Glucose monitoring. Hypoglycemia (glucose level <70 mg/dL) during a 5-day period of continuous type 2 diabetes, took 2 or more insulin injections/d, and had at least 1 episode of insulin glulisine (Apidra; Sanofi-Aventis). All patients were 65 years or older with insulin lispro (Humalog; Lilly), insulin aspart (NovoLog; Novo Nordisk) and Neutral Protamine Hagedorn insulin. Meal-time insulins include meal-time insulins. Long-acting insulins include insulin detemir (Levemir; Novo Nordisk) and insulin glargine (Lantus; Sanofi-Aventis). Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) (http://www.ncbi.nlm.nih.gov/pubmed/25538310). Further simplification agents were chosen based on risk of hypoglycemia, cost, adverse-effect profile, effect on weight, and effectiveness, as recommended. If fasting glucose levels are higher than the goal but prelunch or dinner glucose levels reach the goal, change the glargine dose to bedtime at the same dose. Simplification of Insulin Regimen in Older Adults and Risk of Hypoglycemia Hypoglycemia is a serious adverse event, especially in older patients with diabetes, and is associated with poor outcomes. Intensive insulin regimens add a large burden of self-care to daily life.
older patients and increase the risk of hypoglycemia.\textsuperscript{2,3} Treatment guidelines and expert consensus recommend deintensification of treatment regimens in older adults.\textsuperscript{4} However, the effect of insulin regimen simplification on the risk of hypoglycemia or uncontrolled hyperglycemia is not known. In addition, the lack of an algorithm to guide insulin regimen simplification may account for missed opportunities to deintensify insulin regimens in older patients with diabetes.\textsuperscript{5}

Methods | In a single-arm, intervention study, we recruited 65 adults 65 years or older, with type 2 diabetes (positive stimulated serum C-peptide levels) on 2 or more insulin injections/d with 1 or more episodes of hypoglycemia ($\leq$70 mg/dL) over a 5-day period of continuous glucose monitoring (CGM). Simplification was achieved by switching multiple-dose insulin regimens to once-a-day glargine with or without noninsulin agents over a 5-month period, followed by a 3-month no-contact (no interaction with study staff) period to assess sustainability of the simplified regimen. The algorithm used to simplify the regimen included adding and/or changing long-acting insulin to basal insulin glargine, decreasing and discontinuing meal-time insulin, and simultaneously adding noninsulin agents (Figure).

Results | We simplified the insulin regimen in 65 patients (mean [SD] age, 76 [6] years; diabetes duration, 23 [11] years; insulin injections/d, 3.7 [1.3]; hemoglobin A\textsubscript{1c} [HbA\textsubscript{1c}] level, 7.7% [1.2%]). Overall, 15 patients (23%) were living alone, 16 patients (25%) had cognitive dysfunction, 26 patients (40%) had depression, and 16 patients (26%) had a history of falls within the past 6 months. Hypoglycemia duration decreased at 5 and 8-month ($P < .001$) without any change in HbA\textsubscript{1c} levels (Table) after simplification. There was an improvement in HbA\textsubscript{1c} levels in patients whose baseline HbA\textsubscript{1c} levels were between 8% and 9% (mean [SD] improvement, $-0.52\% [0.5\%]; P < .001$) or above 9% (mean [SD] improvement, $-1.7\% [2\%]; P = .03$). There was a small worsening in those with baseline HbA\textsubscript{1c} levels below 7% (mean [SD] worsening, 0.37% [0.7%]; $P = .03$), while no change was noted in those with HbA\textsubscript{1c} levels between 7% and 8% (mean [SD] change, $-0.06\% [0.6\%]; P = .80$). Diabetes-related distress score, measured by Problem Areas In Diabetes (PAID),\textsuperscript{6} improved at 5 months and remained low at 8 months ($P < .001$). Interestingly, the duration of hypoglycemia was not different when subject were stratified by HbA\textsubscript{1c} levels of less than 7.0%, 7.1% to 8.0%, 8.1% to 9.0%, and more than 9.0% at baseline (mean duration, 278 min/5-day CGM), 5-month (mean duration, 124 min/5-day CGM), or 8-month (mean duration, 88 min/5-day CGM).

Discussion | Our results show that insulin regimen simplification can reduce the risk of hypoglycemia without compromising glycemic control. After simplification, 36 (60%) of the study patients only needed 1 additional agent with basal insulin, 23 (38%) needed 2 agents, and 1 (2%) needed 3 agents. In addition, the total dose of the insulin was significantly reduced after simplification.

<table>
<thead>
<tr>
<th>Table. Characteristics Before and After Simplification at 5 and 8 Months</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<tr>
<td>Duration of hypoglycemia ($\leq$70 mg/dL glucose), min/5-d CGM</td>
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<tr>
<td>(Range)</td>
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<tr>
<td>HbA\textsubscript{1c} (%)</td>
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<tr>
<td>Duration of hyperglycemia ($&gt;250$ mg/dL glucose), min/5-d CGM</td>
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<tr>
<td>(Range)</td>
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<tr>
<td>Insulin dose, unit/kg</td>
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<tr>
<td>Daily insulin injections, No.</td>
</tr>
</tbody>
</table>

Patients taking noninsulin agents, %

| Metformin | 38 | 58 | 58 |
| Sulfonylurea | 17 | 32 | 32 |
| DPP4 Inhibitor | 0 | 20 | 20 |
| GLP-1 RA | 8 | 23 | 23 |

PAID\textsuperscript{6} 26.5 (15.9) 17 (14.5) $<.001$ 17.3 (15.2) .003

SCI-2 66.2 (9.2) 68.2 (8.1) .08 66.7 (10.2) .80

IADL 13.9 (3.2) 13.8 (3.3) .90 14.1 (2.8) .70

ADL 11.5 (1.1) 11.6 (0.8) .70 11.7 (0.5) .60

6-min walk test 331.3 (121) 346 (118.9) .60 353 (115.9) .80

GDS 3.1 (3.2) 2.6 (2.5) .40 2.5 (2.8) .30

CIB test 6.1 (1.8) 6.3 (1.6) .70 6.2 (1.8) .80

Abbreviations: HbA\textsubscript{1c}, hemoglobin A\textsubscript{1c}; ADL, activities of daily living; CGM, continuous glucose monitoring; CIB, Clock-in-a-Box; DPP4, dipeptidyl peptidase-4; GDS, Geriatric Diabetes Scale; GLP-1 RA, glucagon-like peptide-1 receptor agonist; IADL, instrumental activities of daily living; PAID, Problem Areas In Diabetes; SCI-2, Self-Care Inventory-2.
the simplified regimen was that many patients were able to adjust the dose of glargine when glucose levels changed with other health issues during the no-contact period.

Another important finding of the study is that the level of HbA1c did not correlate with duration of hypoglycemia before or after simplification of the regimen, suggesting that HbA1c level is a poor predictor of the risk of hypoglycemia. Our previous study has shown that the HbA1c levels may not correlate with estimated average glucose in older populations. The combination of these findings suggests that liberating the HbA1c goals in frail older patients is not adequate to protect against the risk of hypoglycemia. The type of glucose-lowering agents and the strategy for their use are important to lower the risk of hypoglycemia.

Conclusions | Our study shows that (1) simplification of insulin regimens in older adults can decrease hypoglycemia risk and disease-related distress without compromising glycemic control; and (2) HbA1c levels may not predict the risk of hypoglycemia in the older population and should not be used as the sole parameter for goal setting.

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Drafting of the manuscript: Munshi, Slyne, Saul.

Critical revision of the manuscript for important intellectual content: Munshi, Slyne, Segal, Saul, Lyons, Weinger.

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Editor’s Note

Simplification of Insulin Regimens in Patients With Type 2 Diabetes

In many patients with inadequately controlled type 2 diabetes, insulin is added to the treatment regimen. This often includes a daily dose of a long-acting insulin, as well as rapid-acting or short-acting insulin, sometimes with a sliding scale, to control elevated glucose following meals. Thus, treatment with insulin can impose a major burden, requiring patients to check blood glucose and inject insulin multiple times per day and to appropriately adjust insulin doses. The use of rapid-acting or short-acting insulin can also increase the risk for hypoglycemia, which is of particular concern in the elderly. In a research letter published in this issue of JAMA Internal Medicine,1 Munshi et al provide preliminary data to suggest that, compared with multiple doses of insulin, a single dose of basal insulin results in less hypoglycemia with little effect on glycated hemoglobin.

The study by Munshi et al1 is small and did not include a concurrent control group, so the evidence should be considered preliminary. However, we decided to publish the study because we believe it should inspire larger trials to investigate optimum insulin regimens that minimize hypoglycemia and patient burden. While the participants in the study by Munshi et al were elderly, we see no reason why such a simplified regimen should not also be considered in younger patients with type 2 diabetes.

Deborah Grady, MD, MPH
Conflict of Interest Disclosures: None reported.


Estimated Cost of Injectable Medication Waste Attributable to Syringe Dead Space

Excess waste is a well-known known driver of inefficiency in the US health care system. Medication waste contributes to this inefficiency and has recently been described among cancer medications, but it may also be attributable to the syringes used