JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Australian Type 1 Diabetes Clinical Research Network

Pilot Study of Screening for Type 1 Diabetes in the General Population

Our Vision

To intercept type 1 diabetes (T1D) in the general population during the silent stage of the autoimmune process, prior to clinical diagnosis. Ultimately, the goal is to develop strategies to prevent or delay progression to T1D in at-risk individuals.

Key Points

- JDRF is supporting a pilot study of a population screening program for T1D risk in Australia
- Population screening for T1D risk can identify those with asymptomatic disease before they would traditionally be diagnosed
- T1D affects around 120,000 Australians, and around 30% of people with T1D experience diabetic ketoacidosis (DKA) at diagnosis
- The pilot study will detect markers of T1D risk (islet autoantibodies) and assess the benefits of, feasibility of, and attitudes towards a population screening program
- Benefits from similar overseas studies have been decreased rates of DKA, improved long-term outcomes, and opportunities to receive therapies that can delay or prevent clinical disease

Background

Type 1 diabetes is an autoimmune disease and one of the most common chronic diseases in Australian children. People with T1D have a lifelong reliance on insulin therapy, delivered either through daily injections or an insulin pump. There is no cure, and prevention is a key goal of T1D research.

T1D classically has a sudden and pronounced onset, requiring immediate insulin therapy due to autoimmune destruction of the pancreatic beta cells. Diagnosis is often traumatic, with around 30% of children in Australia experiencing diabetic ketoacidosis (DKA) – a potentially fatal build-up of ketones in the bloodstream.

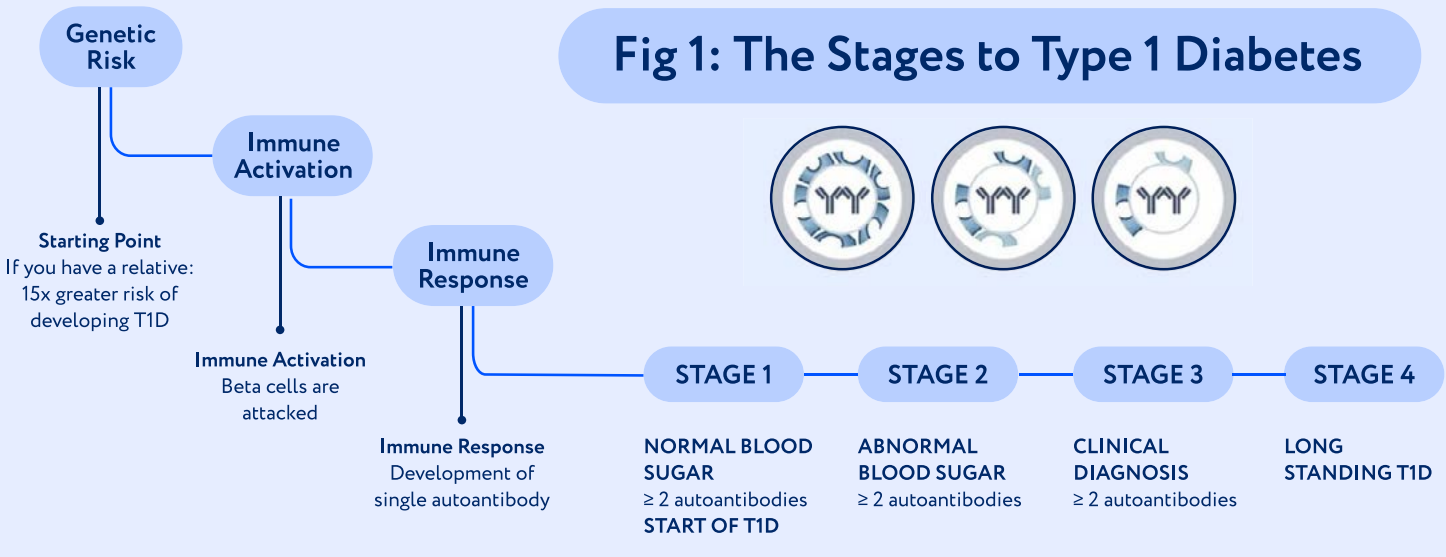
T1D Risk and Susceptibility

It has recently been recognised that there are presymptomatic phases of T1D that can last for months or years prior to clinical diagnosis. Now considered the start of T1D, stages 1 and 2 are characterised by the persistence of circulating autoantibodies to islet antigens in the pancreas. During stage 1 blood sugar levels remain normal, while during stage 2 blood sugar levels become elevated (Fig 1).

Stage 1 begins early in life – most children who develop T1D have detectable islet autoantibodies before the age of 5 years, and some even younger. The time to progression is generally shorter for younger children – 75% of children with two or more islet autoantibodies before age 3 will progress to clinical disease before the age of 10.[1]

T1D susceptibility also involves a genetic component. The risk of a child progressing to clinical disease is 2%, 8% or 30% if the mother, father, or both parents, respectively have T1D.[2] Global cohorts have recently shown a new concept, the T1D genetic risk score, can independently predict progression to islet autoimmunity and T1D in at-risk individuals. [3]

Fig 1: The Stages to Type 1 Diabetes



Benefits of General Population Screening

Screening for the presence of islet autoantibodies can identify those in the population with asymptomatic disease, potentially many years before they would traditionally be diagnosed. Detection of autoantibodies at this stage offers many benefits over a classical diagnosis.

Preservation of beta cell function and access to preventative therapies
A key benefit of presymptomatic T1D screening is the ability to retain some degree of beta cell function. This opens up opportunities for people identified through screening to enrol in clinical trials of preventative therapies, many of which are most effective in early stages of T1D before clinical diagnosis.

In 2019, a landmark clinical trial showed that the monoclonal antibody teplizumab could delay progression to stage 3 T1D. Among children with multiple islet autoantibodies but without an official T1D diagnosis, teplizumab delayed disease onset by a median of 2 years.[8] A screening program will be a crucial tool to identify individuals at risk and facilitate further clinical trials that could lead to delaying or preventing progression to clinical, stage 3 T1D.

Reduction in DKA
DKA is a potentially fatal build-up of ketones in the bloodstream due to unchecked blood glucose levels. It requires hospitalisation, causes significant psychological stress for families, and is associated with poorer long-term glycaemic control.[4] Evidence shows that autoantibody screening can markedly reduce rates of DKA at the time of diagnosis. [6]

Around 30% of children in Australia experience DKA as their first symptom of T1D. [5]

90% of individuals who develop T1D don't have a first-degree relative with the condition.[1] This means that general population screening is crucial to comprehensively identify at-risk individuals.

Improved long-term outcomes
Those identified through screening can receive monitoring and timely initiation of glucose management, which is critical for improving long-term outcomes for people with T1D and in addition, experience less psychological stress and better long-term glycaemic control than those diagnosed through the traditional pathway.[6]

Global Progress

T1D screening is an emerging area of public health research across the globe, and programs in Germany and the US have shown screening to be a cost-effective way of improving health outcomes.

Through screening and close monitoring, the rate of DKA in the Fr1da study in Germany was less than 5%, compared to the usual rate of 20%.[6] Similar reductions have been reported in US-based screening studies.[7,9]

Screening can also be a cost-effective public health measure. The Autoimmunity Screening for Kids (ASK) study in the US showed that a reduction of 20% in DKA events at diagnosis and the subsequent improvement in metabolic control would offset the cost of screening, particularly if combined with existing infrastructure. [9]

What JDRF is Planning in Australia

JDRF will add to its world-leading portfolio of prevention research by commencing this pilot project to investigate the feasibility and cost effectiveness of undertaking the first population-based T1D screening program in Australia.

As opposed to screening in high risk individuals, few global T1D screening programs exist in the general population. Australia is uniquely placed to join the critical global effort due to its well accepted population-based approach to screening in other disease areas.

Led by Dr Kirstine Bell and supported by JDRF's Type 1 Diabetes Clinical Research Network (T1DCRN), the pilot study will consist of design, implementation and evaluation of an autoantibody screening program in the general population.

The pilot is expected to generate evidence on the effectiveness and benefits of screening, as well as attitudes of healthcare professionals and the T1D community. This evidence will be evaluated for its feasibility, acceptability, cost-effectiveness and overall potential to be considered as part of population health framework approaches such as population-based screening within the Australian health system.[10]

Contact Us for Further Information

Dr Kirstine Bell
Principal Research Fellow, Australian Type 1 Diabetes General Population Screening Project and Research Fellow, Charles Perkins Centre, The University of Sydney

kirstine.bell@sydney.edu.au

Dr Dorota Pawlak
Chief Scientific Officer, JDRF and Director, T1DCRN

dpawlak@jdrf.org.au

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