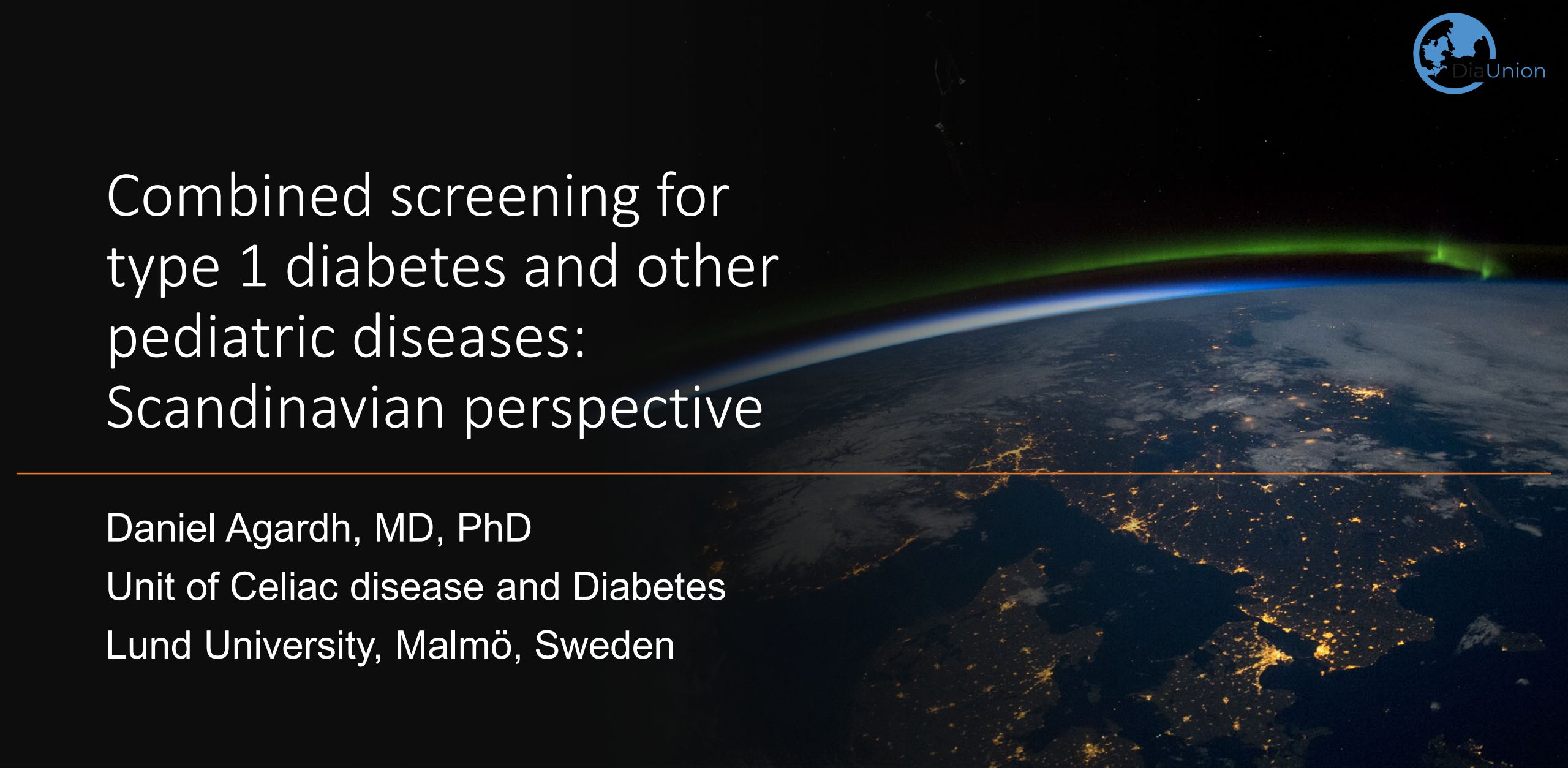

Combined screening for type 1 diabetes and other pediatric diseases: Scandinavian perspective

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Challenges of screenings for T1D in Scandinavia

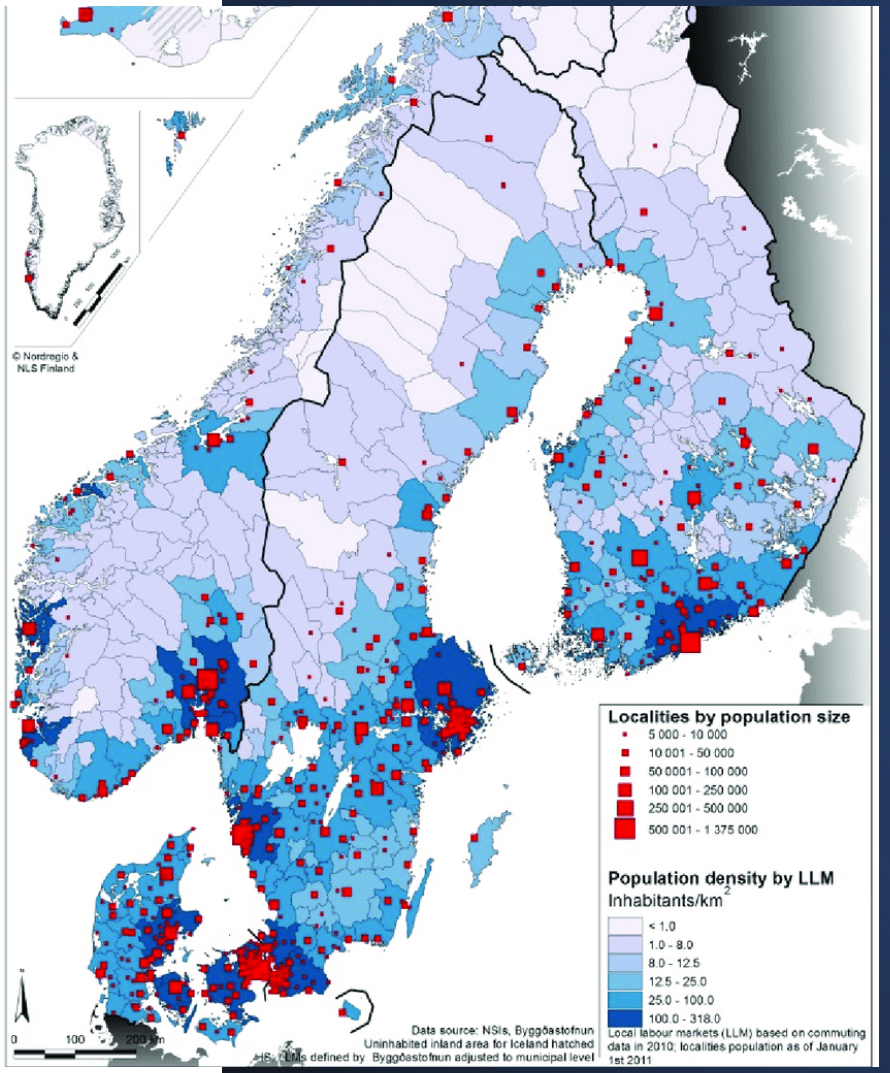
- Which is the optimal target population?
- How do we follow autoantibody positive individuals?
- How do we implement screening programs including health economic evaluations in interaction with societal stakeholders?
- Will applying screening for several diseases be more efficient?

Objectives

- Scandinavian perspective
- Screening practices in Scandinavia
- Disease prevalence in Scandinavia
- Combined screening in pediatric cohorts
- Introduce DiaUnion´s combined screening program

Scandinavian perspective

- Scandinavia (Sweden, Denmark, Norway) has a total population of 22 million people
- Similar health care systems:
  - Public available
  - Majority of health care sector is governmental
  - Politics and taxpayers decide
- Health equality is high
- Nationwide patient registries
- Similar screening policies



Screening Guidelines in Scandinavia

Based on WHO´s criteria and 5 additional criteria

National screening include :
- Cervical, breast & colon cancers
- Newborn screening for congenital metabolic disorders, spinal muscular atrophy (SMA), severe combined immuno-deficiency (SCID), cystic fibrosis (CF; not in Sweden)

Swedish National Board of Social Health´s criteria for national screening

1. The condition must be an important health problem
2. The natural history of the disease must be known
3. The condition must have a symptom-free phase that can be detected
4. There must be an appropriate test method
5. There must be measures that give a better effect in an early phase than with clinical detection
6. The screening must reduce mortality, morbidity or disability caused by the condition.
7. The test method and the further investigation must be accepted by the intended population
8. The measures for the condition must be clear and acceptable to the intended population
9. The health benefits must outweigh the negative effects of the screening program
10. The screening program must be acceptable from an ethical perspective
11. The cost-effectiveness of the screening program must have been evaluated and judged to be reasonable in relation to the need
12. The information to the participants in the screening program must have been evaluated
13. Organizational aspects that are relevant for a nationally equivalent screening program must have been clarified
14. The screening program's resource needs and feasibility must have been assessed
15. There must be a plan to evaluate the screening program's effects

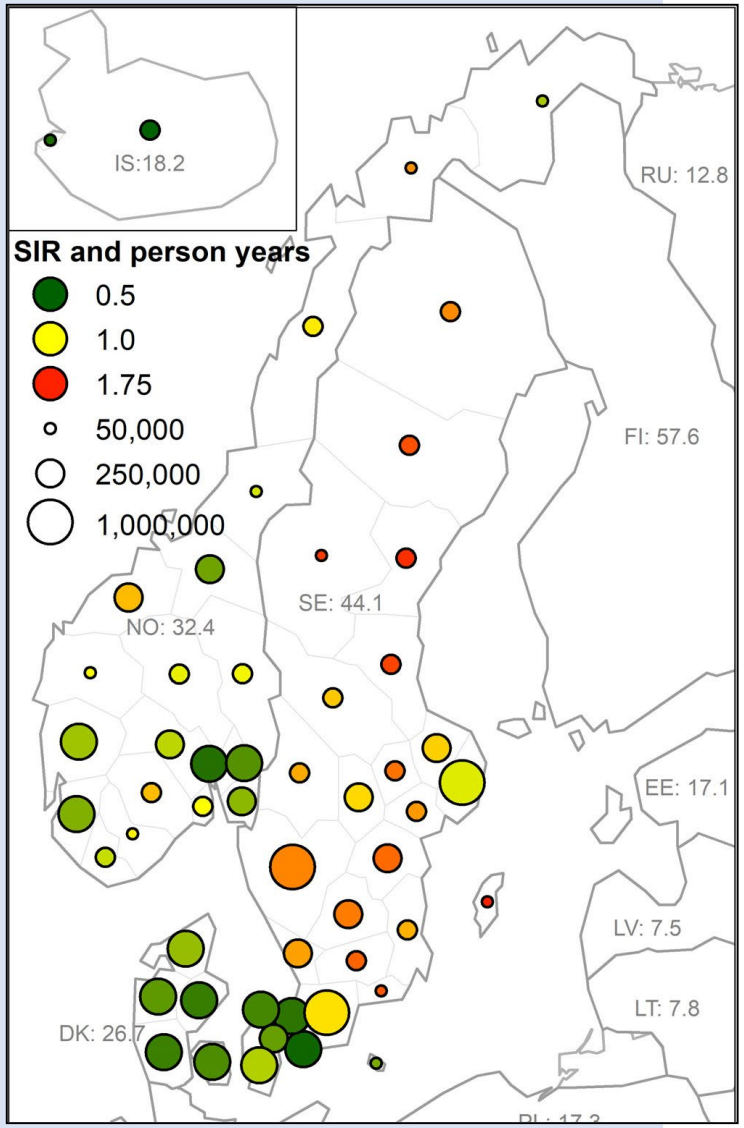
Type 1 diabetes in Scandinavia

Nordic national childhood databases

Total incidence of T1D is 35.6 per 100.000 person years (2006-2011)

Overall incidence highest in Sweden (Finland highest of Nordic countries)

Geographic variation in Sweden and Norway (**Figure**)



Samuelsson et al. Pediatric Diabetes. 2020;21:259–265

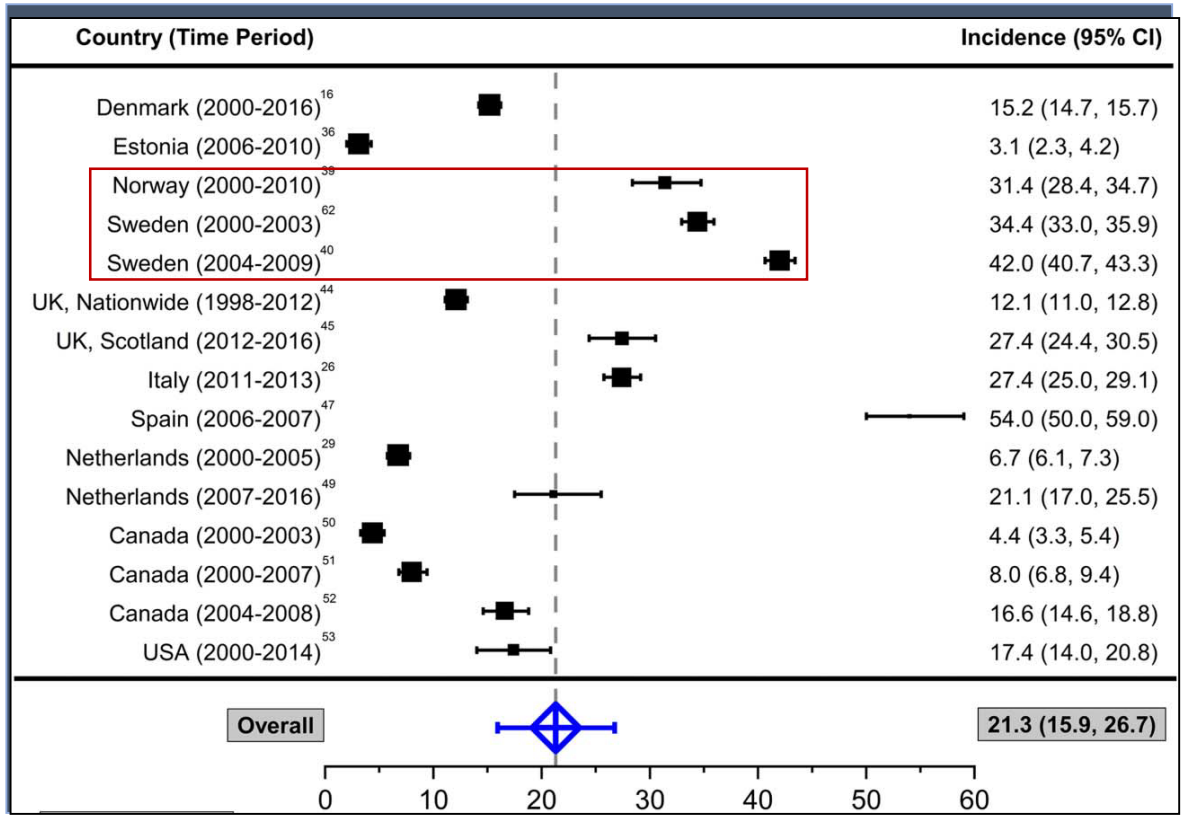
Celiac disease & autoimmune thyroid disease

Incidence of CD in Sweden among the highest in world (prevalence of 2-3%) (**Table**)

Screenings indicate CD is also common in Norway and Denmark

Under-reporting of the health system makes prevalence of AITD uncertain in Scandinavia

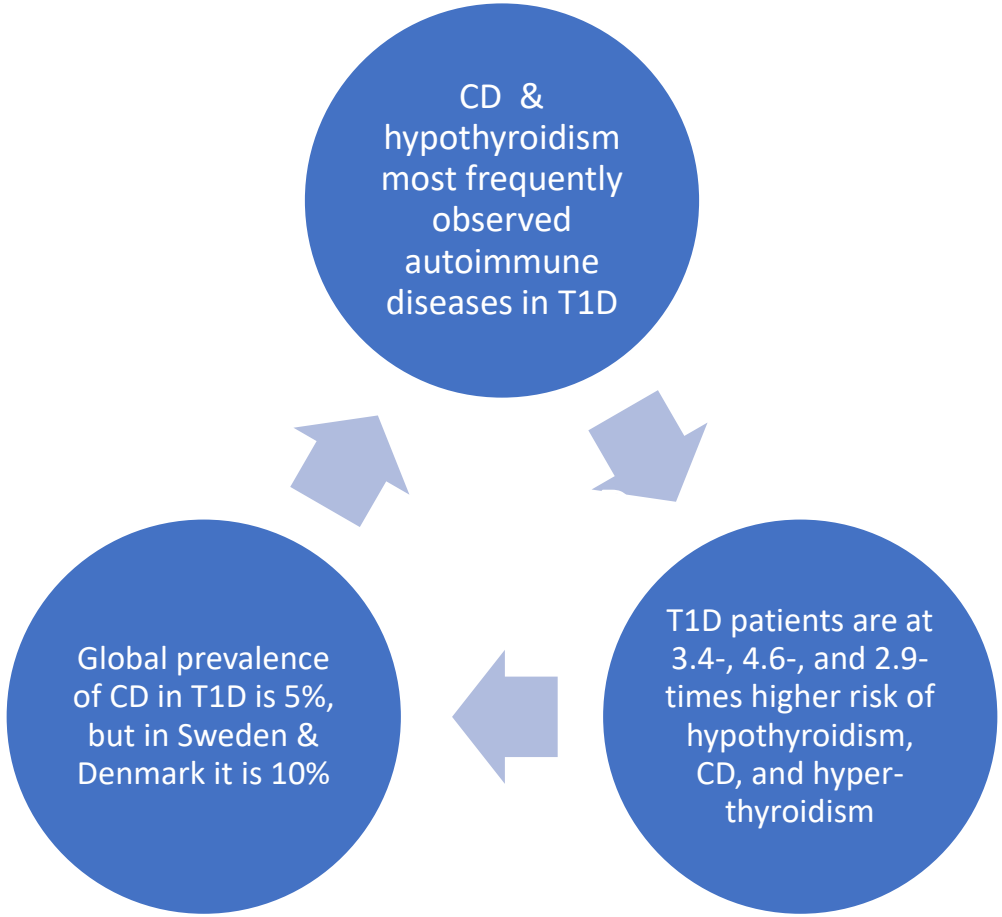
Screening practices for CD and AITD differ between regions and Scandinavian countries



Eaton et al. J Autoimmun. 2007

King et al. Am J Gastroenterol 2020;00:1–19.

Clustering of autoimmune diseases: The TRIAD



Pham-Short et al. Pediatrics 2015; Larsson et al. Pediatr Diabetes 2008; Hansen et al. Acta Paediatr2001; Mäkimattila et al. Diabetes Care 2020;43:1041–1047.

Importance of screening for the TRIAD

Screening for T1D

- Early detection prevents diabetic ketoacidosis

Screening for CD

- Identify the majority of CD children and prevent delayed diagnosis
- Reduce risk of complications (e.g. ostepenia, iron defiency, stunted growth and development)

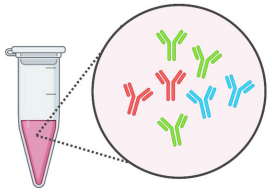
Screening for AITD

- Early detection and treatment will improve mental health and cognitive development in children

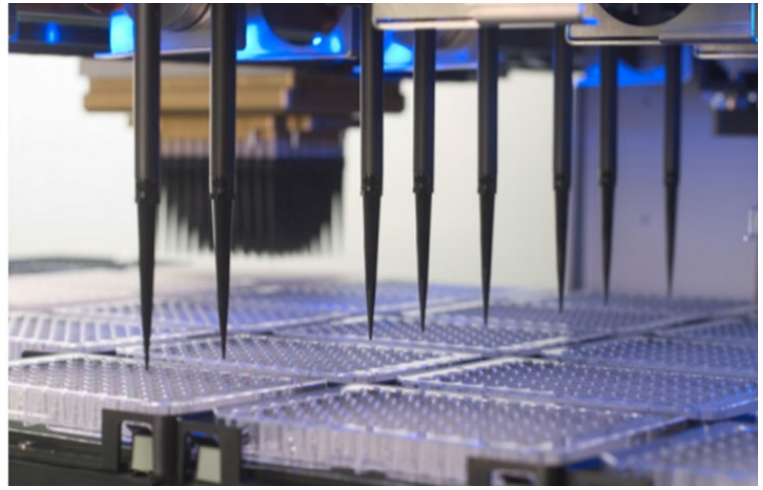
Screening methods

- Autoantibodies, defined HLA haplotypes and genetic risk scores are currently the best available biomarkers used to inform risk for disease development

- TRIAD specific autoantibodies:
  - **T1D**: IAA, GADA, IA-2A, ZnT8A
  - **CD**: IgA-tTG, IgG-tTG
  - **AITD**: TPOA, ThGA



- Radiobinding assays used for decades
- Novel multiplex assays (<4ul) with automated pipetting will increase quantity



Benefits of combined screening

Early Detection and Intervention

- Lead to timely intervention and treatment
- Prevent or reduce the severity of the disease and its associated complications

Efficiency

- More efficient and cost-effective than separate screenings for each disease
- Minimizes the need for multiple healthcare visits and reduces the burden on healthcare systems

Risk Stratification

- Identify children at higher risk based on genetic, familial, or other risk factors
- Targeted monitoring and preventive measures for at-risk individuals

Family Health

- Identifying a disease in a child may prompt family screenings to detect and manage conditions that may also affect other family members

DiaUnion - An interregional screening study

DiaUnion objectives

1. To establish a public screening program to identify healthy people at risk for T1D and two related autoimmune diseases, CD and AITD
2. To establish a framework for monitoring of autoantibody-positive individuals with pre-symptomatic T1D
3. To offer available treatments to T1D autoantibody positive individuals

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Region Hovedstaden

Region Skåne

novo nordisk fonden

Interreg Öresund-Kattegat-Skagerrak European Regional Development Fund

European Union

DiaUnion - Status as of November 2023

DiaUnion is screening the general population in Sweden and first-degree relatives in Denmark for the TRIAD (i.e., T1D, CD and AITD)

General pediatric population
Age 6-9 and 13-16 years (n=3,815)
Multiple islet autoantibodies: 0.6%

First-degree relatives (siblings)
Mean age: 11.4 years (n=2,150)
Multiple islet autoantibodies: 4.7%

The DiaUnion initiative is also to improve prediction and follow-up program of autoantibody positive individuals

Omic technologies

Follow-up on IAb-positive individuals

Systems genetics

Autoantibody screening and affinity

Summary

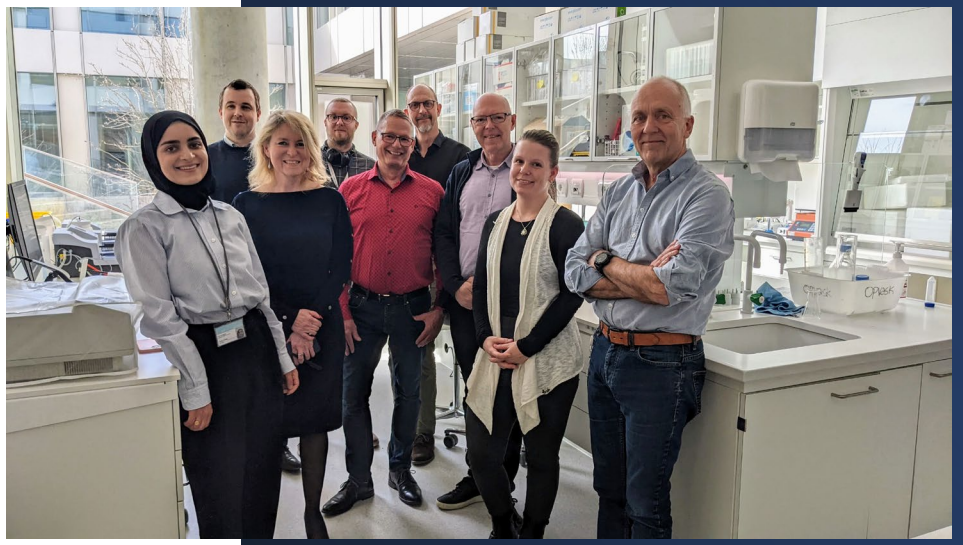
T1D, and two related autoimmune diseases, CD and AITD, are common autoimmune diseases in Scandinavia and cluster in T1D patients

DiaUnion aims to establish a combined autoantibody public screening program to identify children at risk for T1D, CD and AITD (i.e. the TRIAD)

Thank you!

DiaUnion Team & Partners

Finn Kristensen, Anette Steenberg, Maria Naredi Scherman, Samia Hamdan, Alexander Lind, Julie Christine Antvorskov, Rasmus Bennet, Julie Hviid Klæbel, Jesper Johannesen, Markus Lundgren, Jessica Melin, Zeliha Mestan, Johan Svensson, Åke Lernmark, Flemming Pociot, Daniel Agardh.



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