Evaluation of Guideline Recommendations on Oral Medications for Type 2 Diabetes Mellitus

A Systematic Review

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Background: Clinical practice guidelines have an important role in guiding choices among the numerous medications available to treat type 2 diabetes mellitus, but little is known about their quality.

Purpose: To assess whether guidelines on oral medications for type 2 diabetes are consistent with a systematic review of the current evidence and whether the consistency of the guidelines depends on the quality of guideline development.

Data Sources: MEDLINE, CINAHL, and guideline-specific databases were searched between July 2007 and August 2011, after the 2007 publication of a peer-reviewed systematic review on oral diabetes medications.

Study Selection: Two reviewers independently screened citations to identify English-language guidelines on oral medications to treat type 2 diabetes that were applied in the United States, United Kingdom, and Canada.

Data Extraction: Reviewers assessed whether the guidelines addressed and agreed with 7 evidence-based conclusions from the 2007 systematic review. Two reviewers independently rated guideline quality by using 2 domains from the Appraisal of Guidelines Research and Evaluation instrument.

Data Synthesis: Of the 1000 screened citations, 11 guidelines met the inclusion criteria. Seven guidelines agreed with the conclusion that metformin is favored as the first-line agent. Ten guidelines agreed that thiazolidinediones are associated with higher rates of edema and congestive heart failure compared with other oral medications to treat type 2 diabetes. One guideline addressed no evidence-based conclusions, and 5 guidelines agreed with all 7 conclusions. The summary scores of the rigor of development (median, 28.6% [range, 16.7% to 100.0%]) and editorial independence (median, 75.0% [range, 8.3% to 100.0%]) domains varied greatly across guidelines. Guidelines that received higher quality scores contained more recommendations that were consistent with the evidence-based conclusions.

Limitation: Only English-language guidelines targeting users in the United States, United Kingdom, and Canada that contained recommendations on oral medications were included.

Conclusion: Not all practice guidelines on oral treatment of type 2 diabetes were consistent with available evidence from a systematic review. Guidelines judged to be of higher quality contained more recommendations consistent with evidence-based conclusions. The quality of guideline development processes varied substantially.

Primary Funding Source: Agency for Healthcare Research and Quality.


For author affiliations, see end of text.
METHODOLOGY

Data Sources and Search Strategy

Between July 2007 and August 2011, we searched for clinical practice guidelines in MEDLINE (accessed by means of PubMed) and CINAHL, as well as 3 guideline-specific databases: the U.S. National Guideline Clearinghouse, the United Kingdom’s National Library of Guidelines, and the Canadian Medical Association Infobase: Clinical Practice Guidelines. We restricted our search to U.S., United Kingdom, and Canadian databases because we deemed these countries’ guideline developers most likely to access and use the systematic review.

Our search strategy combined terms for type 2 diabetes; treatment or management; and guidelines, consensus, or recommendations and was limited to English-language guidelines. We also searched the Web sites of 15 diabetes-specific organizations and professional organizations about general health that had previously published diabetes guidelines or commonly produce guidelines on chronic diseases to identify new and updated guidelines.

Clinical Practice Guideline Selection

Two reviewers independently reviewed titles and abstracts to identify eligible guidelines. We excluded guidelines that both reviewers agreed met 1 or more of the following criteria: They were not published in English, were published before July 2007, did not contain recommendations on oral medication treatment for type 2 diabetes, or did not meet the 1990 IOM definition of a guideline (that is, “Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” [13]). Conflicts between reviewers about eligibility were resolved by consensus. Third-party arbitration was available but not necessary. Eligible abstracts underwent full article review.

Two independent reviewers also screened the full articles of all included abstracts to determine eligibility for data abstraction. In addition to the exclusion criteria applied to the abstracts, we excluded articles if the guideline was not sponsored or authored by an organization or group; was not intended to be applied in the United States, the United Kingdom, or Canada; applied only to the pediatric population; addressed treatment of type 2 diabetes specifically in patients with HIV infection; or summarized an already published guideline. Differences of opinion about article eligibility were resolved through consensus.

Data Extraction

Two reviewers sequentially extracted relevant information from each eligible guideline. A primary reviewer extracted all of the data for each article, whereas a second reviewer checked the first reviewer’s data abstraction forms for completeness and accuracy. Differences of opinion were resolved through consensus. Data extracted included information on the sponsoring organization and whether the guideline was peer-reviewed and the authors provided references for the recommendations (for example, a systematic review or meta-analysis, literature review, or expert opinion).

Some of the investigators were involved in creating the 2007 systematic review on medications for type 2 diabetes [11, 12] and developed a list of the main evidence-based conclusions of that. We then assessed whether the included guidelines addressed and were consistent with the 7 evidence-based conclusions from the 2007 systematic review. We also assessed whether the guidelines contained an evidence summary statement, which we defined as a statement synthesizing the evidence, weighing the risks and benefits of treatment, and stating whether the guidelines graded their evidence or recommendations.

Assessment of Guideline Quality

We assessed the quality of the guidelines by using the 7-item rigor of development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) instrument [14], which comprised 1) methods used to search for the evidence; 2) criteria for selecting the evidence; 3) methods used for formulating the recommendations; 4) consideration of health benefits, side effects, and risks in formulating the recommendations; 5) an explicit link between the recommendations and supporting evidence; 6) external review by experts; and 7) procedure for updating the guideline. We further clarified item 6 by requiring the peer review to be external to the guideline-developing organization to receive the maximum score. We also included the 2 items from the editorial independence domain: editorial independence from funding organization and recording of conflicts of interest by the guideline development members.

Two reviewers independently rated each item in these 2 domains on a 4-point scale ranging from 1 (strongly agree) to 3 (agree) to 1 (strongly disagree), with midpoints of 2 (agree) and 1 (disagree). We calculated domain summary scores by summing the scores for each item in a domain and standardizing the total as a percentage of the maximum possible score for that domain. We also reported the mean score for each individual item in a domain. We calculated the κ statistic to determine agreement between the reviewers’ “agree” and “disagree” scores; the κ statistic for agreement on quality items was 0.65.

We sought multiple sources to verify our assessment of the guideline development process. We looked for and reviewed any published or unpublished manuals or documents and contacted corresponding authors of the included guidelines; we did not receive e-mail responses from 2 guideline authors. Two reviewers independently evaluated methods manuals and e-mail responses from guideline authors.

Role of the Funding Source

Our work on the systematic review was funded by a contract with the Agency for Healthcare Research and Quality (AHRQ). Although AHRQ staff reviewed an
early stage of this work as it informed topic refinement of a larger project, no one at AHRQ participated in the literature search, data analysis, interpretation of the results, or manuscript preparation. Under the terms of our contract with AHRQ, we obtained copyright release from AHRQ.

RESULTS

Eleven guidelines from 22 publications, including 7 updates, met our inclusion criteria. Six guidelines were from the United States (15–24) (Figure 1). The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) jointly produced 1 guideline (25–30), as did the ADA and the Egyptian Diabetes Center (31). Other organizations that each produced 1 guideline were the International Diabetes Federation (IDF) (32, 33), the Canadian Diabetes Association (34), and the National Institute for Health and Clinical Excellence (NICE) (35, 36) (Table 1). Three guideline developers were medical centers or health systems (15–18, 22–24).

The scope of 8 guidelines was to make general recommendations on the medical treatment of diabetes, but the IDF guideline focused exclusively on the management of postprandial glucose levels (32), including use of oral medications. One guideline from the Joslin Clinic (17) addressed specific considerations when caring for older patients with diabetes, and 1 guideline jointly produced by the ADA and the Egyptian Diabetes Center focused on diabetes management during Ramadan (31).

Three of the 11 guidelines were peer-reviewed by persons external to the guideline developing organizations (32–36). Most guidelines made recommendations based
on a combination of expert opinion and literature review, including published systematic reviews (Table 1).

**Guideline Agreement With Evidence-Based Conclusions From the 2007 Systematic Review**

We evaluated whether guidelines were consistent with each of the 7 conclusions from the 2007 systematic review on the comparative effectiveness of oral medications for adults with type 2 diabetes (11, 12). The IDF guideline, which focused on the management of postprandial glucose levels, made recommendations about use of oral medications but was the only guideline that did not address any of the 7 conclusions (32, 33). Five guidelines contained recommendations that were consistent with all 7 conclusions (Table 2).

Seven of the 11 guidelines were consistent with the conclusion that metformin is favored as first-line agent. The joint ADA/EASD guideline (25, 26), as well as those from Partners HealthCare (18) and the Yale Diabetes Cen-

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**Table 1. Characteristics of 11 Included Clinical Practice Guidelines on Oral Medication for Type 2 Diabetes**

<table>
<thead>
<tr>
<th>Guideline, Year (Reference)</th>
<th>Sponsoring Organization</th>
<th>Guideline Scope</th>
<th>Country Applied</th>
<th>External Peer Review</th>
<th>Basis for the Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA/EASD, 2008 (29, 30) and 2009 (25–28)</td>
<td>ADA and EASD</td>
<td>Consensus report on the medical management of hyperglycemia in type 2 diabetes 2008 update on thiazolidinediones</td>
<td>United States and Europe</td>
<td>No</td>
<td>Expert opinion, nonsystematic literature review, published systematic review, single RCTs, other guidelines</td>
</tr>
<tr>
<td>ADA/EDC, 2010 (31)</td>
<td>ADA and the EDC</td>
<td>Update on the management of diabetes during Ramadan</td>
<td>International</td>
<td>No</td>
<td>2005 guideline, expert opinion, nonsystematic literature review, single RCTs</td>
</tr>
<tr>
<td>IDF, 2008 (32) and 2007 (33)</td>
<td>IDF</td>
<td>Relationship between postprandial glucose levels and diabetes complications and the management of postprandial glucose levels</td>
<td>International</td>
<td>Yes</td>
<td>Systematic review of the literature, single RCTs, other guidelines, observational and basic science studies</td>
</tr>
<tr>
<td>Abrahamson et al, 2007 (15); Joslin Clinical Oversight Committee, 2009 (16)</td>
<td>Joslin Diabetes Center and Joslin Clinic</td>
<td>Pharmacologic management of type 2 diabetes</td>
<td>United States</td>
<td>No</td>
<td>Published systematic review, single RCTs, literature review, other guidelines*</td>
</tr>
<tr>
<td>Joslin Clinical Oversight Committee, 2007 (17)</td>
<td>Joslin Diabetes Center and Joslin Clinic</td>
<td>Care of the older adult with diabetes, including oral medications</td>
<td>United States</td>
<td>No</td>
<td>Single RCTs, nonsystematic literature review, other guidelines</td>
</tr>
<tr>
<td>Partners HealthCare, 2009 (18)</td>
<td>Partners HealthCare</td>
<td>Management of type 2 diabetes</td>
<td>United States</td>
<td>No</td>
<td>Expert opinion, single RCTs, other guidelines</td>
</tr>
<tr>
<td>AACE/ACE, 2009 (19)</td>
<td>AACE and ACE</td>
<td>Consensus panel on an algorithm for glycemic control in type 2 diabetes</td>
<td>United States</td>
<td>No</td>
<td>Expert opinion, published systematic review, single RCTs, FDA prescribing information, other guidelines</td>
</tr>
<tr>
<td>National Collaborating Centre for Chronic Conditions, 2008 (35); NICE, 2009 (36)</td>
<td>Royal College of Physicians and NICE</td>
<td>Management in primary and secondary care Partial update on newer agents</td>
<td>United Kingdom</td>
<td>Yes</td>
<td>Systematic review or meta-analysis, single RCTs, cohort study, health economics data</td>
</tr>
<tr>
<td>CDA Clinical Practice Guidelines Expert Committee, 2008 (34)</td>
<td>CDA</td>
<td>Prevention and management of diabetes</td>
<td>Canada</td>
<td>Yes</td>
<td>Systematic review or meta-analysis, single RCTs, literature review, cohort study, expert opinion</td>
</tr>
<tr>
<td>ICSI, 2009 (20) and 2010 (21)</td>
<td>ICSI</td>
<td>Diagnosis and management of type 2 diabetes mellitus in adults</td>
<td>United States</td>
<td>No</td>
<td>Physicians’ Desk Reference Network†, FDA, package insert, other guidelines</td>
</tr>
<tr>
<td>Yale Diabetes Center, 2009 (22), 2010 (23), and 2011 (24)</td>
<td>Yale Diabetes Center, Yale-New Haven Hospital, Yale School of Medicine, Yale School of Nursing</td>
<td>Diabetes facts and guidelines with a section on pharmacologic therapy for type 2 diabetes</td>
<td>United States</td>
<td>No</td>
<td>Expert opinion, published systematic review, single RCTs, other guidelines</td>
</tr>
</tbody>
</table>

AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; CDA = Canadian Diabetes Association; EASD = European Association for the Study of Diabetes; EDC = Egyptian Diabetes Center; FDA = U.S. Food and Drug Administration; ICSI = Institute for Clinical Systems Improvement; IDF = International Diabetes Federation; NICE = National Institute for Health and Clinical Excellence; RCT = randomized, controlled trial.

* The 2007 guideline did not provide a reference list.
† Accessed at www.pdr.net.
ter (22–24) (which were based on the joint ADA/EASD guideline), supported use of metformin as a “tier one well-validated core” recommendation along with lifestyle changes. The basis for these recommendations was data from the United Kingdom Prospective Diabetes Study (38) and another randomized, controlled trial (39).

The guidelines from the Joslin Clinic provided treatment algorithms but did not recommend one drug over another (15, 16). The joint consensus statement from the American Association of Clinical Endocrinologists/American College of Endocrinology (19) described metformin as the “cornerstone of monotherapy” because of its safety and efficacy. However, its monotherapy algorithm recommended 4 drugs (metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, and α-glucosidase inhibitors) as first-line medication options (19). Five guidelines were consistent with the conclusion that all regimens (except acarbose and nateglinide) produce similar reductions in hemoglobin A\textsubscript{1c} (Table 2).

### Adverse Events

Nine guidelines were consistent with the conclusion that metformin or thiazolidinediones are associated with lower risk of hypoglycemia. The joint ADA/Egyptian Diabetes Center guideline recommended these medications for safely fasting during Ramadan because of their lower risk for severe hypoglycemia (30).

Ten guidelines were consistent with the conclusion that thiazolidinediones are associated with higher rates of edema and congestive heart failure (15–31, 34–36). Eight guidelines (15, 16, 19–31, 35, 36) acknowledged the concern about rosiglitazone and risk for ischemic heart disease that the 2007 systematic review (11, 12) cited. Six guidelines were consistent with the conclusion that metformin and acarbose are associated with weight maintenance (19–30, 34–36), and 9 guidelines were consistent with the conclusion that acarbose is associated with gastrointestinal side effects (15–17, 19–31, 34–36) (Table 2).

#### Table 2. Guideline Agreement With Evidence-Based Conclusions and Evidence Synthesis

<table>
<thead>
<tr>
<th>Guideline, Year (Reference)</th>
<th>Agreement With Evidence-Based Conclusions*</th>
<th>Evidence Synthesis</th>
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<tbody>
<tr>
<td><strong>Met Favored as First-Line Agent</strong></td>
<td>Met or TZDs Are Associated With a Lower Risk For Hypoglycemia</td>
<td>Most Medications Cause Similar Reductions in HbA\textsubscript{1c}</td>
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<tr>
<td>ADA/EASD, 2008 (29, 30), and 2009 (25–26)</td>
<td>Agreed</td>
<td>Agreed</td>
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<tr>
<td>ADA/EDC, 2010 (31)</td>
<td>Not addressed</td>
<td>Agreed</td>
</tr>
<tr>
<td>IDF, 2008 (32) and 2007 (33)</td>
<td>Not addressed</td>
<td>No drug favored</td>
</tr>
<tr>
<td>Abrahamson et al, 2007 (15); Joslin Clinical Oversight Committee, 2009 (16)</td>
<td>No drug favored</td>
<td>Agreed</td>
</tr>
<tr>
<td>Joslin Clinical Oversight Committee, 2007 (17)</td>
<td>Agreed</td>
<td>Agreed</td>
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<tr>
<td>Partners HealthCare, 2009 (18)</td>
<td>Agreed</td>
<td>Agreed</td>
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<tr>
<td>AACE/AACE, 2009 (19)</td>
<td>Agreed</td>
<td>Agreed</td>
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<tr>
<td>National Collaborating Centre for Chronic Conditions, 2009 (33); NICE, 2009 (34)</td>
<td>Agreed</td>
<td>Agreed</td>
</tr>
<tr>
<td>CDA Clinical Practice Guidelines Expert Committee, 2008 (34)</td>
<td>Agreed</td>
<td>Agreed</td>
</tr>
<tr>
<td>ICSI, 2009 (20) and 2010 (21)</td>
<td>Agreed</td>
<td>Agreed</td>
</tr>
<tr>
<td>Yale Diabetes Center, 2009 (22), 2010 (23), and 2011 (24)</td>
<td>Agreed</td>
<td>Agreed</td>
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AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; CDA = Canadian Diabetes Association; EASD = European Association for the Study of Diabetes; EDC = Egyptian Diabetes Center; GI = gastrointestinal; HbA\textsubscript{1c} = hemoglobin A\textsubscript{1c}; ICSI = Institute for Clinical Systems Improvement; IDF = International Diabetes Federation; Met = metformin; NICE = National Institute for Health and Clinical Excellence; TZD = thiazolidinedione.

* Conclusions obtained from a 2007 peer-reviewed, published systematic review on the comparative effectiveness of oral medications for adults with type 2 diabetes (11, 12).

† Except acarbose and nateglinide.

‡ It is safer to fast during Ramadan when using these medications.

§ The evidence statement lists available medications but does not summarize the benefit-harm ratio.

‖ Strength of evidence: Class 1a, Grade: A for obese patients; strength of evidence: Class 4, Grade: D for nonobese patients.

¶ Evidence is graded as “R” on the basis of a joint 2006 ADA/EASD consensus statement (37).
Evidence Synthesis

Seven guidelines provided evidence statements or summaries of the balance of benefits and harms for choices of and recommendations for oral diabetes medication. For example, the guideline from Partners HealthCare (18) mentions medication risk in older adults. It recommends “use of glimepiride or glipizide over glyburide... given the greater hypoglycemia risk associated with glyburide use,” a concern in this population (18), and references a retrospective cohort study (40).

Six guidelines rated the strength of recommendation for some or all of their recommendations (15, 20, 21, 25–30, 32–36). The joint ADA/EASD guideline provided tiers of therapy. “Tier 1 therapy” refers to “well-validated core” treatments, which include metformin as initial therapy and insulin or sulfonylureas as additional therapy. Tier 2 therapy is “less well-validated” and includes thiazolidinediones and glucagon-like peptide-1 receptor agonists (25–30).

Quality of Guideline Development and Risk for Bias

We evaluated the quality of the guideline development process by using the description of the process provided within the guideline text and, if needed, from methods manuals or documents (41–43) and correspondence with corresponding authors.

Table 3. Assessment of Guideline Quality, by Using Domains From the AGREE Instrument*

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<tr>
<td>Rigor of development</td>
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<tr>
<td>The criteria for selecting the evidence are clearly described.</td>
<td>4 4 3.5 1.5 1.5 1.5 1 1 1 1 1 1</td>
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<tr>
<td>The methods used for formulating the recommendations are clearly described.</td>
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<td>The health benefits, adverse effects, and risks have been considered in formulating the recommendations.</td>
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<td>There is an explicit link between the recommendations and the supporting evidence.</td>
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<td>The guideline has been externally reviewed by experts before its publication.</td>
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<td>A procedure for updating the guideline is provided.</td>
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<td>Summary score, %</td>
<td>100 97.6 83.3 47.6 28.6 28.6 23.8 21.4 21.4 19 16.7</td>
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<td>Editorial independence</td>
<td>4 4 4 1 3 3 1.5 1.5 3 1 1 2</td>
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<tr>
<td>The guideline is editorially independent from the funding body.</td>
<td>4 4 4 4 1 3 3 4.5 3 1 2 2</td>
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</tr>
<tr>
<td>Conflicts of interest of guideline development members have been recorded.</td>
<td>4 4 4 4 4 4 4 4 1.5 1 3.5 3 2</td>
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<tr>
<td>Summary score, %</td>
<td>100 100 100 50 83.3 83.3 16.7 8.3 75 33.3 33.3</td>
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</tbody>
</table>

AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; AGREE = Appraisal of Guidelines Research and Evaluation; CDA = Canadian Diabetes Association; EASD = European Association for the Study of Diabetes; EDC = Egyptian Diabetes Center; ICSI = Institute for Clinical Systems Improvement; IDF = International Diabetes Federation; NICE = National Institute for Health and Clinical Excellence.

* Item scores represent the mean score between 2 independent reviewers by using a scale of 1 to 4, where 1 = strongly disagree and 4 = strongly agree. Domain summary scores are calculated by adding all of the item scores in each domain and dividing by the maximum possible score for that domain. Possible summary scores range from 0% (lowest) to 100% (highest). The basis for quality assessment included guideline documents, manuals for guideline development, and responses from corresponding authors.
Guideline Recommendations on Oral Medications for Type 2 Diabetes

We used the 7 rigor of development domain items from the AGREE instrument to evaluate the process used to gather and synthesize the evidence and methods to formulate and update the recommendations (14). Two guidelines received the highest scores (4 on a scale of 1 to 4) for the items “systematic methods used to search for evidence” and “clearly described methods for formulating recommendations” (34–36).

The rigor of development domain summary scores ranged from 0% (lowest) to 100% (highest). The scores for the guidelines that we reviewed ranged from 16.7% to 100% (median, 28.6%). The 3 guidelines that received the highest quality summary scores conducted external peer reviews before publication (32–36). The NICE guideline received the maximum rigor of development summary score (35, 36) (Table 3).

We evaluated the guidelines’ risk for bias by using the 2 editorial independence domain items from the AGREE instrument (14). This domain’s summary scores ranged from 8.3% to 100.0% (median, 75.0%). Six of the 11 guidelines recorded conflicts of interest of guideline development members. The NICE, Canadian Diabetes Association, and IDF guidelines received the maximum score for the editorial independence domain (32, 34–36). The 2 Joslin Diabetes Center guidelines received the lowest scores (8.3% [17] and 16.7% [15, 16]) because they provided minimal information about the guideline development group and did not have available methods guides (Table 3).

Figure 2 demonstrates a linear relationship between the domain summary scores of editorial independence and rigor of development. In general, guidelines with lower editorial independence scores also had lower rigor of development scores, whereas those with higher-quality domain scores scored high in both domains.

Relationship Between Guideline Quality and Consistency With Evidence-Based Conclusions

Figure 3 shows the distribution of the quality summary scores of rigor of development and editorial independence according to the number of recommendations that were consistent with the 7 evidence-based conclusions from the 2007 systematic review (11, 12). In addition, Figure 3 shows that guidelines that received higher quality scores, such as those of the Canadian Diabetes Association and NICE (34–36), had more recommendations that were consistent with the conclusions from the 2007 systematic review of evidence. However, most of the guidelines had multiple recommendations that were consistent with the conclusions from the 2007 review, even those with lower quality scores.

Discussion

In this systematic review of clinical practice guidelines on treating type 2 diabetes with oral medications, we identified 11 guidelines (including their updates) that had been published during the 4 years after the publication of a systematic review on medications for type 2 diabetes (11, 12). Most diabetes guidelines had multiple recommendations that were consistent with the evidence-based conclusions from the 2007 review; we identified no guidelines with contradictory conclusions.

However, overall guideline quality was poor with respect to rigor of the guideline development process, particularly in use of systematic methods to identify evidence. In addition, most guidelines were susceptible to bias because they lacked a description of editorial independence from funders and guideline developers failed to report potential conflicts of interest.

To our knowledge, this is the first review of diabetes guidelines that used a systematic search to identify guidelines, focused on oral medication management of this condition, and compared recommendations with conclusions from a systematic review of available evidence. Burgers and colleagues (44) did not conduct a systematic search to identify guidelines on type 2 diabetes from 13 countries but reported a general consensus of the recommendations among the guidelines. Stone and colleagues (45) selected guidelines on type 2 diabetes from 8 European countries, compared the recommendations, and assessed guideline quality by using the AGREE instrument. Consistent with Burgers and colleagues, they reported little variation in the recommendations among the European guidelines. Neither of these reviews specifically evaluated recommendations about choice of medication or rated the quality of the in...

Figure 2. Relationship between the editorial independence and rigor of development domain summary scores, by using the AGREE instrument.

AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; AGREE = Appraisal of Guidelines Research and Evaluation; CDA = Canadian Diabetes Association; EDC = Egyptian Diabetes Center; ICSI = Institute for Clinical Systems Improvement; IDF = International Diabetes Federation; Joslin = Joslin Clinical Oversight Committee; NICE = National Institute for Health and Clinical Excellence; Partners = Partners HealthCare; Yale = Yale Diabetes Center.
Sixth, no standard tool to rate guideline quality exists, but the AGREE instrument is frequently used. We used 2 methods.

The consistency of guidelines with evidence-based conclusions equals the number of conclusions agreed with out of 7. AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; CDA = Canadian Diabetes Association; EDC = Egyptian Diabetes Center; ICSI = Institute for Clinical Systems Improvement; IDF = International Diabetes Federation; Joslin = Joslin Clinical Oversight Committee; NICE = National Institute for Health and Clinical Excellence; Partners = Partners HealthCare; Yale = Yale Diabetes Center.

included evidence by comparing the recommendations with conclusions from a published systematic review.

Our review included guidelines targeting an audience in the United States, the United Kingdom, and Canada. It was consistent with Stone and colleagues’ finding that the NICE guideline had the highest scores for rigor of development and editorial independence on the AGREE instrument (35, 46).

Reviews of guidelines on cardiovascular disease have also highlighted deficiencies in the rigor and transparency of the guideline development process (6, 47). Choudhry and colleagues (5) reported that 87% of authors of practice guidelines had some relationship with the pharmaceutical industry, according to a survey of 192 guideline authors in the United States and Europe. This finding highlights the need for not only disclosure but also avoidance of conflicts. Such interactions of guideline developers with the pharmaceutical industry are especially concerning in type 2 diabetes because many new drugs to manage this condition have been introduced to the market, only to raise concerns about adverse events (48) and, sometimes, the need for removal from the market (49).

In March 2010, the IOM released Clinical Practice Guidelines We Can Trust, a report that proposed standards for creating clinical practice guidelines. In the report, the IOM redefined clinical practice guidelines as “statements that include recommendations intended to optimize patient care that are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative care options” (3). The new definition emphasizes the importance of using systematic reviews to synthesize the existing evidence and demonstrate the reasoning behind each recommendation, both of which we assessed in this review. The report proposed 8 standards for developing trustworthy practice guidelines, which include disclosing and divesting of conflicts of interest, rating strength of recommendations, and establishing external review (3).

Our review has limitations. First, we focused on guidelines that contained recommendations about oral medications for type 2 diabetes and did not assess recommendations about other treatment options, such as insulin. Second, 3 guidelines had a narrower scope than the 2007 systematic review and therefore did not address each of the 7 evidence-based conclusions.

Third, 4 guidelines that received lower-quality scores were produced by medical centers and therefore might not be fully comparable with guidelines of larger organizations. These 4 guidelines may have had different intended audiences than those of the larger guideline-producing organizations and thus have less rigor and transparency of their methods.

Fourth, guidelines published immediately after the 2007 review may not have had sufficient time to incorporate the new evidence synthesis. However, users accessed the 2007 review thousands of times soon after it was published, and it received numerous citations. These factors indicate that it was readily available when most of the guidelines were published.

Fifth, we included only English-language guidelines with targeted users in the United States, United Kingdom, and Canada because these countries’ guideline developers were most likely to use the 2007 systematic review. We therefore may have excluded other high-quality, international, evidence-based guidelines.

Sixth, no standard tool to rate guideline quality exists, but the AGREE instrument is frequently used. We used 2 domains of the AGREE instrument because they were most relevant to our aims. We did not address the other aspects of guideline quality of the included guidelines, such
as inclusion of stakeholders or whether the recommendations are actionable or implementable by clinicians (50).

Finally, the authors of the 2007 review (11, 12) were among those who assessed the guideline recommendations and the quality of the guideline development process, which may have biased their evaluations. However, those authors had no particular conflict of interest that would favor any one guideline over another.

In summary, most of the 11 practice guidelines on oral medications for type 2 diabetes had recommendations that were consistent with the 7 conclusions from the 2007 systematic review and provided evidence statements summarizing the balance of benefits and harms. The highest-quality guidelines had more recommendations that were consistent with the 7 conclusions from the 2007 systematic review. However, guideline quality was generally low, and few guidelines graded the strength of their recommendations. The new IOM definition of a guideline and guideline development standards will require guideline developers to adapt their processes to improve compliance with these standards and thus increase their trustworthiness to clinician-users and, ultimately, their quality of care for patients with type 2 diabetes.

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