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Re: New seminal research for consideration in the Evidence Review for Screening for Type 2 Diabetes, Impaired Fasting Glucose and Impaired Glucose Tolerance

Dear Drs. Miller and Wolff,

In January 2013, the Diabetes Advocacy Alliance™ (DAA) submitted a letter to the Agency for Healthcare Research and Quality (AHRQ) that outlined seminal research for consideration by the United States Preventive Services Task Force (USPSTF) in anticipation of an update to the recommendations for screening for type 2 diabetes. (See Appendix A).

The DAA, a coalition of 20 members representing patient advocacy organizations, professional societies, trade associations, other nonprofit organizations, and corporations, is committed to changing the way diabetes is viewed and treated in America. As such, the DAA is pleased to submit a compendium of studies that augments our earlier letter submitted to AHRQ and represents new evidence for the Evidence-based Practice Center (EPC) to consider as it conducts its systematic evidence review for screening for type 2 diabetes. We are hopeful that an updated recommendation for screening for type 2 diabetes will take into account the most recent data and seek to identify people with undiagnosed diabetes and risk factors for diabetes to allow for early interventions to prevent or delay the disease and its complications. For type 2 diabetes, screening is the entry point to prevention.

The DAA commends USPSTF for reconsidering this important topic, as type 2 diabetes is a highly prevalent disease that poses a significant burden to people with the disease, the US health care system, and our society.
There are currently 26 million Americans with diabetes, and 90 percent to 95 percent of diagnoses are type 2 diabetes. An additional 79 million people are estimated to have prediabetes, which often progresses to type 2 diabetes within 10 years.\(^1\) Over the past 30 years, the percentage of Americans diagnosed with diabetes has more than doubled\(^2\) and the number of Americans living with diabetes, both diagnosed and undiagnosed, is projected to increase by 64 percent from 2010 to 2025.\(^3\) Additionally, diabetes is intrinsically linked with an increased risk of other chronic diseases and is the leading cause of kidney failure, blindness, and lower-limb amputations.\(^4\) The prevalence of the disease presents a massive economic burden, with the US spending $245 billion on diabetes annually.\(^5\)

The Healthy People 2020 goals call for a 10 percent increase in the proportion of people with diabetes whose condition has been diagnosed, and a 10 percent increase in the proportion of people with prediabetes who are engaged in lifestyle behaviors to reduce their risk of diabetes.\(^6\) There are known risk factors for prediabetes and type 2 diabetes that are easy to assess, including overweight and obesity, family history, age, history of gestational diabetes, and certain racial/ethnic populations.\(^7\) For this reason, the American Diabetes Association (ADA) recommends that adults who are overweight (BMI >25) with one or more risk factors (e.g., use of hypertensive medication, previously recorded high blood glucose levels, family history of diabetes, etc.) undergo screening as part of regular medical care. There is consensus among numerous organizations worldwide for targeted screening of high-risk individuals.\(^8\)

The USPSTF currently recommends screening for type 2 diabetes only in asymptomatic adults with high systolic blood pressure (SBP > 135 mmHg), despite the various other well-known risk factors mentioned above.\(^1\) With type 2 diabetes now reaching epidemic levels, there is a significant need to update and reconsider the current recommendation. Below, we provide a summary of new research published since 2011 that: (1) illustrates the performance of the current USPSTF criteria (sensitivity and specificity) and (2) could be employed to help inform the key and contextual questions in the analytic framework.

These articles include:


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**Performance of 2008 USPSTF Screening Criteria**

**Casagrande SS, Cowie CC, Fradkin JE (2013)**

Casagrande and colleagues conducted a study aimed at determining the effectiveness of the current USPSTF screening criteria for identifying patients with undiagnosed type 2 diabetes. Using data from the National Health and Nutrition Examination Survey, the authors measured the sensitivity and specificity of the USPSTF screening criteria and determined the prevalence of cardiovascular disease (CVD) risk factors and comorbidities among patients with undiagnosed type 2 diabetes. They found that, among patients without diagnosed type 2 diabetes, 4% had undiagnosed type 2 diabetes. Additionally, among those with undiagnosed diabetes, only 44.4% would have been correctly identified using the current USPSTF screening criteria. This study illustrates that employing the current criteria results in missing over half of undiagnosed type 2 diabetes cases, and a substantial portion of this cohort has high low-density lipoprotein or other CVD risk factors. Therefore, expanding the USPSTF type 2 diabetes screening criteria to include additional risk factors could avoid the negative impact of utilizing the current guidelines.

**Evidence to Inform Key and Contextual Evidence Review Questions**

**Chamnan P, Simmons RK, Khaw KT, et al. (2012)**

Chamnan and colleagues used a modeling approach to estimate the potential population impact of several stepwise screening strategies to identify individuals at high risk who would benefit from being offered preventive interventions. The authors used data from the European Prospective Investigation of Cancer-Norfolk to model screening strategies to identify and treat high-risk individuals using different HbA1c cut-off points with and without a stage of prestratification. They found that a stepwise strategy, using routine data for type 2 diabetes risk prestratification before inviting high-risk individuals to a HbA1c diagnostic test and subsequent preventive interventions, could prevent a significant number of type 2 cases with potential cost savings. This study can help to inform two contextual questions outlined in the final USPSTF research plan:
1. What is the yield (incidence) of starting screening at different ages or rescreening at different intervals among nonpregnant adults with an initial normal fasting blood glucose, hemoglobin A1c, or glucose tolerance test?

2. What is the utility of existing modeling studies of type 2 diabetes screening versus no screening in examining important health outcomes?

We are pleased that the USPSTF will be capturing modeling studies in its evidence review. In the absence of randomized clinical trials, modeling studies can mathematically synthesize data from multiple studies, and can be valuable in understanding the dynamics and downstream impact of healthcare decisions.

**Mortaz S, Wessman C, Duncan R, et al. (2012)**

Mortaz and colleagues assessed the health benefits and cost reduction associated with several screening strategies for type 2 diabetes and prediabetes from the perspective of the Canadian healthcare system. The authors developed a ten-year Markov state-transition model, tracking a cohort of individuals with at least one risk factor for type 2 diabetes, to compare the cost-effectiveness of no screening with conventional screening. Conventional screening once every 3 years was superior to no screening, and changing the frequency of screening did not impact the overall results. Screening once every five years yielded the lowest cost per quality-adjusted life year. The authors conclude that a no screening approach would cost the Canadian healthcare system considerably more than screening once every five years. This study can help to inform the following contextual question outlined in the final USPSTF research plan:

1. What is the utility of existing modeling studies of type 2 diabetes screening versus no screening in examining important health outcomes?

**Rahman M, Simmons RK, Hennings SH, et al. (2012)**

Rahman and colleagues examined the impact of diabetes screening on self-rated health and cardiovascular morbidity, by comparing 13-year outcomes in individuals without diabetes from screened and unscreened patients from the Ely Study cohort. The authors found that screening for diabetes is not associated with long-term harms at the population level; however, self-rated functional health status and health utility were identical among screened and unscreened populations. One explanation for the null results is that no advice was given to patients who screened negative in the Ely Study cohort, regardless of risk status. If high-risk non-diabetic patients were provided educational materials on diabetes prevention, the impact of screening may have been more pronounced. This study can help to inform Key Question 2 outlined in the final USPSTF research plan:

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9 Three strategies of conventional screening were examined: (1) once every three years, and once every year if patient found to have prediabetes; (2) once every five years, and once every year if patient found to have prediabetes; (3) once every year

www.diabetesadvocacyalliance.org
1. What are the harms of screening nonpregnant adults for type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance?

**Simmons RK, Rahman M, Jakes RW, et al. (2011)**

Simmons and colleagues measured the impact of invitation for type 2 diabetes screening on population mortality in the Ely Study cohort. The authors found that compared to patients not randomly invited to screening from 1990-1992, those who were randomly invited to screening had a non-significant reduction in all-cause mortality. However, the non-significant reduction (21%) approaches statistical significance (CI: 0.63-1.00, p=0.05), indicating a strong trend in mortality outcomes in favor of invitation to screening. Additionally, the marginally non-significant reduction in mortality in the Ely Study cohort materialized without specification of a standard intervention for people with newly diagnosed type 2 diabetes – potentially underestimating the true impact of screening and early intervention. Also, the study design included patients who were randomly invited to the screening but did not attend, which could confound the results. The authors evaluated the impact of screening on all-cause mortality when the screening group was comprised only of individuals who were invited to screening and actually attended the screening. In this cohort, screening was found to have a statistically significantly lower risk of all-cause mortality compared to those not randomly invited to screening. This study can help to inform Key Question 1 outlined in the final USPSTF research plan:

1. Is there direct evidence that systematic screening (either targeted or universal) for type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance among asymptomatic, nonpregnant adults improves health outcomes?


Simmons and colleagues estimated the impact of a population-based stepwise screening program on mortality in patients aged 40-69 years and previously identified as at high risk of undiagnosed diabetes using data from the ADDITION-Cambridge trial. The authors found that all-cause mortality over a median of almost 10 years was not reduced by one round of screening. However, because the follow-up period was only 10 years on average, the study may not be able to capture the true mortality risk-reduction associated with risk-based screening, which may take many more years to materialize. This study can help to inform Key Question 1 outlined in the final USPSTF research plan:

1. Is there direct evidence that systematic screening (either targeted or universal) for type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance among asymptomatic, nonpregnant adults improves health outcomes?
Conclusion
Diabetes screening is essential for timely diagnosis of type 2 diabetes, and enables early initiation of individual treatment with the potential to improve individual health outcomes and reduce major public health burdens. Research shows that the current USPSTF guideline for screening for type 2 diabetes may be missing many people with undiagnosed diabetes and risk factors for diabetes (Casagrande SS, Cowie CC, Fradkin JE (2013)). Because screening for type 2 diabetes is effective, noninvasive, and can be quickly and easily conducted, at a minimum, screening criteria should be expanded to incorporate multiple risk factors linked to developing diabetes (e.g., obesity, age, family history) in order to identify as many people with undiagnosed type 2 diabetes as possible. The current body of literature, including additional evidence published since the last USPSTF review, indicates that screening asymptomatic adults at high risk for type 2 diabetes can provide a clear net clinical benefit. Given the importance of the USPSTF screening recommendations, and their impact on access to screening services, consideration should be given to strategies that incorporate multiple risk factors for developing type 2 diabetes.

Thank you for your consideration of the evidence we have outlined above. The DAA commends the USPSTF for its review of the evidence on screening for type 2 diabetes, and will remain engaged in the review process through TOPS Workgroup participation and submission of comments during the public comment opportunity.

Sincerely,

Academy of Nutrition and Dietetics
American Association of Clinical Endocrinologists
American Association of Diabetes Educators
American Clinical Laboratory Association
American Diabetes Association
American Optometric Association
American Medical Association
Endocrine Society
Healthcare Leadership Council
National Association of Chronic Disease Directors
Novo Nordisk Inc.

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USPSTF recommends screening in asymptomatic adults with sustained blood pressure (BP) greater than 135/80 mmHg (B grade), and concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening in asymptomatic adults with BP of 135/80 mmHg or lower (I statement).
http://www.uspreventiveservicestaskforce.org/uspstf/uspsdiab.htm