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Can Type 1 Diabetes Be Prevented? Screening and Risk Assessment in Clinical Trials: A Narrative Review

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Abstract

Background. This review summarises recent clinical trials on type 1 diabetes (T1D) and emerging screening and prevention strategies. The increasing incidence of T1D raises interest in early detection and potential prevention. Ongoing studies focus on newborn risk assessment, islet autoantibody screening and preventive strategies.

Aim. This review aims to present current knowledge on T1D prevention, screening methods for risk assessment and identification of preclinical disease, and to highlight recent directions in clinical research.

Material and methods. A literature search was conducted in PubMed, Scopus and Google Scholar. Retrospective and cohort studies, literature reviews, systematic reviews, guidelines, clinical trial protocols and randomised controlled trials were included. The following keywords were used: 'type 1 diabetes', 'risk factors', 'ketoacidosis', 'screening', 'newborn screening', 'genetic risk', 'prevention', 'preclinical stage'. The search focused on recent clinical trials.

Results. Clinical studies demonstrate a shift towards earlier detection of T1D through screening strategies combining genetic risk assessment with islet autoantibody testing. These strategies allow identification of at-risk individuals and long-term monitoring. Studies confirm that detection of preclinical stages is associated with reduced incidence of diabetic ketoacidosis at diagnosis and a milder disease course. Early diagnosis enables access to disease-modifying therapy with teplizumab, which can delay disease progression. Preventive approaches, including oral insulin immunotherapy and microbiome-targeted interventions, are under investigation, with mixed results.

Conclusions. T1D can be identified at earlier stages using combined genetic and immunological screening strategies, improving clinical outcomes at diagnosis. However, effective prevention remains limited. Further research is required to optimise screening and its implementation in clinical practice.

Keywords: type 1 diabetes, screening, risk assessment, prevention, preclinical stage.

1. Introduction

Type 1 diabetes is one of the most common endocrine and metabolic disorders in children. A patient with type 1 diabetes must manage their condition continuously, which involves administering insulin, monitoring blood glucose levels, engaging in physical activity and following a well-balanced diet (1). Type 1 diabetes is an autoimmune disease in which the immune system destroys the pancreatic β-cells responsible for producing insulin. This results in a permanent, complete deficiency of this hormone, which must be replaced for the rest of the patient's life. This condition significantly affects quality of life, is associated with a risk of serious complications in the future, can shorten life expectancy, and generates significant costs for both patients and healthcare systems, even in high-income countries (2–5).

The incidence of type 1 diabetes is rising. It is estimated that around 9.5 million people worldwide have type 1 diabetes – this is more than in 2021, when the figure stood at 8.4 million (an increase of 13%). Of these, around 1 million are children aged 0–14, and a further 0.8 million are teenagers aged 15–19 (6). Projections indicate a significant increase in the number of people with type 1 diabetes over the coming decades – from around 8.4 million in 2021 to as many as 13.5–17.4 million in 2040, representing an increase of between 60% and 107%. At the same time, life expectancy for people with this condition remains highly variable depending on a country's level of development – in high-income countries it may be close to the general population average, whereas in lower-income countries it is significantly shorter, mainly due to limited access to diagnosis, insulin treatment and medical care (7). Given the rising incidence of type 1 diabetes, there is growing interest in identifying individuals at increased risk and in developing effective strategies for its prevention.

2. Research materials and methods

The literature review was conducted using three main databases: PubMed, Scopus and Google Scholar. The search was focused on publications from the past five years (2020–2025) to capture the most recent clinical trials. Earlier studies were included only to provide historical context on the development of clinical research. The search was based on the following keywords and their combinations: 'type 1 diabetes', 'risk factors', 'ketoacidosis', 'screening', 'newborn screening', 'genetic risk', 'prevention', 'preclinical stage', and 'treatment'.

Retrospective and cohort studies, literature reviews, systematic reviews, clinical guidelines, clinical trial protocols, and randomised controlled trials were included in the analysis. Exclusion criteria comprised case reports, conference abstracts, articles without available full texts, non-English publications, duplicate records, and studies not directly related to current strategies for the screening, risk assessment, or prevention of type 1 diabetes. This study was conducted as a narrative review, and articles were selected based on their scientific relevance and contribution to the understanding of early detection and preventive approaches in type 1 diabetes.

Artificial intelligence tools were used exclusively for linguistic correction and stylistic improvement to ensure the clarity of the text and its compliance with academic writing standards. All stages of the analysis, the interpretation of results and the formulation of conclusions were carried out independently by the authors, without the involvement of artificial intelligence in the processing of the research results.

3. Research results

3.1. Identification of the risk of type 1 diabetes in newborns

Type 1 diabetes is largely genetically determined – this is confirmed by the fact that the concordance rate among twins is as high as 70% (8), while the risk among siblings is around 8% (9). The majority of disease risk is driven by genetic variation in a few strongly linked regions, particularly the HLA class II DR-DQ loci and the HLA class I region, as well as more than 50 non-HLA single nucleotide polymorphisms (SNPs), including variants in genes such as INS and PTPN22 (9).

An improved genetic risk score for type 1 diabetes (GRS2) has been developed, which combines 67 SNP variants and better accounts for the complexity of the HLA region and genetic interactions. Compared to previous models, it achieves higher diagnostic accuracy (AUC ROC 0.93), better distinguishing between individuals with type 1 diabetes, type 2 diabetes, and healthy individuals. The use of this indicator increases the efficiency of screening, as it allows for the detection of more future cases of the disease while requiring fewer individuals to be monitored, thereby reducing costs. It is particularly useful in early childhood, when other risk factors are not yet available and the risk of sudden onset of the disease is highest (10).

The Freder1k study shows that an increased risk of type 1 diabetes in newborns can be identified on the basis of specific HLA variants and family history. An increased risk is primarily associated with the presence of the HLA DR3/DR4-DQ8 or DR4-DQ8/DR4-DQ8 genotypes, as well as situations where a child has the DR4-DQ8 haplotype and a first-degree relative has type 1 diabetes. Children classified as being at risk are then regularly monitored in the following years of life (including at 6 months, 2 and 4 years of age) to detect autoantibodies and the early stages of the disease. In the study, approximately 2.6% of newborns met the criteria for increased risk, and the majority of families agreed to further monitoring.
The results demonstrate that using HLA markers, especially DR3, DR4, and DQ8, together with a family history of type 1 diabetes enables reliable identification of children at highest risk of developing the disease and supports the introduction of early clinical follow-up. They also demonstrate that genetic screening for type 1 diabetes can be feasibly implemented within population-wide newborn screening programmes (11).

3.2. Screening for early, asymptomatic stages of type 1 diabetes in children

The early, asymptomatic stages of type 1 diabetes can be identified by the presence of numerous autoantibodies directed against pancreatic islets, such as antibodies against insulin (IAA), glutamic acid decarboxylase (GADA), insulinoma-associated antigen-2 (IA-2A) and the zinc transporter (ZnT8A) (12). On this basis, stage 1 (normoglycaemia) and stage 2 (dysglycaemia) of type 1 diabetes are distinguished (13, 14).

For many patients, type 1 diabetes is not diagnosed until their health has deteriorated significantly, often requiring hospitalisation. One of the most serious and, at the same time, most common complications at the time of admission is diabetic ketoacidosis. Despite numerous educational initiatives, this problem still affects up to half of all children at the time of diagnosis. This condition requires treatment in hospital and, in more severe cases, also in an intensive care unit (15).

The FR1DA study conducted in Bavaria was one of the pioneering population-based programmes aimed at detecting the early, asymptomatic stages of type 1 diabetes in children (16). This study has demonstrated that identifying the disease at the preclinical stage brings significant clinical benefits for both patients and their families. Above all, a significant

reduction in the risk of ketoacidosis at the time of clinical diagnosis is observed. Additionally, children diagnosed in the presymptomatic phase are less likely to experience severe clinical symptoms and weight loss at the time of disease onset. This group of patients also exhibits a more favourable metabolic profile, including higher C-peptide concentrations and lower levels of glycated haemoglobin (HbA1c) and blood glucose at the time of diagnosis (17–19). A significant benefit of early risk identification is also the possibility of qualifying patients for disease-modifying therapy using teplizumab, an anti-CD3 antibody that slows the progression of diabetes (20).

The European EDENT1FI programme (European Diagnosis of Early Non-clinical Type 1 Diabetes For disease Interception) is an innovative initiative aimed at improving the early detection of type 1 diabetes through the implementation of screening within healthcare systems. The project aims to harmonise and standardise diagnostic procedures and patient care in the early stages of the disease. Screening for pancreatic islet autoantibodies is being carried out in eight European countries (the Czech Republic, Denmark, Germany, Italy, Poland, Portugal, Sweden and the United Kingdom), and between 2023 and 2028, it is planned to cover approximately 200,000 children and young people aged between 1 and 17.

The EDENT1FI initiative, modelled on the FR1DA study, aims to improve care for children and young people with type 1 diabetes by detecting the condition at an early, asymptomatic stage. The programme comprises three main components: screening for autoantibodies, assessment of disease severity (including OGTT, HbA1c, and blood glucose levels) and educational initiatives as well as patient monitoring. The project serves as a model for implementation across various European countries, taking local differences into account, and also includes an assessment of the impact of the tests on mental health, as well as long-term follow-up and therapeutic interventions (21).

3.3. Evaluation of the efficacy of high-dose, once-daily oral insulin immunotherapy in children with a genetic risk

Oral immunotherapy involves gradually increasing amounts of a food allergen until a stable maintenance dose is achieved, with the goal of reducing the body’s immune reactivity. This approach aims to lower the patient’s sensitivity to the allergen over time. As a result, patients typically develop desensitisation – meaning a higher threshold is required to trigger an

allergic reaction during treatment and, in some cases, long-term tolerance that persists even after therapy has ended (22). The question was raised as to whether such an approach might be useful in autoimmune diseases, including type 1 diabetes.

Insulin is one of the earliest and most important autoantigens involved in the development of type 1 diabetes in children. In individuals with a genetic predisposition, antibodies against insulin often appear in early childhood (23). The subsequent loss of immune tolerance to insulin can trigger a broader autoimmune response against pancreatic islet cells, which results in the onset of clinical diabetes (24).

The Global Platform for the Prevention of Autoimmune Diabetes (GPPAD) has launched a multicentre, randomised, double-blind, placebo-controlled clinical trial, which was conducted at seven centres across Europe between 2018 and 2024. The Primary Oral Insulin Trial (POInT) was the first study to evaluate the effectiveness of early oral exposure to an autoantigen before the onset of autoimmune processes. It was designed to determine whether daily oral insulin administration from infancy is safe and can reduce the risk of developing autoantibodies and type 1 diabetes in children with an increased genetic risk. It included infants aged 4–7 months with a high genetic risk of developing type 1 diabetes, defined as a greater than 10% probability of developing two or more islet autoantibodies before the age of six. Participants were given oral insulin in gradually increasing doses or a placebo, and their health was monitored over several years during regular follow-up visits. During each visit, the presence of autoantibodies against pancreatic islets was assessed through blood tests. The study demonstrated that daily administration of high-dose oral insulin did not significantly reduce the risk of developing pancreatic islet autoantibodies or type 1 diabetes itself across the entire population of children analysed. At the same time, it was confirmed that the treatment was safe and well tolerated. However, additional analyses indicated that in children who developed autoimmunity, oral insulin may have slowed the progression of the disease. Furthermore, the treatment effect varied depending on the insulin gene variant, suggesting that the efficacy of this therapy may depend on genetic factors and requires a personalised approach (25).

3.4. The use of Bifidobacterium longum subsp. infantis EVC001 supplementation in reducing autoimmunity associated with type 1 diabetes

SINT1A (Supplementation with B. Infantis for Mitigation of Type 1 Diabetes Autoimmunity) (26), a randomised, placebo-controlled trial, is investigating whether daily probiotic supplementation during the first year of life can reduce the risk of beta-cell autoimmunity in children with a high genetic risk of type 1 diabetes, identified by the GPPAD (27). The study builds on evidence indicating that the gut microbiota plays an important role in developing immune tolerance (28–31), including tolerance to insulin, as well as on studies reporting beneficial effects of early probiotic supplementation in preventing peanut allergy (32). It is hypothesised that early modulation of the microbiome may promote the development of tolerogenic immune responses, including through the action of metabolites, especially short-chain fatty acids (SCFAs) (33–37).

Evidence linking the gut microbiome to the risk of type 1 diabetes comes from several large prospective studies showing that microbial alterations precede the development of beta-cell autoimmunity and clinical disease. In the BABYDIET study, changes in microbial interaction networks were detected at 0.5 and 2 years of age in children who later developed beta-cell autoimmunity (29). Similarly, Finnish cohort studies reported reduced microbial diversity and increased abundance of certain bacteria, including Bacteroides dorei, in genetically susceptible children prior to disease onset (38). The TEDDY study further confirmed these findings, demonstrating that children who did not develop autoimmunity more frequently harboured microbial genes involved in fermentation and short-chain fatty acid biosynthesis, supporting a potential protective role of SCFAs in early disease development (30). In addition, TEDDY data indicated that very early probiotic supplementation (within the first 27 days of life) was associated with a reduced risk of islet autoimmunity, suggesting that early modulation of dysbiosis may influence disease risk (28). The SINT1A study builds on the concept used in the POInT study, which involves early exposure of the immune system to antigens to prevent autoimmune processes (25).

The study is a randomised, double-blind, placebo-controlled trial. It included infants aged between 7 days and 6 weeks at the time of randomisation who were found to have a high genetic risk of developing type 1 diabetes, defined as at least a 10% risk of developing multiple autoantibodies against beta cells before the age of 6, similar to the POInT study. Participants

are randomly assigned to the probiotic or placebo group. The intervention involves daily administration of the probiotic for a period of 12 months; the preparation contains selected bacterial strains with potential immunomodulatory effects, aimed at supporting the development of immune tolerance by influencing the gut microbiome. The children are then followed up over a long-term period of approximately 6–6.5 years, during which blood samples are taken at regular check-ups to measure autoantibodies against pancreatic islet cells, and the development of autoimmunity and other clinical parameters are monitored. It is hypothesised that early modulation of the microbiota may reduce the risk of beta-cell autoimmunity and thus potentially lower the risk of type 1 diabetes in high-risk children. The results of the study are currently unknown, as the project is still ongoing (26).

4. Discussion

Until recently, type 1 diabetes was typically diagnosed at the symptomatic stage, often accompanied by diabetic ketoacidosis, which remains a common and serious complication at the time of diagnosis. This review highlights a trend towards earlier detection, including the identification of genetic susceptibility in newborns and the recognition of preclinical stages through islet autoantibody screening. These approaches reflect a shift towards a more proactive and preventive model of care.

Screening strategies for type 1 diabetes risk based on HLA genotyping and improved genetic risk scores, such as GRS2, enable early identification of individuals at increased risk. These approaches allow for long-term monitoring and, if necessary, early intervention. However, the predictive value of genetic risk alone remains limited, as not all individuals with a high-risk genotype will develop the disease. Therefore, the most effective approach appears to be the combination of genetic risk assessment with screening for islet autoantibodies.

Population-based screening programmes implemented within international initiatives demonstrate that early detection of asymptomatic stages of type 1 diabetes is clinically beneficial. Their key advantage is a significant reduction in the incidence of diabetic ketoacidosis at diagnosis, as well as a milder clinical course and better metabolic status in affected children. Early diagnosis also enables timely education of families and facilitates access to treatments that can slow disease progression.

Teplizumab is currently an approved therapy that delays the progression from the preclinical stage to symptomatic type 1 diabetes. However, it does not fully prevent disease onset, highlighting the need for further therapeutic development. Similarly, attempts to induce immune tolerance through oral insulin administration have shown a favourable safety profile, but their efficacy appears to be limited to specific subgroups, suggesting that genetic and immunological heterogeneity plays an important role in treatment response.

Preventive approaches targeting the gut microbiome, such as early-life probiotic supplementation, remain promising; however, results from ongoing studies are not yet available. This suggests that environmental factors may play an increasingly important role in the development of type 1 diabetes and may influence disease risk.

Despite these advances, several important challenges remain. Large-scale screening programmes raise important ethical issues, particularly related to the psychological impact of identifying children at increased risk. It is also important to consider the potential burden that such programmes may place on healthcare systems. Therefore, further research is needed to improve screening strategies and develop more effective ways of preventing the disease.

5. Conclusions

In conclusion, type 1 diabetes is increasingly being identified at earlier stages through screening strategies that combine genetic and immunological markers. Early detection is associated with improved clinical outcomes and reduced disease severity at diagnosis. However, effective prevention remains a challenge, although ongoing trials may help to delay or prevent disease onset. Further research is needed to support the implementation of these screening programmes in clinical practice.

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