Type 1 diabetes screening: need for ethical, equity, and health systems perspective

As of October, 2024, the ICD-10 codes include presymptomatic type 1 diabetes, whereas previously these codes only included type 1 diabetes once it was diagnosed. The codes now present the different stages of type 1 diabetes, with stage 1 (characterised by the β-cell autoimmunity with people testing positive for two or more islet autoantibodies, when blood sugar concentrations are in the normal range); stage 2 (in case of abnormal blood sugar concentrations); and stage 3 (when clinical diabetes features are detectable).

Given that these presymptomatic stages are now recognised as distinct diseases, different international and national consensus statements and guidelines have put forward the need for population screening of type 1 diabetes to identify individuals at stages 1 and 2.[1,2] These guidelines are the precursors of changing type 1 diabetes care in clinical practice.

Implementation of consensus statements raises questions about how methods, previously used in academic research settings, can be translated into policy and practice. Firstly, there is the question of medicalising of presymptomatic stages of type 1 diabetes. Screening for different conditions is a key public health intervention. Although reliable tests for screening of type 1 diabetes have been available for many decades, mainly in research, until recently there were no therapeutic options available for people identified in their presymptomatic stages of type 1 diabetes. The advent of teplizumab has changed this framework; this agent is the first to be authorised in the USA for the secondary prevention of type 1 diabetes by delaying progression to stage 3 (ie, clinical onset). Beyond the possible use of teplizumab, another rationale put forward for the screening of type 1 diabetes is the prevention, or at least reduction, of the incidence of diabetic ketoacidosis at the time of clinical diagnosis, as shown in people who have been screened for islet autoantibodies.[1]

Decisions about screening require careful consideration. Whether to be screened or not should be the decision of the individual and their family. For children, parents might need to make that decision, and some children might want to know the results even if their parents do not. The psychological and emotional effect of a positive screening result for type 1 diabetes should be considered and carefully evaluated. Although individuals with stage 2 type 1 diabetes have a 75% risk of clinical diagnosis within 5 years,[3] there is no absolute certainty as to if and when the person will

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	Current considerations
The condition should be recognised as a considerable health burden	Daily management of diabetes is a major burden for people with diabetes and their caregivers. How should this burden be quantified and how does it relate to the delay in clinical diagnosis, which the use of teplizumab might result in? Should the focus be on absolute numbers of people? Is there a possibility of diagnosis in diabetic ketoacidosis? Are there acute versus chronic complications?
There should be an accepted treatment for people with the given condition	Can teplizumab be considered an accepted treatment? Teplizumab has to be accepted by people who will be using it and not only the clinical and scientific community, therefore, more efforts are needed to ensure that the voices of people with lived experience are included in development of consensus statements and guidelines. Teplizumab as a treatment needs to be clearly explained to people (ie, the psychological burden for children and parents resulting from a positive screening test). How is a negative test result managed? Teplizumab might affect the disease course for some people, but does it affect prognosis? Are there any cost considerations? Currently, teplizumab is only indicated for children older than age 8 years; what happens to children screened at younger ages?
Facilities should be able to diagnose and treat people with the identified condition	Is there a need for wide availability of testing and treatment facilities to ensure equity? Which treatment is recommended when someone is screened and considered to be at risk? Which treatment is recommended once someone has received a course of teplizumab? How do health systems need to adapt to this new treatment?
There should be a recognisable latent or early symptomatic stage	Staging of type 1 diabetes is not a linear process. Staging has been used in trials and academic settings, but not necessarily widely in clinical practice.
A suitable test or examination should be available	There are issues of sensitivity and specificity—type 1 diabetes is a multicomponent disease. Identification of genetic risk or antibodies does not necessarily translate into developing type 1 diabetes and actual onset cannot be precisely predicted.
The test should be acceptable to the population	Blood tests are seen as acceptable by the general population, however, acceptability with regards to its predictive value could be debated, as well as staging specifically for the administration of teplizumab at stage 2 of type 1 diabetes.
The natural history of the condition should be well understood	True causes of type 1 diabetes are unknown. Positive genetic and antibody test results do not necessarily translate into development of type 1 diabetes. Staging exists, but transition between stages is not clear, well understood, and is variable between individuals.
Policies should be in place to treat people	These policies are currently scarce and need to be defined with the aim of strengthening existing services for people with type 1 diabetes. Equity within and between countries needs to be considered as not all countries will be able to access screening and disease-modifying therapies.
Balance between the costs of case finding with regards to medical expenditure as a whole	Screening is expensive, as is teplizumab; however, these are not the only associated costs. The new costs that the introduction of this new approach will generate need to be assessed compared with the existing practice.
Case finding should be ongoing and not single occurrence	Ongoing case finding will require systems to be established. As many people will be identified at stage 1, there is the need for ongoing monitoring of their progression to enable them to benefit from teplizumab.

Table: **Criteria proposed by Wilson and Jungner[7] for population screening applied to type 1 diabetes, with considerations for ethical, equity, and health system factors**

develop type 1 diabetes. Studies have highlighted anxiety associated with screening,[4] as well as concerns about the effectiveness of teplizumab.[5] The wider effect of a positive result needs to be assessed carefully regarding health, insurance, and other social factors that might be affected by having a disease. Similarly, the implications of a negative result also warrant consideration.

Access to teplizumab and other disease modifying therapies will be determined by their price and by whether this will be paid for by the individual or the health system. This access raises issues of equity between and within countries, with some individuals or health systems being able to pay for these therapies themselves and others not.[4] The private sector's role in screening and introducing teplizumab should not be ignored. In discussing genetic screening in general, Turnball and colleagues[6] warn of commercial interests, government targets, and patient groups pushing a particular agenda versus a focus on the scientific benefits.

In their well recognised criteria for the justification of population screening, Wilson and Jungner[7] discuss that screening should enable the discovery of a given condition with a view to provide a solution to the individual. However, applying these criteria for the general population screening of type 1 diabetes raises questions that require the consideration of ethical, equity, and health system perspectives before translating scientific advances to policy and practice (table).

Considering how the voices of those with lived experiences are integrated when addressing such complex factors and fundamental shifts in type 1 diabetes care is crucial. Finally, the implementation of population screening and use of teplizumab will have substantial financial implications for both individuals and health systems. Careful consideration of this effect on existing type 1 diabetes care and services needs to be reflected upon.

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David Beran, Aude Bandini, Emanuele Bosi, Claudia Boettcher, Marie-Anne Burckhardt, Matthieu Colange, Nina Tousch, Valérie Schwitzgebel

david.beran@unige.ch

Division of Tropical and Humanitarian Medicine, Faculty of Medicine, University of Geneva, Geneva 1211, Switzerland (DB); Diabetes Center, Faculty of Medicine, University of Geneva, Geneva, Switzerland (DB, VA); Philosophy Department, University of Montreal, Montreal, QC, Canada (AB); Diabetes Research Institute, IRCCS San Raffaele Hospital, Milan, Italy (EB); Pediatric Endocrinology and Diabetology, University Children's Hospital Bern, Inselspital Bern, Bern, Switzerland (CB, M-AB); Department of Clinical Research, University of Basel, Basel, Switzerland (M-AB); Glucose toujours, Paris, France (MC, NT); Pediatric Endocrine and Diabetes Unit, Department of Pediatrics, Obstetrics, and Gynecology, Geneva University Hospitals, Geneva, Switzerland (VS); Institute of Genetics and Genomics (iGE3), University of Geneva, Geneva, Switzerland (VS)

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6 Turnbull C, Firth HV, Wilkie AOM, et al. Population screening requires robust evidence-genomics is no exception. *Lancet* 2024; **403:** 583–86.

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Mpox and diabetes: a needed public health research agenda

In August, 2024, WHO announced that the surge of mpox cases in the Democratic Republic of the Congo constituted a public health emergency of international concern, and endorsed a continuation of that status on Nov 28, 2024.[1] Mpox is a viral infectious disease caused by the monkeypox virus. Since January, 2022, and until time of writing, there have been 124 753 laboratory-confirmed cases of mpox and 272 deaths reported across 128 WHO Member States globally.[2] With this ongoing public health crisis, an opportunity has arisen to deepen our understanding of the risk of mpox transmission, severity, and clinical outcomes in people with diabetes and the associated public health implications of the intersection of these two conditions.

People with diabetes have a well documented increased risk of severe or prolonged diseases from viral infections.[3] This risk of more severe infection-related health outcomes has been attributed to changes in the immune response in people with diabetes including lowered production of interleukins, reduced chemotaxis and phagocytic activity, and immobilisation of polymorphonuclear leukocytes.[3] Although poor glycaemic control is often associated with an increased risk of adverse outcomes from infections,