Predizione del diabete tipo 1

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Fonti di finanziamento

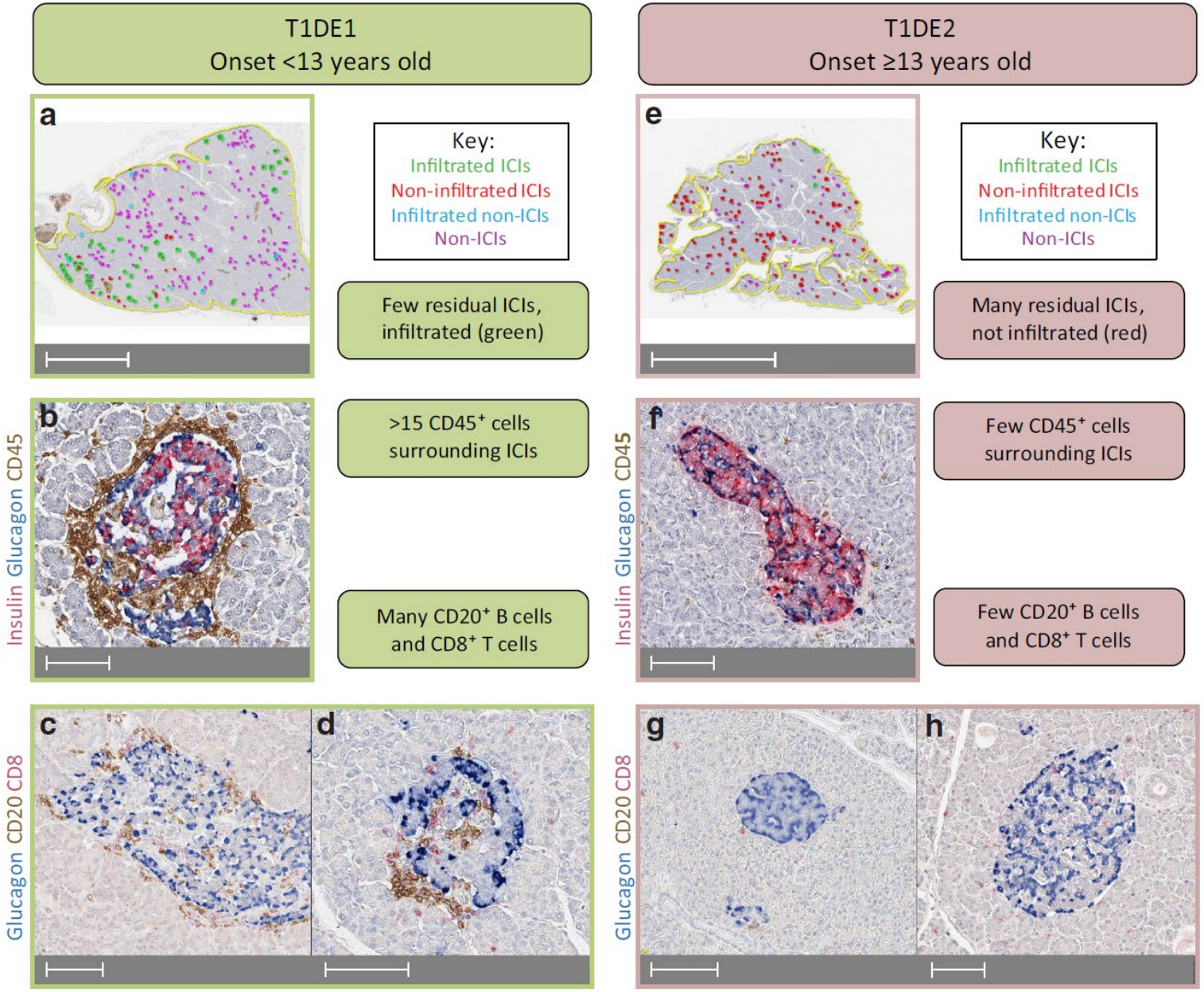
Il sottoscritto Prof. Francesco Dotta dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- **Sanofi**
- **Novo Nordisk**
- **Eli Lilly**
- **Boehringer Ingelheim**
- **Biontech**

T1D heterogeneity

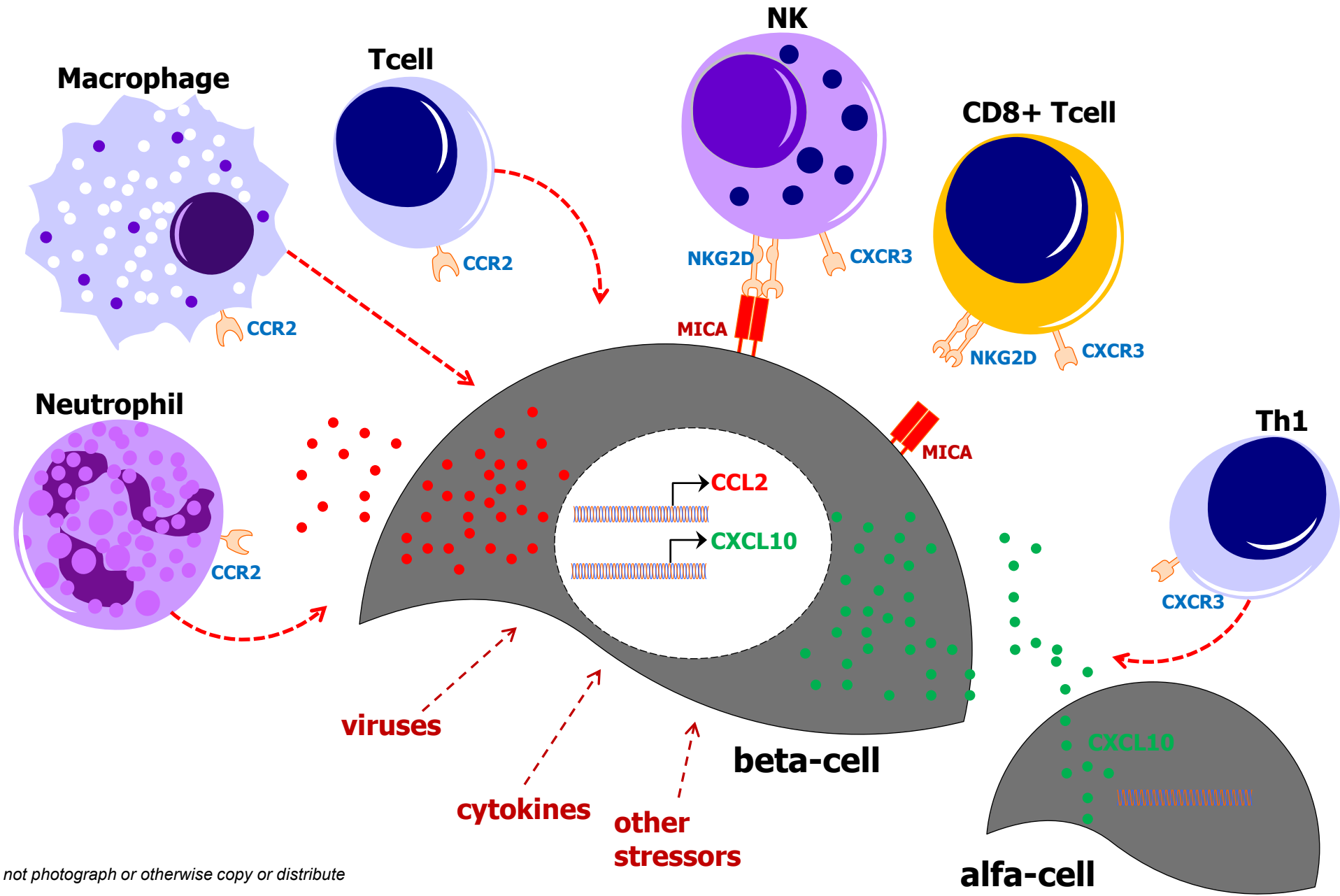
Clinical	• Age of onset of β cell–directed autoimmunity and hyperglycemia (from 6 months to adult); up to 40% onset in individuals over 30 years old • Other autoimmune endocrinopathies or diseases (thyroid, adrenal, celiac, etc.) • Degree and rate of development of diabetes-related complications (e.g., retinopathy, nephropathy, neuropathy)
Genetic	• Presence of HLA DR3/DR4 haplotypes • More than 50 genetic loci
Immunological	• Autoantibody frequency, profile, and target epitopes • Type 1 IFN, innate immunity, and T cell signatures
Metabolic	• Rate of decline in β cell function and mass in stages 2 and 3 • Degree and duration of residual C-peptide production • Response to immunomodulatory therapy
Pathological	• Insulitis (degree, location) differs between and within individuals • CD20+ B lymphocytes in younger-onset T1D • Degree of β cell loss • Differences between insulin-negative islets and islets with β cells

Age-related T1D Endotypes



Diabetologia (2021) 64:15–25

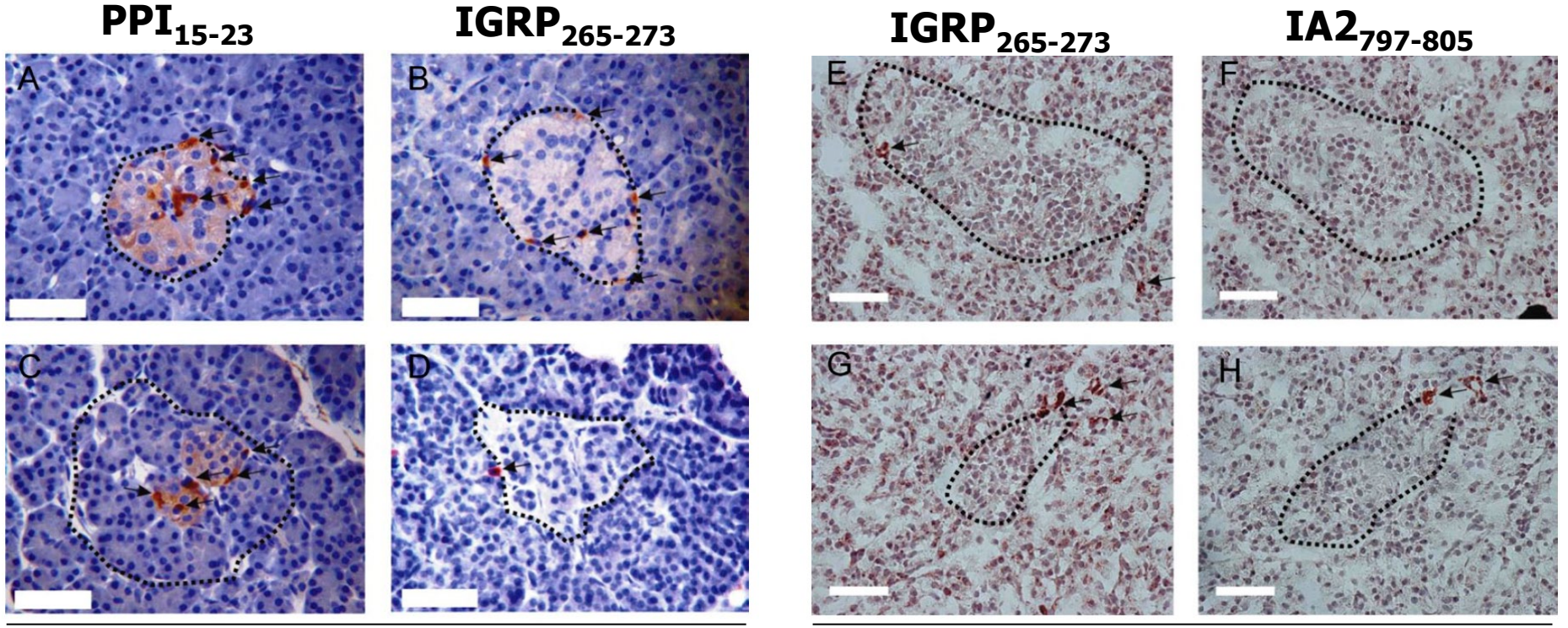
Type 1 diabetes: Complex dialogue between islet and immune system



Autoreactive CD8$^+$ T cells are enriched in pancreata from T1D donors

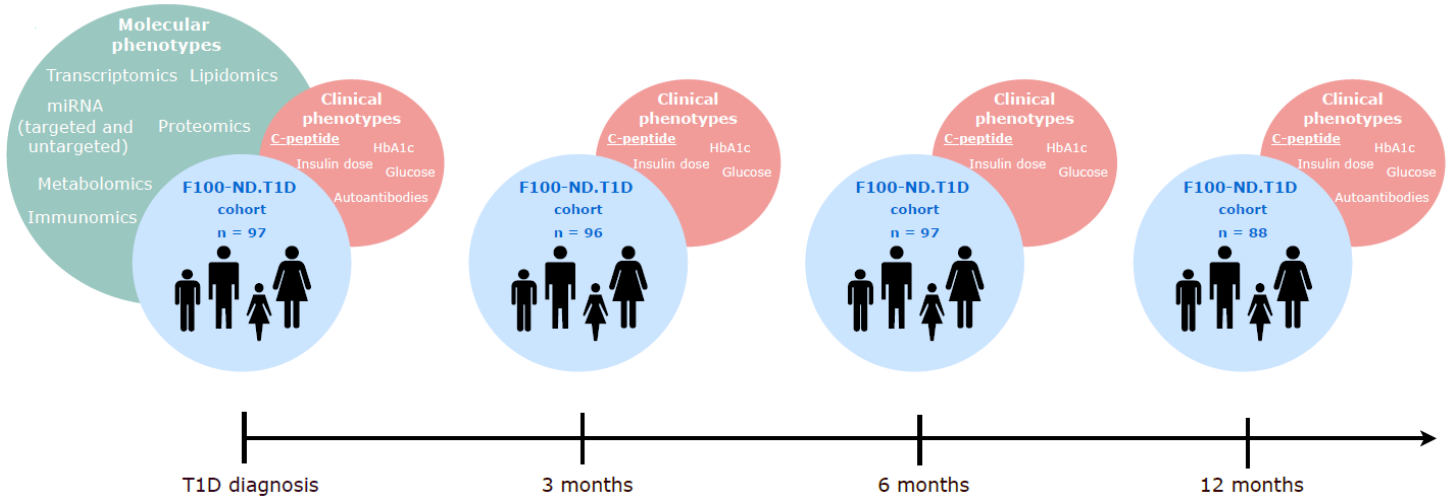
Demonstration of islet-autoreactive CD8 T cells in insulitic lesions from recent onset and long-term type 1 diabetes patients

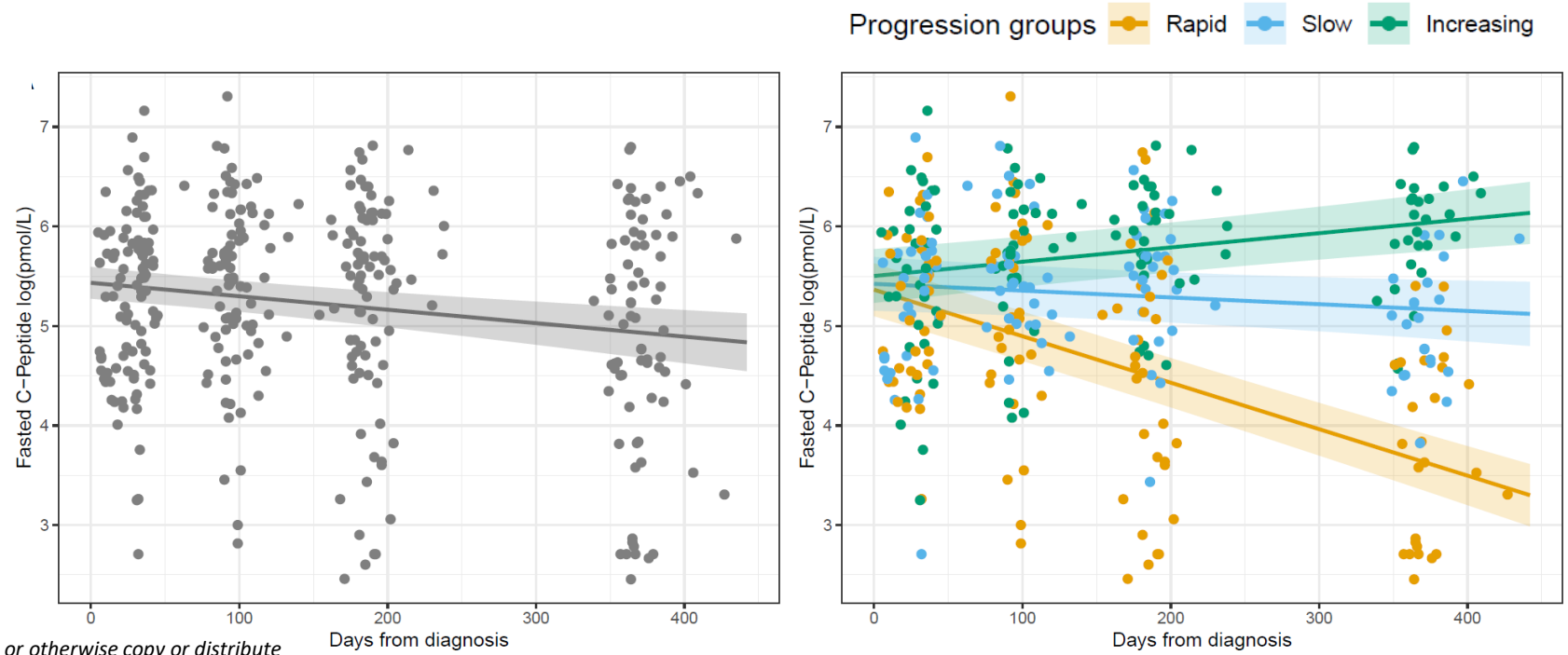
Ken T. Coppieters,[1] Francesco Dotta,[2] Natalie Amirian,[1]
Peter D. Campbell,[3] Thomas W.H. Kay,[3] Mark A. Atkinson,[4]
Bart O. Roep,[5] and Matthias G. von Herrath[1]



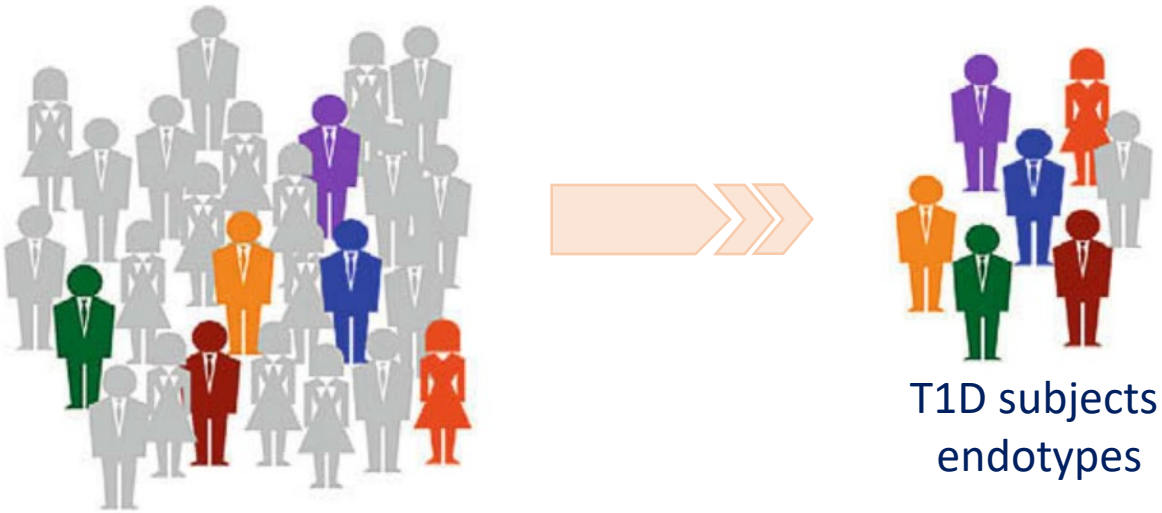
J.Exp. Med. 2012

Heterogeneous beta-cell functional decline during Type 1 Diabetes progression





E' possibile identificare specifici endotipi di soggetti T1D sulla base dei profili di espressione dei biomarcatori circolanti e della loro correlazione con parametri clinici e altre caratteristiche molecolari?



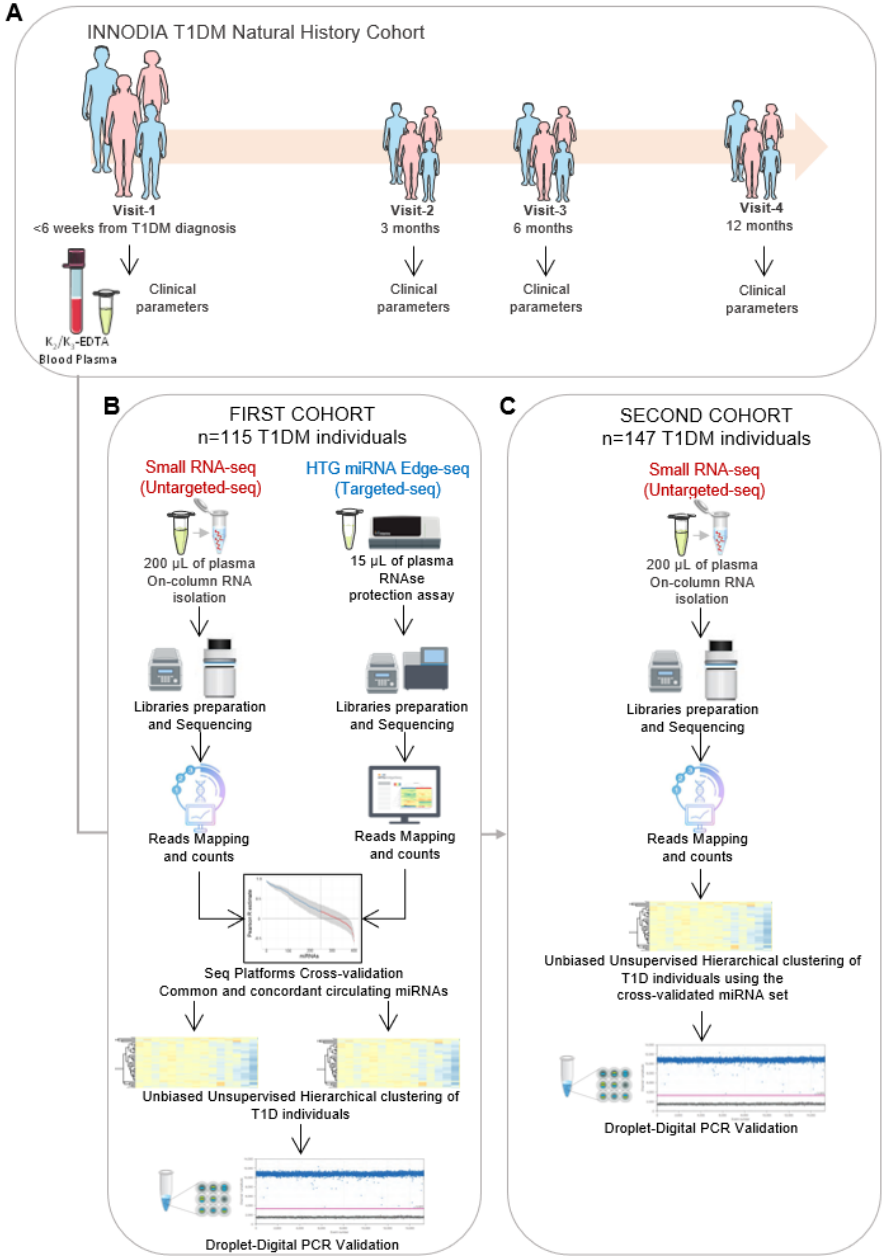
INNODIA Biomarkers Research study to identify novel T1D endotypes

MMTT		✓	✓	✓	✓
C-pep	✓	✓	✓	✓	✓
Serum	✓	✓	✓	✓	✓
Cells	✓	✓	✓	✓	✓
AA	✓			✓	✓
Omics*	✓			✓	✓
Stool /urine	✓	✓	✓	✓	✓

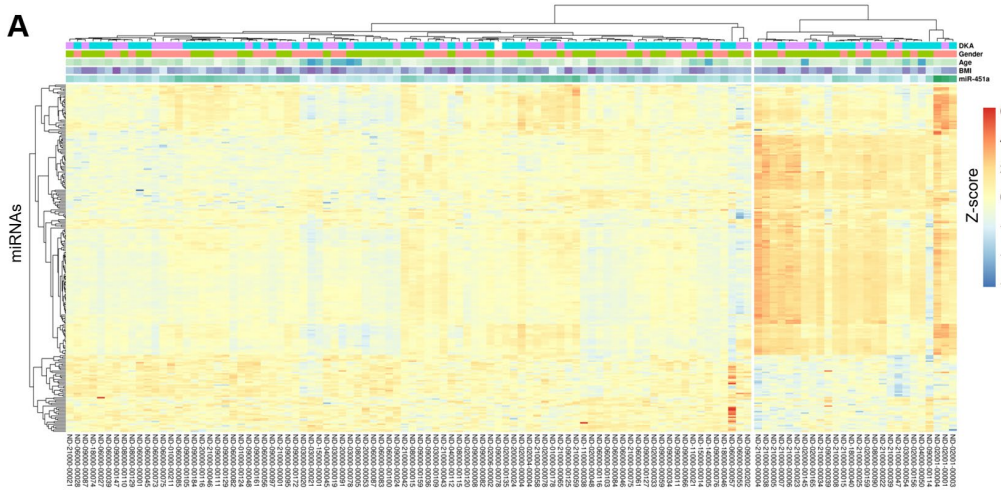
* Including micro-RNA and whole blood RNA

- Genotyping
- Immunomics
- Lipidomics
- Trancriptomics
- Proteomics
- Microbiome
- miRNA/Small RNAs

Cluster A and Cluster B T1DM individuals show distinct features at baseline and follow-up



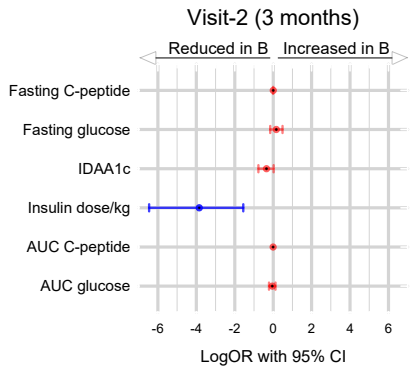
Circulating MicroRNAs

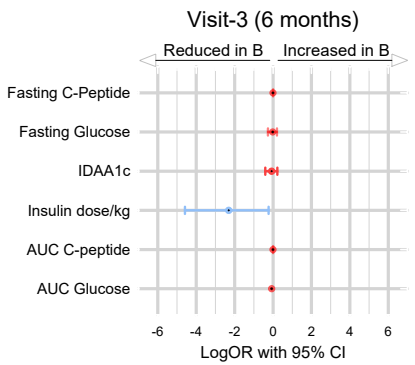


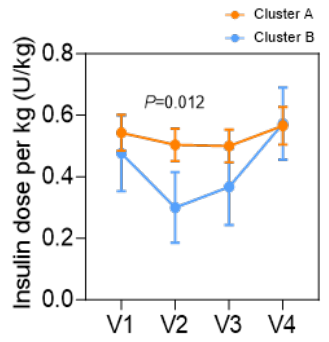
Cluster B enriched of 14q32 miRNAs

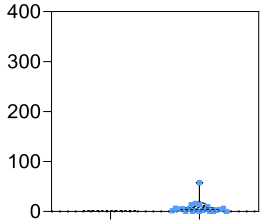
- hsa-miR-127-3p
- hsa-miR-134-5p
- hsa-miR-323a-3p
- hsa-miR-337-5p
- hsa-miR-370-3p
- hsa-miR-376c-3p
- hsa-miR-381-3p
- hsa-miR-382-5p
- hsa-miR-409-3p
- hsa-miR-431-5p
- hsa-miR-485-3p
- hsa-miR-494-3p
- hsa-miR-589-5p
- hsa-miR-654-3p

Clinical Parameters

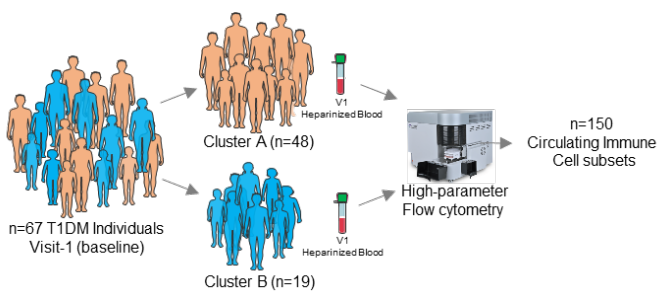








Immunomics

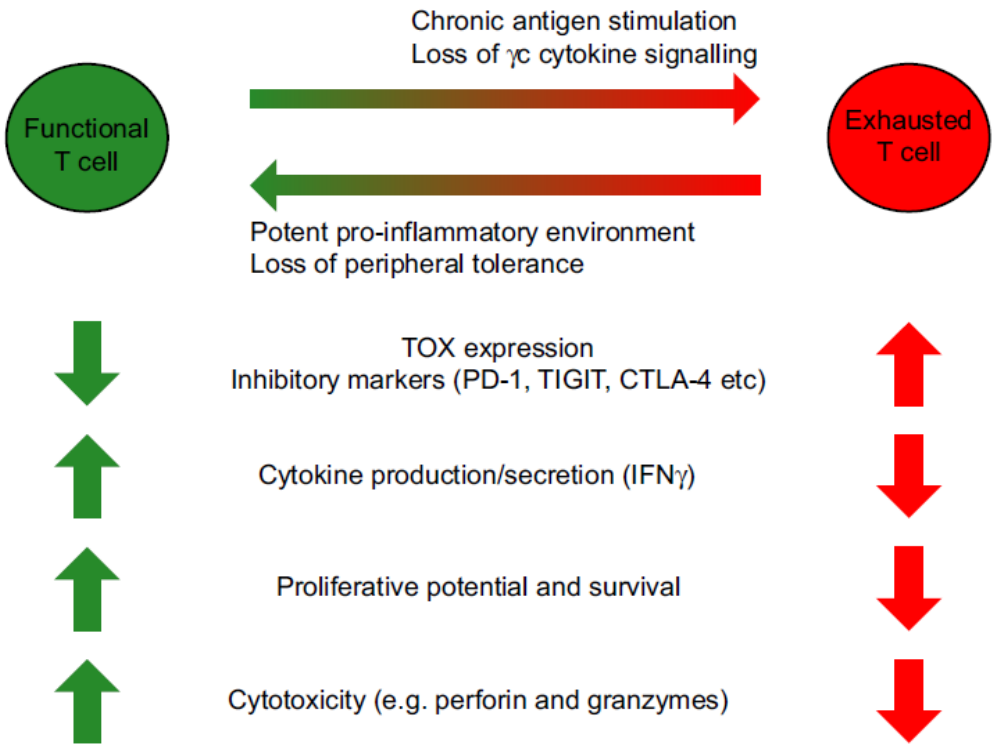


Immune cell subset	FC [B vs A]	P value
CD8+ Tscm	1,61	0,002
Th1-Th2-like Tfh	1,50	0,00008
TIGIT+ KLRG1- CD8+ Tem	1,26	0,002
TIGIT+ Tconv Tcm	1,12	0,002

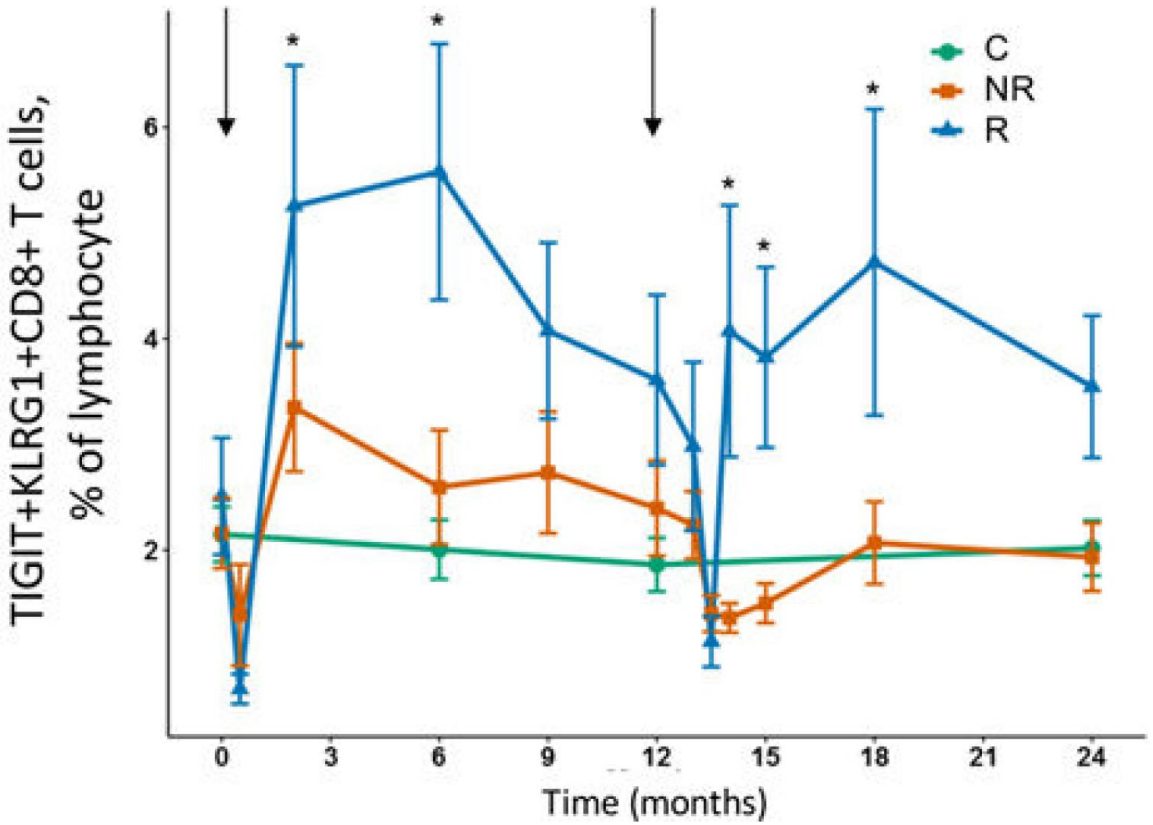
Sebastiani G. et al., 2024, Cell Reports Medicine, 2024

T-cell exhaustion in T1D

T-cell exhaustion is associated with reduced cytokines production



T1D subjects, **RESPONDERS** to aCD3 immunotherapy, showed higher levels of partially exhausted CD8 Tem KLRG1^{+} TIGIT^{+}

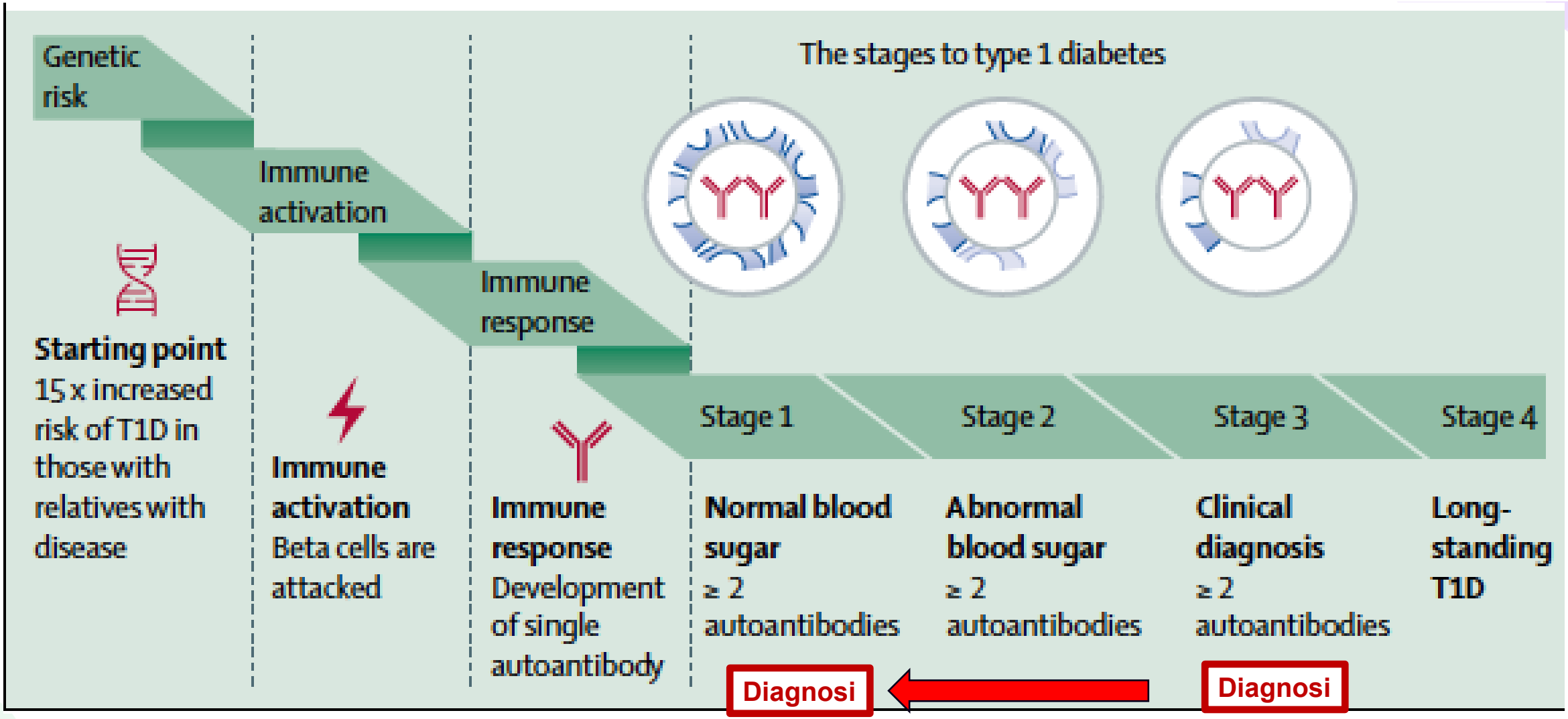


Long SA, et al .2016- *Sci. Immunol.*

Come troviamo chi è a rischio?
Come identifichiamo chi trattare?...e con quali strategie?

Storia naturale del diabete tipo 1

European Diabetes Forum Italia



12 aprile 2024: ICD10 codifica ora per stadio 1 e 2 (oltre allo stadio 3), rendendo queste fasi una MALATTIA riconosciuta

Type 1 diabetes stages

The American Diabetes Association recognizes three stages:

- ✓ Stage 1 (normoglycaemic and positive for autoantibodies to β-cell antigens)
- ✓ Stage 2 (asymptomatic with dysglycaemia)
- ✓ Stage 3 defined by glucose levels consistent with the definition of diabetes mellitus

Gli atteggiamenti nei confronti delle pratiche di screening sono divergenti tra i paesi europei, e le **autorità politico-sanitarie richiedono prove di beneficio** nel proprio paese prima di introdurre nuovi programmi di screening come parte della normale assistenza sanitaria.

Le aspettative fondamentali riguardano **un beneficio per la salute e un basso onere della diagnosi di malattie asintomatiche**; la disponibilità di cure mediche efficaci che prevengano o ritardino almeno in parte la malattia sintomatica e ne riducano le complicanze; lo screening e il monitoraggio devono essere efficaci sotto il profilo dei costi e competitivi rispetto ad altre esigenze e priorità sanitarie

In che modo lo screening per il diabete tipo 1 attraverso il dosaggio autoanticorpale è in linea con questi criteri?

La risposta è positiva in base ai dati della letteratura scientifica, sia in termini di benefici clinici che di sostenibilità economica.

Dal punto di vista dei costi e della sostenibilità economica, è stato suggerito che lo screening per il T1D nei bambini è sostenibile grazie a metodi di screening anticorpale più economici, alla prevenzione dei ricoveri per DKA e alla prevista riduzione dell'incidenza e dell'impatto economico delle complicanze del diabete.

In uno studio condotto in Colorado, i pazienti con DKA al momento della diagnosi hanno avuto HbA1c superiore dell'1,4% rispetto a quelli senza DKA, fino a 15 anni dopo la diagnosi. Inoltre, l'Autoimmunity Screening for Kids (ASK) ha dimostrato che la prevenzione della DKA alla diagnosi, combinata con una HbA1c persistentemente più bassa nei pazienti senza DKA e una ridotta incidenza di complicanze del diabete, rende lo screening della popolazione generale economicamente vantaggioso.

In Italia, coerentemente con i dati della letteratura prodotti da oltre 20 anni di ricerca scientifica, lo screening nazionale nella popolazione pediatrica è previsto dall'art. 1 comma 1 della legge 15 settembre 2023 n. 130, che si propone l'obiettivo 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.

Lo screening è attuato nelle Regioni e nelle Province Autonome di Trento e Bolzano e si inserisce nell'ambito dell'attività di "sorveglianza e prevenzione delle malattie croniche, inclusi la promozione di stili di vita sani ed i programmi organizzati di screening; sorveglianza e prevenzione nutrizionale" previste dal Piano Nazionale di Prevenzione 2020-2025.

Lo screening viene effettuato su campioni di sangue capillare e prevede la misurazione dei marcatori autoanticorpali del diabete di tipo 1 presso Laboratori di riferimento, individuati dalle Regioni e dalle Province Autonome, muniti della strumentazione analitica e di dispositivi adeguati a garantire la continuità, la qualità e l'adeguatezza delle prestazioni erogate.

Il coordinamento nazionale e regionale del sistema di screening spetta all'Istituto Superiore di Sanità che opera in stretta collaborazione con il Ministero della Salute.

Lo screening per il diabete tipo 1 in età pediatrica **è realizzabile e pienamente giustificato** anche nella popolazione generale ed ha mostrato efficacia nella prevenzione della DKA nei bambini.

Legge 130 pone il nostro paese in una situazione di avanguardia nel contesto internazionale per la diagnosi e la cura del diabete tipo 1.

Implementazione necessaria con il coinvolgimento di tutti gli attori necessari alla sua realizzazione, quali i centri clinici specialistici, i pediatri di libera scelta, le società scientifiche e le associazioni di pazienti, in collaborazione con le Regioni e le Province Autonome, il Ministero della Salute e l'Istituto Superiore di Sanità.

- The first step in achieving valid results in prevention is **to strengthen screening in the general population, and make them a part of the "Standard of Care"**. Screening strategies could allow to identify individuals at risk for T1D in order to enroll them in clinical trials.

- Another possible benefit of screening programs is the purpose of reducing the incidence of DKA at the time of diagnosis, as well as the opportunity to offer psychological, emotional and social support to children and families at the time of diagnosis.

JAMA | Original Investigation

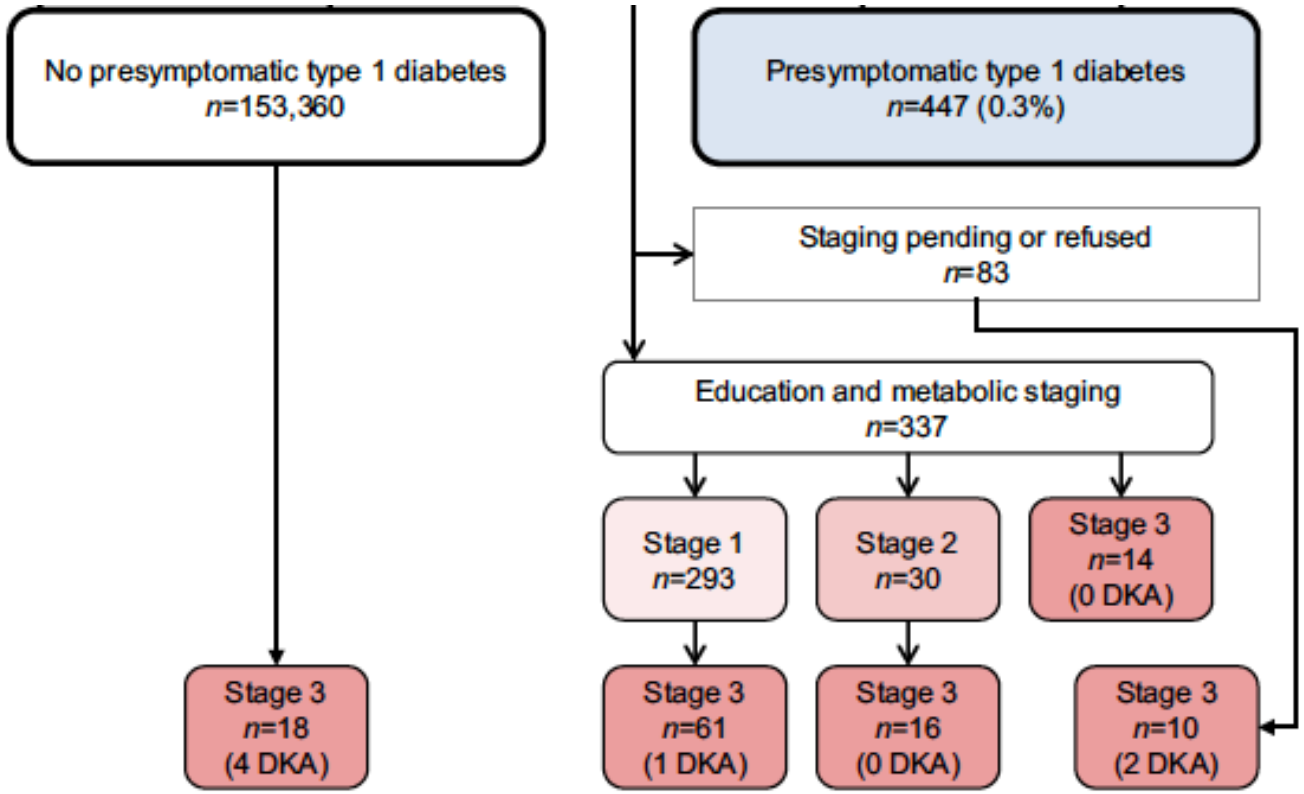
Yield of a Public Health Screening of Children for Islet Autoantibodies in Bavaria, Germany

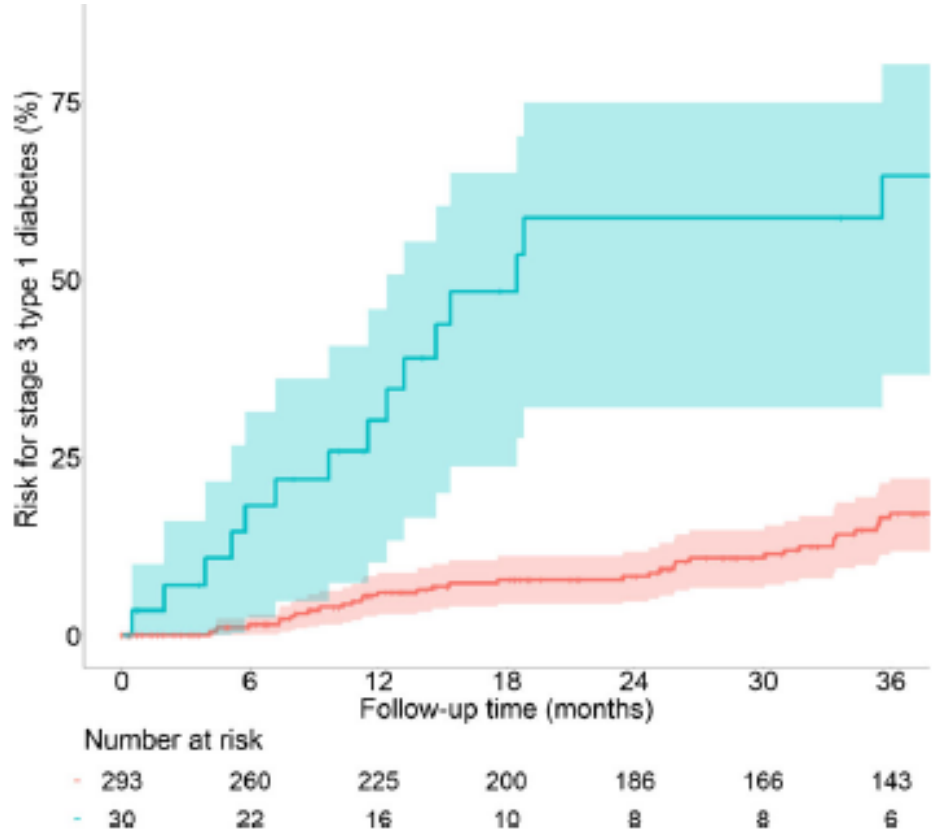
Fr1da

Typ 1 Diabetes: Früh erkennen – Früh gut behandeln

Progression likelihood score identifies substages of presymptomatic type 1 diabetes in childhood public health screening

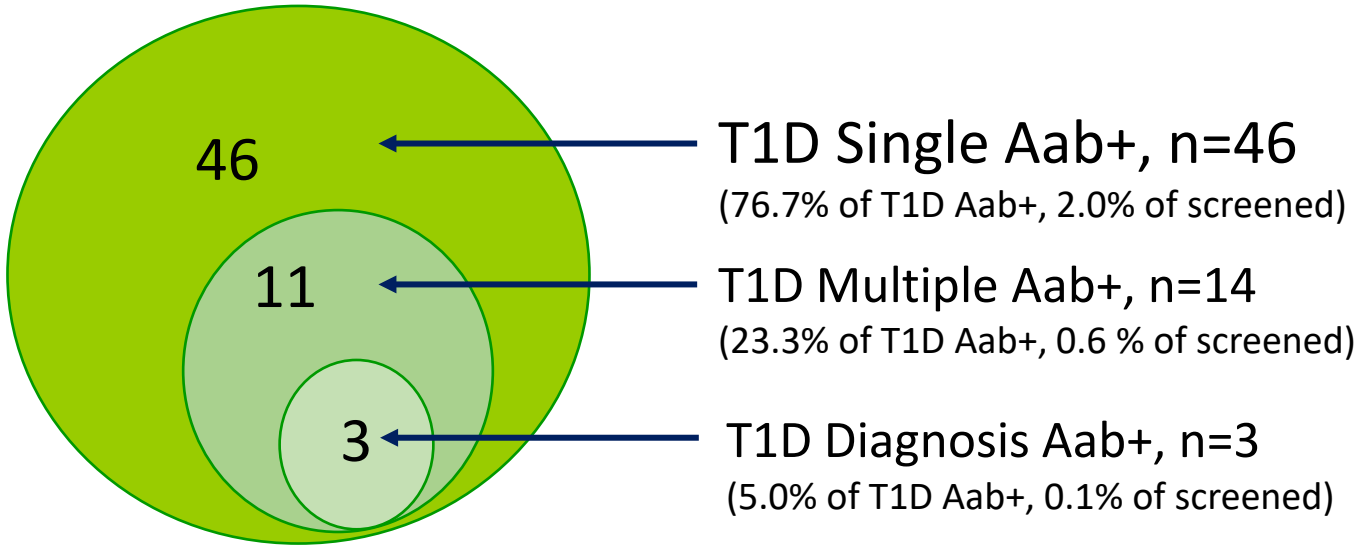
Andreas Weiss [1,2] · Jose Zapardiel-Gonzalo [1,2] · Franziska Voss [1] · Manja Jolink [1] · Joanna Stock [1] · Florian Haupt [1,2,3] · Kerstin Kick [4] · Tiziana Welzhofer [4] · Anja Heublein [1] · Christiane Winkler [1,2,3] · Peter Achenbach [1,2,3,4] · Anette-Gabriele Ziegler [1,2,3,4] · Ezio Bonifacio [2,5,6] · for the Fr1da-study group





Update 2023: 600 double Ab+ / 200.000 screened (0.3%)

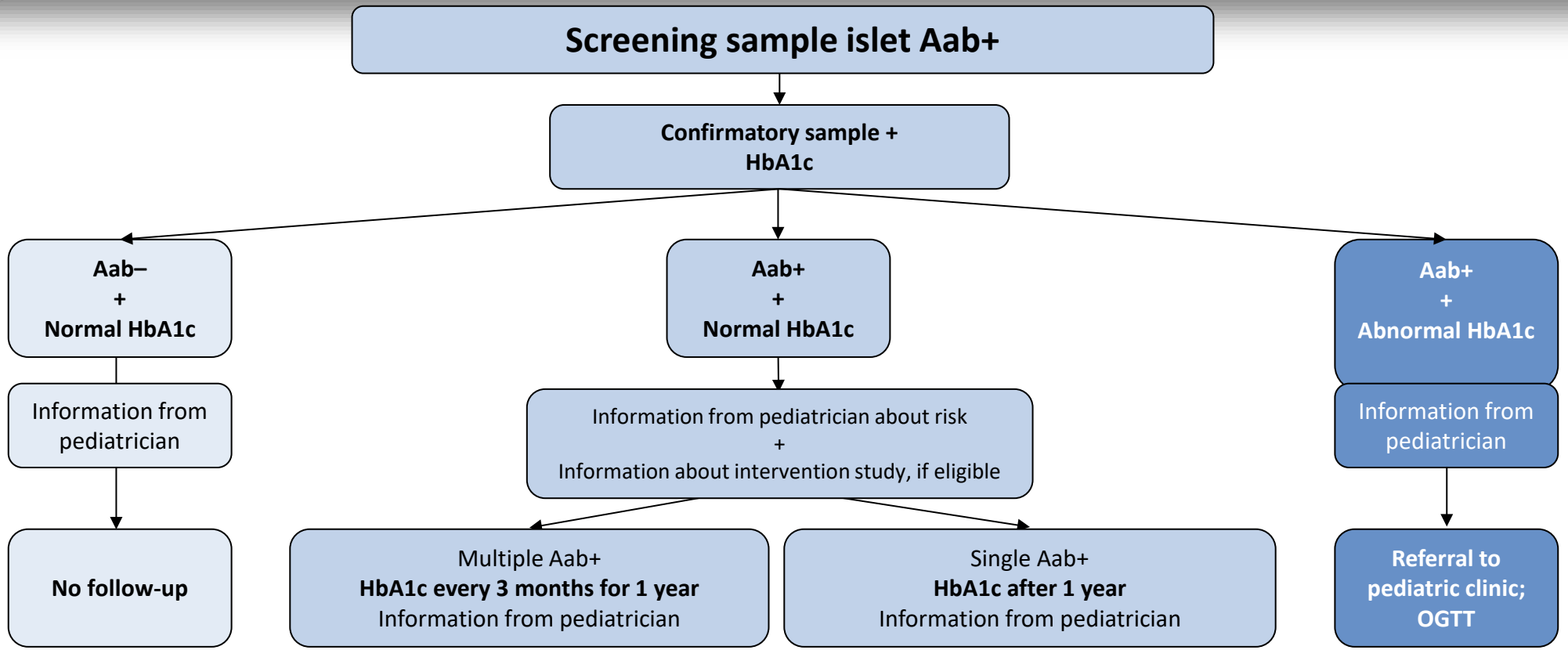
Islet Aab+ (n=60)



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

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].

Clinical follow-up



Monitoring program of autoantibody positive children is under evaluation

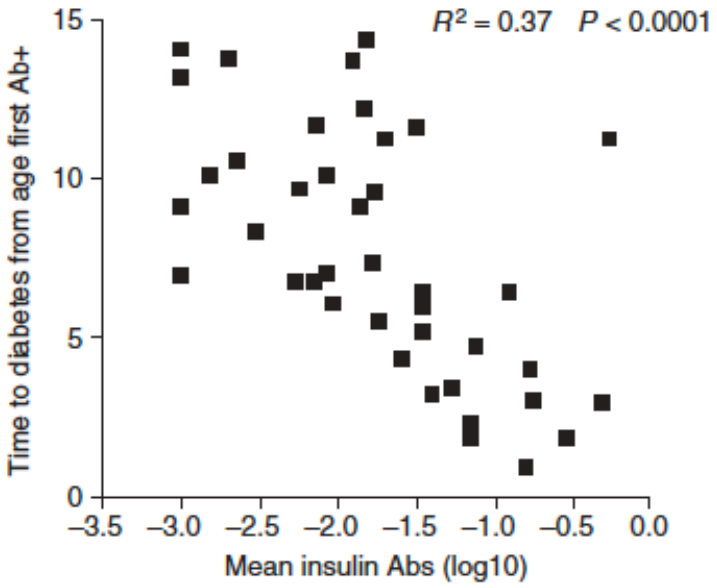
OGTT, oral glucose tolerance test. **Communication provided by speaker.** The DiaUnion TRIAD study is a collaboration between Lund University, Steno Diabetes Center Copenhagen and Medicon Valley Alliance, for early detection of T1D and two genetically related autoimmune diseases (CD and AITD). For more 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].

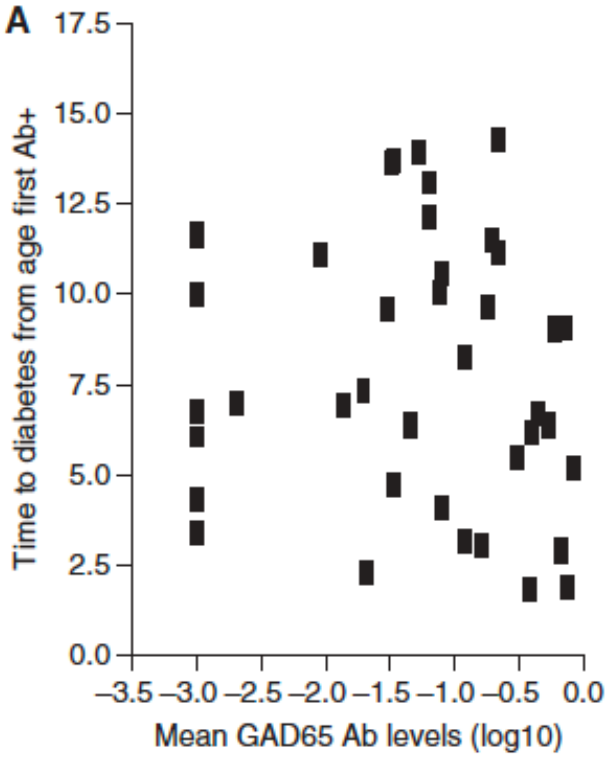
Follow-up (Consorzio EDENT1FI)

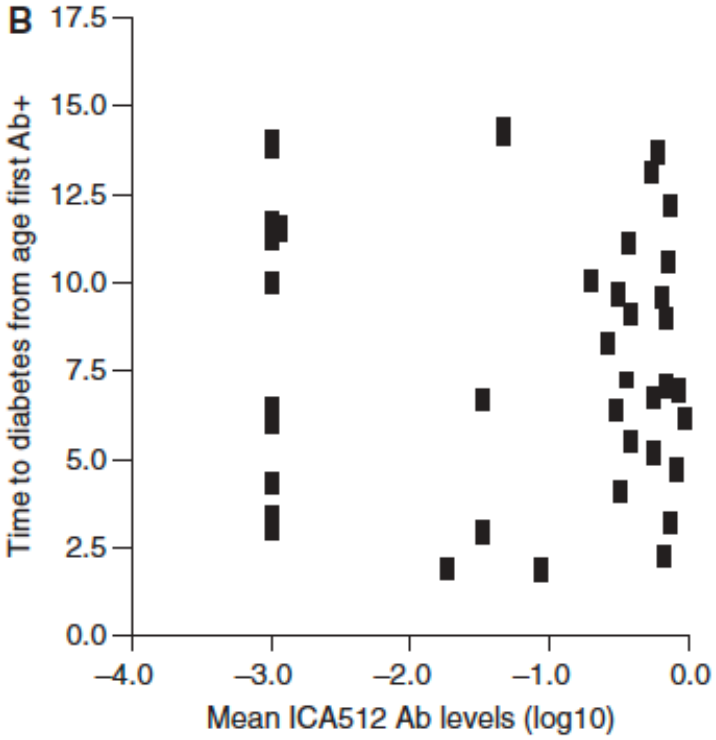
Tier	Progression rate	Explanation of risk	Suggested Follow up
1	Low (2 yr rate: <5%)	Normoglycaemia* Age over 2 y Progression score**<0.5	Random capillary glucose, HbA1c and autoantibody profiles at baseline and every 12 months, OGTT after 2 years
2	Moderate (2 yr rate: 5-20%)	Normoglycaemia and age <2 y or with progression score 0.5 – 4.0	6-monthly OGTT, HbA1c, autoantibody profiles
3	High (2 yr rate 50%)	Dysglycaemia (Stage 2)* Or Progression score >4.0	6-monthly OGTT, HbA1c, CGM, 1-2 weekly home self-glucose monitoring
4 (opt out)		-	Random capillary glucose, HbA1c and autoantibody profiles at baseline- Contact every 6 to 12 months

**** Progression score based on IA-2A antibodies, HbA1c, OGTT, CGM**

Aab titers vs time to diabetes progression in first-degree relatives







Cold Spring Harb Perspect Med 2012;2:a012831

nature communications

Article

https://doi.org/10.1038/s41467-024-47918-w

Distinct cellular immune responses in children en route to type 1 diabetes with different first-appearing autoantibodies

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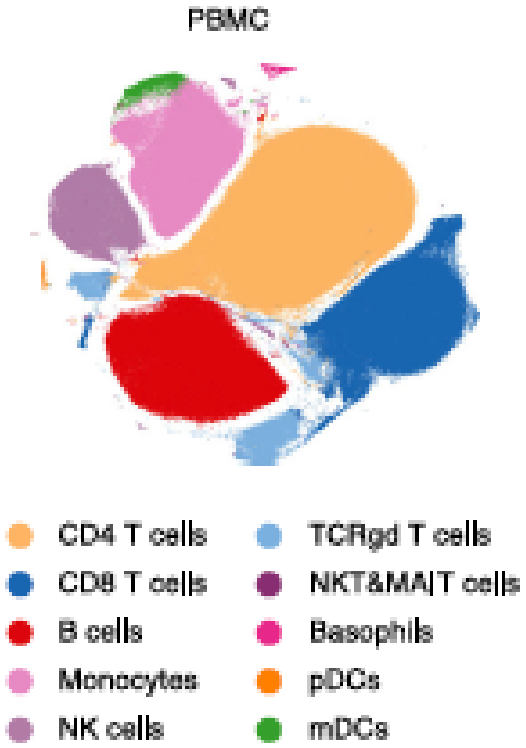
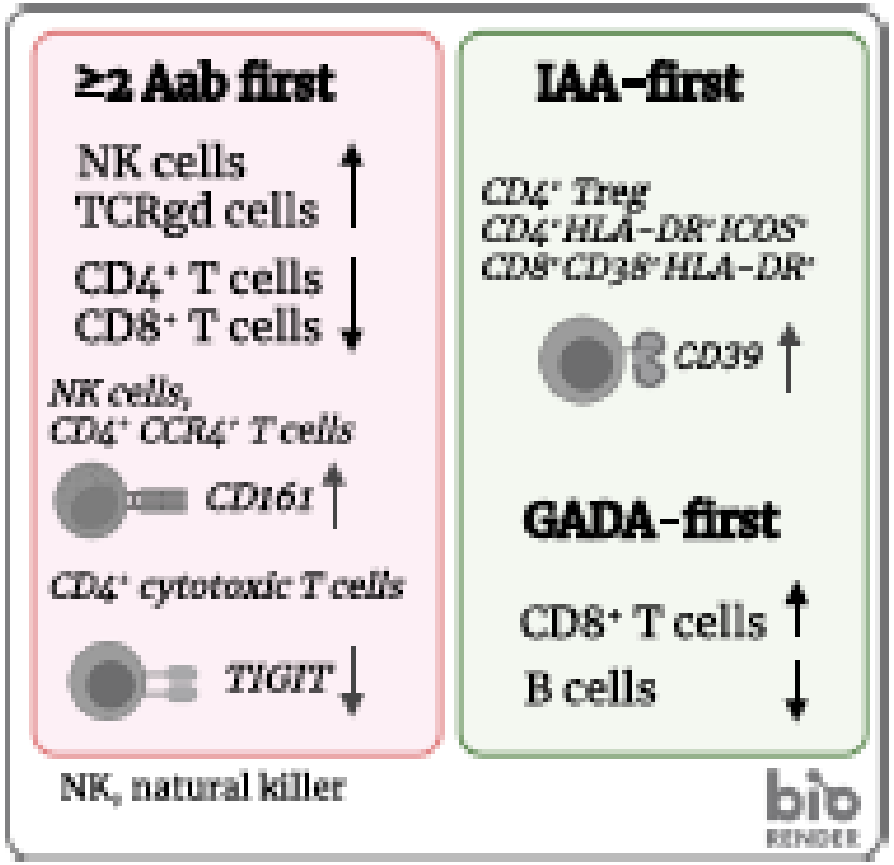
Published online: 07 May 2024

Check for updates

Inna Starskaia[1,2,3,14], Milla Valta[3,4,14], Sami Pietilä[1,2,14], Tomi Suomi[1,2,14], Sirpa Pahkuri[3,4], Ubaid Ullah Kalim[1,2], Omid Rasool[1,2], Emilie Rydgren[1,2], Heikki Hyöty[5], Mikael Knip[6,7], Riitta Veijola[8], Jorma Ilonen[4], Jorma Toppari[2,9,10,11], Johanna Lempainen[4,11,12] ✉, Laura L. Elo[1,2,13] ✉ & Riitta Lahesmaa[1,2,13] ✉





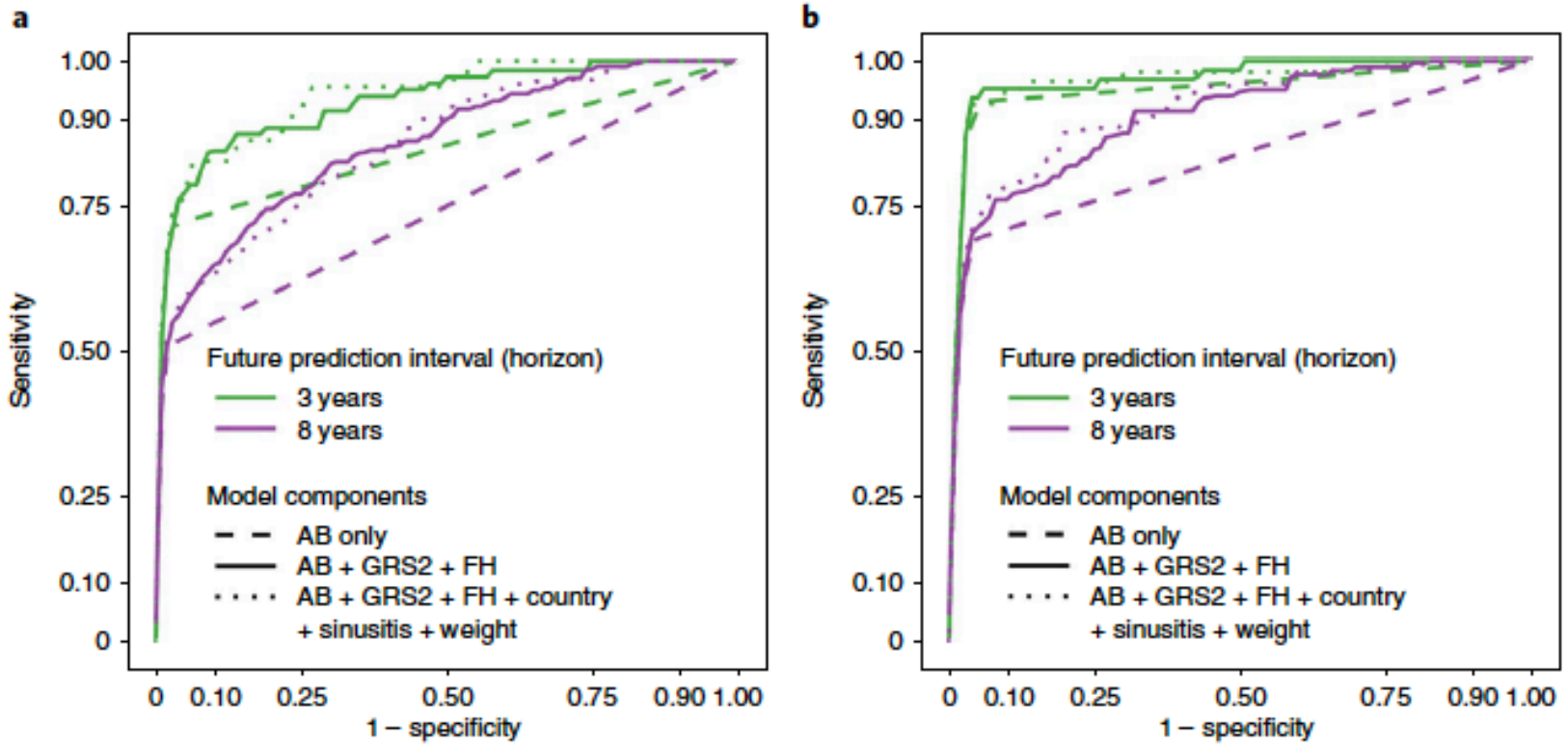
«We identify differences in immune cell composition of children who later develop disease depending on the type of autoantibodies that appear first. Notably, we observe an increase in CD161 expression in natural killer cells of children with ≥ 2 autoantibodies and validate this in an independent cohort»

A combined risk score enhances prediction of type 1 diabetes among susceptible children

Lauric A. Ferrat[1], Kendra Vehik[2], Seth A. Sharp[1], Åke Lernmark[3], Marian J. Rewers[4], Jin-Xiong She[5], Anette-G. Ziegler[6,7,8], Jorma Toppari[9,10], Beena Akolkar[11], Jeffrey P. Krischer[2], Michael N. Weedon[1], Richard A. Oram[1,12,37], William A. Hagopian[13,37] ✉ and TEDDY Study Group*

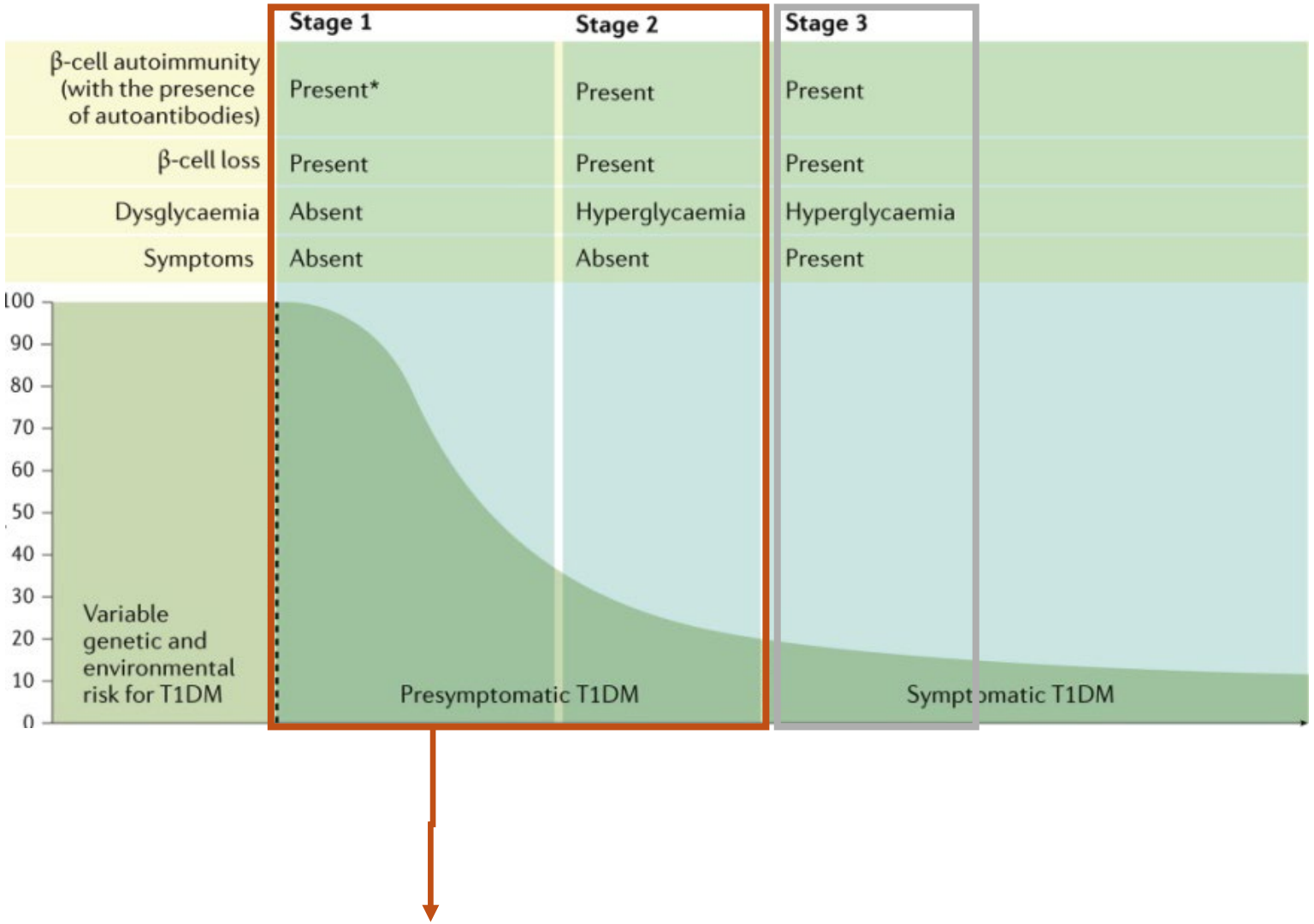
- **Autoanticorpi**
- **Storia familiare**
- **GRS2 (67 SNPs)**

- Nazione
- Sinusite
- Peso



NATURE MEDICINE | VOL 26 | AUGUST 2020 | 1247–1255

Analysis of circulating miRNAs across natural history of T1DM



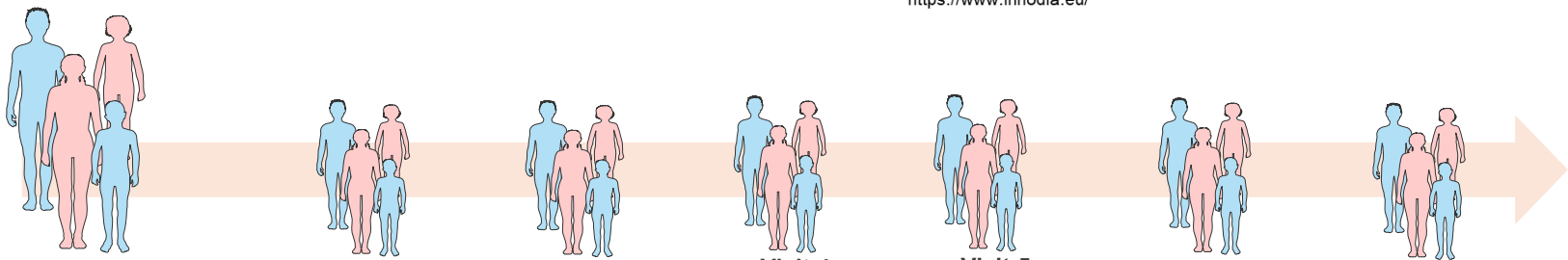
MiRNAs in the prediction of Stage-3 onset in UFM

Circulating miRNAs analysis in UFM Progressor vs Non-Progressor individuals

n=65
UFM Aab+

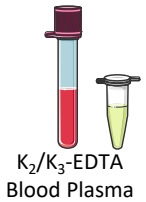
INNODIA Unaffected Family Members (UFM) Cohort
Aab-positive individuals followed up

https://www.innodia.eu/



n=21
Progressors

n=44
Non-Progressors



Small RNA seq → Differential Expression and LASSO model analysis → Cellular specificity using IsomiRDB database

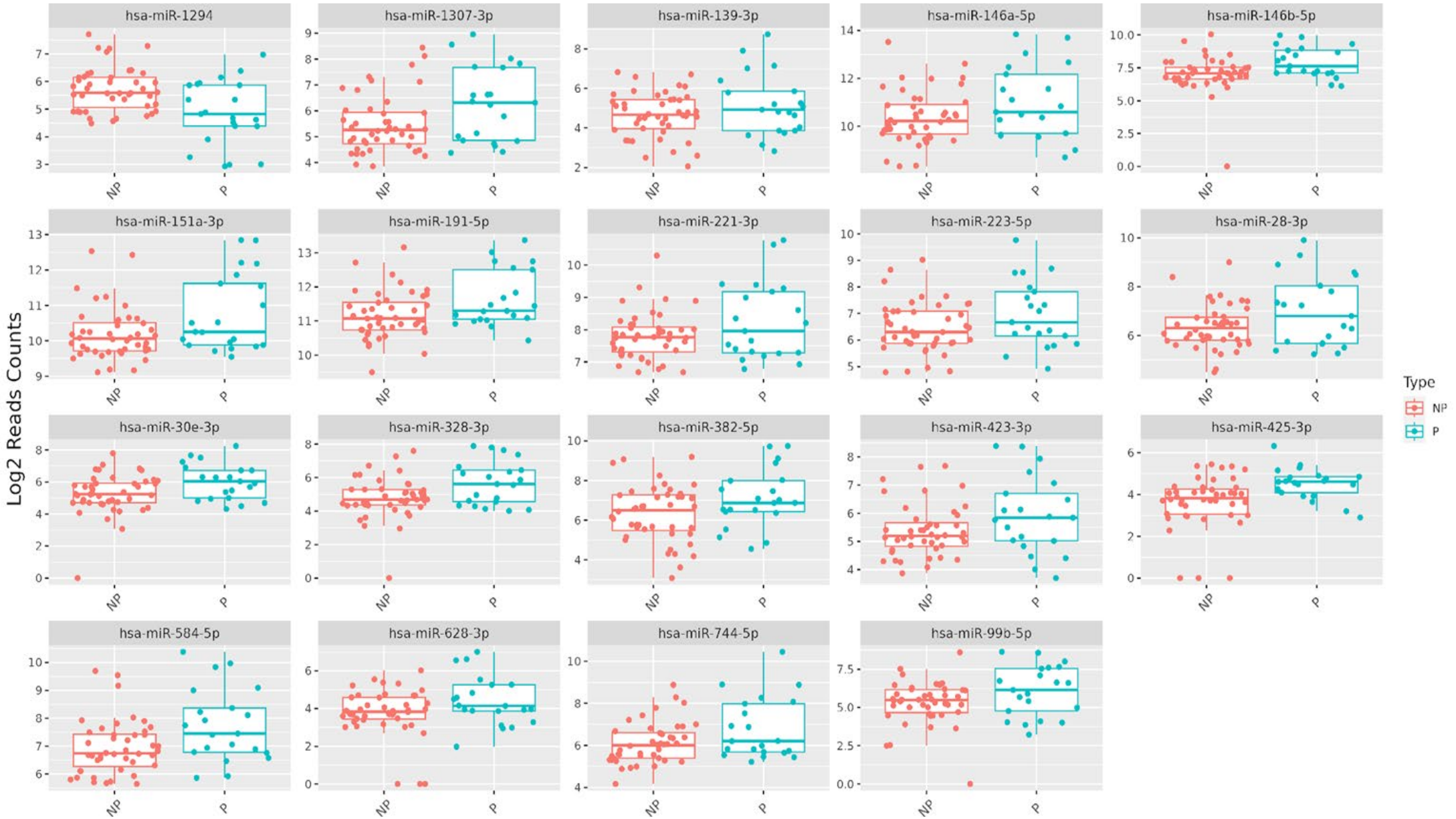
Pedace E. et al., Unpublished

Circulating miRNAs analysis in UFM Progressors vs Non-Progressors individuals

SUBJECT DEMOGRAPHICS								
AAB	1 AAB		2 AAB		3 AAB		4 AAB	
P/NP	UFM Progressor	UFM Non Progressor	UFM Progressor	UFM Non Progressor	UFM Progressor	UFM Non Progressor	UFM Progressor	UFM Non Progressor
n (M/F)	3 (0/3)	9(0/9)	4(4/0)	11(11/0)	7(5/2)	13(8/5)	7(4/3)	11(8/3)
Age [years, mean±SD (range)]	28,3± 13,3 (13-37)	29,0±11,6 (13-38)	14,8± 16,8 (2-39)	15,8±14,7 (2-44)	12,9±2,0 (10-16)	12,8±1,6 (10-16)	8,1±3,7 (3-13)	9,1±4,8 (2-16)
Follow-up [months, mean±SD, (range)]	13,7± 2,8 (10,8-16,3)	30,4±5,8 (24,0-36,4)	21,8± 10,6 (8,7-31,3)	17,4±9,4 (7,6-36,8)	12,4± 7,4 (2,0-21,9)	16,0±8,1 (6,2-35,4)	14,0± 9,1 (5,7-31,2)	19,3±12,6 (2,6-36,1)
Total Progr - Non Progr	3	9	4	11	7	13	7	11
Total	12		15		20		18	
Matching Prog:Non Progr	1:3		1:2,8		1:1,9		1:1,6	

Which MicroRNAs, in addition to a set of clinical parameters, define the progression to T1D in a specific time frame?

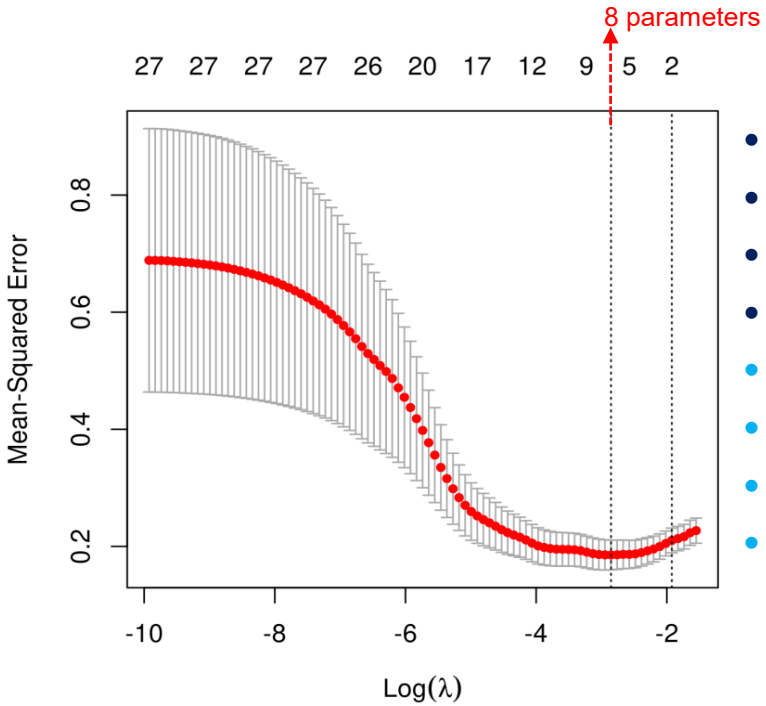
19 circulating miRNAs are differentially expressed between Progressor (P) and Non-Progressors (NP) UFM individuals



DeSeq2 Wald test P<0.05 FDR adjusted, NP vs P (Age, Gender, Aab+ as covariates)

Pedace E et al., Unpublished

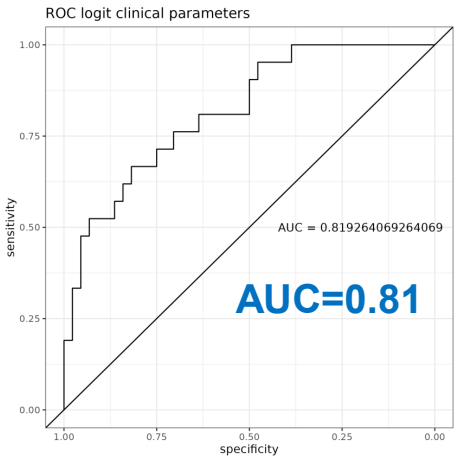
A LASSO model built using clinical parameters and differentially expressed miRNAs prioritizes a composite signature of 8 features to predict Stage-3



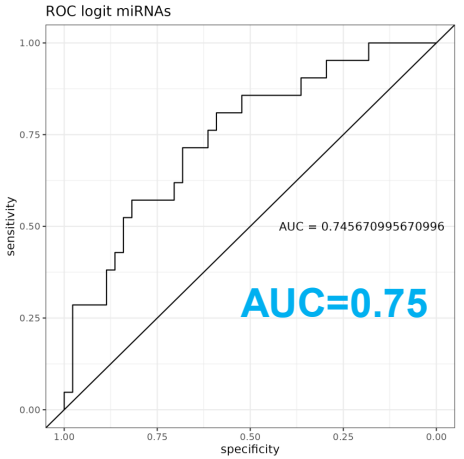
- IA2A titers
- HbA1c
- AUC C-peptide
- AUC Glucose
- miR-1294
- miR-328-3p
- miR-628-3p
- miR-425-3p

Parameters at V1	s0
hba1c_result	6,33E-03
ogtt_auc_c_pep	-3,47E-05
ogtt_auc_glucose	7,46E-02
IA-2A_result_value	1,81E-02
hsa-miR-1294	-1,28E-03
hsa-miR-328-3p	5,16E-04
hsa-miR-628-3p	9,15E-04
hsa-miR-425-3p	5,25E-03

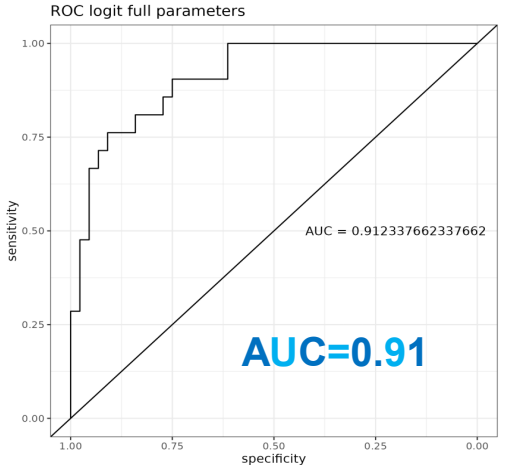
Clinical Parameters



miRNAs



Clinical Parameters + miRNAs



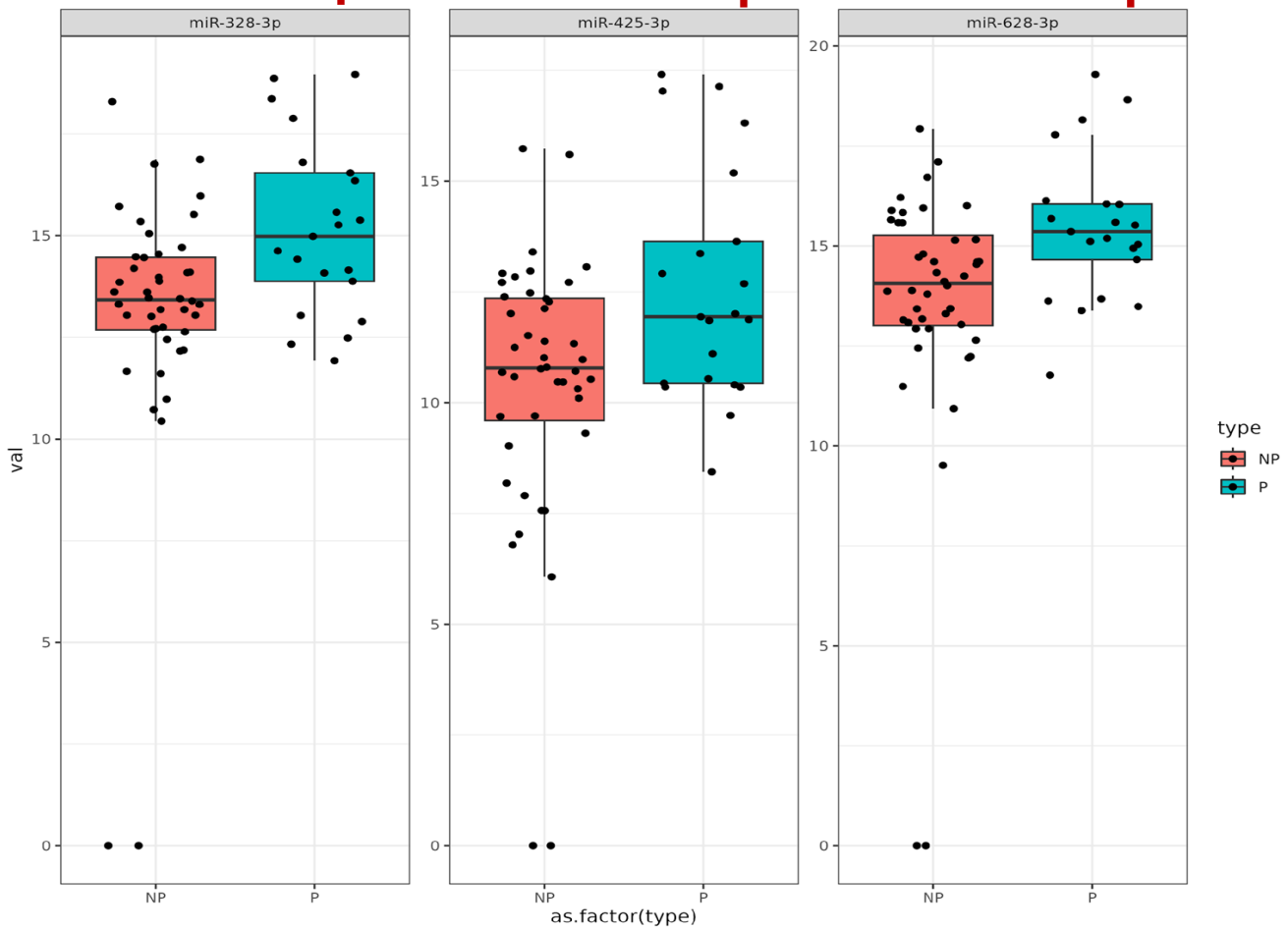
Pedace et al., Unpublished

ddPCR validated miR-328, miR-425 and miR-628 while a cell specificity analysis showed their putative neutrophil-origin

miR-328-3p

miR-425-3p

miR-628-3p



miR-628 and miR-425 are neutrophils-enriched

MATURE NAME	CELL	EXPR	Z SCORE
hsa-miR-1294	Neutrophil	10,33333	5,85
hsa-miR-1294	T Lymphocyte	6,44	3,26
hsa-miR-628-3p	Neuron	63,765	6,41
hsa-miR-628-3p	Neutrophil	45,70667	4,36
hsa-miR-425-3p	Smooth Muscle Cell Vascular	242,34	5,01
hsa-miR-425-3p	Neutrophil	217,8733	4,42
hsa-miR-425-3p	Mononuclear Immune Cell	186,9084	3,67
hsa-miR-425-3p	Platelet	174,0922	3,36
hsa-miR-425-3p	Monocyte	168,1467	3,22
hsa-miR-328-3p	Platelet	1075,553	7
hsa-miR-328-3p	Fibroblast Breast	786,8833	4,96

Pedace et al., Unpublished

SUMMARY

- 19 circulating miRNAs are differentially expressed between UFM progressor and non-progressor
- A LASSO model prioritizes 8 features to predict Stage-3 onset in a specific time-frame
- 4 miRNAs, included in the model, significantly improve the prediction over clinical parameters
- 2 miRNAs (miR-425 and miR-628) are neutrophils-enriched thus being putatively secreted by these innate immune cells

Prevention of T1D – is there potential?

The identification of those at risk for T1D is key to development of potential prevention strategies

Potential primary prevention

Aimed at preventing the autoimmunity against islet autoantigens

Potential secondary prevention

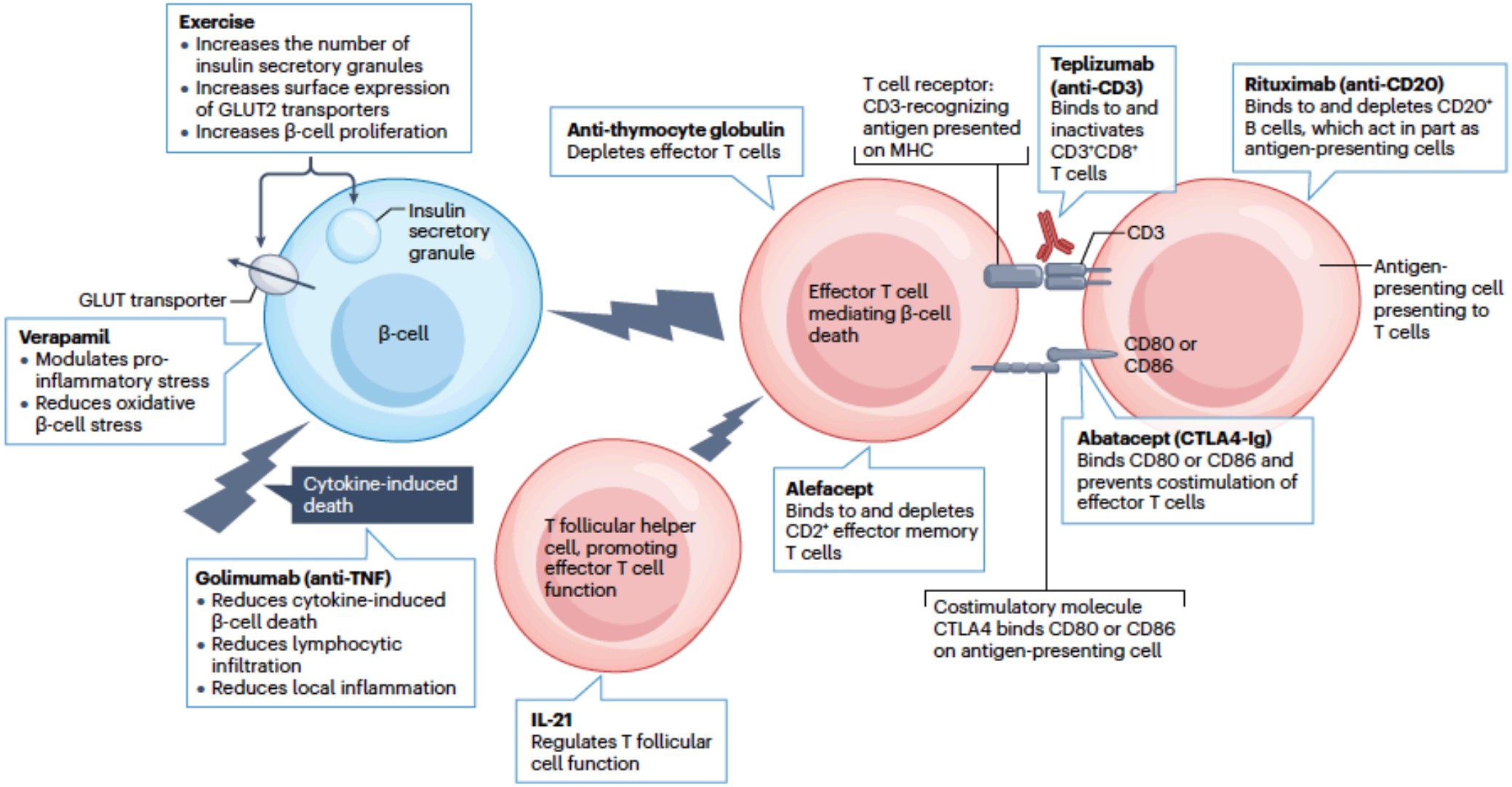
Aimed at halting autoimmunity processes and potentially avoiding the clinical onset of diabetes

Potential tertiary prevention

Attempting to reduce or minimize the complications associated with T1D

Primavera M, et al. Front Endocrinol (Lausanne) 2020;11:248.

Sites of action of therapeutic interventions for β-cell preservation.



Moving towards treating the autoimmune process: Example of 12 immunobiologics licensed for psoriasis

Anti-TNF
- Infliximab
- Etanercept
- Adalimumab
- Certolizumab

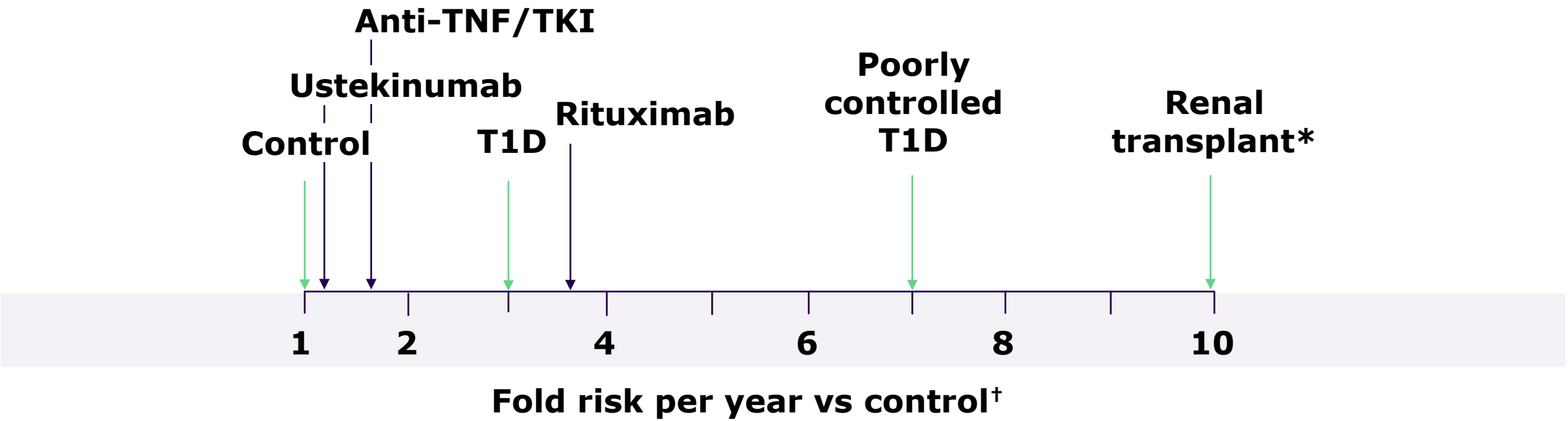
Anti-IL-12/IL-23
- Ustekinumab

Anti-IL-17
- Ixekizumab
- Secukinumab
- Brodalumab (IL-17RA)
- Bimekizumab

Anti-IL-23p19
- Guselkumab
- Risankizumab
- Tildrakizumab

Therapies included on this slide are approved for use in psoriasis in the EU. Please refer to individual SmPCs for further prescribing information.
Smith CH, et al. British Journal of Dermatology 2020;183:628–37; Van der Kraaij GE, et al. Br J Dermatol 2019;180:31.

Summary of risk of hospitalization for infection



T1D and glycemic control: *Balintescu et al 2023[1]; Simonsen et al 2015[2]; Carey et al 2018[3]*
Renal transplant: *Dharnidharka et al 2007[4]*
Psoriasis/Arthritis and biologics : *Davila-Seijo et al[5]; Jin et al 2021[6]*
IBD and biologics: *Singh et al 2020[7]; Cheng et al 2022[8]*

*Only a proportion of renal transplant patients had diabetes. †Subjects without diabetes.

1. Balintescu, et al. Diabetes Obes Metab 2023;25:1942–49; 2. Simonsen JR, et al. BMJ Open Diabetes Research & Care 2015;3:e000067;
3. Carey IM, et al. Diabetes Care 2018;41:513–21; 4. Dharnidharka VR, et al. American Journal of Transplantation 2007;7:653–61.

The NEW ENGLAND JOURNAL of MEDICINE

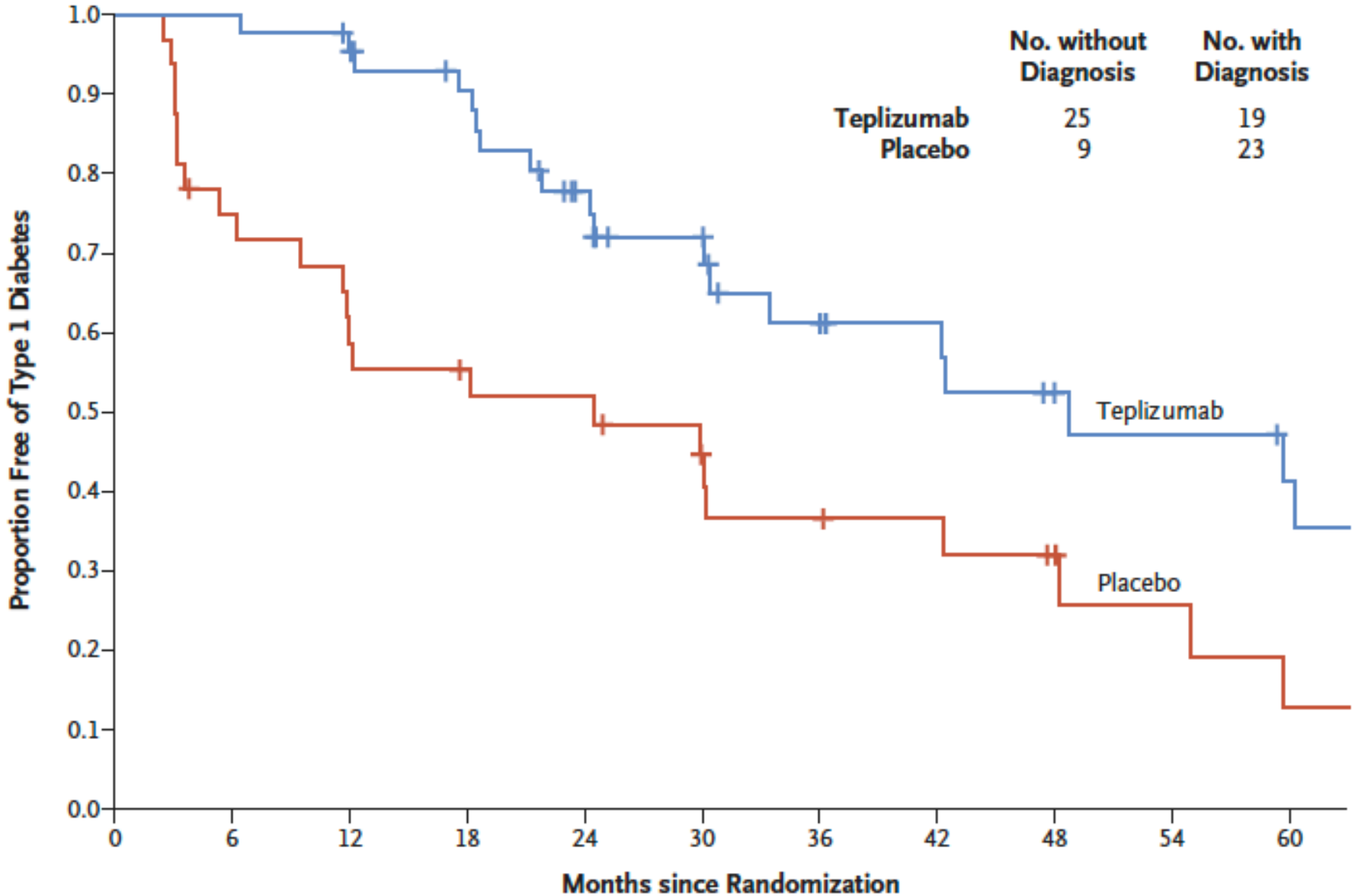
ORIGINAL ARTICLE

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

Kevan C. Herold, M.D., Brian N. Bundy, Ph.D., S. Alice Long, Ph.D., Jeffrey A. Bluestone, Ph.D., Linda A. DiMeglio, M.D., Matthew J. Dufort, Ph.D., Stephen E. Gitelman, M.D., Peter A. Gottlieb, M.D., Jeffrey P. Krischer, Ph.D., Peter S. Linsley, Ph.D., Jennifer B. Marks, M.D., Wayne Moore, M.D., Ph.D., Antoinette Moran, M.D., Henry Rodriguez, M.D., William E. Russell, M.D., Desmond Schatz, M.D., Jay S. Skyler, M.D., Eva Tsalikian, M.D., Diane K. Wherrett, M.D., Anette-Gabriele Ziegler, M.D., and Carla J. Greenbaum, M.D., for the Type 1 Diabetes TrialNet Study Group*

N Engl J Med. 2019 August 15; 381(7): 603–613.

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes



Considerations for improving intervention trials in type 1 diabetes

- Combination therapies (combined at onset)
- Sequential therapies (induction and maintenance)
- Concepts for retreatment with primary agents
- Long-term safety considerations for retreatment with primary agents
- Identification of biomarkers that would suggest when retreatment would be needed or beneficial
- Cost-effectiveness
- Patient choice and autonomy
- Address the challenge of competing interests for pharmaceutical entities in settings of combination therapy

www.thelancet.com/diabetes-endocrinology Published online October 3, 2023

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SANOFI

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Turku team

Riitta Lahesmaa

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Shari Messinger (Miami, USA)

INNODIA Team Science, T1D subjects and their families

STRATEGIA, METODI e COSTI

Risultati di stidi epidemiologici e di screening suggeriscono il test a tre punti tra 1 e 18 anni:

- Tra i 2 e i 5 anni,
- tra i 7 e i 9 anni
- tra i 12 e i 14 anni

- Screening capillare con kit 3Screen e successiva determinazione autoanticorpale su siero in tutti i positivi (3/4 saranno single-Ab+)

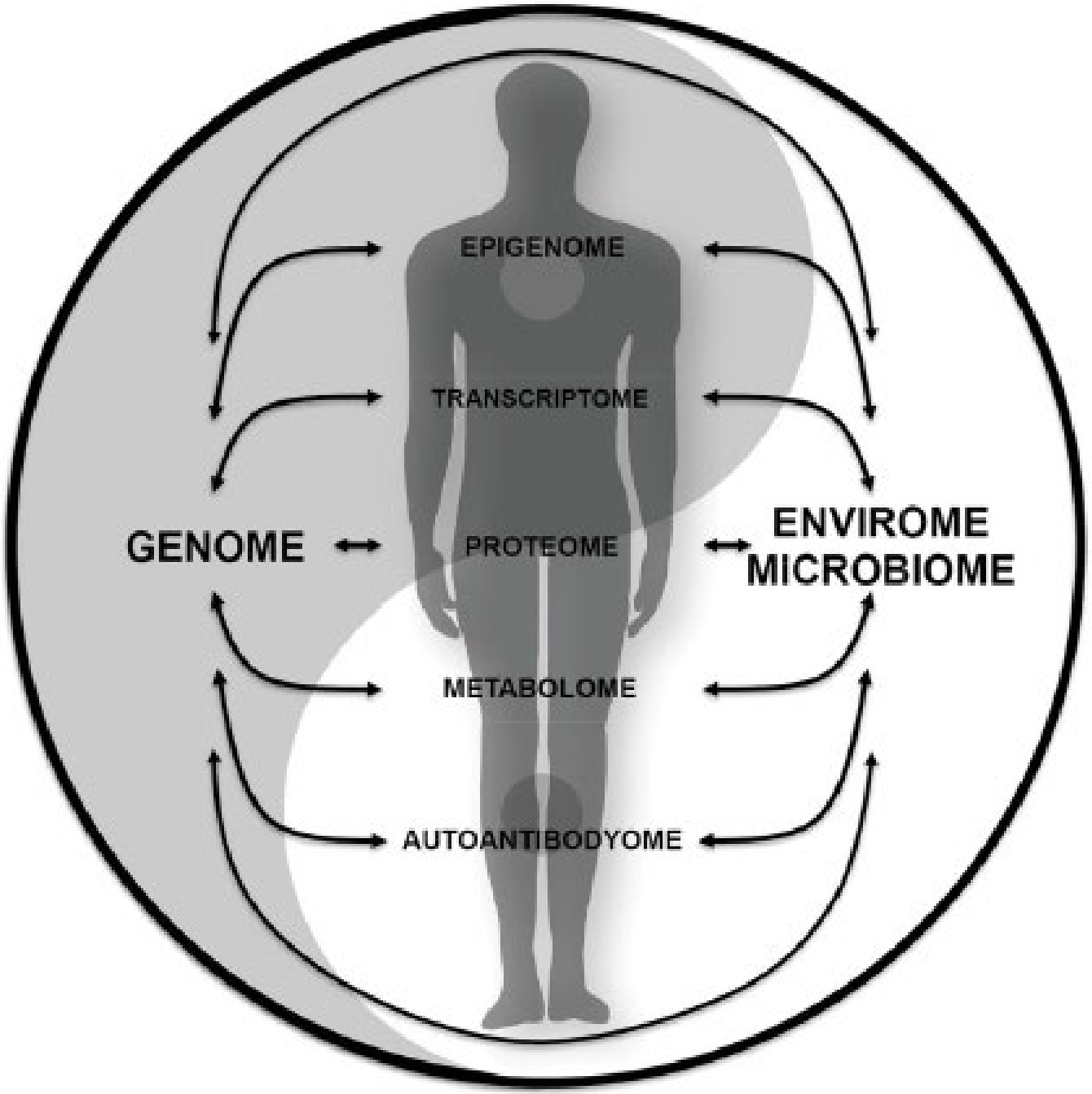
OPPURE

- Screening capillare con kit CLIA (Enable Bioscince) con immediata identificazione dei double-positive

- Costi per lo screening (spese personale) **13€/ campione**

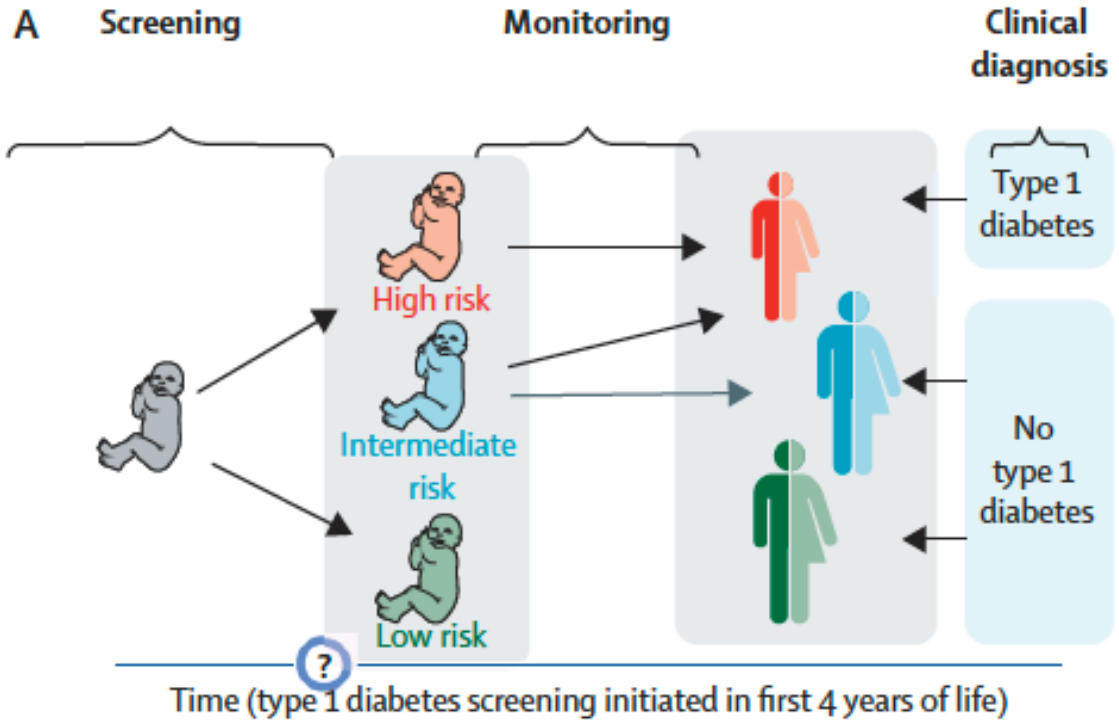
- Costi per il test di screening capillare su Kit ELISA (3Screen, RSR) **10€/campione**
- Costi per il test di screening capillare su Kit CLIA (Enable Biosciences) **??€/campione (50-70€?)**

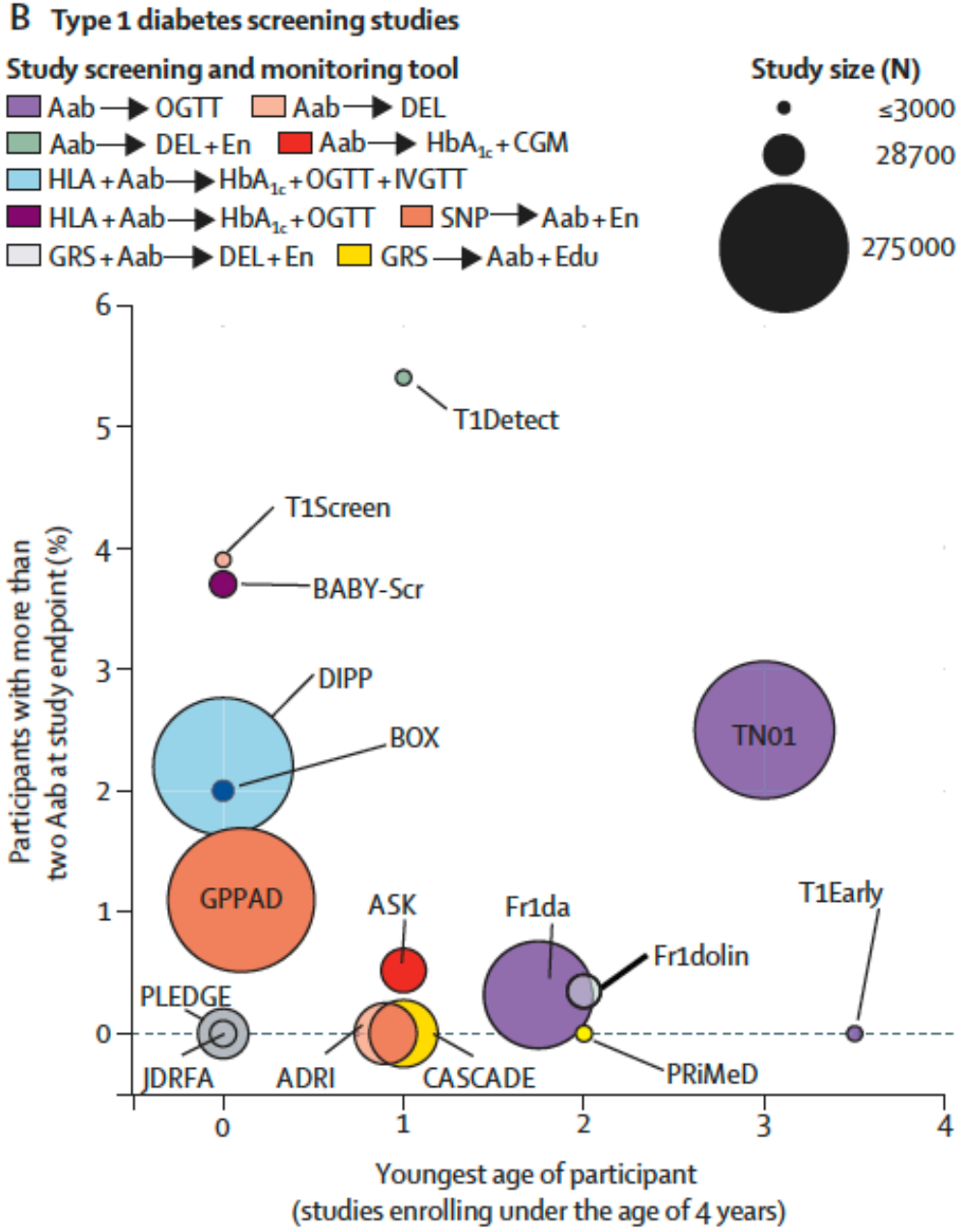
- Costi per la misurazione della validazione su siero Kit ELISA (RSR): 16€/campione/Autoab; Totale: **48€/campione**



Prediction of progression to type 1 diabetes with dynamic biomarkers and risk scores

Mugdha V Joglekar*, Simranjeet Kaur*, Flemming Pociot, Anandwardhan A Hardikar





Lancet Diabetes Endocrinol 2024
Published Online May 23, 2024
https://doi.org/10.1016/ S2213-8587(24)00103-7

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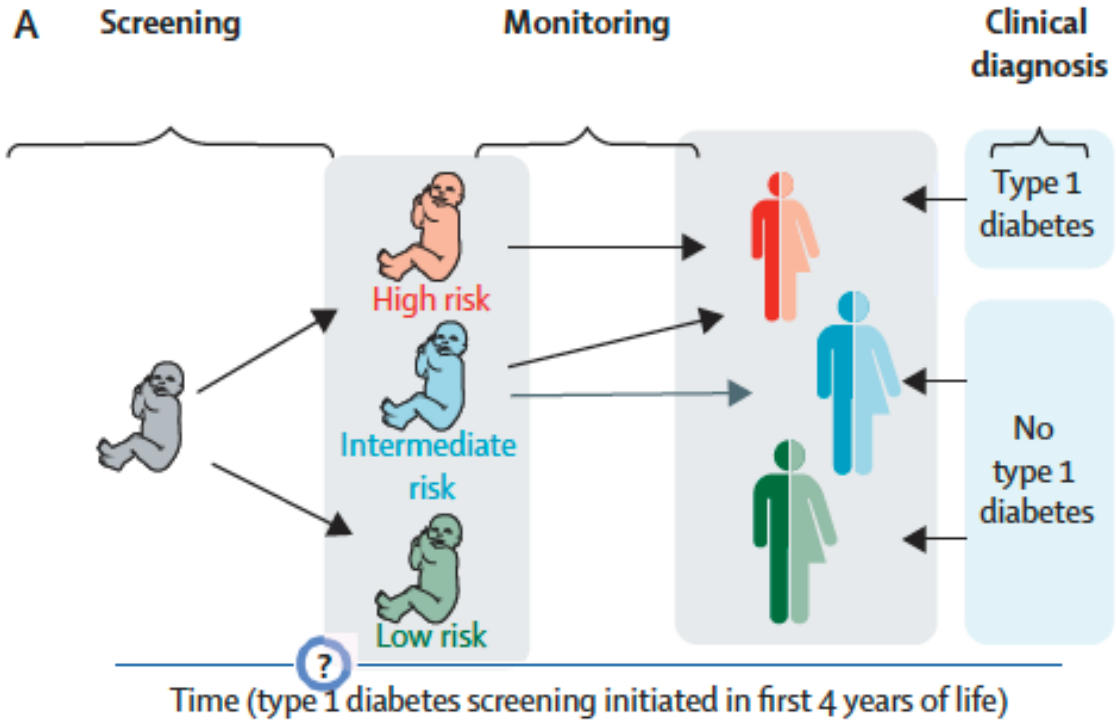
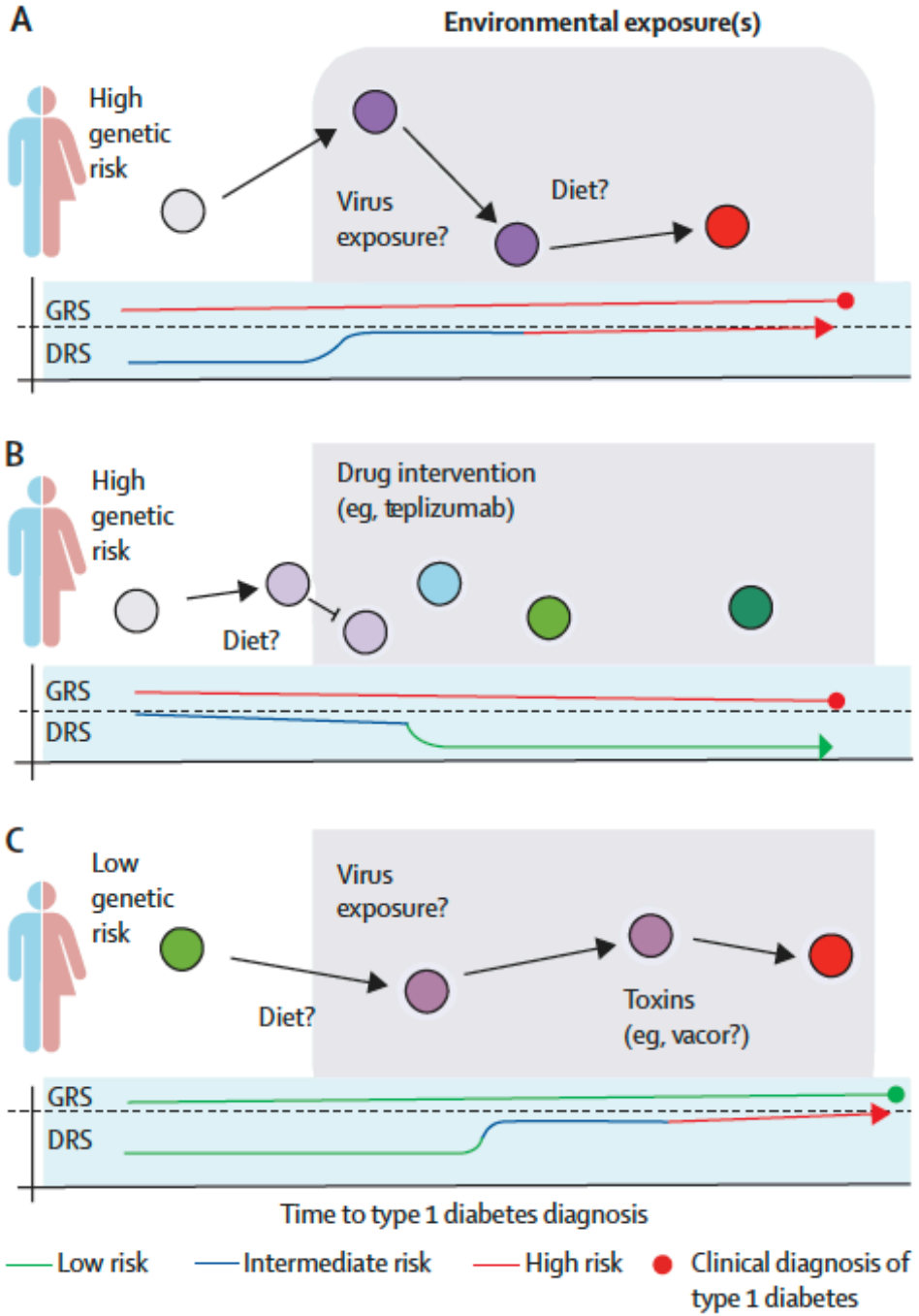




Lancet Diabetes Endocrinol 2024
Published Online May 23, 2024
https://doi.org/10.1016/ S2213-8587(24)00103-7

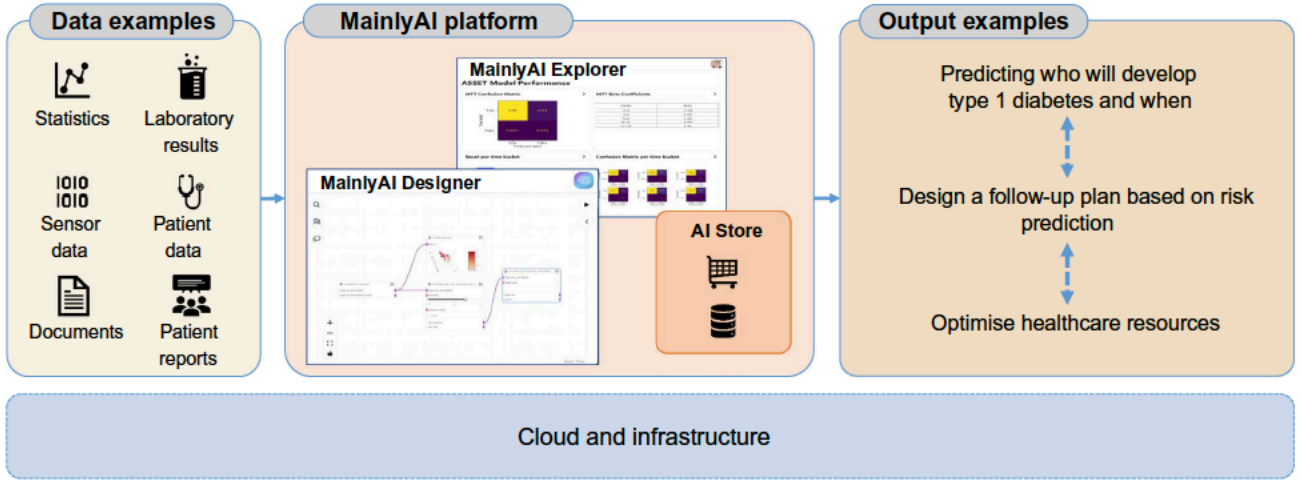
European Diabetes Forum Italia

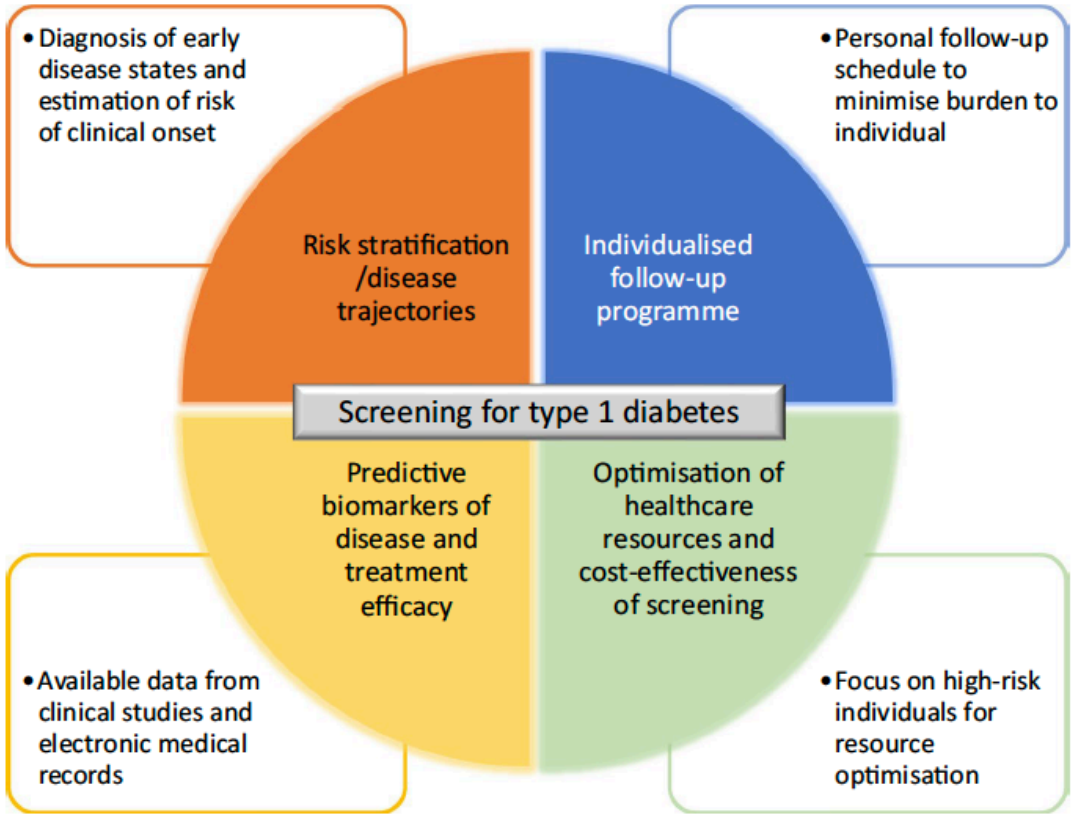
Disposizioni concernenti la definizione di un programma diagnostico per l'individuazione del diabete di tipo 1 e della celiachia nella popolazione pediatrica (n. 727)

Programma pluriennale di screening su base nazionale nella popolazione pediatrica, da avviare a decorrere dall'anno 2024 per l'individuazione degli anticorpi del diabete di tipo 1 e della celiachia, finalizzato al 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, oltre che ottenere diagnosi precoci della celiachia.

Assisting the implementation of screening for type 1 diabetes by using artificial intelligence on publicly available data

Pedro F. Teixeira[1] · Tadej Battelino[2,3] · Anneli Carlsson[4] · Soffia Gudbjörnsdottir[5,6] · Ulf Hannelius[1] · Matthias von Herrath[7,8] · Mikael Knip[9,10] · Olle Korsgren[11,12] · Helena Elding Larsson[4,13] · Anton Lindqvist[1] · Johnny Ludvigsson[14] · Markus Lundgren[15,16] · Christoph Nowak[1] · Paul Pettersson[17,18] · Flemming Pociot[19,20] · Frida Sundberg[21,22] · Karin Åkesson[23,24] · Åke Lernmark[4] · Gun Forsander[21,22]





Diabetologia (2024) 67:985–994

Treating type 1 diabetes mellitus before insulin is needed

Table 1 | Proposed subclassification of stage 3 T1DM

Stage	Insulin requirement	Clinical features
Stage 3a	Early T1DM not requiring insulin	Not insulin-requiring; random C-peptide >600 pmol/l; HbA_{1c} 6.4–7.0% (47–53 mmol/mol) without insulin; very low ketosis risk; no hypoglycaemic risk; immunotherapy and/or β-cell-preserving therapy appropriate
Stage 3b	Requiring insulin, but clinically relevant β-cell function remains	Insulin-requiring; random C-peptide 200–600 pmol/l; immunotherapy and/or β-cell-preserving therapy appropriate; moderate ketosis and hypoglycaemia risk
Stage 3c	Requiring insulin and no clinically significant β-cell function	Random C-peptide <200 pmol/l; advanced insulin therapy and/or β-cell replacement required; high ketosis and hypoglycaemia risk

Possible criteria for the timing of introducing insulin in stage 3a type 1 diabetes mellitus

C-peptide level
- Non-fasting <600 pmol/l

Glycaemic control
- HbA_{1c} >53 mmol/mol (7%)
- Frequent home postprandial blood levels of glucose >8 mmol/l
- Time above 8 mmol/l on a continuous glucose monitor is >10%

Diabetic ketoacidosis risk
- Episode of ketosis or ketoacidosis
- Persistent home blood levels of ketones of >0.6 mmol/l

Clinical symptoms
- Weight loss
- Reduced exercise performance
- Intercurrent illness, pregnancy, nausea or vomiting

Nature Reviews Endocrinology | Volume 19 | June 2023 | 361–370