Breakthrough T1D USPSTF Application

Below is the application Breakthrough T1D submitted to USPSTF recommending the topic of screening for early detection of T1D.

We encourage other individuals and organizations to also nominate T1D as a new topic to USPSTF. Individuals and organizations can adapt our nomination submission and supporting evidence as needed to reflect your priorities and/or the priorities of your organization. Parts of the application can be copied and pasted directly into the USPSTF nomination form for your application. The more applications submitted to USPSTF on a given topic, even if not aligned in all areas, show broad interest and support which increase the likelihood of USPSTF taking up T1D screening as a new topic.

The USPSTF new topic nomination form is available [here](https://urldefense.com/v3/__https%3A/www.uspreventiveservicestaskforce.org/uspstf/public-comments-and-nominations/nominating-recommendation-statement-topics/new-topic__;!!DSSadoo!3npU4AP5q8M2g_D1AY1T1SATkBj767X97R7gZ73ZeYxWRnfp-Aox0L5KhXCl39IqHyBYQ9YPrNpadbpNBynIGWHQqilBXB5z$).

**USPSTF Topic Nomination for Type 1 Diabetes (T1D)**

Topic Details

**New Preventive Service Topic you are nominating** *[open text box; no word count limit]*

We are nominating the topic of screening for early detection of type 1 diabetes (T1D) in the general pediatric population for a USPSTF recommendation. Early screening for Type 1 Diabetes (T1D) is crucial as it enables timely intervention, reduces the risk of life-threatening complications, and improves long-term health outcomes for affected individuals.

T1D is an autoimmune disease that up to now, often strikes suddenly, and can be fatal if not identified quickly. Incidence rates of both T1D and the life-threatening T1D complication of diabetic ketoacidosis (DKA) are increasing in children [1]. Currently, approximately 9.4 million people are living with T1D globally, with an increase in incidence resulting in a projected 16.4 million people living with T1D by the year 2040, making it one of the fastest-growing, noncommunicable, chronic diseases globally [2]. People with T1D require lifelong insulin therapy coupled with medical products to monitor and regulate blood glucose levels to live.

These tools support the management of this complex chronic disease and help avoid its acute and persistent life-threatening complications. Too much insulin causes hypoglycemia (low blood glucose levels) which can result in seizures, coma, or death, whereas too little insulin causes hyperglycemia (high blood glucose levels) which can lead to complications such as DKA, and, over time, leads to devastating kidney, heart, nerve, and eye damage. Not only do people living with T1D encounter increased economic burdens associated with managing their chronic disease, but they are also at elevated risk of developing mental health related issues such as eating disorders and depression. [21]

T1D can be diagnosed at any age, with a peak incidence in childhood and adolescence. T1D does not discriminate – it strikes children and adults regardless of their socioeconomic status. While most people currently living with T1D in the US are White, the fastest rates of diagnosis are among Black and Hispanic children [12].

T1D develops in stages over time and can first be detected by a simple blood test (islet autoantibody test) before glucose levels rise and insulin is required. The presence of islet autoantibodies indicates the body’s immune system is attacking the insulin-producing cells in the pancreas. The stages of T1D progression include:

Stage 1: Multiple islet autoantibodies, normal plasma glucose, presymptomatic.

Stage 2: Autoimmunity, abnormal glucose tolerance, presymptomatic.

Stage 3: Autoimmunity, hyperglycemia (plasma glucose levels above American Diabetes Association (ADA) diagnostic thresholds), typically symptomatic [4].

While the exact causes of T1D remain unclear, a combination of genetic predisposition, environmental factors, and immune system responses may lead to a higher likelihood of developing T1D. Certain genetic variations increase the likelihood of an individual developing T1D, as can a family history of the condition. 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. However, about 85% of those who will be diagnosed with T1D do not have a family history of the disease [2]. The risk of a T1D diagnosis is not influenced by factors such as lifestyle, activity level, socioeconomic status, or habits.

Currently, T1D cannot be prevented or reversed in individuals already diagnosed. **Once the immune system is activated, early detection of T1D autoantibodies through screening can identify the disease prior to the onset of symptoms**. Screening positive for two or more confirmed persistent autoantibodies indicates a 69.7% chance of progression to clinical T1D within 10 years, and a nearly 100% chance over a lifetime among pediatric populations [3]. FDA-authorized assays [insulin autoantibody (IAA), glutamic acid decarboxylase antibody (GADA), insulinoma-associated antigen protein 2 autoantibody (IA-2A), and Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA] are currently used in clinical care for classification of diabetes type and are also used to identify autoantibodies prior to stage 3 T1D. Any individual who screens positive for one or more autoantibodies should have follow-up monitoring which has been shown to reduce the risk of life-threatening DKA. As beta cells are destroyed, insulin production decreases, leading to abnormal blood glucose levels and eventual T1D symptom onset. T1D can now be delayed in some individuals who receive an immunotherapy, which can be prescribed during stage 2 of T1D, if autoantibodies are identified through screening.

**Screening of T1D has proven benefits, including a reduced risk of DKA at stage 3 diagnosis, providing time for patients and their families to plan and prepare, giving providers more treatment options, and providing opportunities for additional research aimed at delaying and preventing T1D progression.** DKA is more prominent in pediatric patients. Screening and monitoring can reduce DKA rates from 30-60% to 2.5-6.1%, amplifying a lifetime of improved health outcomes [5,6,14]. Additional details on the benefits of screening are discussed in the responses below.  Previous and ongoing T1D screening programs demonstrate feasible and effective clinical implementation based on current clinical guidelines. These studies have also identified potential harms, including those common among screening programs (e.g. false positives, false negatives, psychological harm, physical harm associated with blood collection, increased provider burden associated with increased diagnosis) [19]. Particularly relevant for T1D screening programs is the potential harm related to increased anxiety associated with positive test results [14, 20]. However, these potential harms may be managed through education and follow up monitoring [14].

While the USPSTF has issued recommendation grades for prediabetes and type 2 diabetes (T2D) in adults (Grade B; last updated in 2021), prediabetes and T2D in children and adolescents (I Statement; last updated in 2022), and gestational diabetes (B Grade and I Statement; last updated in 2021), there is no USPSTF recommendation for T1D. Though they share some similarities in symptoms and long-term complications, T1D and T2D have different etiologies and treatments. T1D is an autoimmune condition in which the body cannot produce insulin because of beta cell destruction. T2D is a metabolic disease in which the body makes insulin but does not use it properly, developing symptoms slowly over time.

Modeled on the USPSTF template and previous recommendations, an example of the USPSTF analytic framework and key questions applicable to a T1D evidence review is available for reference here: <https://www.breakthrought1d.org/wp-content/uploads/2025/03/USPSTF-Analytic-Framework_T1D.pdf>. The analytic framework and the associated key questions support the understanding that, based on the current evidence, the benefits of screening for T1D in general population children outweighs the potential harms, as outlined in the responses below.

**Rationale for Topic**

*[Select all that apply]*

**ü Screening**

 Preventive medication

**ü Counseling**

**Primary Care Relevance**

*[Select one]*

**ü Provided in the primary care setting**

 Referable from a primary care setting

**Public Health Importance**

**Please describe the public health importance of the topic. Include burden of disease and suffering and the potential of preventive service to reduce that burden.** *(maximum: 449 words)*

T1D is a growing public health issue affecting over 9.4 million people globally. In the US, approximately 2 million individuals are living with T1D, 304,000 of whom are children [8]. Additionally, 18,000 children and adolescents under 20-years old are diagnosed with T1D in the US annually [7]. By 2033, it is projected the US T1D population will grow by about 10%, affecting approximately 2.29 million [11]. T1D impacts all races, ages, and genders. Half of those newly diagnosed are children, and incidence rates are increasing among Black and Hispanic populations [12]. People who have a family member with T1D are up to 15 times more likely to develop T1D. Although guidelines recommend familial T1D screening in the clinical or research setting, 85% of diagnoses occur in individuals without family history [2].

Health-adjusted life years lost for individuals diagnosed with T1D at 10 years old range from 14-55 years [9]. The mortality rate is approximately 2-3 times higher than those without type 1 diabetes [10].

While curative treatments are in development, none have been approved yet. Screening for T1D can identify individuals in early stages, crucial for improving outcomes by reducing life-threatening DKA complications at clinical onset that occur in over half of diagnosed individuals. It also allows access to an immunotherapy that delays the onset of clinical diagnosis and insulin dependence. A German population-based screening study, Fr1da, found 0.31% of screened children had early-stage T1D [13]. Fr1da also showed less need for insulin treatment at the time of clinical presentation of T1D for those identified through screening [14]. Screening for autoantibodies, recognizing early signs, and creating a monitoring plan can prevent hospitalization, reduce DKA risk at clinical onset and allow time to prepare a care plan optimizing access to research or treatments.

DKA, a serious condition caused by insulin insufficiency, occurs when the body seeks energy from stored fat and leads to high blood ketone levels. Without prompt treatment, DKA can lead to hospitalization and be fatal. According to ADA standards, approximately half of children diagnosed with T1D present with DKA as the first manifestation of disease [5,17].

T1D increases the risk of chronic complications including kidney, eye, and cardiovascular disease, with risk growing over time. Screening allows autoantibody-positive individuals to be treated with FDA-approved therapies and/or join ongoing clinical trials aimed at delaying stage 3 T1D, as well as be referred to specialists for treatment and monitoring.

Providers can screen for islet autoantibodies, monitor progression in early stages, educate families on signs and symptoms, initiate prompt interventions, and offer management strategies to improve glycemic control and reduce complications.

**Potential Impact**

**Please describe the potential impact of USPSTF's review of the topic, for example, expected changes in clinical practice.** *(maximum: 119 words)*

Screening for pre-symptomatic T1D reduces acute life-threatening complications, provides opportunities for therapies that delay onset, enable clinical trial participation, and improve preparation. Studies consistently show the status quo has made no meaningful impact on DKA reduction at diagnosis [5,17]. However, screening and monitoring can reduce DKA rates from 30-60% to 2.5-6.1% [5,6,14].

International consensus guidelines support autoantibody screening and follow-up monitoring. ADA guidelines recommend autoantibody screening for early stage T1D in relatives of people with T1D. With 85% of T1D cases occurring in people without family history of the disease, a USPSTF recommendation for universal pediatric screening would improve long-term outcomes and enable delivery of evidence-based care.

**Supporting Documentation**

**Please list the evidence that supports your topic nomination. Specific citations will allow the USPSTF to give fullest consideration to the details of your nomination. (All nominations will be fully considered.) Documentation must be research published in peer-reviewed journals. Please note that the USPSTF does not evaluate cost-effectiveness studies of preventive services in developing its recommendations. Please list full citation(s) here and include a link to the article or its abstract.** *[open text box; no word count limit]*

The supporting documentation is grouped into three sections: A) Bibliography for T1D Topic Nomination Submission, B) T1D Supporting Evidence, and C) T1D Scientific Background Evidence. In the T1D Supporting Evidence below, we have noted the applicable Key Questions the research supports following the citation. The Key Questions align to the T1D USPSTF Analytic Framework and Key Questions developed here: <https://www.breakthrought1d.org/wp-content/uploads/2025/03/USPSTF-Analytic-Framework_T1D.pdf>

A: Bibliography for T1D Topic Nomination submission:

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