

# Prediction and prevention of type 1 diabetes (T1D) in neonates: a new trial program in Europe

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## Background

Type 1 diabetes is the **n°1 metabolic disease in childhood** and is **increasing in incidence**, making primary prevention a **major public-health goal**.

**We must focus on early identification** of neonates and infants who are at risk of type 1 diabetes. Genetic markers arise before the auto-immune attack against  $\beta$  cells occurs, and are therefore a key role in early detection.

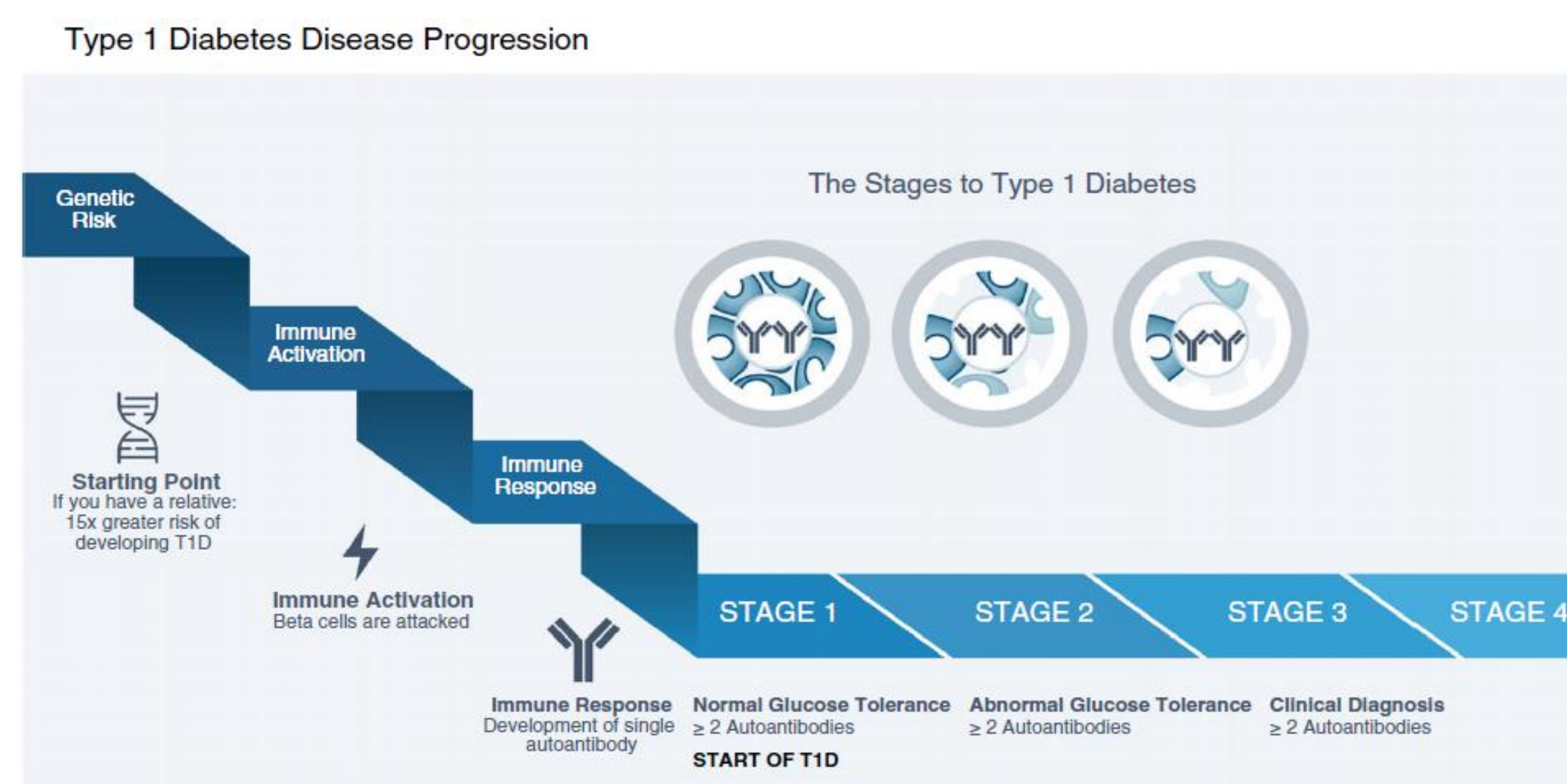


Fig 1 : DiMeglio et al (2018). The Lancet.

**Global Platform for the Prevention of Autoimmune Diabetes (GPPAD)** has established :

- 1) Screening program (GPPAD-02) to identify high genetic risk newborns
- 2) If screening is positive, this infants can participate in a primary prevention study : the Primary Oral Insulin Trial (POInT).

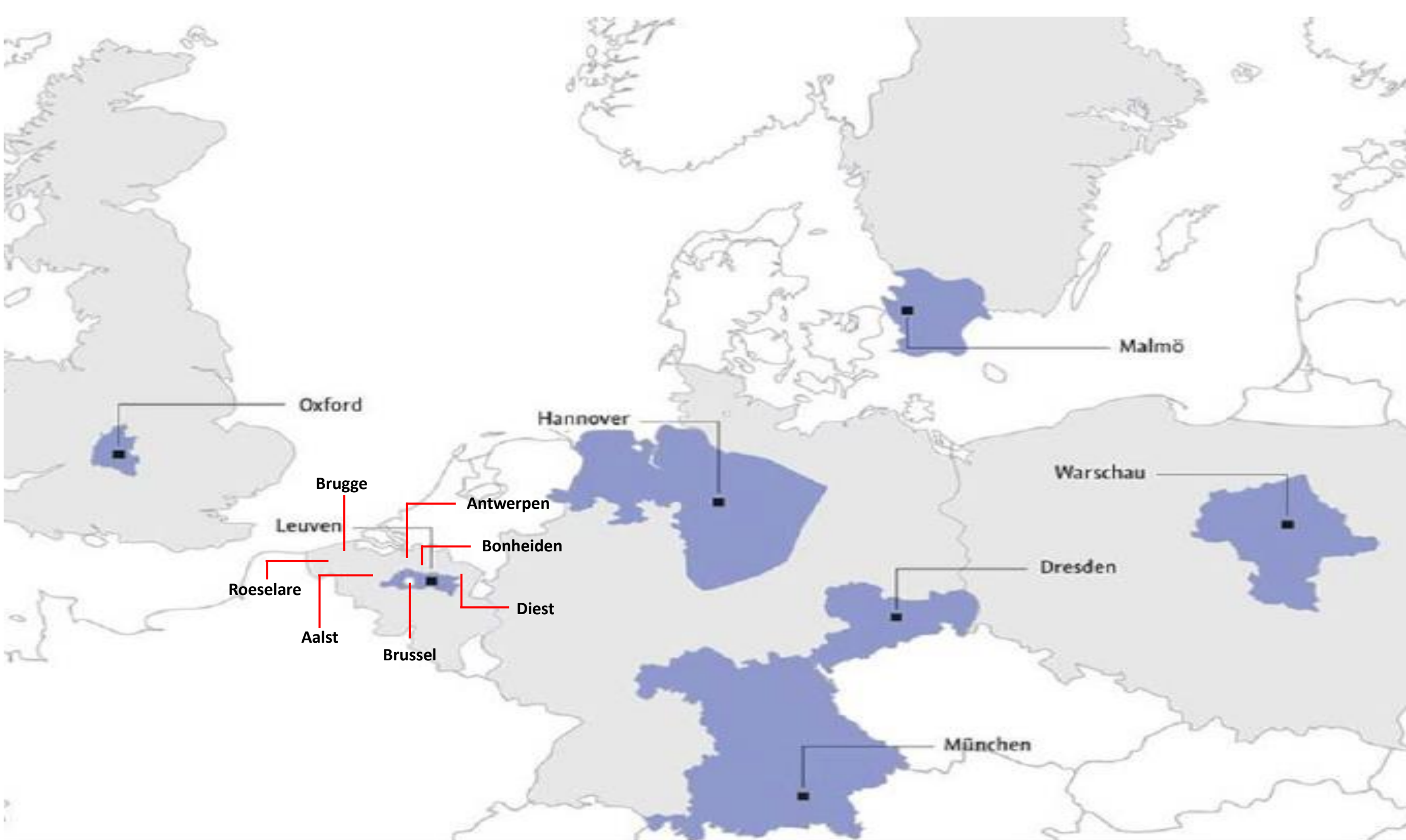


Fig 2. : Map showing GPPAD recruitment centers active in 2019

## GPPAD-02 - freder1k study:

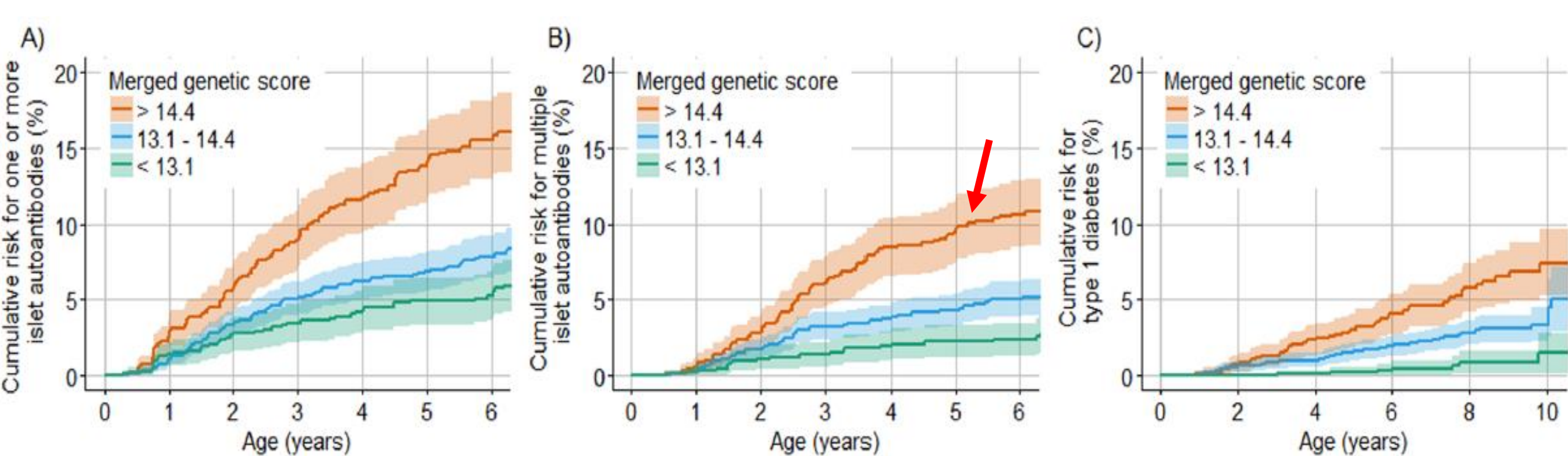


Fig. 3 : Cumulative risks of 1 or more islet autoantibody, multiple islet autoantibody, and type 1 diabetes development in TEDDY children with the HLA DR3/DR4-DQ8 or DR4-DQ8/DR4-DQ8 genotype stratified by their merged score. The cumulative risk of developing 1 or more islet autoantibodies (A), multiple islet autoantibodies (B), and type 1 diabetes (C) (y-axis) is shown relative to age in years (x-axis) and was calculated using the Kaplan-Meier method. Curves are shown for children with genetic scores in the upper (orange line), lower (green line), and 2 middle (blue line) quartiles. The shaded areas represent the 95% confidence interval of the cumulative risk. The numbers at risk indicate the number of children included in the analysis at each age. (Bonifacio, E. et al. (2018), PLoS medicine, 15(4), e1002548.)

**GPPAD-02** : Determination of **individual genetic risk** based on 47 T1D susceptibility SNPs and the first degree-family history for T1D (**merged algorithm**).

**Method** : **Capillary blood samples** from newborns and infants before the age of 3 months.

**Primary outcome**: Identification in infants with a **high genetic risk** for multiple  $\beta$  cell autoantibodies (>10%) by the age of 6 years.

- 1% of screened general population
- Multiple Aab+ = stage 1 diabetes
- Evolve to stage 3 in 90% of cases (within 20 years)

## GPPAD03 – POInT study

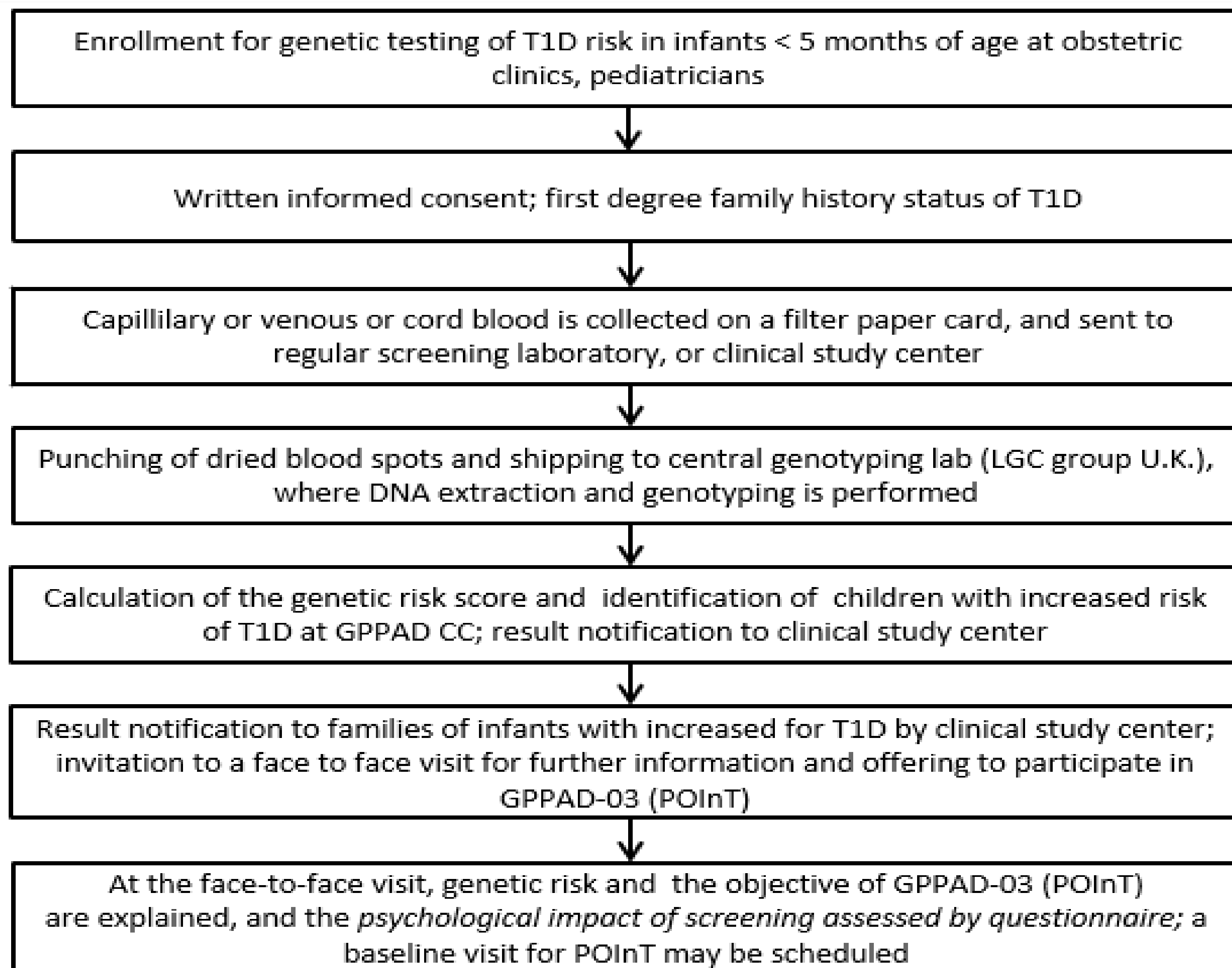


Fig 4 : Flowchart explaining recruitment in GPPAD-02 and GPPAD-03

**POInT** : randomized, double-blinded, multicenter **phase IIb/III primary prevention trial**.

**Method** : High-risk infants identified in GPPAD-02 are offered participation in POInT trial. Daily administration of oral insulin from age 4-7 months until age of 3 years in children with elevated genetic risk for T1D.

**Primary endpoint** : Reduction of the cumulative incidence of  $\beta$  cell autoantibodies and diabetes in childhood.

## Results in February 2019

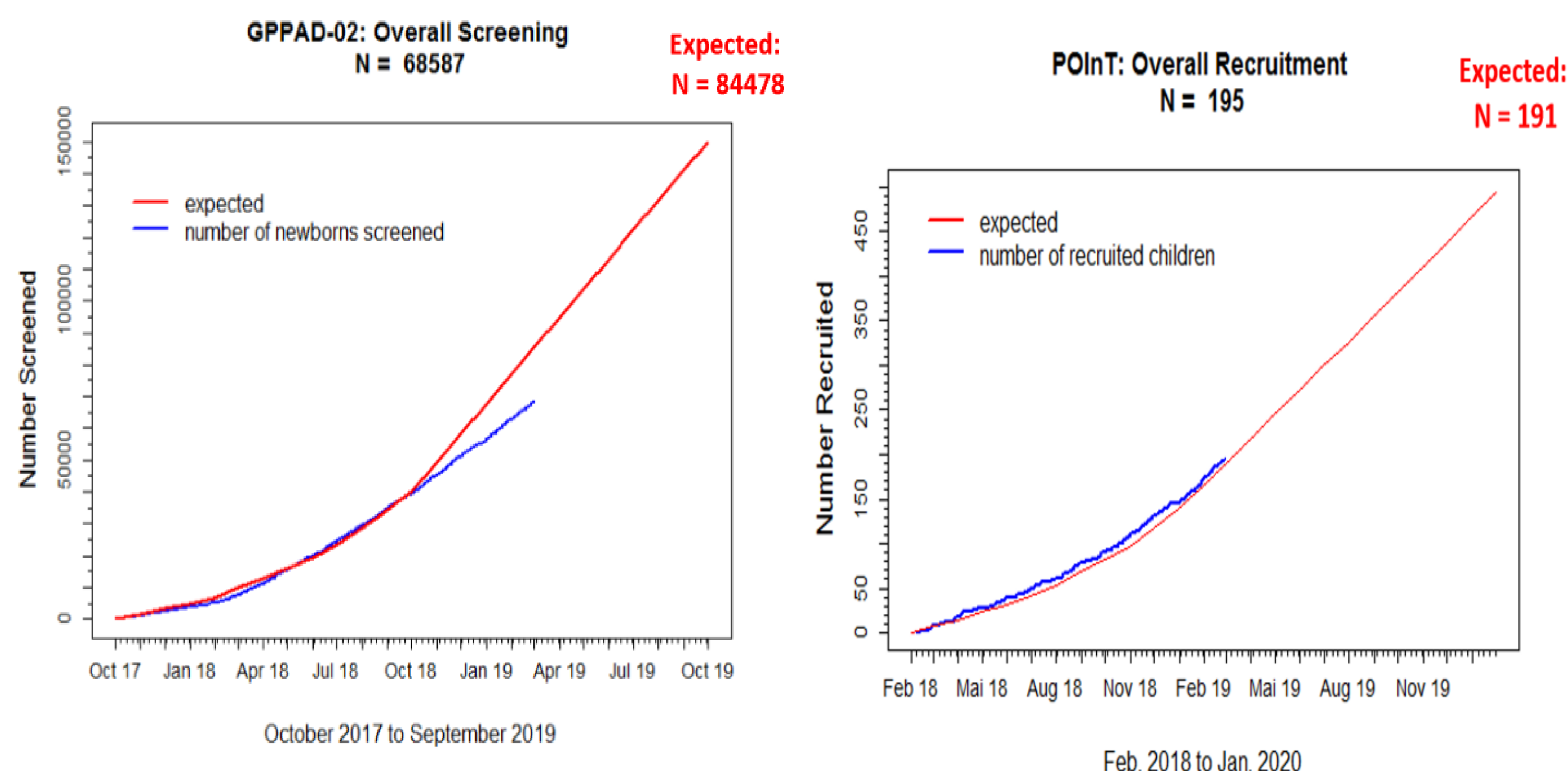


Fig 4 : GPPAD-02 and GPPAD-03 recruitment data and expectations for 2019

## What about Belgium ?

**GPPAD-02** : Running in Belgium (Universitair Ziekenhuis Leuven) since July 2018 with 900 infants screened and initiation in eight other centers is imminent.

**GPPAD-03** : Starting soon.

→ We are expecting to screen 17000 infants and enroll 66 children in the 3 next years within GPPAD.

## Conclusion

- 1) Primary results show that screening for genetic risk in newborns is feasible and well accepted by parents.
- 2) Enrollment in POInT is running well and number of patients participating is within the expected range.