



Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS



Children's Hospital Colorado

Combined Screening for T1D and Celiac Disease: ASK Perspective

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Colorado Center for Celiac Disease

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A SIMPLE TEST TO DETECT
Childhood Diabetes
+ **Celiac Disease**

Disclosures

- MS has consulted for:
 - Pfizer:** Data safety and monitoring board for a celiac disease clinical trial
 - Takeda:** Advisory board for celiac disease pathology
- EL has consulted for:
 - Takeda:** Advisory board

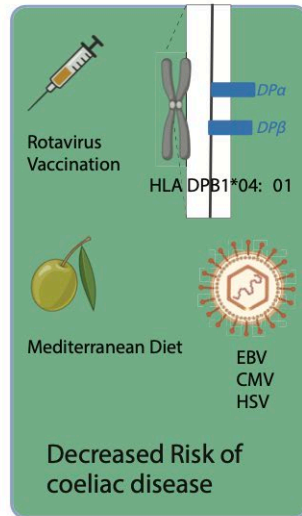
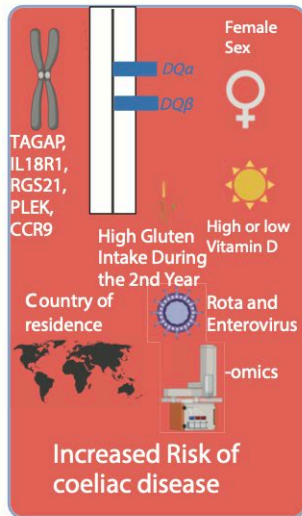
*These consulting responsibilities are not related to any of the data we will be presenting today

Outline

- Briefly review available data on overlap of type 1 diabetes and celiac disease.
- Present data pertinent to both celiac disease and islet autoimmunity in the ASK study.
- Discuss practical aspects of celiac disease screening and how we can combine resources to advance screening efforts for both of these autoimmune diseases.

TYPE 1 DIABETES AND CELIAC DISEASE

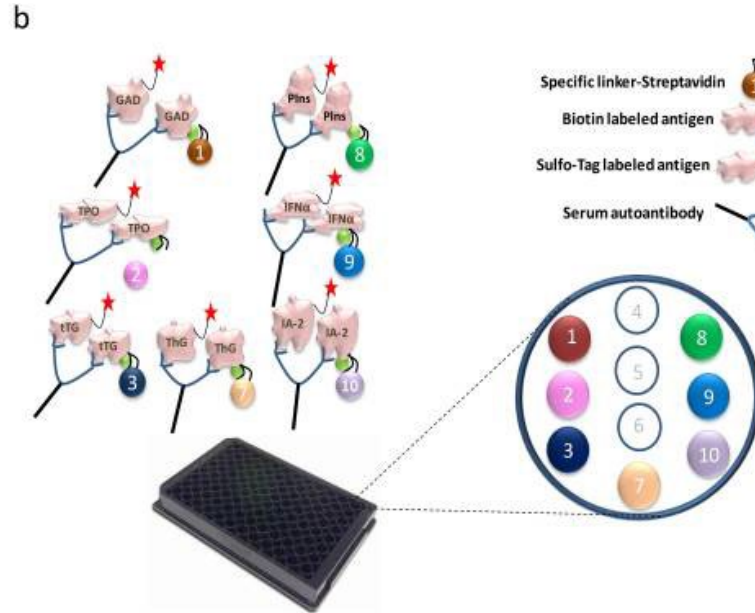
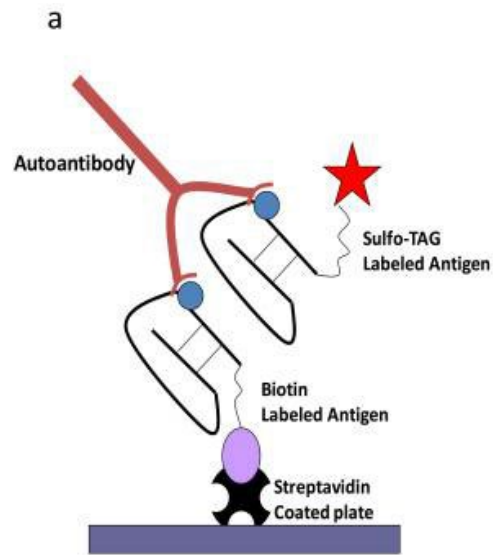
Overlapping Genetic & Environmental Risk Factors



Proposed Risk Factors:

- Genetic: Both HLA and non-HLA contributions
- Intestinal Barrier and Microbiome
- Early life infections
- Dietary factors
- Metabolome and other -omics

We Can Efficiently Screen for Both Diseases



- Cut labor time and supply cost by 30%
- Sensitivity and specificity identical to single ECL

Screening Tests for tTGA

- In clinical settings, we typically use the Enzyme Linked Immunosorbent Assay (ELISA).
- For the ASK study, we use highly sensitive and quantitative assays:
 - Radiobinding Assay (RBA)- **IgA**
 - Electrochemiluminescence Assay (ECL)-**IgA, IgG, IgM**

ASK RESULTS

Autoimmunity Screening for Kids (ASK) and ASK the Experts

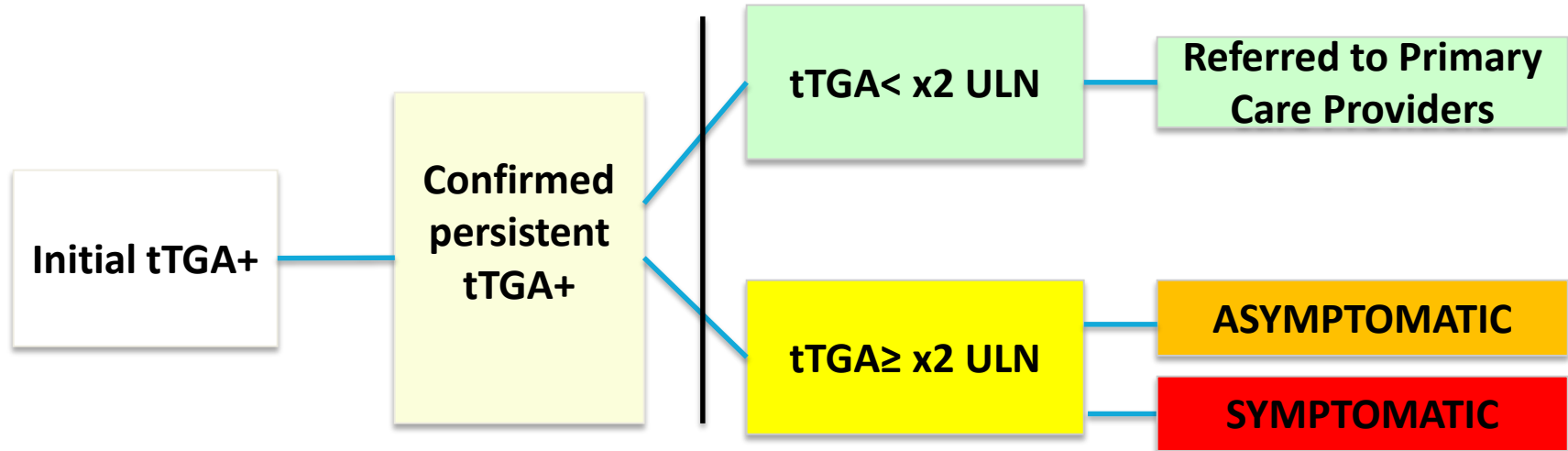
- Mass screening program for Celiac Disease and Type 1 Diabetes in Colorado
- Children 1 yo to 17 yo
- Screen 50,000 children for tissue transglutaminase IgA (tTGA) and islet autoantibodies
- Fully implemented in February 2017
- Beyond Colorado, ASK the Experts strives to do the following for CD screening: access to mass screening, knowledgeable providers, and GFD education

Pathway Based on RBA tTGA

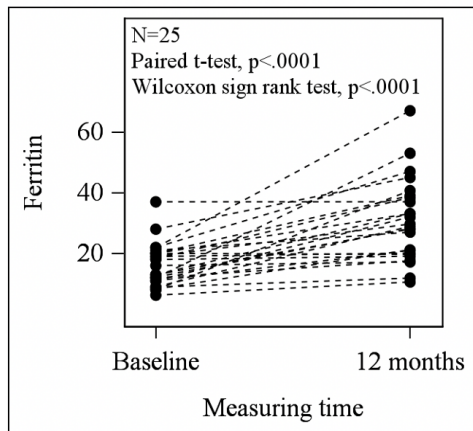
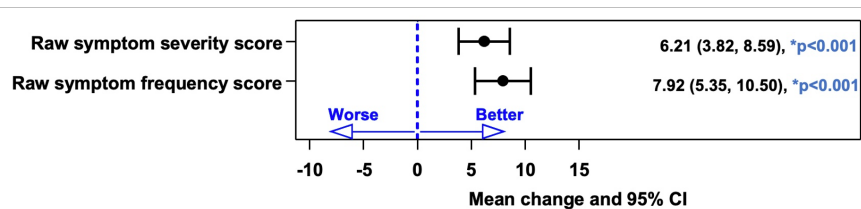
Initial Screen

Confirmation

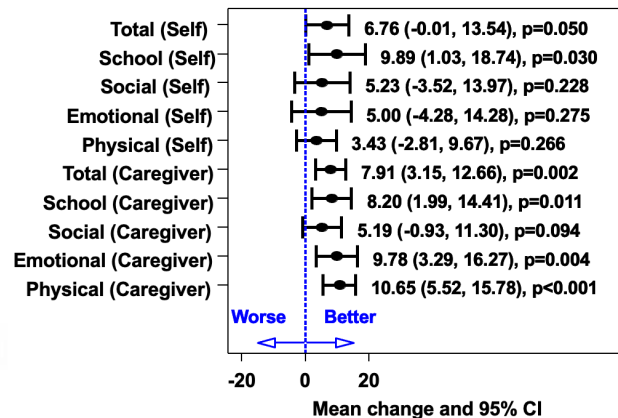
Follow-up



What Have We Learned from Children Diagnosed with Celiac Disease through ASK?



Symptoms Improve with



Iron Deficiency Improves with GFD

Quality of Life Improves with GFD

What Have We Learned From Screening for T1D and Celiac?

- 996/>33,000 (3.0%) screened positive for tTGA
 - 487/568 (85.7%) with a positive tTGA confirmation
 - 255 diagnosed with CD
- 45/28,465 (0.16%) screened positive for BOTH islet autoimmunity and celiac disease autoimmunity
- 15/271 (5.5%) with a prior celiac disease diagnosis screened positive for islet autoimmunity
- 8/649 (1.2%) followed for islet autoimmunity and subsequently developed celiac disease autoimmunity

CAN SCREENING FOR BOTH HELP US ADVANCE UNIVERSAL SCREENING?

It's the law



- Starting in 2024, Italy will be the first to require screening for T1D and CD for all children 0-17 years
- “provisions concerning the definition of a diagnostic program for the identification of T1D and CD in the pediatric population”
 - Years 2024-25 3.85 mil Euro per year
 - Years 2026- 2.85 mil Euro per year

What would it take to get this done in other countries?

Research partners:

Why might we tie mass screening of CD with efforts in T1D?

Mass screening to identify presymptomatic T1D:

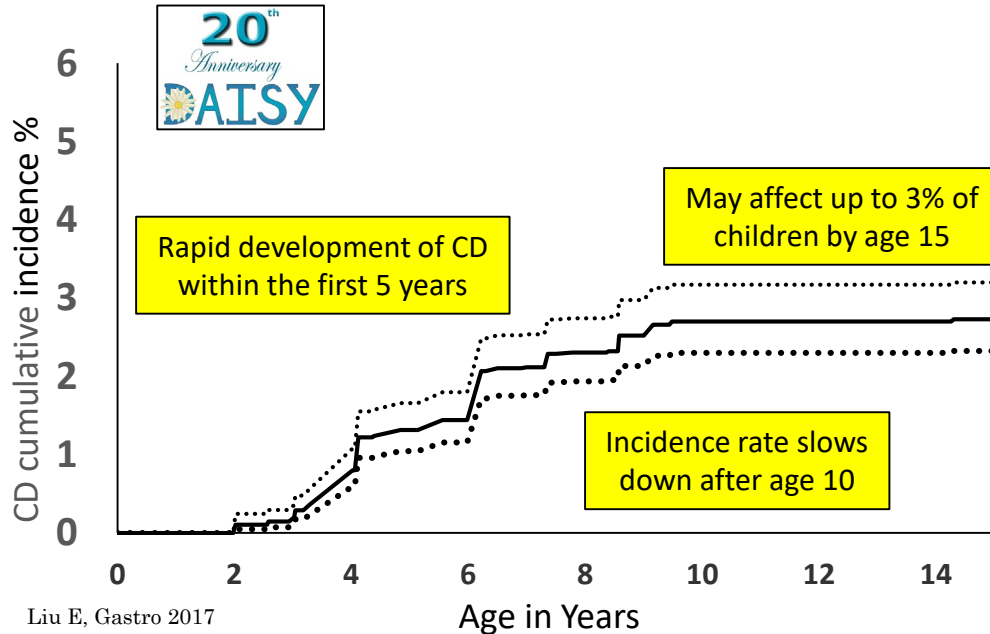
- Prevalence of 1% (ASK)
- 90% have no family history of T1D
- Awareness and minimal home glucose monitoring can prevent >80% hospitalizations for DKA
- Can be cost-effective in high prevalence areas with proper screening infrastructure
- Availability of trials (and treatment) for the delay or prevention of disease progression

Mass screening to identify early and unrecognized CD:

- Prevalence of 1-3% depending on region
- 90% have no family history of CD
- 2/3 are asymptomatic or subclinical
- Healing rates in children >> adults
- Screened CD patients get health benefits from treatment
- QoL is not worsened, may improve with treatment of previously undetected disease
- Cost effectiveness studies underway

Practical aspects of screening

What would it look like?



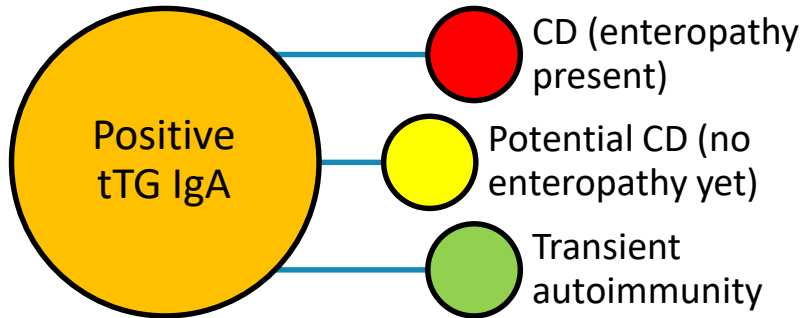
- Decreased incidence after age 10
- Cross-sectional vs **serial tTG testing**
- Testing up to 3 times still cheaper than initial HLA testing*
- Opportunistic testing (ie. with lead and dyslipidemia screening)
- Total IgA testing?

*Corrado M et al. "Cost minimization analysis of celiac disease screening strategies." NASPGHAN 2023 poster

Practical aspects of monitoring

Potential CD, transients, natural history

How to handle a positive tTG IgA test?



Will need Best Practices – apply lessons learned from ASK

- How to handle a low-positive vs high-positive tTG IgA test?
- When to refer?
- When to “watch and wait”?
- When to biopsy?
- How to reduce “loss to follow up”?
- How to manage the “asymptomatic” patient?

Priorities and challenges

- Best Practices for a positive screening test
- Public awareness and understanding of CD
- Cost studies
- Partner perspectives
 - Patient groups
 - Health care providers
 - Professional healthcare associations
 - Payors
 - Pharmaceutical industry (in the near future!)
 - Policy makers



So what's keeping us (in the US) from implementing mass screening for CD?

- Data – more supportive evidence of a benefit to impact recommendations
- Shape public perception – public awareness, willingness to undergo screening. Patient preference!
- Provider perception – provider education, willingness to screen
- Money – Cost effectiveness, overall dollars
- Policymakers – is this a priority

Last thought: Dual⁺ screening for autoimmunity

- There is benefit for both CD and T1D to be pushed together in mass screening.
 - Has mostly been one-sided
- It would be good for efforts in CD to be closer to equal footing with efforts in T1D
- **How can we help from the CD perspective to push mass screening forward?**



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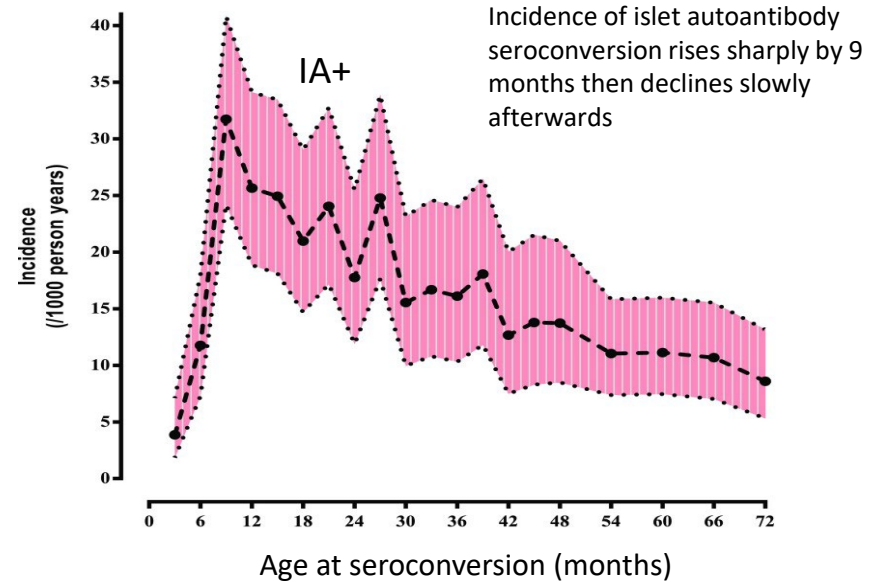
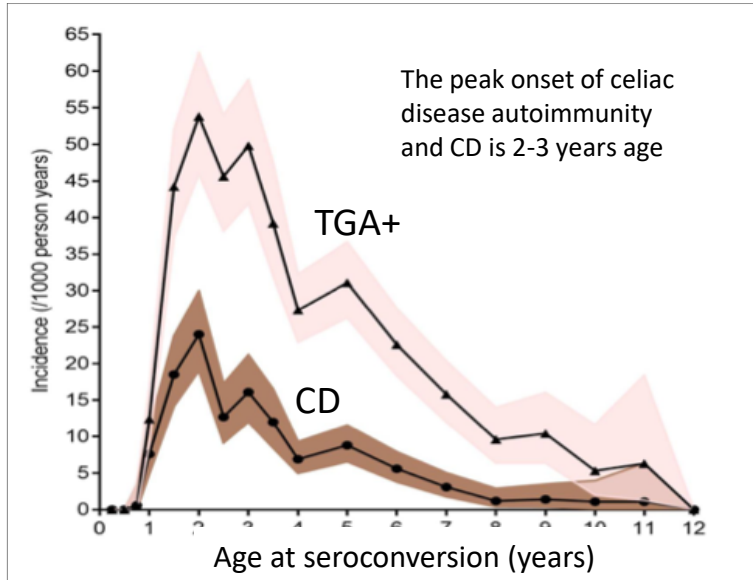
Autoimmunity Screening for Kids



Ask the Experts

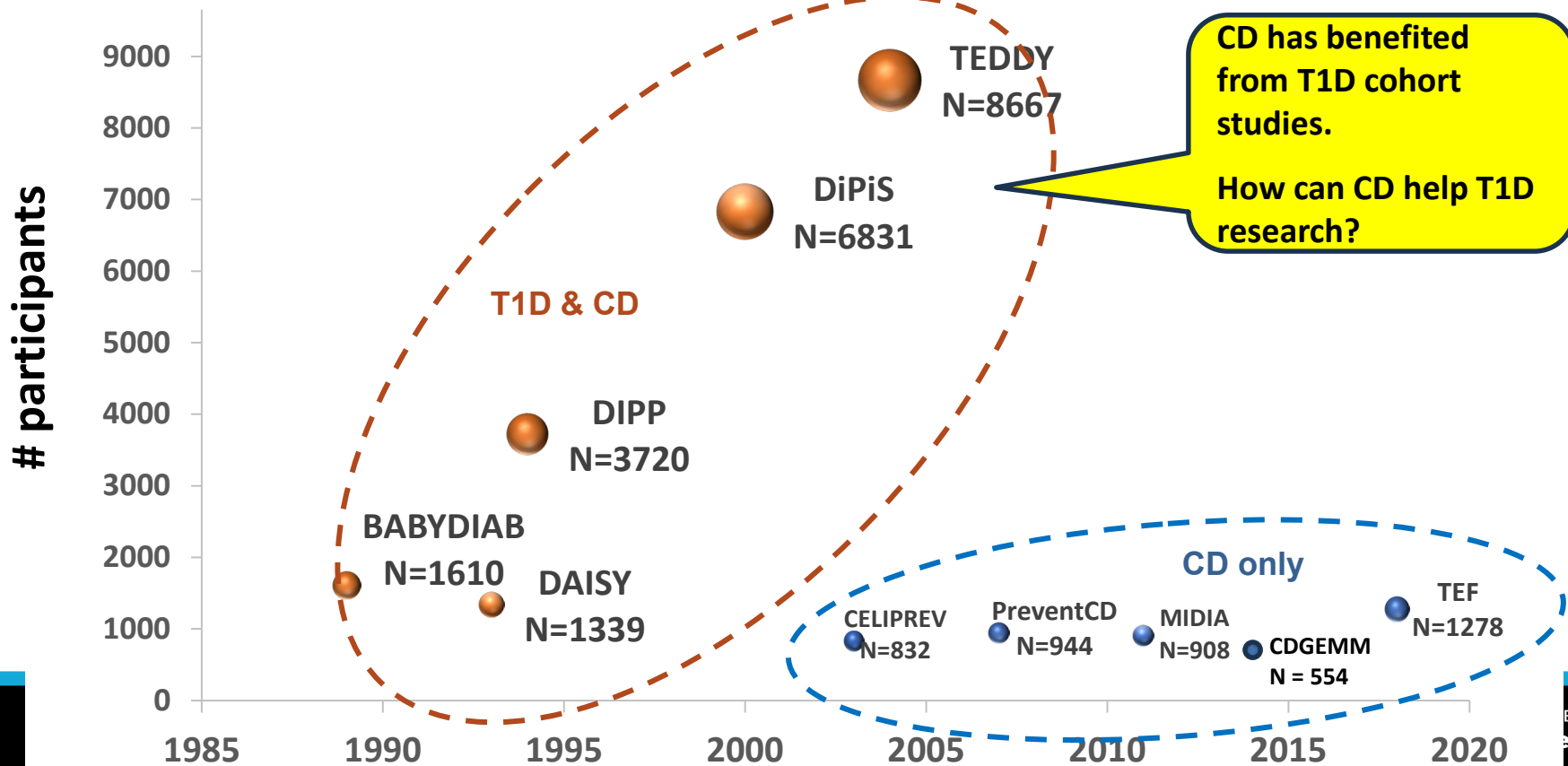
Autoimmunity begins in early childhood for both T1D and CD

Shared comorbidity, HLA predisposition and childhood onset



Good research partners:

Birth cohorts that prospectively follow children for T1D and celiac disease



CD has benefited from T1D cohort studies.

How can CD help T1D research?