

## CLINICAL DECISIONS

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## Management of Type 2 Diabetes — Polling Results

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In mid-January, we presented the case of a patient with type 2 diabetes in Clinical Decisions,<sup>1</sup> an interactive feature designed to assess how readers would manage a clinical problem for which there may be more than one appropriate treatment. Our patient was a 55-year-old woman with type 2 diabetes, obesity, and hypertension. Her morning fasting glucose levels ranged between 110 and 140 mg per deciliter (6.1 and 7.8 mmol per liter), and her glycated hemoglobin level was 8.1%. Her medication regimen included metformin (1000 mg twice daily) and glipizide (10 mg twice daily).

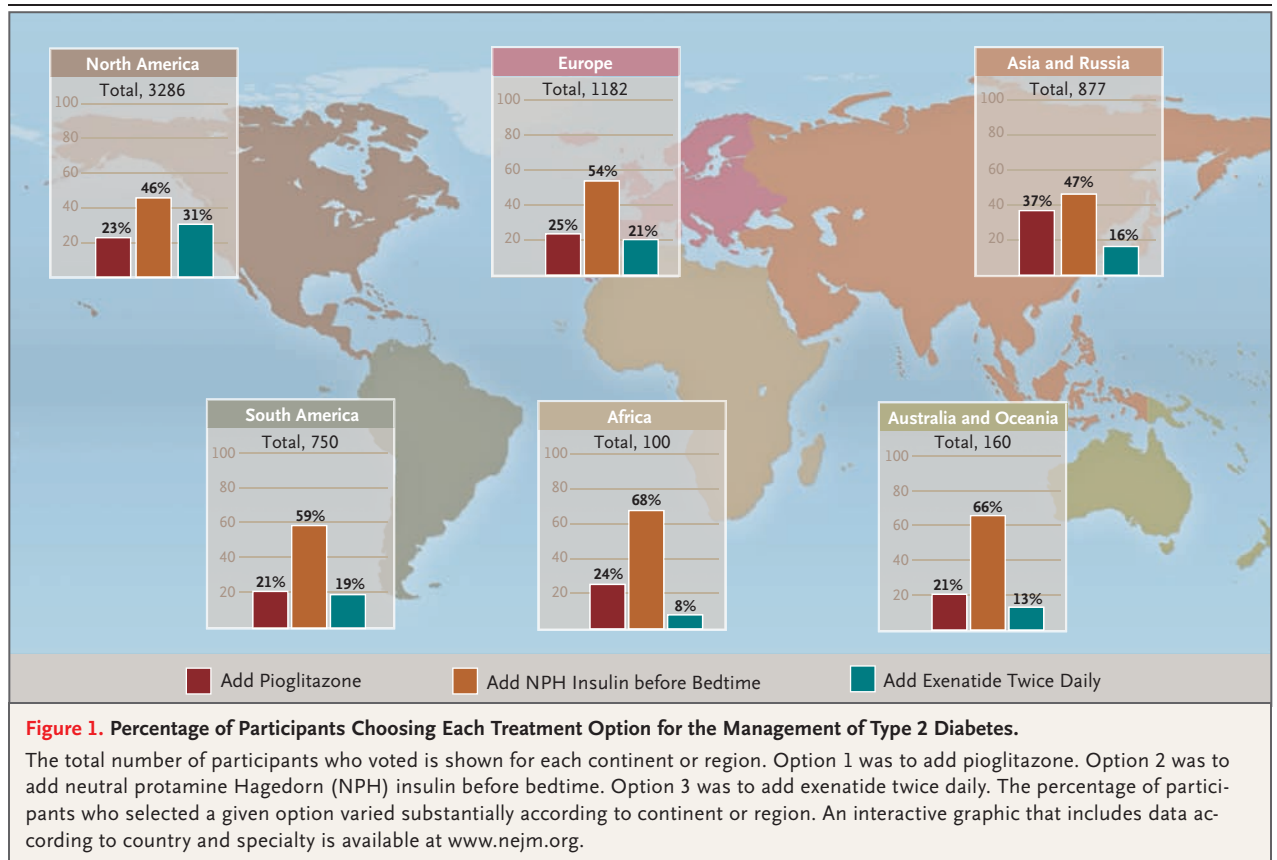
Of the three management options proposed, the most popular — receiving 3243 votes (50% of the 6455 votes cast) — was to add neutral protamine Hagedorn (NPH) insulin before bedtime. The other two options (to add pioglitazone or to add exenatide twice daily) were tied, each receiving 25% of the votes cast. The 6455 participants who voted were from 123 countries and regions and indicated that they were physicians specializing in diabetes (18%), physicians with other specialties (49%), medical students or physicians-in-training (17%), other health professionals (12%), or other (4%). Detailed results are displayed according to country and specialty at [www.nejm.org](http://www.nejm.org). The percentage of participants who selected a given treatment varied substantially when the responses were stratified according to the participants' locations (Fig. 1).

The percentage of respondents who selected a given option also varied significantly when the votes were stratified according to the respondents' self-reported specialties. Among voters from North America, the first choice among diabetologists was to add exenatide twice daily (53%); the second choice was to add NPH insulin before bedtime (32%); and the third choice was to add pioglitazone (15%). In contrast, among North American physicians with other specialties, the leading choice was to add NPH before bedtime (52%), and votes for adding pioglitazone and add-

ing exenatide twice daily were divided evenly (24% each). In Europe and Asia, all physicians who voted, irrespective of specialty, gave NPH insulin before bedtime as their first choice. Among voters from Europe, the second-most favored choice among diabetes specialists was adding exenatide twice daily (31%), whereas adding pioglitazone was the second-most favored choice among physicians with other specialties (22%). In contrast, the addition of pioglitazone was the second-most favored choice among all physicians from Asia who voted.

In addition to votes, we received 492 comments, 93% of which were posted at [www.nejm.org](http://www.nejm.org) (after being reviewed for appropriateness). The majority of comments were in favor of the addition of NPH insulin before bedtime, and the rest were divided between the other two treatment options, reflecting the overall voting trends. Reasons given in favor of a particular management strategy were varied but included some recurrent themes, as detailed below. Many additional management options were suggested, but none of these alternatives were overwhelmingly favored.

The majority of respondents who favored adding NPH insulin before bedtime considered this option to be the most efficacious at lowering glycated hemoglobin levels, as well as the most cost-effective. Many believed insulin to be the safest choice, noting that it has been in use longer than the other two choices, has fewer adverse effects, and has been shown to reduce the risk of complications of diabetes, not just surrogate end points. Several respondents remarked that insulin administration is ultimately inevitable, given the progressive nature of type 2 diabetes. However, many participants would have preferred the addition of a longer-acting insulin, such as insulin glargine or insulin detemir. Participants who did not opt to initiate insulin cited two main objections to this choice: reluctance of patients to carry out self-injections, and the possibility of weight gain.



Almost all the respondents who chose to add exenatide twice daily mentioned weight loss as a primary reason for their selection. Several noted that exenatide therapy would be particularly effective in the patient in the case vignette, whose glycated hemoglobin level was more markedly elevated than her fasting blood glucose levels, suggesting high postprandial glucose excursions. Other justifications provided for this choice included low risk of hypoglycemia, as well as possible improvement of pancreatic beta-cell function. Indeed, many respondents favored stopping sulfonylurea therapy or decreasing the dose to decrease the risk of hypoglycemia further. Those who were not in favor of adding exenatide twice daily expressed concern about the cost of the medication, its considerable gastrointestinal side effects (which may include pancreatitis), and the lack of long-term safety and efficacy data.

Respondents who opted to add pioglitazone to the current medical regimen considered this to be the simplest and most convenient choice for the patient. The oral route of administration was perceived to be a major advantage as compared

with the injectable alternatives and was considered likely to increase adherence to therapy. In addition, in some countries, such as India and China, voters considered the addition of pioglitazone to be the most cost-effective. Proponents of pioglitazone therapy highlighted its insulin-sensitizing properties and its beneficial effects on other features of the metabolic syndrome, such as levels of high-density lipoprotein cholesterol. Many respondents opined that recent reports suggesting that rosiglitazone may be associated with increased cardiovascular risk<sup>2,3</sup> do not apply to pioglitazone, whereas several respondents who voted for other treatment options expressed concern that such risks may be common to all thiazolidinediones. Other objections to the use of a thiazolidinedione included increased risks of weight gain, edema, osteoporosis, and fracture. A few participants expressed a preference for oral incretin therapy with dipeptidyl peptidase IV inhibitors.

As is evident from these results, the care of patients with diabetes whose glycated hemoglobin remains above target levels, despite dual oral hypoglycemic therapy, remains controversial. Thus,

more data are needed to direct our clinical decisions. Current approaches used by physicians vary on the basis of their experience, the availability and cost of medications, and stated or perceived preferences of patients. Indeed — as many respondents appropriately noted — given a clinical problem without a clear, evidence-based solution, it is essential to inform patients of all treatment options and the risks and benefits of each and to engage them in the decision-making process. Finally, as the participants emphasized, the successful management of type 2 diabetes necessitates not only pharmacologic interventions for glycemic control but also sustained lifestyle modification and aggressive management of other cardiovascular risk factors.

Comments from this interactive feature will remain available at [www.nejm.org](http://www.nejm.org), along with data on the voting results. We thank you for your input, and we look forward to hearing from you again soon about another challenging case.

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2. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med* 2007;356:2457-71. [Erratum, *N Engl J Med* 2007; 357:100.]
3. Singh S, Loke YK, Furberg CD. Long-term risk of cardiovascular events with rosiglitazone: a meta-analysis. *JAMA* 2007;298:1189-95.

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