Treatment Trends in Type 2 Diabetes

The Evolving Role of A1c, Metformin & Newer Medications

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Abstract

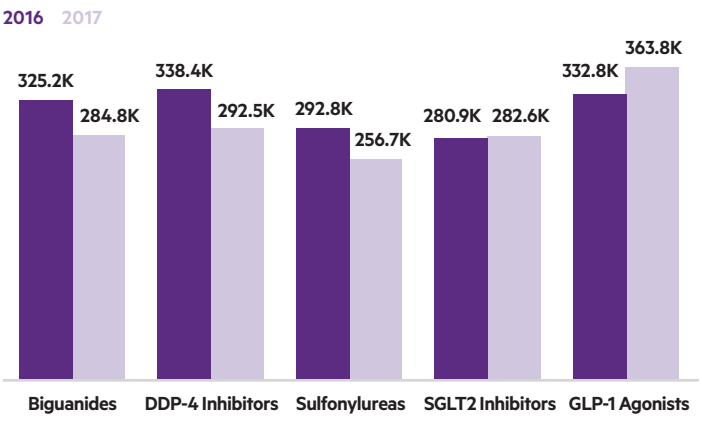
Expenditures nearly doubled in recent years, from $25.6 billion (2013) to $51.5 billion (2016).[1,2]

For prescription medicines for Type 2 diabetes, this increase may be associated with a number of trends, including fewer patients on monotherapy, a decline in the use of sulfonylureas and the introduction of newer therapies, such as DPP-4 and SFLT2 inhibitors, GLP-1 agonists, and non-insulin injectable diabetic medications.

"While prescribing trends reflect physician behaviors, understanding the attitudes and perceptions determining medication choices requires additional research."

To better understand the thinking behind type 2 diabetes prescribing decisions, Epocrates surveyed 50 primary care physicians on topics ranging from A1c targets, the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial and the importance of blood pressure control.

Epocrates TapStream Data® Diabetes Drug Class LookUps (January-June)



Epocrates TapStream data reflects number of times clinicians using Epocrates Rx looked up certain classes of type 2 diabetes drugs. Epocrates TapStream data does not represent actual prescribing data.

Findings:
Highlights from the Epocrates HCPView survey appear below.

74% of physicians agreed that A1c ought to be tightly controlled (<6.5) for most patients. **This perception is inconsistent with 2010/2011 Veterans Administration (VA) and American Diabetes Association (ADA) guidelines.**

94% physicians agreed that the combination of metformin + glipizide is to be avoided due to high degree of hypoglycemia. **This perception is consistent with marketing claims.**

70% of physicians agreed that the ACCORD trial showed that intensive glucose control reduces cardiovascular mortality. **This perception is inconsistent with ACCORD results showing that intensive control increased mortality and did not significantly reduce major cardiovascular events.**

68% of physicians agreed that metformin is contraindicated for diabetes patients with mild renal impairment due to the potential for lactic acidosis. **This is inconsistent with published evidence from the past ten years.**

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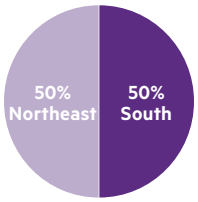
Participant Profile

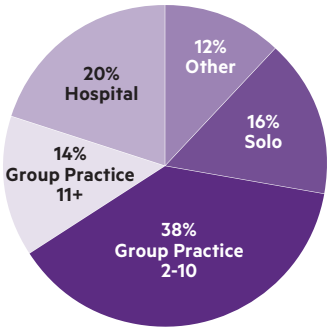
We surveyed a total of 50 primary care physicians using the Epocrates MedInsight platform. Participating physicians treated at least 10 type 2 diabetes patients weekly and wrote 16 or more type 2 diabetes prescriptions per month.

We surveyed doctors from two distinct geographic regions to assess whether there would be geographic variation in physician responses. Physicians surveyed represented various practice settings.

Geographic composition of participating physicians



Practice Settings of Participating Physicians

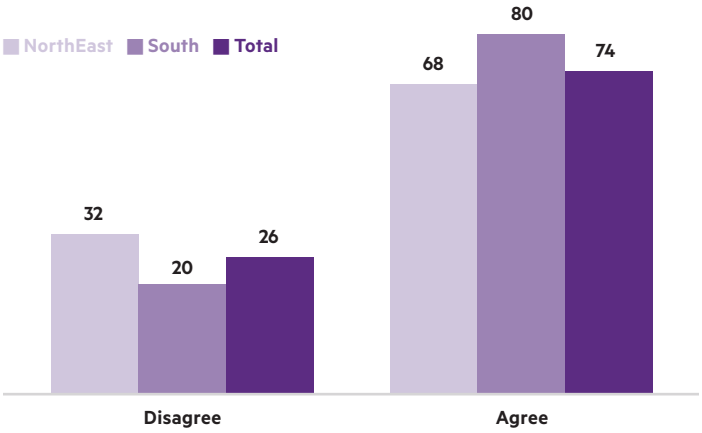


Methods

Physicians were presented with statements concerning type 2 diabetes (questions 1 through 8) and asked to what extent they disagreed or agreed using a 4-part Likert Scale – Strongly Disagree, Disagree, Agree and Strongly Agree. **For purposes of analysis, responses were combined in a binary fashion (agree or disagree) and presented as percentages**. Question 9 uses a multiple choice format.

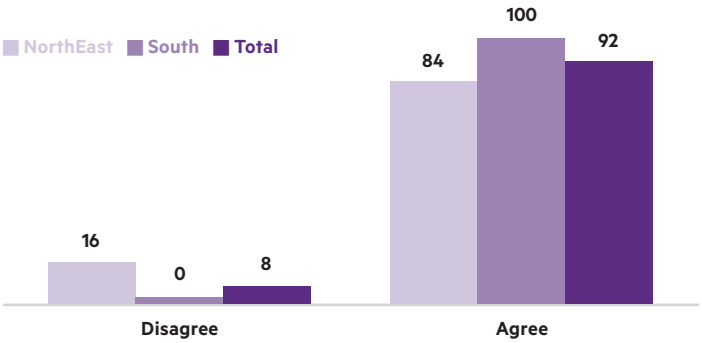
Q1 *Current evidence suggests that aggressive targets for HbA1c (<6.5%) are desirable for most patients.*

74% of total physicians surveyed agreed with this statement, with 26% of respondents disagreeing. The majority response is inconsistent with current evidence and recent guidelines.[3-5] Current ADA and VA guidelines, which are based on evidence from multiple clinical studies, recommend individualizing A1c target (range 7% to 9%) depending on factors including physiologic age, presence/severity of major comorbidities and duration of diabetes.[3,4] For frail older adults and individuals with a life expectancy of less than five years, the American Geriatrics Society suggests an A1c target of 8 percent.[6]



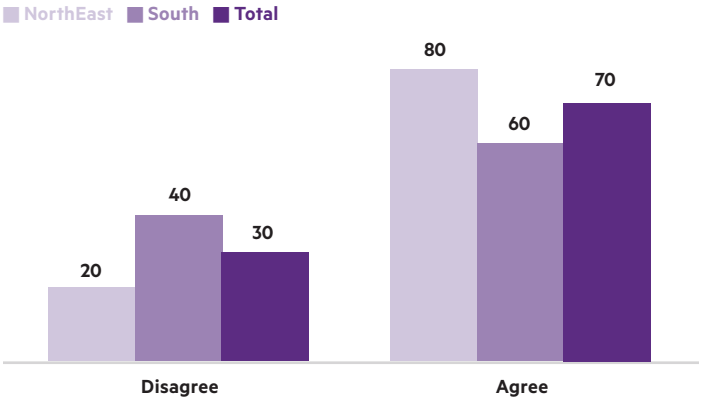
Q2 *Metformin is the first drug of choice for the great majority of diabetes patients.*

92% of total physicians surveyed agreed with this statement, with 8% of respondents disagreeing. The majority responded in a manner that is consistent with evidence and guidelines showing that metformin is the preferred first-line oral agent for treatment of type 2 diabetes.[7]



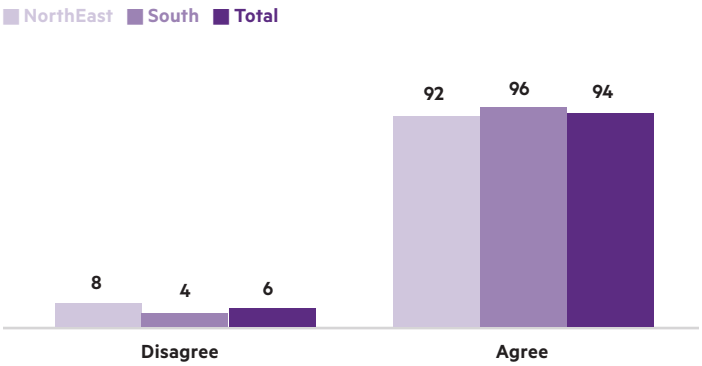
Q3 *Metformin + sulfonylurea is the preferred oral combination for patients who do not have adequate glycemic control on monotherapy with either drug.*

The majority of respondents agreed with this statement which is consistent with recommendations.[7] However, 20% of the physicians in the Northeast and 40% of the doctors in the South disagreed.



Q5 *Januvia (sitagliptin) + metformin may be preferred to metformin + glipizide to avoid hypoglycemia.*

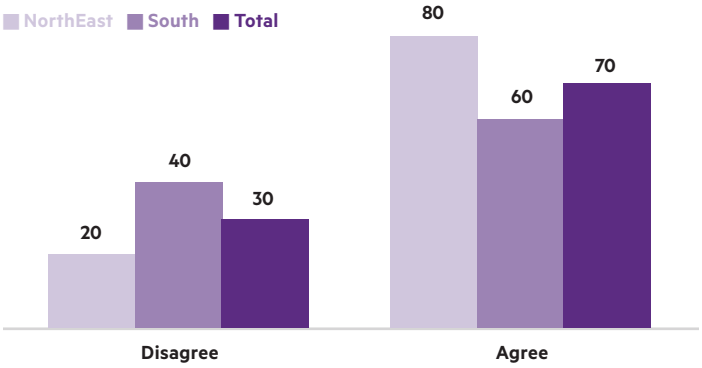
94% of respondents agreed with this statement, which is made in marketing materials. This claim is based on a clinical trial sponsored, and a paper authored, by industry.[9] In this paper, patients taking metformin + glipizide experienced rates of hypoglycemia higher than those reported in drug compendia.[9,10]



Q4 *The ACCORD trial demonstrated that intensive glycemic control reduced CVD mortality in patients with Type 2 diabetes.*

70% of total physicians surveyed agreed with the statement. However, the statement is incorrect; ACCORD did not demonstrate reduced CVD mortality with intensive control.

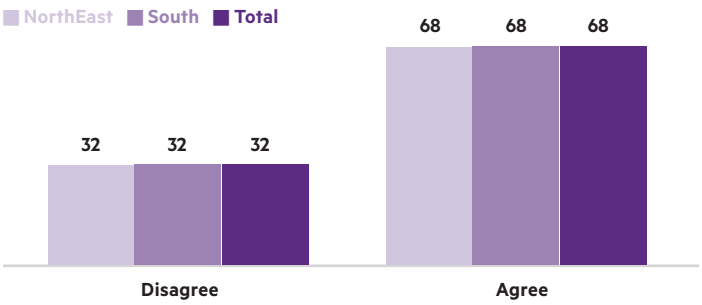
In ACCORD, 10,250 patients with long-standing type 2 diabetes were randomly assigned to intensive or standard glycemic control.[8] After a median follow-up of 3.7 years, intensive therapy was stopped due to a higher number of total and cardiovascular deaths in subjects assigned to intensive therapy compared with the standard treatment group.[8]



Q6 *The risk of lactic acidosis with metformin use is substantially elevated for diabetes patients with mild renal impairment (creatinine 1.3-1.8 mg/dL).*

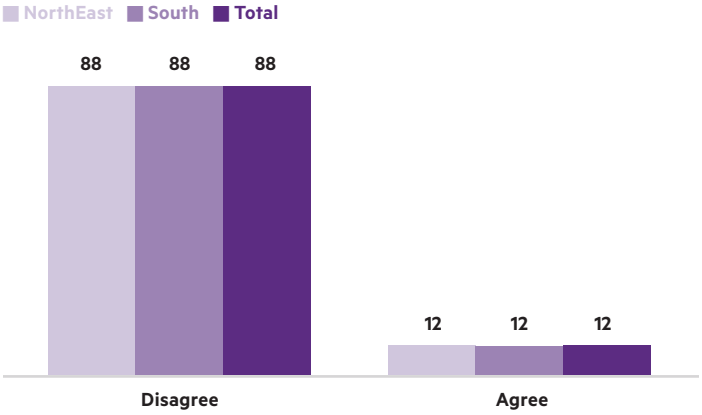
68% of total physicians surveyed agreed with this statement; however there appears to be little evidence to support this.[11,12]

In a 2010 Cochrane Review, 324 (97%) of the 334 prospective studies allowed for the inclusion of patients taking metformin with at least one contraindication, including renal insufficiency. Analysis of these trials and studies (as well as previous Cochrane Reviews) showed no increased risk of lactic acidosis, or increased level of lactate, for metformin compared to other agents.[11] In another study of 393 patients with chronic kidney disease (plasma creatinine levels of 1.5 to 2.5 mg/dl), no cases of lactic acidosis occurred over the four year trial duration.[12]



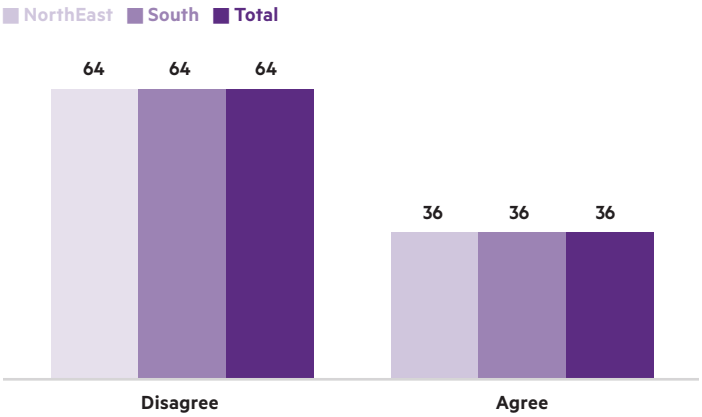
Q7 *An ARB is preferred to an ACEI for treating hypertension in most patients with Type 2 diabetes.*

88% of total physicians surveyed disagreed with this statement, which indicates that the majority of physicians' responses were consistent with evidence. The benefits of ACE inhibitors in patients with diabetes and hypertension are well established, with strong evidence demonstrating their beneficial effects on multiple adverse outcomes, including both macrovascular and microvascular complications.[13]



Q8 *For my patients with Type 2 diabetes, good blood pressure control takes priority over getting HbA1c <7%.*

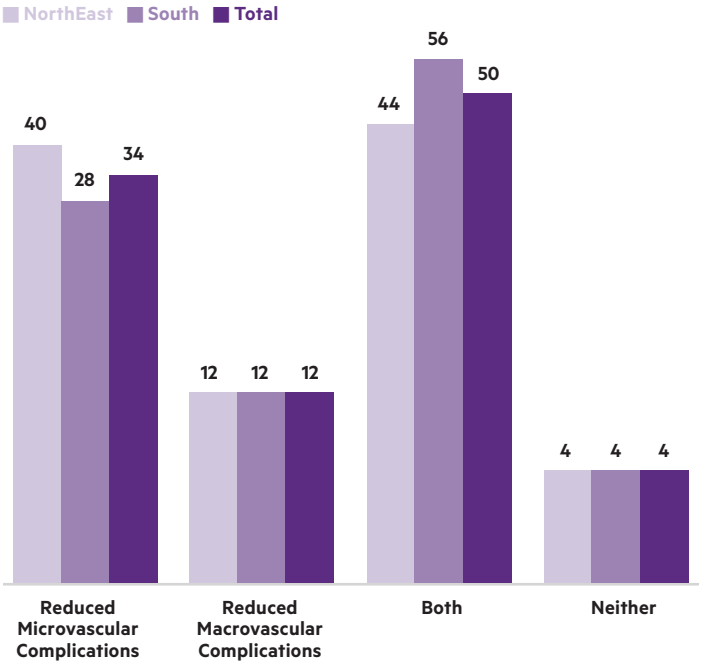
64% of respondents disagreed with this statement. However, according to the 2010 VA guidelines, BP control ought to take priority over getting a low A1c in patients with type 2 diabetes.[4] While glucose control early in the course of diabetes appears to confer some long-term benefit in CVD risk reduction, research clearly indicates that achieving hypertension and dyslipidemia targets confers the greatest benefit.[4,13]



Q9 *In clinical trials, better glycemic control has been associated with reductions in which of the following outcomes?*

50% of total physicians surveyed indicated that better glycemic control is associated with both reduced microvascular and macrovascular advantages. This is inconsistent with the evidence which shows that intensive glycemic control is only proven to reduce the risk for diabetes microvascular and neuropathic disease.[14]

In contrast, most randomized clinical trials show that intensive therapy does not improve macrovascular outcomes in patients with type 2 diabetes.[5] VADT (Veterans Affairs Diabetes Trial), ACCORD, and ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) were all designed to study the impact of intensive vs. conventional therapy on cardiovascular outcomes in patients with long-standing type 2 diabetes (duration 8 to 12 years). None of these trials showed reductions in cardiovascular risk with intensive therapy.5 ACCORD, in fact, showed that intensive therapy was associated with significant increases in total and CVD mortality in patients with type 2 diabetes.[5, 8] Furthermore, in a 2011 meta-analysis published in BMJ of 34,533 patients with type 2 diabetes (mean baseline A1c of 7.9%) randomized to intensive (n=18,315) or standard (n= 16,218) treatment, there were no reductions in all-cause mortality or cardiovascular causes of death with intensive treatment and more than a doubling in severe hypoglycemia.[15]



Conclusion

According to the Institute of Medicine, it takes "an average of 17 years for new knowledge generated by randomized controlled trials to be incorporated into practice, and even then application is highly uneven."[16] Factors influencing a slow uptake in evidence-based practice include: 1) lack of consistent knowledge and adoption of clinical guidelines, 2) lack of balanced sources of summarized evidence, 3) the inherent bias of patients and prescribers towards use of new therapies, and 4) insulation of consumers and prescribers from health care costs.[17] Numerous reasons have been sought to explain this evidence "adoption gap"- the extended time it takes for research to be incorporated into physician prescribing practices.[18] One key reason is the challenge of transferring evidence-based information to practicing clinicians. This problem arises from information overload and the growing complexity of research findings.[18]

Our survey of physician knowledge of type 2 diabetes treatment suggests that a) many physicians are unfamiliar with newer guidelines, b) older evidence (> 15 years) is more likely to be incorporated into practice, c) physician concerns around certain drugs may be unfounded, and 4) physicians have strong recall of claims made in marketing materials.

Physician respondents were unfamiliar with new A1c target goals reflected in recent guidelines. Additionally, over two thirds of respondents misunderstood the results of the ACCORD trial, leading to a perception that cardiovascular mortality could be reduced through intensive glycemic control. Data from the ACCORD trial, in fact, suggests that intensive control of A1c can be unsafe, particularly in patients with a long history of diabetes who are at high risk for cardiovascular disease.[5]

Recommendations such as those for treatment of hypertension in patients with diabetes appear to have better diffusion and adoption. 88% of physicians surveyed were aware, for example, that angiotensin converting enzyme (ACE) inhibitors are as effective as an ARB for treating hypertensive diabetic patients, with benefits that are well established and have been aggressively disseminated by the Joint National Commission.[18,19]

The majority of physicians saw metformin use as contraindicated in patients with renal impairment due to concerns regarding lactic acidosis. However, the evidence shows that diabetic patients who are treated with metformin and who tolerate it well may continue taking it, even when mild renal impairment develops.[11,12]

Many attempts to rectify the paradox of high cost/low quality practice have failed due to a failure to address the complex behavioral, cultural, and social contexts of professional practice.[20] New strategies for communicating evidence to physicians are required to accelerate adoption of optimal prescribing practices.

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About HCPView

Epocrates HCPView offers access to the nation's largest verified and opted-in physician panel. The service allows organizations to conduct primary research with a panel of specialists. Insights gleaned from these physician surveys can assist in developing communication programs and interventions designed to improve quality of care and manage prescription drug utilization.

About RxBalance

RxBalance is a 501(c)(3) organization that seeks to balance the influence of commercial marketing on pharmaceutical care. We aim to prevent overtreatment and underutilization by promoting healthcare media literacy and numeracy. Visit us at www.rxbalance.org.

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Thanks to Randall Stafford, MD, PhD, Program Director, Program on Prevention Outcomes and Practices, Stanford Prevention Research Center, Stanford University School of Medicine for assistance with development of this survey and report.

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