

# General population screening for T1D: Experience from Sweden

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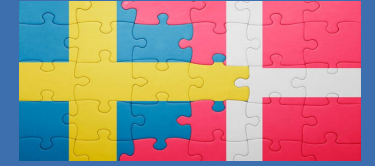
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# DiaUnion est. 2020



**DiaUnion** is a collaboration between **Lund University** and **Steno Diabetes Center Copenhagen**

**DiaUnion** started in 2020 with the aim to create a screening program in Sweden and Denmark for type 1 diabetes and related autoimmune diseases

**DiaUnion's first focus** is to build an infrastructure for early detection of type 1 diabetes, celiac disease and autoimmune thyroid disease in the Öresund Region



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Steno Diabetes Center  
Copenhagen



## Why the TRIAD?

- Type 1 Diabetes (T1D), Celiac Disease (CD), Autoimmune Thyroid Disease (AITD)
- Common chronic diseases affecting children and adolescents (0.5–3%)
- Frequently co-occurs in families
- No cure – lifelong treatment (insulin, gluten-free diet, levothyroxin)
- Clinical onset is preceded by the presence of disease-specific autoantibodies





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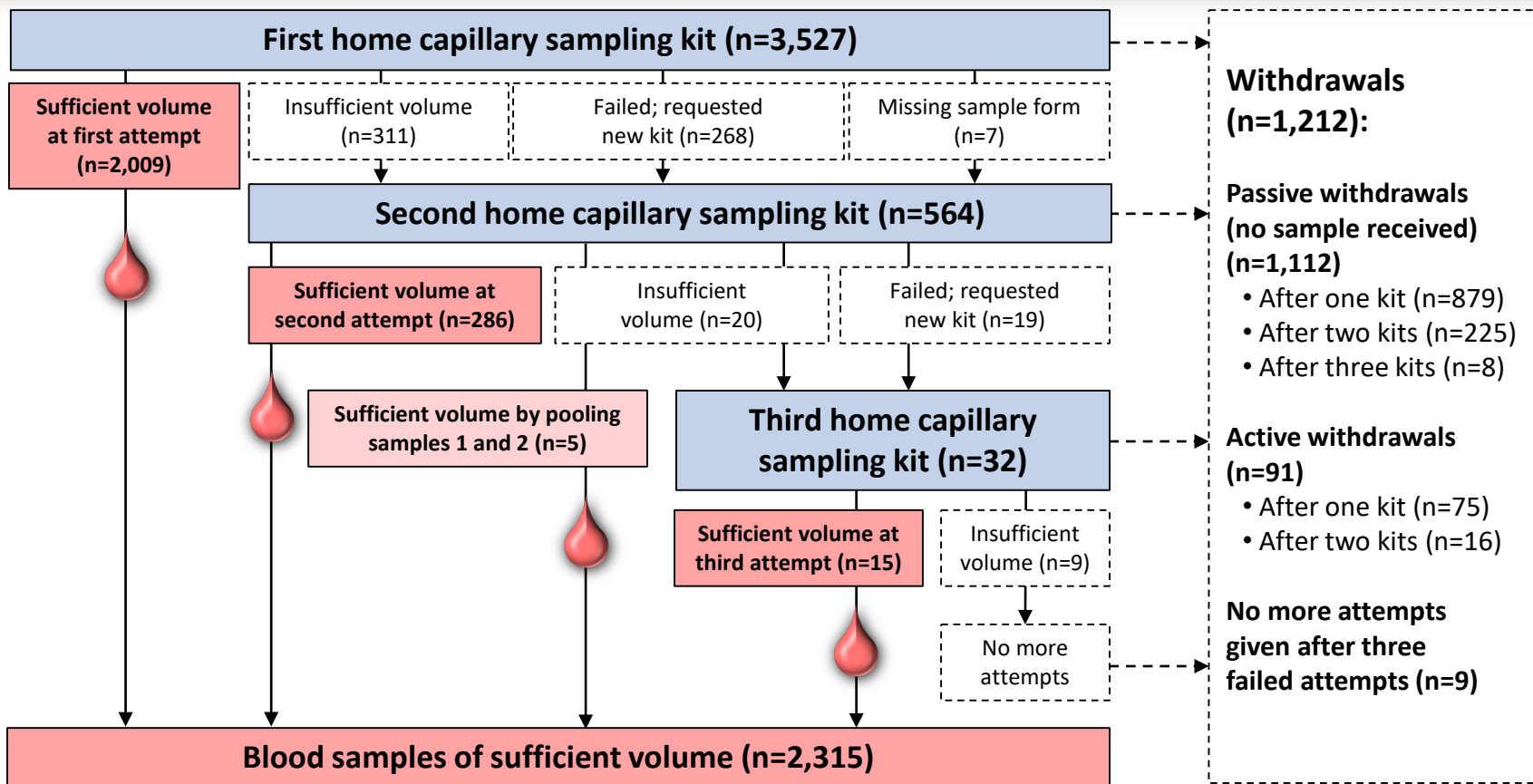
Steno Diabetes Center  
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Screening of children randomly invited from the general pediatric population in the Skåne County, Sweden

Screening of siblings (i.e., FDRs) of patients with T1D in Copenhagen, Denmark

FDR, first degree relatives.

**Communication provided by speaker.** The DiaUnion TRIAD study is a collaboration between Lund University, Steno Diabetes Center Copenhagen and Medicon Valley Alliance, for early detection of T1D and two genetically related autoimmune diseases (CD and AITD). For more information on the DiaUnion TRIAD study, including the predicted end date, see: <https://portal.research.lu.se/en/projects/screening-for-Type-1-diabetes-celiac-disease-and-thyroiditis-in-c> [Last accessed October 2023]



- **3,527** consents (**18.0%**)
- **4,123** kits sent out
- **2,315** blood samples of sufficient volume (**65.6%**)
- **1,112** no sample (**31.5%**)
- **91** active withdrawals
  - **58** due to concerns about blood draw (**63.7%**)

## Step 1. Invitation



### Skåne County, Sweden (n=1.4 million)

- Two age groups:
  - 6–9 years
  - 13–16 years
- General population (n=68,000)
- Invitation to screening (n=20,000)

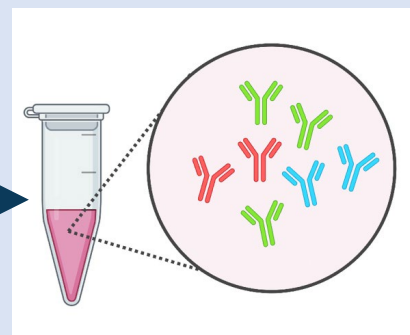
## Step 2. Sampling



### Home capillary sampling kit

- Kit sent to home address
- Finger prick (>250 uL)
- Samples sent back to the lab by regular mail

## Step 3. Testing



### Detection of eight autoantibodies:

- **T1D** (IAA, GADA, IA-2A, ZnT8A)
- **CD** (IgA-tTG, IgG-tTG)
- **AITD** (TPOA, THGA)
- 1. Radiobinding assays (RBA); chemiluminescent immunoassay
- 2. Antibody-detection by agglutination-PCR (ADAP)

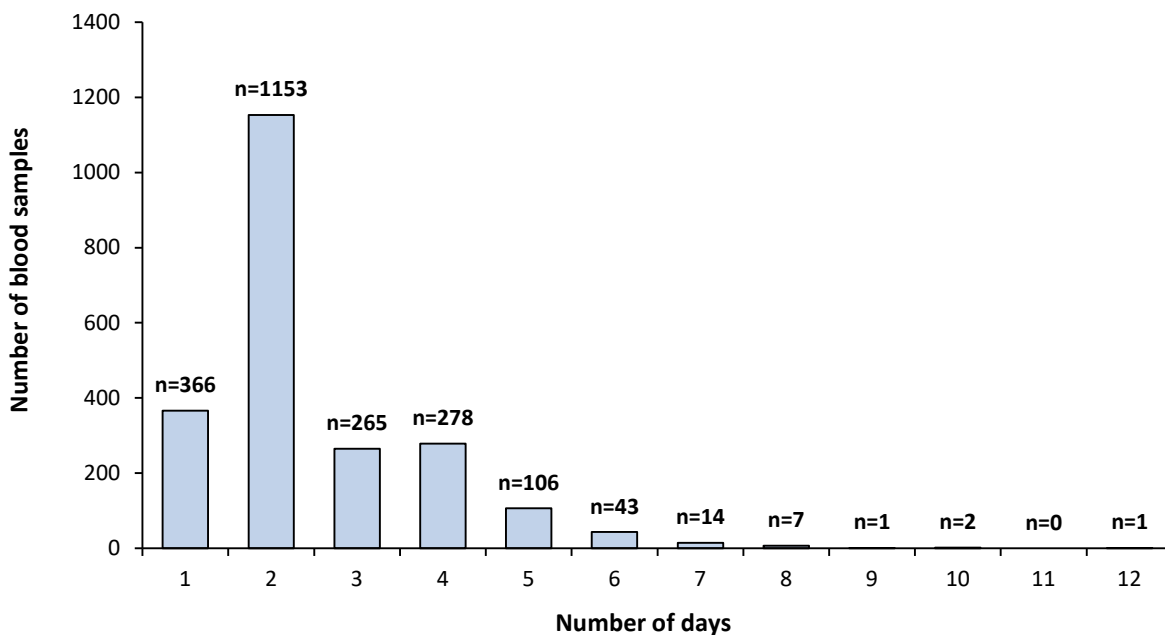
## Step 4. Follow-up



### (Aab+) children:

- A second sample median 3.8 (range 1.9–15) mo
- Persistent Aab+ children referred to pediatrician for clinical follow-up

## Days between sample draw date and sample process date (registered in 2,236 samples)



**Median: 2 days**

## HEMOLYSIS? (registered in 2,301 samples)



**No hemolysis**  
n=1,471 (63.6%)



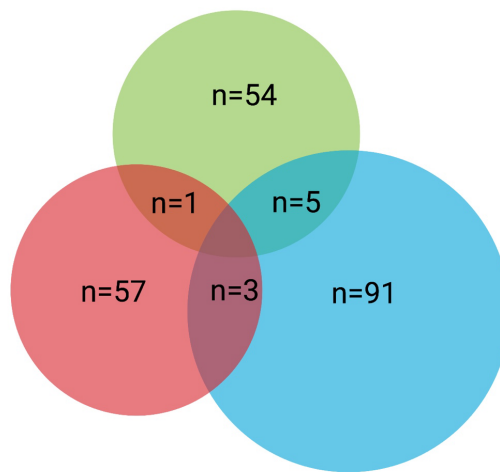
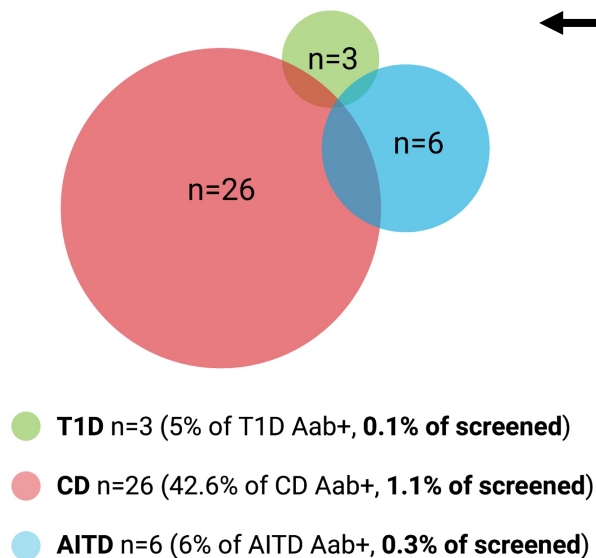
**Moderate hemolysis**  
n=620 (26.9%)



**Gross hemolysis**  
n=210 (9.1%)

## AAb+ in screening n=211 (9.3%)

## Diagnosed after screening n=35 (1.5%)



- T1D Aab+ n=60 (2.6% of screened)
- CD Aab+ n=61, (2.7% of screened)
- AITD Aab+ n=99, (4.4% of screened)
- ● ● Aab+ for multiple TRIAD diseases n=9 (0.4% of screened)

## Positive autoantibodies Normal clinical investigation "At risk individuals"

n=176

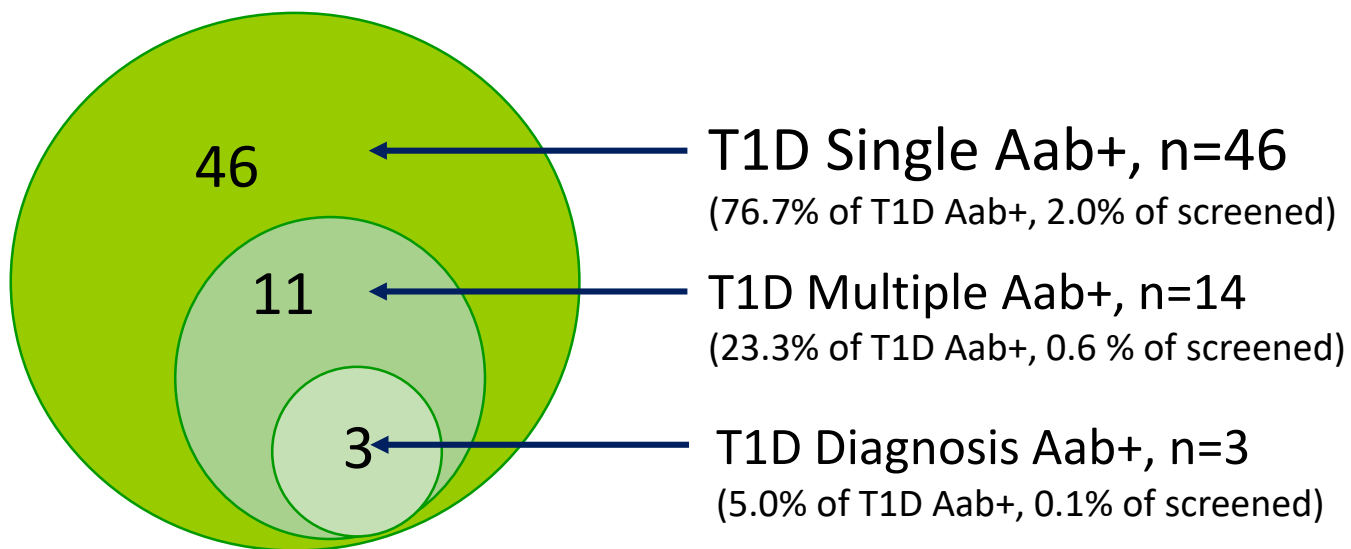
## Recruited to clinical intervention study (PAL) n=65

**PAL**

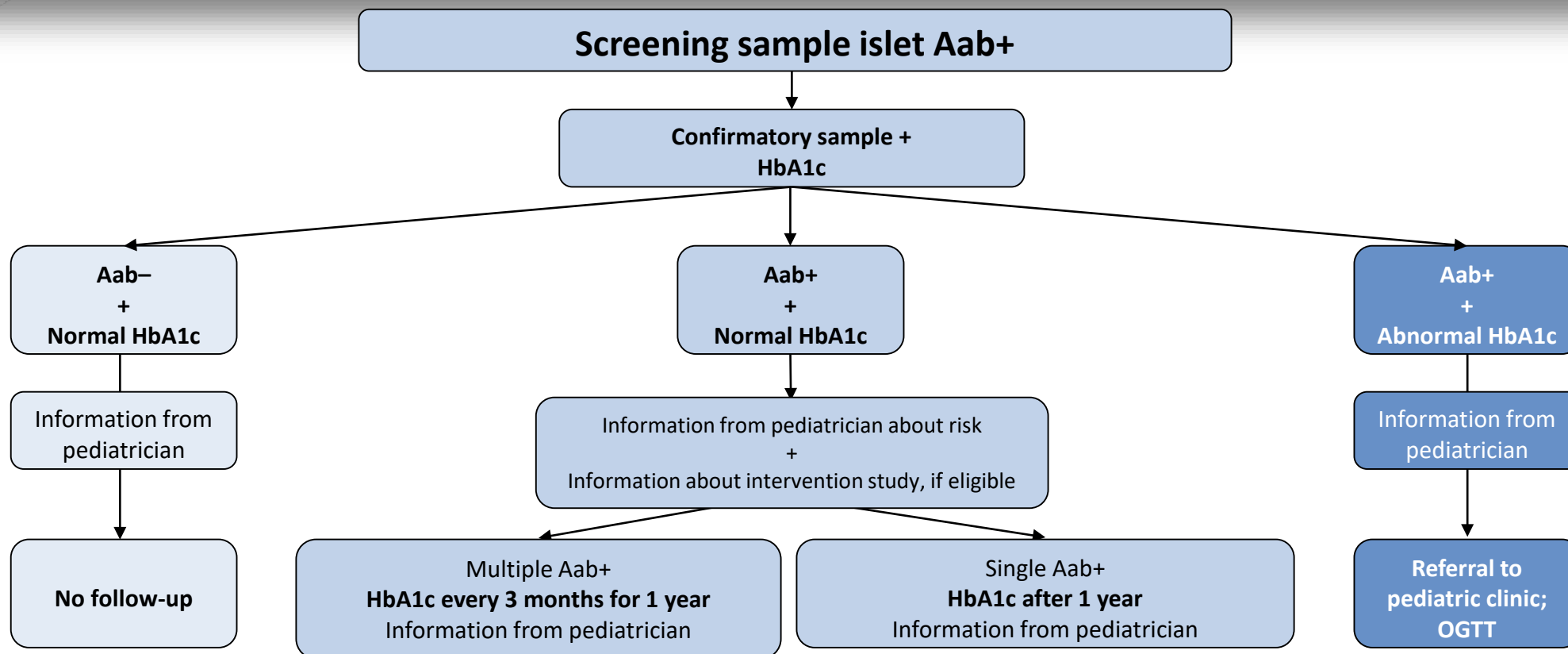
Prevention av Autoimmunitet med Laktobaciller



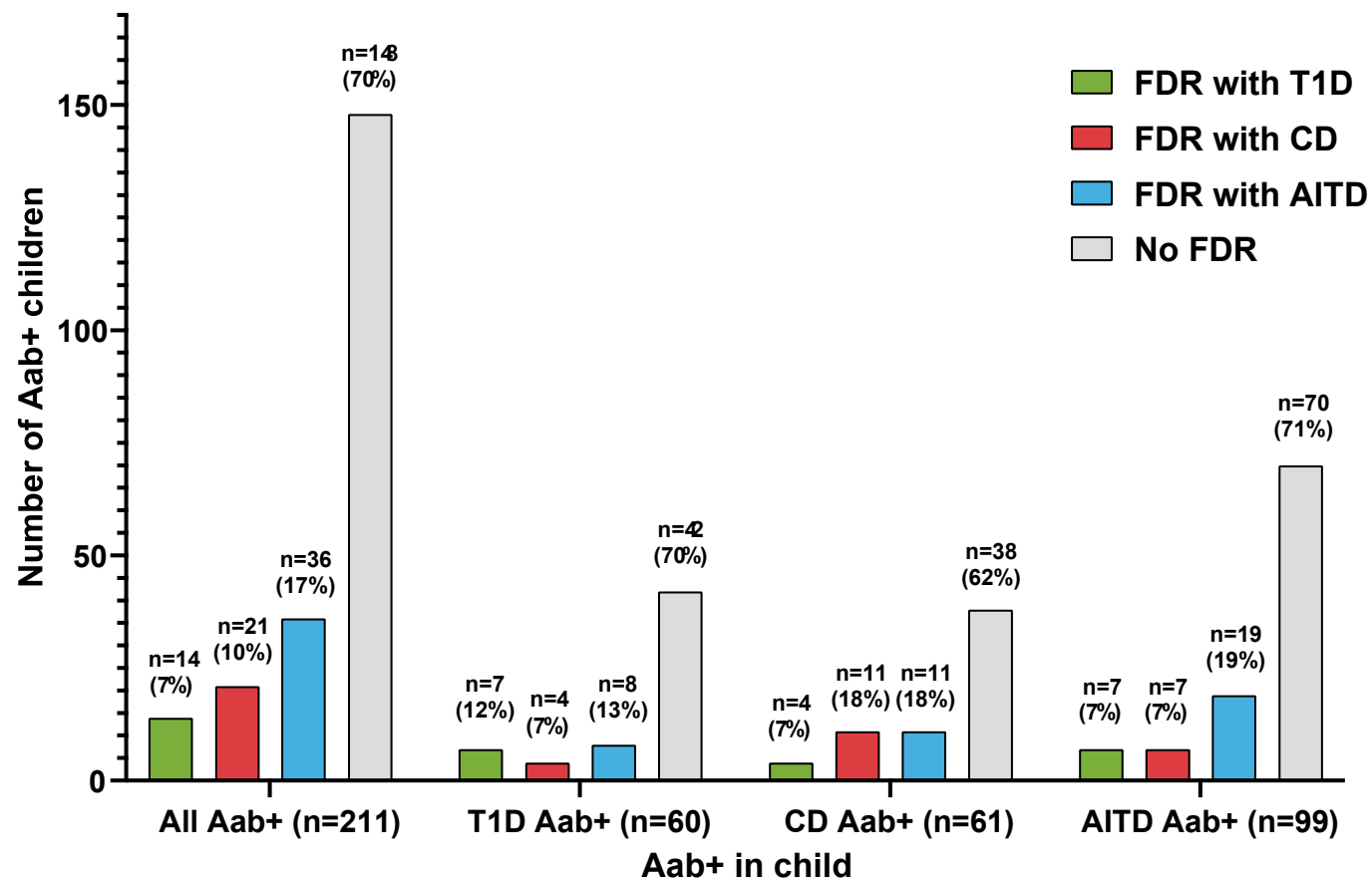
# Islet Aab+ (n=60)



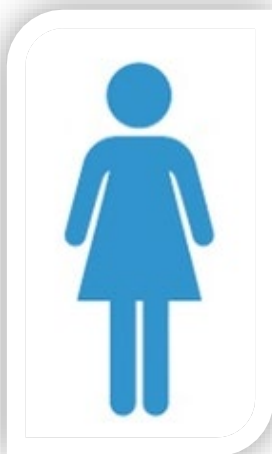
	No. (%)
All screened	2,271 (100)
<b>Islet Aab+</b>	<b>60 (2.6)</b>
IAA	30 (1.3)
GADA	37 (1.6)
IA-2A	10 (0.4)
ZnT8A	9 (0.4)



## Diagnosis in FDR to Aab+ children (n=211)

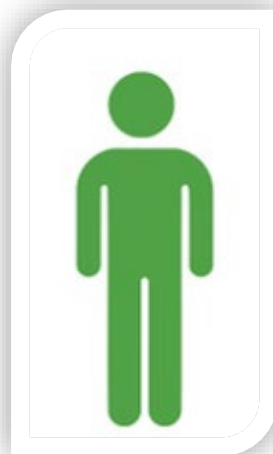


30% of Aab+ children had an FDR with a TRIAD-disease



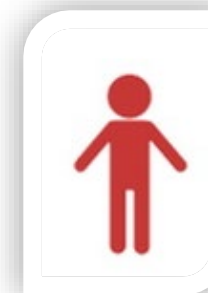
>2/3 were mothers

**AITD** was the most common disease in mothers (70%)



>1/6 were fathers

**T1D** was the most common disease in fathers (50%)



<1/6 were siblings

**CD** was the most common disease in siblings (63%)

In 52% the FDR had another disease than the child was screened positive for



1. Biobank samples (no follow up; n=1,420)
2. ADAP used as the screening assay
3. RBA used to confirm Aab+

## **Aab+ results confirmed by RBA showed:**

### **Any TRIAD autoantibody:**

- 13.5% Danish T1D FDRs
- 5.6% of Swedish pediatric GP

### **Any T1D autoantibody:**

- 7.5% of Danish T1D FDRs
- 1.1% of Swedish pediatric GP

### **Multiple T1D autoantibodies:**

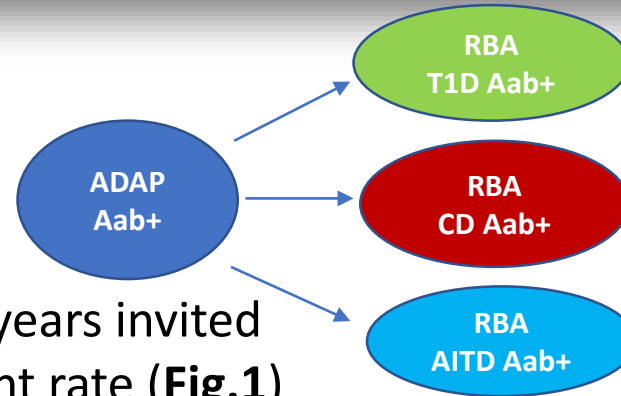
- 4.6% of Danish T1D FDR
- 0.6% of Swedish pediatric GP

Aab+	Danish T1D FDRs N=192/1,420 (13.5%) n/N (%)	Swedish children N=127/2,271 (5.6%) n/N (%)
<b>GADA</b>	89/1,420 (6.3%)	22/2,272 (1.0%)
<b>IAA</b>	43/1,420 (3.0%)	8/2,272 (0.4%)
<b>IA-2A</b>	38/1,420 (2.7%)	8/2,272 (0.4%)
<b>ZnT8</b>	28/1,420 (2.0%)	3/2,271 (0.1%)
<b>TPOA</b>	55/1,420 (3.9%)	52/2,272 (2.3%)
<b>tTGA</b>	55/1,420 (3.9%)	55/2,272 (2.4%)

## DiaUnion 1.5 (2022–2023):

### 1. Swedish general pediatric population:

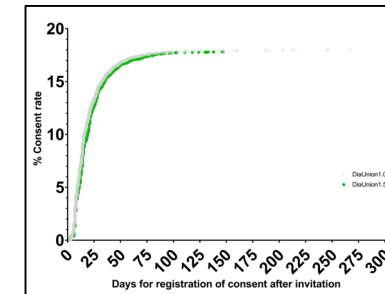
- 1. ADAP screening assay
- 2. RBA confirmation assay
- 13,498 children ages 6–9 years and 13–16 years invited
- So far 2407 children enrolled, 17.8% consent rate (**Fig.1**)
- So far 1553 samples collected, 11.5% participating rate (**Fig.2**)
- 31 (2.0%) reported a TRIAD disease (1.0% CD, 0.2% T1D, 0.1% AITD)
- 333 (21.4%) children reported to have a FDRs with TRIAD disease



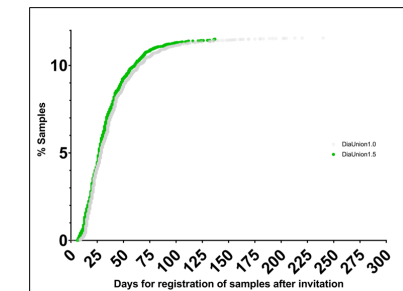
### 2. Danish T1D-FDRs (siblings, children, parents):

- Age <40 years, 1,500 invited to screening
- ADAP screening assay
- RBA confirmation assay
- Analysis pending

**Fig. 1. Consent rate**

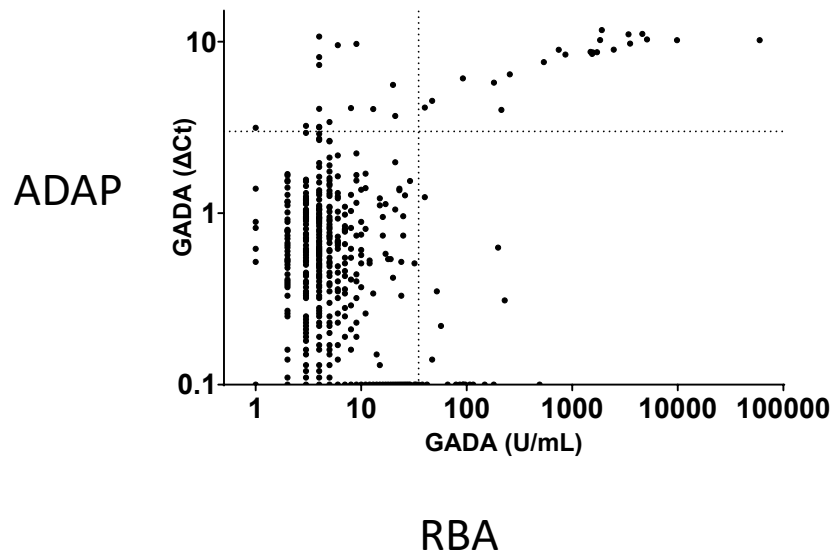


**Fig. 2. Sample rate**



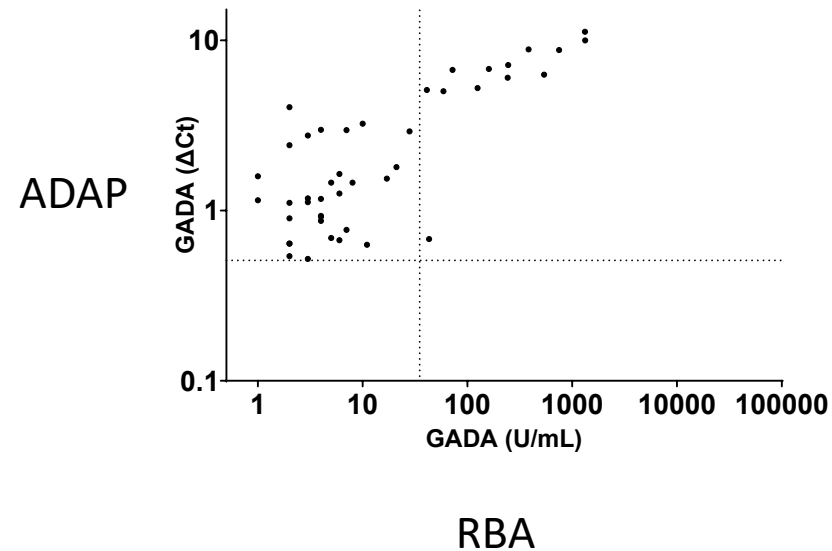
## DiaUnion 1.0 (2021-2022)

- 2273 samples analysed in both ADAP and RBA
- The concordance agreement, Cohen's kappa  $\kappa$  coefficient, between the assays were 0.542
- **Prevalence of confirmed GADA 1.0%**



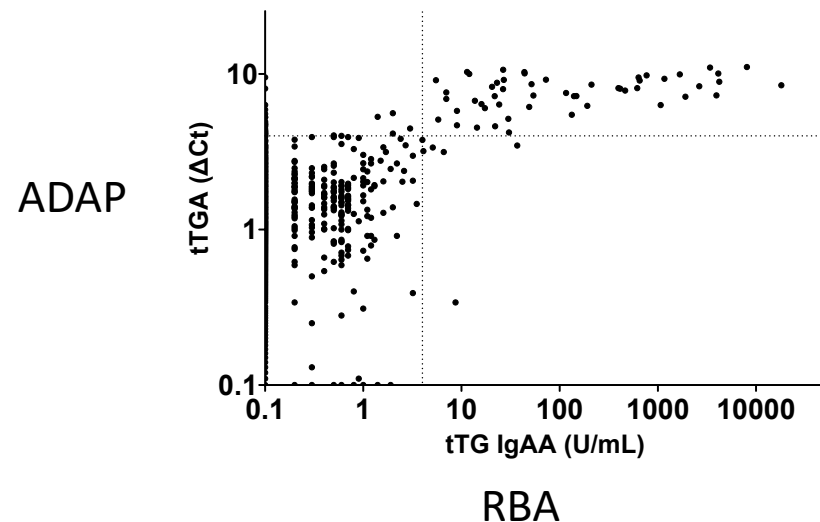
## DiaUnion 1.5 (2023)

- ADAP first-line screening (cut-off 98th percentile)
- RBA confirmation assay
- 44/957 (4.6%) above cut-off in ADAP
- 13/44 (29.5%) confirmed GADA positive in RBA
- **Prevalence of confirmed GADA 1.4%**



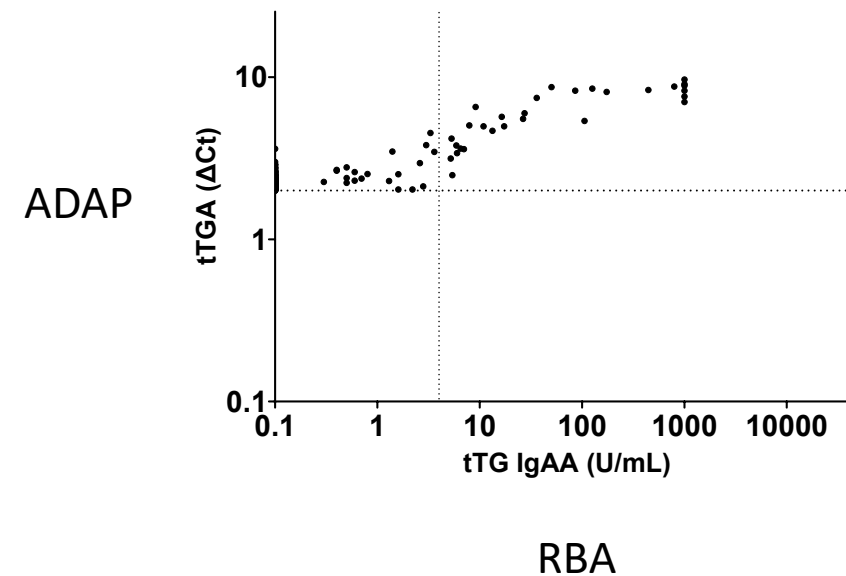
## DiaUnion 1.0 (2021-2022)

- 2273 samples analysed in both ADAP & RBA
- The concordance agreement, Cohen's kappa  $\kappa$  coefficient, between the assays were 0.698 (IgA) and 0.675 (IgG)
- **Prevalence of confirmed tTGA 2.4%**



## DiaUnion 1.5 (2023)

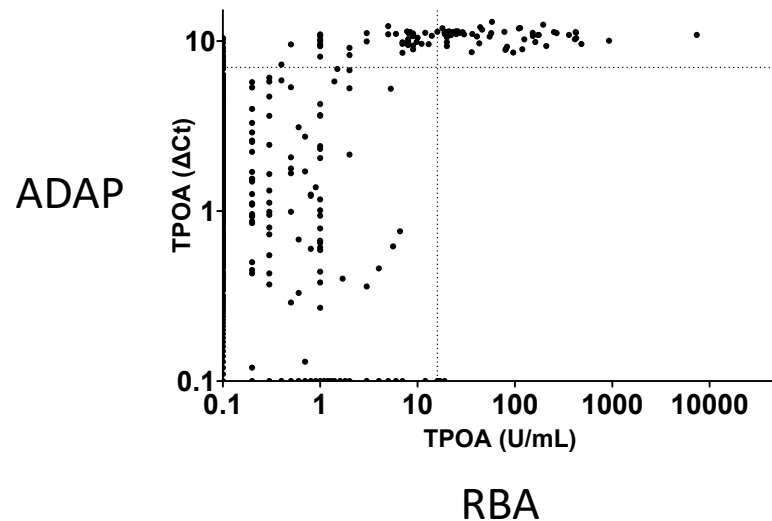
- ADAP first-line screening (cut-off 75th percentile)
- RBA confirmation assay
- 222/957 (23.2%) above cut-off in ADAP
- 33/222 (14.9%) confirmed tTGA (IgA+IgG) positive in RBA
- **Prevalence of confirmed tTGA 3.4%**





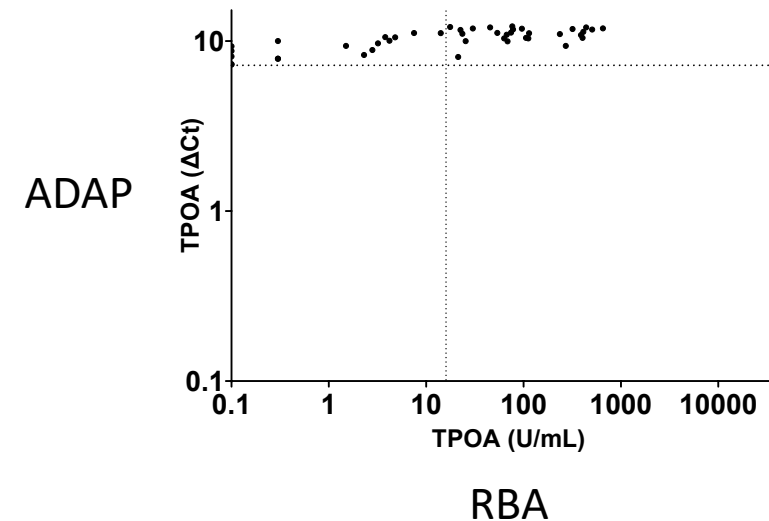
## DiaUnion 1.0 (2021-2022)

- 2273 samples analysed in both ADAP & RBA
- The concordance agreement, Cohen's kappa  $\kappa$  coefficient, between the assays were 0.595
- **Prevalence of confirmed TPOA 2.3%**



## DiaUnion 1.5 (2023)

- ADAP first-line screening (cutoff 90th percentile)
- RBA confirmation assay
- 44/957 (4.6%) above cut-off in ADAP
- 27/44 (61.4%) confirmed positive in RBA
- **Prevalence of confirmed TPOA 2.8%**



- DiaUnion boosts screening for T1D by including CD and AITD
- DiaUnion's 1<sup>st</sup> screening of the Swedish GP population found islet autoimmunity in 2.6%, multiple islet autoantibodies in 0.6%, and T1D in 0.1%
- Results DiaUnion's 2<sup>nd</sup> screening of the Swedish GP population pending, but confirms consent rate (18%) and successful participation rate (12%).
- Home sampling is feasible, but can be optimized by collecting smaller sample volumes for multiplex assays
- The multiplex ADAP assay is promising as a screening method, but further evaluation is needed before considering it as first-line screening for the GP
- DiaUnion's next goal is to scale up screening to 30,000 Swedish children from the GP and 15,000 Danish T1D FDRs



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