

Physician Reasons for Nonpharmacologic Treatment of Hyperglycemia in Older Patients Newly Diagnosed with Type 2 Diabetes Mellitus

Elizabeth Marrett · Qiaoyi Zhang · Claudia Kanitscheider ·
Michael J. Davies · Larry Radican · Mark N. Feinglos

To view enhanced content go to www.diabetestherapy-open.com

Received: April 5, 2012 / Published online: June 15, 2012

© The Author(s) 2012. This article is published with open access at Springerlink.com

ABSTRACT

Introduction: To identify reasons why primary care physicians (PCPs) do not treat older patients newly diagnosed with type 2 diabetes mellitus (T2DM) with antihyperglycemic agents following diagnosis.

Results from this survey study were presented in abstract form at the 2009 ADA meeting in New Orleans, LA, USA.

E. Marrett (✉)
Global Health Outcomes, WS2E85, 1 Merck Drive,
Whitehouse Station, NJ 08889, USA
e-mail: elizabeth.marrett@merck.com

E. Marrett
University of Medicine and Dentistry of New Jersey,
Piscataway, NJ, USA

Q. Zhang · M. J. Davies · L. Radican
Merck Sharp & Dohme Corp., Whitehouse Station,
NJ, USA

C. Kanitscheider
KantarHealth, Munich, Germany

M. N. Feinglos
Duke University Medical Center, Durham, NC, USA



Enhanced content for this article is
available on the journal web site:
www.diabetestherapy-open.com

Methods: US PCPs were surveyed via the internet regarding their reasons for not treating patients aged >65 years diagnosed with T2DM and had not yet initiated antihyperglycemic therapy for ≥ 6 months after diagnosis. PCPs were requested to provide relevant clinical information for untreated older patients and select applicable reasons for not initiating treatment from a list of 35 possibilities, grouped into five categories.

Results: A total of 508 PCPs completed the online survey and provided complete clinical data for 770 patients. The reasons provided by the first-ranked physician for not initiating antihyperglycemic therapy were related to diet and exercise (57.5%); mild hyperglycemia (23.8%); patient's concerns (13.4%); concerns about antihyperglycemic agents (3.0%); and comorbidities and polypharmacy (2.3%). The "diet and exercise" category was the most common first-ranked non-treatment reason, regardless of recent hemoglobin A_{1c} (HbA_{1c}) stratum. Reasons within the "patient's concerns," "concerns related to antihyperglycemic agents," and "comorbidities and polypharmacy" categories tended to be selected more often as first-ranked reasons by

physicians for patients with higher HbA_{1c} values. Of the 158 patients whose physicians planned to initiate antihyperglycemic therapy within the next month, 54.4% already had a most recent HbA_{1c} value above their physician-stated threshold for treatment initiation.

Conclusion: In the PCPs studied, there was a tendency to select appropriate reasons for non-treatment with antihyperglycemic agents given their patients' glycemic status. However, there was inertia related to the initiation of pharmacological therapy in some older patients with newly diagnosed T2DM. Important factors included physicians' perceptions of "mild" hyperglycemia and the HbA_{1c} threshold for using antihyperglycemic agents.

Keywords: Antihyperglycemic agents; Clinical inertia; Elderly; Non-treatment; Type 2 diabetes mellitus

INTRODUCTION

The number of people aged ≥ 65 years is increasing, and currently represents approximately 13.0% of the US population. At the same time, the incidence and prevalence of diagnosed type 2 diabetes mellitus (T2DM) among adults aged ≥ 65 years have increased to values of 2.7% annually and 24.8%, respectively [1]. Persons aged ≥ 65 years diagnosed with T2DM in the US have morbidity and mortality rates far in excess of their counterparts without diabetes, including microvascular complications and cardiovascular disease [2]. In the UK Prospective Diabetes Studies, treatment with antihyperglycemic therapies reduced the risk of microvascular and, in the metformin arm, macrovascular disease endpoints among patients with newly diagnosed T2DM [3, 4]. Importantly,

this early treatment led to sustained benefits related to the development and progression of microvascular disease as well as to emergent risk reduction in macrovascular disease and all-cause mortality [5]. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes recommend initiating treatment with metformin, in combination with lifestyle changes, immediately after the diabetes diagnosis, with a target hemoglobin A_{1c} (HbA_{1c}) value of $<7.0\%$ for adults [6]. The American Geriatrics Society also recommends a target HbA_{1c} of $\leq 7.0\%$ for relatively healthy, older adults [7]. However, specific glycemic targets may need to be re-evaluated for higher-risk patients with T2DM in light of the increased mortality observed in patients aggressively treated with antihyperglycemic agents to achieve intensive glucose lowering glycemic targets [8].

However, many patients aged ≥ 65 years are not prescribed antihyperglycemic agents after diagnosis of T2DM. In a US employer-based health insurance data set, 44.0% of individuals aged ≥ 65 years received no antihyperglycemic therapy in the 12-month period following T2DM diagnosis [9]. Similarly, in a retrospective US cohort study, older patients (age ≥ 65 years) with newly diagnosed T2DM were less likely to have oral antihyperglycemic therapy initiated following diagnosis than younger patients [10]. Among patients who showed disease progression in a 1-year follow-up period (defined as a HbA_{1c} increase from <7.0 to $\geq 7.0\%$), the likelihood of initiating antihyperglycemic therapy decreased by 40.0% with every decade increase in age [11].

Although there have been studies of physicians' attitudes toward recommending lifestyle changes after a diagnosis of T2DM [12, 13], or their attitudes toward treatment intensification with

insulin [14–17], there are limited data evaluating the reasons given by primary care physicians for not initiating antihyperglycemic therapy in older patients with T2DM. Therefore, the objectives of the present study were, first, to describe the clinical characteristics of patients aged ≥ 65 years who had not been treated with oral antihyperglycemic therapy in the 6 or more months following diagnosis of T2DM, and second, to report the reasons given by primary care physicians for not initiating oral antihyperglycemic therapy in their patients.

MATERIALS AND METHODS

Physicians and Patients

This study was an internet-based survey of a panel of US primary care physicians, conducted in November to December 2008. The study was reviewed and approved by a central institutional review board (IntegReview, Austin, TX, USA). The physician panel (TNS Jstreet's online panel) used for this study was maintained by TNS Healthcare at the time of the study and included approximately 25,000 physicians in the US covering 37 specialties, including primary care ($n = 5,600$ primary care physicians). The geographical distribution of primary care physicians in this panel shows more physicians from the South (32.0%) and Northeast (26.0%) relative to the Midwest and West (21.0% each). Primary care physicians in general practice, family practice, and internal medicine who regularly participated in panel-related survey studies were identified and randomly sent an invitation to participate in the present survey study ($n = 3,401$ invitees). If an invited physician provided satisfactory responses to a screening questionnaire, the physician was

allowed to enter the survey site and to complete the patient-related survey. The survey site was closed shortly after 500 physicians completed the survey and provided the required information for their patients. Physicians were compensated for a completed survey.

Each participating physician was requested to provide data for one or two older patients with T2DM, selected randomly on the basis of an assigned patient's last name initial to limit selection bias. Patients, provided by the physician, had to meet the following inclusion criteria: age ≥ 65 years at the time of T2DM diagnosis, no antihyperglycemic treatment up to the time of the survey and for at least 6 months after diagnosis, and at least one office visit for management of their diabetes within the previous 6 months. The following data were collected from patients' charts and entered by the physician into online forms: patient demographics, comorbidities and associated medication use, and laboratory measurements (values closest to diagnosis and the most recent values [i.e., closest to the time of the survey]). Laboratory measurements at the time closest to diagnosis included HbA_{1c} and fasting blood glucose (FBG). The most recent laboratory measurements included HbA_{1c}, FBG, blood pressure, lipids, and serum creatinine.

Patients with a body mass index >25 kg/m² were included in the classification of overweight/obese. The estimated glomerular filtration rate (eGFR) was calculated from the abbreviated Modification of Diet in Renal Disease study equation [18]. Microvascular complications were defined as any history of neuropathy, retinopathy, or renal disease. Cardiovascular conditions included any history of congestive heart failure, ischemic heart disease, myocardial infarction, peripheral vascular disease, or stroke.

Survey

The online survey was developed based on extensive interviews with an expert panel of community and academic physicians. Interviews included discussions regarding the treatment of older patients, scenarios where patients are not treated with antihyperglycemic agents for at least 6 months after an initial diabetes diagnosis, and potential reasons relevant to not initiating antihyperglycemic treatment. After the survey was drafted according to the experts' opinions, it was presented back to the panel for review and approval. A list of 35 possible reasons for non-treatment was subsequently provided to the study physicians. Physicians selected the reasons why their patients had not been treated with antihyperglycemic agents in the 6 months or more after diagnosis and also ranked the selected reasons in order of importance. A physician could check all the applicable reasons. Physicians were also asked if they intended to initiate antihyperglycemic therapy in the next month for their patient and, if yes, they were asked to further specify what threshold HbA_{1c} level would trigger a decision to start drug therapy.

Data Analysis

Descriptive statistics were used to summarize patient demographics, disease characteristics, and reasons for non-treatment with antihyperglycemic agents. For purposes of analysis, the 35 reasons for non-treatment were grouped into five high-level categories: "diet and exercise" (one item); "mild hyperglycemia" (three items); "patient's concerns" (nine items); "concerns related to antihyperglycemic agents" (17 items); and "comorbidities and polypharmacy" (five items). Reasons for

non-treatment were expressed as frequency of selection for each reason (all reasons analyses) and for the first-ranked reason (first-ranked reasons analyses). Descriptive analyses included the distribution of first-ranked reasons for non-treatment, by most recent HbA_{1c} stratum (<7.0, 7.0–7.4, ≥7.5%), and the distribution of all reasons for non-treatment by selected patient characteristics. A small number of patients had a most recent HbA_{1c} value ≥7.5% and, thus, were considered one group in the stratified analysis.

RESULTS

Physicians Who Completed the Survey

Of the 3,401 primary care physicians invited to participate, 1,093 accessed the online link until the survey was closed after reaching the target number of physicians. Of the 1,093 physicians, 414 were screened out for the following reasons: 258 had less than two older patients with T2DM currently being treated with diet and exercise only; 40 had the incorrect specialty; 35 had less than 3 years of clinical practice; 34 had an insufficient number of patients meeting all inclusion criteria; and 47 for various other reasons. Of those who satisfied the criteria in the screening questions ($n = 679$), 508 fully completed the survey and provided the required information for their patients. These 508 physicians (77.0% men) had a mean age of 47 years and a mean number of years in clinical practice of 16 years since post-graduate medical training.

Patient Characteristics

Complete information was provided by participating physicians for 770 older patients with T2DM not treated with antihyperglycemic

therapy for at least 6 months following diagnosis (Table 1). These patients had a mean (\pm SD) age of 72 (6) years, a mean (\pm SD) HbA_{1c} at diagnosis of 7.2% (0.8), and a mean (\pm SD) duration of diabetes (i.e., time from diagnosis to survey date) of 20.9 (23.7) months. In the cohort of patients ($n = 738$) with a most recent HbA_{1c} measurement, the mean (\pm SD) HbA_{1c} was 6.7% (0.6; Table 1). Of these patients, 67.0% had a most recent HbA_{1c} value <7.0%, 21.0% had an HbA_{1c} of 7.0–7.4%, and 12.0% had an HbA_{1c} \geq 7.5% (including 31 patients with an HbA_{1c} \geq 8.0%).

In a subset of patients with HbA_{1c} measurements at both “closest to diagnosis” and “most recent” time points ($n = 656$, or 85.0% of the sample), 15.0% ($n = 100$) experienced an increase in HbA_{1c}, with a mean (\pm SD) HbA_{1c} increase of 0.37% (0.29).

Physicians’ Reasons for Non-Treatment with Antihyperglycemic Agent

The frequency of selection of each physician’s reason for non-treatment is shown in Table 2. When evaluated by category of reasons, the “diet and exercise” category was selected most (92.5%) followed by “mild hyperglycemia” (83.6%), “patient’s concerns” (61.3%), “concerns related to antihyperglycemic agents” (49.1%), and “comorbidities and polypharmacy” (36.9%). Within these five categories, the most commonly cited reasons by physicians were: “try diet and exercise first before starting drug treatment” (92.5%); “HbA_{1c} value close to ADA recommended threshold” (69.6%); “patient does not want to take (additional) medication” (51.6%); “may cause hypoglycemia” (29.5%); and “patient is taking several other medications already” (25.3%). The cumulative frequency of first-ranked reasons for non-treatment in the five categories was 57.5%

Table 1 Characteristics of 770 patients provided by the physicians

| Characteristics | Mean \pm SD or proportion |
|--|-----------------------------|
| Males (%) | 54 |
| Age (years) | 72 \pm 6 |
| Age at diabetes diagnosis (years) | 71 \pm 5 |
| Duration of diabetes (months) | 20.9 \pm 23.7 |
| BMI (kg/m ²) | 29.7 \pm 4.9 |
| Overweight/obese (%) | 74 |
| Laboratory values | |
| HbA _{1c} closest to diabetes diagnosis (%) | 7.2 \pm 0.8 |
| Most recent HbA _{1c} ^a (%) | 6.7 \pm 0.6 |
| Most recent HbA _{1c} ^a <7.0% (%) | 67 |
| FBG closest to diagnosis (mg/dL) | 155 \pm 38 |
| Most recent FBG (mg/dL) | 124 \pm 23 |
| Most recent FBG \geq 126 mg/dL (%) | 43 |
| Serum creatinine (mg/dL) | 1.15 \pm 0.30 |
| eGFR (mL/min/1.72 m ²) | |
| \geq 60–89 (%) | 56 |
| 30–59 (%) | 42 |
| 15–29 (%) | 2 |
| Microvascular complications (%) | 12.7 |
| Neuropathy (%) | 3.4 |
| Retinopathy (%) | 0.8 |
| Renal disease (%) | 10.3 |
| Cardiovascular conditions (%) | 17.3 |
| Congestive heart failure (%) | 9.0 |
| Ischemic heart disease (%) | 8.1 |
| Myocardial infarction (%) | 4.7 |
| Peripheral vascular disease (%) | 3.9 |
| Stroke (%) | 2.6 |

of patients (diet and exercise), 23.8% (mild hyperglycemia), 13.4% (patient’s concerns), 3.0% (concerns related to antihyperglycemic

Table 1 continued

| Characteristics | Mean \pm SD or proportion |
|--|-----------------------------|
| Medications | |
| Prescription(s) for lipid-modifying therapy (%) | 57 |
| Prescription(s) for antihypertensive therapy (%) | 69 |
| Total number of medications, median (range) | 3.0 (0–20) |

BMI body mass index, *HbA_{1c}* hemoglobin A_{1c}, *eGFR* estimated glomerular filtration rate, *FBG* fasting blood glucose

^a When the most recent HbA_{1c} was missing, the value closest to diagnosis was imputed ($n = 738$)

agents), and 2.3% (comorbidities and polypharmacy; Table 2).

Physicians' First-Ranked Reasons by Categories for Non-Treatment by HbA_{1c} Stratum

The “diet and exercise” category was the first-ranked reason for non-treatment in all HbA_{1c} strata, with a decrease in selection with increasing HbA_{1c} levels (Fig. 1). In addition, while “mild hyperglycemia” was cited as the first-ranked reason category for non-treatment by physicians for 27.0% of patients with a most recent HbA_{1c} <7.0%, it was also the first-ranked reason for 19.0% with an HbA_{1c} of 7.0–7.4%, and 13.0% with an HbA_{1c} \geq 7.5% (Fig. 1). In contrast, “patient’s concerns”, “concerns related to antihyperglycemic agents”, or “comorbidities and polypharmacy” tended to be selected as the first-ranked reason category for non-treatment by physicians for more patients with higher HbA_{1c} values (Fig. 1).

Reasons Selected for Non-Treatment by Patient Characteristics or Comorbid Conditions

Physicians appeared to select reasons (using all reasons analysis) within “concerns related to antihyperglycemic agents” or “comorbidities and polypharmacy” categories more often for patients with pre-existing microvascular complications, cardiovascular conditions, renal impairment (i.e., eGFR <60 mL/min/1.72 m²), or already taking more than three medications. Duration of diabetes above the median (i.e., >12 months) did not appear to impact selected reasons (Fig. 2).

Physician-Stated Threshold for Initiating Antihyperglycemic Treatment

Physicians designated 158 patients to begin treatment with antihyperglycemic agents within the next month. When physicians were asked for the HbA_{1c} threshold to initiate treatment among these patients, the mean (\pm SD) HbA_{1c} was 7.1% (0.6). Of these patients, 86 (54.4%) already had a most recent HbA_{1c} value above their physician-stated threshold for treatment initiation (median difference between the most recent HbA_{1c} value and the threshold value equals 0.5% [min, max: 0.1, 2.8]).

DISCUSSION

This survey of over 500 US primary care physicians examined their reasons for not initiating antihyperglycemic treatment in older patients who had not been treated for at least 6 months following diagnosis of T2DM. The characteristics of the present cohort of patients were generally similar to those of a

Table 2 All and first-ranked reasons for non-treatment with antihyperglycemic agents

| Reasons | All (<i>n</i> = 770) | | First-ranked (<i>n</i> = 756) | |
|---|-----------------------|------|--------------------------------|------|
| | <i>n</i> | % | <i>n</i> | % |
| Diet and exercise | 712 | 92.5 | 435 | 57.5 |
| Try diet and exercise first before starting drug treatment | 712 | 92.5 | 435 | 57.5 |
| Mild hyperglycemia | 644 | 83.6 | 180 | 23.8 |
| HbA _{1c} value stable, drug therapy not necessary | 478 | 62.1 | 65 | 8.6 |
| HbA _{1c} value close to ADA recommended threshold | 536 | 69.6 | 81 | 10.7 |
| Blood glucose values under control with diet and exercise | 507 | 65.8 | 34 | 4.5 |
| Patient's concerns | 472 | 61.3 | 101 | 13.4 |
| Patient's follow-up visit is overdue | 59 | 7.7 | 5 | 0.7 |
| Patient does not want to take (additional) medication | 397 | 51.6 | 86 | 11.4 |
| Fear of hypoglycemia | 149 | 19.4 | 0 | 0 |
| Fear of weight gain | 135 | 17.5 | 0 | 0 |
| Fear of other treatment side effects | 162 | 21.0 | 2 | 0.3 |
| Fear to change from diet/exercise to oral agents | 119 | 15.5 | 0 | 0 |
| Fear to change from diet/exercise to insulin | 100 | 13.0 | 0 | 0 |
| Financial burden (health insurance coverage/patient co-pay) | 134 | 17.4 | 7 | 0.9 |
| Drug therapy decreases quality of life | 64 | 8.3 | 1 | 0.1 |
| Concerns related to antihyperglycemic agents | 378 | 49.1 | 23 | 3.0 |
| May cause hypoglycemia | 227 | 29.5 | 7 | 0.9 |
| May cause fluid retention | 147 | 19.1 | 2 | 0.3 |
| May cause weight gain | 179 | 23.2 | 1 | 0.1 |
| May cause GI side-effects | 175 | 22.7 | 0 | 0 |
| May increase risk of fracture | 70 | 9.1 | 0 | 0 |
| May increase cardiovascular risk | 93 | 12.1 | 1 | 0.1 |
| May increase risk of lactic acidosis | 118 | 15.3 | 0 | 0 |
| Uncertainty how to dose certain drug for older patients | 46 | 6.0 | 1 | 0.1 |
| Not clear if several agents are safe for older patients | 59 | 7.7 | 0 | 0 |
| Efficacy of agents not clear for older patients | 48 | 6.2 | 0 | 0 |
| Safety of agents not clear for older patients | 67 | 8.7 | 0 | 0 |
| Cognitive burden of therapy administration too high for older patient | 67 | 8.7 | 4 | 0.5 |
| Cognitive burden of monitoring blood glucose too high for older patient | 67 | 8.7 | 1 | 0.1 |
| Difficulties/ability to change patient's lifestyle | 93 | 12.1 | 2 | 0.3 |
| Risk of noncompliance (not related to side-effects) | 101 | 13.1 | 4 | 0.5 |

Table 2 continued

| Reasons | All (n = 770) | | First-ranked (n = 756) | |
|--|---------------|------|------------------------|-----|
| | n | % | n | % |
| Risk of noncompliance due to side-effects | 95 | 12.3 | 0 | 0 |
| Lack of monitoring due to physical limitations (e.g., dexterity) | 55 | 7.1 | 0 | 0 |
| Comorbidities and polypharmacy | 284 | 36.9 | 17 | 2.3 |
| Patient has other severe disease(s) | 118 | 15.3 | 7 | 0.9 |
| Medical diabetes treatment is contraindicated | 22 | 2.9 | 1 | 0.1 |
| Patient is taking several other medications already | 195 | 25.3 | 8 | 1.1 |
| Risk of side effects | 184 | 23.9 | 1 | 0.1 |
| Risk of drug–drug interactions | 110 | 14.3 | 0 | 0 |

ADA American Diabetes Association, GI gastrointestinal, HbA_{1c} hemoglobin A_{1c}

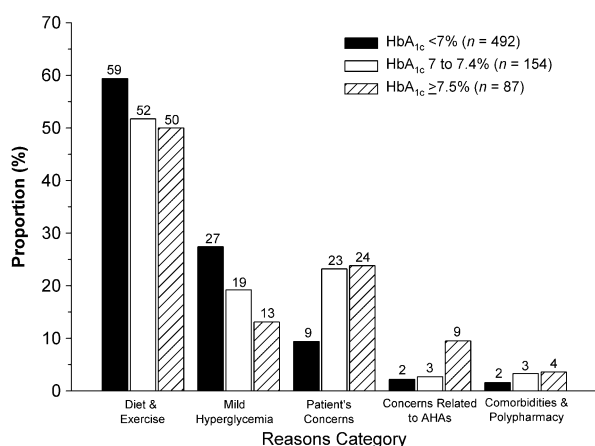


Fig. 1 First-ranked physician’s reasons for non-treatment with antihyperglycemic agents (AHAs), stratified by most recent HbA_{1c} level before the survey. HbA_{1c} hemoglobin A_{1c}

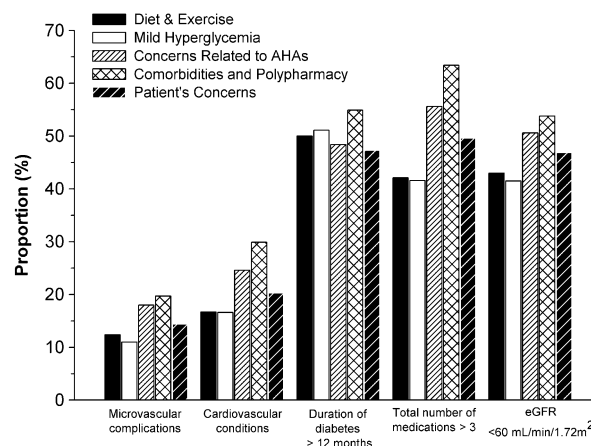


Fig. 2 Reasons provided by physicians for non-treatment with antihyperglycemic agents (AHAs) by select patient characteristics and comorbidities (all reasons analysis). eGFR estimated glomerular filtration rate

US cohort of older patients with newly diagnosed T2DM [10]. The survey found that the reasons cited by physicians were overwhelmingly related to a preference for diet and exercise or a perception that the patient had mild hyperglycemia and was in good glycemic control. The specific reason “try diet and exercise first” was selected by 92.5% of physicians. Moreover, 57.5% of physicians

ranked this reason first. The second-most cited reasons included those in the “mild hyperglycemia” category, with physicians selecting any one of the items in this category 83.6% of the time (ranked first by 23.8% of physicians). Collectively, these two categories accounted for over 80.0% of first-ranked reasons for not initiating treatment. Using a similar survey in the UK, 79.0% of general practitioners

selected their first-ranked reason for not initiating antihyperglycemic therapy from the “mild hyperglycemia” category (the “diet and exercise” category was not a standalone category in this survey) for their older and younger patients with newly diagnosed T2DM [19].

The proportion of physicians selecting reasons related to “diet and exercise,” or “mild hyperglycemia” as reasons for non-treatment with antihyperglycemic agents tended to decline as the patients’ HbA_{1c} values increased. Although these reasons may have been appropriate for patients with a most recent HbA_{1c} value <7.0%, selection of these reasons continued for many untreated patients whose most recent HbA_{1c} value was ≥7.0%. Furthermore, when physicians were asked if they planned to initiate antihyperglycemic therapy within the next month for their patients, the mean HbA_{1c} threshold for initiating therapy indicated by the physicians was approximately 7.0%. However, more than half the patients identified by the physicians for future pharmacologic treatment already had an HbA_{1c} level above this threshold. These results demonstrate discordance between physicians’ theoretical and actual clinical actions for their older patients with T2DM.

For patients whose most recent HbA_{1c} level was ≥7.0%, physicians tended to select patient-centric reasons for not initiating glycemic therapy in the present study. The most-selected reasons within the “patient’s concerns” category were related to taking additional medications, fear of side effects, including hypoglycemia and weight gain, and increased financial burden. In the aforementioned UK survey by Zhang et al. [19], general practitioners were more likely to select reasons related to side effects, disease or medication burden for patients, and well-being

of the patient for their older patients compared to younger ones. Interestingly, “not wanting to take additional medication” was behind only “try diet and exercise” as a first-ranked reason for not initiating therapy in the present study. Although patient fear or physician concern of the common side effects with antihyperglycemic agents (e.g., hypoglycemia, weight gain, gastrointestinal intolerance, and fluid retention) was selected as reasons by approximately 17.0–30.0% of physicians, none of these reasons were selected by more than 1.0% of physicians as a first-ranked reason. This is in agreement with the findings of Grant et al. [20], who reported that a patient’s tendency to complain about side effects was not a major consideration when initiating antihyperglycemic therapy.

Consistent with the main reasons for not initiating an antihyperglycemic agent (diet and exercise, and mild hyperglycemia) observed in this study, physicians generally report that lifestyle change was a key component of diabetes treatment. However, physicians have also indicated that it was difficult for patients to change their lifestyle or diet [12, 13]. In response to a questionnaire given to healthcare providers in Finland regarding a lifestyle change, almost all (98.0%) physicians reported that lifestyle change was always or nearly always a central part of treatment [13]. Most (83.0%) reported that the biggest barrier to treatment of diabetes was always or nearly always the patients’ unwillingness to change their lifestyle [13]. Likewise, most (87.0%) doctors in Denmark, responding to a questionnaire regarding a change in patient diet, thought that changing their diabetic patients’ food habits was difficult or very difficult [12]. Furthermore, the proportion of T2DM patients treated with diet alone was positively associated with the level of their

doctors' dietary counseling skills, suggesting physicians who were less skilled in providing dietary advice prescribed antihyperglycemic agents [12]. Information on recommended lifestyle changes and dietary advice was not collected from the physicians in the present study.

There is a paucity of evidence regarding the factors that influence the initiation of oral antihyperglycemic agents in clinical practice. Pani et al. [11] found that, despite disease progression in untreated patients with T2DM, the likelihood of initiating therapy was lower as the patient's age increased. In an observational study of US patients with newly diagnosed T2DM, age ≥ 65 years was a significant factor for not initiating oral antihyperglycemic therapy after adjusting for baseline and time-varying covariates [10]. In newly diagnosed T2DM patients ≥ 40 years of age, general practitioners tended to set the goal of normoglycemia for patients who were younger and in better overall health at diagnosis [21]. Conversely, age does not always appear to be a major factor for initiating therapy in untreated patients with T2DM. In 603 newly diagnosed T2DM patients from a Dutch town, the time to first treatment with an oral antihyperglycemic agent was shortest in patients with the highest fasting plasma glucose values at the time of diagnosis, whereas age, body weight, and history of cardiovascular disease did not influence the initiation of therapy [22]. Grant et al. [20] surveyed US physicians (specialists and generalists) to determine the factors they considered when deciding the initial antihyperglycemic therapy to prescribe to untreated patients with T2DM. The most common factors were the patient's overall health status and comorbidities (89.0% of all respondents), HbA_{1c} value (74.0%), and patient's weight (66.0%). Patient's age tended

to be considered more by specialists (38.0%) compared with generalists (22.0%) [20]. In the present study, physicians selected reasons within the "concerns related to antihyperglycemic agents" or "comorbidities and polypharmacy" categories more often for non-treatment in patients with pre-existing microvascular complications, cardiovascular conditions, renal impairment, or already taking numerous medications. Collectively, the research suggests that patient's disease and comorbidity status, glycemic control at diagnosis, and younger age influence the initiation of antihyperglycemic therapy.

This study has several limitations. The survey was developed and approved by experts, but no external validation was performed. To limit selection bias, physicians were instructed to select a patient on the basis of a randomly assigned last name initial and to provide information on the first patient with this initial who met entry criteria. However, because of the online nature of the survey, it could not be verified whether the physicians adhered to this specific protocol for patient selection. All reported laboratory measures closest to diagnosis were included in the analysis, regardless of the timing of the measurement. The question regarding the physician's intent to treat a patient within the next month may have produced responses biased in favor of treatment. The results pertain to a sample of US primary care physicians and may not be generalizable to all primary care physicians or to endocrinologists and other diabetes specialists. Although nearly one-third of invited physicians accessed the survey invitation link, the final response rate could affect the generalizability of the results. Lastly, participating physicians may have been more confident in their management of T2DM in older patients than nonparticipating

physicians. Thus, the present findings may underestimate the issue of non-treatment in the general population.

In conclusion, in this survey study of physicians, two-thirds of patients had appropriate glycemic control (i.e., HbA_{1c} <7.0%) and selection of reasons for non-treatment with antihyperglycemic agents related to this appears to be an appropriate clinical decision for many of these patients. The data from the present study also indicate that, in the group of physicians surveyed, there is substantial inertia related to the initiation of pharmacological therapy in older patients with newly diagnosed T2DM. Physician-reported reasons for non-treatment suggest that there are substantial barriers to drug use in clinical practice, including physicians' perceptions of "mild" hyperglycemia and the HbA_{1c} threshold for the use of antihyperglycemic agents. One-third of the patients had an HbA_{1c} above goal (with HbA_{1c} 7.0–7.4% in 21.0% of patients and HbA_{1c} ≥7.5% in 12.0%), and many of these patients already had cardiovascular or microvascular complications and risk factors. The timing of initiation of drug therapy for T2DM in the older population is an issue requiring further clarification. The present study suggests the need for more explicit guidelines for physicians who treat such patients.

ACKNOWLEDGMENTS

E.M., Q.Z., C.K., L.R., and M.N.F. were involved in the concept and design of the study. E.M., Q.Z., and C.K. were involved in the data collection and/or analysis. All authors were involved in interpretation of the results. M.J.D. and E.M. drafted the article and all authors were involved in the critical revision and approval of the article. E.M. is the guarantor

for this article, and takes responsibility for the integrity of the work as a whole. Medical writing assistance was provided by Julia Vishnevetsky and Melissa Stauffer, PhD (SCRIBCO, Newtown, PA, USA) on an early draft of this manuscript with funding provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ, USA.

Conflict of interest. This study was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ, USA. E.M., Q.Z., M.J.D., and L.R. are employees of Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA. C.K. and M.N.F. have no disclosures related to this study.

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

REFERENCES

1. Sloan FA, Bethel MA, Ruiz D Jr, Shea AM, Feinglos MN. The growing burden of diabetes mellitus in the US elderly population. *Arch Intern Med.* 2008;168:192–9.
2. Bethel MA, Sloan FA, Belsky D, Feinglos MN. Longitudinal incidence and prevalence of adverse outcomes of diabetes mellitus in elderly patients. *Arch Intern Med.* 2007;167:921–7.
3. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet.* 1998;352:837–53.
4. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight

- patients with type 2 diabetes (UKPDS 34). *Lancet*. 1998;352:854–65.
5. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359:1577–89.
 6. American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care*. 2012;35(Suppl. 1):S11–63.
 7. Brown AF, Mangione CM, Saliba D, Sarkisian CA. Guidelines for improving the care of the older person with diabetes mellitus. *J Am Geriatr Soc*. 2003;51:S265–80.
 8. Action to Control Cardiovascular Risk in Diabetes Study Group; Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med*. 2008;358:2545–59.
 9. Erwin G, Iyer S, Rajagopalan R, et al. Type 2 diabetes mellitus treatment patterns and healthcare costs in the elderly population. *Dis Manag Health Outcomes*. 2006;14:75–83.
 10. Zhang Q, Rajagopalan S, Marrett E, Davies MJ, Radican L, Engel SS. Time to treatment initiation with oral antihyperglycaemic therapy in US patients with newly diagnosed type 2 diabetes. *Diabetes Obes Metab*. 2012;14:149–54.
 11. Pani LN, Nathan DM, Grant RW. Clinical predictors of disease progression and medication initiation in untreated patients with type 2 diabetes and A1C less than 7%. *Diabetes Care*. 2008;31:386–90.
 12. de Fine Olivarius N, Palmvig B, Andreasen AH, Thorgersen JT, Hundrup C. An educational model for improving diet counselling in primary care: a case study of the creative use of doctors' own diet, their attitudes to it and to nutritional counselling of their patients with diabetes. *Patient Educ Couns*. 2005;58:199–202.
 13. Jallinoja P, Absetz P, Kuronen R, et al. The dilemma of patient responsibility for lifestyle change: perceptions among primary care physicians and nurses. *Scand J Prim Health Care*. 2007;25:244–9.
 14. Agarwal G, Nair K, Cosby J, et al. GPs' approach to insulin prescribing in older patients: a qualitative study. *Br J Gen Pract*. 2008;58:569–75.
 15. Hayes RP, Fitzgerald JT, Jacober SJ. Primary care physician beliefs about insulin initiation in patients with type 2 diabetes. *Int J Clin Pract*. 2008;62:860–8.
 16. Peyrot M, Rubin RR, Lauritzen T, et al. Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. *Diabetes Care*. 2005;28:2673–9.
 17. van Avendonk MJ, Gorter KJ, van den DM, Rutten GE. Insulin therapy in type 2 diabetes is no longer a secondary care activity in the Netherlands. *Prim Care Diabetes*. 2009;3:23–8.
 18. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130:461–70.
 19. Zhang Q, Marrett E, Jameson K, et al. Reasons given by general practitioners for non-treatment decisions in younger and older patients with newly diagnosed type 2 diabetes mellitus in the United Kingdom: a survey study. *BMC Endocr Disord*. 2011;11:17.
 20. Grant RW, Wexler DJ, Watson AJ, et al. How doctors choose medications to treat type 2 diabetes: a national survey of specialists and academic generalists. *Diabetes Care*. 2007;30:1448–53.
 21. Hansen LJ, Olivarius NF, Siersma V, Drivsholm T, Andersen JS. Individualised treatment goals in diabetes care. *Scand J Prim Health Care*. 2004;22:71–7.
 22. Spoelstra JA, Stolk RP, Klungel OH, et al. Initiation of glucose-lowering therapy in type 2 diabetes mellitus patients in general practice. *Diabet Med*. 2004;21:896–900.