Breakthrough T1D™
Formerly JDRF

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Dear Dr. Michael Silverstein, Dr. John Wong, and Dr. Esa Davis,

Breakthrough T1D, formerly JDRF, has recently organized an effort to develop and submit an application to the United States Preventive Services Task Force (USPSTF) for a new preventive service topic: pediatric general population screening for type 1 diabetes (T1D). Based on nearly three decades of global research seeking interventions to detect, delay, and reverse the effect of T1D, we now have the first FDA approved immunotherapy to delay the onset of T1D. We also now have the knowledge and ability to detect the disease prior to clinical onset and can provide interventions that improve health outcomes at the point of diagnosis. As those signed on to this letter demonstrate, there is broad support among the key clinical organizations and clinical leaders to advance a USPSTF topic nomination.

The evidence supporting the nomination of T1D screening in the pediatric general population was submitted via the USPSTF "New Topic" form on 05/19/2025. The bibliography follows in the Appendix at the conclusion of this letter. In the following sections we outline the context in which we hope the USPSTF will evaluate and accept T1D screening as a new preventive service topic.

T1D is an autoimmune disease that is caused by the destruction of insulin-producing β-cells by multiple immune mechanisms. There are nearly 9.4 million people living with T1D today globally, approximately 2 million people in the US. Studies suggest that more than 50,000 Americans are diagnosed with T1D each year.[1,2,3] The prevalence of T1D per 1000 people for those 19 years or

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[3] CDC. Prevalence of diagnosed diabetes. https://www.cdc.gov/diabetes/php/data-research/index.html [updated May 15, 2024].

younger increased significantly from 1.48 in 2001 to 1.93 in 2009 to 2.15 in 2017.[4] The mortality rate for people with T1D is approximately 2-3 times higher than for those without diabetes.[5,6]

As a result of nearly three decades of research led by many institutions, namely NIH's TrialNet, we now know that the autoimmune response in T1D occurs in stages often over years. The ability to stage T1D allows for the development of therapies and care plans to target early interventions to improve outcomes at the time of diagnosis.[7] As our understanding of disease progression in T1D has improved, so has our understanding and ability to care for those living with T1D. Historically T1D was understood to be a childhood disease, but data now indicate that roughly half of all people newly diagnosed with T1D are adults.[8] Further studies indicate that relatives of people with T1D have an approximate 15-fold increased risk of disease compared to those without a relative with T1D. [9,10] However, 85% of those who will be diagnosed with T1D do not have a family history with the disease.[11]

Regardless of any familial connection to T1D, it is all too common for people to be diagnosed after presenting with preventable life-threatening complications, chiefly diabetic ketoacidosis (DKA). DKA is characterized by hyperglycemia, ketosis, and acidosis, resulting from insulin insufficiency and increased levels of counterregulatory hormones (glucagon, catecholamine, cortisol, and growth hormone). DKA must be recognized and treated immediately, often necessitating hospitalization in intensive care for management and monitoring, to avoid acute morbidity (e.g., cerebral edema) and death.[12] Rates in the US vary but several studies show increasing rates of DKA at diagnosis with some estimates as high as 58%.[13,14,15] Younger children are at greater risk for presentation in DKA at diagnosis because of the rapid disease progression in this age group and unrecognized

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symptoms.[16,17] In addition to significant reductions in hospitalization for DKA at diagnosis, studies indicate better long-term health outcomes, including improved glycemic outcomes over time and lower risk for neurocognitive complications associated with avoiding DKA.[18,19]

For nearly 30 years, government, research institutions, and clinicians have explored ways to identify those at risk of developing T1D and to intervene prior to diagnosis with hopes, in part, to avoid life-threatening complications like DKA at diagnosis. This research led to our ability to identify the staging for T1D and supported the development of the first-ever FDA approved immunotherapy for T1D in 2022. This disease modifying therapy, teplizumab-mzwv, delays the clinical onset of T1D (Stage 3 T1D) and is a critical step in efforts to move the treatment of T1D from treating symptoms to treatment focused on changing the course of the disease itself.

In addition to screening people for research and clinical trial purposes, global efforts have also focused on screening people for risk via familial and pediatric general population screening programs. These programs in both the US and across the globe clearly show that screening for detection of early stage T1D provides better outcomes for those screened. For example, the feasibility of general population T1D screening in children has been demonstrated in Germany through the Fr1da study.[20]

As is the case with all preventive screening programs, there are potential harms associated with T1D screening such as false positives, false negatives, inducing fear, physical harm associated with blood collection, and the additional provider burden associated with increased diagnosis.[21] In addition to these common potential harms, global studies have shown increased anxiety levels in parents when their child is identified as potentially being diagnosed with early stage T1D.[22] These potential harms are able to be managed with our current clinically available tools, further underscoring the positive benefit of T1D screening.[23] In fact, current standards of care by the American Diabetes Association emphasize the importance of screening for early stage T1D in individuals with an elevated genetic risk, including individuals with a family history of T1D.[24]

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[24] American Diabetes Association Professional Practice Committee; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. *Diabetes Care* 1 January 2025; 48 (Supplement_1): S27–S49. https://doi.org/10.2337/dc25-S002

Significant studies are ongoing to test and understand T1D screening in a general population that includes both adults and children (e.g. ASK, EDENT1FI, ELSA, DIPP, ADIR, T1DRA).

It is now possible to identify presymptomatic children and adults likely to develop T1D and take action to prevent poor outcomes at diagnosis as well as the potential to delay the need to replace insulin. There is a preponderance of evidence about the impact of screening in the general pediatric population. Given this base of evidence, we encourage the USPSTF to accept the nomination of T1D screening as a new topic for consideration.

If there are any questions or additional information any of the undersigned members can provide, please contact Aaron Turner-Phifer at aturner-phifer@breakthrought1d.org. We thank USPSTF for its ongoing efforts to expand access to preventive services and improve public health.

Sincerely,

Organizations

Clinical Experts

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Appendix

Bibliography of Relevant T1D Screening Studies

A: Bibliography for T1D Topic Nomination submission:

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