

How Doctors Choose Medications to Treat Type 2 Diabetes: A National Survey of  
Specialists and Academic Generalists

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Richard W. Grant MD MPH (1,2), Deborah J. Wexler MD (2), Alice J. Watson MD (3),  
William T. Lester MD (4), Enrico Cagliero MD (2), Eric G. Campbell PhD (5), and  
David M. Nathan MD (2)

General Medicine Unit (1), Diabetes Center (2), Partners Telemedicine Program (3),  
Laboratory of Computer Science (4), and Institute for Health Policy (5), Massachusetts  
General Hospital and Harvard Medical School, Boston, MA

Corresponding Author:  
Richard W. Grant, MD MPH  
50-9 Staniford St, Boston, MA 02114  
Rgrant@partners.org

## Abstract

**Background:** Glycemic control remains sub-optimal despite the wide range of available medications. More effective medication prescription might result in better control. However, the process by which physicians choose glucose-lowering medicines is poorly understood.

**Methods:** We surveyed 886 physician members of either the Society of General Internal Medicine (“academic generalists”, response rate 30%) or the American Diabetes Association (“specialists”, 23%) currently managing patients with type 2 diabetes. Respondents weighed the importance of 15 patient, physician, and non-clinical factors when deciding which medications to prescribe for type 2 diabetes at each of three management stages (initiation, use of 2<sup>nd</sup> line oral agents, and insulin).

**Results:** Respondents reported using a median of five major considerations (Interquartile range: 4-6) at each stage. Frequently cited major considerations included: overall assessment of the patient’s health/comorbidity, HbA1c level, and patient’s adherence behavior, but not expert guidelines/hospital algorithms or patient age. For insulin initiation, academic generalists placed greater emphasis on patient adherence (76% vs. 60% of specialists,  $p < 0.001$ ). These generalists also identified patient fear of injections (68%) and patient desire to prolong non-insulin therapy (68%) as major insulin barriers. Overall, qualitative factors (e.g. adherence, motivation, overall health assessment) were somewhat more highly considered than quantitative factors (e.g. HbA1c, age, weight) with mean aggregate scores of 7.3 vs. 6.9 on a scale of 0 to 10,  $p < 0.001$ .

**Conclusions:** The physicians in our survey considered a wide range of qualitative and quantitative factors when making medication choices for hyperglycemia management. The apparent complexity of the medication choice process contrasts with current evidence-based treatment guidelines.

There are over 30 unique medicines from nine different drug classes currently approved for the treatment of hyperglycemia in type 2 diabetes, with dozens more medicines and several new drug classes in development (1-4). Given the wide array of options, it is not surprising that physicians demonstrate wide variation in the choice and sequence of medications prescribed for diabetes management (5-7). Few studies, however, have evaluated how physicians decide which medicines to prescribe (8), and no studies, to our knowledge, have focused on glycemia-lowering medicines.

In contrast to hyperlipidemia treatment (9) and, to a lesser extent, hypertension management (10), until recently there have been no widely accepted treatment guidelines for hyperglycemia that specifically recommend which medicines to prescribe and in what sequence. A recent ADA consensus statement developed in part to address sub-optimal glycemic control emphasizes three common, inexpensive medications (metformin, sulfonylureas, and insulin) and advocates a simple algorithm with branch point decisions based on HbA1c level, cost, and effectiveness of medications in lowering glycemia (11). Although data are lacking to determine whether dissemination of this new algorithm will change practice patterns or improve glycemic control, prior research suggests that many physicians do not conform to standard practice or expert recommendations (12, 13).

Population-based studies have repeatedly demonstrated that current glycemic management continues to fall short of evidence-based HbA1c goals (14, 15). To the extent that variation from

“best practice” results in less effective glucose control, understanding practice variation in choice of glycemic medicines may inform more effective interventions to improve type 2 diabetes management. We hypothesized that prescription choices may be driven by patient factors (e.g. weight, motivation to improve), physician-specific variables (e.g. usual practice patterns), and/or non-clinical issues (e.g. patient out-of-pocket expenses). To address these hypotheses, we conducted a survey to elicit physicians’ considerations when making prescription choices at various stages of glycemic management. Because evidence-based guidelines typically rely on objectively measurable criteria such as HbA1c level and weight, we also sought to compare the relative importance respondents gave to qualitative vs. quantitative criteria.

## Methods

### Survey Development

We designed our survey to address three key steps in the medication prescription pathway for type 2 diabetes: 1) Choice of first agent; 2) Use of thiazolidinediones (glitazones), which are often considered 2<sup>nd</sup> line agents; and 3) Initiation of insulin.

We convened four focus groups that included both primary care physicians and diabetologists to generate a list of potential factors considered by physicians when making glycemic medication choices. Based on feedback from these groups and data available from the literature (16-18), we grouped our variables of interest into the following four mutually exclusive categories:

- 1) Objective patient clinical data: patient’s age, weight, last

measured HbA1c, and for the questions about insulin, pattern of self-measured glucose levels.

- 2) Subjective patient factors: adherence behavior, specific medication requests, patients desire to delay or avoid insulin injection; and for the questions about insulin, patient's motivation to improve.
- 3) Non-clinical factors: medication costs.
- 4) Physician factors: physician's usual or prior practice, expert guidelines or hospital algorithms, and physician's assessment of patient's health status and co-morbid conditions. For glitazones we asked about physicians' desire to improve patient's lipid profile and/or to reduce insulin resistance and their desire to delay or avoid need for insulin. For insulin we also asked about the influence of the doctor-patient therapeutic relationship.

For each section of the survey, respondents were asked to indicate to what extent each factor was a "major consideration", "minor consideration", or "not a consideration" when making their medication prescription decision. Each question also clearly asked respondents to exclude any medical contra-indications from consideration. Respondents were given the opportunity to list additional criteria not included in the survey.

#### Survey Sample and Administration

Society of General Internal Medicine (SGIM) and the American Diabetes Association (ADA) members were invited via e-mail in April, 2006 to participate in the web-based survey. These two organizations were chosen as representative professional societies for academic generalist (SGIM) and

physicians with particular clinical interest in diabetes care (ADA). Eligibility criteria for study participation included: U.S. or Canadian physician, valid e-mail address voluntarily listed in the published membership directory, and currently managing patients with diabetes. Additional criteria for ADA members included a self-designated clinical emphasis (vs. administration or research). The 12 eligible physicians with membership in both societies were included with the ADA cohort under the assumption that ADA membership connoted a special interest in diabetes care. Endocrinologists comprised 54% of the ADA respondents. Compared to non-endocrinologists ADA physicians, a similar proportion of ADA endocrinologists worked in a community practice setting; the endocrinologists had similar years of training and a higher caseload of diabetes patients.

All physicians meeting eligibility criteria received an initial e-mail briefly describing the study, enrollment in \$40 gift card lottery after survey completion, and a link to the web-based survey site. In the next 1-2 weeks a second reminder e-mail was sent. Overall, 886 surveys were returned within four weeks of distribution, including 450 responses from SGIM members (30% response rate) and 436 responses from ADA members (23% response rate).

#### Statistical Analysis

For each stage of management, the proportion of respondents indicating that an item was a "major consideration" was tabulated and the proportions ranked. Generalist and specialist responses were compared using chi-square tests. In an exploratory analysis, we also grouped the individual survey items into two categories (quantitative vs. qualitative) and calculated an aggregate score for each

category using the following method: For each item, a response of “major consideration” was assigned “+2”, “minor consideration” was assigned “+1” and “not a consideration” was assigned “0”. Scores were then summed, divided by the total number of items in the category, and converted to a 10-point scale. This average aggregate score was used to compare the relative weight given to quantitative factors (e.g. clinically measured patient variables and medication costs) vs. qualitative factors (e.g. subjective patient data and physician factors). Scores were compared using t-tests, stratified by specialty status. We repeated this analysis using an alternative weighting approach [“major consideration” = “+1”, “minor consideration” and “not a consideration” = “0”] and obtained qualitatively similar results [data not shown]. SAS v9.1 (SAS Institute, Cary, North Carolina) was used for all analyses. This study was approved by the Massachusetts General Hospital Institutional Review Board.

## Results

### Survey Respondents

Of the 886 eligible survey respondents, 97% were staff physicians and 3% were fellows or residents. Compared to SGIM respondents, ADA respondents were in practice longer (22 vs. 15 years since medical school graduation,  $p < 0.01$ ), and were more likely to work in private practice (38% vs. 2%,  $p < 0.01$ ) than in an academic center (40% vs. 78%,  $p < 0.01$ ). Over two-thirds of ADA members (67%) reported treating > 100 patients with type 2 diabetes in the prior year, compared to 41% of SGIM respondents ( $p < 0.01$ ). Overall 92% of physicians treated more than 20 patients with type 2 diabetes in the preceding year.

### Choice of First Glycemic Medicine

Table 1 presents the list of variables considered when choosing which medicine to prescribe first for glycemic control in type 2 diabetes, ranked by proportion of respondents designating each variable as a “major consideration”. Respondents indicated a median of 5 major considerations (Interquartile range: 4-6) when choosing which medicine to prescribe first. The three most frequently cited major considerations were: “Assessment of the patient’s health status and co-morbid conditions” (89% of respondents), “Extent of HbA1c elevation” (74%), and “Patient’s weight” (66%). Although specialists and generalists differed significantly in the absolute percentage of respondents ranking each factor as a major consideration, the rank order of factors was similar except for a greater relative emphasis by generalists on patients’ adherence behavior, out-of-pocket costs, and published guidelines.

In addition to the list of survey items, 314 respondents (35%) wrote in additional considerations. These respondent comments could be grouped into four broad categories: 1) Unique patient factors (e.g. alcoholism, history of injection drug use, long-distance truck driving, dementia, eating habits, etc), 2) External forces (hospital formulary restrictions and availability of free samples), 3) Evidence-based approach (results from clinical trials and efficacy of HbA1c lowering), and 4) Physiologic approach (estimate of insulin resistance, drug mechanisms, and pattern of recent glucose values).

### Use of Glitazones

Specialists were more likely to prescribe glitazones than generalists (54% vs. 16% prescribed glitazones frequently,  $p < 0.001$ ). Among glitazone prescribers, respondents listed a median of 5 major

considerations (IQR 4-6). Specialists listed their assessment of the patient's health status and co-morbid conditions, extent of HbA1c elevation, and motivation to improve lipid profiles/reduce insulin resistance as their three leading considerations. In contrast, generalists prescribed glitazones primarily to avoid insulin (Table 2). Generalists also considered patient's health status and co-morbid conditions, extent of HbA1c elevation, and out-of-pocket expenses, but not lipid profile/insulin resistance when considering this drug class. Twenty-five percent of specialists reported that existing guidelines or local hospital algorithms were "not a consideration" when considering glitazones compared with 18% of generalists ( $p = 0.01$ , Table 4).

#### Insulin Use and Barriers

Extent of HbA1c elevation, patient-measured blood glucose profiles, and concurrent health status/co-morbid conditions were the three most frequently selected major considerations by both specialists and generalists when deciding to initiate insulin therapy (Table 3). Overall, each respondent listed a median of 5 major considerations (IQR 4-7). As with their prescribing attitudes regarding the glitazones, specialists were less concerned than generalists with existing guidelines, with 26% vs. 15% reporting that guidelines/algorithms were "not a consideration",  $p < 0.001$  (Table 4).

We also asked survey respondents to indicate whether specific factors were a "Major Barrier", "Minor Barrier", or "Not a Barrier" to insulin initiation. The majority of generalists listed patients' fear or resistance to insulin injections (68%) and patients' preference to give lifestyle modification and oral medicines more time to succeed (68%) as major barriers to insulin initiation. In contrast, few

specialists indicated any major barriers to insulin initiation. The majority of respondents also indicated that their own level of experience prescribing insulin (86% of specialists, 65% of generalists) and concerns about extra time required to address insulin dose adjustment (63% of specialists, 53% of generalists) were not barriers to insulin prescription.

#### Aggregate Measures of Quantitative vs. Qualitative Factors

The aggregate mean scores of quantitative items (extent of HbA1c elevation, age, weight, medication costs, pattern of measured glucoses) were compared to aggregate mean scores for qualitative items (adherence, assessment of health status and co-morbid conditions, usual practice, patient requests, tendency to complain about side effects, patient and physician attitudes towards insulin, patient motivation, and strength of therapeutic relationship). In this exploratory analysis, the qualitative criteria were given greater overall consideration than the quantitative criteria (7.3 vs. 6.8 on a scale of 0-10,  $p < 0.001$ ). Qualitative criteria were given an aggregate weight of 7.2 by academic generalists vs. 7.3 by specialists ( $p = 0.09$ ), and quantitative criteria 6.6 (academic generalists) vs. 7.1 (specialists,  $p < 0.001$ ).

#### Conclusions

This survey of over 850 practicing physicians examined which factors were considered when making medication choices at three distinct stages of glycemic management. In one of the largest and most detailed surveys of physician decision-making of its kind, we found that survey respondents reported considering a range of issues when choosing drug treatment options, such as their overall assessment of their patients' health and co-morbid conditions, and the

patient's HbA1c level, adherence, and motivation to improve and/or avoid insulin. Many physicians also reported that their choices were constrained by medication costs and/or formulary restrictions but not by expert guidelines or hospital algorithms.

What are the implications of our survey for diabetes management? Although there are many contributors to the observed difficulty in achieving national goals of glycemic control, effective medication prescription remains a central task for physicians. Our survey respondents considered a median of 5 qualitative and quantitative factors when choosing which medications to prescribe. The apparent complexity of their medication decision-making contrasts with a recently published algorithm that begins with metformin (when not contraindicated), followed by one of three choices (sulfonylureas, insulin, or glitazones) depending on subsequent HbA1c level, side effects, and medication cost (11). Our findings suggest that efforts to effectively implement parsimonious guidelines may be hindered by the current complexity of decision-making reported by physicians.

The relative importance of different factors varied at each management stage. When choosing to initiate drug therapy, survey respondents often considered patient weight and adherence behavior, two factors particularly relevant to metformin prescription. The prescription attitudes regarding glitazones differed markedly by specialty status, both in frequency and rationale. Specialists were much more likely to consider prescribing these agents and in doing so often considered intermediate physiologic end-points (e.g. insulin sensitivity, lipid profile) not necessarily supported by large clinical

trials of diabetes-related complications. In contrast, academic generalists appeared to view glitazones as a means of delaying or avoiding insulin.

Although we did not ask specifically about frequency of insulin prescription, other studies have consistently reported greater insulin use by diabetes specialists, a reflection in part of their management of patients with more severe disease (19, 20). Prior studies have shown that patients cared for by specialists tend to have longer duration of diabetes, more diabetes-related comorbidity, more complex medical regimens, and higher levels of motivation (21-24). Regarding barriers to insulin use, academic generalists highlighted patient-derived barriers (patients' fears/resistance to insulin and patients' preference to extend non-insulin therapy) while specialists indicated no major barriers to insulin treatment. This stark contrast in perceived patient preferences may either reflect very different patient populations treated or reluctance by generalists to pursue aggressive insulin strategies in their patients with type 2 diabetes (25). Our findings underscore the importance of lowering barriers to starting insulin by developing means to support insulin initiation and titration in the primary care setting.

Implementing guidelines, particularly static flow sheets, has had minimal impact for many clinical conditions (26-28). In systems with electronic medical records, sophisticated decision support driven by evidence-based treatment algorithms can be used to guide appropriate prescription. In one recent example involving hyperlipidemia management, physicians choosing to initiate or increase dose of statin therapy for their patients with elevated LDL levels were presented a list of statins ranked by

calculated LDL-lowering effect and relative out-of-pocket expense based on patient co-pays (29). This advanced decision support intervention was effective in increasing statin prescription and LDL control in study patients. Many would argue that hyperglycemia treatment is more complex than statin adjustment. Given the emphasis our respondents placed on difficult-to-measure factors such as overall health, adherence, and motivation, implementing advanced decision support for glycemia management may present a difficult challenge.

These data must be interpreted in the context of the study design. Our relatively low response rate, while not unusual for e-mail-based surveys, falls short of ideal rates for survey research. More intensive subject recruitment may have led to higher response rates and possibly some qualitative differences in our results. Moreover, the academic generalists in our survey are likely not representative of community-based primary care physicians who may have very different practice styles and patient populations. Our findings may therefore not be generalizable to other health care systems or practice environments.

Given the paucity of evidence regarding how glycemia-lowering medicines are prescribed in clinical practice, our survey of a select sub-group of practicing US and Canadian physicians serves to generate hypotheses to guide future efforts to change prescribing behavior. In addition, our survey was designed with a list of 15 a priori items for physicians to evaluate and thus our results necessarily focus on our pre-specified factors. Given the very limited body of published work in this area, we relied on focus groups of generalists and specialists within our institution to develop these

items and may have excluded other critical factors. We addressed this limitation to some degree by collecting additional “free text” comments from respondents, a process that highlighted the powerful role of formularies and sample availability in influencing medication choice. The additional comments also underscored the apparent contrast between “clinical trial evidence” vs. “patient physiology”-based approaches to making management decisions. Future studies investigating the process of medication initiation and adjustment should include this “evidence vs. physiology” dichotomy.

In summary, our results suggest that in the face of limited evidence-based data to guide specific medication prescription choices (30), the physicians in our survey relied on a wide range of both clinically objective and patient-focused factors when managing hyperglycemia. Respondents reported integrating their overall clinical assessment with their perception of patients’ adherence, motivation, and concerns about treatments, a more complicated view of medication prescribing than that recommended by recent guideline algorithms. Achieving more uniform and cost-effective hyperglycemic medication management may require both better evidence in favor of specific treatment strategies and further insight into why physicians make individual exceptions from standard care.

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Table 1: Major Considerations when choosing initial hypoglycemic medical therapy, and percentage (rank) of specialists vs. academic generalists listing each major consideration			
Major Considerations, % (Rank)	Specialist n = 379	Generalist n = 440	P-value*
Assessment of patient's health and co-morbid conditions	93 (1)	85 (1)	<0.001
Extent of HbA1c elevation	86 (2)	64 (2)	<0.001
Patient's weight	70 (3)	63 (3)	0.06
MD Usual Practice	68 (4)	54 (5)	<0.001
Patient's adherence behavior	59 (5)	57 (4)	0.7
Patient's out-of-pocket costs	49 (6)	52 (6)	<0.001
Expert Guideline/Hospital Algorithm	37 (8)	47 (7)	0.01
Patient's Age	38 (7)	22 (9)	<0.001
Patient's Request	16 (10)	26 (8)	<0.001
Patient's Tendency to complain about side effects	22 (9)	18 (10)	0.003

\*Comparing specialist and generalist responses;  
Considerations are listed in order of overall combined rank

Table 2: Major Considerations when choosing to prescribe a glitazone, and percentage (rank) of specialists vs. academic generalists listing each major consideration

Major Considerations, % (Rank)	Specialist n = 369	Generalist n = 403	P-value*
Assessment of patient's health and co-morbid conditions	88 (1)	68 (2)	<0.001
Patient's desire to avoid insulin	47 (7)	76 (1)	<0.001
Extent of HbA1c elevation	65 (2)	60 (3)	0.26
MD desire to improve lipid profile/reduce insulin resistance	63 (3)	39 (6)	<0.001
Patient's out-of-pocket costs	50 (6)	50 (5)	1.0
MD desire to avoid/delay insulin	36 (8)	56 (4)	<0.001
MD Usual Practice	57 (4)	32 (8)	<0.001
Patient's weight	53 (5)	25 (9)	<0.001
Expert Guideline/Hospital Algorithm	24 (9)	36 (7)	<0.001
Patient Request	13 (11)	15 (10)	0.03

Patient Age	— 14 (10)	13 (11)	0.47
*Comparing specialist and generalist responses; Considerations are listed in order of overall combined rank			

Table 3: Major Considerations when choosing to initiate insulin therapy, and percentage (rank) of specialists vs. academic generalists listing each major consideration

Major Considerations, % (Rank)	Specialist n = 370	Generalist n = 434	P-value*
Extent of HbA1c elevation	93 (1)	92 (1)	0.82
Pattern of Measured Glucoses	83 (2)	74 (4)	0.012
Assessment of patient's health and co-morbid conditions	81 (3)	75 (3)	0.06
Patient's motivation to improve	67 (4)	71 (5)	0.06
Patient's adherence behavior	60 (5)	76 (2)	<0.001
Strength of therapeutic relationship with patient	46 (6)	38 (6)	<0.001
Expert Guideline/Hospital Algorithm	26 (7)	37 (7)	<0.001
Patient's weight	20 (9)	24 (8)	<0.001
Patient Age	20 (9)	20 (9)	0.92
Patient's out-of-pocket costs	22 (8)	24 (8)	0.65

\*Comparing specialist and generalist responses;  
Considerations are listed in order of overall combined rank

Table 4: Factors most frequently listed as "Not a Consideration" at each management stage, comparing percentage of specialist vs. academic generalist respondents			
	<u>Specialist</u>	<u>Generalist</u>	<u>P-value</u>
<b>When choosing initial hypoglycemic agent</b>	<b>n = 379</b>	<b>n = 440</b>	
Patient tendency to complain about side effects, %	16	25	0.001
Patient's specific medication request, %	15	16	0.59
Expert Guideline/Hospital Algorithm, %	17	14	0.23
<b>When choosing to prescribe a glitazone</b>	<b>n = 369</b>	<b>n = 403</b>	
Patient's Age, %	23	27	0.22
Patient's specific medication request, %	20	27	0.23
Expert Guideline/Hospital Algorithm, %	25	18	0.01
<b>When deciding to initiate insulin</b>	<b>n = 370</b>	<b>n = 434</b>	
Patient's Out-of-Pocket Expenses, %	25	26	0.81
Expert Guideline/Hospital Algorithm, %	26	15	<0.001
Patient's Age, %	18	17	0.7

Numbers are percentages.