47 (3.5)	.37
Medication use				
Insulin use at age 75 y				<.01
Long acting and short acting	2205 (54.1)	1601 (58.4)	604 (45.2)	
Long acting	1702 (41.8)	1046 (38.2)	656 (49.1)	
Short acting	169 (4.1)	94 (3.4)	75 (5.6)	
Metformin	1358 (33.3)	893 (43.3)	465 (46.1)	.14
Sulfonylurea	1487 (36.5)	986 (36.0)	501 (37.5)	.33
ACE inhibitors	1776 (43.6)	1185 (43.2)	591 (44.3)	.53
Statins	3490 (85.6)	2358 (86.0)	1132 (84.8)	.29
Functional status				
Prescription for walker	464 (11.4)	303 (11.1)	161 (12.1)	.34
Self-reported weekly exercise	1468 (36.0)	990 (41.9)	478 (40.2)	.32

Abbreviations:
ACE, angiotensin-converting enzyme; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; COPD, chronic obstructive pulmonary disease; ESRD, end stage renal disease; HbA_{1c}, hemoglobin A_{1c}.

[a] Numbers are column percentages except where noted to be means (SD). Column percentages add up to less than 100% for some variables owing to missing data (<2%).

[b] Neighborhood Deprivation Index is defined using data from the US Census Bureau's American Community Survey from 2006 through 2010 with 5-year estimates divided into quartiles.

short-acting insulin use to long-acting alone) was relatively uncommon (prevalence, 7.9%) but was more frequent in patients with poor health. This finding underscores the clinical utility of insulin regimen simplification to reduce hypoglycemia risk in certain situations when clinicians or patients are less willing to discontinue insulin. For example, patients with long-standing diabetes may become insulin-dependent owing to progressive beta-cell dysfunction.[37] Indeed, we found that characteristics indicative of reduced beta-cell function, such as longer diabetes duration and use of both long-acting and short-acting insulin, predicted insulin persistence. Patients with renal insufficiency may have contraindications to noninsulin medications, and their HbA_{1c} may be artificially low, which makes clinical decisions about insulin use more challenging. In these situations, insulin regimen simplification may allow clinicians to pri-

oritize practical aspects of diabetes management while also reducing risk of iatrogenic hypoglycemia.

Limitations

The results of this study must be interpreted in the context of the study design. First, the observational design precludes any definitive inference about causality. However, the cohort had few exclusion criteria and likely represents the general population better than that of a clinical trial. Second, we studied an insured population in an integrated health system, which may limit generalizability, but using the KPNC closed pharmacy system allowed us to capture near-complete insulin prescribing information. Third, without being present with patients, we are unable to evaluate the discussion (or lack thereof) that informed the decision to continue or discontinue insulin therapy in this older, higher-risk patient population. Rather, we provide a population-level perspective of the scope of insulin use in different older patient subgroups. Further work is now needed that can inform system-level efforts to guide safer and more standardized insulin continuation, discontinuation, and simplification frameworks for older patients. Fourth, because we measured insulin dispensing rather than insulin ordering, we were unable to determine whether insulin discontinuation was because of the clinician (ie, stopped prescribing insulin) or patient (ie, stopped picking up prescriptions). This measure has the advantage of capturing true discontinuation but requires further research to better understand the role of clinician vs patient in the discontinuation process. Fifth, despite robust pharmacy data, we were unable to examine insulin dose reductions because doses are not reliably captured in prescription information in the pharmacy data. Finally, the health status classification scheme used EHR data and was susceptible to underrepresentation of medical comorbidities such as dementia, a condition often underdiagnosed.[38] Nonetheless, this approach was empirically validated by the strong association of worse health status with death and hospitalizations.

Conclusions

As the population with type 2 diabetes continues to age, there is a growing need for evidence-based treatment strategies related specifically to the use of insulin for these older patients. We found that the older adults in poorest health were most likely to use insulin and that subsequent insulin discontinuation was most common among healthier individuals. The substantial and persistent insulin use among older adults with a high risk of hypoglycemia and limited future benefit suggests that more work is needed to develop systems-based approaches that support guideline-concordant insulin use in people older than 75 years.

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REFERENCES

1. Centers for Disease Control and Prevention. United States Diabetes Surveillance System. https://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html. Accessed August 14, 2018.

2. Gerstein HC, Miller ME, Byington RP, et al; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med*. 2008;358(24):2545-2559. doi:10.1056/NEJMoa0802743

3. Patel A, MacMahon S, Chalmers J, et al; ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2008;358(24):2560-2572. doi:10.1056/NEJMoa0802987

4. Lipska KJ, Krumholz H, Soones T, Lee SJ. Polypharmacy in the aging patient: a review of glycemic control in older adults with type 2 diabetes. *JAMA*. 2016;315(10):1034-1045. doi:10.1001/jama.2016.0299

5. Huang ES, Laiteerapong N, Liu JY, John PM, Moffet HH, Karter AJ. Rates of complications and mortality in older patients with diabetes mellitus: the diabetes and aging study. *JAMA Intern Med*. 2014;174(2):251-258. doi:10.1001/jamainternmed.2013.12956

6. ORIGIN Trial Investigators. Predictors of nonsevere and severe hypoglycemia during glucose-lowering treatment with insulin glargine or standard drugs in the ORIGIN trial. *Diabetes Care*. 2015;38(1):22-28. doi:10.2337/dc14-1329

7. Bruderer SG, Bodmer M, Jick SS, Bader G, Schlienger RG, Meier CR. Incidence of and risk factors for severe hypoglycaemia in treated type 2 diabetes mellitus patients in the UK: a nested case-control analysis. *Diabetes Obes Metab*. 2014;16(9):801-811. doi:10.1111/dom.12282

8. American Diabetes Association. 11. Older Adults: *Standards of Medical Care in Diabetes—2018*. *Diabetes Care*. 2018;41(suppl 1):S119-S125. doi:10.2337/dc18-S011

9. Moreno G, Mangione CM, Kimbro L, Vaisberg E; American Geriatrics Society Expert Panel on Care of Older Adults with Diabetes Mellitus. Guidelines abstracted from the American Geriatrics Society Guidelines for Improving the Care of Older Adults With Diabetes Mellitus: 2013 update. *J Am Geriatr Soc*. 2013;61(11):2020-2026. doi:10.1111/jgs.12514

10. Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care. https://www.healthquality.va.gov/guidelines/CD/diabetes/VADoDDMCPGFinal508.pdf. Published April 2017. Accessed August 14, 2018.

11. Qaseem A, Wilt TJ, Kansagara D, Horwitch C, Barry MJ, Forciea MA; Clinical Guidelines Committee of the American College of Physicians. Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: a guidance statement update from the American College of Physicians. *Ann Intern Med*. 2018;168(8):569-576. doi:10.7326/M17-0939

12. Lipska KJ, Yao X, Herrin J, et al. Trends in drug utilization, glycemic control, and rates of severe hypoglycemia, 2006-2013. *Diabetes Care*. 2017;40(4):468-475. doi:10.2337/dc16-0985

13. Pathak RD, Schroeder EB, Seaquist ER, et al. Severe hypoglycemia requiring medical intervention in a large cohort of adults with diabetes receiving care in U.S. integrated health care delivery systems: 2005-2011. *Diabetes Care*. 2016;39(3):363-370. doi:10.2337/dc15-0858

14. Lee SJ. So much insulin, so much hypoglycemia. *JAMA Intern Med*. 2014;174(5):686-688. doi:10.1001/jamainternmed.2013.13307

15. Tseng CL, Soroka O, Maney M, Aron DC, Pogach LM. Assessing potential glycemic overtreatment in persons at hypoglycemic risk. *JAMA Intern Med*. 2014;174(2):259-268. doi:10.1001/jamainternmed.2013.12963

16. Lipska KJ, Ross JS, Miao Y, Shah ND, Lee SJ, Steinman MA. Potential overtreatment of diabetes mellitus in older adults with tight glycemic control. *JAMA Intern Med*. 2015;175(3):356-362. doi:10.1001/jamainternmed.2014.7345

17. Arnold SV, Lipska KJ, Wang J, Seman L, Mehta SN, Kosiborod M. Use of intensive glycemic management in older adults with diabetes mellitus. *J Am Geriatr Soc*. 2018;66(6):1190-1194. doi:10.1111/jgs.15335

18. Sussman JB, Kerr EA, Saini SD, et al. Rates of deintensification of blood pressure and glycemic medication treatment based on levels of control and life expectancy in older patients with diabetes mellitus. *JAMA Intern Med*. 2015;175(12):1942-1949. doi:10.1001/jamainternmed.2015.5110

19. Thorpe CT, Gellad WF, Good CB, et al. Tight glycemic control and use of hypoglycemic medications in older veterans with type 2 diabetes and comorbid dementia. *Diabetes Care*. 2015;38(4):588-595.

20. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in Pacific Islanders and Asian subgroups: the Diabetes Study of Northern California (DISTANCE). *Diabetes Care*. 2013;36(3):574-579. doi:10.2337/dc12-0722

21. Messer LC, Laraia BA, Kaufman JS, et al. The development of a standardized neighborhood deprivation index. *J Urban Health*. 2006;83(6):1041-1062. doi:10.1007/s11524-006-9094-x

22. Stoddard PJ, Laraia BA, Warton EM, et al. Neighborhood deprivation and change in BMI among adults with type 2 diabetes: the Diabetes Study of Northern California (DISTANCE). *Diabetes Care*. 2013;36(5):1200-1208. doi:10.2337/dc11-1866

23. Centers for Disease Control and Prevention. Defining adult overweight and obesity. https://www.cdc.gov/obesity/adult/defining.html. Updated April 11, 2017. Accessed August 7, 2018.

24. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612. doi:10.7326/0003-4819-150-9-200905050-00006

25. Campbell KH, Huang ES, Dale W, et al. Association between estimated GFR, health-related quality of life, and depression among older adults with diabetes: the Diabetes and Aging Study. *Am J Kidney Dis*. 2013;62(3):541-548. doi:10.1053/j.ajkd.2013.03.039

26. Parker MM, Moffet HH, Adams A, Karter AJ. An algorithm to identify medication nonpersistence using electronic pharmacy databases. *J Am Med Inform Assoc*. 2015;22(5):957-961. doi:10.1093/jamia/ocv054

27. Karter AJ, Moffet HH, Liu J, et al. Glycemic response to newly initiated diabetes therapies. *Am J Manag Care*. 2007;13(11):598-606.

28. Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. Review of deprescribing processes and development of an evidence-based, patient-centred deprescribing process. *Br J Clin Pharmacol*. 2014;78(4):738-747. doi:10.1111/bcp.12386

29. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med*. 2015;175(5):827-834. doi:10.1001/jamainternmed.2015.0324

30. Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice. *Br J Clin Pharmacol*. 2015;80(6):1254-1268. doi:10.1111/bcp.12732

31. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. *BMJ Open*. 2014;4(12):e006544. doi:10.1136/bmjopen-2014-006544

32. Anderson K, Foster M, Freeman C, Luetsch K, Scott I. Negotiating "unmeasurable harm and benefit": perspectives of general practitioners and consultant pharmacists on deprescribing in the primary care setting. *Qual Health Res*. 2017;27(13):1936-1947. doi:10.1177/1049732316687732

33. Wallis KA, Andrews A, Henderson M. Swimming against the tide: primary care physicians' views on deprescribing in everyday practice. *Ann Fam Med*. 2017;15(4):341-346. doi:10.1370/afm.2094

34. Reeve E, Wolff JL, Skehan M, Bayliss EA, Hilmer SN, Boyd CM. Assessment of attitudes toward deprescribing in older Medicare beneficiaries in the United States. *JAMA Intern Med*. 2018;178(12):1673-1680. doi:10.1001/jamainternmed.2018.4720

35. Thompson W, Lundby C, Graabaek T, et al. Tools for deprescribing in frail older persons and those with limited life expectancy: a systematic review. *J Am Geriatr Soc*. 2019;67(1):172-180. doi:10.1111/jgs.15616

36. Munshi MN, Slyne C, Segal AR, Saul N, Lyons C, Weinger K. Simplification of insulin regimen in older adults and risk of hypoglycemia. *JAMA Intern Med*. 2016;176(7):1023-1025. doi:10.1001/jamainternmed.2016.2288

37. Fonseca VA. Defining and characterizing the progression of type 2 diabetes. *Diabetes Care*. 2009;32(suppl 2):S151-S156. doi:10.2337/dc09-S301

38. Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ Open*. 2017;7(2):e011146. doi:10.1136/bmjopen-2016-011146