How Doctors Choose Medications to Treat Type 2 Diabetes

A national survey of specialists and academic generalists

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OBJECTIVE — Glycemic control remains suboptimal 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. We sought to study the means by which physicians choose medications for type 2 diabetic patients.

RESEARCH DESIGN AND 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, response rate 23%) currently managing patients with type 2 diabetes. Respondents weighed the importance of 15 patient, physician, and nonclinical factors when deciding which medications to prescribe for type 2 diabetic subjects at each of three management stages (initiation, use of second-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, A1C 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 noninsulin 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., A1C, age, weight) with mean aggregate scores of 7.3 vs. 6.9 on a scale of 0–10, $P < 0.001$.

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.

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There are over 30 unique medicines from 9 different drug classes currently approved for the treatment of hyperglycemia in type 2 diabetic patients, 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 American Diabetes Association (ADA) and European Association for the Study of Diabetes consensus statement (11), developed in part to address suboptimal glycemic control, emphasizes three common, inexpensive medications (metformin, sulfonylureas, and insulin) and advocates a simple algorithm with branch-point decisions based on A1C level, cost, and effectiveness of medications in lowering glycemia. 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 A1C 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 nonclinical 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 A1C level and weight, we also sought to compare the relative importance respon-

dents gave to qualitative versus quantitative criteria.

RESEARCH DESIGN AND METHODS

Survey development
We designed our survey to address three key steps in the medication prescription pathway for type 2 diabetic patients: *1*) choice of first agent; *2*) use of thiazolidinediones (glitazones), which are often considered second-line agents; and *3*) initiation of insulin.

We convened four focus groups that included 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, including patient's age, weight, last-measured A1C, and for the questions about insulin, pattern of self-measured glucose levels; *2*) subjective patient factors, including adherence behavior, specific medication requests, patient's desire to delay or avoid insulin injection, and for the questions about insulin, patient's motivation to improve; *3*) medication costs; and *4*) physician factors, including physician's usual or prior practice, expert guidelines or hospital algorithms, and physician's assessment of patient's health status and comorbid 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 a medication prescription decision. Each question also clearly asked respondents to exclude any medical contraindications from consideration. Respondents were given the opportunity to list additional criteria not included in the survey.

Survey sample and administration
The Society of General Internal Medicine (SGIM) and 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 generalists (SGIM) and for physicians with particular clinical interest in diabetes care (ADA). Eligibility criteria for study participation included status as a U.S. or Canadian physician, valid e-mail address voluntarily listed in the published membership directory, and that the physician be 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 with ADA physicians who were not endocrinologists, a similar proportion of ADA endocrinologists worked in a community practice setting; the endocrinologists had similar years of training and a higher caseload of diabetic patients.

All physicians meeting eligibility criteria received an initial e-mail briefly describing the study, enrollment in a $40.00 gift card lottery after survey completion, and a link to the web-based survey site. In the next 1–2 weeks, a reminder e-mail was sent. Overall, 886 surveys were returned within 4 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 χ^2 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) versus qualitative factors (e.g., subjective patient data and physician factors). Scores were compared using Student's *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 (Version 9.1; SAS Institute, Cary, NC) 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. ADA respondents were in practice longer compared with SGIM respondents (22 vs. 15 years since medical school graduation, respectively, $P < 0.01$) 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 with 41% of SGIM respondents ($P < 0.01$). Overall, 92% of physicians treated >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 diabetic patients, ranked by proportion of respondents designating each variable as a "major consideration". Respondents indicated a median of five 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 the fol-

Choosing medications to treat type 2 diabetes

Table 1—*Major considerations when choosing initial hypoglycemic medical therapy*

Major considerations	Specialist (n = 379)	Academic generalist (n = 440)	P
Assessment of patient's health and comorbid conditions	93 (1)	85 (1)	<0.001
Extent of A1C elevation	86 (2)	64 (2)	<0.001
Patient's weight	70 (3)	63 (3)	0.06
Physician's 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

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.

lowing 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 A1C 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 were generalists (54 vs. 16%, respectively, prescribed glitazones frequently, $P < 0.001$). Among glitazone prescribers, respondents listed a median of five major considerations (4–6). Specialists listed their assessment of the patient's health status and comorbid conditions, the extent of A1C 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 comorbid conditions, the extent of A1C 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 A1C elevation, patient-measured blood glucose profiles, and concurrent health status/comorbid 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 five major considerations (4–7). As with their prescribing attitudes regarding the glitazones, specialists were less concerned than generalists with existing guidelines, with 26 vs. 15%, respectively, 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% specialists, 65% generalists) and concerns about extra time required to address insulin dose adjustment (63% specialists, 53% generalists) were not barriers to insulin prescription.

Aggregate measures of quantitative versus qualitative factors
The aggregate mean scores of quantitative items (extent of A1C elevation, age, weight, medication costs, pattern of measured glucose levels) were compared with aggregate mean scores for qualitative items (adherence, assessment of health status and comorbid conditions, usual practice, patient requests, tendency to complain about side effects, patient and physician attitudes toward 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, respectively, on a scale of 0–10, $P < 0.001$).

Table 2—*Major considerations when choosing to prescribe a glitazone*

Major considerations	Specialist (n = 369)	Academic generalist (n = 403)	P
Assessment of patient's health and comorbid conditions	88 (1)	68 (2)	<0.001
Patient's desire to avoid insulin	47 (7)	76 (1)	<0.001
Extent of A1c elevation	65 (2)	60 (3)	0.26
Physician's 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
Physician's desire to avoid/delay insulin	36 (8)	56 (4)	<0.001
Physician's 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

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.

Table 3—*Major considerations when choosing to initiate insulin therapy*

Major considerations	Specialist (n = 370)	Academic generalist (n = 434)	P
Extent of A1C elevation	93 (1)	92 (1)	0.82
Pattern of measured glucose levels	83 (2)	74 (4)	0.012
Assessment of patient's health and comorbid 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

Data are percentage (rank) of specialists vs. academic generalists listing each major consideration. Considerations are listed in order of overall combined rank.

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 vs. 7.1 by academic generalists and specialists, respectively, $P < 0.001$.

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 overall assessment of their patients' health and comorbid conditions and the patient's A1 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 five 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 A1C levels, 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 specifically ask 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 noninsulin therapy) while specialists indicated no major barriers to insulin treatment. This stark contrast in perceived patient preferences may reflect either very different patient populations treated or reluctance by generalists to pursue aggressive insulin strategies in 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

Table 4—*Factors most frequently listed as "not a consideration" at each management stage*

	Specialist	Academic generalist	P
When choosing initial hypoglycemic agent			—
n	379	440	—
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
When choosing to prescribe a glitazone			—
n	369	403	—
Patient's age	23	27	0.22
Patient's specific medication request	20	27	0.23
Expert guideline/hospital algorithm	25	18	0.01
When deciding to initiate insulin			—
n	370	434	—
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

Data are percentages.

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 with a list of statins ranked by calculated LDL-lowering effect and relative out-of-pocket expense based on patient copays (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 subgroup of practicing U.S. 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; thus, our results necessarily focus on our prespecified 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–versus patient physiology–based approaches to making management decisions. Future studies investigating the process of medication initiation and adjustment should include this 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 overall clinical assessments with perceptions 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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