

Preventing DKA

Early Screening For Pancreatic Islet Cell Autoantibodies

Dr. Herb Bravo

Disclosures

- Medical Advisory Board for Sanofi USA
- National Speaker Bureau T1D for Sanofi USA- STR1DE
- Consultant to Med Tech, Independent Practices, and Pharma
- Will not discuss experimental or brand-name therapies



About Dr. Bravo

Dr. Bravo is a distinguished US pediatrician and serial entrepreneur known for his significant contributions to healthcare and beyond. Trained as a medical student at Hospital Nacional De Ninos in Costa Rica, he completed his internship at MSU-KCMSBronson Children's Hospital in Michigan and residency at Rush University Children's Hospital in Chicago.

Dr. Bravo's career spans diverse settings, from establishing a rural practice in Appalachia to spearheading pediatric emergency services in Northern Virginia. He notably designed the first pediatric emergency department in a community hospital and founded the region's first pediatric urgent care service, Pediatrics@Nite.

As co-founder of the Pediatric Lounge Podcast, Dr. Bravo facilitates knowledge sharing among pediatricians across North America. He also co-founded the Pediatric Executive Development System (P.E.D.S.), a data analytics platform and mastermind program that has helped independent pediatric practices achieve up to 10X growth in just two years.

Dr. Bravo's expertise is widely recognized. He was invited as the sole pediatrician in the USA to join Sanofi's STRIDE speaker panel, educating primary care clinicians on the importance of early autoantibody screening to prevent diabetic ketoacidosis (DKA).

His passion for children's healthcare drives his commitment to exceptional patient care and fostering strong communication between pediatricians and parents.

Dr. Herb Bravo MD

Co-host

The Pediatric Lounge Podcast

CEO & Founder

**Pediatric Executive Development
System**

Bravo Pediatrics and Consultants

[Work : \(703\) 783-7978](tel:(703)783-7978)

<https://thepediatriclounge.com/meet-the-hosts>

Case Presentation

- 13 year old white male
- Chief Complaint: Mom wants AAb Testing, recommended by her endo
- Family History: Mother 40 years Hx of T1D with Thyroid Disease
- ROS : (-) Weight Loss, (-) Getting Up at night to urinate, (-) Polyuria, (-) Polyphagia
- Physical Exam: BMI 30
- Diagnosis Codes :
 - BMI 30.0-30.9 Z68.30 and Family History of DM Z83.3
- Labs: WHAT DO YOU ORDER?

15X

First Degree Relatives Risk
3 to 5%

Family History of T1D	Risk of T1D Autoantibodies
None- Population in General	1/300
Maternal	1/40
Paternal	1/15
Siblings (ALL)	1/12
HLA-Identical Twins	1/4
Monozygotic Twins	1/3

90%

Will Not Have A Risk Factor

1 in 300 Screened

WHAT DO YOU ODER

Diagnosis

Autoantibodies 2+

- **GAD65: glutamic acid decarboxylase antibodies**
- **IA2: tyrosine phosphatase antibodies**
- **IAA: insulin autoantibodies**
- **TnZ8: zinc transporter antibodies**

HOW DO YOU ORDER

Clinical guidelines support autoantibody screening for early detection of type 1 diabetes. Confirmatory testing is indicated for individuals with positive results.¹

Labs to order (4)	Related diagnosis codes
• Insulin Autoantibody (IAA)-CPT 86337 • Glutamic Acid Decarboxylase (GAD) Autoantibody-CPT 86341 • Islet Antigen 2 (IA-2) Autoantibody-CPT 86341 • Zinc Transporter 8 (ZnT8) Autoantibody-CPT 86341	• Z83.3 - Family history of diabetes • R73.9 - Hyperglycemia, unspecified • Z13.1 - Screening for diabetes mellitus

Expert support at no cost for clinical management available at asktheexperts.org

Negative Result?

Consider additional testing in future if at risk for developing T1D.

Positive Result?

- Order confirmatory testing for persistent autoantibody status
- Consider referral to TrialNet for free confirmatory testing and possible referral to research studies
- Additional testing: HbA1c, random blood glucose
- Provide patient education including T1D symptoms
- If multiple autoantibodies present or dysglycemia, refer to Endocrinology



Screening Options for Patients

Option 1: Screen Through a Research Study

TrialNet

- For people 2 to 45 years old who have a parent, brother/sister, or child with T1D, or
- For people 2 to 20 years old who have an aunt/uncle, cousin, grandparent, niece/nephew, or half-brother/sister with T1D
- Lab or at-home tests available



ASK

- For all children ages 1-17
- No family history of type 1 diabetes is required
- At-home tests available
- Also screens for Celiac Disease



Option 2: Screen Through Your Doctor's Office

Your doctor (or your child's doctor) can order labs to detect type 1 diabetes autoantibodies and the cost may be covered by your insurance. Consider contacting your insurance company regarding coverage prior to testing.

Positive Result?

- Confirmatory testing must be performed, either through TrialNet (free for ages 2-45 years) or your doctor's office
- Ask the Experts can provide individualized support for you in partnership with your doctor (visit www.asktheexperts.org or scan QR code)



GETTING AHEAD OF TYPE 1

Case Presentation

- Lab Corp Diabetes Autoimmune Profile 504050
 - **GAD : 15 u/mL (Normal Less than 5 u/mL)**
 - **ZNT8: 373 u/mL (Normal Less than 15 u/mL)**
 - IA : 1 u/ml (Normal Less than 5 u/mL)
 - IA-2 : 1 u/ml (Normal Less than 7.5 u/mL)

**POSITIVE
INSULITIS**

Autoimmune Insulinitis (T1D) leads to Pancreatic Beta-cell failure, necessitating exogenous insulin for survival. It is a complex genetic, environmental, and immune disorder that starts early in life, with autoantibodies peaking at 9 months to 24 months of age.

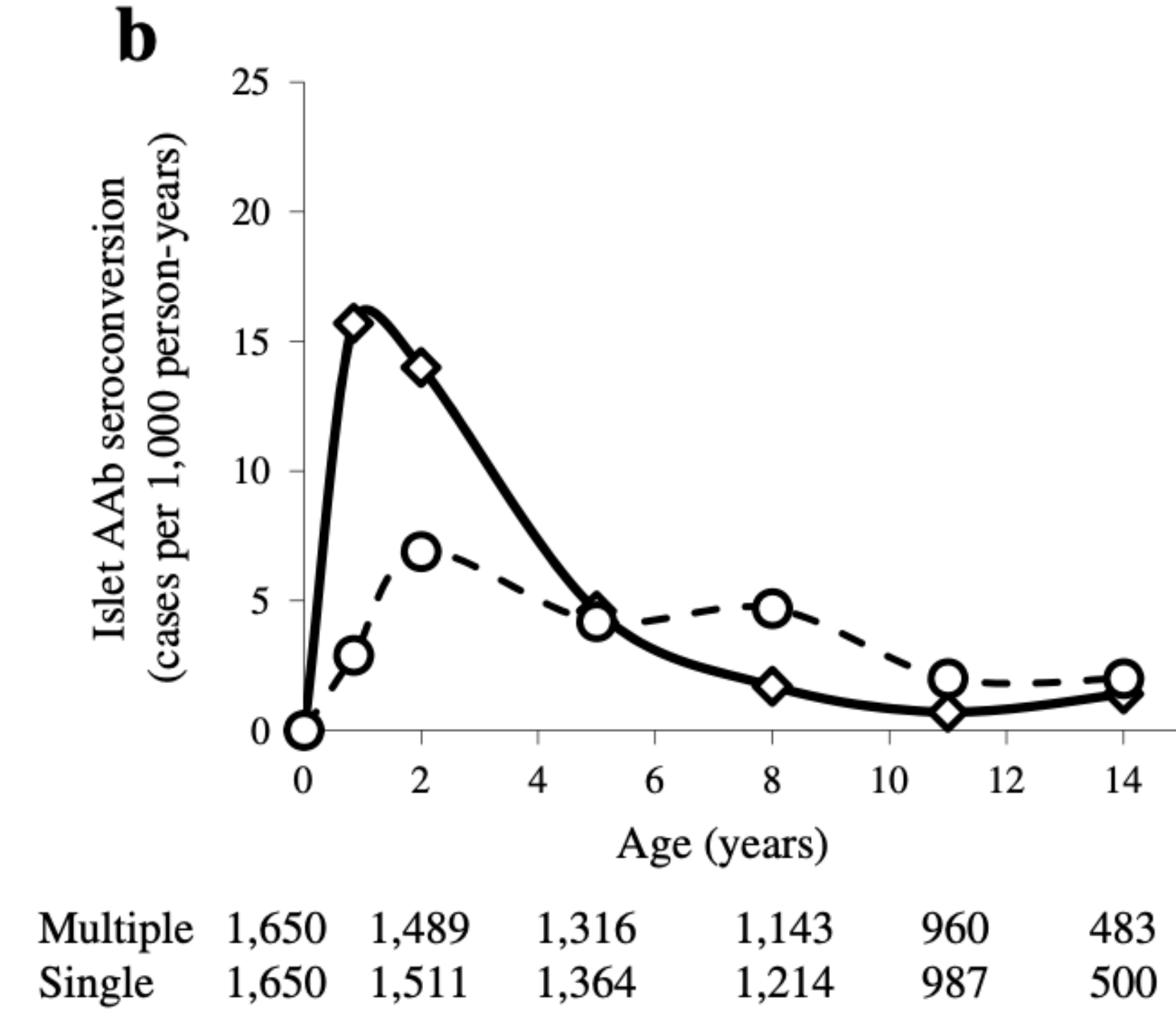
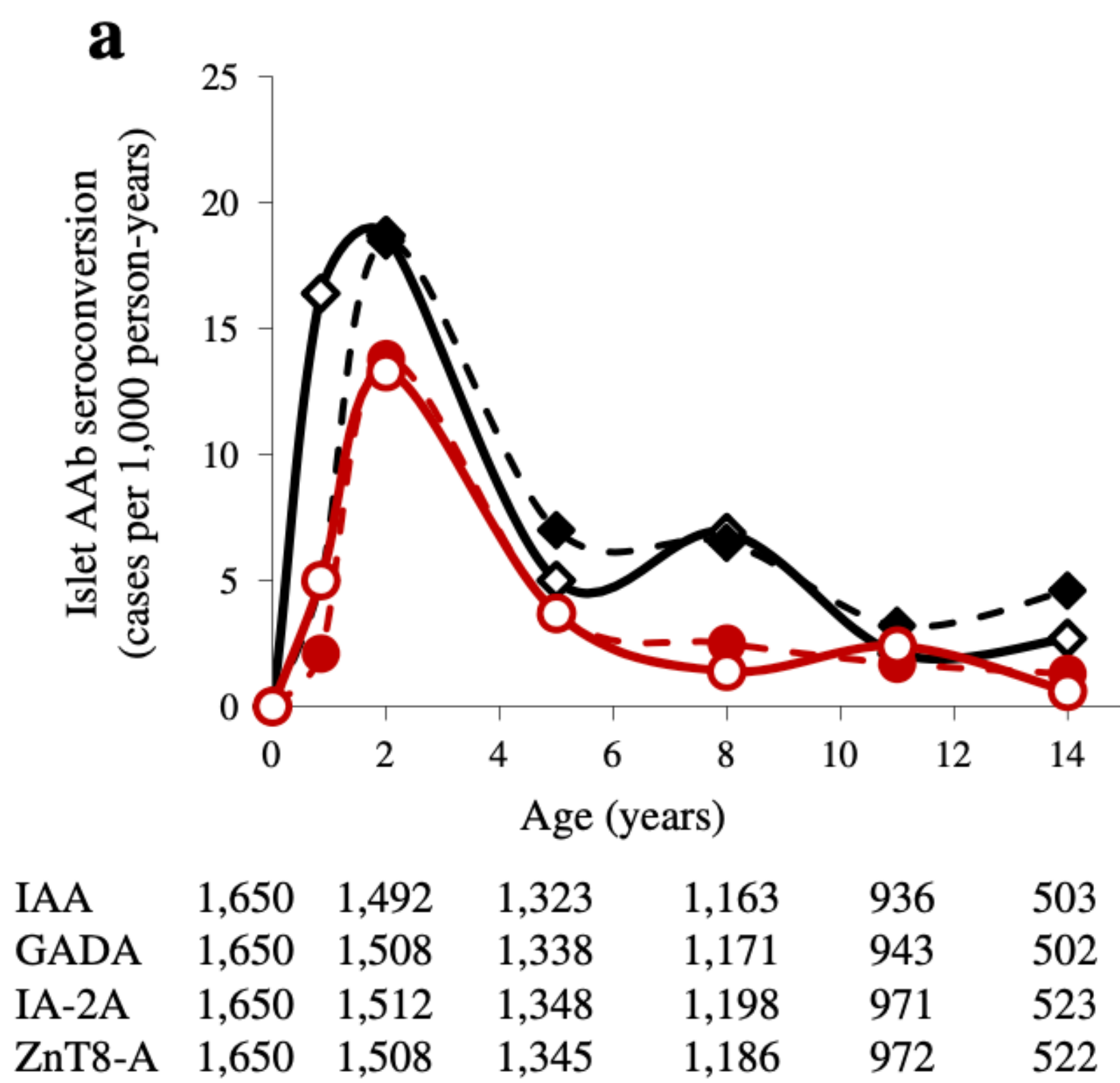
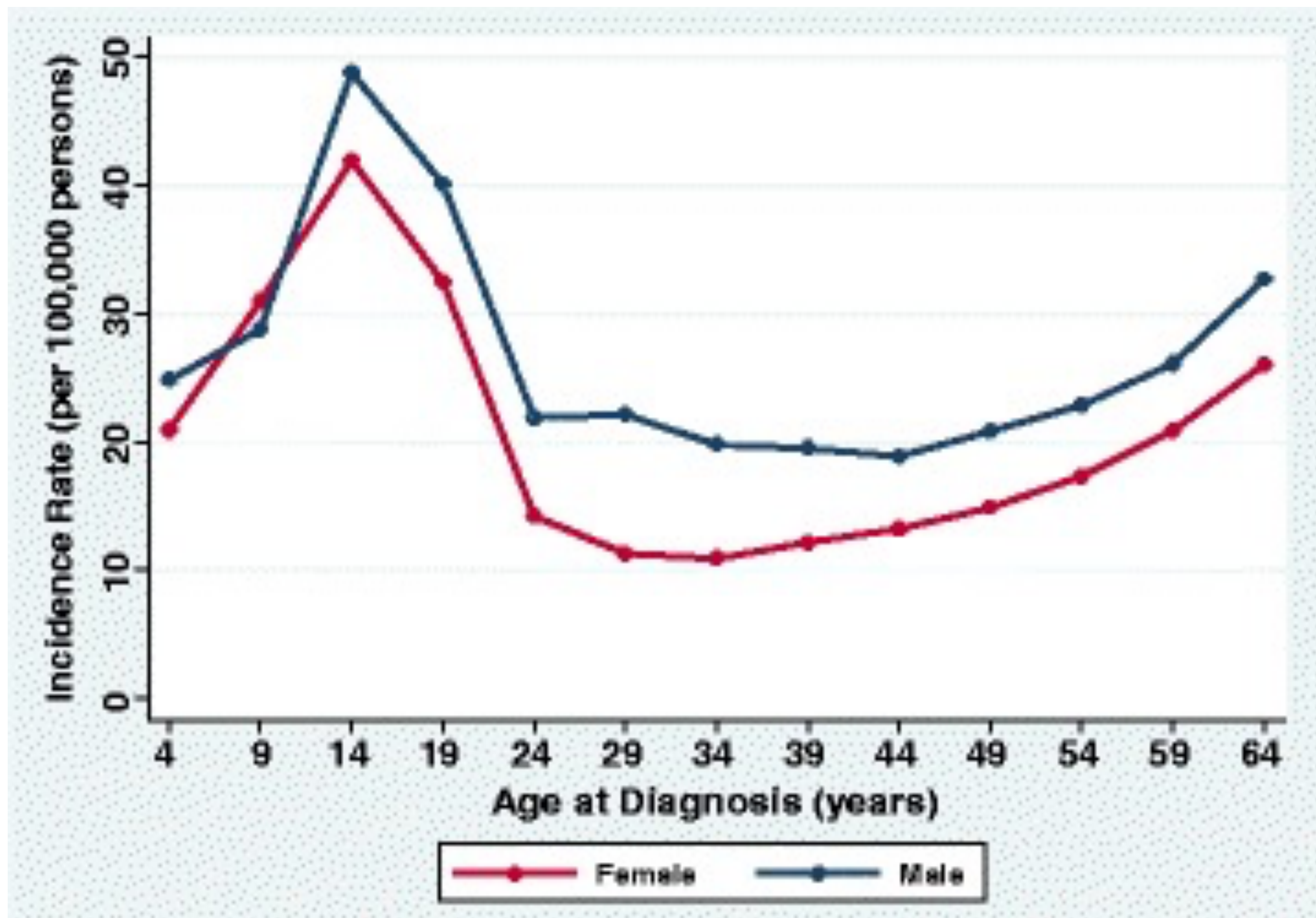
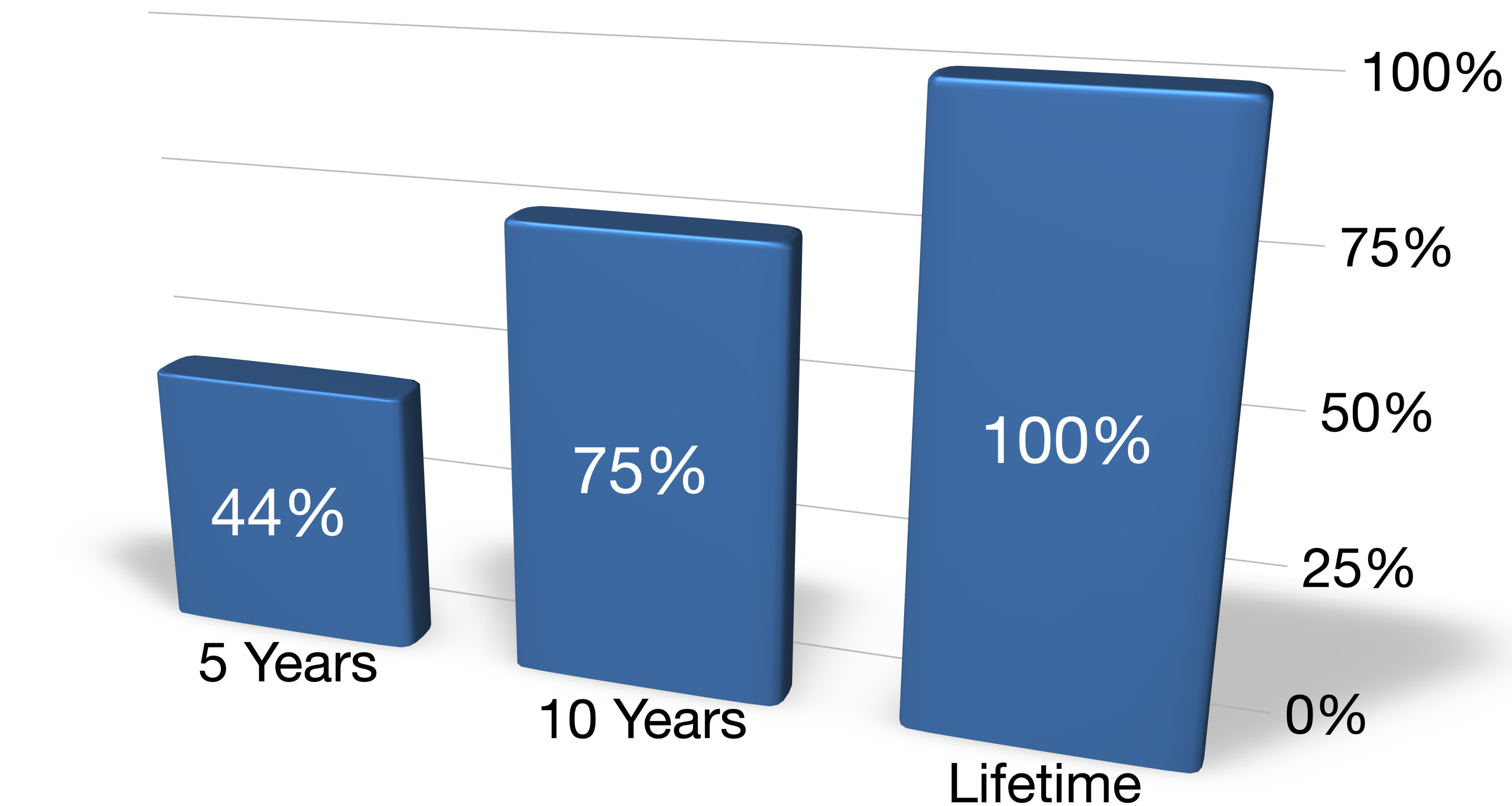


Fig. 2 Incidence (cases per 1,000 person-years) of specific islet autoantibodies (AAb). **a** IAA (solid black line), GADA (dashed black line), IA-2A (solid coloured line) and ZnT8-A (dashed coloured line) in offspring of parents with type 1 diabetes (BABYDIAB Study).

b Incidence of multiple (solid line) and single (dashed line) islet autoantibodies. Incidence is shown at the ages of islet autoantibody testing (9 months and 2, 5, 8, 11 and 14 years). Numbers under the x-axes are the numbers of children still followed at each time point



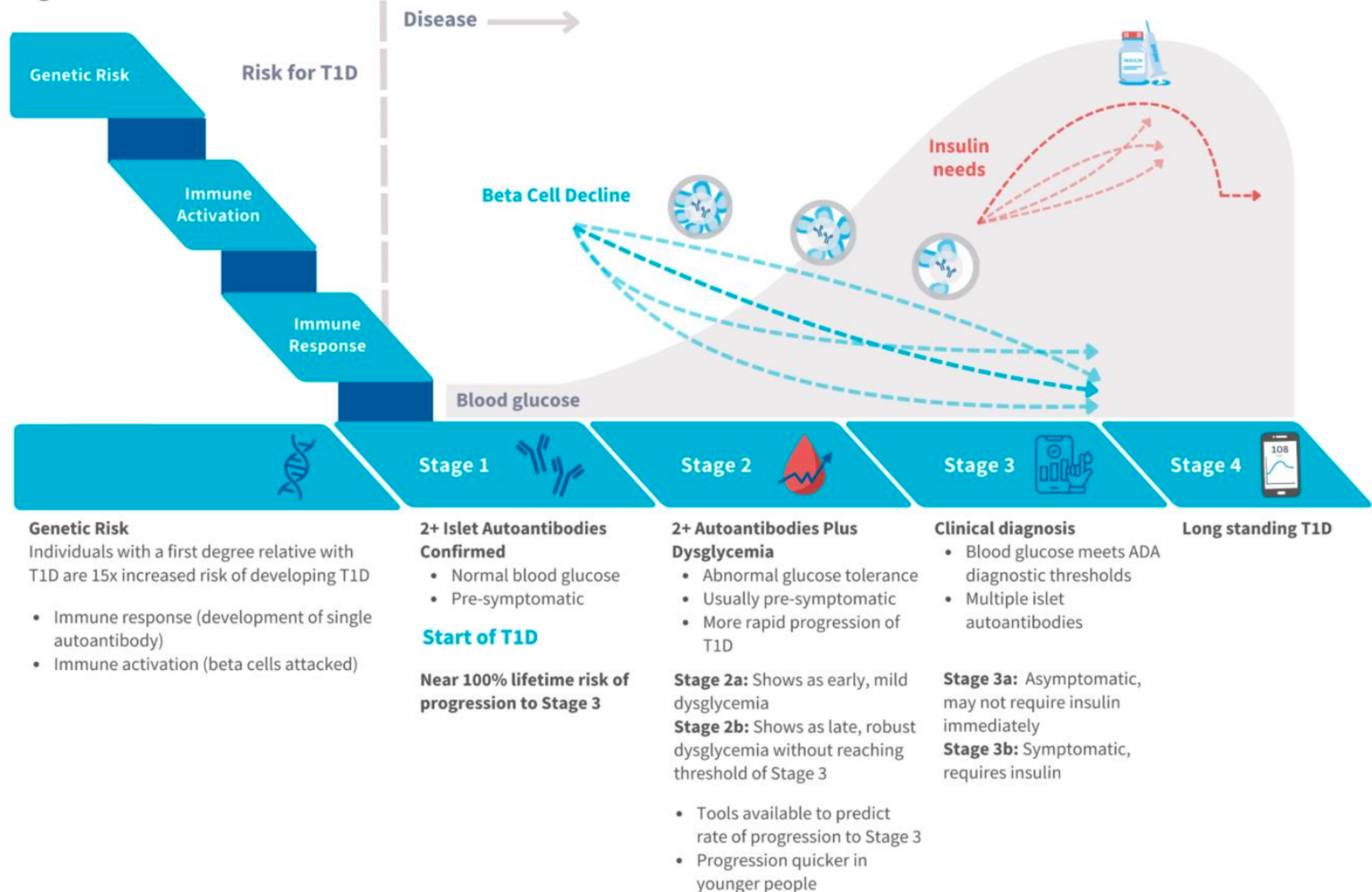
A longitudinal study comprising 32,476 commercially insured Americans aged 0-64 years who developed T1D between 2001 and 2015. T1D=type 1 diabetes. Rogers MAM, et al. *BMC Med.* 2017;15(1):199.



■ Risk Of T1D Stage1 to 3 Insulin Dependency When 2X 2+AA

Richard A. Insel, Jessica L. Dunne, Mark A. Atkinson, Jane L. Chiang, Dana Dabelea, Peter A. Gottlieb, Carla J. Greenbaum, Kevan C. Herold, Jeffrey P. Krischer, Åke Lernmark, Robert E. Ratner, Marian J. Rewers, Desmond A. Schatz, Jay S. Skyler, Jay M. Sosenko, Anette-G. Ziegler; Staging Presymptomatic Type 1 Diabetes: A Scientific Statement of JDRF, the Endocrine Society, and the American Diabetes Association. *Diabetes Care* 1 October 2015; 38 (10): 1964–1974. <https://doi.org/10.2337/dc15-1419>

Progression of T1 Diabetes



Now What?

Two antibody Positive -Monitoring

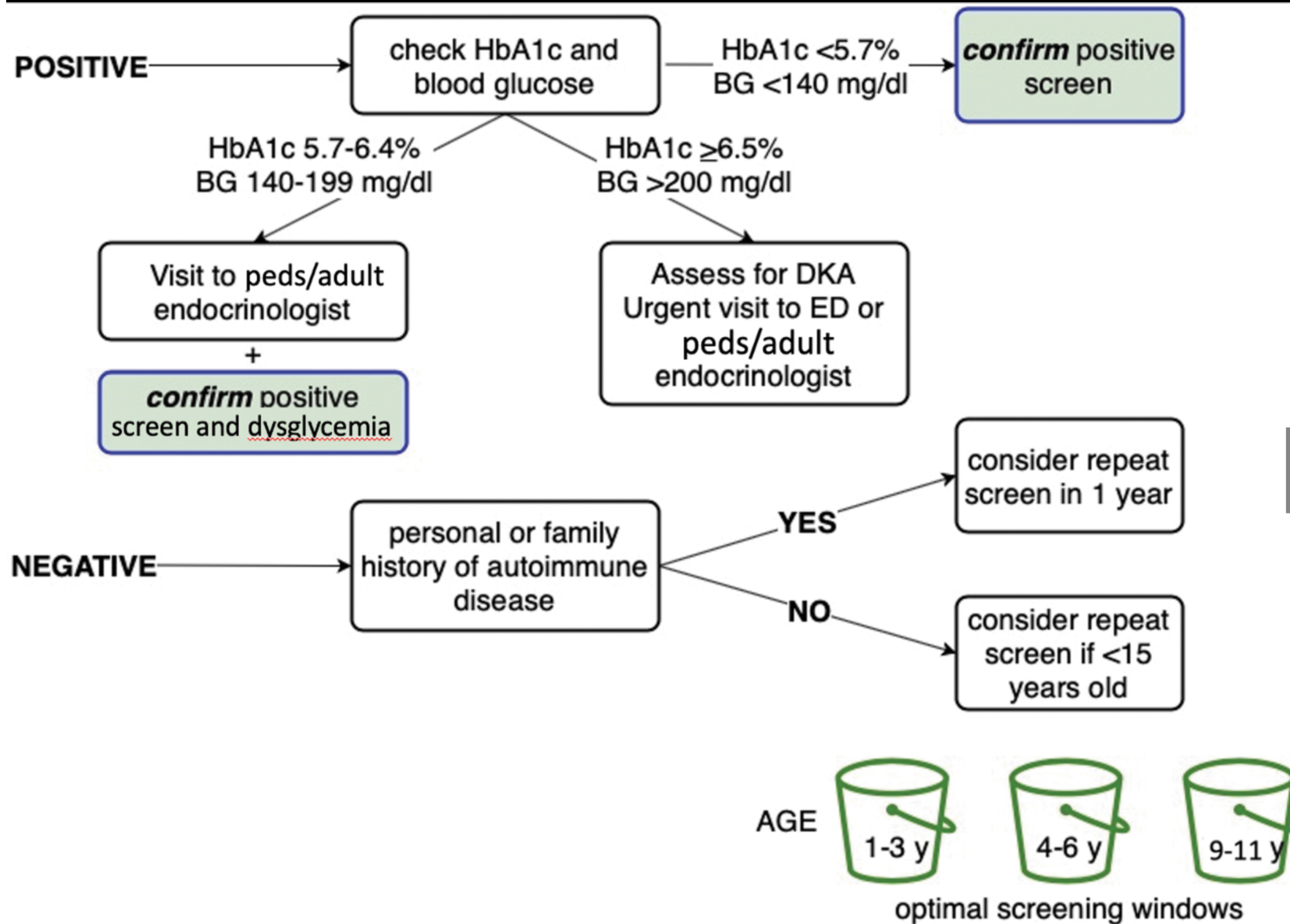


FIG. 1. Algorithm for management of a person screened for T1D. Confirmation of a positive screening test by measuring all four biochemical (GADA, IA-2A, mIAA, and ZnT8A) and excluding hyperglycemia are critical. IA, islet autoantibodies; T1D, type 1 diabetes.

Case Presentation

WHAT DO YOU DO NEXT?

- Glucose Random 91
- Counsel Mother and Aunt on DKA

- A1C 5.1%
- May consider 2 H GTT and C-peptide fasting

- CPT Codes
 - 99215 E&M Visit
 - 36416 Collection Capillary Sample
 - 82948 Blood Glucose

- ICD-10
 - R89.9 Abnormal Lab
 - Z09 Follow Up
 - E10.A1 Diabetes Stage 1

Stage 1
E10.A1

Stage 2
E10.A1

Stage 3
E10.9

Stage 4
E10.9

2 Abb +

2 Abb +

2 Abb +/-

2 Abb +/-

**Normal
Glucose**

Disglycemia

Hyperglycemia

Hyperglycemia

A1C $\leq$ 5.6%

**A1C $\geq$ 5.7%
 $\leq$ 6.4%**

A1C $\geq$ 6.5%

A1C $\geq$ 6.5%

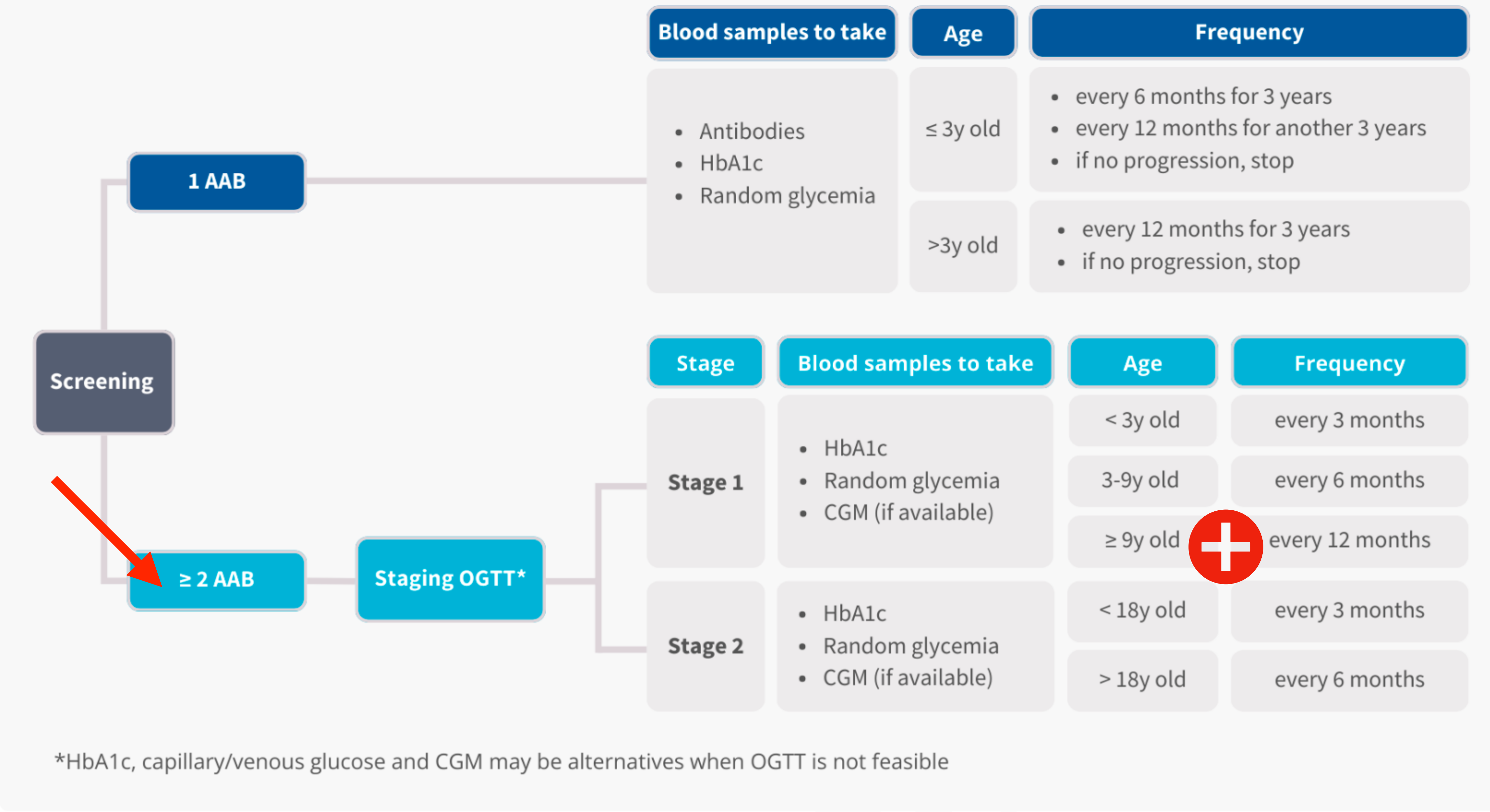
Diagnosis

Insulinitis Euglycemia

- ****Stage 1****: 2 or more positive autoantibodies from two samples and normoglycemia **E10.A1**
 - Fasting plasma glucose <100 mg/dL,
 - HbA1c <5.7%,
 - 2-hour oral glucose tolerance test <140 mg/dL

Collobarotive Management with Peds Diebetologist

Metabolic Monitoring



Why?



Prevents 93% of DKA at Presentation

Disease Modifying FDA-Approved Treatment Options

Participation in Research Studies



1. **Prevention of DKA and its associated short- and long-term morbidity and mortality.** Rates of DKA at diagnosis of Stage 3 T1D are 15–80% worldwide in the general population, whereas screening programs combined with long-term follow-up reduce DKA rates to less than 5%. DKA prevention at diagnosis has potential lifelong benefits, including avoidance of acute morbidity (cerebral edema, shock), neurocognitive impairment, and mortality. There are also non-causal associations between DKA at onset and risk of future DKA episodes, severe hypoglycemia, and suboptimal long-term glycemic outcomes identified in some but not all studies which, in turn, increase the risk of future diabetes-related complications.
 2. **Improving short-term outcomes** (symptoms, weight loss, DKA, prolonged hospitalization).
 3. **Improving quality of life and reducing psychological burden at the time of T1D diagnosis.** Caregiver anxiety and depressive symptoms increase in response to their child's multiple islet AAB positive test results. Preparation for insulin therapy, education, and psychological support may help reduce caregiver anxiety and smooth the transition to Stage 3 T1D and insulin therapy....
- Despite the benefits associated with screening for T1D, potential harms must also be considered.**

Teplizumab Treatment is Associated with a Sustained Effect on Type 1 Diabetes Progression Over 923 Days of Follow-up



Sims EK, Bundy BN, Stier K, Serti E, Lim N, Long SA, Geyer SM, Moran A, Greenbaum CJ, Evans-Molina C, Herold KC; Type 1 Diabetes TrialNet Study Group. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. *Sci Transl Med.* 2021 Mar 3;13(583):eabc8980.

WHO?

Who Do I Screen ?

- First Degree Relative living with T1D
 - 1/20
- Family or Self History of Autoimmunity
 - 1 to 3 / 100
- None of the above
 - 1/300
- Dysglycemic Patients
 - Up To 40% of T1D are misdiagnosed as Type 2



- General population screening programs using autoantibody testing alone or combinations of genetic and autoantibody testing can identify children and young adults with or at risk of T1D. [A]
- Screening and follow up should be completed to identify people with Stage 1,2, and 3a T1D, reduce incidence of diabetic ketoacidosis (DKA) and hospitalization, and to direct individuals towards interventions or studies seeking to delay or prevent ongoing beta cell loss. [A]
- Screening for islet autoantibodies repeated twice during childhood may provide the most cost-effective means of identifying those who will develop T1D. Optimal ages for screening may depend on background population risk.[B]