ICSI
Institute for Clinical Systems Improvement

Response Report for Review and Comment – May 2014

Diagnosis and Management of Type 2 Diabetes Mellitus in Adults Guideline

Member Groups Requesting Changes:

Mayo Clinic

Member Groups that Reviewed the Guideline, No Changes Requested:

River Falls Medical Clinic

Member Groups that Responded but the Guideline Does Not Pertain to Practice:

None

Sponsoring Health Plans Requesting Changes:

HealthPartners Health Plan
Metropolitan Health Plan
UCare

Sponsoring Health Plans that Reviewed the Guideline, No Changes Requested:

Medica

MEDICAL CONTENT:

1) Page 7), Clinical Highlights, 5th Bullet: Prefer "once in.." just to avoid confusion. (Mayo Clinic)

Thank you this section has been revised.

2) Annotation #3 page 10, 3rd bullet: Please add this sentence, "though less effective than intensive lifestyle modification". (Mayo Clinic)

Thank you this section has been revised.

3) Annotation #3 page 10, 8th bullet: "Biguanides" credit should state "(Tuomilehto, 2001 [High Quality Evidence])". (Mayo Clinic)

Thank you this resource is no longer used after the current revision.

4) Annotation #5, page 12: MHP and UCare recently submitted a performance improvement project to DHS in which we will strive to increase the LDL-C screening rate of our members with diabetes. It was in the process of doing that research that we discovered the very timely findings regarding fasting state. Although fasting is ideal, it appears that a non-fasting state is not a reason to delay screening. This became an even greater concern when we reviewed the disparity between HEDIS rates of HgbA1c screening (94.74%) vs LDL-C screening (81.42%) for an identical sample of members. It appears that opportunities are indeed being missed. (Metropolitan Health Plan)

Thank you for your comments. We did not recommend that LDL levels should be obtained after fasting and have forwarded your comment to the Lipid Management in Adults work group for review in their upcoming revision.

5) Annotation #7 page 14, Consider adding: All hospitalized patients should have a plasma glucose measured, even if they are not known to have diabetes. (Umpierrez et al 2012) (Mayo Clinic)

After a thorough review of the literature the work group felt that at this time there was not enough evidence to recommend screening for all hospitalized patients, but will continue to monitor the literature for upcoming revisions.

6) Annotation #10 page 15, 5th bullet: Poor evidence (Bergenstal RM, Johnson M, Powers MA, et al. Adjust to target in type 2 diabetes: comparison of a simple algorithm with carbohydrate counting for adjustment of mealtime insulin glulisine. Diabetes Care 2008; 31:1305-1310) (Mayo Clinic)

Thank you for your submission of literature, when we complete a systematic review using our search criteria this article was not included, as we look to expand our criteria and recommendations in upcoming revisions we will hold on to this article for future use.

7) Annotation #10 page 20, 3rd paragraph: The role of bariatric surgery for people with type 2 diabetes who have a BMI less than 35 k/m2 is not established. (Mayo Clinic)

After a thorough review of the evidence the work group felt as though the patients with a BMI greater than 35 k/m2 may consider bariatric surgery if they feel the benefits outweigh the harms if their diabetes or other comorbidities are difficult to control with lifestyle and pharmacologic therapy. There have been several studies that have reviewed and discussed efficacy but have lacked long-term follow-up at this time.

8) Annotation #11 page 21 1st bullet, 2nd paragraph, 2nd sentence: Add "using medications" in the "<7%" section. We ought to mention 1. A lower HbA1c should be targeted if safe. For example, in a person with type 2 diabetes being treated with therapeutic

lifestyle changes and/or metformin alone. 2. A lower HbA1c should be targeted in women planning pregnancy. (Mayo Clinic)

Thank you for your comments. We refer all prenatal/pregnancy related topics to the Prenatal Guideline and have revised our guideline recommendations to be reflective of a glycemic control range and also depending on individual patient factors. The work group felt that being inclusive of all individual patient factors would potentially make the guideline exclusive when each patient's goals should truly be individualized.

9) Annotation#11, Page 23, 2nd paragraph: We should use the targets of therapy of these trials while discussing the implications of the results, not the HbA1c achieved. Our take: In ACCORD for example it was targeting a glycated hemoglobin level below 6.0% led to achieving 6.4% and possibly increased CV events. Therefore, the conclusion is that targeting glycated Hb below 6% in people with (avg 65 Y old) type 2 diabetes for about 10 years and increased cardiovascular risks using multiple medications (including the combination of rosiglitazone and insulin in 70%) was not associated with a reduction in CV events/death when compared to targeting HbA1c 7.7.9%. To us we should not conclude that A1c target below 7% is not safe in a young newly diagnosed person on metformin/TLC etc. (Mayo Clinic)

The excess mortality in ACCORD was in a group of patients with mean A1c about 6.8% and median A1c about 6.5%. ACCORD and ADVANCE and the VADT were the only large RCTs that have even achieved and maintained A1c < 7% and they showed little in the way of CV benefit, with 22% increased mortality in ACCORD. Based on this data, there is no evidence that achieving near-normal glucose control, using the agents used in ACCORD is something that can be broadly recommended for most diabetes patients. In ACCORD, achieving A1c < 7% using an average of three glucose-lowering medications was linked to higher mortality.

The work group discussed that the lower the A1c the better, if this can be achieved by lifestyle or lifestyle plus metformin, based in part on the Diabetes Prevention Program (DPP) results and recommended glycemic control be based upon the patients individual factors.

10) Annotation #13 Page 25 2ND bullet: Not ALL diabetes is coronary disease equivalent. Magri and Fava J CV Med 2012 (Mayo Clinic)

Thank you, We have revised the recommendations after a thorough evidence review and recommended that the patient be assessed for cardiovascular risk and given different strategies based upon increased risk.

11) Annotation #18 page 34 5th paragraph, Retinopathy: Retinal imaging may be used to screen for diabetic retinopathy, esp. in resource limited setting. Abramoff JAMA Ophthalmol. 2013 Mar;131(3):351-7 (Mayo Clinic)

Thank you for your comment. We will continue to review the literature for retinal imaging for our next revision.

12) Annotation #20 page 39 There seems to be a need to reduce the emphasis on lactic acidosis and risk of lactic acidosis with metformin use. Salpeter et al Cochrane Database Syst Rev. 2010 Apr 14;(4):CD002967 (conclusion of the abstract: There is no evidence from prospective comparative trails or from observational cohort studies that metformin is associated with an increased risk of lactic acidosis, or with increased levels of lactate, compared to other anti-hyperglycemic treatments.); Eurich et al Circ Heart Fail. 2013;6:395-402 (Conclusion of the abstract: The totality of evidence indicated that metformin is a least as safe as other glucose-lowering treatments in patients with diabetes mellitus and HF and even in those with reduced left ventricular ejection fraction or concomitant chronic kidney disease. Until trial data become available, **metformin should be considered the treatment of choice for patients with diabetes mellitus and HF**.) (Mayo Clinic)

The work group agrees that FDA product labeling for metformin with contraindications for use in patients with creatinine ≥ 1.4 in women and 1.5 mg/dl in men, and cautions in patients with pharmacologically treated CHF, due to increased risk of lactic acidosis is based on unsubstantiated evidence. We appreciate and have reviewed the references that you forwarded supporting metformin as a safe drug in these situations, and outlining the overall very low rates of lactic acidosis. We also acknowledge that international guidelines have been shifting toward less stringent contraindications for metformin use. In addition, we recognize that the use of estimated glomerular filtration rate (eGFR) is now more preferred over absolute creatinine levels as a reliable estimate of renal dysfunction. However, FDA guidelines have remained static despite the emerging evidence and changes in clinical care, creating a difficult practice conflict for providers. The work group reflected the above information in the harms to benefit of the metformin recommendation and that lactic acidosis is rare, but believed that it is up to the discretion of the provider since FDA labeling has not changed.

13) Annotation #20 page 39, first large paragraph: Re-write this section to state: A recent consensus report of the American Diabetes Association and the European Association for the Study of Diabetes emphasizes on a patient centered approach for the decision of treatment of a person with type 2 diabetes. It is generally agreed that metformin, if not contraindicated and if tolerated, is the preferred and most cost-effective first agent. If metformin alone is unable to achieve/maintain the target, the report suggests adding a second oral agent, a GLP-1 receptor agonist, or basal insulin. The choice of the second line-agent is based on one of a combination of various factors: Efficacy in reducing HbA1c, risks of hyopgylcemia, expected change in weight and other side effects, and, costs (Mayo Clinic)

This section was rewritten and recommendations were made by the ICSI work group after a thorough review of the literature and will continue to be reviewed and updated in upcoming revisions.

14) Annotation #20 page 40, Renal Dysfunction, - General comment and suggestion for re-write of this section: This is rather a vague statement re metformin use in "renal dysfunction. I would recommend: "FDA recommends against using metformin if the serum creatinine is >=1.4 (women) and>=1.5 mg/dL(men) mg/dL. (Mayo Clinic)

Thank you. We have revised this document and recommend clinicians use package inserts to other up-to-date information before prescribing.

15) Annotation #20 page 40, Cardiopulmonary Comorbidities , 1st para 1st sentence: Decompensated (not necessarily any CHF/COPD/OSA) (Mayo Clinic)

Thank you. We have revised this section and cardiopulmonary comorbidities are no longer labeled this way.

16) Annotation #20 page 40, Cardiopulmonary Comorbidities, 3rd paragraph: In compensated heart failure patients on meformin do better than those not on metformin. (Mayo Clinic)

Thank you. We have revised the metformin section to include heart failure patients.

17) Annotation #20 page 40 Hepatic Disease, 2nd sentence: We Disagree. It is at least safe, if not effective in reducing liver enzymes in Non-alcoholic Fatty Liver Disease related elevations of AST and ALT. Reference: Bugianesi et al Am J Gastroenterol. 2005 May;100(5):1082-90 (Mayo Clinic)

Thank you. We have revised this document extensively and these changes have been incorporated.

18) Annotation #21 page 40 2nd bullet: Add to end: or intermediate-acting or NPH. (Mayo Clinic)

Thank you. We have revised this document extensively and will continue to review the evidence in adding insulin and different oral agents in future revisions.

19) Annotation #21 page 41, 6th bullet: Meal times….add: in patients on premixed insulin or NPH twice a day. (Mayo Clinic)

Thank you. We have revised this document extensively and will continue to review the evidence in adding insulin and different oral agents in future revisions.

20) Annotation #21 page 41 3rd, 4th and 5th bullet from the bottom of the page: - Patients should not be treated only with sliding scale rapid acting insulin. However, pump therapy is expensive and requires substantial patient education and involvement in care. There is no evidence in patients with type 2 diabetes showing benefit of pump over multiple daily insulin dose plan. Yeh et al Ann Intern Med. 2012 Sept 4;157(5):336-47. Nevertheless it is recommended and can be helpful in patients with type 2 diabetes who have failed multiple daily insulin injection plan. Reference: Bode et al Diabetes Technol Ther.2010 June;12(Suppl 1):S-17-S-21 (Mayo Clinic)

Thank you. Monotherapy with rapid-acting insulin dosed by "sliding scale" is not recommended. The work group did a thorough review and found there to be a lack of evidence supporting benefit of pump therapy compared to multiple daily insulin injections, particularly in patients with type 2 diabetes. However, pump therapy is more expensive and requires substantial patient education and involvement in care. Insulin pump therapy may be helpful for patients who are interested in more intensified management of blood glucose and want more flexibility, or if pregnancy is desired. Insulin pump therapy is more commonly used in type 1 patients but may be a suitable option for type 2 patients that have not reached their glycemic goals with multiple daily insulin injections. The work group will continue to review the evidence for incorporation into recommendations for future revisions.

21) Annotation #22: page 43: Additions to this section: and the only agent besides insulin and metformin to show prevention of diabetes complications (Mayo Clinic)

The work group reviewed the literature and is unable to make a recommendation at this time. If you have literature you would like to provide for the next revision, please send for further review.

22) Page 44 Table: GLP-1 agonist liraglutide and the DPP-4 inhibitors saxagliptin, alogliptin, and linagliptin should be added to the list of agents associated with weight loss or weight maintenance. This information is listed in the drug table in annotation 22. To be consistent, it should be included in the text of annotation 20 as well.

References
Liraglutide package insert (http://www.novo-pi.com/victoza.pdf)
Alogliptin package insert (http://www.takeda.us/products/)
Linagliptin package insert (http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/PIs/Tradjenta/Tradjenta.pdf)

Saxagliptin package insert (http://packageinserts.bms.com/pi/pi_onglyza.pdf (HealthPartners Health Plan)

Thank you for your comment. We have removed the table regarding weight loss medications with our current revision.

23) Sulfonylureas should be added to the list of agents associated with weight gain along with insulin and thiazolidinediones. This information is listed in the drug table in annotation 22. To be consistent, it should be included in the text of annotation 20 as well.

References
Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach (http://care.diabetesjournals.org/content/early/2012/04/17/dc12-0413) Inzucchi, 2012. (HealthPartners Health Plan)

Thank you for your comment. We have removed the table regarding weight loss medications with our current revision.

24) For consistency, the information regarding renal dysfunction and DPP-4 inhibitors and GLP-1 agonists contained in the drug table in annotation 22 p. 44 should be in the text of annotation 20 as well. (HealthPartners Health Plan)

Thank you for your comment. We have extensively revised this document and will continue to review evidence for additional recommendations in future revisions.

25) Annotation # 22; Non-insulin Agents Table: Recommendations: Exenatide is spelled incorrectly in the table. The new DPP-4 inhibitor alogliptin should be added to the table. (HealthPartners Health Plan)

Thank you for your comment. We have removed the table regarding weight loss medications with our current revision.

26) Table in Annotation #22**:** To 1st row, safety/monitoring column, 3rd bullet add: "Despite FDA".
To 2nd row, safety/monitoring column add: Start with the lowest possible dose, titrate up slowly.
Question: add canagliflozin to the table? (Mayo Clinic)

Thank you for your comment. We have removed the table in our current revision and will continue to review evidence for additional recommendations in future revisions.

27) Annotation #24: Recommendation- In the insulin alone section ".2-.4 units/kg" should be changed to "0.2-0.4 units/kg" for ease of reading. (HealthPartners Health Plan)

Thank you for your comment. We have revised the document throughout to include the appropriate number of significant figures for ease of reading.

AIMS AND MEASURES:

30) Page 50: Measurement #1 a, b, c: Optimal Diabetes Care: Percentage of patients with type 2 diabetes mellitus age 18-75 years old who achieve any or all of the following diabetes controls….. Comment: Several composite measures on NQF, and also in Minnesota Community Measurement also have a tobacco component, i.e. optimal includes being tobacco free. Can ICSI consider adding this outcome to optimal care? (HealthPartners Health Plan)

The work group has updated the Optimal Diabetes Care measure to include percentage of patients who are tobacco free, and in upcoming revisions will systematically review the evidence for recommendations as part of the document.

31) Aims and Measures, page 48 2nd paragraph:-However, efforts to achieve…
Comment on this section: Suggest HbA1c instead of A1c.
Same issue as before: in the intensive groups the "efforts to achieve lower A1c" were as follows: ACCORD: below 6%; ADVANCE: below 6.5%; VADT: below 6% or below 1.5SD above ULN. There is no evidence that "efforts to achieve lower A1c" below 7% increases risk of mortality..... etc. *Mayo Clinic)*

The measures have been updated to be HbA1c instead of A1c. The excess mortality in ACCORD was in a group of patients with mean A1c about 6.8% and median A1c about 6.5%. ACCORD and ADVANCE and the VADT were the only large RCTs that have even achieved and maintained A1c < 7% and they showed little in the way of CV benefit, with 22% increased mortality in ACCORD. Based on this data, there is no evidence that achieving near-normal glucose control, using the agents used in ACCORD is something that can be broadly recommended for most diabetes patients. In ACCORD, achieving A1c < 7% using an average of three glucose-lowering medications was linked to higher mortality. The work group discussed that the lower the A1c the better, if this can be achieved by lifestyle or lifestyle plus metformin, based in part on the DPP results and recommended a range of glycemic control based upon the patients individual factors.

32) Aims and Measures page 49 #3e: or retinal *photography (Mayo Clinic)*

Thank you for your comment. We will continue to review the literature for retinal imaging for our next revision and update the affected Aims and Measure if a recommendation is produced.

Order Set

33) Appendix A – Order Set, page 115. Blood glucose goals: Comment on this section: On IV insulin therapy in ICU the glucose level should be maintained between 140 and 180 mg/dl; below 110 mg/dL using insulin is not recommended. (ADA 2009) (Mayo Clinic)

As noted on the first page of the order set, this order set is intended for management of patients receiving subcutaneous insulin and is not intended to cover critical care patients. While we would agree with the above recommendation it is outside the scope of this order set.

34) Glucose Monitoring Order Set- Comment on this section: Medical Record should show the duration after the last meal at the time of glucose check.
(Mayo Clinic)

As is noted in the documentation of the order set, we are not aware of evidence supporting any particular glucose monitoring regimen. In order to avoid making the order set overly detailed or burdensome, we would prefer to maintain the current structure of the order set and allow individual organizations to modify it to fit their own practices and procedures.

35) Order Set Types of Insulin : Comment on this section:
Do not use "Sliding Scale Insulin" as the sole therapy in any patient with persistent (>2 days) of hyperglycemia above 180 mg/dL. (Mayo Clinic)

We have updated the documentation of the order set to include new data from recent randomized trials comparing "sliding scale" insulin regimens with basal-bolus regimens. As there may be some situations where "sliding scale" insulin may be non-inferior to basal-bolus regimens (patients receiving enteral nutrition – Korytkowski, et al. Diabetes Care, 32(4) 594, 2009), we do not wish to be overly proscriptive or dogmatic as far as recommendations for specific insulin regimens. As we note in the documentation section Basal insulin: "Basal insulin would generally be appropriate for any patient being managed with subcutaneous insulin …".

36) Transition from Intravenous to Subcutaneous Insulin page 117, Add to this section: or enteral/ parenteral nutrition (Mayo Clinic)

We are not clear what the suggested change is for this section. Perhaps the member group could expand on this or provide a suggested change.

37) Order Set: Insulin administration (if going home on insulin) Add to this section: Do not use "Sliding Scale Insulin" as the sole therapy while being sent home. (Mayo Clinic)

As per our response to 35) above, in the absence of data to support a particular management approach, we would prefer to avoid specific proscriptive statements, and will continue to monitor the evidence for upcoming revisions.