OLTRE LA DIAGNOSI: STRATEGIE INNOVATIVE PER LA PREVENZIONE DEL DIABETE TIPO 1

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Genova 15/11/2025

DIABETE MELLITO = LA PUNTA DI UN ICEBERG

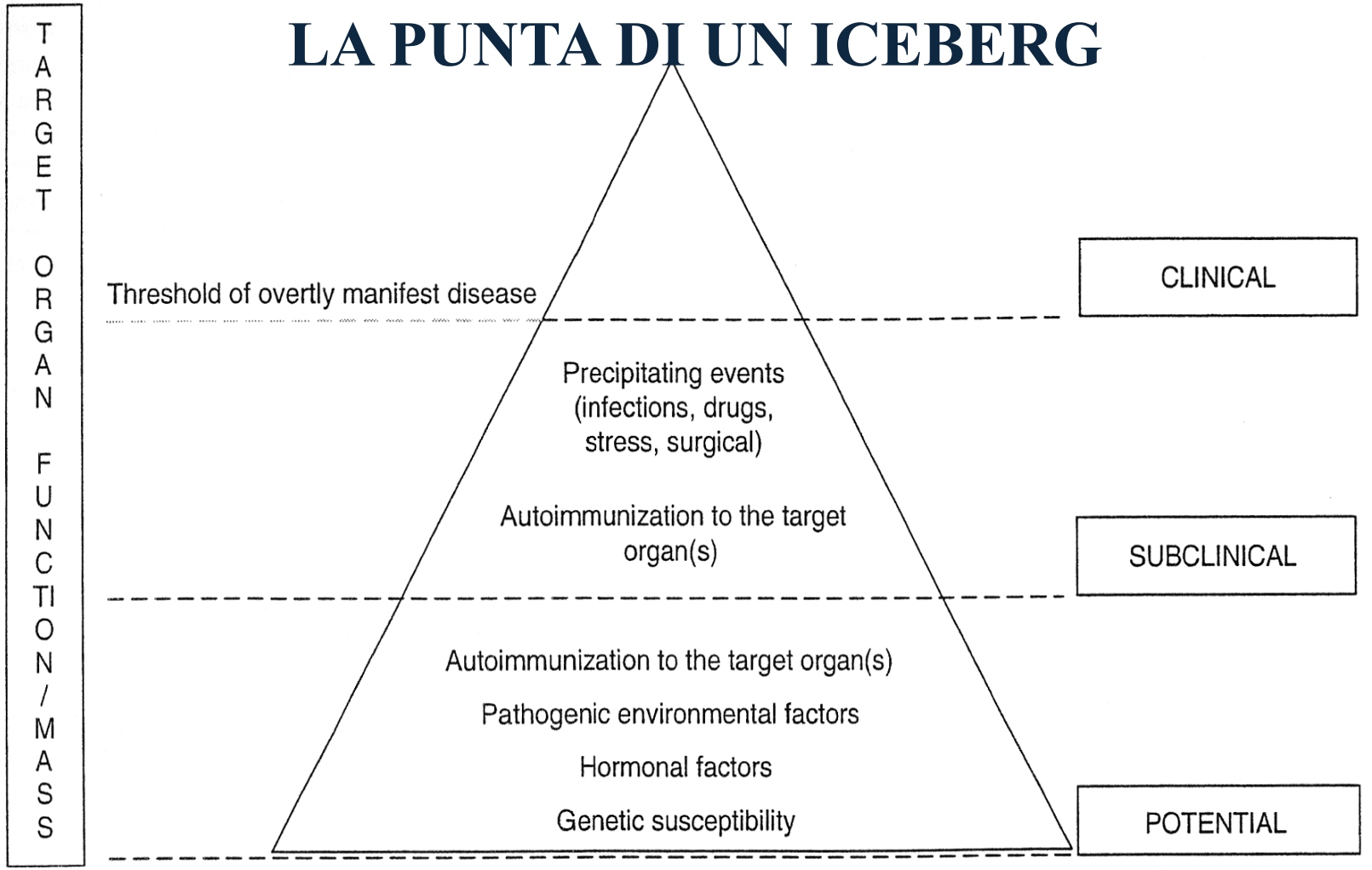
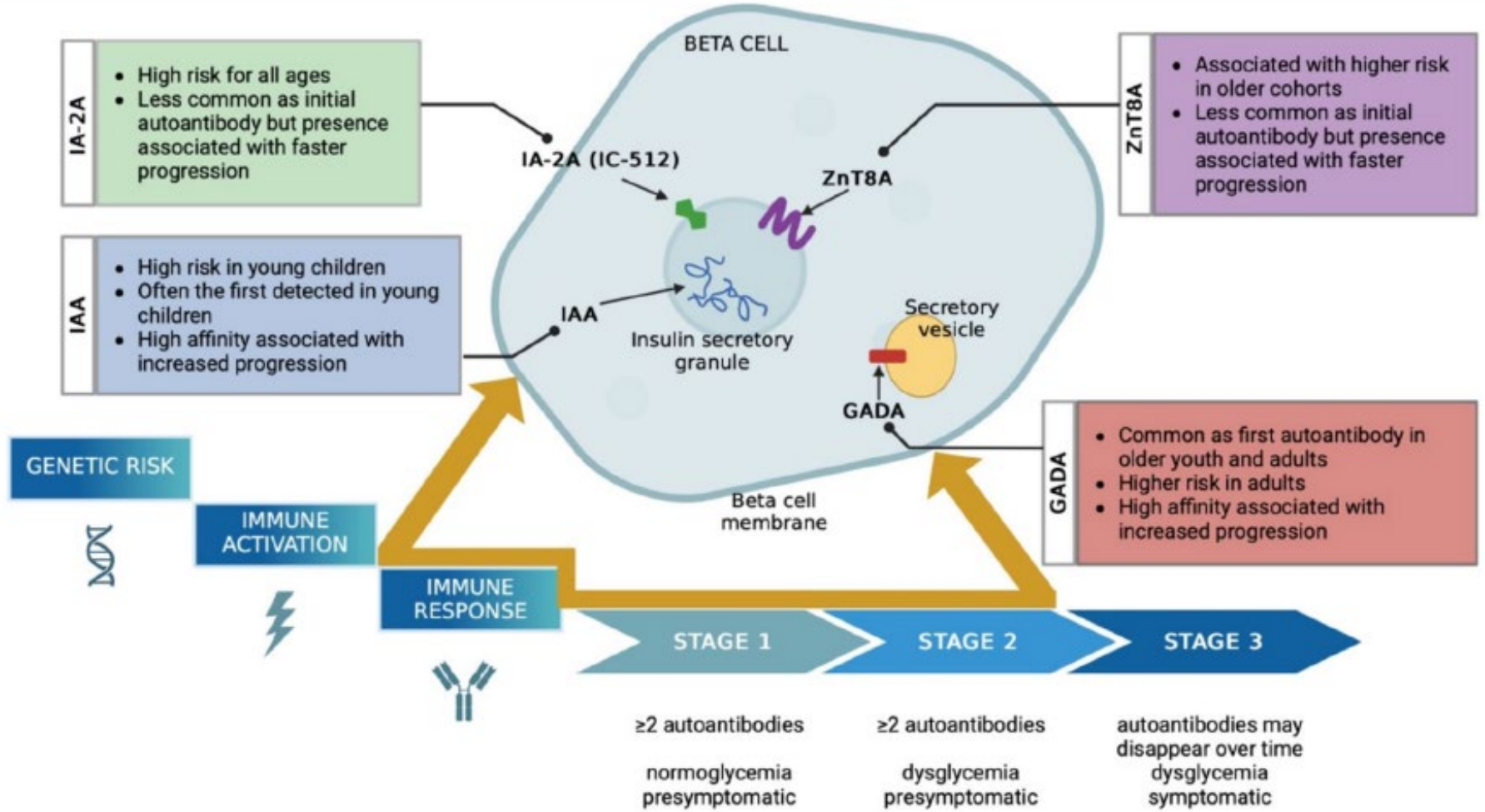
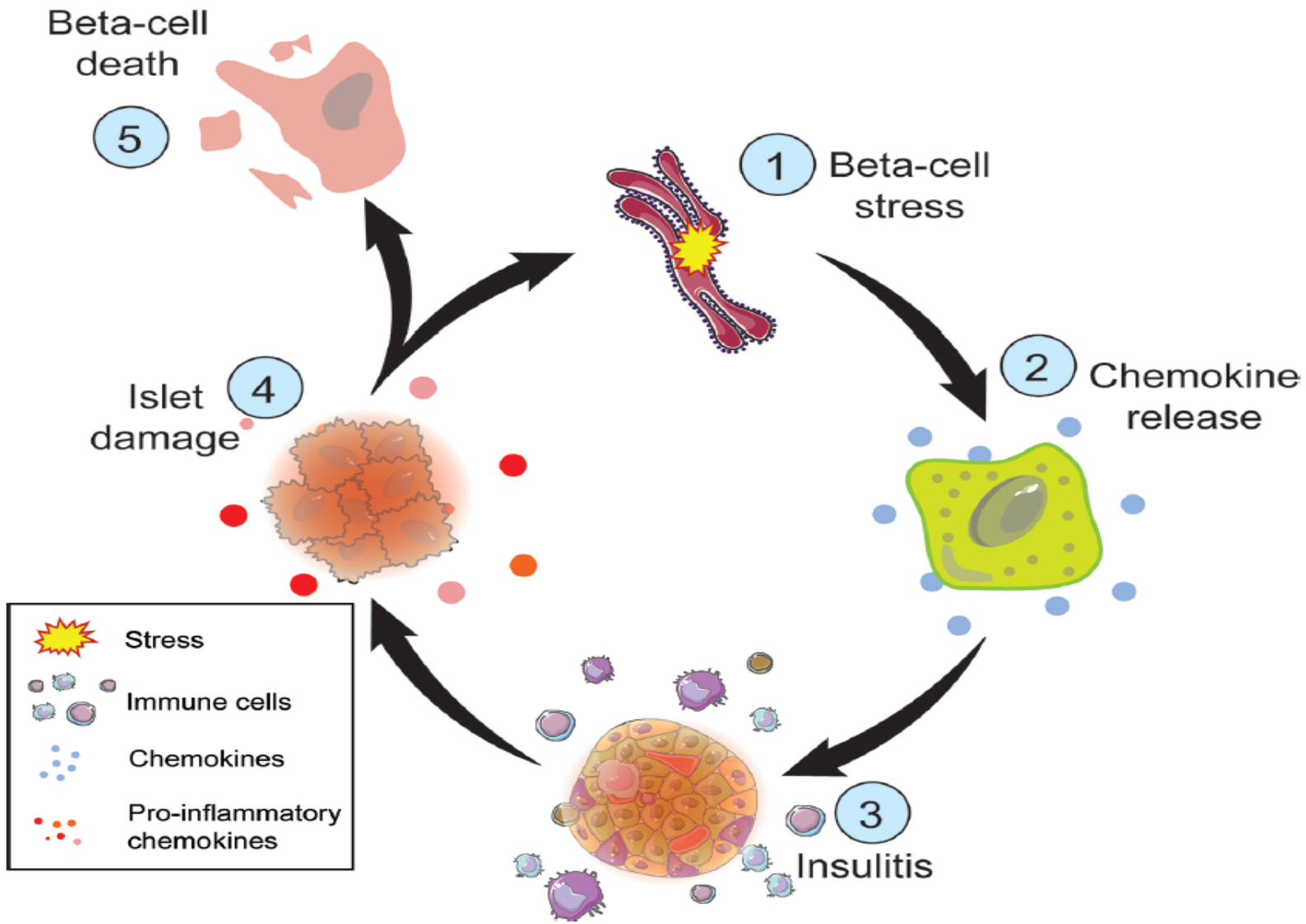
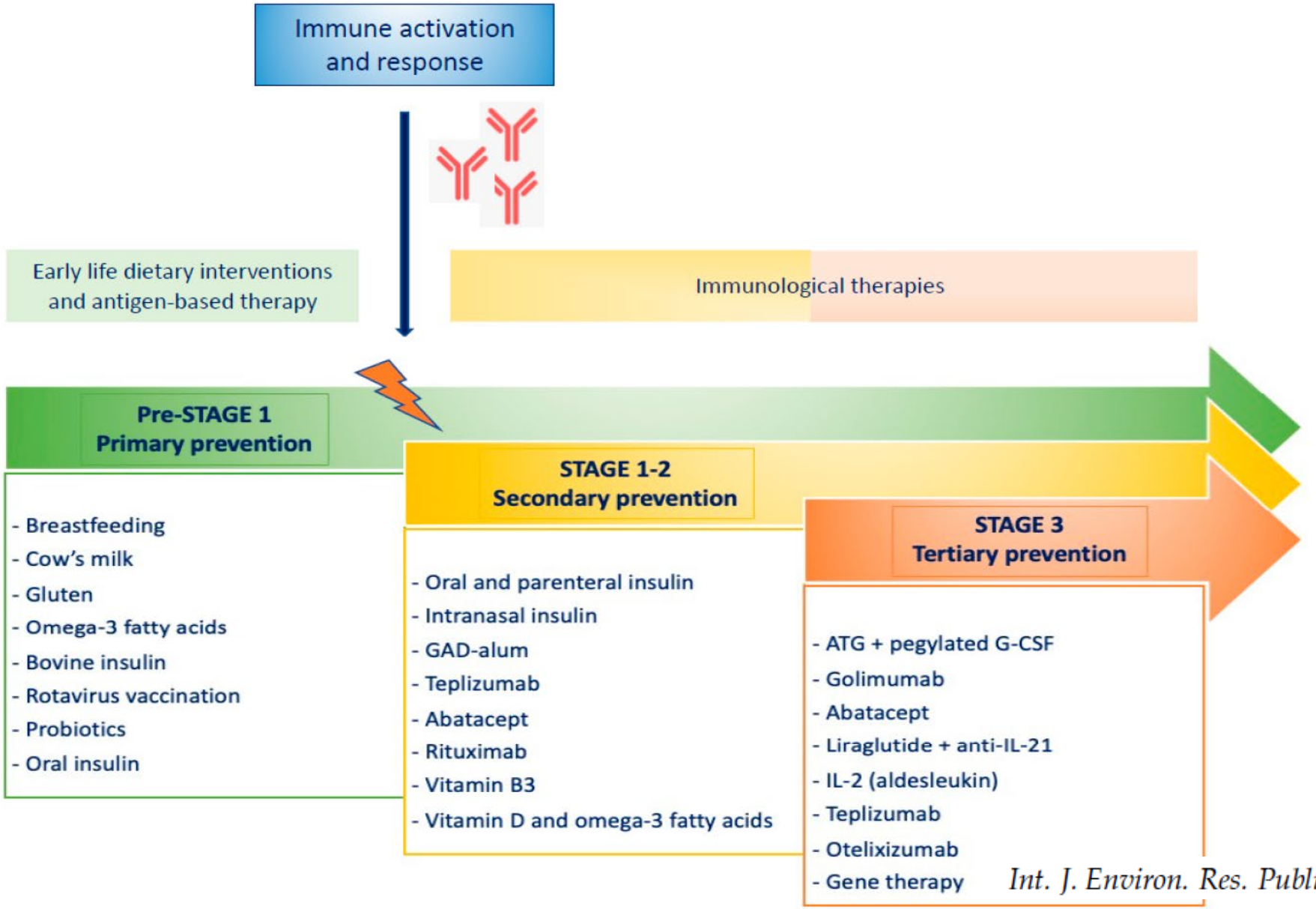


Figure 1. The autoimmune iceberg.


BETA CELL
IA-2A
High risk for all ages
Less common as initial autoantibody but presence associated with faster progression
IA-2A (IC-512)
ZnT8A
ZnT8A
Associated with higher risk in older cohorts
Less common as initial autoantibody but presence associated with faster progression
IAA
High risk in young children
Often the first detected in young children
High affinity associated with increased progression
IAA
Insulin secretory granule
Secretory vesicle
GADA
GADA
Common as first autoantibody in older youth and adults
Higher risk in adults
High affinity associated with increased progression
Beta cell membrane
GENETIC RISK
IMMUNE ACTIVATION
IMMUNE RESPONSE
STAGE 1
STAGE 2
STAGE 3
≥2 autoantibodies
normoglycemia
presymptomatic
≥2 autoantibodies
dysglycemia
presymptomatic
autoantibodies may disappear over time
dysglycemia
symptomatic


Beta-cell death
5
1 Beta-cell stress
2 Chemokine release
3 Insulitis
Islet damage
4
Stress
Immune cells
Chemokines
Pro-inflammatory chemokines



Int. J. Environ. Res. Public Health **2023**, *20*, 5962.

Diabetologia (2019) 62:1823–1834
https://doi.org/10.1007/s00125-019-4942-x

REVIEW

Early-life factors contributing to type 1 diabetes

Maria E. Craig[1,2,3] · Ki Wook Kim[1,4] · Sonia R. Isaacs[1,4] · Megan A. Penno[5,6] · Emma E. Hamilton-Williams[7] · Jennifer J. Couper[5,6] · William D. Rawlinson[1,4,8]

Environmental factors associated with initiation of, or protection from, IA and progression to type 1 diabetes

Prenatal initiators of IA

- Maternal enterovirus infection
- Pre-conception maternal and paternal obesity
- Maternal obesity in pregnancy
- Higher birthweight
- Caesarean section
- Maternal gluten intake
- Older maternal age

Postnatal initiators of IA

- Enterovirus infection +/− viral load
- Respiratory infection
- Infant weight gain
- Early exposure to cereals, root vegetables
- Greater cows' milk protein intake
- Stressful life events

Postnatal progressors to type 1 diabetes

- Persistent or recurrent enterovirus infections
- Accelerator hypothesis (overweight/greater height velocity)
- Puberty/insulin resistance
- High glycaemic load
- Lower microbial diversity
- Psychological stress

Prenatal protective factors of IA

- Higher maternal vitamin D
- Gestational respiratory infections

Postnatal protective factors of IA

- Breastfeeding in early life
- Early introduction of gluten or egg
- Higher *n*-3 fatty acids
- Probiotics
- Rotavirus vaccination

Postnatal protection from progression to type 1 diabetes

- Limited evidence

Infections in the first year of life and development of beta cell autoimmunity and clinical type 1 diabetes in high-risk individuals: the TRIGR cohort

Olga Kordonouri[1] · David Cuthbertson[2] · Malin Belteky[3] · Bärbel Aschemeier-Fuchs[1] · Neil H. White[4] · Elisabeth Cummings[5] · Mikael Knip[6,7,8] · Johnny Ludvigsson[3]

Table 4 Univariable and multivariable (adjusted for HLA, gender, breastfeeding duration and birth order) Cox regression results based on time to initial AB+ development, initial multiple AB+ development and type 1 diabetes

	Univariable unadjusted model				Multivariable model			
Outcome	HR	Lower 95% CI	Upper 95% CI	*p* value	HR	Lower 95% CI	Upper 95% CI	*p* value
Any AB+								
Age at first viral infection (reference = those with no infections in first year)								
< 3 months	0.909	0.756	1.093	0.313	0.928	0.771	1.117	0.430
3 to < 6 months	0.952	0.789	1.149	0.610	0.997	0.825	1.205	0.979
6–12 months	0.823	0.686	0.988	0.036	0.828	0.690	0.994	0.043
Number of infections before 3 months (reference = 0)								
1–3	1.088	0.941	1.257	0.255	1.093	0.945	1.265	0.229
4–6	0.377	0.094	1.510	0.168	0.395	0.098	1.584	0.190
7 or more	8.002	1.122	57.09	0.038	9.166	1.277	65.81	0.028
Occurrence of any unspecified bacterial infection	1.379	1.051	1.808	0.020	1.412	1.075	1.854	0.013
Multi-AB+								
Age at first viral infection (reference = those with no infections in first year)								
< 3 months	0.939	0.676	1.305	0.709	0.954	0.684	1.330	0.782
3 to < 6 months	0.709	0.484	1.040	0.079	0.745	0.506	1.097	0.136
6–12 months	0.669	0.457	0.978	0.038	0.664	0.453	0.972	0.035
Number of infections between 6 and 12 months (reference = those with no infections)								
1–3	0.752	0.573	0.988	0.041	0.760	0.578	0.999	0.049
4–6	0.780	0.487	1.251	0.303	0.779	0.485	1.253	0.304
7 or more	1.094	0.508	2.355	0.819	1.076	0.498	2.325	0.852
Occurrence of any unspecified bacterial infection	1.620	1.014	2.589	0.044	1.652	1.030	2.649	0.037
Development of T1D								
Occurrence of any unspecified bacterial infection	2.193	1.261	3.814	0.005	2.066	1.182	3.613	0.011
Occurrence of any unspecified viral infection	0.536	0.289	0.992	0.047	0.525	0.283	0.975	0.041

Diabetologia (2022) 65:2098–2107

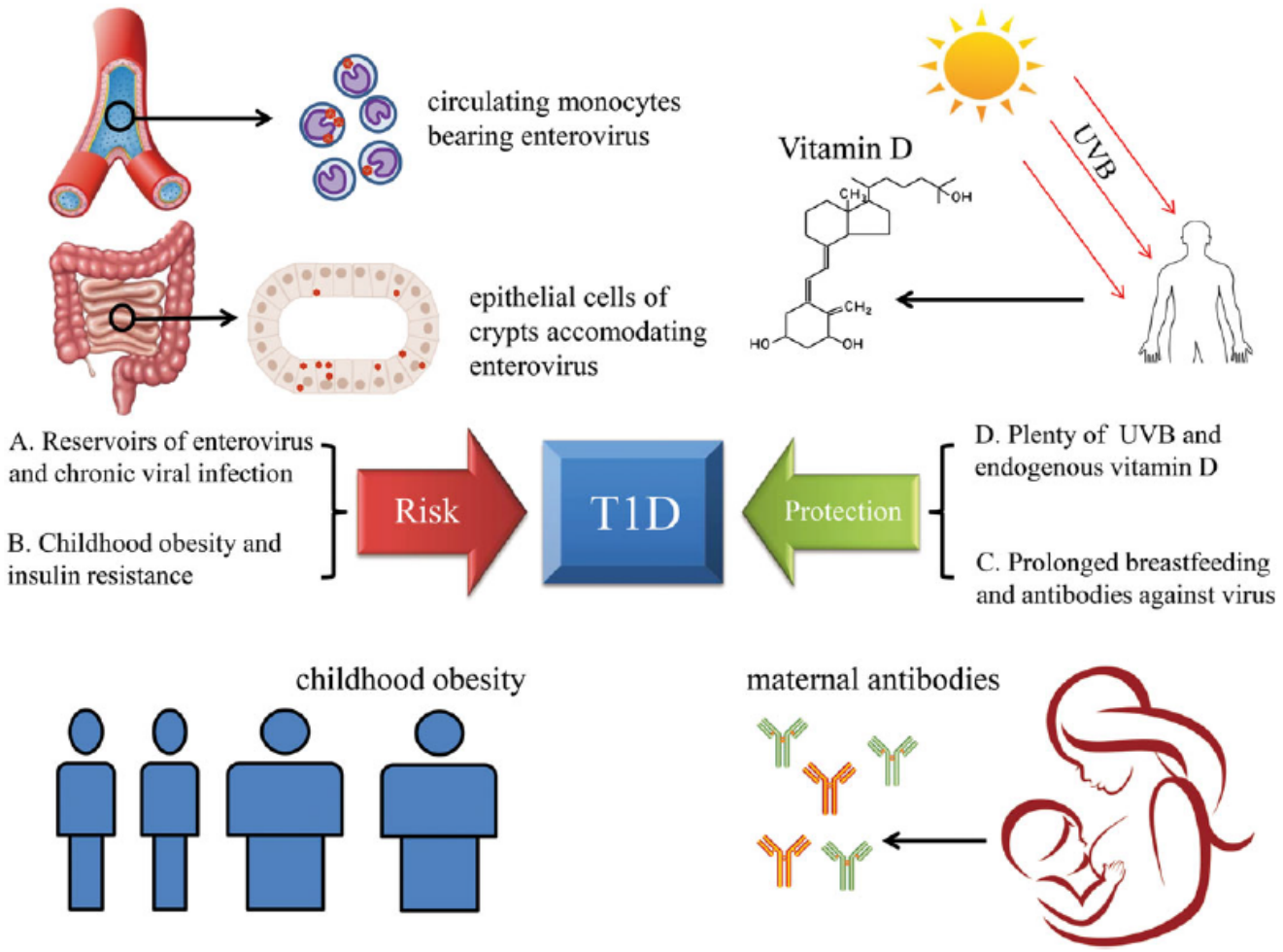


FIGURE 2 Schematic diagram of 4 putative environmental determinants of T1D risk. A. Red dots represent enterovirus. Circulating monocytes and epithelial cells of crypts in small intestine have both been assumed to act as reservoirs of enterovirus, responsible for chronic viral infections and monocytes might serve as vehicles of virus' moving into pancreas. B. Obese children are likely to be at a higher risk for the development of T1D, sharing the common mechanism of insulin resistance with T2D. C. Prolonged breastfeeding has been linked to lower risk for T1D and partly explained by providing maternal antibodies against virus. D. Individuals residing close to the equator are exposed to abundant UVB from sunlight, which initiates the endogenous synthesis of vitamin D and associates with reduced risk for T1D

Diabetes Metab Res Rev. 2019;35:e3075.
https://doi.org/10.1002/dmrr.3075

Rotavirus Infections and Development of Type 1 Diabetes: An Evasive Conundrum

Serena Ballotti and Maurizio de Martino

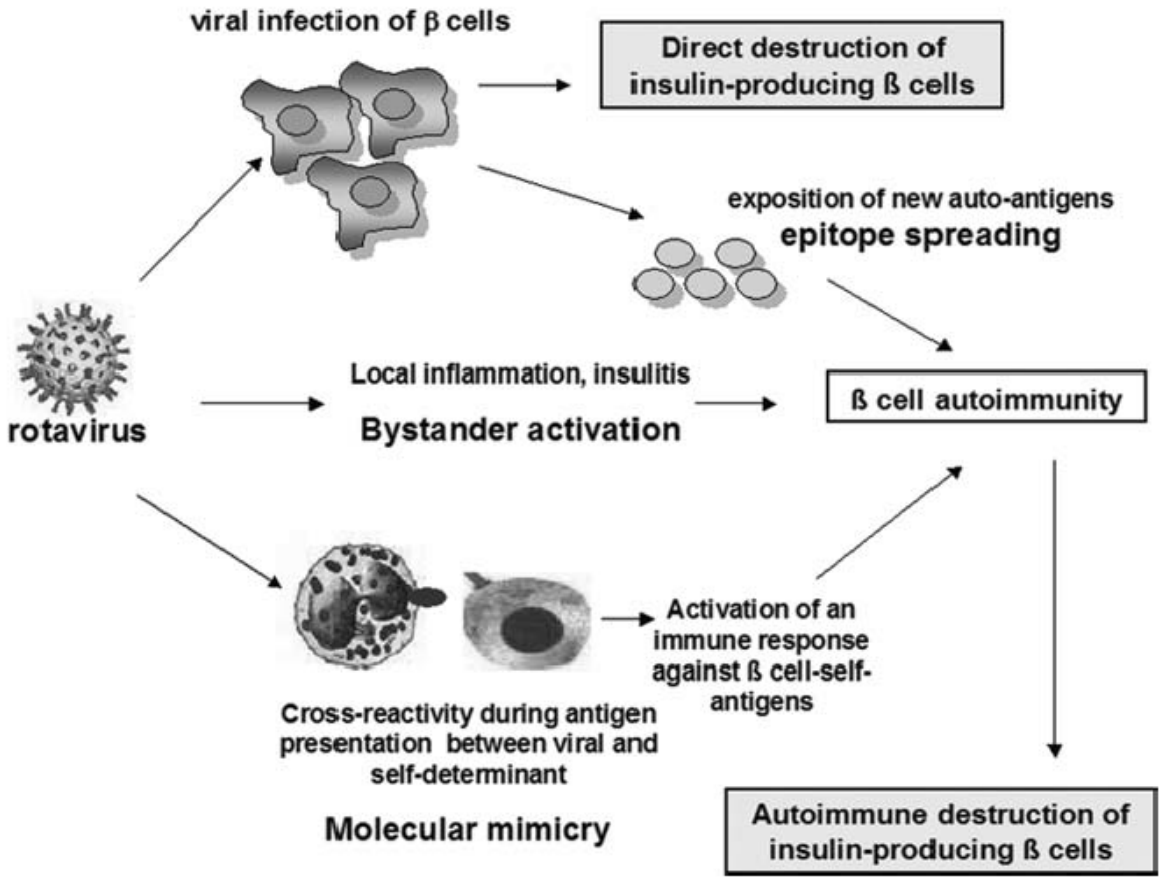
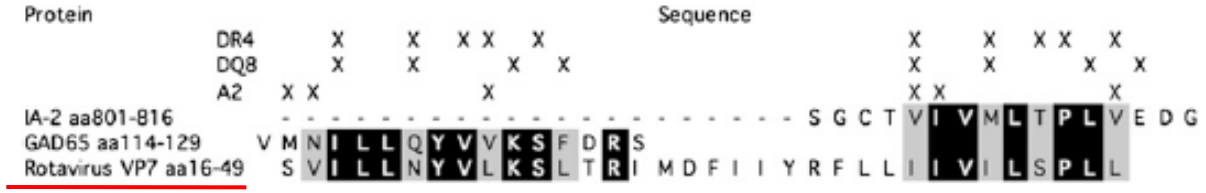


FIG. 1. Potential mechanisms involved in RV-mediated β cell destruction. An involvement of the pancreas by RV infections is possible, with a direct cytotoxic effect on β cells. Alternatively, β cell damage may be immune mediated, with several potential mechanisms including molecular mimicry and epitope spreading, generally together with bystander processes.

Evidence for Molecular Mimicry between Human T Cell Epitopes in Rotavirus and Pancreatic Islet Autoantigens

Margo C. Honeyman,* Natalie L. Stone,* Ben A. Falk,† Gerald Nepom,† and Leonard C. Harrison*

- Epitopo VIVMLTPLVEDGVKQC di IA2A
- 56% identità, 100% similarità con VP7
- Epitopo GAD65 HLA-DR4 restricted
- 78% identità, 100% similarità con VP7



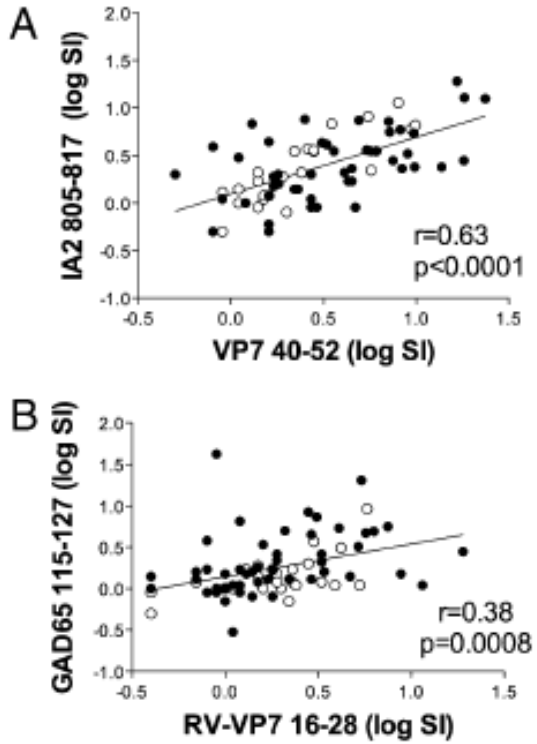
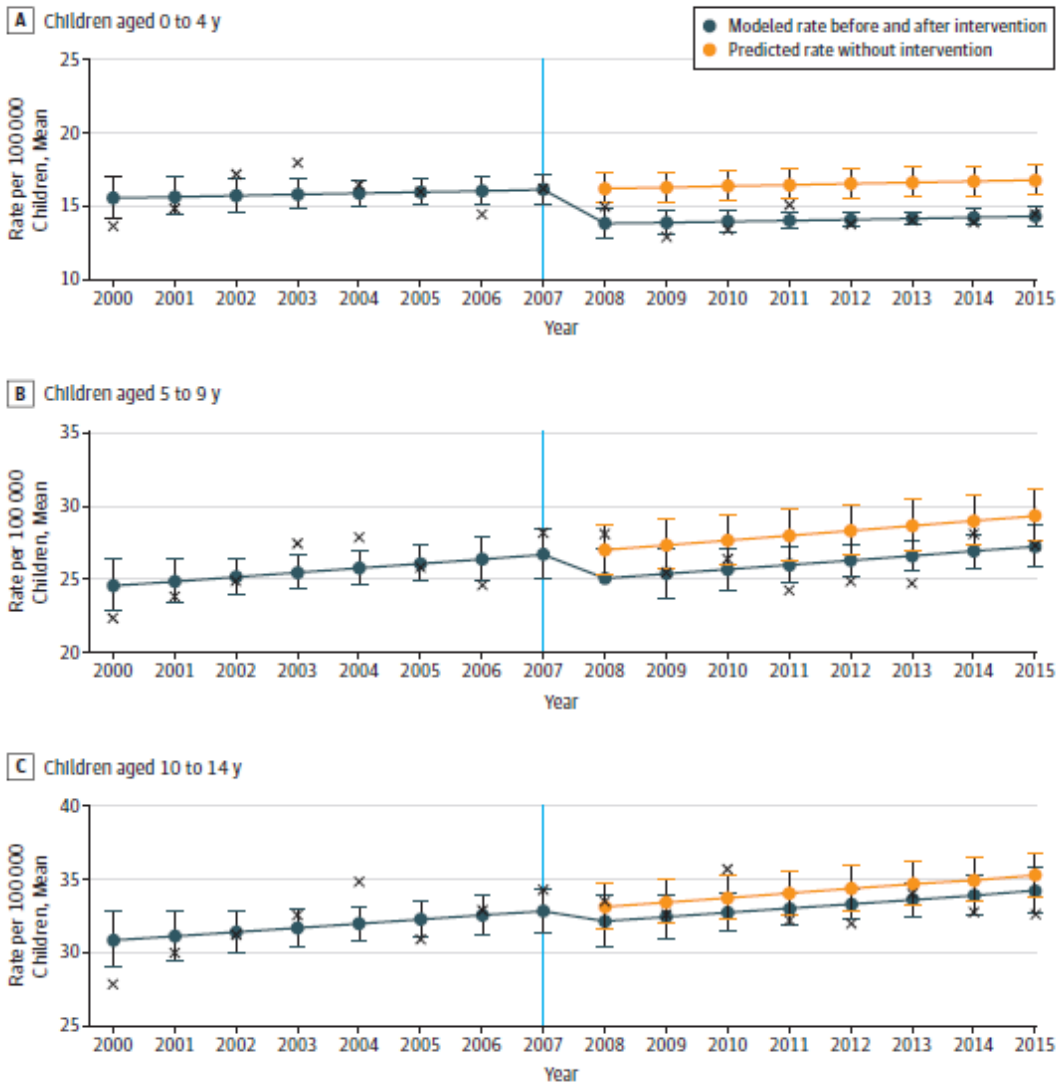


FIGURE 4. Correlation of T cell proliferative responses to sequence-similar peptides from IA2 and RV-VP7 (*A*) and GAD65 and RV-VP7 (*B*).

The Journal of Immunology, 2010, 184: 2204–2210.

Figure. Age Group–Based Modeling of Type 1 Diabetes Incidence Rate Ratios Before and After Introduction of Oral Rotavirus Vaccine



Association of Rotavirus Vaccination With the Incidence of Type 1 Diabetes in Children

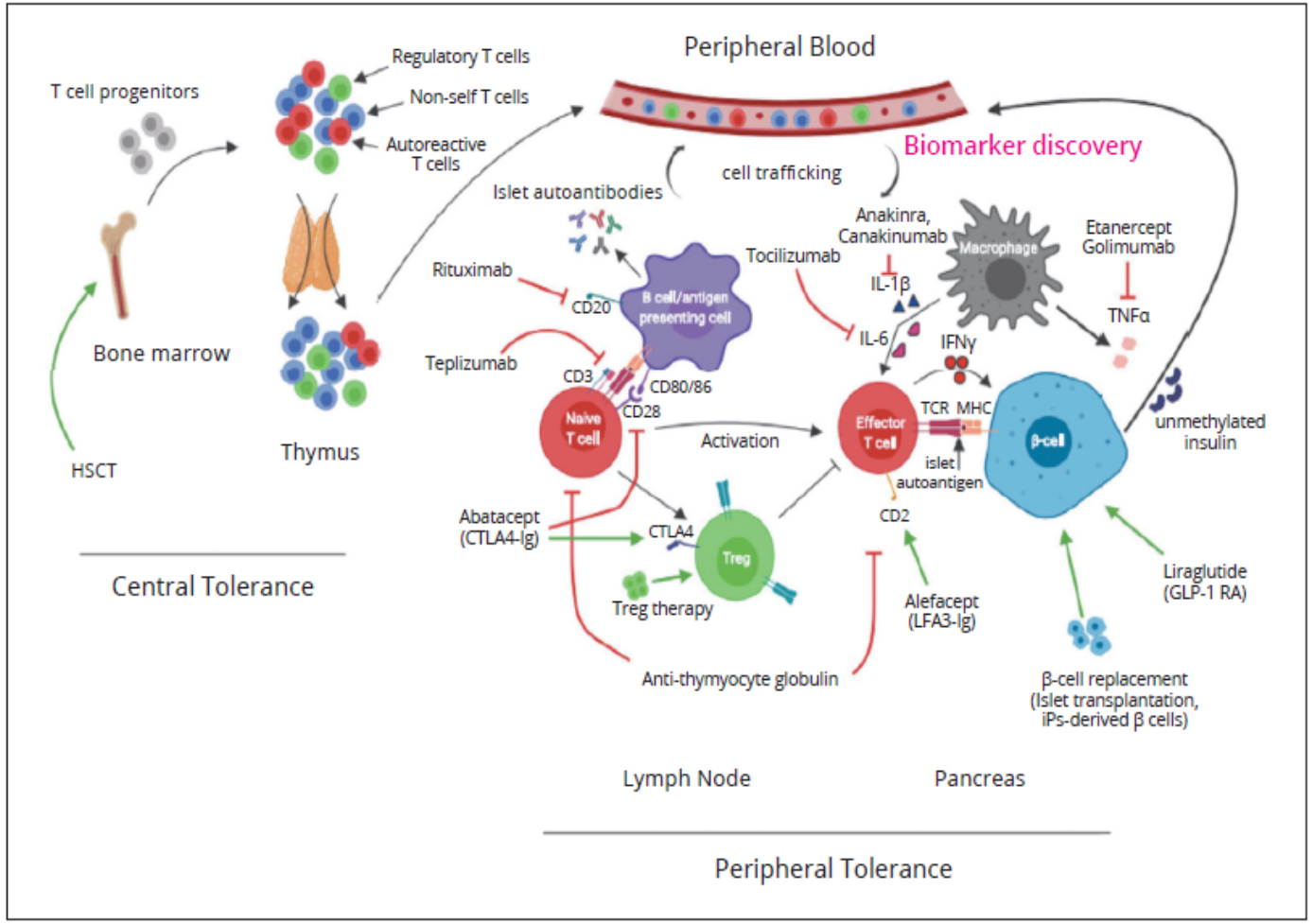
Terry M. Nolan, MBBS, PhD, FRACP, FAFPHM, FAHMS
Leonard C. Harrison, MBBS, MD, DSc, FRACP, FRCPA, FAHMS

- **Studio australiano di confronto 8 anni prima e dopo vaccino anti RV**
- **Tasso di incidenza DM1: 24.4/1000.0000**
- **Riduzione 15% gruppo 0-4 anni**

JAMA Pediatrics March 2019 Volume 173, Number 3

IMMUNOTERAPIA

- **IMMUNOSOPPRESSIONE ASPECIFICA**
  - Ciclosporina, effetto durata-dipendente, nefrotossicità
  - Cortisone
- **IMMUNOMODULAZIONE**
- Antigen-based therapy: induzione immunotolleranza
  - GAD Alumn
  - Insulin-derived peptides
  - Heat shock protein 60
- Cellule staminali mesenchimali ipoimmuni
  - Riduzione espressione antigeni HLA classe I e II,
  - Iperespressione CD47
- Anticorpi anti CD3
  - Teplizumab
- Blocco costimolazione
  - Abatacef
  - Alefacept
- Anticorpi anti CD20
  - Rituximab
- Terapia citochinica
  - TNF-α, IL1, IL2, IL6, Januskinasi



Intralymphatic GAD-Alum (Diamyd®) Improves Glycemic Control in Type 1 Diabetes With HLA DR3-DQ2

Christoph Nowak,[1,2] Marcus Lind,[3] Zdenek Sumnik,[4] Terezie Pelikanova,[5] Lía Nattero-Chavez,[6] Elena Lundberg,[7] Itxaso Rica,[8] Maria A Martínez-Brocca,[9] MariSol Ruiz de Adana,[10] Jeanette Wahlberg,[11,12] Ragnar Hanas,[13] Cristina Hernandez,[14] Maria Clemente-León,[15] Ana Gómez-Gila,[16] Marta Ferrer Lozano,[17] Theo Sas,[18] Stepanka Pruhova,[4] Fabricia Dietrich,[19] Sara Puente-Marin,[19] Ulf Hannelius,[2] Rosaura Casas,[20] and Johnny Ludvigsson[20]

Aims: Residual b
(Diamyd) given in
antigen (HLA) DR
glucose recorded

Methods: DIAGN
aged 12 to 24 yea
4 µg GAD-alum ar
Treatment arms w

Results: We inclu
treated). In DR3-D
treated compared
and significant be
pared to placebo
was correlated wi

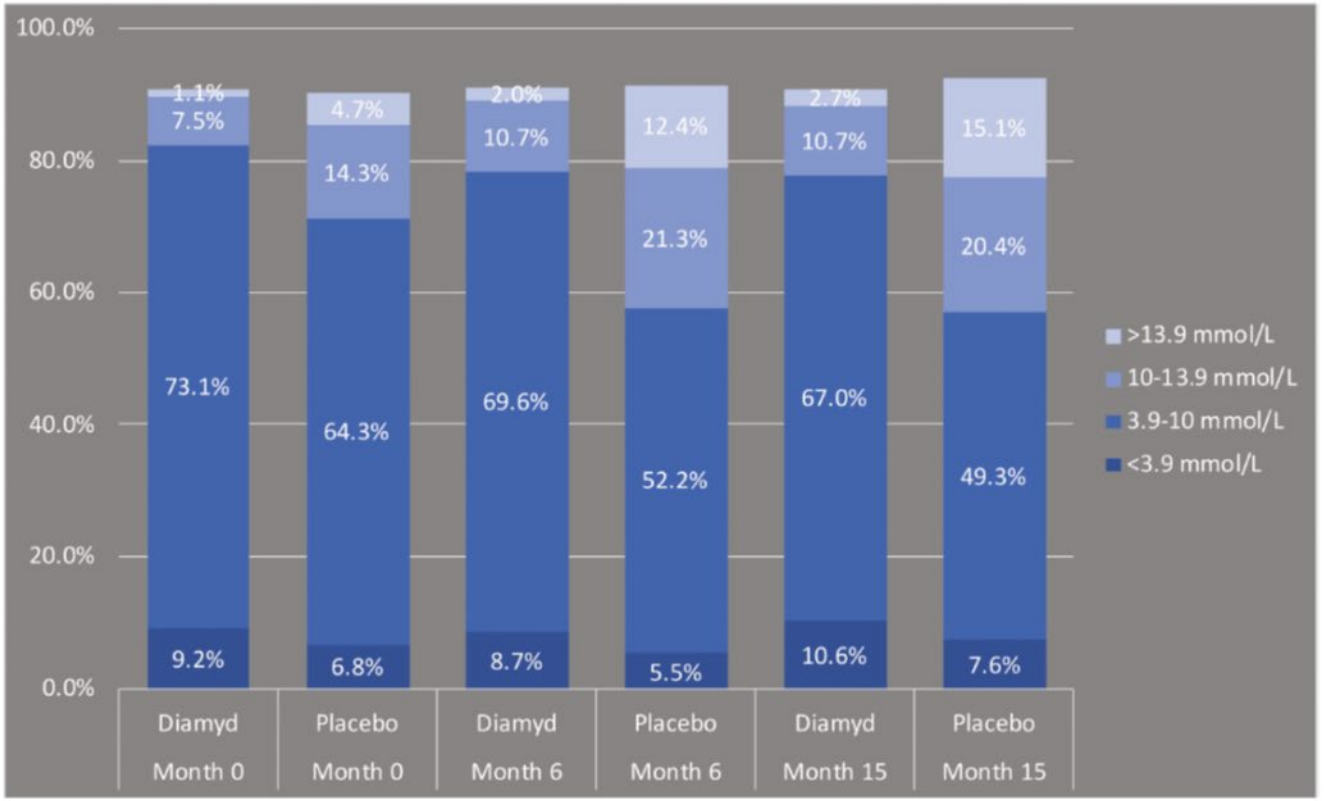


Figure 2. Mean percent of time during the 14-day CGM recording periods spent in different glycemic ranges (individuals with HLA DR3-DQ2).

herapy with GAD-alum
g the human leukocyte
ic GAD-alum on blood

ent-onset T1D patients
ymphatic injections of
t months 0, 6, and 15.

eated and 15 placebo-
nonth 15 in GAD-alum-
) mmol/L ($P = 0.0036$),
emia. GAD-alum com-
). Change in C-peptide

Oral insulin therapy for primary prevention of type 1 diabetes in infants with high genetic risk: the GPPAD-POInT (global platform for the prevention of autoimmune diabetes primary oral insulin trial) study protocol

Anette-Gabriele Ziegler,[1,2] Peter Achenbach,[1,2] Reinhard Berner,[3] Kristina Casteels,[4,5] Thomas Danne,[6] Melanie Gündert,[1] Joerg Hasford,[7] Verena Sophia Hoffmann,[1] Olga Kordonouri,[6] Karin Lange,[8] Helena Elding Larsson,[9,10] Markus Lundgren,[9] Matthew D Snape,[11,12] Agnieszka Szypowska,[13] John A Todd,[14] Ezio Bonifacio,[15] and the GPPAD Study group

ANTIGEN-BASED THERAPY: INDUZIONE DI IMMUNOTOLLERANZA

- Insulina: antigene coinvolto nel danno β-cellulare
- Anticorpi antiinsulina: si positivizzano nei primi anni di vita
- Studi precedenti non hanno evidenziato effetti collaterali

- Studio multicentrico
  - Germania, Polonia, UK, Belgio, Svezia
- Lattanti 4-7 mesi a rischio genetico di autoanticorpi anti β-cellula
- Randomizzati a insulina orale
  - 7,5 mg per 2 mesi, 22.5 mg per 2 mesi, 67.5 mg fino a 36 mesi
  - Placebo
- Follow up 7 anni
- Obiettivo: indurre immunotolleranza e prevenire il processo autoimmune

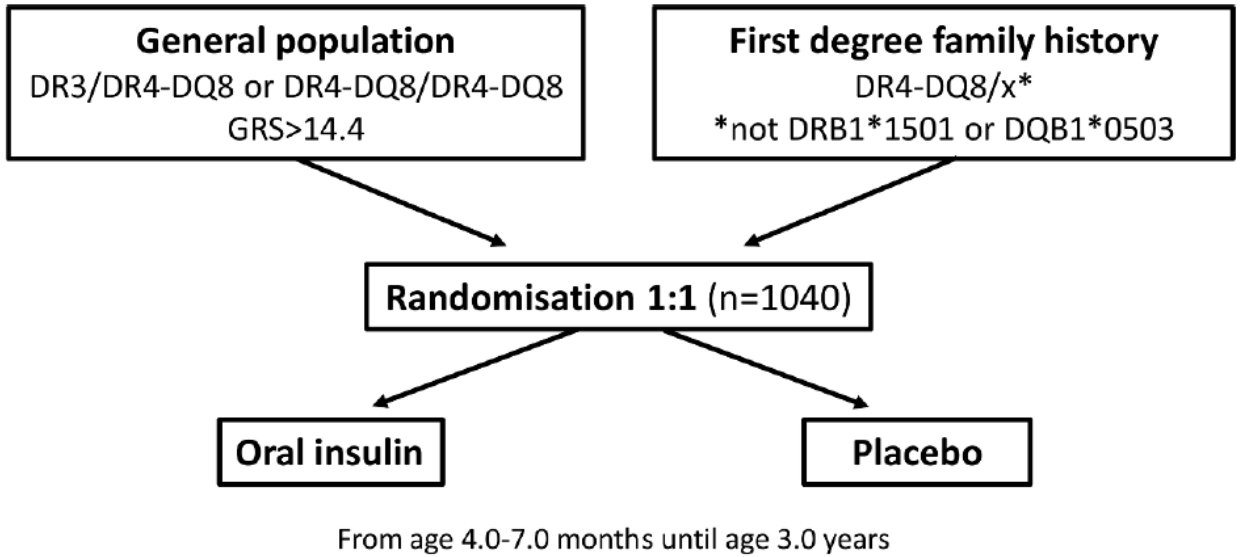
Table 1 Number of people already treated with the study medication

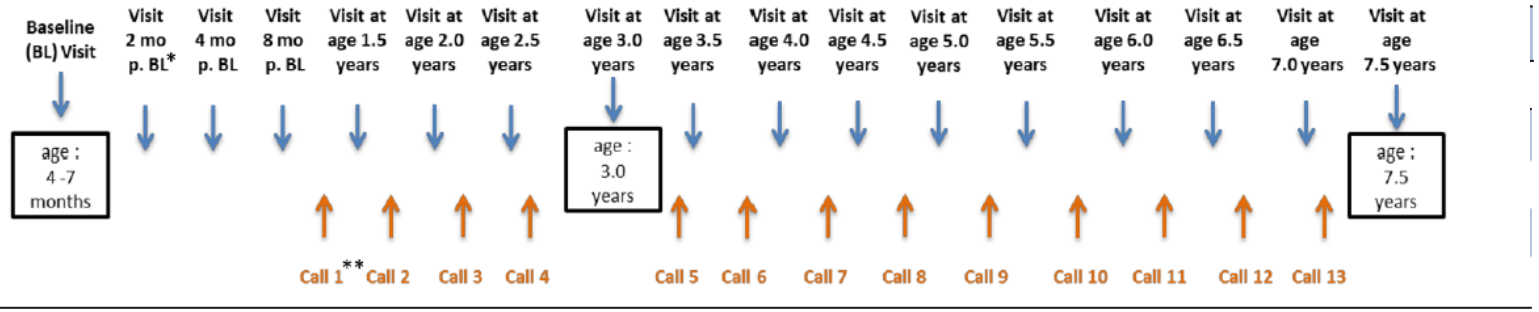
Study	Reference	Dose of oral insulin	Number of participants	Duration of treatment
DPT-1	26	7.5 mg	186 (incl. children)	4.3 years (median period)
Pre-POINT	11	7.5 mg, 22.5 mg, 67.5 mg	15 children	up to 18 months
TrialNet TN07	27	7.5 mg	276 (incl. children)	up to 8.0 years
Pre-POINT Early	Unpublished data	7.5 mg, 22.5 mg, 67.5 mg	22 children	12.0 months

BMJ Open 2019;**9**:e028578.
doi:10.1136/bmjopen-2018-028578

Oral insulin therapy for primary prevention of type 1 diabetes in infants with high genetic risk: the GPPAD-POInT (global platform for the prevention of autoimmune diabetes primary oral insulin trial) study protocol

Anette-Gabriele Ziegler,[1,2] Peter Achenbach,[1,2] Reinhard Berner,[3] Kristina Casteels,[4,5] Thomas Danne,[6] Melanie Gündert,[1] Joerg Hasford,[7] Verena Sophia Hoffmann,[1] Olga Kordonouri,[6] Karin Lange,[8] Helena Elding Larsson,[9,10] Markus Lundgren,[9] Matthew D Snape,[11,12] Agnieszka Szypowska,[13] John A Todd,[14] Ezio Bonifacio,[15] and the GPPAD Study group





BMJ Open 2019;**9**:e028578.
doi:10.1136/bmjopen-2018-028578

Oral insulin immunotherapy in children at risk for type 1 diabetes in a randomised controlled trial

Robin Assfalg[1,2,3] · Jan Knoop[1] · Kristi L. Hoffman[4] · Markus Pfirrmann[5] · Jose Maria Zapardiel-Gonzalo[1] · Anna Hofelich[2] · Anne Eugster[6,7] · Marc Weigelt[6] · Claudia Matzke[1] · Julia Reinhardt[6] · Yannick Fuchs[6] · Melanie Bunk[1] · Andreas Weiss[1] · Markus Hippich[1] · Kathrin Halfter[5] · Stefanie M. Hauck[8] · Jörg Hasford[5] · Joseph F. Petrosino[4] · Peter Achenbach[1,2,3] · Ezio Bonifacio[3,6,7,9] · Anette-Gabriele Ziegler[1,2,3]

What are the new findings?

- High-dose oral insulin in children aged <2 years appears safe
- The trial failed to find immune effects previously observed in older children
- Exploratory analyses suggested: (1) an oral insulin-associated immune response in children with type 1 diabetes-susceptible *INS* genotypes; (2) that *INS* genotype may influence the gut microbiome; and (3) that inflammatory monocyte profiles were remarkably frequent and associated with insulin-directed T cell responses in very young children

How might this impact on clinical practice in the foreseeable future?

- Oral insulin can be safely administered to very young children in primary prevention trials, and these trials should consider stratification for *INS* genotype

Diabetologia (2021) 64:1079–1092

Heat-shock protein peptide DiaPep277 treatment in children with newly diagnosed type 1 diabetes: a randomised, double-blind phase II study

L. Lazar[1,2]
R. Ofan[1]
N. Weintrob[1,2]
A. Avron[3]
M. Tamir[3]
D. Elias[3]
M. Phillip[1,2]*
Z. Josefsberg[1,2]

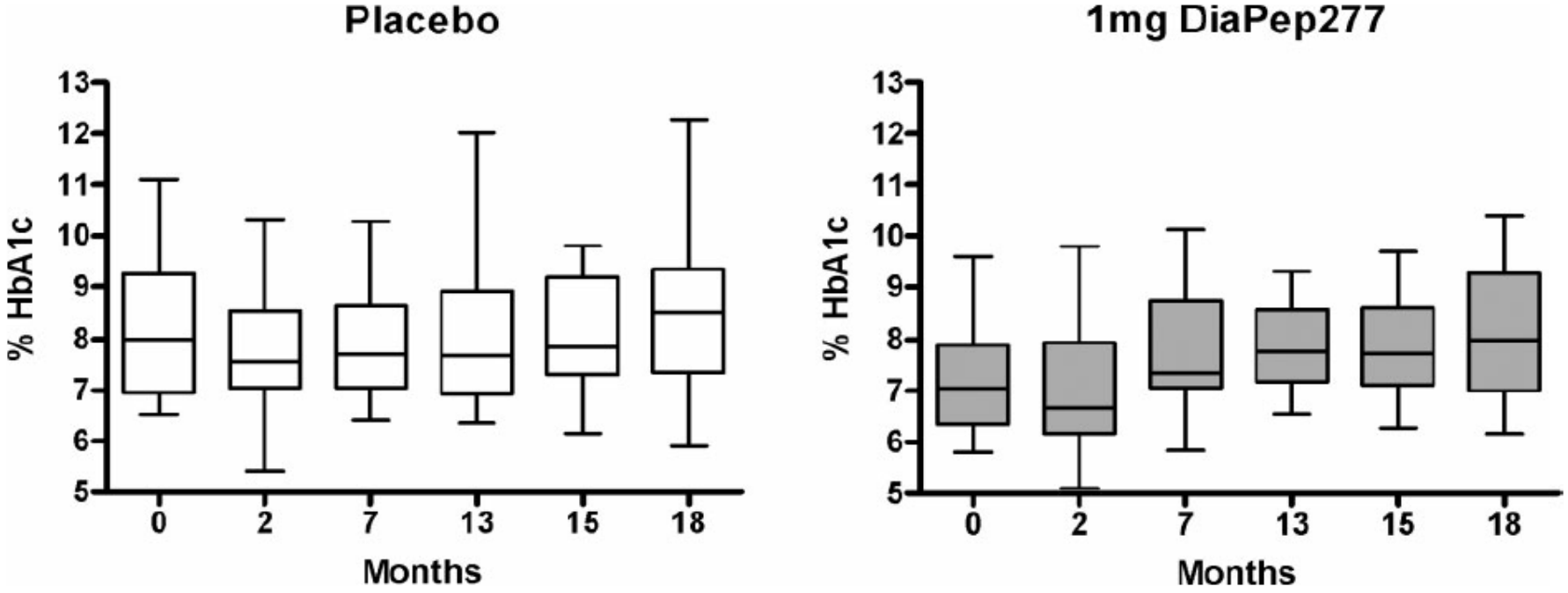


Figure 4. Metabolic control % HbA_{1c}: prospective data on HbA_{1c} at 0, 2, 7, 13, 15 and 18 months of follow-up. Shown are median, interquartile range and total range

DIABETES/METABOLISM RESEARCH AND REVIEWS
Diabetes Metab Res Rev 2007; **23**: 286–291.

Teplizumab: type 1 diabetes mellitus preventable?

Saurav Misra[1] · Ajay Kumar Shukla[2]

ANTICORPO MONOCLONALE ANTI CD3

- Storicamente impiegato nel post trapianto
- Si lega alle molecole CD3 sulla superficie di CD4 e CD8
- Previene l'attivazione delle cellule T inibendo il riconoscimento dell'antigene
- Agonista parziale di T Cell Receptor
- Per pazienti con DM1 in stadio 2 di età > 8aa
- Per ritardare (2.75 aa in media) esordio
- Infusione per 14 giorni
  - Deplezione T linfociti, infezione da EBV, reazione di ipersensibilità, cytokine release syndrome

European Journal of Clinical Pharmacology (2023) 79:609–616

Efficacy of anti-CD3 monoclonal antibodies in delaying the progression of recent-onset type 1 diabetes mellitus: A systematic review, meta-analyses and meta-regression

Muhammad Talal Ashraf MBBS[1] | Syed Hassan Ahmed Rizvi MBBS[1] | Muhammad Arham Bin Kashif MBBS[1] | Muhammad Khuzzaim Shakeel Khan MBBS[1] Syed Hassan Ahmed MBBS[1] | Muhammad Sohaib Asghar MBBS, MD[2]

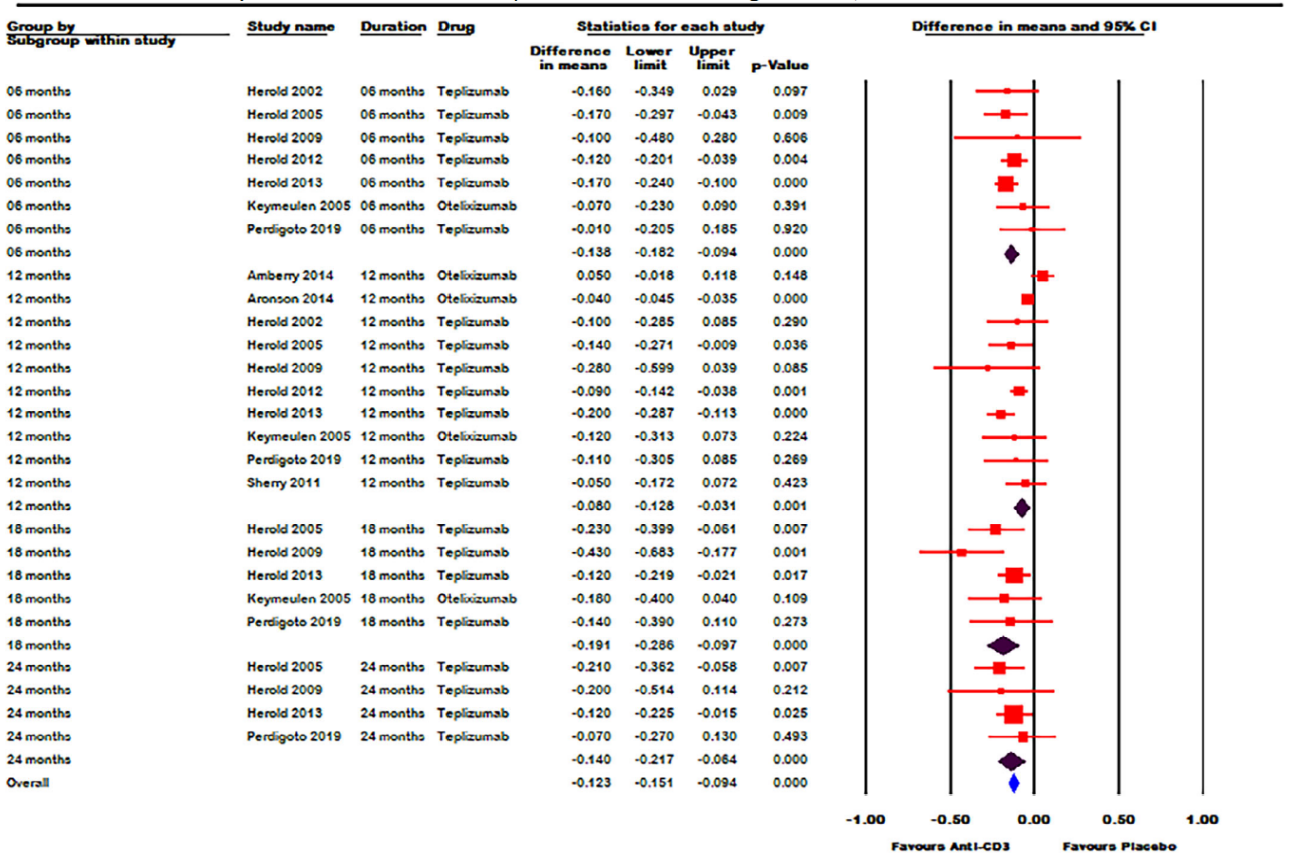


FIGURE 7 Forest plot for change in insulin dose.

Teplizumab and β-Cell Function in Newly Diagnosed Type 1 Diabetes

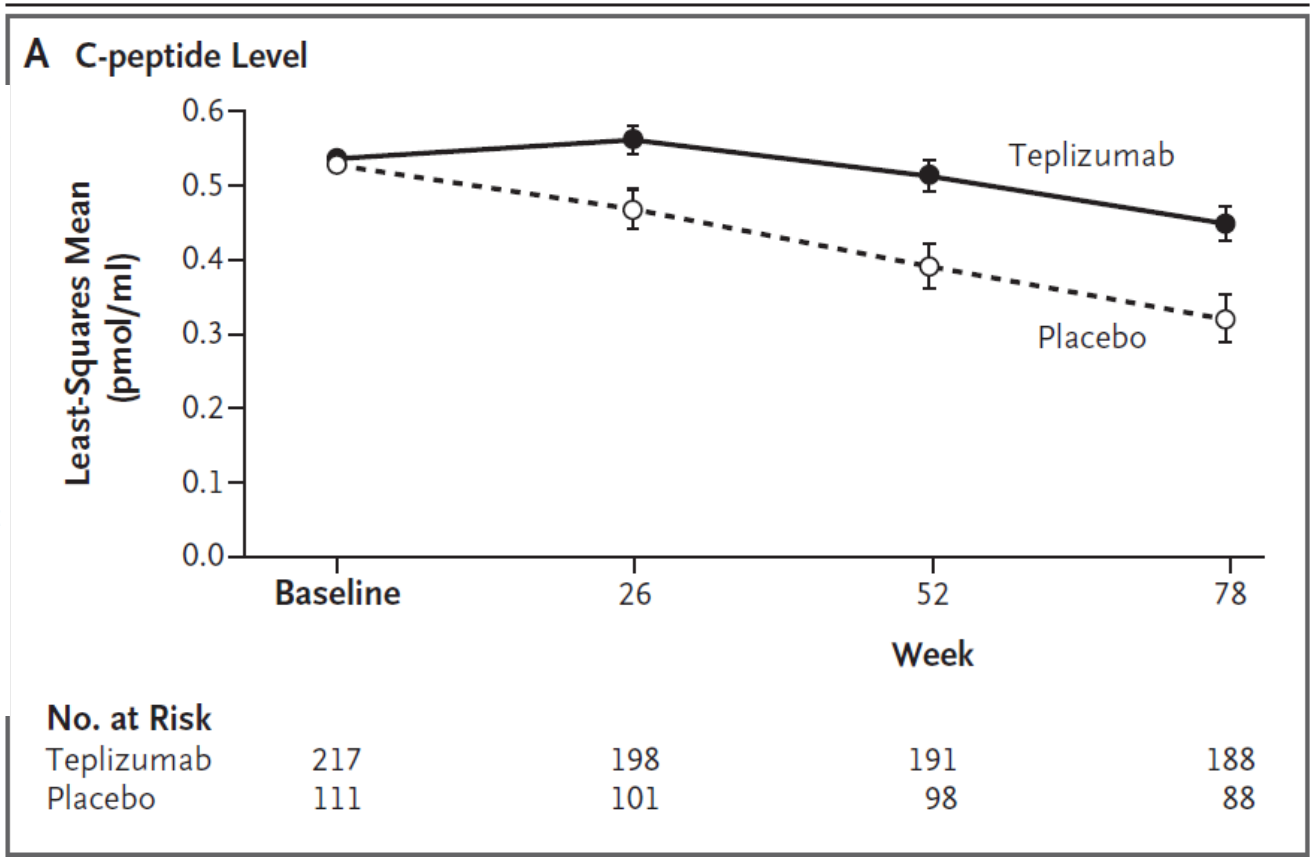
Eleanor L. Ramos, M.D., Colin M. Dayan, M.B., B.S., Ph.D., Lucienne Chatenoud, M.D., Ph.D., Zdenek Sumnik, M.D., Ph.D., Kimber M. Simmons, M.D., Agnieszka Szypowska, M.D., Ph.D., Stephen E. Gitelman, M.D., Laura A. Knecht, M.D., Elisabeth Niemoeller, M.D., Wei Tian, Ph.D., and Kevan C. Herold, M.D., for the PROTECT Study Investigators*

BACKGROUND

Teplizumab, a humanized monoclonal antibody to CD3 on T cells, is approved by the Food and Drug Administration to delay the onset of clinical type 1 diabetes (stage 3) in patients 8 years of age or older with preclinical (stage 2) disease. Whether treatment with intravenous teplizumab in patients with newly diagnosed type 1 diabetes can prevent disease progression is unknown.

METHODS

In this phase 3, randomized, placebo-controlled trial, we assessed β-cell preservation, clinical end points, and safety in children and adolescents who were assigned to receive teplizumab or placebo for two 12-day courses. The primary end point was the change from baseline in β-cell function, as measured by stimulated C-peptide levels at week 78. The key secondary end points were the insulin doses that were required to meet glycemic goals, glycated hemoglobin levels, time in the target glucose range, and clinically important hypoglycemic events.



Teplizumab and β-Cell Function in Newly Diagnosed Type 1 Diabetes

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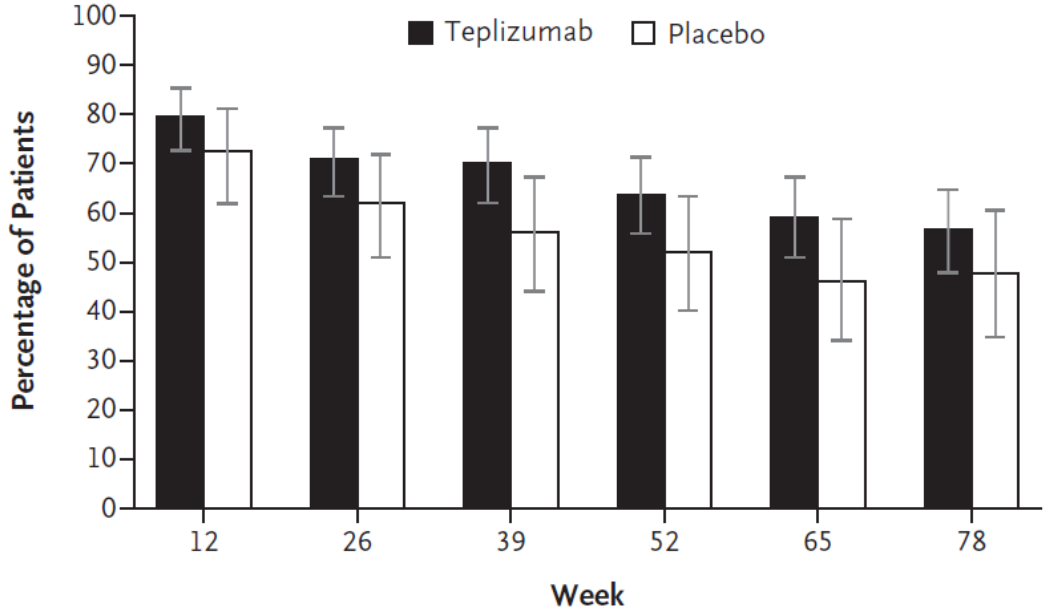
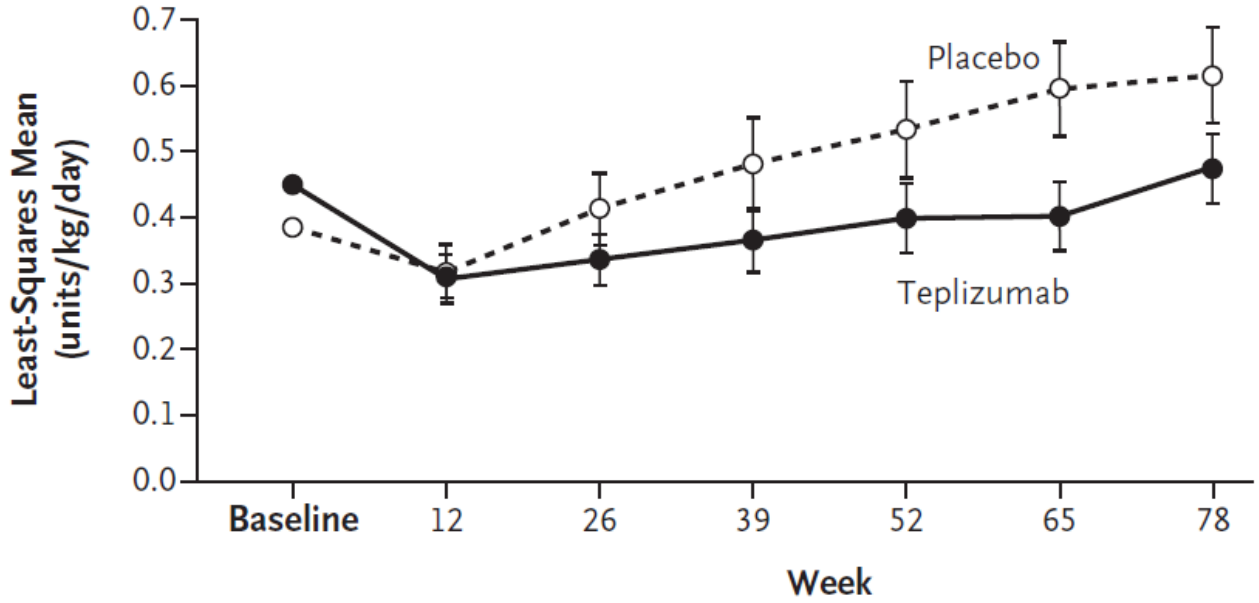
B Patients with Glucose Levels in the Target Range ≥70% of the Time



No. Events/ No. at Risk						
Teplizumab	132/166	123/174	105/150	100/157	87/147	79/140
Placebo	65/90	55/89	43/77	40/77	32/69	30/63

C Daily Insulin Dose



Sci Transl Med. 2021 March 03; 13(583): . doi:10.1126/scitranslmed.abc8980.

Teplizumab improves and stabilizes beta cell function in antibody positive high-risk individuals

Emily K. Sims[1], Brian Bundy[3], Kenneth Stier[4], Elisavet Serti[5], Noha Lim[5], S Alice Long[6], Susan M Geyer[7], Antoinette Moran[8], Carla J Greenbaum[6], Carmella Evans-Molina[2], Kevan C. Herold[4] Type 1 Diabetes TrialNet Study Group

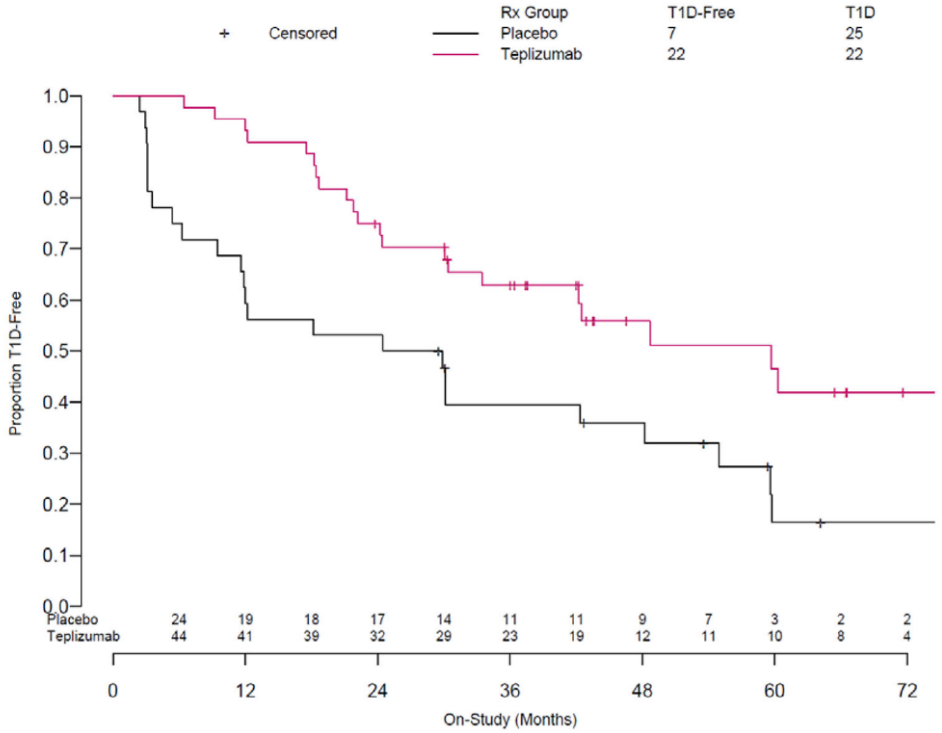


Figure 1. Teplizumab Treatment is Associated with a Sustained Effect on Type 1 Diabetes Progression Over 923 Days of Follow-up.

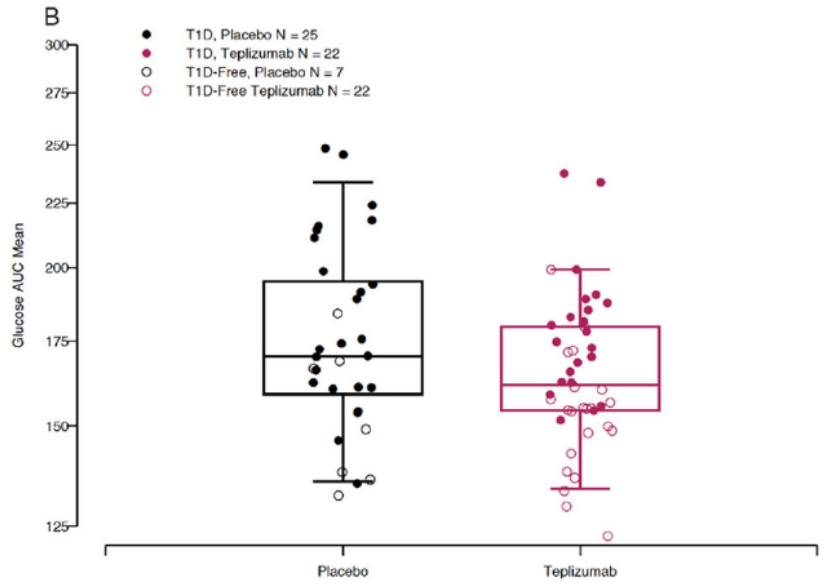


Figure 2. Improved glycemia in teplizumab treated participants is associated with maintenance of dysglycemic status.

Subcutaneous Abatacept in New Onset Type 1 Diabetes: Clinical and Immunological Effects

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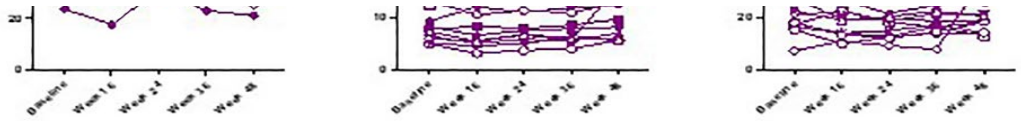
ABSTRACT

Abatacept is a CTLA4-Ig fusion protein that blocks CD80/CD86-dependent T-cell co-stimulation. When administered, Abatacept limits, to a variable degree, loss of stimulated C-peptide secretion in patients with newly-diagnosed type 1 diabetes (T1D), while reducing both circulating memory $CD4^+$ T-cells and T follicular helper (Tfh) cells; however, its precise mechanism of action is not known. To investigate this effect, we studied 12 patients, using multi-parameter flow cytometry, who each self-administered Abatacept in subcutaneous formulation for 6 months within 100 days of diagnosis. Abatacept treatment impacted the $CD4^+$ T cell memory compartment, inducing a reduction in T-effector cells across both conventional (Tconv) and regulatory (Treg) sub-populations. A reduction in activated Tfh cells ($CXCR5^+PD1^+ICOS^+$), previously described with intravenous therapy, was replicated and extended. An integrated baseline immunological phenotype predicted Abatacept-induced preservation of C-peptide.

Mean time from diagnosis to first sample (days)

Mean glycated haemoglobin (mmol/mol)



Abatacept for Delay of Type 1 Diabetes Progression in Stage 1 Relatives at Risk: A Randomized, Double-Masked, Controlled Trial

William E. Russell, Brian N. Bundy, Mark S. Anderson, Laura A. Cooney, Stephen E. Gitelman, Robin S. Goland, Peter A. Gottlieb, Carla J. Greenbaum, Michael J. Haller, Jeffrey P. Krischer, Ingrid M. Libman, Peter S. Linsley, S. Alice Long, Sandra M. Lord, Daniel J. Moore, Wayne V. Moore, Antoinette M. Moran, Andrew B. Muir, Philip Raskin, Jay S. Skyler, John M. Wentworth, Diane K. Wherrett, Darrell M. Wilson, Anette-Gabriele Ziegler, Kevan C. Herold, and the Type 1 Diabetes TrialNet Study Group

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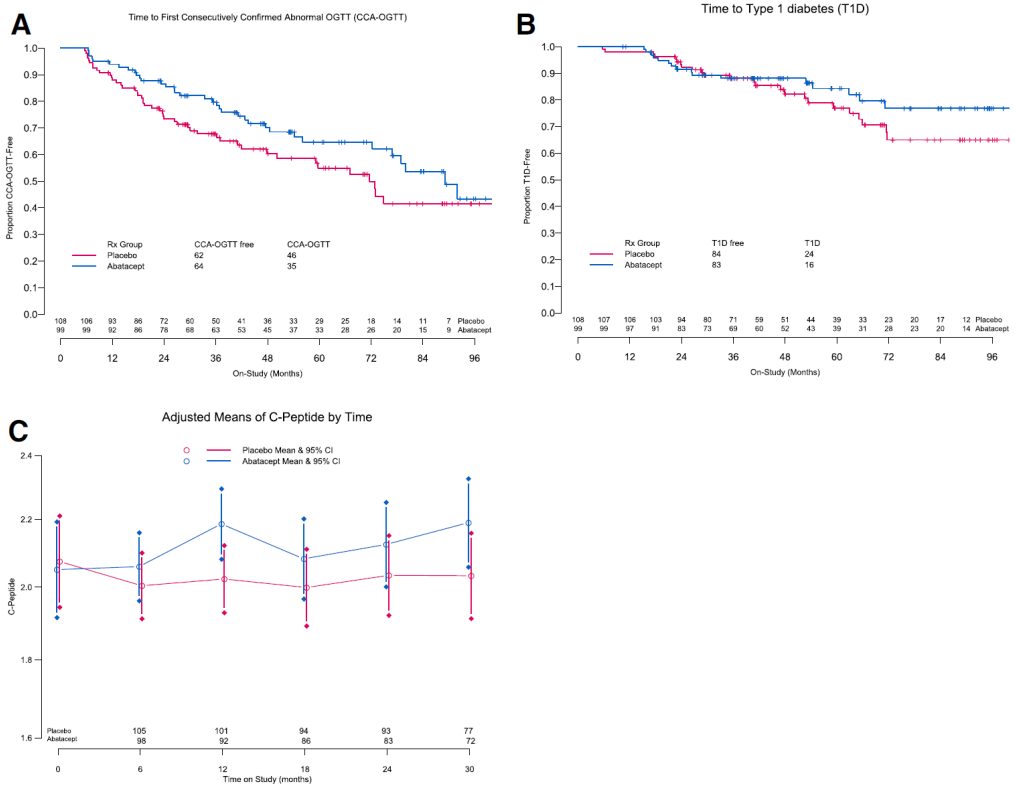
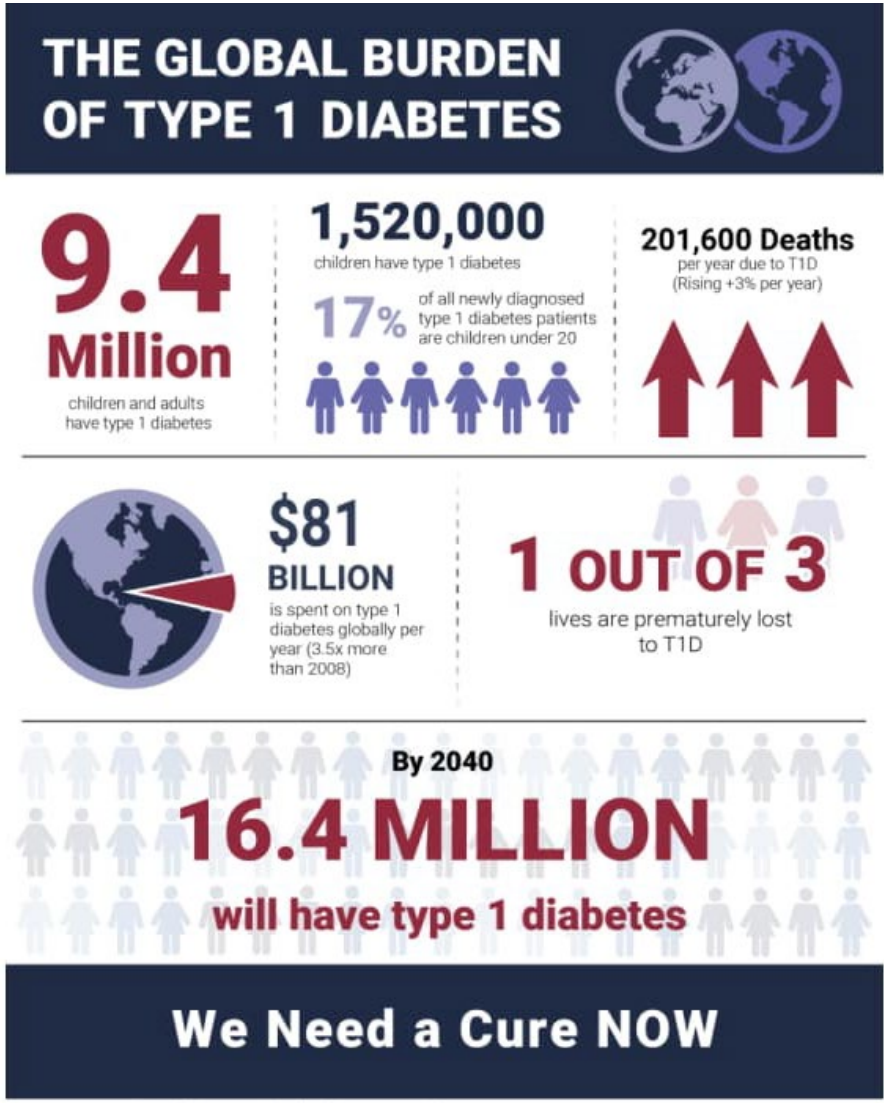
ABATACEPT (CTLA4Ig)

- Previene attivazione dei T linfociti attraverso asse CD80/86
- Costimulation blockade
- Rallenta la distruzione delle β-cellule

STUDIO RANDOMIZZATO FASE II SU SOGGETTI A RISCHIO DI DM1

- 134 età < 18 anni, 78 età > 18 anni
- 101 trattati
- 111 placebo
- Infusione di Abatacept 10 mg/kg
- End point: OGTT, Progressione fase III, C peptide





Source: T1D Index and the International Diabetes Foundation

Report 2024, available online at: https://www.thejdca.org/publications/report-library/archived-reports/2024-reports/diabetes-awareness-month-the-t1d-burden-grows-heavier-each-year.html

LEGGE 130/2023

IL PRESIDENTE DELLA REPUBBLICA

Promulga

la seguente legge:

Art. 1

Programma di screening nazionale
per diabete di tipo 1 e celiachia

1. Al fine di prevenire l'insorgenza di chetoacidosi in soggetti affetti da diabete di tipo 1 e di rallentare la progressione della malattia mediante l'impiego delle terapie disponibili, nonché di effettuare la diagnosi precoce della celiachia, con decreto del Ministro della salute, da emanare entro centoventi giorni dalla data di entrata in vigore della presente legge, previo parere della Conferenza permanente per i rapporti tra lo Stato, le regioni e le province autonome di Trento e di Bolzano e sentite le associazioni maggiormente rappresentative delle persone affette da diabete di tipo 1 e da celiachia e dei loro familiari e le fondazioni di rilevanza nazionale operanti in materia, è adottato un programma pluriennale di screening su base nazionale nella popolazione pediatrica per l'individuazione degli anticorpi del diabete di tipo 1 e della celiachia, da avviare a decorrere dall'anno 2024. Lo schema di decreto di cui al primo periodo è sottoposto al parere delle competenti Commissioni parlamentari, che si esprimono entro il termine di trenta giorni dalla data della sua trasmissione, decorso il quale il Ministro della salute può comunque procedere.

STUDY PROTOCOL

Study protocol of D1Ce Screen: A pilot project of the Italian national screening program for type 1 diabetes and coeliac disease in the paediatric population

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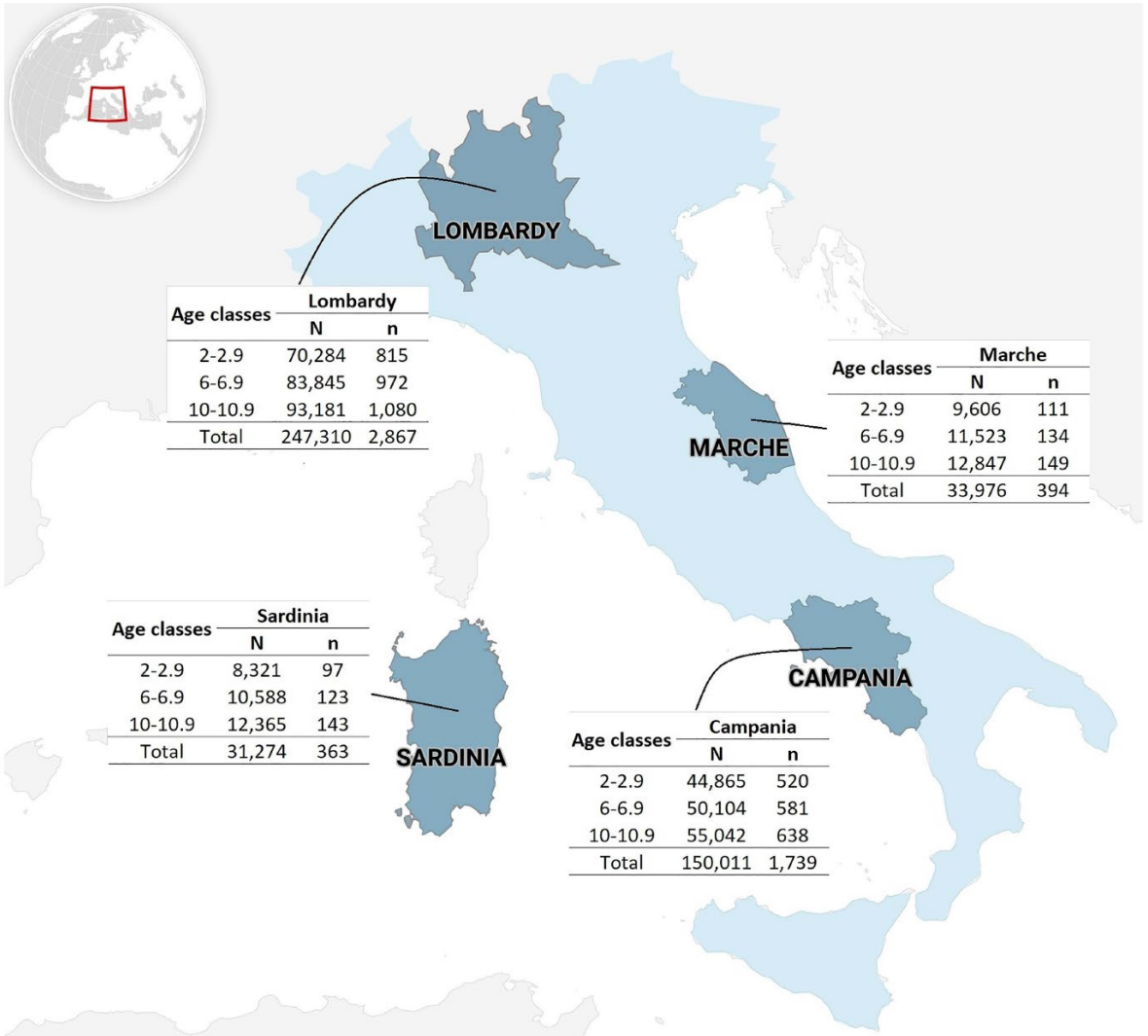

Age classes	Lombardy	
	N	n
2-2.9	70,284	815
6-6.9	83,845	972
10-10.9	93,181	1,080
Total	247,310	2,867

Age classes	Marche	
	N	n
2-2.9	9,606	111
6-6.9	11,523	134
10-10.9	12,847	149
Total	33,976	394

Age classes	Sardinia	
	N	n
2-2.9	8,321	97
6-6.9	10,588	123
10-10.9	12,365	143
Total	31,274	363

Age classes	Campania	
	N	n
2-2.9	44,865	520
6-6.9	50,104	581
10-10.9	55,042	638
Total	150,011	1,739

PLOS One | https://doi.org/10.1371/journal.pone.0328624 August 13, 2025

Initial observations on the frequency of diabetic ketoacidosis following pilot screening for type 1 diabetes in the general Italian population

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TABLE 1 New diagnoses of type 1 diabetes and the proportion of DKA and severe DKA at type 1 diabetes diagnosis by year of onset, age group, and regions included and not included in the D1Ce Screen study.

	2023			2024		
Regions included in the D1Ce Screen study	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**
Age groups						
0.5–5	118	31.4	5.9	88	27.3	9.1
6–11	213	30.0	8.9	174	27.6	9.8
12–17	127	31.5	8.7	150	30.7	8.7
Total	458	30.8	8.1	412	28.6	9.2
Regions not included in the D1Ce Screen study	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**
Age groups				Total	Total	Total
0.5–5	230	41.3	20.9	209	45.9	19.1
6–11	359	35.9	12.8	312	34.3	16.3
12–17	201	33.3	15.9	217	31.3	11.1
Total	790	36.8	15.9	738	36.7	15.6
Both regions						
Total	1248			1150		

Real-world experiences of adult individuals or caregivers of children who received teplizumab treatment in stage 2 type 1 diabetes

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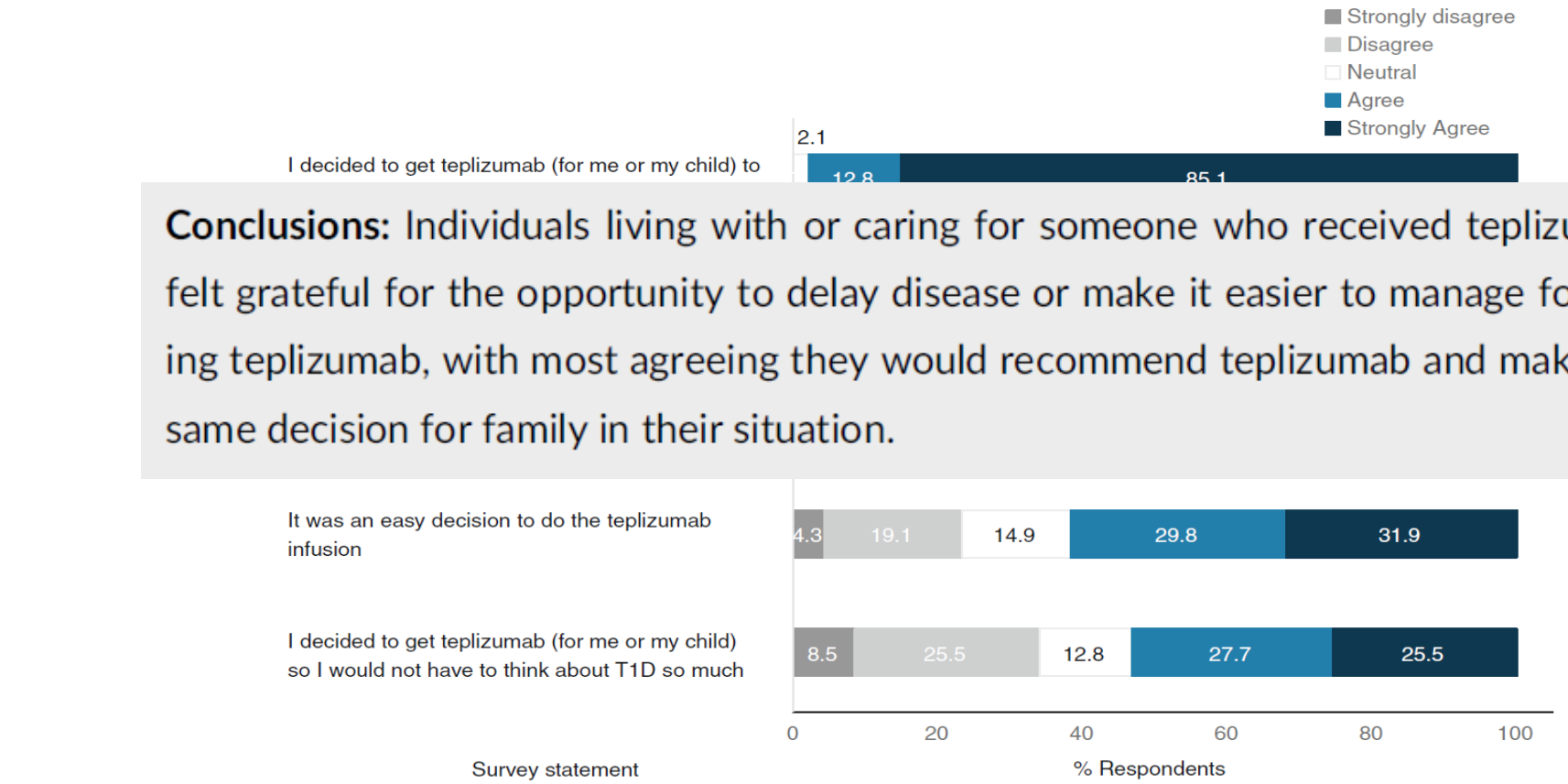
Stephen E. Gitelman MD[2] | Terry Dex PharmD[3] | Robert Hill BSc (Hons)[4] |
Mattias Wieloch MD[3,5] | Julia Zaccai PhD[6] | Jennifer D'Souza PhD[7] |
France Ginchereau Sowell PhD[7] | James Turnbull MPH[7] | Korey K. Hood PhD[8]



Conclusions: Individuals living with or caring for someone who received teplizumab felt grateful for the opportunity to delay disease or make it easier to manage following teplizumab, with most agreeing they would recommend teplizumab and make the same decision for family in their situation.

Diabetes Obes Metab. 2025;27:2495–2506.

GRAZIE PER L'ATTENZIONE