Rates of Deintensification of Blood Pressure and Glycemic Medication Treatment Based on Levels of Control and Life Expectancy in Older Patients With Diabetes Mellitus

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IMPORTANCE Older patients with diabetes mellitus receiving medical treatment whose blood pressure (BP) or blood glucose level are potentially dangerously low are rarely deintensified. Given the established risks of low blood pressure and blood glucose, this is a major opportunity to decrease medication harm.

OBJECTIVE To examine the rate of BP- and blood glucose–lowering medicine deintensification among older patients with type 1 or 2 diabetes mellitus who potentially receive overtreatment.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study conducted using data from the US Veterans Health Administration. Participants included 211 667 patients older than 70 years with diabetes mellitus who were receiving active treatment (defined as BP-lowering medications other than angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, or glucose-lowering medications other than metformin hydrochloride) from January 1 to December 31, 2012. Data analysis was performed December 10, 2013, to July 20, 2015.

EXPOSURES Participants were eligible for deintensification of treatment if they had low BP or a low hemoglobin A1c (HbA1c) level in their last measurement in 2012. We defined very low BP as less than 120/65 mm Hg, moderately low as systolic BP of 120 to 129 mm Hg or diastolic BP (DBP) less than 65 mm Hg, very low HbA1c as less than 6.0%, and moderately low HbA1c as 6.0% to 6.4%. All other values were not considered low.

MAIN OUTCOMES AND MEASURES Medication deintensification, defined as discontinuation or dosage decrease within 6 months after the index measurement.

RESULTS The actively treated BP cohort included 211 667 participants, more than half of whom had moderately or very low BP levels. Of 104 486 patients with BP levels that were not low, treatment in 15.1% was deintensified. Of 25 955 patients with moderately low BP levels, treatment in 16.0% was deintensified. Among 81 226 patients with very low BP levels, 18.8% underwent BP medication deintensification. Of patients with very low BP levels whose treatment was not deintensified, only 0.2% had a follow-up BP measurement that was elevated (BP \(\geq\)140/90 mm Hg). The actively treated HbA1c cohort included 179 991 participants. Of 143 305 patients with HbA1c levels that were not low, treatment in 17.5% was deintensified. Of 23 769 patients with moderately low HbA1c levels, treatment in 20.9% was deintensified. Among 12 917 patients with very low HbA1c levels, 27.0% underwent medication deintensification. Of patients with very low HbA1c levels whose treatment was not deintensified, fewer than 0.8% had a follow-up HbA1c measurement that was elevated (\(\geq\)7.5%).

CONCLUSIONS AND RELEVANCE Among older patients whose treatment resulted in very low levels of HbA1c or BP, 27% or fewer underwent deintensification, representing a lost opportunity to reduce overtreatment. Low HbA1c or BP values or low life expectancy had little association with deintensification events. Practice guidelines and performance measures should place more focus on reducing overtreatment through deintensification.
Clinical practice guidelines and quality of care initiatives for glucose and blood pressure (BP) control have long focused on intensifying therapy to achieve target risk factor levels, such as reducing hemoglobin A₁c (HbA₁c) levels to less than 7.0% and BP levels to under 140/90 mm Hg. As a result of this focus on medication intensification, undertreatment has decreased dramatically.¹,² Unfortunately, the same focus has also likely led to substantial overtreatment.³⁻⁷

Such overtreatment is not harmless. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, providing treatment for patients with diabetes mellitus to achieve a target systolic BP (SBP) of less than 120 mm Hg increased the rate of serious adverse events,⁶ and treating to a target HbA₁c level of 6.0% increased all-cause mortality.⁷ Overtreatment is common even in older, medically complex patients, in whom it can be especially dangerous.⁸⁻¹¹ The most recent guidelines of the American Diabetes Association and the American Geriatrics Society, as well as the American Board of Internal Medicine’s Choosing Wisely campaign,¹²⁻¹⁴ have started to acknowledge the harms of overtreatment resulting in very low BP and HbA₁c levels. The new guidelines and the Choosing Wisely campaign specifically recommend less aggressive treatment for older patients and those with limited life expectancy, such as a target HbA₁c level of 7.5% or 8.0%. The report from the panel members appointed to the Eighth Joint National Committee¹⁵ now recommends treatment in older patients to achieve an SBP level below 150 mm Hg—no longer to a level below 140 mm Hg.

To meet these new goals, many patients will need to discontinue medications within their present regimen. This process of medication deintensification may be difficult. From the patients’ perspective, deintensifying treatment could mean moving away from goals that they had worked hard to reach for many years. For health care professionals, promoting deintensification means informing patients that previously recommended treatments are no longer useful; this alteration could also worsen health care professionals’ performance assessments on profiles that continue to promote tight BP and glucose level control for many patients. There are no specific recommendations on deintensifying treatment.

We know little about the process of medication deintensification, including how often it happens or for whom. Therefore, we describe the frequency of treatment deintensification among older patients with diabetes mellitus who are potentially receiving overtreatment and examine whether patients with limited life expectancy (the people who are least likely to benefit) are more likely to undergo medication deintensification.

Methods

Study Population

We used the Corporate Data Warehouse from the Department of Veterans Affairs (VA) to construct 2 cohorts: one to assess blood glucose medication deintensification and the other to assess BP medication deintensification. The cohorts included all active primary care patients 70 years or older with a diagnosis of diabetes mellitus who were receiving active treatment for elevated glucose level control or BP control between January 1 and December 31, 2012.⁴ Diabetes mellitus was defined using previously published methods.⁴ Patients in the BP cohort had at least 1 BP measurement and primary care appointment on the same day in 2012, and those in the HbA₁c cohort had at least 1 HbA₁c measurement in 2012. The index BP or HbA₁c was the last measurement in 2012. We included all VA clinics in which primary care services are delivered. We excluded patients who died within 180 days of their index measurement. The Ann Arbor VA Human Studies Committee approved this study with a waiver of informed consent.

We defined a patient receiving active medical therapy for BP control as having prescriptions for hypertension medications other than low-dose angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. We excluded these patients because these drugs are often appropriately prescribed for renal protection in patients with diabetes mellitus rather than exclusively for BP. Active medical therapy for blood glucose level control was defined as receiving treatment with any diabetes medication other than metformin hydrochloride. We excluded treatment with metformin alone because this drug usually does not cause hypoglycemia and may have clinical benefits apart from lowering HbA₁c, including possible direct cardiovascular benefits.¹⁶

Patients with diagnoses of congestive heart failure or cirrhosis were excluded from the low BP cohort since there are reasons for antihypertensive treatment for these conditions even in the presence of low BP. These exclusions were made to conservatively ensure that we studied individuals who would most likely benefit from deintensification.

Variable Construction and Definition

We stratified each cohort based on their index BP or HbA₁c level. For BP, we defined very low as an SBP less than 120 mm Hg or a diastolic BP (DBP) less than 65 mm Hg, moderately low as an SBP of 120 to 129 mm Hg or a DBP less than 65 mm Hg, not low as an SBP of 130 mm Hg or greater and a DBP of 65 mm Hg or greater, and high as an SBP of 140 mm Hg or greater or a DBP of 90 mm Hg or greater. For HbA₁c, we defined very low as less than 6.0%, moderately low as 6.0% to 6.4%, not low as 6.5% or greater, and high as greater than 7.5%. Safe was defined as all values that are neither low nor high.

The cut points chosen to define our very low BP and blood glucose level groups were based on the ACCORD randomized trial¹⁷ of diabetes mellitus treatment as well as other studies⁶⁻¹⁸ documenting adverse consequences of low DBP. The ACCORD trial found that treatment resulting in an SBP less than 120 mm Hg or HbA₁c less than 6.0% increased adverse events and all-cause mortality, respectively, in a population of patients who were substantially younger and healthier than those in our cohorts.

The cut points chosen to define our moderately low BP and blood glucose-level groups were selected because they were substantially lower than recommendations of clinical practice guidelines.¹²⁻¹⁵,¹⁹ These cut points are within the range for which there is an absence of evidence of benefit.¹⁵,²⁰ Patients receiving active treatment who were experiencing very low or moderately low levels of HbA₁c or BP were considered to be receiving potential overtreatment. The values for high BP and HbA₁c were based on clinical practice guidelines of the time.

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The VA guidelines recommended an HbA1c level less than 8.0%; thus, our choice of less than 7.5% was more conservative with respect to our study question.

Our primary outcome was the percentage of patients receiving potential overtreatment who underwent medication deintensification. In brief, therapy was considered to have been deintensified if the patients did not have a refill of a previously prescribed BP- or HbA1c-lowering medication for 180 days after the index measurement or if their next medication refill after the index measurement was at a lower dose. Details on our definition of deintensification are available in the eAppendix and eFigure 1 in the Supplement. We did not have dosage information on insulin; therefore, an insulin deintensification event required stopping at least one type of insulin.

Comorbidity was measured with the Deyo et al adaptation21,22 of the Charlson Comorbidity Index and derived from VA administrative data. We estimated patients' remaining life expectancy using a technique based on the patient's age and his or her Charlson-Deyo score.23 In this technique, patients aged 70 to 79 years with a Charlson-Deyo score of 0 are recognized to have a life expectancy of more than 10 years, those aged 70 to 84 years with a Charlson-Deyo score of 1 to 3 or those aged 80 years or older with a Charlson-Deyo score of 0 have a life expectancy of 5 to 10 years, and patients aged 70 to 84 years with a Charlson-Deyo score of 4 or more or those who are 85 years or older whose score is 1 or more have a life expectancy of less than 5 years.

Statistical Analysis
After defining the cohorts, we stratified them based on the defined BP and HbA1c cut points and then on whether the patients underwent deintensification of treatment. For patients who did not receive deintensification, we used the next available BP and HbA1c measurements within 6 months of the index visit to describe how many patients had a follow-up value that was persistently very low or moderately low and could therefore still prompt deintensification, those whose value entered a range that could be considered to be high (conservatively defined as a BP ≥140/90 mm Hg or an HbA1c level ≥7.5%), and those whose BP or HbA1c level entered a safe “in-between” zone. If there were multiple values on the same date, we used the lowest one. This choice examines the risk and benefit of making no change when encountering a very low or moderately low BP or HbA1c level.

We then examined whether the level of HbA1c, or BP or the patient's life expectancy influenced the rate of deintensification. After dividing each cohort into 9 groups for each of 3 levels of BP or HbA1c and 3 levels of life expectancy, we performed a logistic regression analysis to predict deintensification for each group. We also did this in models that did not include life expectancy. These analyses helped to differentiate between deintensification because of low BP or HbA1c levels vs other reasons. Preventing potential overtreatment is unlikely the reason for deintensification in patients whose BP and HbA1c levels are not low. These results were considered baseline deintensification rates representing ordinary attrition of medications, adverse reactions, patient-driven discontinuation, or medication nonadherence.24 Rates of deintensification in the low BP and HbA1c groups beyond these baseline rates were considered deintensification responses more likely to be attributable to the low HbA1c or BP levels.

In another supplementary analysis, we compared rates of deintensification and follow-up values based on how consistently patients' BP and HbA1c levels had been recorded as low. Statistical analysis was conducted using Stata, version 13 (StataCorp).
Treatment Deintensification in Older Patients With Diabetes Mellitus

Original Investigation Research

The cohort evaluated was patients with diabetes mellitus who were older than 70 years and receiving active BP-lowering treatment. We defined active BP-lowering treatment as receiving treatment with medications other than low-dose angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. The BP level stratification is explained in the Variable Construction and Definition subsection of the Methods section.

In the BP cohort, 25,955 of 211,667 patients (12.3%) received treatment to achieve a moderately low BP level, and 81,226 individuals (38.4%) developed a very low BP level associated with treatment (Figure 1). With results reported as percentage with 95% CI, patients whose BP was not low had a 15.1% (14.9%-15.4%) chance of having a BP medication deintensified, those with moderately low BP had a 16.0% (15.5%-16.4%) chance, and those with a very low BP had an 18.8% (18.5%-19.1%) chance.

In the HbA1c cohort, 23,769 of 179,991 patients (13.2%) received treatment to achieve a moderately low HbA1c level, and 12,917 (7.2%) received treatment resulting in a very low HbA1c level (Figure 2). With results reported as percentage with 95% CI, patients whose HbA1c was not low had a 17.5% (17.3%-17.7%) chance of having a glucose-lowering medicine deintensified; those with a moderately low HbA1c had a 20.9% (20.3%-21.4%) chance, and those with a very low HbA1c had a 27.0% (26.2%-27.8%) chance.

Although BP and HbA1c values fluctuated between measurements, among patients who were eligible for but had not undergone deintensification, low values of BP and HbA1c rarely increased to elevated levels (Figures 1 and 2). In fact, among 65,951 patients with very low index BPs whose treatment was not deintensified, during the next 6 months, 28.1% of these patients had persistently low BP levels, only 0.2% had measured values of 140/90 mm Hg or greater, and 61.6% had no measurement documented. Among 9,428 individuals with very low index HbA1c values whose treatment was not deintensified, during the next 6 months, 16.9% of these patients had a low follow-up HbA1c level, fewer than 0.8% had an HbA1c level of 7.5% or greater, and 79.8% had no measured HbA1c documented.

Because we were able to assess only the presence or absence of prescriptions for short- and long-acting insulin and not the insulin dosages, we repeated the analyses excluding all patients receiving only metformin (as before), receiving any insulin, or receiving both therapies. Similarly, on the possibility that some patients were receiving therapy with high-dose angiotensin agents (namely, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) for renal protection, we repeated the analyses with all angiotensin agent use not considered active treatment. Although removing insulin from the analysis decreased the size of the cohort by 40%, neither of these exclusions had a substantial effect on the outcomes (eFigure 2 and eFigure 3 in the Supplement).

We also looked at the effect of consistency of BP and HbA1c levels on deintensification (eFigure 4 and eFigure 5 in the Supplement). For both BP and HbA1c, in patients with at least 1 moderately or very low measurement, we found that those with 2 or more low values and those with only 1 low value had similar rates of deintensification. Those with only 1 value measured had slightly lower rates of deintensification. After that, patients with only 1 value documented in the previous 6 months were much less likely to have any follow-up measurement. Those with 2 or more low values were more likely to have low values on follow-up than were those with only 1 low value.

Role of Life Expectancy on Deintensification

We found a weak association between a patient’s estimated life expectancy and rate of deintensification (Figure 3). In the BP cohort, people with less than 5 years of life expectancy had a 19.8% chance of deintensification, those with 5 to 10 years had a 16.9% chance, and those with more than 10 years had a 14.7% chance.

Both low life expectancy and low BP were weakly predictive of deintensification rate, but their effects were not syn-
Only 1 of 8 possible interactions between a patient’s life expectancy, BP, and the rate of deintensification was significant even before adjustment for multiple comparisons (eTables 1 and 2 in the Supplement).

In the HbA1c cohort, patients with less than 5 years of life expectancy had a 21.3% chance of deintensification, those with 5 to 10 years had a 18.5% chance, and those with more than 10 years had a 17.2% chance. There were no interactions between life expectancy, HbA1c levels, and the rate of deintensification.

Discussion

We found that in a cohort of older patients with diabetes mellitus receiving treatment for BP and blood glucose-level control, a patient's BP or HbA1c level had only a weak association with the likelihood of deintensification. More than half of our cohort received treatment resulting in moderately low or very low BP, and more than 20% developed moderately low or very low HbA1c levels. Deintensification rates for people with low...
BP and HbA1c levels were only minimally above the rates found in people with normal BP and HbA1c levels who received treatment. In fact, most patients with low values did not have a BP or HbA1c measure documented in the electronic medical record in the 6 months after the low value was reported, suggesting that health care professionals did not view very low values as a problem in need of monitoring. Patients with the combination of low life expectancy and low HbA1c or BP level were no more likely to have deintensification than would be expected for those with either of the risk factors alone, even though these patients have a particularly small possibility of receiving clinical benefit.

There could be several explanations for why a low BP or HbA1c level has a weak association with deintensification. First, stopping a medication requires a shift in how treatment is understood by patients and explained by health care professionals; it requires a transition from a simplistic focus on “one size fits all” to the more nuanced balancing of risks and benefits. These explanations are more difficult to offer, to understand, and often to accept. Furthermore, clinical uncertainty about the reliability of a single BP and HbA1c measurement and unwillingness to risk undertreatment may influence decisions on whether to deintensify. Second, guidelines and performance measures remain more focused on preventing underuse than overuse. Some guidelines have recommended more modest BP and HbA1c level goals for older patients or those with multiple comorbidities; however, to our knowledge, none of the guidelines have explicitly defined circumstances for deintensification. Until guidelines and performance measures specifically call for deintensification for patients who are at risk for being harmed by overtreatment, rates are likely to remain low.

We considered patients to be eligible for deintensification if persistent intensive treatment would be unlikely to yield clinical benefit or could cause substantial adverse effects based on consultation with clinical experts and randomized evidence. For middle-aged patients with type 2 diabetes mellitus, there is evidence that an intervention that yields an HbA1c level of 7.0% produces slightly better outcomes than an HbA1c level of 7.9%, but an intervention with a goal of less than 6.0% has greater mortality than does one with a goal of less than 8.0%. Therefore, we believe that in the elderly population, achieving an HbA1c value of less than 6.5% is a reasonable level of potential deintensification because it is directly connected to values known to be safe and those known to be dangerous. Similarly, there is strong evidence that, in middle-aged patients with diabetes mellitus, an SBP goal of 150 mm Hg is more effective than 180 mm Hg, but 120 mm Hg provides no clear benefit over 140 mm Hg while increasing adverse treatment effects.

Although we and others have shown that overtreatment for patients with diabetes mellitus and hypertension is common, we know of no previous study that has examined rates of deintensification in these conditions. One strength of the present study is its direct relevance to current treatment choices. The Choosing Wisely campaign recommends that people “avoid using medications to achieve HbA1c of less than 7.5% in most adults age 65 and older,” and the American Diabetes Association guidelines say that, for older patients, “an HbA1c of less than 7.5% to 8.0% may be acceptable, transitioning upward as age and [and] illness burden increase.” We conservatively chose cut points well below these values to strengthen the chance that many of these patients were receiving overtreatment. Our results are notable for the large sample size within the VA Healthcare System.

Our study has limitations. First, pharmacy records underestimate medication intensity for patients who obtain medications outside the VA. Therefore, we may have missed patients who were eligible for deintensification as well as those who underwent deintensification via outside pharmacies. Second, we could not calculate changes in dosing of insulin from VA Healthcare System medication data, only whether one or more insulin types was discontinued. However, results from a sensitivity analysis that examined this limitation did not differ substantially from our main results. Third, some patients with transiently low HbA1c or BP levels may not require deintensification. We did find, however, that few patients whose therapy was not deintensified had significantly higher levels of HbA1c or BP within 6 months after the previous value. Fourth, we lacked detailed functional status information. Finally, we do not know whether deintensification resulted in better overall outcomes for the patients.

There is no data source that will indicate why therapy was and was not deintensified. We estimated a baseline deintensification rate for patients with BP and HbA1c measurements that were within the normal treatment range. This rate is similar to 6-month discontinuation rates seen during active treatment in other studies and presumably measures discontinuation for reasons other than overtreatment. Patients with low BP and HbA1c values had treatment deintensified at a rate only slightly greater than this baseline rate.

Conclusions

Deintensification of therapy following low measurements of BP or HbA1c is uncommon, even among older patients whose treatment is well beyond recommended levels of BP and HbA1c. The harms of overuse have rarely been integrated into guidelines, quality measures, and pay-for-performance efforts. The VA recently started the Hypoglycemia Safety Initiative, a national program to limit overtreatment of blood glucose in VA patients with diabetes mellitus. Future performance management systems should consider how to create incentives against both overuse and underuse to motivate appropriate treatment, including deintensification of treatment that is personalized to individual needs, risks, and benefits. In addition, health care professionals should assess the harms of intensive therapy just as they do the benefits. These changes may require new clinical decision support tools, new performance measures, and, most important, a new perspective focusing on personalized, appropriate care.


Targeting Vascular Risk Factors in Older Adults From Polypill to Personalized Prevention

Enrico Mossello, MD, PhD

For many years vascular disease prevention strategies have been focused on reducing undertreatment, often using a “one-size-fits-all” approach to increase patient adherence. The paradigm of this approach has been the proposal of a polypill targeting multiple vascular risk factors, a standard treatment aimed at maximizing vascular protection. Conversely, during recent years an increasing emphasis has been placed on the issue of potential overtreatment, frequently resulting from the same treatment approach in all patients despite significant individual differences in comorbidity and life expectancy. In type 2 diabetes mellitus (T2DM), data from randomized clinical trials have shown uncertain or negative benefit-risk trade-offs associated with aggressive treatment of hypertension and hyperglycemia. These results, added to the well-known exclusion of elderly individuals with multiple morbidities from nearly all clinical trials, have informed recent guidelines, which now recommend more moderate targets for treatment of T2DM and hypertension in older participants, especially those considered frail or affected by important comorbidities.

These treatment recommendations raise the possible strategy of treatment deintensification for high blood pressure and hyperglycemia in patients with values previously identified as optimal and now labeled as low. This issue was addressed by Sussman and colleagues in a large retrospective sample of older individuals with T2DM (mean age, 78 years) from the Veterans Health Administration actively treated for T2DM or high blood pressure. They found that treatment deintensification (ie, dosage reduction or drug withdrawal) was performed in one-quarter or less of participants with low blood pressure (systolic blood pressure <130 mm Hg or diastolic blood pressure <65 mm Hg) or a low hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) level (<6.5%) (to convert to a proportion of total hemoglobin, multiply by 0.01). Moreover, whether treatment reduction occurred was only weakly associated with a patient’s blood pressure or HbA\textsubscript{1c} level and predicted life expectancy, suggesting that physicians are generally reluctant to deintensify treatment even in conditions that make benefits of therapy limited in comparison with potential harms.

This interpretation is confirmed by a further study from the Department of Veterans Affairs in the present issue of *JAMA Internal Medicine*. Caverly et al surveyed a national sample of health care professionals providing primary care, showing that almost half of them would not worry about harms of tight glycometabolic control obtained with an insulin secretagogue in an older patient at high risk for hypoglycemia. This approach to therapy was largely explained by the concern of making the patient’s HbA\textsubscript{1c} level fall out of Department of Veterans Affairs performance measures, which, as the authors point out, have never targeted values less than 7.0%. Nearly one-quarter of the health care professionals interviewed would even be concerned about malpractice liability risk with deintensification of hypoglycemic medications.

In keeping with these data, Sussman and colleagues call for a change in guidelines, quality measures, and clinical performance management that should include recommendations and incentives to avoid overtreatment. This statement is also consistent with a recent analysis of outpatient and emergency department performance measures in the United States that shows a lack of measures addressing overuse, especially regarding treatments. Yet, some caveats should be raised. Although studies of more aggressive control of risk factors have generally failed to show a reduction of cardiovascular events in T2DM, few data exist regarding the prognostic effect of deintensification, especially in patients with good treatment tolerance. Conversely, more stringent targets are still recommended, although with a low level of evidence, for younger patients with a low risk for adverse events. In addition, incentives for treatment withdrawal might carry a risk of avoiding potentially useful preventive strategies, especially in the present time of resource constraints. Less is not always more, and we should not risk eliminating the benefits of therapy while attempting to lower the risk.

A proposed stratification of antihypertensive and antidiabetic treatment strategies according to patient vulnerability is described in the Figure, including issues that should be further clarified and possible solutions. A first step is represented by the need for simple but clear indicators of vulnerability, which...