

50th Anniversary



ISPAD 20

ON, PORTUGAL | OCTOBER

ion & Innovation in Pediatrics

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ISPAD 2024: Nuevas perspectivas

27 de noviembre 2024



Este evento está dirigido a profesionales de la salud de Argentina, facultados para prescribir

AGENDA



18 a 18:05	Bienvenida y presentación de agenda	Carolina Salvioli
18:05 a 18:20	Nuevos horizontes en diabetes tipo 1	Liliana Trifone
18:20 a 18:35	Experiencias Internacionales en implementación de la detección temprana de la diabetes	Carolina Martinez Mateu
18:35 a 18:55	Puesta al día en terapias automatizadas	Marcela Raggio
18:55 a 19:15	¿Qué hay de nuevo en diabetes tipo 2?	Adriana Roussos
19:15 a 19:35	La educación a través de las distintas etapas de la diabetes	Florencia Grabois
19:35 a 19:45	TRIVIA ¿Qué sabemos de las insulinas de 2da generación?	Carolina Salvioli
19:45 a 20	Q&A - Cierre & Conclusiones	Todo el panel



Disertantes



**Liliana
Trifone**

- Médica Pediatra SAP
- Especialista en Nutrición UBA
- Especializada en Diabetes
- Ex Jefa de Nutrición y Diabetes Hospital de Niños R. Gutiérrez
- Directora de Posgrado en Nutrición Pediátrica UBA



**Carolina
Martinez Mateu**

- Médica pediatra
- Especialista en Nutrición Infantil
- Equipo Multidisciplinario de Diabetes Hospital J. P. Garrahan
- Docente de la Carrera de Especialistas en Nutrición Pediátrica de Universidad de Bs As.



**Marcela
Raggio**

- Médica pediatra
- Especialista en nutrición infantil (UBA)
- Magister en Diabetes (USAL)
- Médica de staff Nutrición infantil Htal Universitario Austral y HMIT (Hospital Materno Infantil Tigre)
- Coordinación Módulo de pediatría Maestría diabetes SAD
- Docente Maestría de diabetes Universidad Austral



**Adriana
Roussos**

- Médica pediatra
- Especialista en Nutrición.
- Jefa Sección Nutrición y Diabetes, Hospital de Niños R. Gutiérrez, CABA.
- Docente adscripta UBA, Pediatría.
- Docente de posgrado UBA, USAL, Barceló.



**Florencia
Grabois**

- Médica pediatra
- Especialista en Nutrición Infantil UBA
- Docente de medicina Infantil UNCO
- Educadora Certificada en Diabetes UNSAM
- Hospital Provincial Neuquén
- Comité de Pediatría SAD
- Comité de Educación SAD



ISPAD's 50th Annual Conference

Lisbon, Portugal | October 16 - 19, 2024

Nuevos Horizontes en Diabetes tipo 1 **#ISPAD50**

Dra Liliana Trifone

consulta.ltrifone@gmail.com





Trifone Liliana

- Médica Pediatra SAP
- Especialista en Nutrición UBA
- Especializada en Diabetes
- Ex Jefa de Nutrición y Diabetes Hospital de Niños R. Gutiérrez
- Directora de Posgrado en Nutrición Pediátrica UBA

Conflictos de interés:

- Disertante: Elli Lilly, Novo Nordisk, Sanofi, Medtronic
- Asesor: Sanofi, Elli Lilly, Novo Nordisk
- Investigación: Sanofi, Novo Nordisk, Medtronic

Inteligencia Artificial en Diabetes

Tratamiento de la Diabetes

Esperanza y promesas por delante

VISIÓN INNOVADORA
DE LA DT1

Detección de DT1

Nuevas

Plantas de seguimiento



CGM vs OGTT

Cambio de Paradigma

Consenso y nuevas guías de monitoreo

Revolucionando el Cuidado
De la DT1

Terapias de Vanguardia

*Nuevos Biomarcadores en
Predicción de DT1*

**TERAPIA CELULAR EN DT1
HACIA PRÁCTICA CLÍNICA**

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Vision: Type 1 Diabetes Therapies on the Horizon

Sanjoy Dutta, Ph.D.
Chief Scientific Officer



Simposio conjunto **Breakthrough T1D**
(anteriormente JDRF)-ISPAD: Tratamientos
para la diabetes tipo 1 (DT1):
Esperanza y promesas por delante

To accelerate life-changing breakthroughs to cure, prevent, and better treat type 1 diabetes and its complications.



Sanjoy Dutta



Loredana Marcoveccio

Cell Therapy for T1D: Gearing up
toward Clinical Practice



Tabitha Randall

Prevención e Intervención
en Diabetes tipo 1



Michaels Rickets



Chantal Mathieu



Colin Dayan



Kimberly Simmons

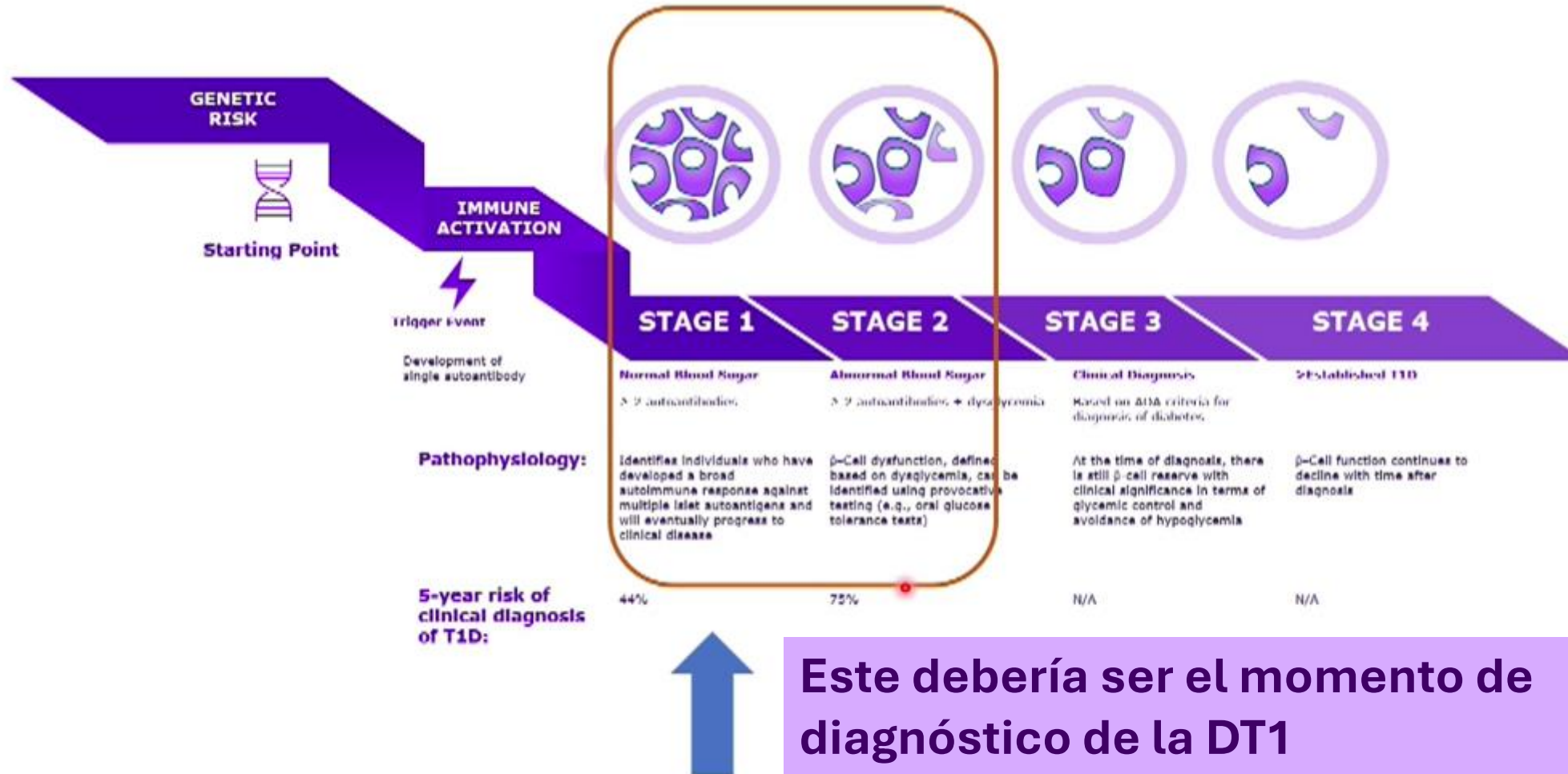
Hay una oportunidad de tratamiento para cada estadio de la DT1

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DT1: Tiempo de cambio



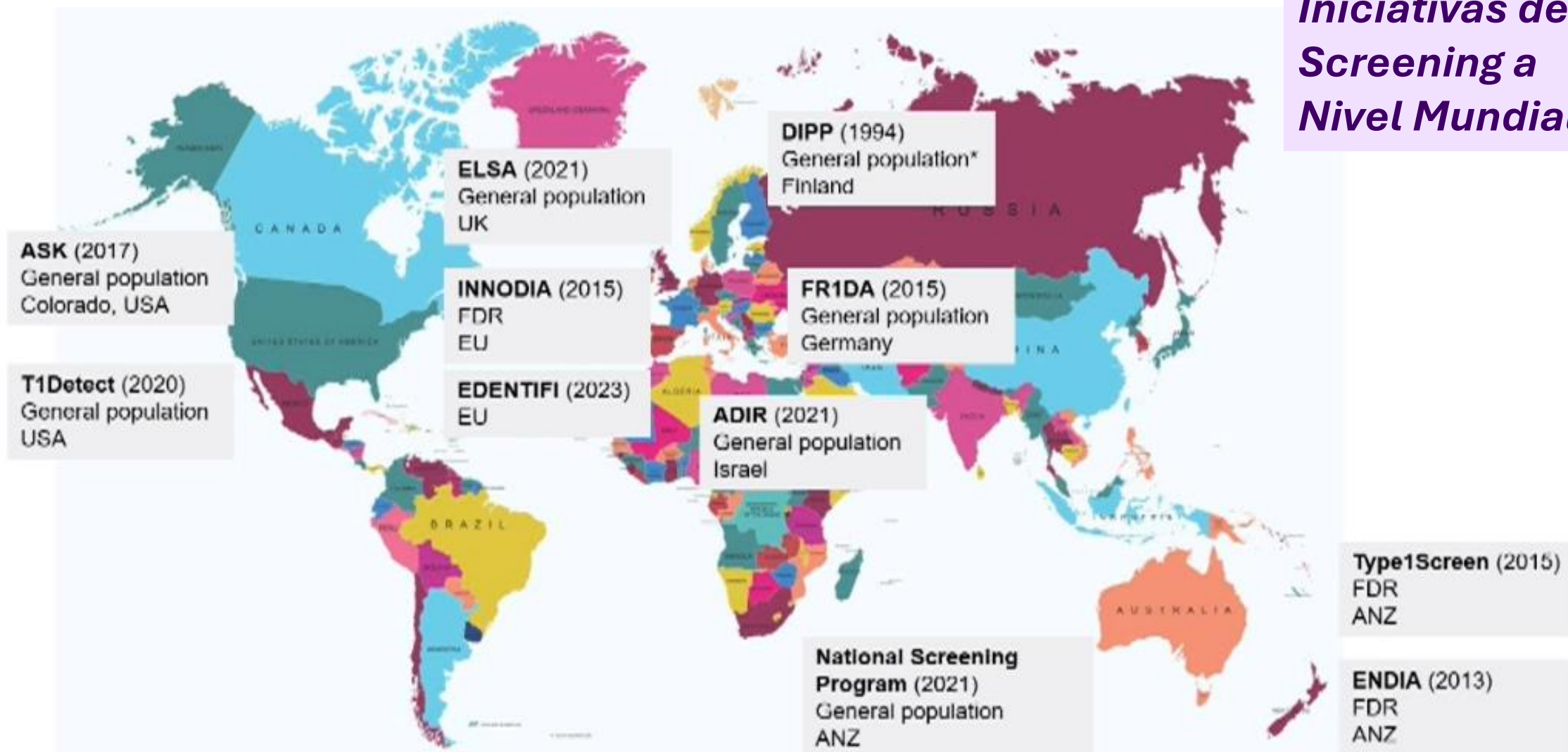
Chantal Mathieu



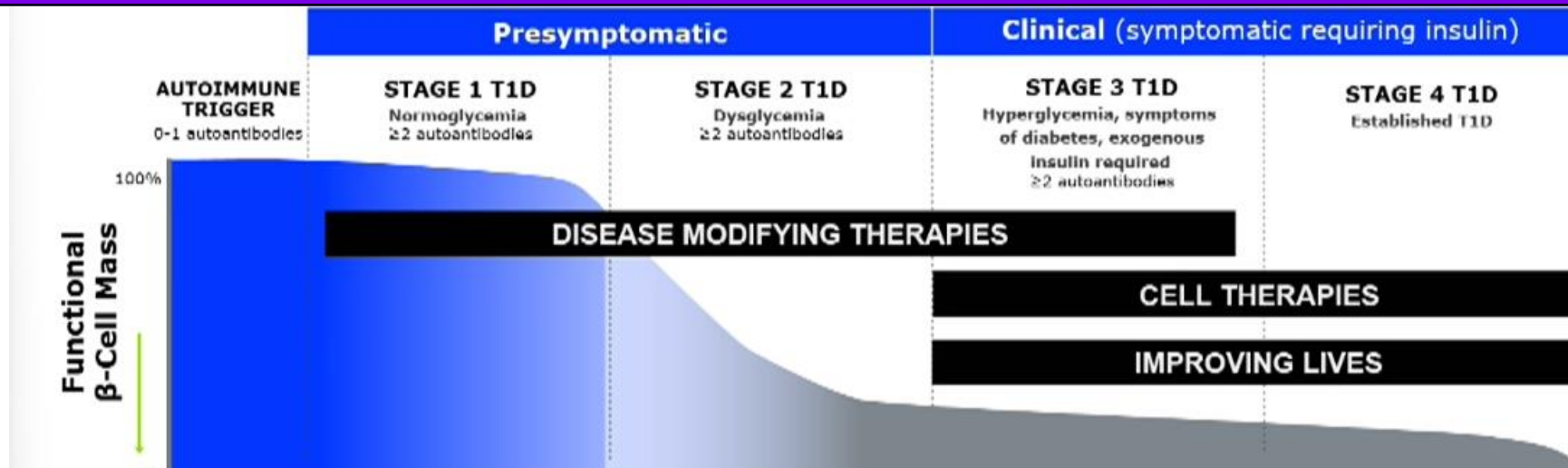
Sims EK, et al. Diabetes 2022;71:610-3; Besser RE, et al. Pediatr Diabetes 2022;23:1175-87

La detección temprana de la DT1 tiene beneficios inmediatos y a largo plazo

Iniciativas de Screening a Nivel Mundial



Misión Estratégica 2030: Crear estrategias focalizadas y prioritarias en todas las iniciativas de investigación hacia la cura de la Diabetes.



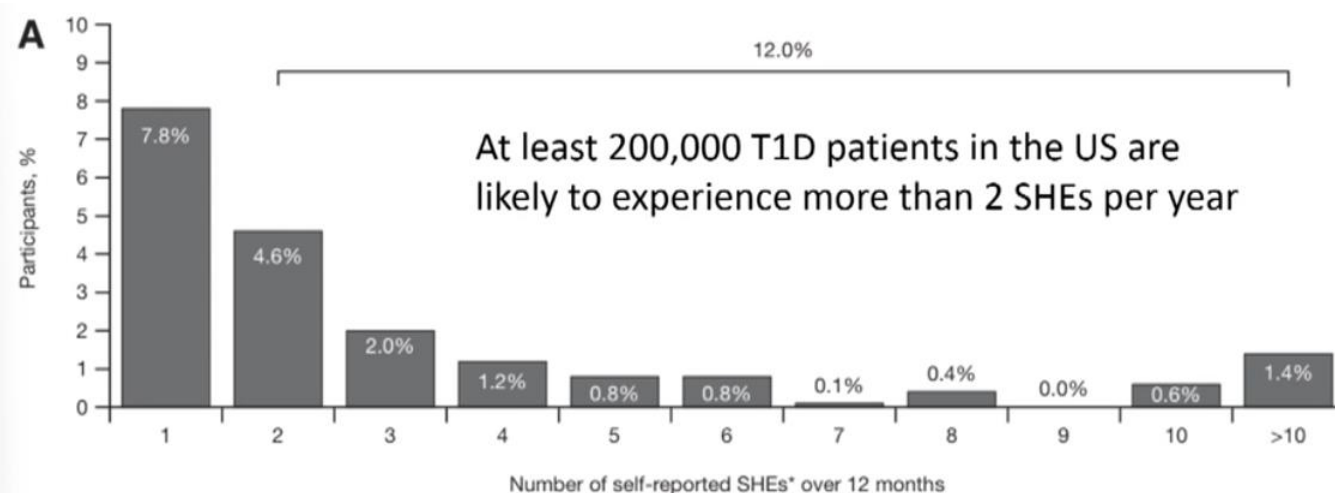
Objectives	Cure		Improve Lives
	Restore Insulin Independence	Delay and ultimately prevent T1D	Improve outcomes + reduce burden
Strategic Initiatives	Cell therapies	Disease modifying therapies	Devices
			Drugs
			Psychosocial
			Complications
			Global responsibility



Severe Hypoglycemia and Impaired Awareness of Hypoglycemia Persist in People With Type 1 Diabetes Despite Use of Diabetes Technology: Results From a Cross-sectional Survey

Jennifer L. Sherr, Lori M. Laffel, Jingwen Liu, Wendy Wolf, Geoffrey Bispham, Katherine S. Chapman, Daniel Finan, Lina Titievsky, Tina Liu, Kaitlin Hagan, Jason Gaglia, Keval Chandarana, Richard Bergenstal, and Jeremy Pettus

Diabetes Care 2024;47(6):941–947 | <https://doi.org/10.2337/dc23-1765>



Key results

Only **57.7%** of all respondents reported achieving target HbA_{1c} <7%

~**20%** of all respondents reported having **≥1 SHEs in past 12 months** including CGM users (16.6% of A1D users, 19% of pump users, and 23% of MDI users)

12% of respondents had **≥2 SHEs** in previous 12 months

Approximately **one-third** of all respondents reported **IAH in past 12 months**, regardless of CGM or A1D usage



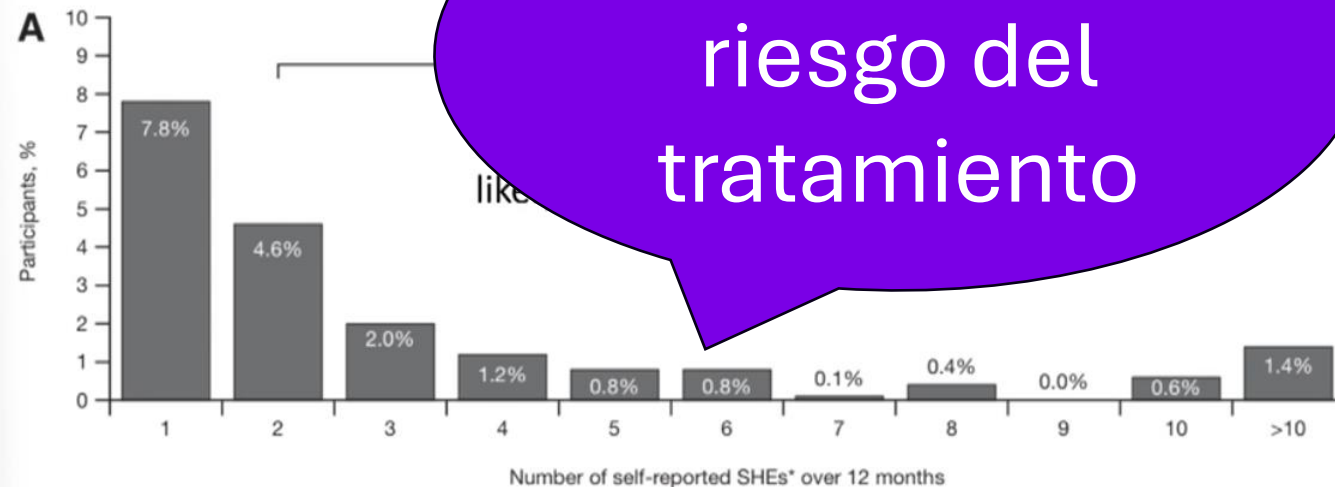
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Diabetes Care 2024;47(6):941–947 | <https://doi.org/10.2337/dc23-1771>



Gran carga y riesgo del tratamiento



Key results

Only **57.7%** of all respondents reported achieving target HbA_{1c} <7%

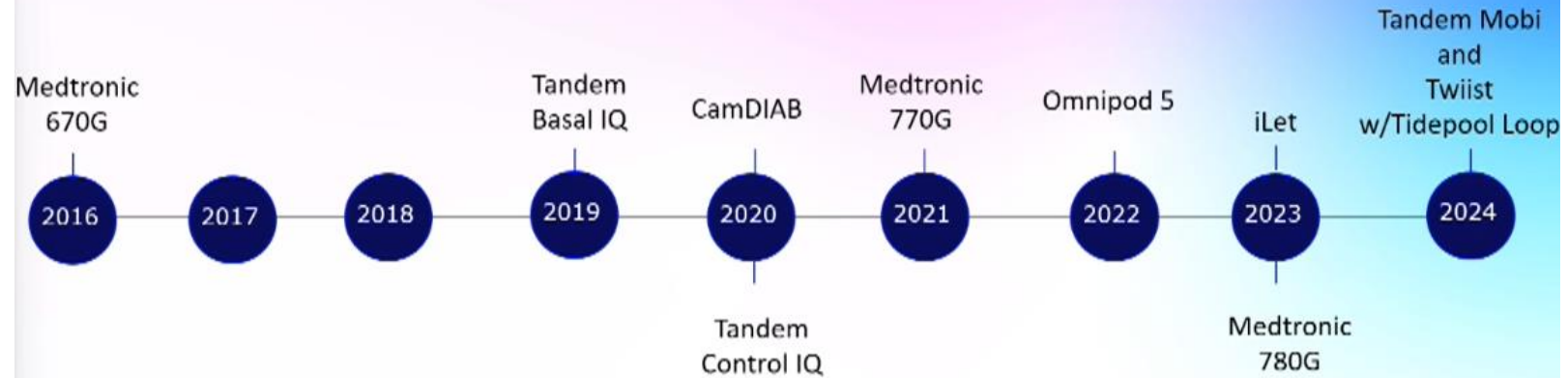
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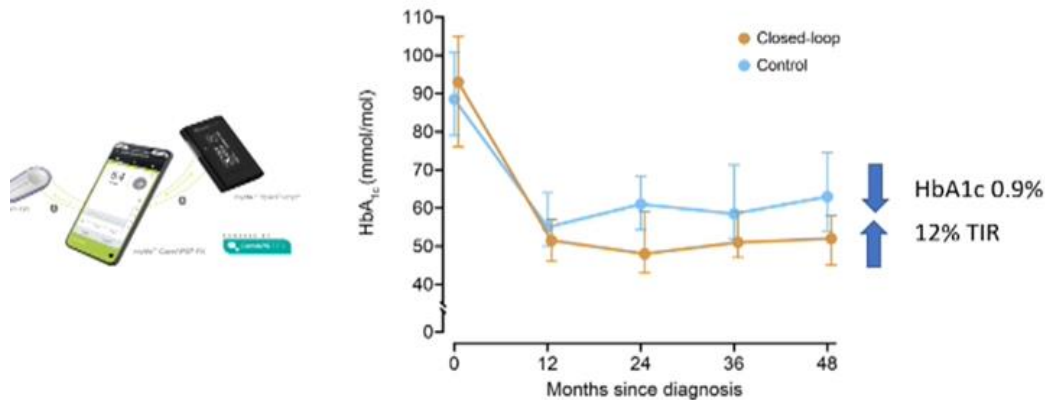
Approximately **one-third** of all respondents reported **IAH in past 12 months**, regardless of CGM or A1D usage



An explosion of AID systems



Are advanced technologies good enough?



¿Son suficientes estos tratamientos desde el inicio en conservación de función celular β ?

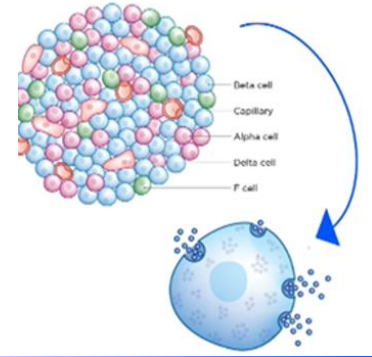
59% meet ADA target <7% (53mmol/mol)
34% meet ISPAD target <6.5% (48mmol/mol)

re et al CLOuD Diab Care 2024

Restaurar la Producción de Insulina:

Terapias celulares

Objetivo: prevenir, detener o revertir la pérdida funcional de célula β



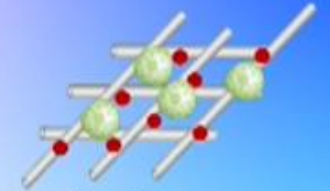
Our strategy: multiple approaches

Encapsulation



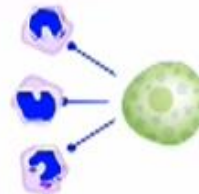
Physical barrier blocks immune attack while ensuring cell survival and function

Scaffolds



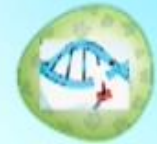
Engineered local environment keeps cells alive – multipurpose platform

Immune Modulation



Locally delivered drugs alter immune response, allowing cells to thrive

Gene Editing



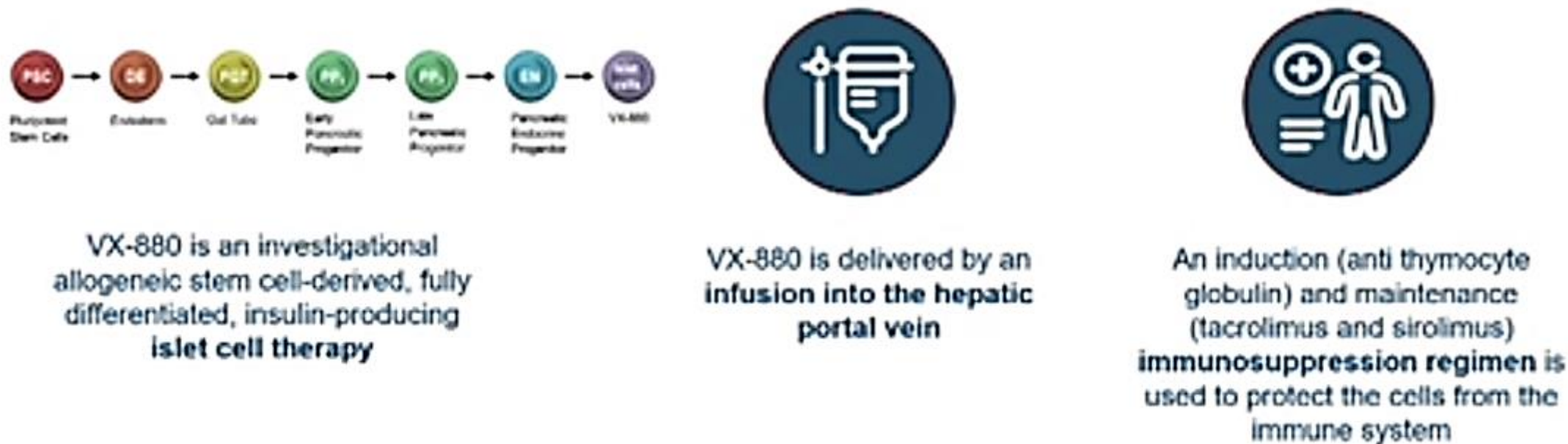
Engineered cells to confer immune evasion and enhance survival



Nueva fuente celular para la terapia con células de los islotes en desarrollo clínico para la diabetes tipo 1 complicada por hipoglucemia grave



Michael
Ricketts



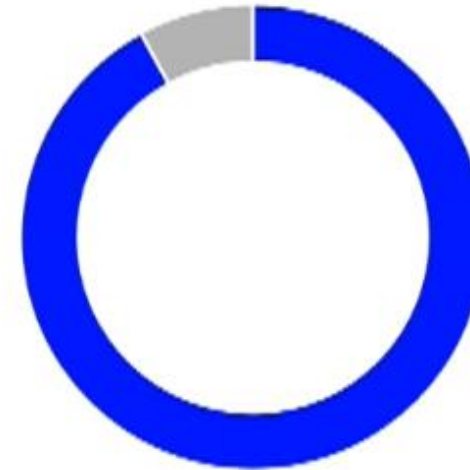
The cellular delivery protocol and immunosuppression regimen have been established for deceased donor islet cell therapy (PHPI)

Figure adapted from Pagliuca et al. *Development* 140: 2472, 2013



El ensayo clínico de Vertex para evaluar VX-880, una terapia de reemplazo de células Gen 1, está en marcha!

- **12** participants have received the full, target dose of cells
- All 3 individuals who received the therapy at least 12 months ago have eliminated hypoglycemic events and are fully off external insulin—**meeting the primary and secondary endpoints**
- There were **no significant side effects** related to VX-880
- The **trial has expanded** to enroll 20 more participants, to 37



11/12

participants have reduced or eliminated the need for external insulin

<https://news.vrtx.com/news-releases/news-release-details/vertex-announces-positive-results-ongoing-phase-1-2-study-vx-880>

Enfoques actuales y futuros para el reemplazo de células de los islotes



Michael Rickets

KEY: Current Proof-of-Concept Future		
β-cell source	Transplant site	Protection from the immune system
Allogeneic islets isolated from a deceased donor	Intrahepatic, via portal vein infusion	Induction and maintenance immunosuppression
Allogeneic islets derived from a human pluripotent stem cell line ³	Intra-omental, via thrombin bio-scaffold ¹	Induction immunomodulation with operational tolerance ²
Autologous islets derived from an inducible pluripotent stem (iPS) cell line ⁴	Sub-anterior rectus sheath ⁴	Immune evasion via genetic engineering ⁵ or local immunosuppression
Xenogeneic islets isolated from a pathogen-free porcine herd	Intramuscular	Immune protection via macroencapsulation device
	Subcutaneous, via a device-less space or cell-permeable or -impermeable device	

1. Baldal et al. *N Eng J Med* 378: 1887, 2017 3. Reichman et al. *EASD LBA31(OP6)*, 2024 5. Hu et al. *Cell Stem Cell* 31: 334, 2024
2. Wisel et al. *Transplant Int* 36: 1, 2023 4. Wang et al. *Cell* 187, 1, 2024



Reversing the Course of T1D

Disease-modifying therapies (DMTs) are therapies that change the course of a disease aimed at people **at every stage of T1D**

Goal:

Prevent, halt, or reverse the loss of functional beta cells

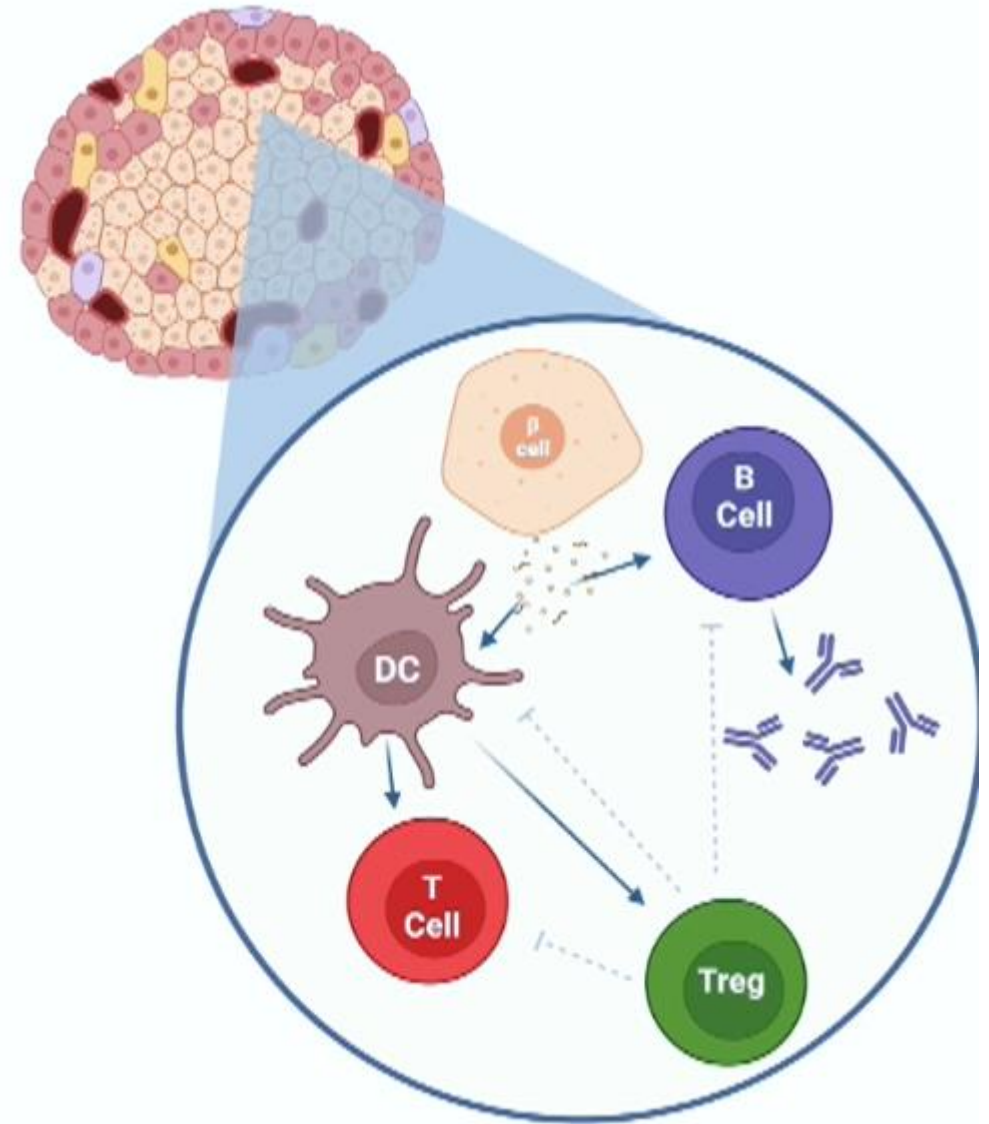
How?:

- Rebalancing the immune system
- Preserving/regrowing beta cells

Several DMTs are in Breakthrough T1D-supported clinical trials around the world- and one has been approved by the FDA!



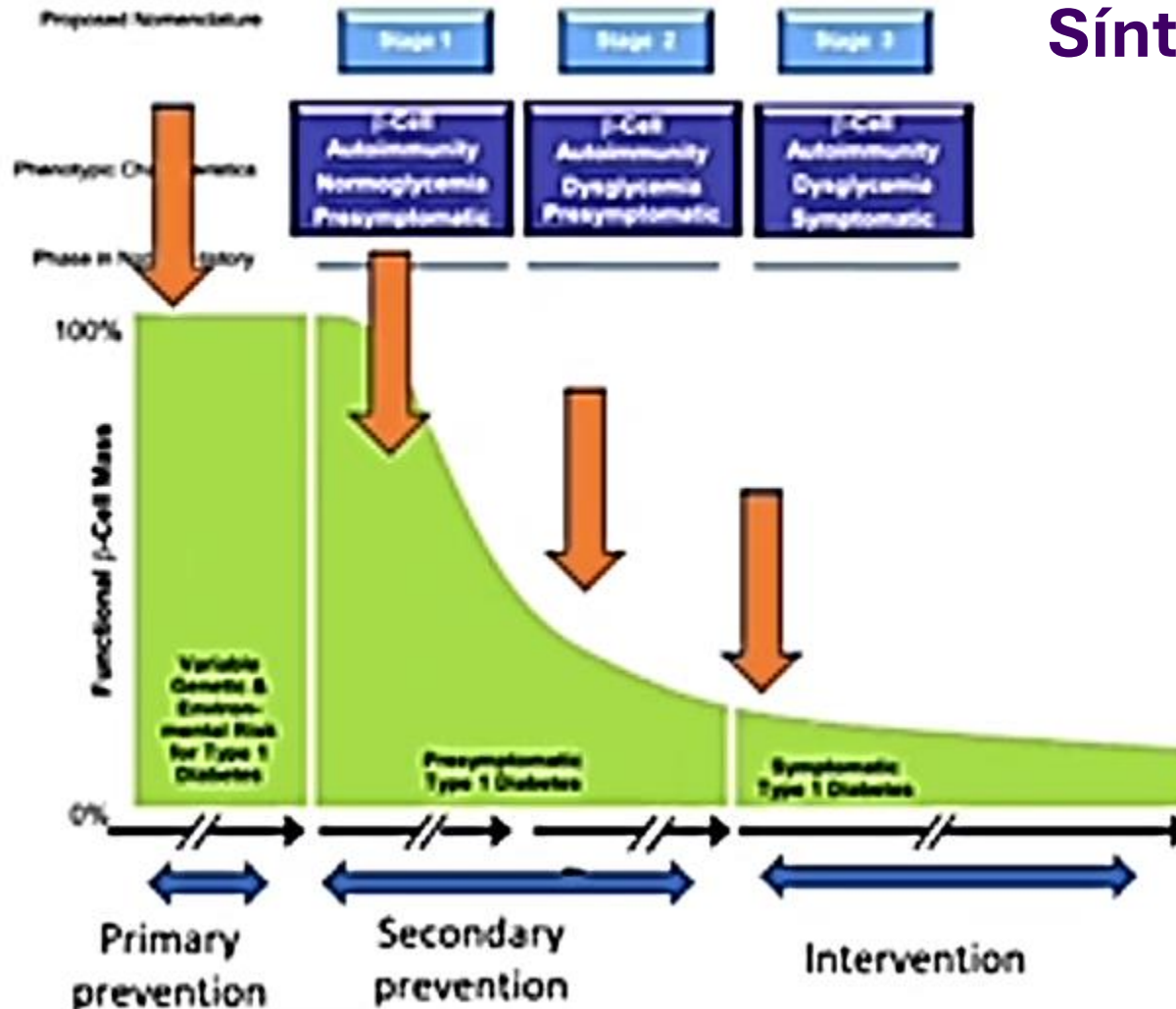
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Cambiando el Paradigma en el manejo de la Diabetes tipo 1



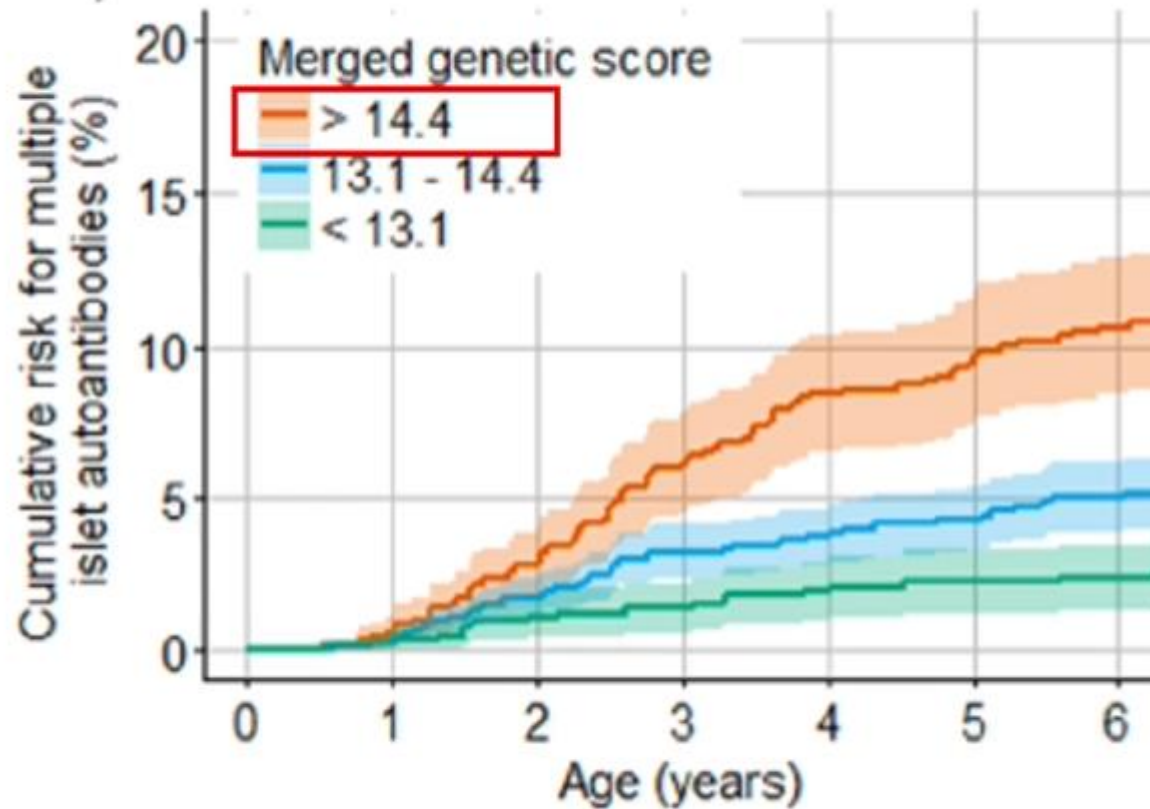
Tabitha
Randall



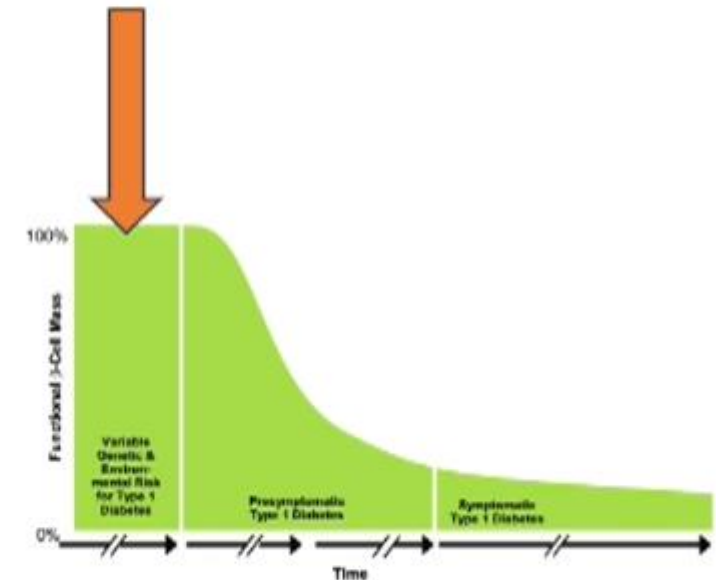
Síntoma → Intervención

1. Novedades en la Intervención
2. Desafíos en la implementación

Prevención Primaria: Prevención de anticuerpos



Bonifacio Plos Medicine 2018



Ziegler BMJ Open 2019 and 2021





Freder1k: Detección temprana para recién nacidos de hasta 7 días de edad

5 Countries, 9 clinical sites



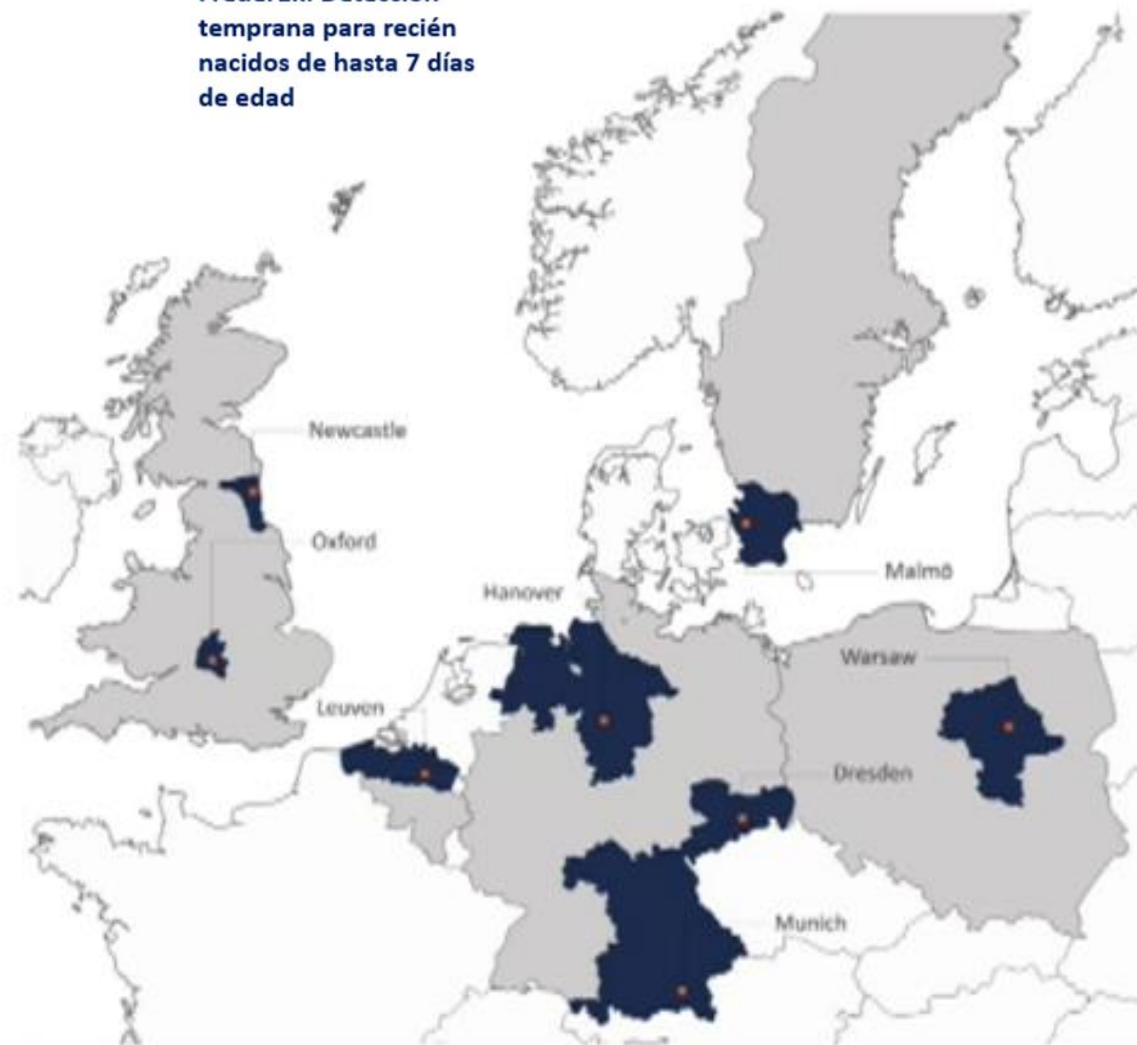
Oral insulin v Placebo
Age 4-7 months



Probiotic v Placebo
Up to 6 weeks



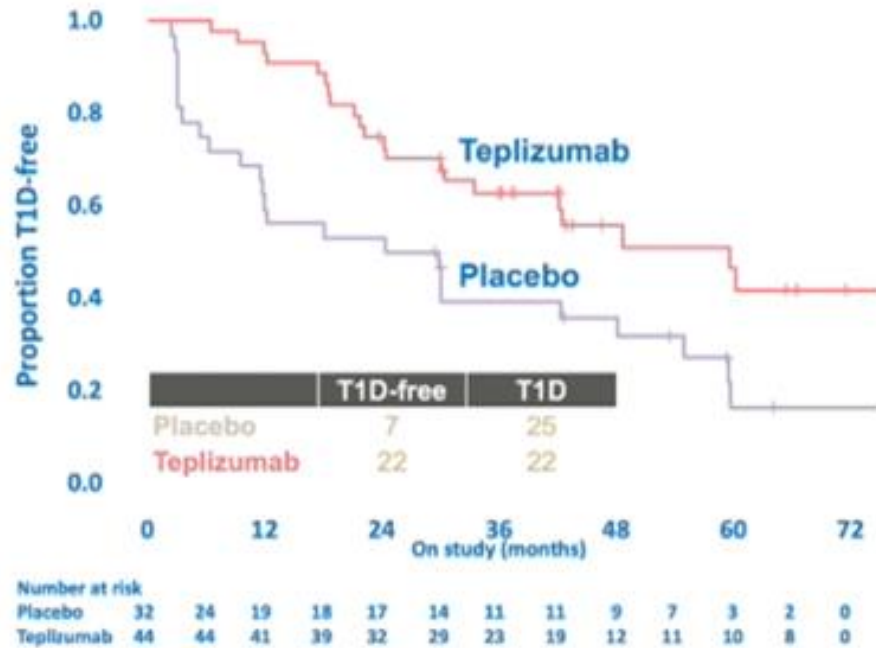
Covid 19 vaccine v Placebo
By age 6m, 6 weeks later, further 8 weeks





Comienza una nueva era

Estadio 2: Tratamiento temprano



The NEW ENGLAND JOURNAL of MEDICINE

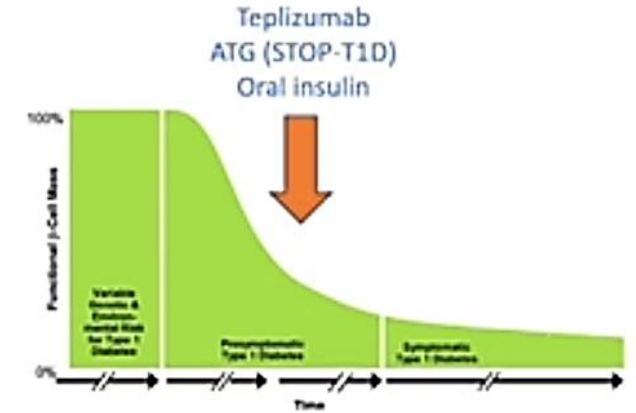
ESTABLISHED IN 1812

AUGUST 15, 2019

VOL. 381 NO. 7

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.,



Teplizumab aprobado por la FDA como el primer y único tratamiento indicado en Estadio 2 de DM para retrasar la aparición de la etapa 3 de la diabetes tipo 1 (DT1)

Noviembre 2022

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Teplizumab no se encuentra aprobado en Argentina

No hay tratamientos disponibles para atacar la fisiopatología autoinmune subyacente y afectar la trayectoria de la enfermedad

Dos tipos de terapias que pueden ser utilizadas en la DT1:

Terapia con Insulina



Reemplazar insulina endógena con inyecciones regulares o bombas

Inmunoterapia



Reprogramar el Sistema immune para que no destruya células beta



La inmunoterapia tiene el potencial de retrasar el debut de la DT1 e incluso prevenirla por completo



Kimberly Simmons

Estadios y Metabolismo HC

Stage of T1D by Monitoring Tool Used in Early T1D Clinic (n=36)

	Stage 1	Stage 2	Stage 3
HbA1c	16	18	2
Fasting Blood Glucose	24	16	6
2-Hour OGTT Glucose	14	9	13

Stage 1 (n=9), CGM time $\geq$ 140 mg/dl (7.8 mmol/L) 2 to 21%

Stage 2 (n=25), CGM time $\geq$ 140 mg/dl (7.8 mmol/L) 2 to 67%

Stage 3 (n=2), CGM time $\geq$ 140 mg/dl (7.8 mmol/L) 46% to 56%

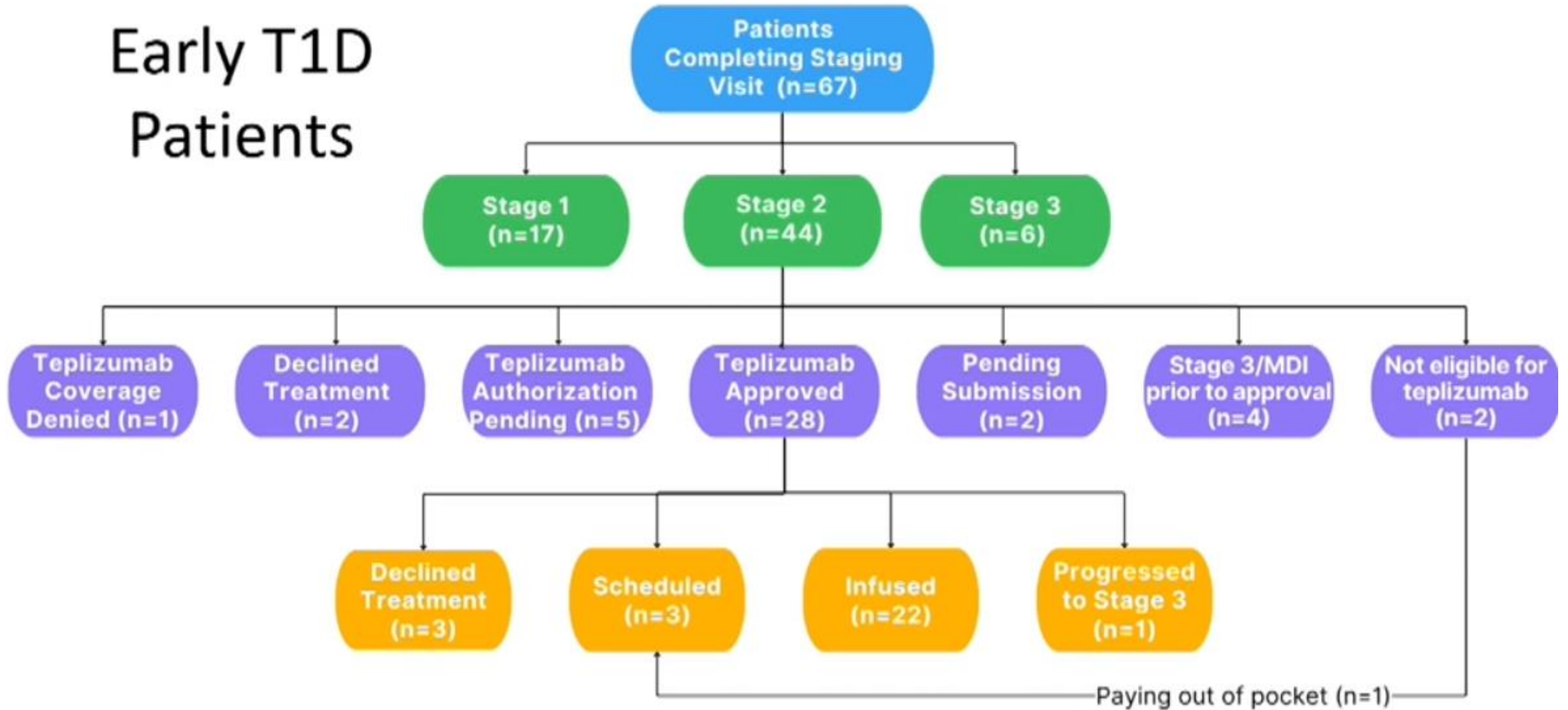
***Patient eligibility varies by tool used to evaluate for dysglycemia.
To date, only 4 of 67 patients in stage 2 met stage 2 criteria for all categories.***



Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS



Early T1D Patients



Apertura del centro 10 /04/2023
Completaron el tratamiento
22 individuos al 14/10/2024

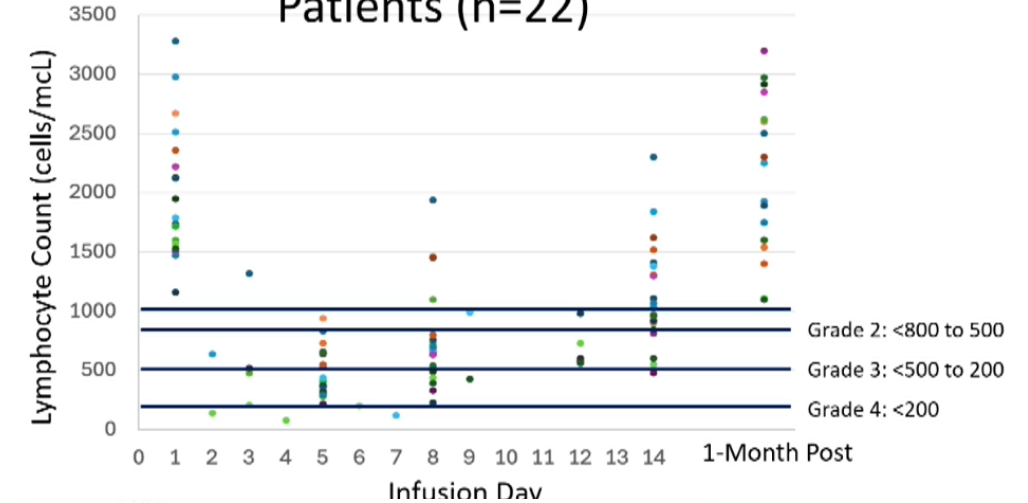
Age: Mean 23 years, Range 10-55 years
 50% <20 years, 50% >20 years

Sex: 59% (n=13) female, 41% (n=9) male

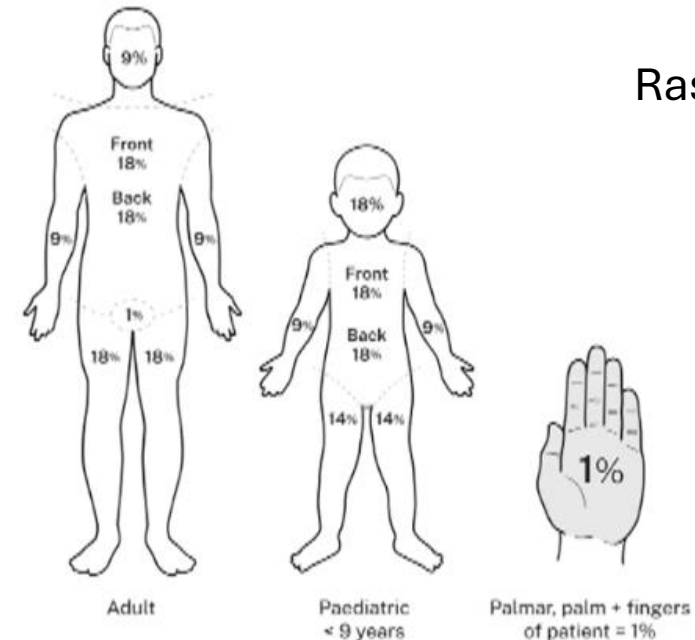
Race: 82% (n=18) White, 14% (n=3) Hispanic,
 4% (n=1) Asian

FDR : 32% (3 sibs, 2 parents, 1 aunt, 1 uncle)

Lymphopenia Occurred AND Recovered in All Patients (n=22)



Rash



Teplizumab Side Effects

	Clinical Trials N=791	BDC N=22
Lymphopenia	80% (632)	100% (22)
Nausea	20% (155)	91% (20)
Leukopenia	63% (501)	82% (18)
Rash	35% (273)	77% (17)
Headache	27% (215)	59% (13)
AST increased	28% (222)	41% (9)
ALT increased	27% (210)	41% (9)
Neutropenia	40% (313)	36% (8)
Thrombocytopenia	22% (172)	18% (4)
Cytokine Release Syndrome (CTCAE Version 5.0 grade 2, with hypotension responsive to IV fluids)	5.8% (4)	14% (3)
Anemia	29% (228)	5% (1)

Side Effect Mitigated with Pre-Medications and OTC and RX Treatments

- Pre-medications
 - Diphenhydramine
 - Ibuprofen
 - Famotidine
- PRN
 - Tylenol
 - Zofran
 - Topical Benadryl cream, hydrocortisone cream
 - Loratidine
 - Lansoprazole, Miralax



Tabitha
Randall

Estadio 3

Objetivo: Preservar la Función pancreática que queda

Shown efficacy



Teplizumab

ATG

Ritiximab

Abatacept

Alefaccept

Golimumab



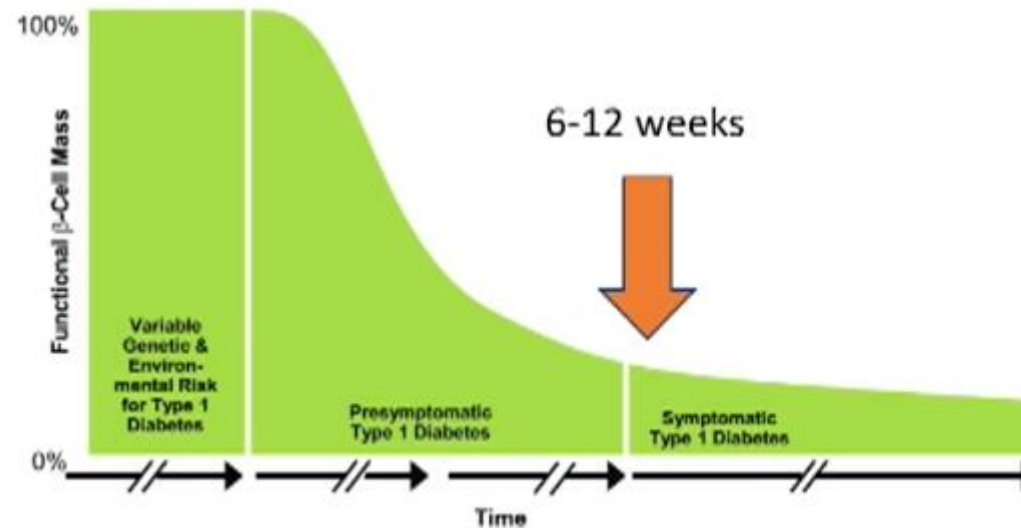
Ustekinumab

Imatinib



Baracitinib

Verapamil

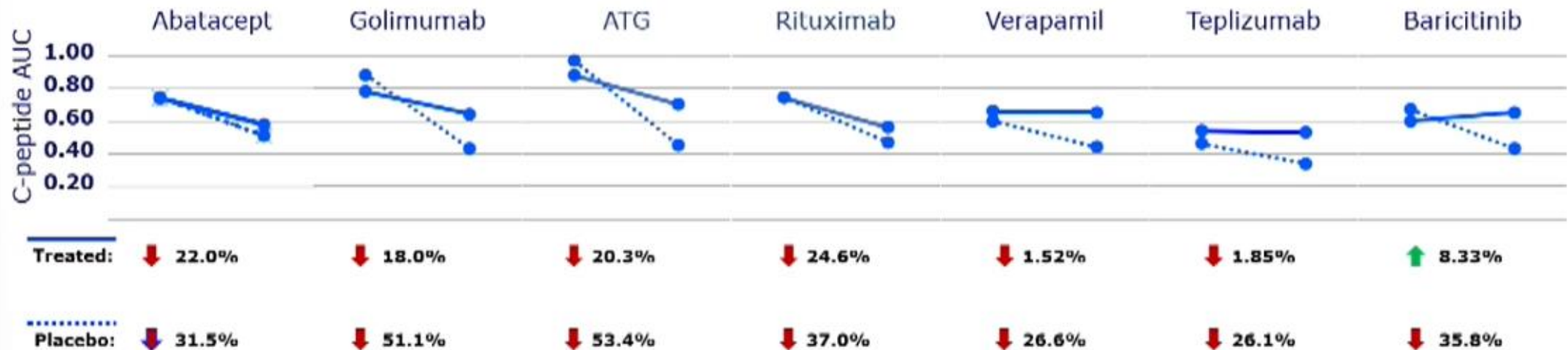




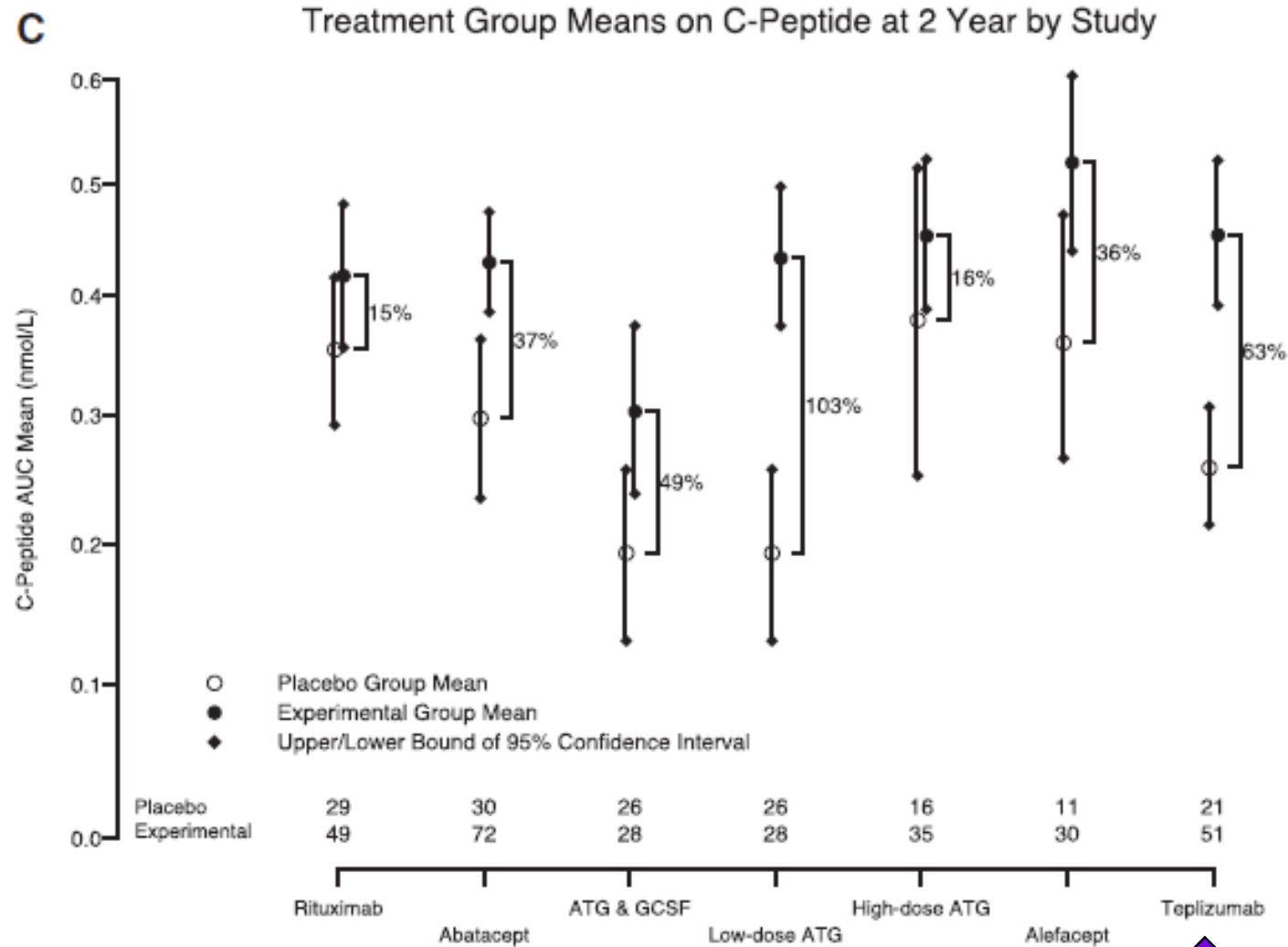
Sanjoy Dutta

7 DMTs Showing Preservation of C-peptide following 1 Year of Treatment in Stage 3

(C-peptide, baseline vs endpoint)



¿Todas las inmunoterapias son iguales?

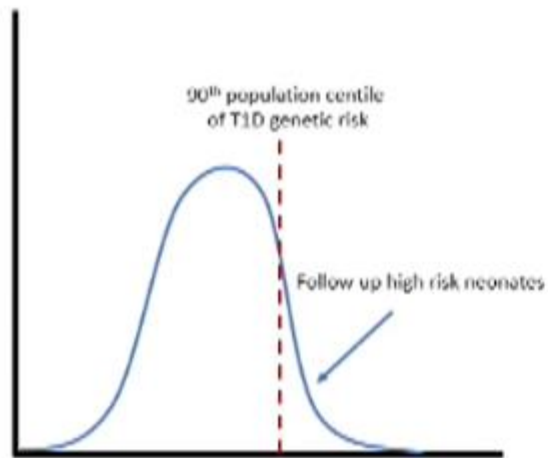


New studies
Recruitment complete
 Vera T1D
 MELD (ATG)
 IMPACT
 CFZ533 (Iscalelimab)
 ITAD

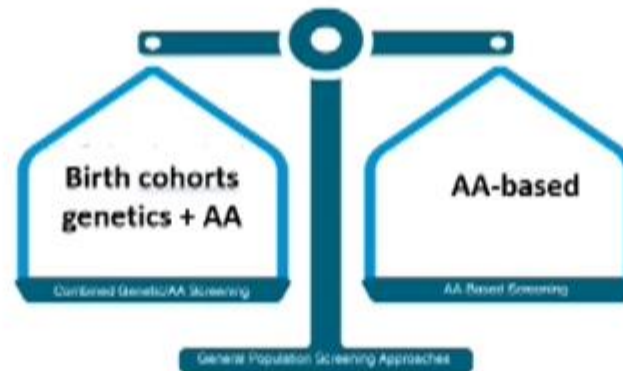
JACOBSEN ET AL.
 DIABETES TECHNOLOGY & THERAPEUTICS
 Volume 22, Number 12, 2020



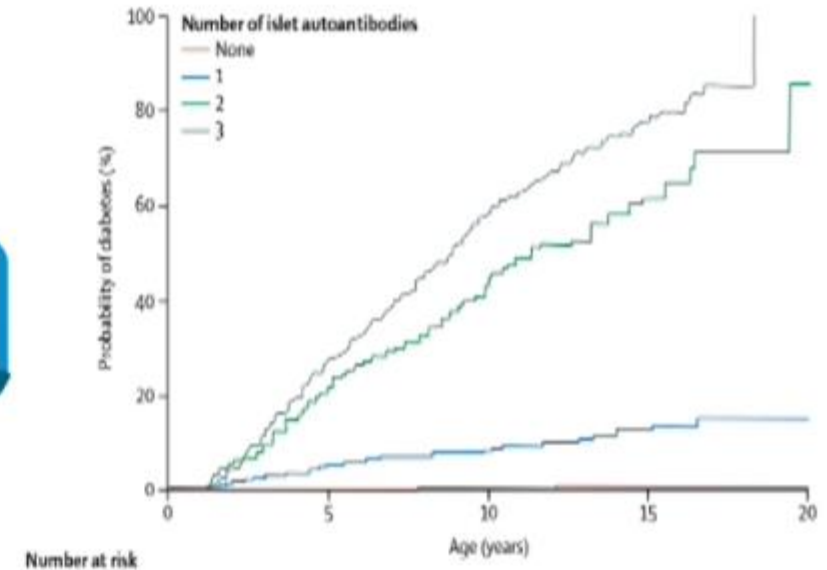
Screening, ¿Cómo?



Dayan Besser Science 2021



Adapted from Sims Diabetes 2022



Ziegler JAMA 2013



Screening, ¿quiénes?

**Familiares de pacientes con
Diabetes vs población general**

**15 veces más riesgo en
familiares**

**5% vs 0,3 % en población
general**

1. Eurodiab Ace Study Group and The Eurodiab Ace Substudy 2 Study Group. Diabetologia. 1998;41(10):1151-6. 2. Karges B, et al. Diabetes Care. 2021;44(5):1116-24. 3. Hemminki K, et al. Diabetologia. 2009;52(9):1820-8. 4. Parkkola A, et al. Diabetes Care. 2013;36(2):348-54. 5. Turtinen M, et al. Diabetologia. 2019;62(11):2025-39. 6. Sims EK, et al. Diabetes 2022;71:610-3. 7. Besser REJ, et al. Arch Dis Child. 2022;107:790-5.



Screening, ¿quiénes?

Individuals diagnosed with T1D:

EURODIAB
ACE Study¹

2–17%

Diabetes Prospective
Follow-up Registry²

6.6%

Swedish Multigeneration
Register³

10.3%

Finnish Pediatric
Diabetes Register^{4,5}

10.4–12.2%

Have a first-degree relative with aT1D

Given that **only ~10% of cases** of aT1D are familial,^{1–5} **screening for T1D in the general population is important** to identify individuals with presymptomatic disease but no family history of T1D. Benefits of screening include^{6,7}:

Reduction of DKA

Fewer hospitalizations

Time to prepare for T1D

Access to clinical trials

1. Eurodiab Ace Study Group and The Eurodiab Ace Substudy 2 Study Group. Diabetologia. 1998;41(10):1151-6. 2. Karges B, et al. Diabetes Care. 2021;44(5):1116-24. 3. Hemminki K, et al. Diabetologia. 2009;52(9):1820-8. 4. Parkkola A, et al. Diabetes Care. 2013;36(2):348-54. 5. Turtinen M, et al. Diabetologia. 2019;62(11):2025-39. 6. Sims EK, et al. Diabetes 2022;71:610-3. 7. Besser REJ, et al. Arch Dis Child. 2022;107:790-5.

General population screening for early T1D



Typ 1 Diabetes: Früh erkennen – Früh gut behandeln

In cooperation
with > 600
primary care
pediatricians in
Bavaria, Germany



Capillary blood



Since 2015:
160,631 participants;
Age 1.75 – 10.99 years

461 children
(0.3 %)

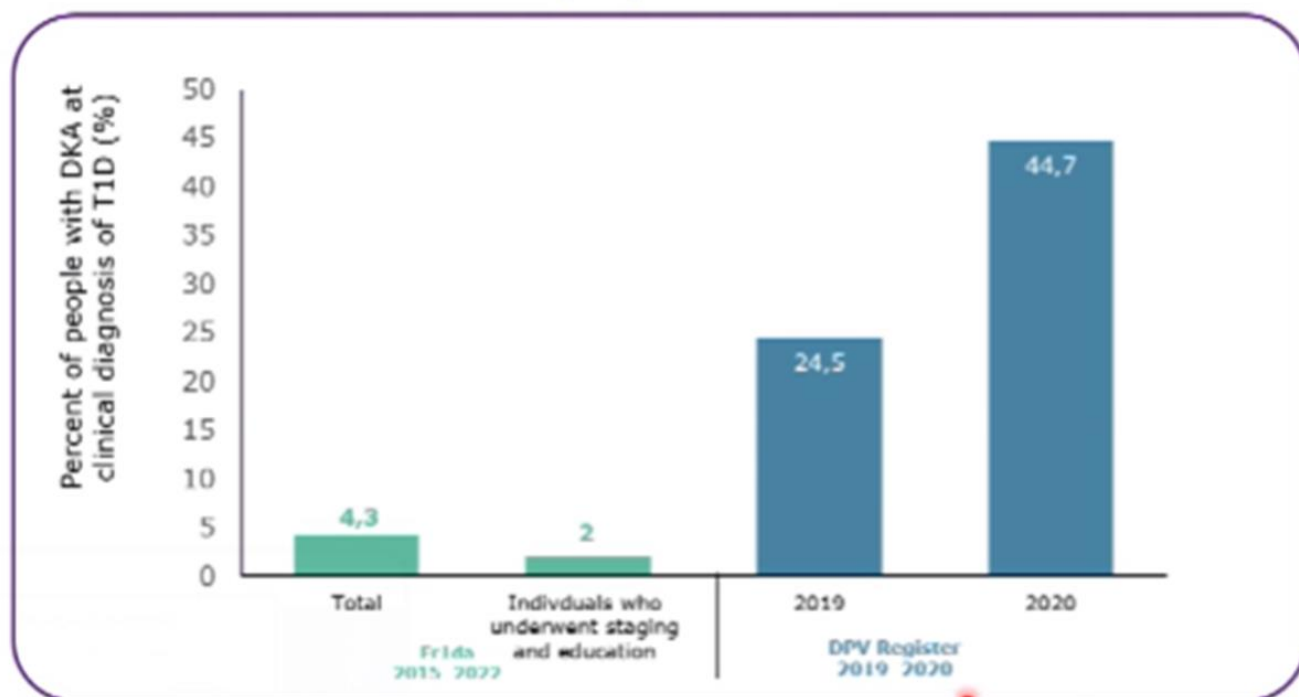
with multiple islet
autoantibodies

T1D
Stage 1 (0.19%)
Stage 2 (0.019%)
Stage 3 (0.027%)

Ziegler, JAMA 2020;
Raab, BMJ open 2016
Ziegler, Diabetes Technol Ther 2016

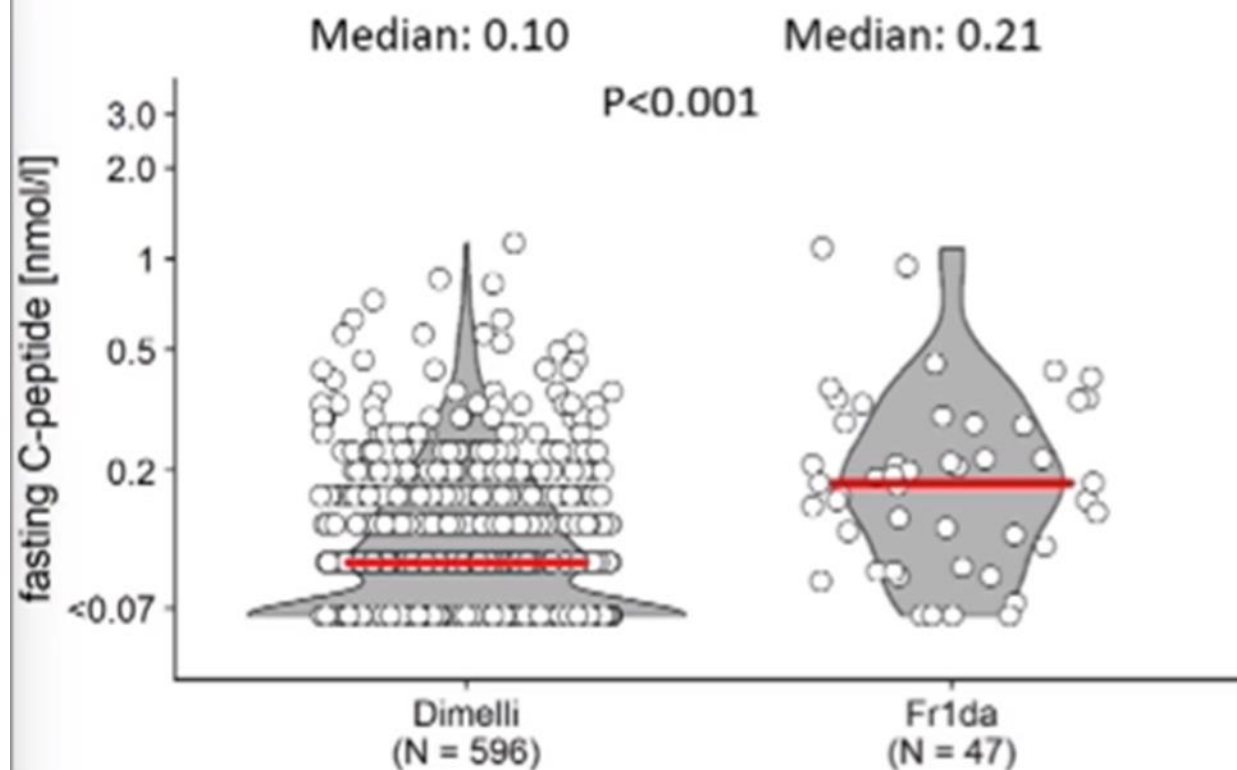
Courtesy of A. Ziegler

The rate of diabetic ketoacidosis is drastically reduced in individuals previously screened for early stage T1D compared with those from the background population

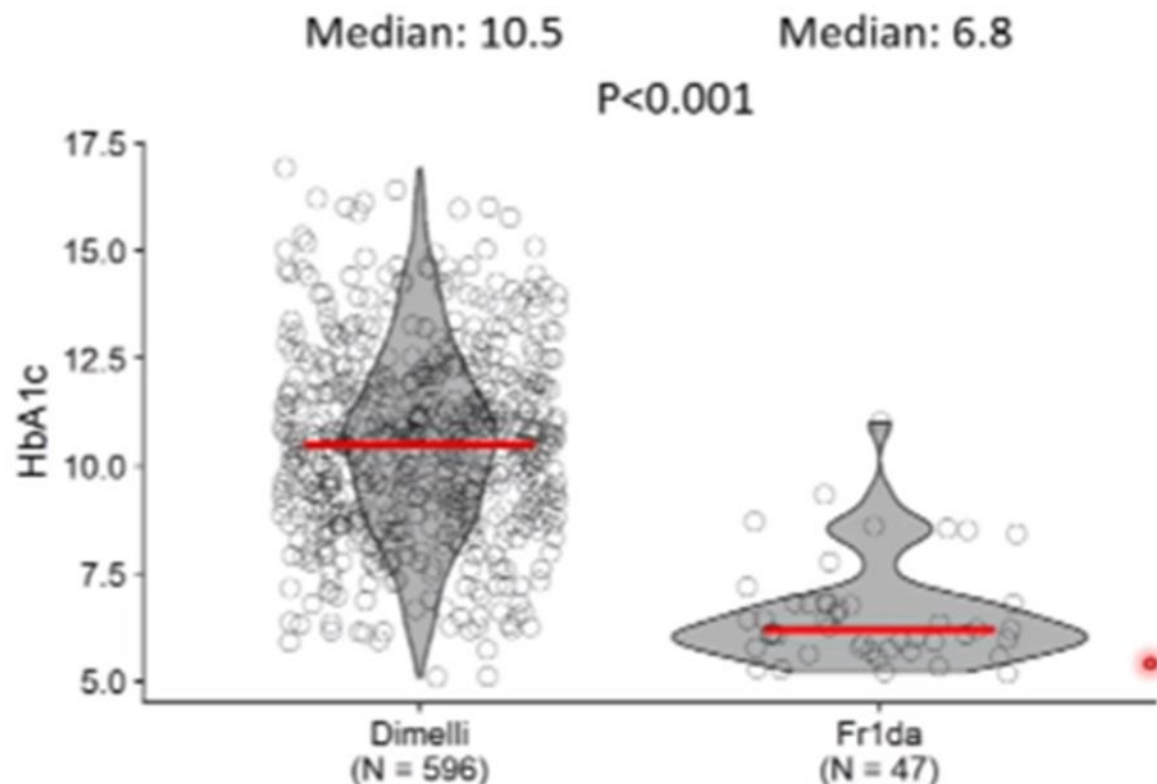


Children diagnosed with presymptomatic T1D through public health screening have milder diabetes at clinical manifestation

Fasting C-Peptide at clinical manifestation



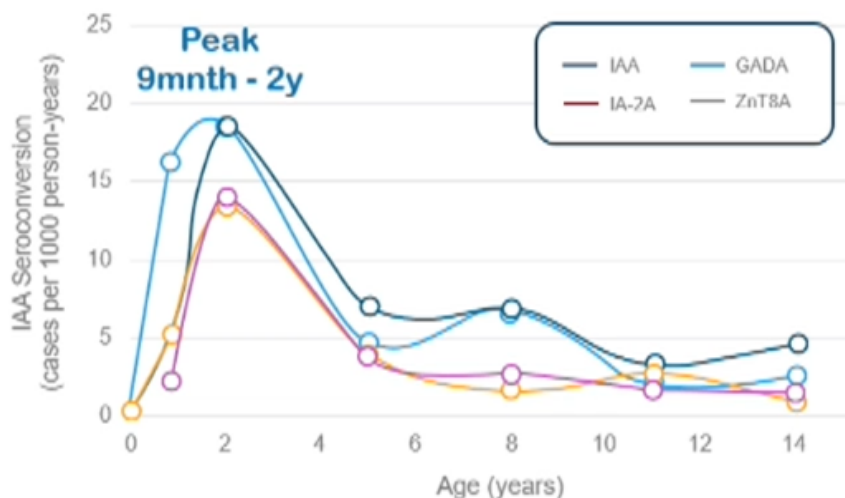
HbA1c at clinical manifestation



Screening, ¿cuándo?

Challenge 3: Screening – when?

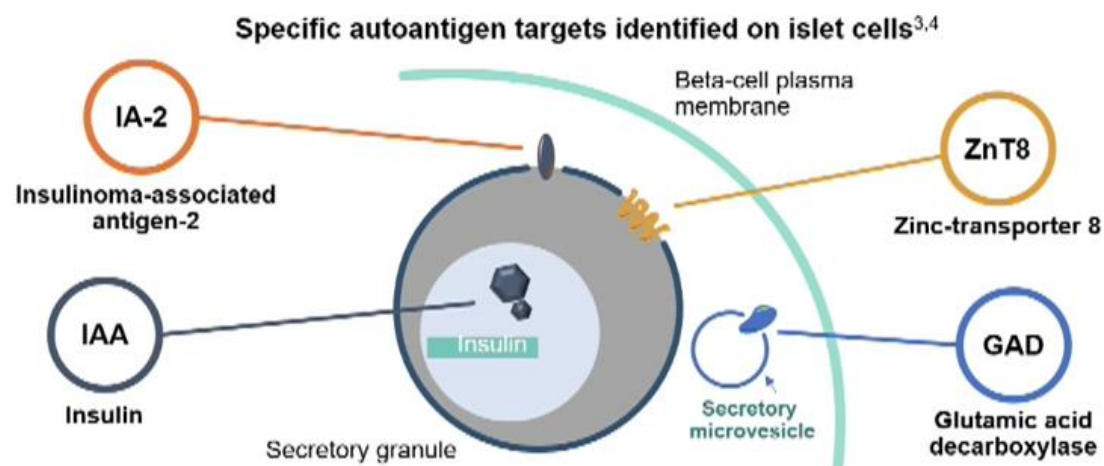
80% children develop antibodies by 6 years



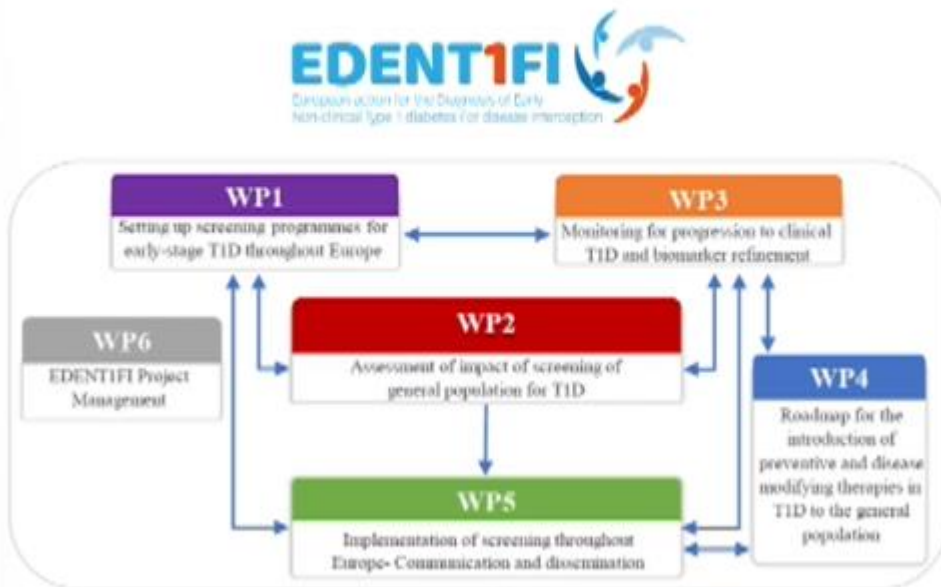
Ziegler et al. Diabetologia 2012, Bonifacio Diab Care 2019, Ghalwash Lancet Diab End 2022

One screen approach: 3-4 y

Multiple time points improves sensitivity e.g. 2,6,10 y



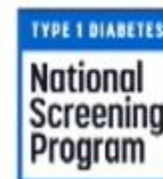
Integrar el screening en los Sistemas de control de salud



Well child check 2-5y → 11y



Hb testing 9-18mth, 2-5y



Newborn, 2 + 6 + 10y
< 1y vaccinations, school

UNISCREEN

Health check 2+ 6 + 10y



Vaccination 3-5y

Estandarización de los ensayos utilizados en el screening poblacional



Loredana Marcoveccio

Highlights

Monitoreo post Screening

1. Actualización Guías ISPAD 2024 en screening, estadios y estrategias de preservación de célula β
2. CONSENSO en guías de monitoreo en individuos con Auto anticuerpos positivos

Por qué necesitamos GUÍAS



Prevención de CAD Menor internación

Identificar y monitorear intervenciones terapéuticas para retrasar el Debut

Educar sobre inicio Insulinoterapia

Evitar diagnóstico erróneo de DM2 y retrasar inicio de insulina

Referir para estudios de investigación



Loredana Marcoveccio



Michael
Haller

Clinical guidance





Clinical Care Advice for Monitoring of Islet Autoantibody Positive Individuals with Presymptomatic Type 1 Diabetes

Diabetes/Metabolism Research and Reviews

RESEARCH ARTICLE [Open Access](#) 

Clinical care advice for monitoring of islet autoantibody positive individuals with presymptomatic type 1 diabetes

A. Emile J. Hendriks, M. Loredana Marcovecchio, Rachel E. J. Besser, Elio Bonifacio, Kristina Casteels, Helena Elding Larsson, Gita Gemulla, Markus Lundgren, Olga Kordonouri, Roberto Mallone, Flemming Podot, Agnieszka Szypowska, Jorma Toppari, Thekla von dem Berge, Anette G. Ziegler, Chantal Mathieu, Peter Achtenbach, on behalf of the INNODIA consortium, the Fr1da Study Group and the GPPAD Study Group.

First published: 20 February 2024 <https://doi.org/10.1002/dmrr.3777>

Expert consensus was obtained from members of the Fr1da, GPPAD, and INNODIA consortia, three European diabetes research groups.



Loredana
Marcovecchio

Consensus Guidance for Monitoring Individuals With Islet Autoantibody-Positive Pre-Stage 3 Type 1 Diabetes

Moshe Phillip, Peter Achtenbach, Ananta Addala, Anastasia Albanese-O'Neill, Tadej Battelino, Kirstine J. Beil, Rachel E.J. Besser, Elio Bonifacio, Helen M. Colhoun, Jennifer J. Couper, Maria E. Craig, Thomas Danne, Carine de Beaufort, Klemen Dovič, Kimberly A. Driscoll, Sanjoy Dutta, Osagie Ebekodien, Helena Elding Larsson, Daniel J. Feten, Brigitte I. Frohnert, Robert A. Gabbay, Mary P. Gallagher, Carla J. Greenbaum, Kurt J. Griffin, William Hagopian, Michael J. Haller, Christel Hendrickx, Emile Hendriks, Richard I.G. Holt, Lucille Hughes, Hoba M. Ismail, Laura M. Jacobson, Suzanne B. Johnson, Leslie E. Kolb, Olga Kordonouri, Karin Lange, Robert W. Lash, Åke Lemmark, Ingrid Libman, Markus Lundgren, David M. Maahs, M. Loredana Marcovecchio, Chantal Mathieu, Kelley M. Miller, Holly K. O'Donnell, Tali Oron, Shivajirao P. Patil, Rodica Pop-Busui, Marian J. Fawcett, Stephen S. Rich, Desmond A. Schatz, Rifka Schulman-Rosenbaum, Kimber M. Simmons, Emily K. Sims, Jay S. Skyler, Laura R. Smith, Cate Spasick, Andrea K. Steck, Nicholas P.B. Thomas, Kaena N. Tonyushkina, Ritta Vejola, John M. Wentworth, Diane K. Wilenett, Jamie R. Wood, Anette-Gabriele Ziegler, and Linda A. DiMeglio

Developed by



In collaboration with international experts and societies

Monitoring guidance for children, adolescents and adults

Diabetes Care

Diabetes Care 2024;47(8):1-22 | <https://doi.org/10.2337/dci24-0042>

Diabetologia

Diabetologia (2024) 67:1731–1739

<https://doi.org/10.1007/s00125-024-06205-5>

This consensus report was endorsed by

- European Society for the Study of Diabetes (EASD)
- American Diabetes Association (ADA)
- American Association of Clinical Endocrinology (AACE)
- American College of Diabetology (ACD)
- Association of Diabetes Care & Education Specialists (ADCES)
- Australian Diabetes Society (ADS)
- International Society for Pediatric and Adolescent Diabetes (ISPAD)
- Advanced Technologies & Treatments for Diabetes (ATTD)
- DiaUnion
- Endocrine Society
- Breakthrough T1D



Michael
Haller



Loredana
Marcoveccio

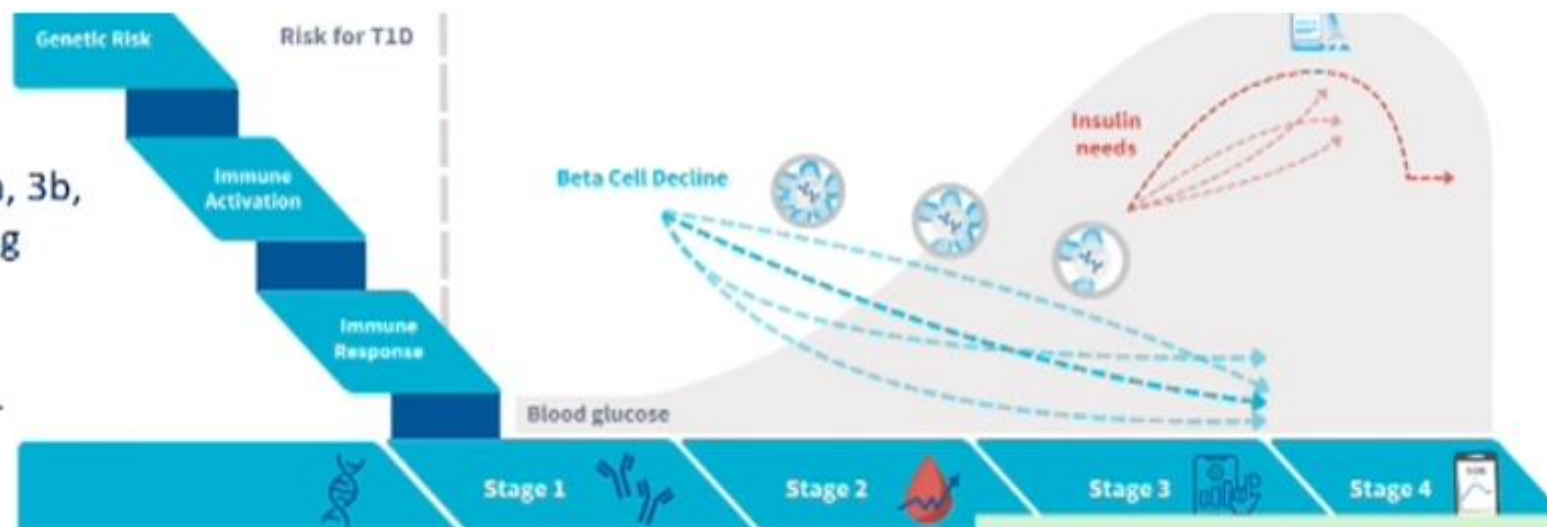
ISPAD Clinical Practice Consensus Guidelines 2024

Screening, Staging, and Strategies to Preserve Beta Cell Function in Children and Adolescents with Type 1 Diabetes

*Michael J Haller, Kirstine J Bell, Rachel E J Besser, Kristina Casteels, Jenny J Couper, Maria E Craig,
Helena Elding Larsson, Laura Jacobsen¹, Karin Lange, Tal Oron, Emily K Sims, Cate Speake, Mustafa
Tosur, Francesca Ulivi, Anette-G Ziegler, Diane K Wherrett, M Loredana Marcovecchio*

¿Qué hay de nuevo?

Stages 1, 2a, 2b, 3a, 3b, and 4 T1D are being used in clinical, research, and regulatory settings.



Genetic Risk
Individuals with a first degree relative with T1D are 15x increased risk of developing T1D

- Immune response (development of single

Stage 1

2+ Islet Autoantibodies Confirmed

- Normal blood glucose
- Pre-symptomatic

Stage 2

2+ Autoantibodies Plus Dysglycemia

- Abnormal glucose
- Usually pre-symptomatic
- More rapid progression to Stage 3

Stage 3

- **Stage 3a:** asymptomatic, may not require insulin immediately
- **Stage 3b:** symptomatic, requires insulin

Stage 4

- **Stage 2a:** early, mild dysglycemia
FPG= 5.6-6.4 mmol/L (100-115 mg/dL)
- **Stage 2b:** late, robust dysglycemia but not reaching threshold for stage 3
FPG 6.5-6.9 mmol/L (116-125 mg/dL)

Stage 2a: Shows as early, mild dysglycemia
Stage 2b: Shows as late, robust dysglycemia without reaching threshold of Stage 3

- Tools available to predict rate of progression to Stage 3
- Progression quicker in younger people

Stage 3a: Asymptomatic, may not require insulin immediately
Stage 3b: Symptomatic, requires insulin

Haller MJ et al, ISPAD Clinical Practice Consensus Guidelines 2024 Screening, Staging, and Strategies to Preserve Beta Cell Function in Children and Adolescents with Type 1 Diabetes.

Indicadores Metabólicos de Monitoreo Glucémico

Method	Pros	Cons	Metrics obtained
Reference OGTT*	- Gold standard in research settings - Used to stage disease and predict progression	Requires glucose load and 2–5 blood draws over 2 h	- Glycemic staging - Risk scores for progression (DPTRS, DPTRS60, Index60, M60, M120, PLS) (94,165–169)
Standard OGTT†	Similar to test for GDM: OGTT with 2 × blood draws (compared with 3 × draws in GDM test), performed routinely in clinical care	Requires 2 blood draws: fasting and at 2 h	120-min OGTT-derived glucose - M120
Random glucose	- One-off sample - Low cost	- Requires a blood draw or fingerstick test - Less sensitive than 120-min OGTT	Similar to 120-min OGTT-derived glucose (96) if obtained 2 h postprandially
Standard HbA _{1c} test	- Highly specific for clinical diagnosis of stage 3 T1D - Can use capillary sample - Longitudinal HbA_{1c} may be as informative as OGTT (66)	- Indicates 3-month mean glucose. Often normal in asymptomatic or recent-onset stage 3 T1D - May be affected by age, nondiabetes disease states (e.g., renal, hematological syndromes) - Not suitable in the home setting	- Risk of progression to “clinical disease”: HbA_{1c} > 39 mmol/mol (>5.7%) (170) 10% rise from baseline (at first positive islet autoantibody) over 3–12 months (66,67) suggests dysglycemia and progression to stage 2 T1D - Consider use of CGM if 10% rise in HbA_{1c} is confirmed, or higher frequency of SMBG, to monitor risk for progression
CGM‡	- Can be used at home - Can be blinded for physician review only in some regions - Optimal duration of CGM wear is validated in adults and children >2 years of age with diagnosed T1D, at all glycemic levels (171)	- Risk of anxiety for unblinded user seeing CGM fluctuations and experiencing alarms - Requires appropriate education on use and interpretation - Many primary care HCPs are unfamiliar with interpretation - Cost and access issues - Duration of wear not validated in early-stage T1D	- Sensitive in detecting individuals with asymptomatic stage 3 T1D and dysglycemia in stage 2 T1D (73) - Risk of progression to “clinical disease,” i.e., 10% of time with glucose >7.8 mmol/L (>140 mg/dL) has been associated with an 80% risk of progression to T1D within 12 months (72) ≥5% time with glucose

Indicadores Metabólicos de Monitoreo Glucémico

Method	Pros	Cons	Metrics obtained
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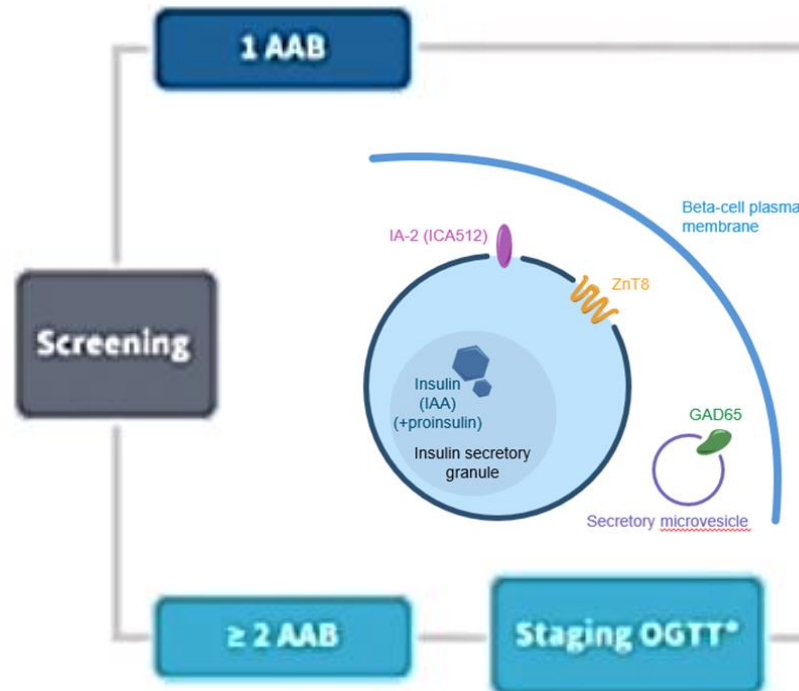
Auto
Monitoreo
glucémico

Simple uso
Hogar
Baja adherencia

Frecuencia no
determinada

Resultado
inmediato

Monitoreo Post screening



Blood samples to take	Age	Frequency
- Antibodies - HbA1c - Random glycemia	≤ 3y old	- every 6 months for 3 years - every 12 months for another 3 years - if no progression, stop
	>3y old	- every 12 months for 3 years - if no progression, stop

Stage	Blood samples to take	Age	Frequency
Stage 1	- HbA1c - Random glycemia - CGM (if available)	< 3y old	every 3 months
		3-9y old	every 6 months
		≥ 9y old	every 12 months
Stage 2	- HbA1c - Random glycemia - CGM (if available)	< 18y old	every 3 months
		> 18y old	every 6 months

*HbA1c, capillary/venous glucose and CGM may be alternatives when OGTT is not feasible

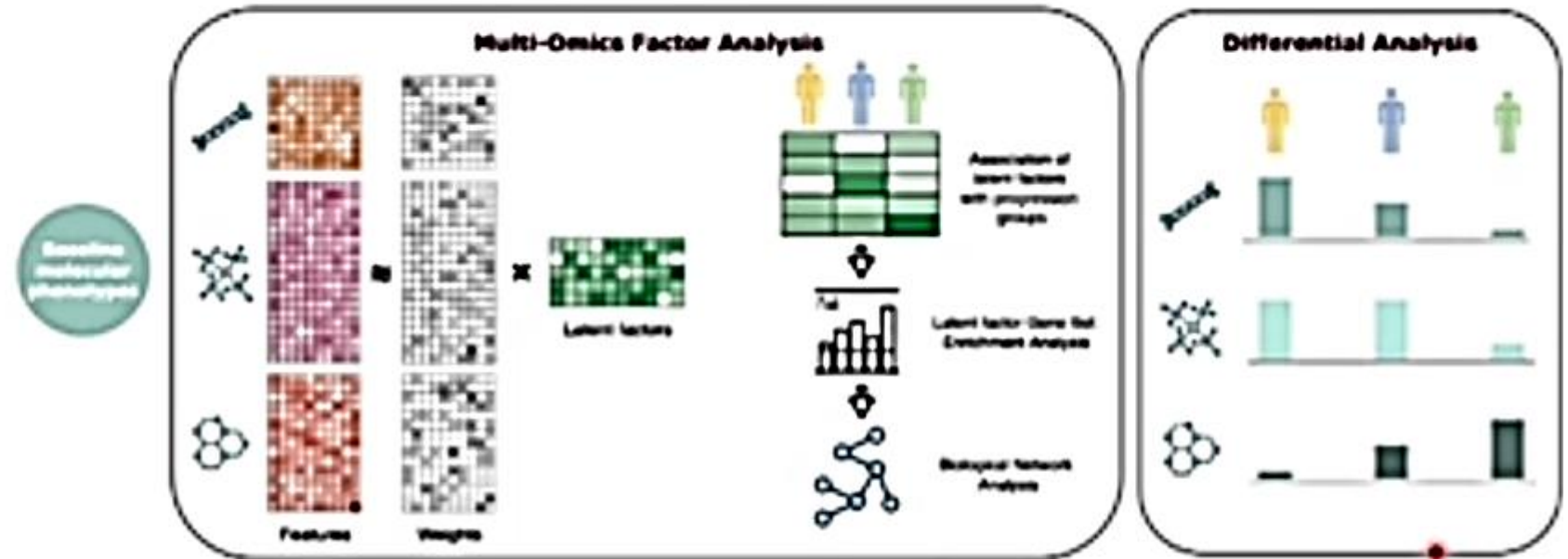


Multi-Omics data

- Transcriptomics
- miRNA (targeted and untargeted)
- Proteomics
- Lipidomics
- Metabolomics
- Immunomics

Objective

Integration of multi-omics dataset and association with disease progression groups

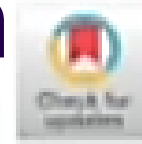


Methods

Multi-Omics Factor Analysis (MOFA) and differential analysis



Nuevos Diseños de Investigación



Innovative Designs and Logistical Considerations for Expedited Clinical Development of Combination Disease-Modifying Treatments for Type 1 Diabetes

Randy L. Anderson,¹ Linda A. DiMeglio,²
Adrian R. Mander,³ Colin M. Dayan,⁴
Peter S. Lindsay,⁵ Kevin C. Harold,⁶
Marjana Marinac,¹ and Simi T. Ahmed⁷



Colin Dayan

Diabetes Care 2022;45:2189–2201 | <https://doi.org/10.2337/dc22-0308>

1. Las plataformas adaptativas incrementan la eficiencia, reducen costos y establecen principios profundos de investigación.
2. Son valiosas en terapias combinadas

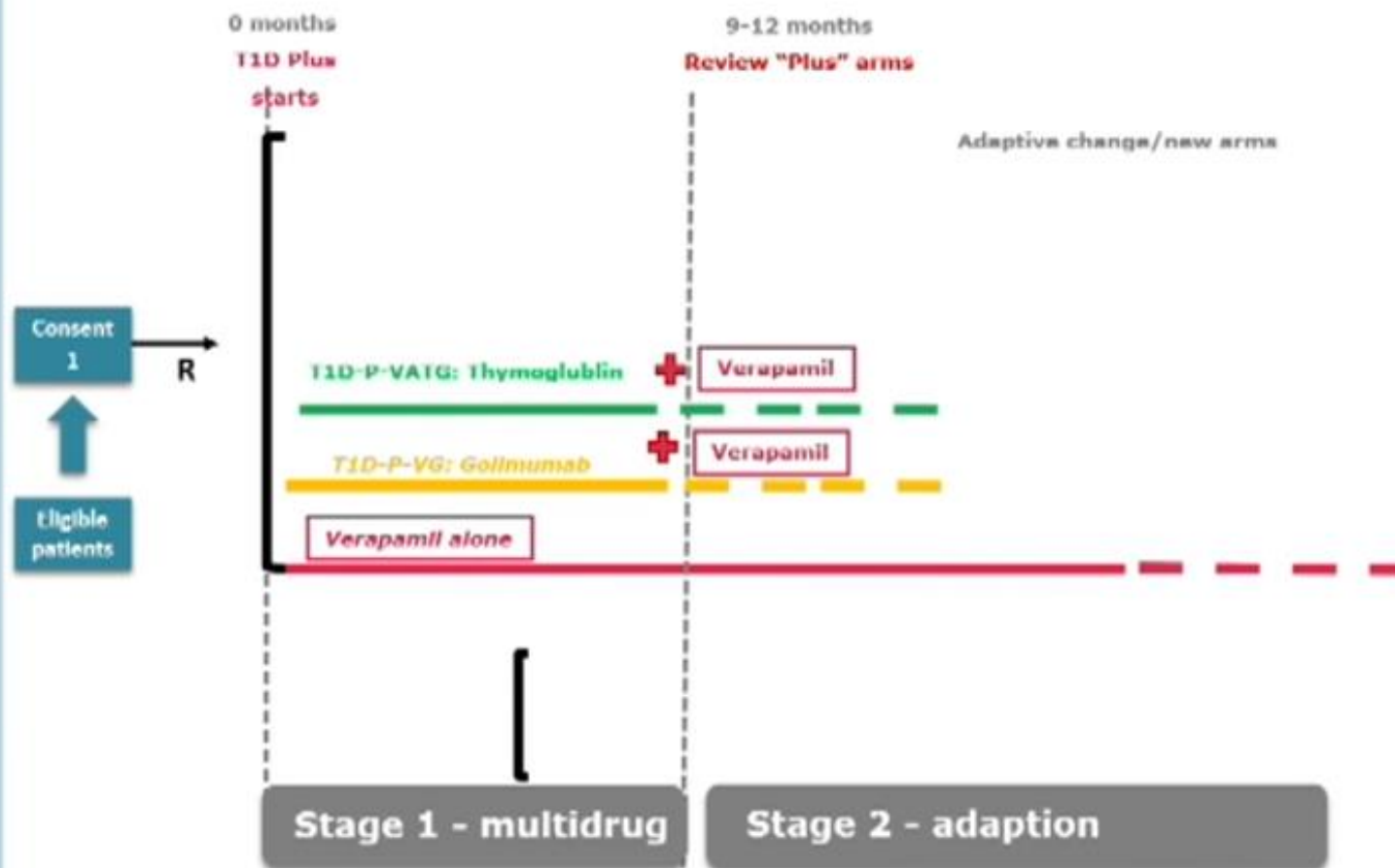


T1D-Plus

A CLINICAL TRIAL BY INNODIA

INNODIA

T1D-Plus



Colin Dayan

sanofi





Puntos clave



1. Realización de ensayos abiertos (Open label)
2. Todas las terapias modificadoras de enfermedad tienen al menos un estudio de Fase 2 de monoterapia.
3. Análisis Internos cada 12 meses.
4. Tres financiadores separados.
5. Objetivo ofrecer todos los tratamientos a todos los sitios.
6. Comparación combinada y con Verapamilo sólo.
7. Investigación y ensayos en Reino Unido, Europa y Australia.

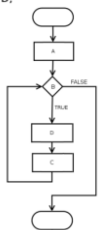


¿Qué nos queda aún por responder en el screening temprano de DT1?



1. *¿Cómo organizar el screening en determinado país según su sistema de salud?*

for(A,B,C)
D;



2. *¿Cómo organizar screening según contexto sociocultural (religión, creencias, verdades)?*

3. *¿Qué piensan los pacientes con DT1?*

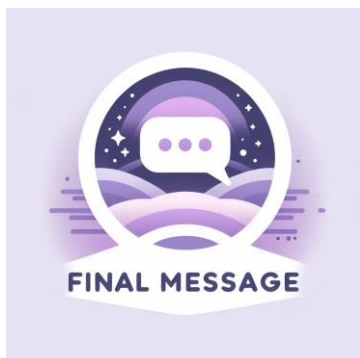


4. *¿Cómo comunicar a la población la Importancia de la detección temprana de DT1?*



5. *¿Cómo definir el beneficio de detección temprana de DT1?*

6. *¿Cómo organizar el monitoreo y acordar con reguladores de salud?*



Nuevos horizontes en las terapias y prevención de la diabetes tipo 1

Terapias de vanguardia que modifiquen la enfermedad

Nuevos biomarcadores de riesgo: Quiénes, cuándo y cómo

Ensayos terapéuticos adaptados
Consenso y Guías
ISPAD

Individuos de riesgo susceptibles, familiares y población general

Muchas Gracias

sanofi



Experiencias internacionales en la implementación de la detección temprana de la diabetes

Carolina Martinez Mateu

- Médica pediatra
- Especialista en Nutrición Infantil
- Equipo Multidisciplinario de Diabetes Hospital J. P. Garrahan
- Docente de la Carrera de Especialistas en Nutrición Pediátrica de Universidad de Buenos Aires



Conflictos de interés:

- Sin conflictos para esta presentación

Hoja de ruta



- ¿Por qué hacer detección en estadios tempranos?
- ¿En quiénes?
- ¿Qué determinaciones realizar?
- ¿Cuándo?
- Experiencias: Israel e Italia.
- Educacion y manejo nutricional.



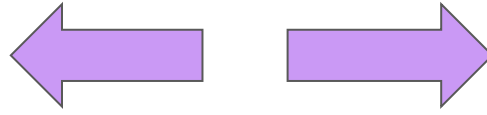
Los principios de la detección de enfermedades

1. La enfermedad debe representar un problema importante de salud pública
2. Debe existir un tratamiento aceptado para los casos detectados
3. Debe ser posible identificar la enfermedad en su fase asintomática
4. El proceso de cribado debe ser seguro, preciso y aceptado por la población
5. Debe existir una política clara para los casos detectados
6. El costo del cribado debe ser razonable en relación con los beneficios obtenidos
7. La historia natural de la enfermedad debe ser bien comprendida
8. El cribado debe ser un proceso continuo

¿Por qué hacer detección en estadios tempranos?

1. Prevenir la cetoacidosis y evitar la hospitalización.
2. Intervenciones terapéuticas para retrasar el comienzo del estadio 3.
3. Minimizar el daño por hiperglucemia.
4. Evitar confusión con diabetes tipo 2 y el retraso de la insulinización.
5. Posibilidad de enrolarse en ensayos clínicos.

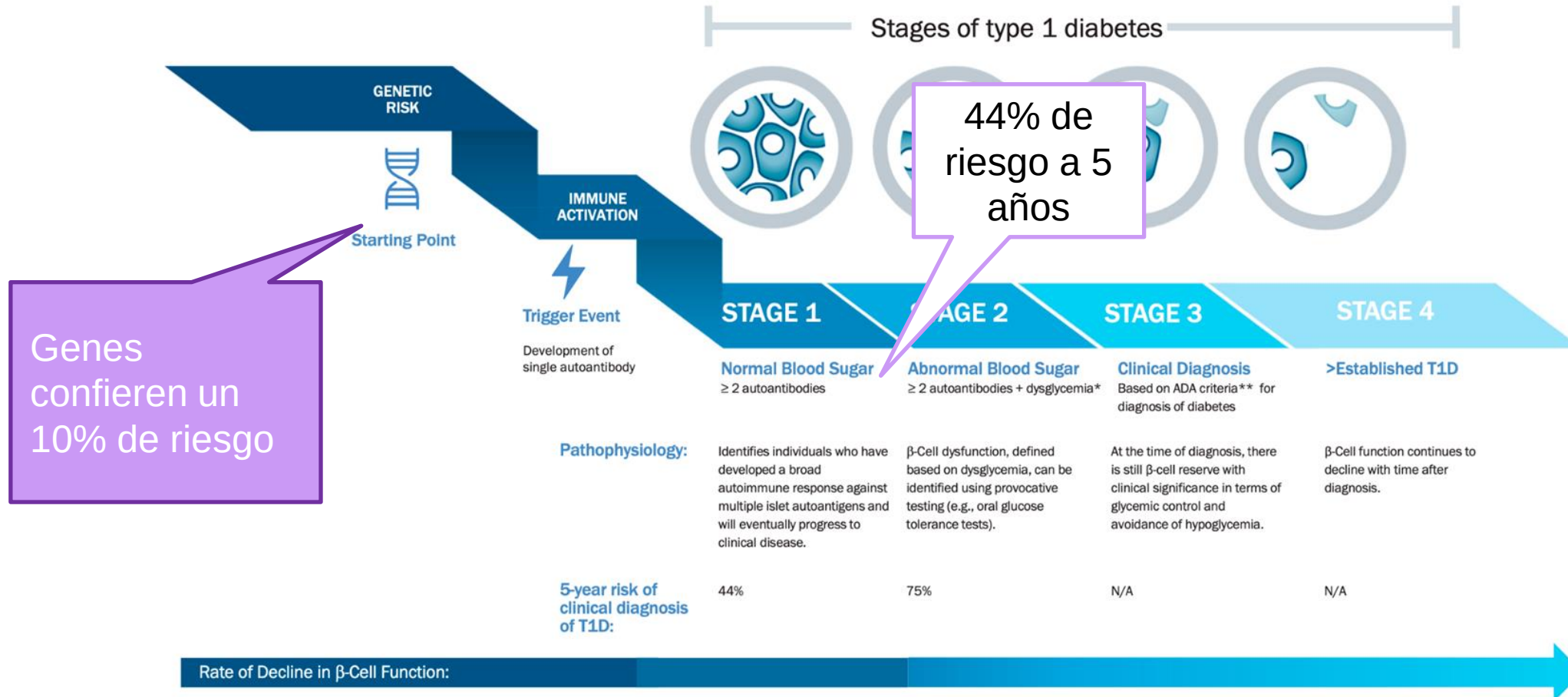
Familiares 1



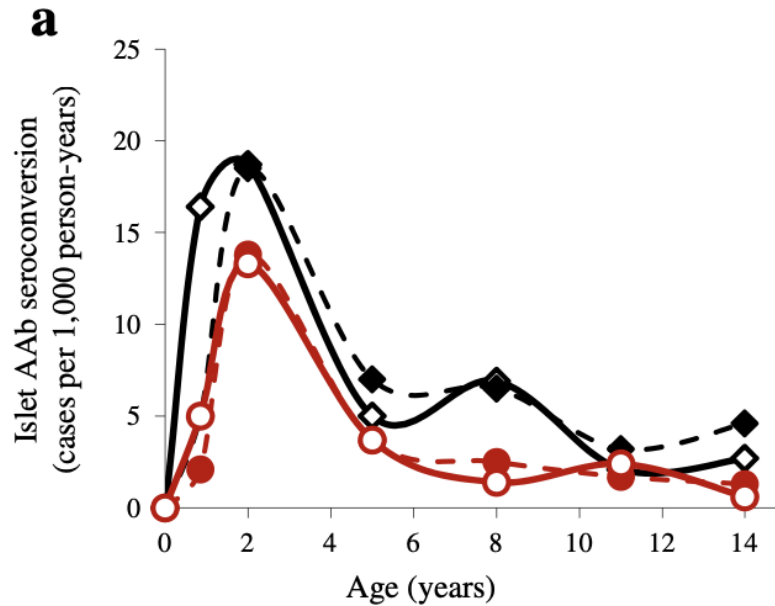
Población 9



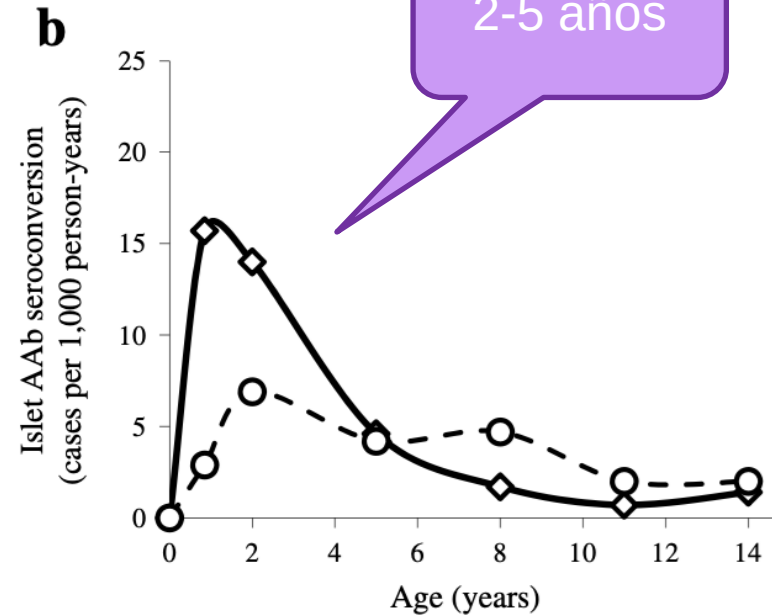
¿Qué determinaciones realizar?



Tasa de conversión de autoanticuerpos ¿Cuándo?



IAA	1,650	1,492	1,323	1,163	936	503
GADA	1,650	1,508	1,338	1,171	943	502
IA-2A	1,650	1,512	1,348	1,198	971	523
ZnT8-A	1,650	1,508	1,345	1,186	972	522



Multiple	1,650	1,489	1,316	1,143	960	483
Single	1,650	1,511	1,364	1,214	987	500



The Antibody Detection Israeli Research



Moshe Phillip

The Institute for Endocrinology and Diabetes
Schneider Children's Medical Center of Israel

Lisbon Oct. 19th



ADIR

Demostrar una disminución en los casos de CAD para que se apruebe un programa nacional de detección.

- 1 PREVENIR CETOACIDOSIS
- 2 TERAPIAS EFECTIVAS
- 3 PREVENIR ENFERMEDAD
- 4 BIOMARCADORES
- 5 INVESTIGACIÓN



Enrollment
Community clinics



Study lab

Central HMO labs



Research center



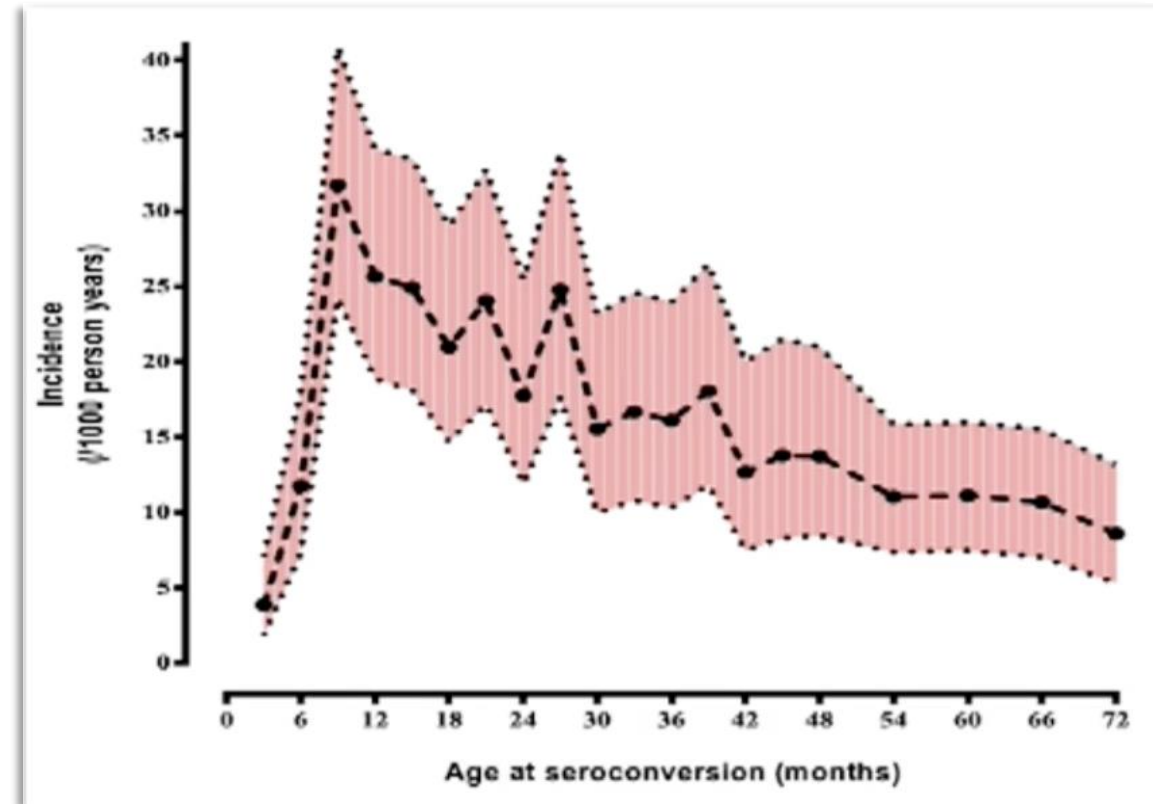
Follow up
Diabetes centers



61 clínicas
6 centros de diabetes

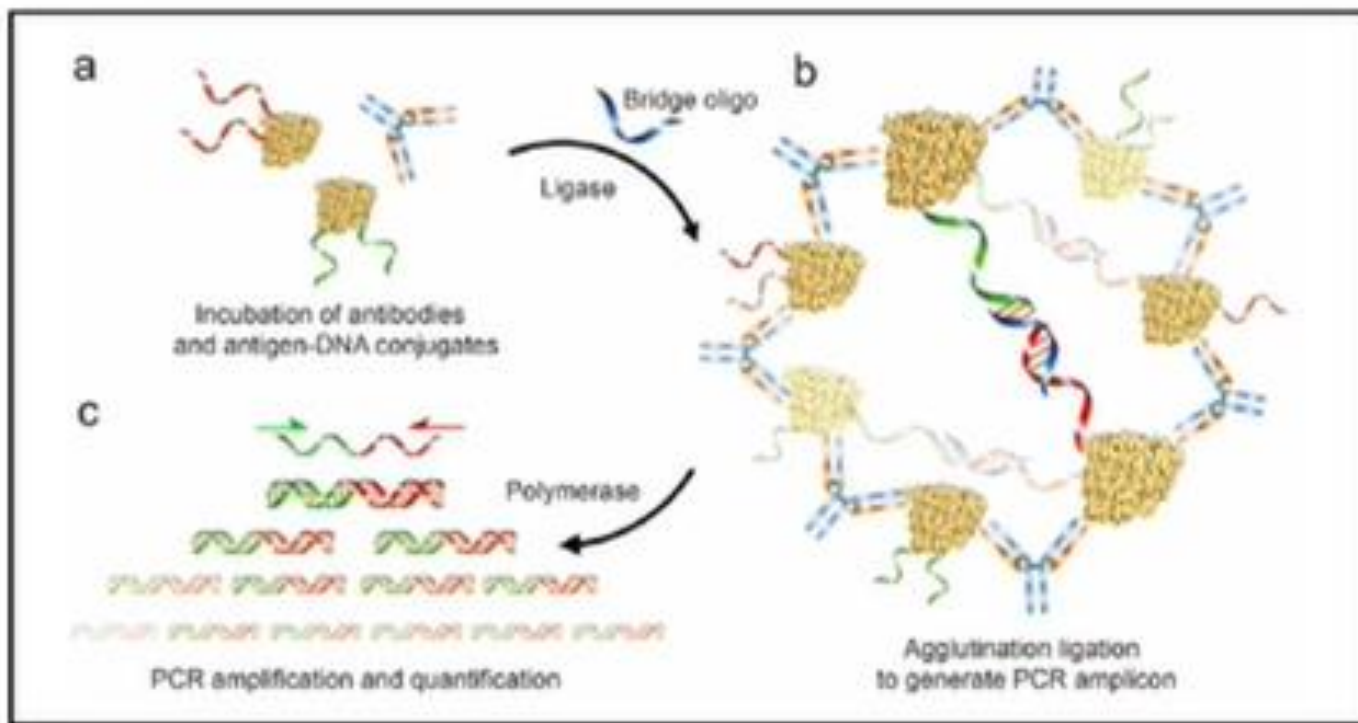
Detección de DT1 Estadío 1

- Sistema Nacional de Salud.
- Historia clínica electrónica.
- Optimizaron recursos: aprovecharon el programa de detección de anemia, que captaba el 97% de los niños en edad 9-18 meses.
- Mejoraron la sensibilidad del test.



Krischer et al. Diabetes Care 2017 (40)
Rogers et al. BMC Medicine 2017 (15)

Anticuerpos: ADAP



ADAP

Técnica de aglutinación
PCR-Sensible
IA-2, IAA, GADA
4μL sangre

Oron, Tal, Cortez, Felipe de Jesus, Shtauf, Biana, et al. Detection of Islet Autoantibodies in Whole Blood by Antibody Detection by Agglutination-PCR (ADAP) Technology Is Sensitive and Suitable for General Population Screening Programs, *Pediatric Diabetes*, 2024.

ADIR Diseño

- **Población:**
 - 35.000 niños a los **9 meses**.
 - 5.000 niños a los **5 años**.
- **Metodología:**
 - Técnica **ADAP** (Antibody Detection by Agglutination-PCR) para detectar autoanticuerpos relacionados con diabetes tipo 1.
 - **Seguimiento de 5 años:**
 - Niños con **≥ 2 autoanticuerpos positivos**.
 - Posterior inclusión de niños con **1 anticuerpo y antecedentes familiares** tras consenso.



Resultados preliminares

GADA+ IA-2A	GADA+ INS-A	IA2-A+ INS-A	All 3
27	12	7	8

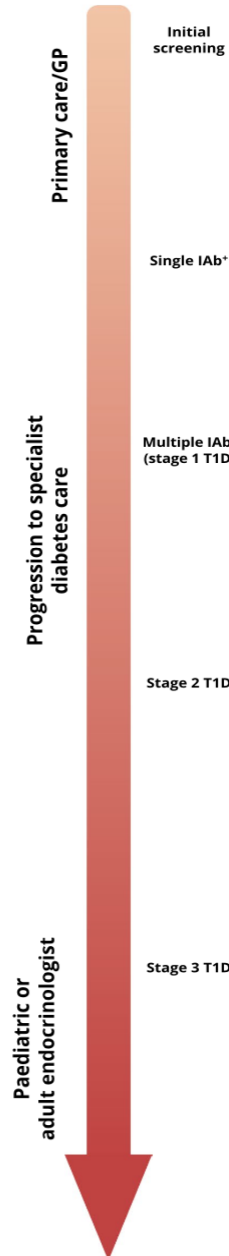
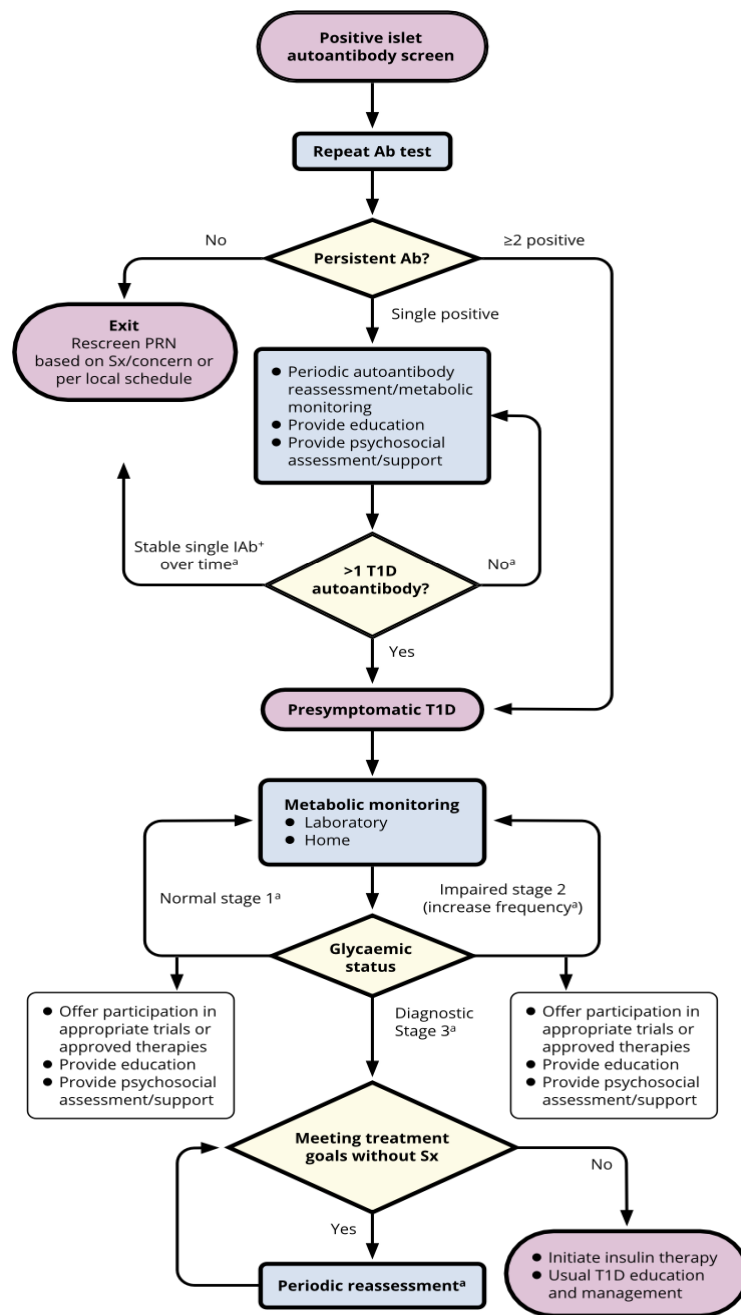
- Población estudiada:
 - Total: 14,608 niños.
 - <18 meses: 10,980.
 - 18 meses - 5 años: 3,628.
- Muestras analizadas: 9,100.
- Resultados positivos:
 - 54 niños (0.59%) con múltiples autoanticuerpos.
 - 5 niños con un autoanticuerpo y antecedentes familiares de diabetes

54/9100: 0,59%

¿¿¿Y después???

Seguimiento 2 anticuerpos: investigadores.

Seguimiento a los que tiene 1 anticuerpo: pediatra, guías y número telefónico.



Guía para el monitoreo de personas con autoanticuerpos positivos en estadios tempranos de la DT1

Phillip, M., Achenbach, P., Addala, A. *et al.* Consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes. *Diabetologia*, 2024.



Screening program for type 1 diabetes in Italy

Valentino Cherubini
SOD Diabetologia Pediatrica
Azienda Ospedaliero Universitaria delle Marche

2024.ispad.org



Programa Nacional por Ley

GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA

PARTE PRIMA Roma - Martedì 17 settembre 2023

AVVISO ALLE AMMINISTRAZIONI

SOMMARIO

LEGGE 15 settembre 2023, n. 130.

Disposizioni concernenti la definizione di un programma diagnostico per l'individuazione del diabete di tipo 1 e della celiachia nella popolazione pediatrica. (23G00140)

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

LEGGE 15 settembre 2023, n. 130.

Disposizioni concernenti la definizione di un programma diagnostico per l'individuazione del diabete di tipo 1 e della celiachia nella popolazione pediatrica. (23G00140)

Pag. 1



Bosi E, Catassi C. Screening type 1 diabetes and celiac disease by law. Lancet Diabetes Endocrinol. 2024



Diabetes y Enfermedad celíaca



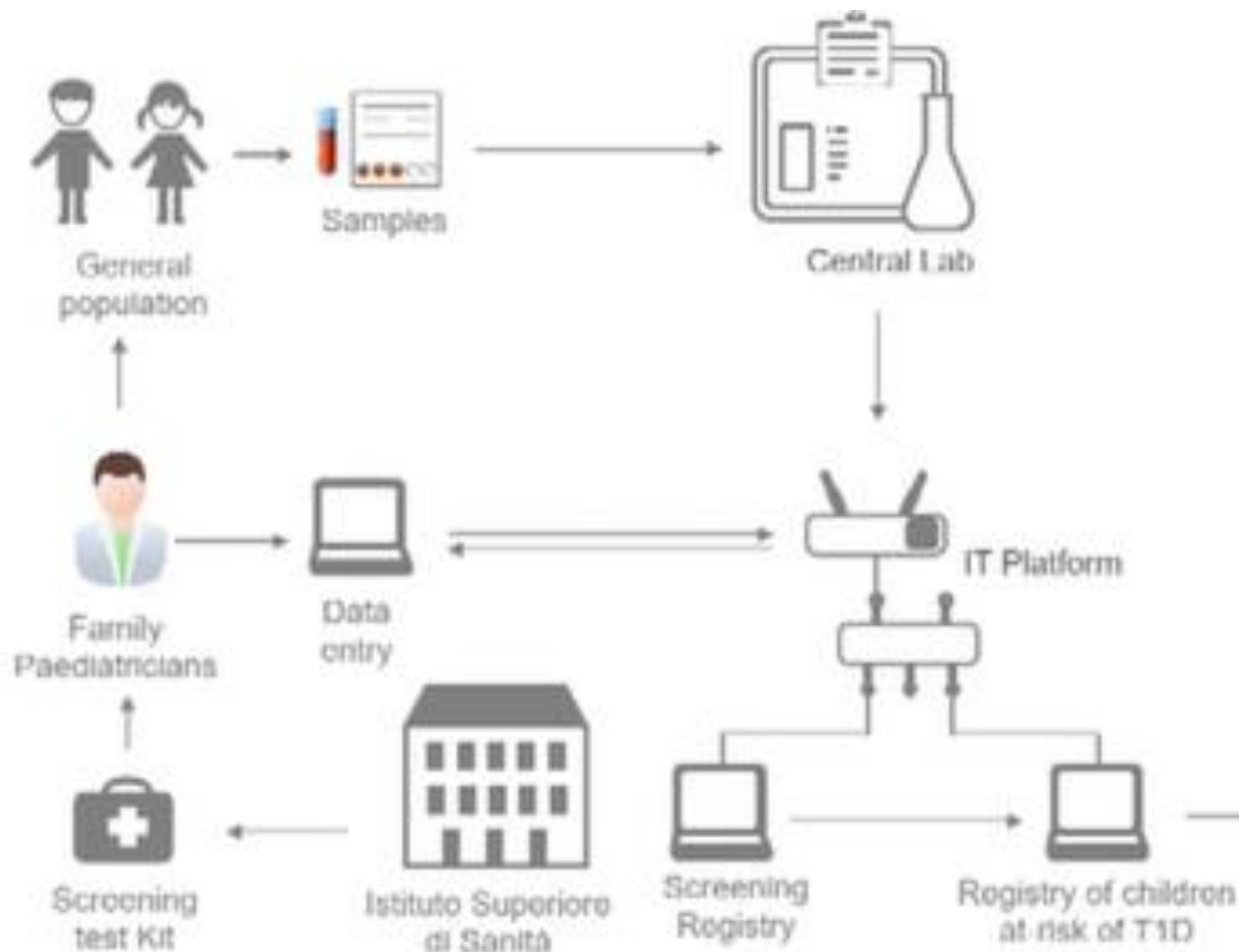
Componentes Principales

1. Registro de personas en riesgo.
2. Colaboración con pediatras de atención primaria.
3. Centros especializados en T1D para seguimiento.
4. Educación para pacientes y familias.
5. Pruebas de anticuerpos confiables.
6. Pruebas metabólicas adecuadas.
7. Encuestas de viabilidad y aceptación.
8. Acceso a terapias innovadoras.
9. Monitoreo de resultados (incidencia de DKA).
10. Análisis de costos.



Seguimiento de personas con un solo IA positivo, además de múltiples IA positivos.

Uso de monitoreo continuo de glucosa (CGM) para evaluar la progresión del riesgo.



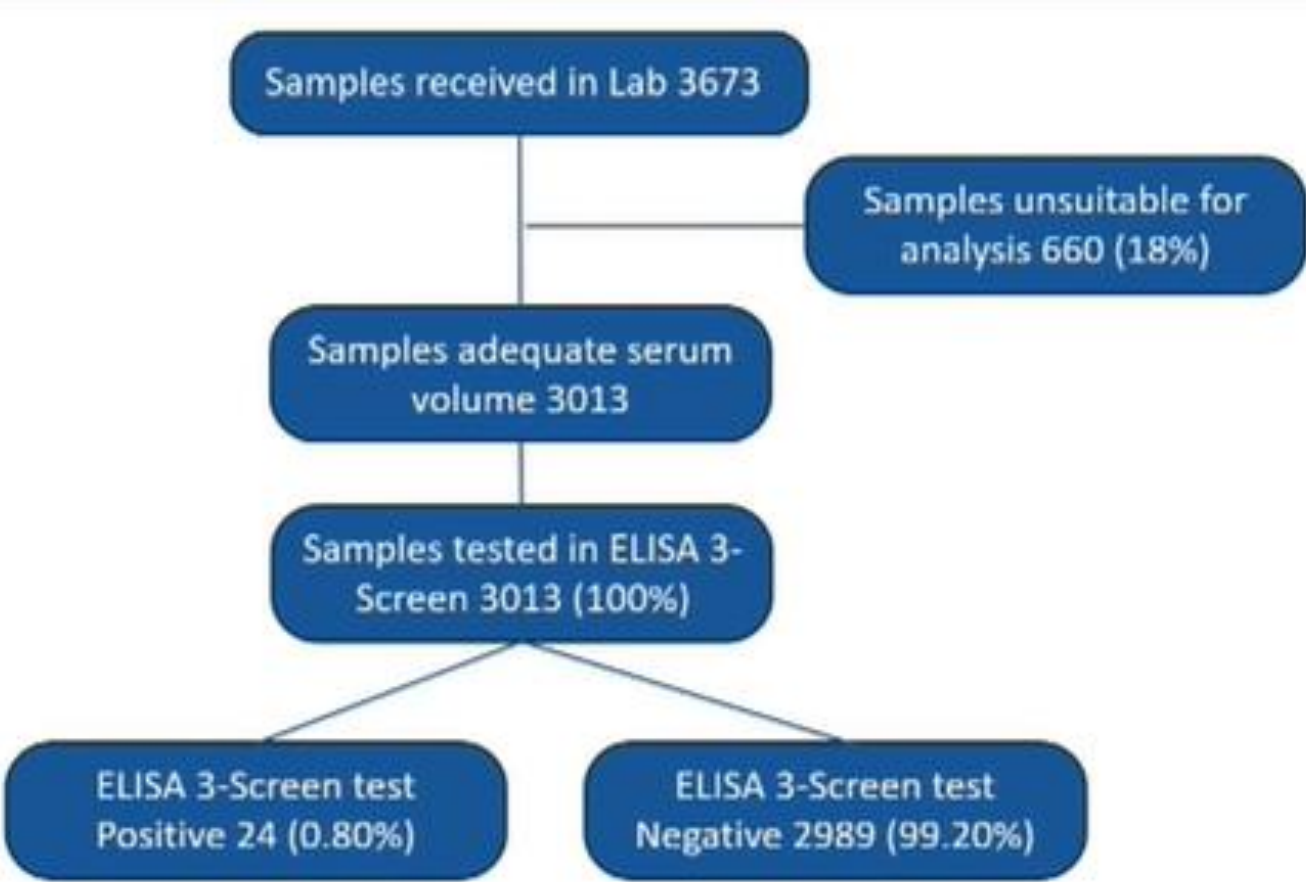
Edad de screening: 2, 6 y 9 años.

Detección de anticuerpos:

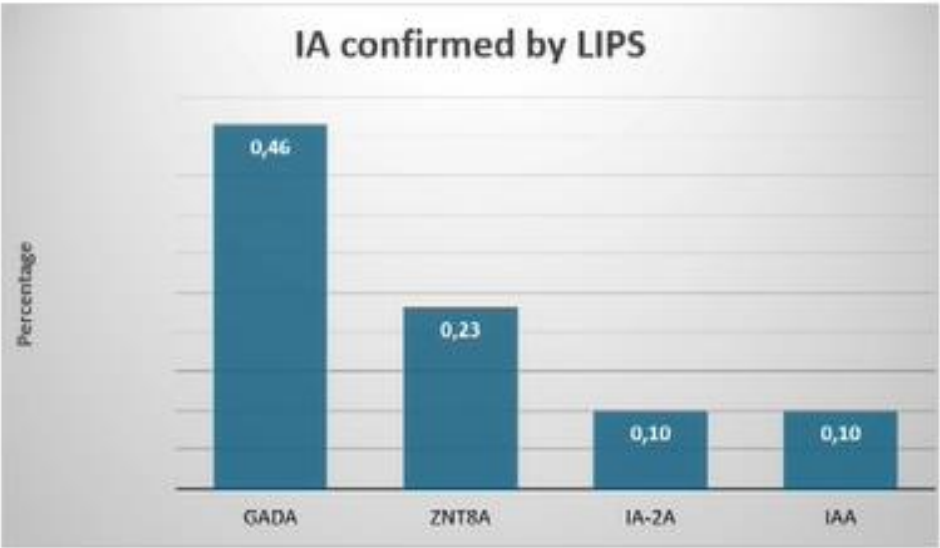
- **Primera etapa:** ELISA (ZnT8, IA2A, GADA).
- **Confirmación:** LIPS (Luciferase Immunoprecipitation System).

Resultados

15/3013:0,49%



n. 24 9 15



n. 14 7 3 3

Cherubini V et al. Follow-up and monitoring programme in children identified in early-stage type 1 diabetes during screening in the general population of Italy. Diabetes Obes Metab. 2024





Resultados

- **Alta motivación** de las partes involucradas.
- Los pediatras muestran **buena capacidad para involucrar a las familias**.
- **Dificultades técnicas:**

Muestras capilares complejas en niños mayores.

La muestra no es estable para almacenamiento y transporte.

- **Costos:** El 50% del presupuesto se destina a recolección de muestras y transporte.

Desafíos y Recomendaciones

1. **Optimización de recolección de muestras:**
 - Evaluar el uso de muestras en **papel filtro**.
 - **Agrupación de muestras** para reducir costos.
2. **Educación y sensibilización:**
 - Mejorar la información sobre el screening a médicos y familias.
 - Proveer soporte educativo continuo.
3. **Recursos humanos y logísticos:**
 - Incrementar el **personal en centros de referencia**.
 - Incorporar un **psicólogo dedicado** al programa.
4. **Diagnóstico y monitoreo:**
 - Definir los laboratorios para confirmación de positivos.
 - Incluir un código **ICD-10** específico para el screening como parte del cuidado en DT1.

¿Y si lo hiciéramos en Argentina?



Argentina 2022 Población 45.892.285 (INDEC)

0-14 años =1.076.302

76.878 tienen 2 años de edad

453 positivos por año.





Information brochure for parents and children



Early diagnosis and care of type 1 diabetes

- ¿Nuestro hijo está en peligro?
- ¿Podemos hacer algo para evitar que la diabetes progrese?
- ¿Qué significa esta enfermedad para nuestra familia y nuestros planes futuros?
- ¿Cuál es la mejor manera de cuidar a nuestro hijo ahora y en el futuro?
- ¿Dónde podemos encontrar apoyo y asesoramiento especializado?



Psychology of Screening and Follow up of high-risk children

JESSICA MELIN, PHD
LUND UNIVERSITY, SWEDEN



Pros y contras del screening de la diabetes

Pros

Sentimientos de satisfacción y seguridad



Contras

Sobreprotección del niño.

El niño es tratado como enfermo.

Impacto negativo en las relaciones padres-hijo.

Preocupación y ansiedad.

ESTRÉS Y ANSIEDAD

Es mayor si hay un familiar con diabetes.

Es mayor en madres que padres.

Correlación entre padres e hijo.

Recomendación del experto

- ✓ TIEMPO!!!
- ✓ Consistencia del equipo. Es mejor tener un referente para cada familia.
- ✓ Comunicar repetidas veces, diversas formas.
- ✓ Evaluación en cada visita



Information material - Children

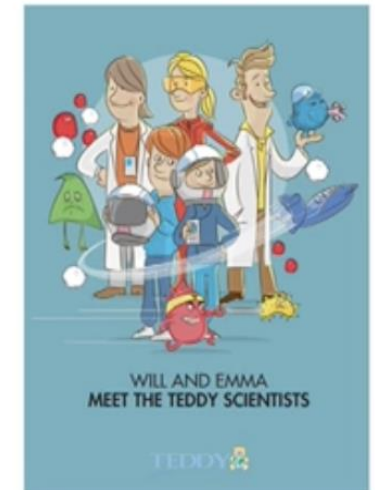
At 2 years



At 5-6 years



At 10 years



<http://www.teddy.lu.se/>

Educación nutricional en los estadios tempranos de la DT1



Dietary education in early stages of type 1 diabetes

Monica Marino, RD and PhD candidate

*Pediatric Diabetology Unit,
Women's and Children's Health,
Azienda Ospedaliero-Universitaria
Ospedali Riuniti Ancona, Marche
Polytechnic University, 60121
Ancona, Italy.*

monicamarino96@gmail.com







Educación nutricional en el programa de detección temprana DT1

¿Quién?

¿Qué?

¿Cómo?

¿Cuándo?



¿Modificar la dieta puede detener o retrasar el desarrollo de la DT1?

¿Quién?



¿Cuándo?

INMEDIATAMENTE



¿Qué?

Macronutrientes, carga glucémica, efecto de las comidas mixtas en la excursión prandial y la glucemia.

Promover hábitos saludables.

Dieta no detiene la progresión de la DT1.



Mensajes clave

- ✓ La detección temprana está en marcha y es factible.
- ✓ Se requiere estructura y personal dedicado.
- ✓ Mejoras en los métodos de laboratorio.
- ✓ Planificación del monitoreo.
- ✓ Se presenta ansiedad y requiere abordaje profesional.
- ✓ La educación debe ser temprana, adecuada y sostenida.
- ✓ Se necesita un código ICD-10 específico para el screening como parte del cuidado en diabetes tipo 1.



¡Muchas Gracias!



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ISPAD's 50th Annual Conference

Lisbon, Portugal | October 16 - 19, 2024

PUESTA AL DÍA EN TERAPIAS AUTOMATIZADAS

#ISPAD50

Dra. Marcela Raggio

Médica de staff Nutrición Infantil Hospital Universitario Austral y HMIT





Marcela Raggio

- Médica Pediatra, especialista en nutrición infantil (UBA)
- Magister en Diabetes (USAL)
- Médica de staff Nutrición infantil Hospital Universitario Austral y HMIT (Hospital Materno Infantil Tigre)
- Coordinación Módulo de pediatría Maestría diabetes SAD
- Docente Maestría de diabetes Universidad Austral



Conflictos de interés

- ✓ Disertante de Simposios de la Industria de Abbott Diabetes, Medtronic Latam, Roche Diabetes, Novo Nordisk.
- ✓ Asesoría científica Roche Diabetes, Sanofi Diabetes.

AGENDA

#ISPAD50



Sistemas AID: Evidencia y resultados

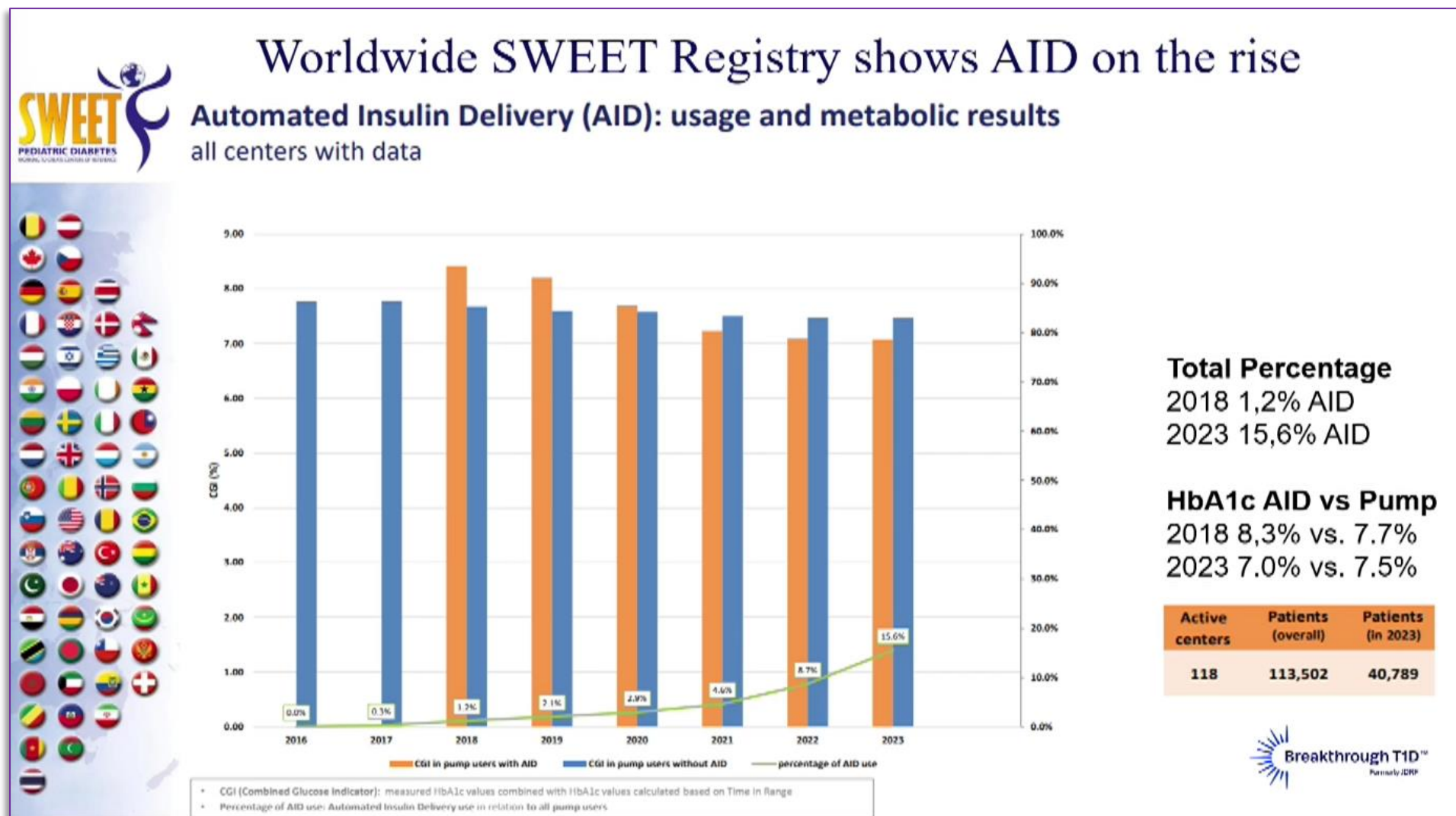


Foco en alcanzar la normoglucemia (TITR)



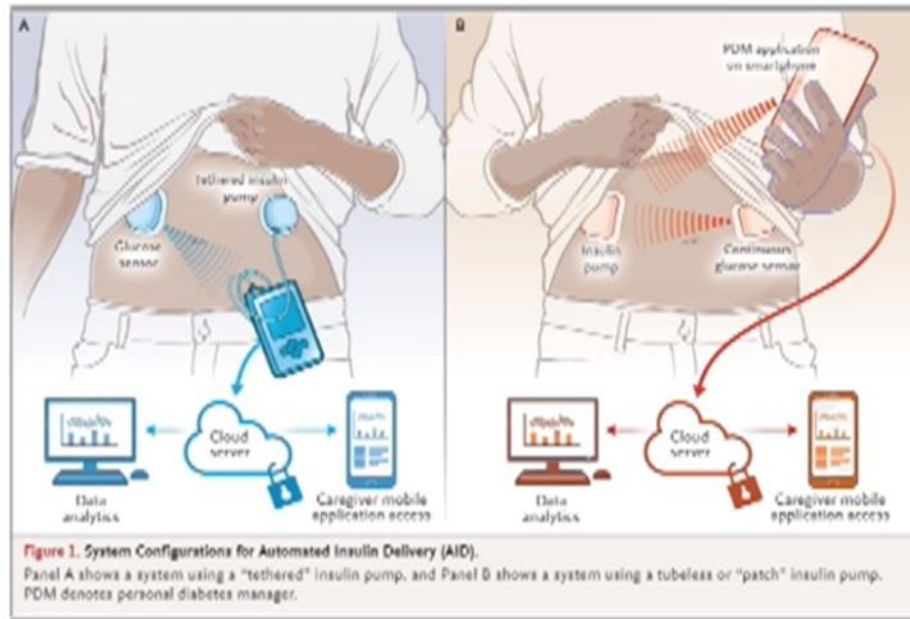
Resultados en poblaciones desafiantes

Registro mundial SWEET muestra crecimiento de la AID



Los blancos tienen que ser alcanzables. AID es un *game changer*

AID (Automated Insulin Delivery) → Transforming Glucose Variability to Insulin Variability



Digital Technology for Diabetes

Michael J. Hughes, M.D., Anne M. Mulla, D.O., M.B.A., and Bruce Buckingham, M.D.

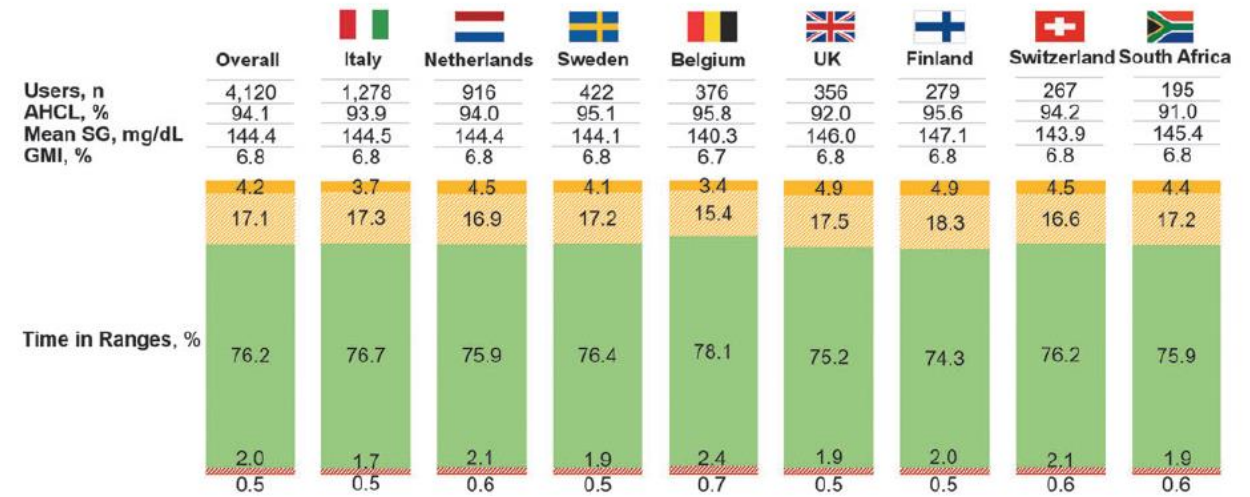
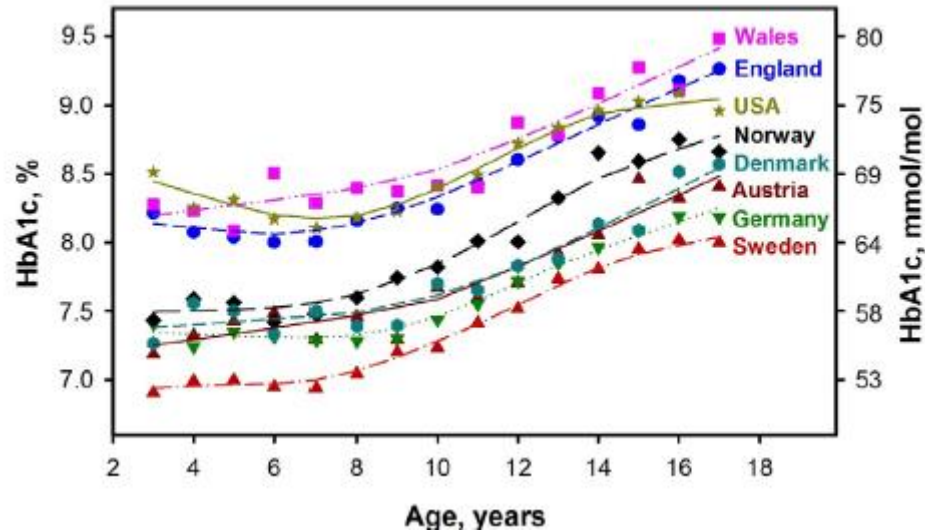
November 30, 2023

N Engl J Med 2023; 389:2076-2086

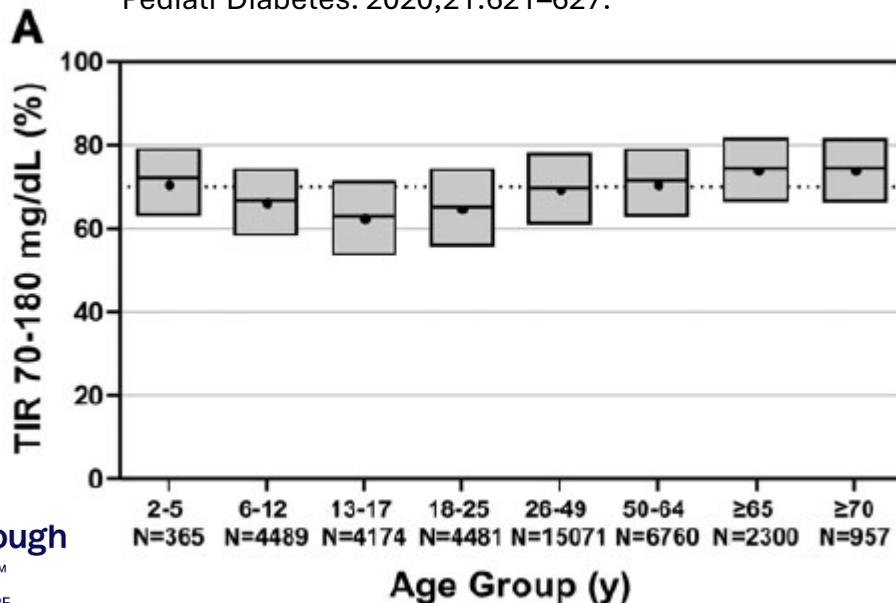


Diferencias en control entre países y distintos grupos etarios

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Pediatr Diabetes. 2020;21:621–627.



Real-World Performance of the MiniMed™ 780G System: First Report of Outcomes from 4120 Users

Julien Da Silva, MS,¹ Giuseppe Lepore, MD,² Tadej Battelino, MD,^{3,i} Arcelia Arrieta, MS,⁴ Javier Castañeda, MS,⁴ Benyamin Grossman, PhD,⁵ John Shin, PhD,⁵ and Ohad Cohen, MD^{1,ii}

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 24, Number 2, 2022
Mary Ann Liebert, Inc.

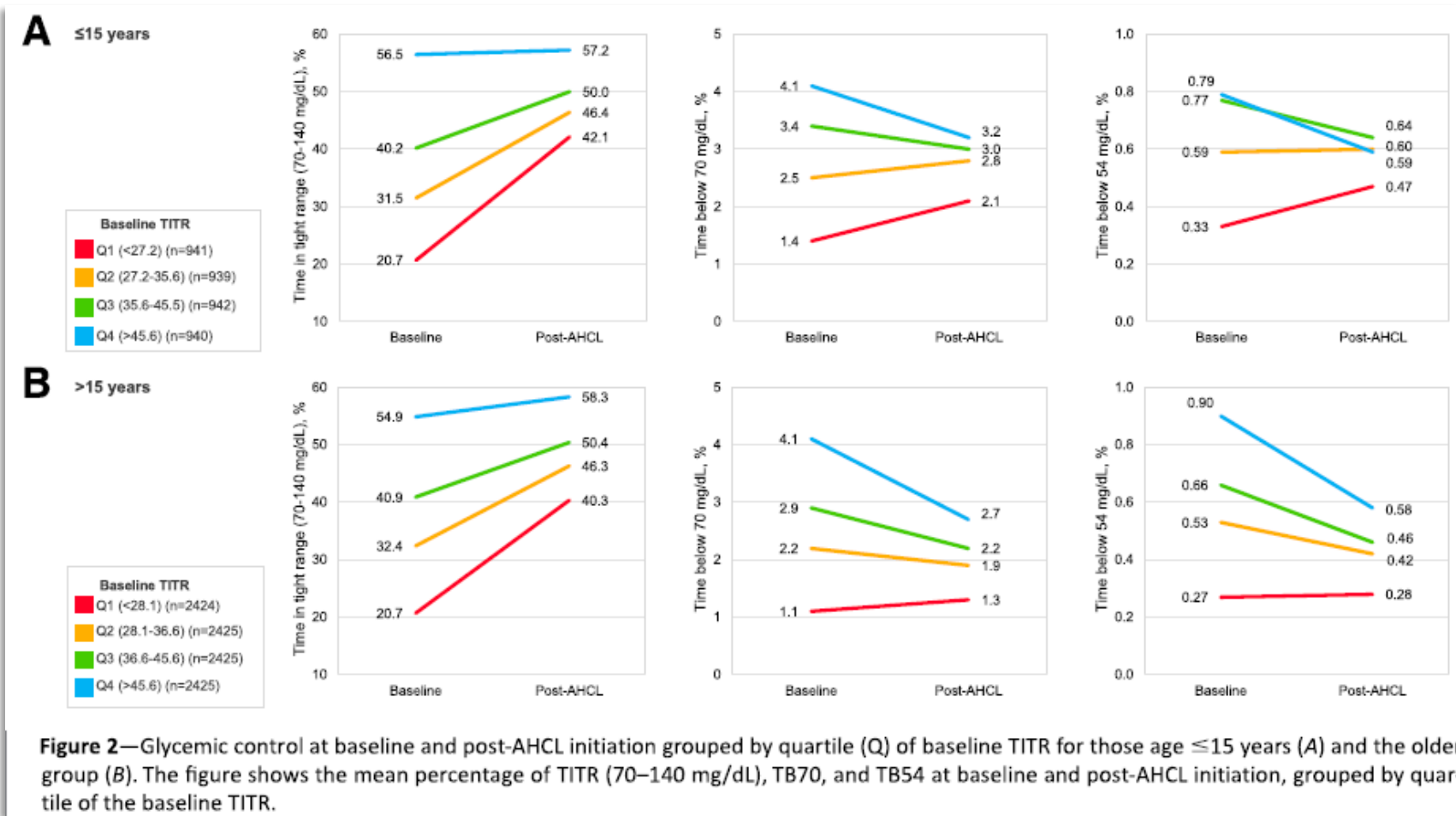
Real-World Evidence of Omnipod® 5 Automated Insulin Delivery System Use in 69,902 People with Type 1 Diabetes

Gregory P. Forlenza, MD,¹ Daniel J. DeSalvo, MD,² Grazia Aleppo, MD, FACE, FACP,³ Emma G. Wilmot, MBChB, PhD,⁴ Cari Berget, RN, MPH, CDCES,¹ Lauren M. Huyett, PhD,⁵ Irene Hadjiyianni, PhD,⁵ José J. Méndez, MS,⁵ Lindsey R. Conroy, PhD,⁵ Trang T. Ly, MBBS, FRACP, PhD,⁵ and Jennifer L. Sherr, MD, PhD⁶

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 26, Number 8, 2024
Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2023.0578

Diferencias entre control al inicio resultan en TTIR comparables con AID

Time in tight glucosa range in type 1 diabetes: predictive factors and achievable targets in real-World users of the MiniMed 780G System



AGENDA

#ISPAD50



Sistemas AID: Evidencia y resultados



Foco en alcanzar la normoglucemia (TITR)



Resultados en poblaciones desafiantes

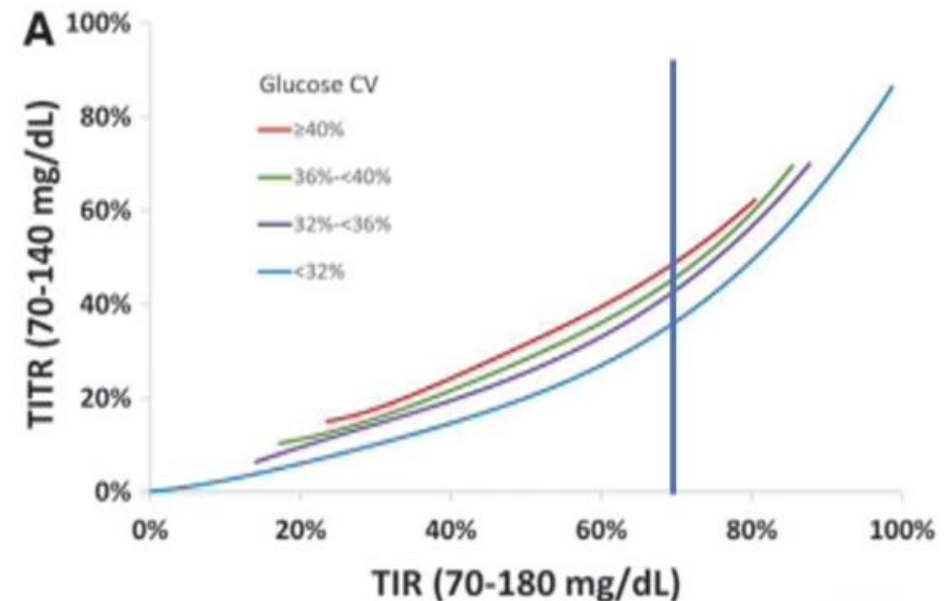
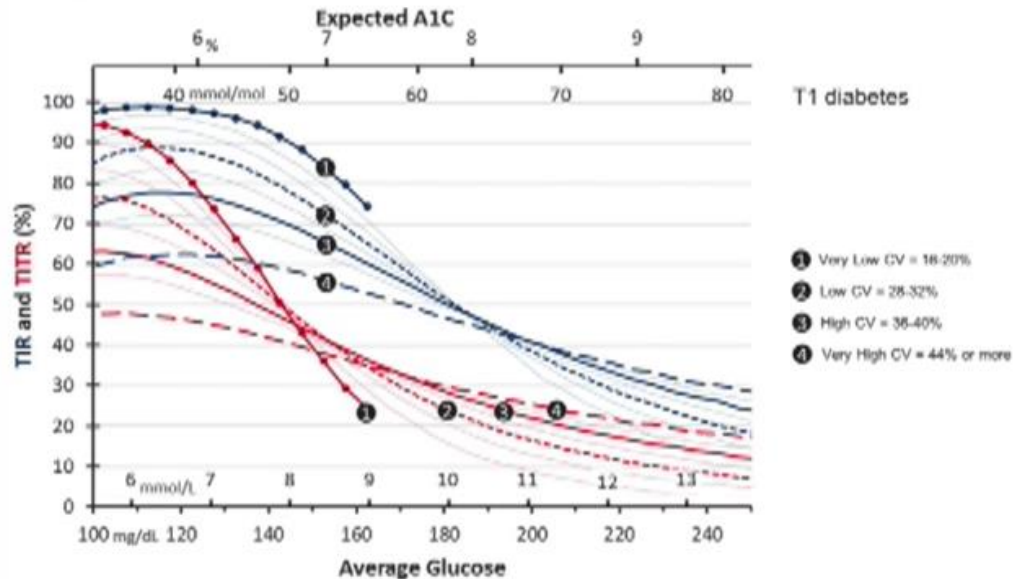
Is It Time to Move Beyond TIR to TITR? Real-World Data from Over 20,000 Users of Continuous Glucose Monitoring in Patients with Type 1 and Type 2 Diabetes

Timothy C. Dunn, PhD,¹ Ramzi A. Ajjan, MD, PhD,² Richard M. Bergenstal, MD,⁴ and Yongjin Xu, PhD¹

The relationship between TIR and TITR = nonlinear → with a higher ratio of TITR:TIR observed as TIR increased → approaching euglycemia

A Comparison of Continuous Glucose Monitoring-Measured Time-in-Range 70–180 mg/dL Versus Time-in-Tight-Range 70–140 mg/dL

Roy W. Beck, MD, PhD,¹ Dan Raghinaru, MS,¹ Peter Calhoun, PhD,¹ and Richard M. Bergenstal, MD²



Time in range – más cerca de la euglucemia

Fuerte correlación:

TITR – GMI < 7% (-0.93, n=36110)

Correlación débil para:

TIR – GMI ≥ 7% / -0.84 n=20542)

Fuerte correlación:

TIR – GMI ≥ 7% (-0.89)

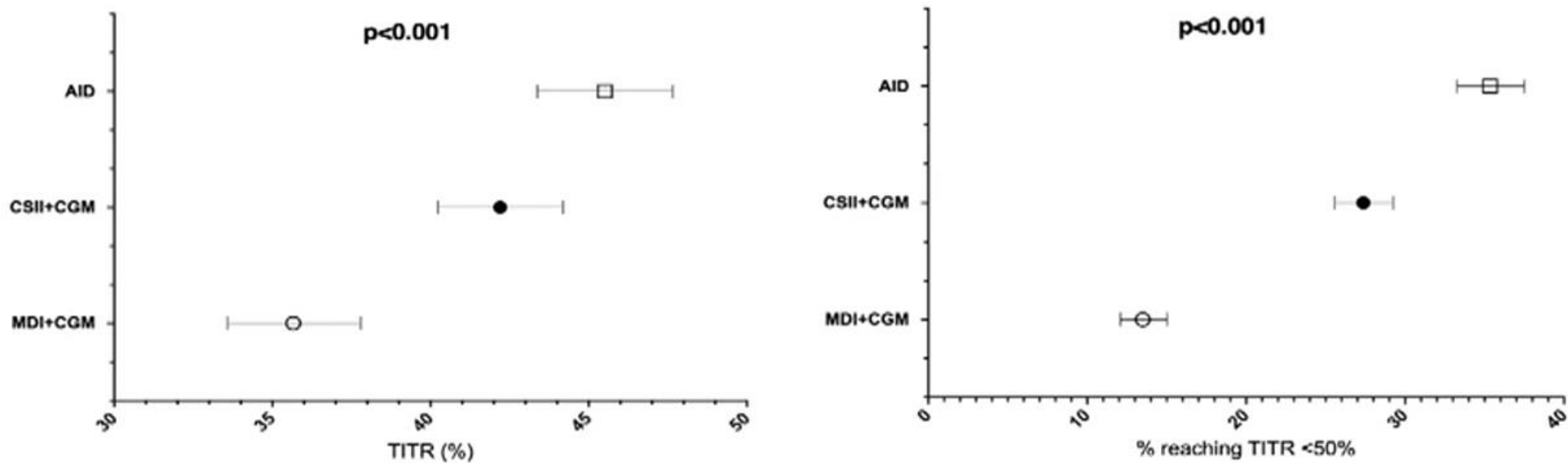
Correlación débil para:

TIR – GMI < 7% (-0.79)



TITR puede ser un mejor target para pacientes con diabetes tipo 1 con un control de glucosa que está más cercano a la euglucemia lo que se logra mediante tecnología de avanzada.

TITR con diferentes modalidades de tratamiento. Registro SWEET



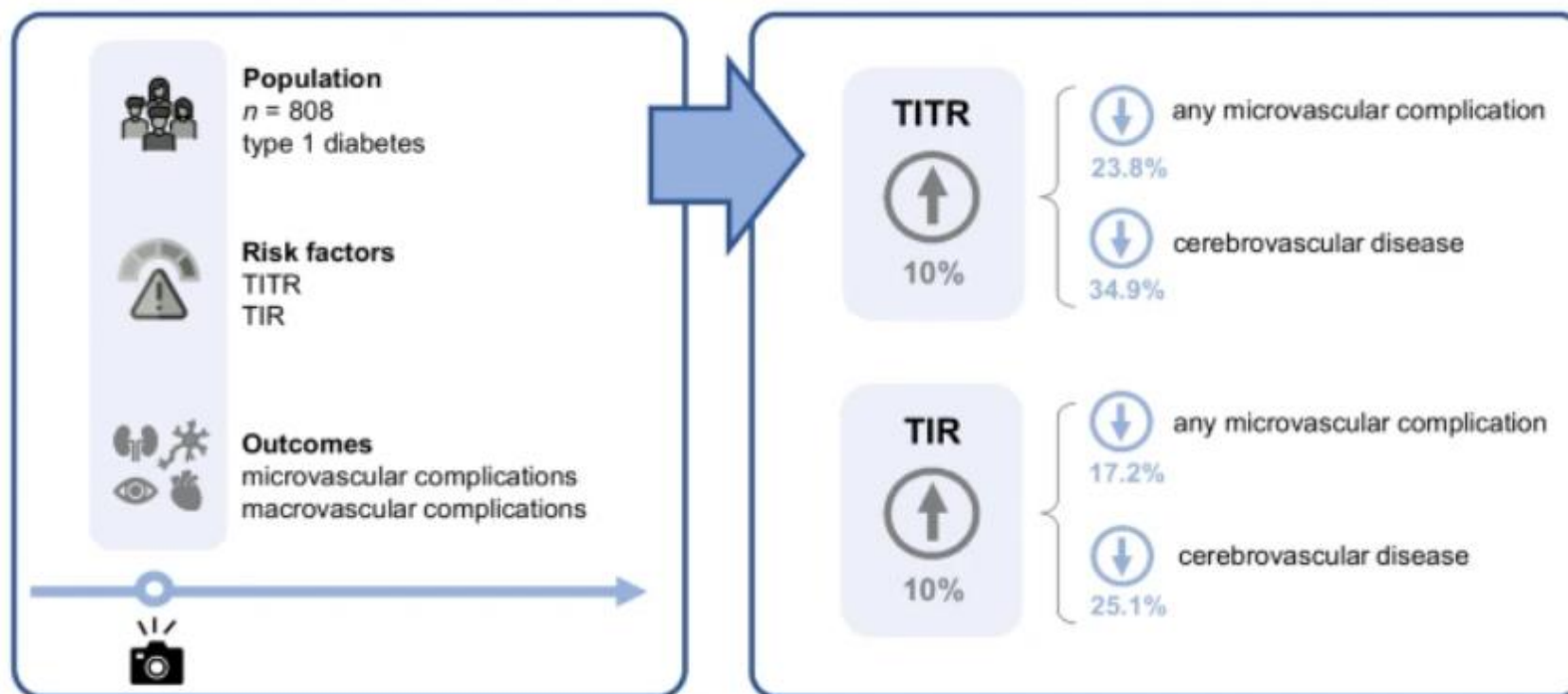
6741 personas con diabetes tipo 1 y perfiles de MCG disponibles. Datos no publicados

TITR: tiempo en rango estrecho; GMI: Indicador de Gestión de Glucosa: TIR: tiempo en rango

Von Dem Berge T et al. Stringent Glycemic Goals. Achievement. Tis vs. Titr in the sweet registry. ATTD 2024, abstrac.
MianowskaB. Cgm-base glycemic variability and its relation to TBR in the sweet registry. ATTD 2024, abstract.

Asociación de complicaciones crónicas y el tiempo en rango en pacientes con DT1: estudio cross retrospectivo de la vida real

The association of chronic complications with time in tight range and time in range in people with type 1 diabetes: a retrospective cross-sectional real-world study



T1R, time in tight range (3.9–7.8 mmol/l); TIR, time in range (3.9–10.0 mmol/l)

Beneficios T1R

- ✓ Aportar más información (TIR>70%)
- ✓ Mayor utilidad en A1D, remisión parcial y estadio 2 DT1
- ✓ Estudios de intervención (para evaluación)

Conclusions/interpretation: T1R and TIR are inversely associated with the presence of microvascular complications and CVA in people with type 1 diabetes. Although this study was not designed to establish a causal relationship, this analysis adds validity to the use of T1R and TIR as key measures in glycaemic management.

AGENDA

#ISPAD50



Sistemas AID: Evidencia y resultados



Foco en alcanzar la normoglucemia (TITR)



Resultados en poblaciones desafiantes

The Lenny trial: The use of closed loop system in young pediatric users (2-6 years old) is safe and effective

Tadej Battelino, on behalf of the LENNY investigators

University Medical Center Ljubljana
University of Ljubljana,
Slovenia

Estudio LENNY

Evaluación del sistema MiniMed 780G en pacientes jóvenes (2-6 años) con diabetes tipo 1 en el ámbito domiciliario



Objective

to evaluate the safety and performance of the MiniMed™ 780G system in Auto Mode in comparison to the MiniMed™ 780G system in Manual Mode with Suspend before low.



Design

- prospective, open-label, multi-center, randomized crossover study
- 12 centers Finland, Italy, Slovenia and UK



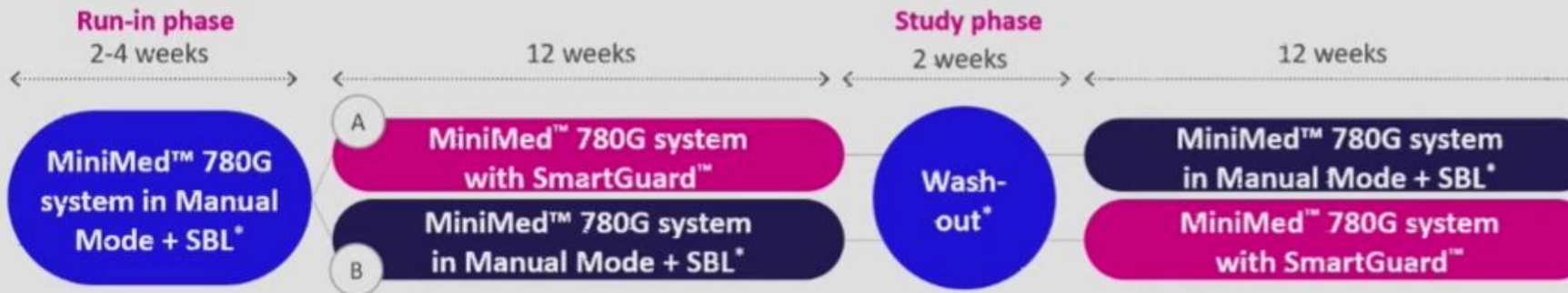
Population

- 98 children aged 2-6 at time of screening
- T1D ≥6 months
- On MDI therapy or CSII with or without CGM
- TDD ≥6 units
- HbA1c <11%



Primary endpoints

- between-treatment difference in time in target range 70-180 mg/dL (3.9-10.0 mmol/L)



*MiniMed™ 780G system with Guardian 4 sensor, suspend-before-low feature activated; ClinicalTrials.gov ID: NCT05574062; The MiniMed™ 780G insulin pump is indicated for use by patients aged 7-80 years with Type 1 diabetes, whose total daily dose of insulin is 8 units per day or more.



Sistema usado

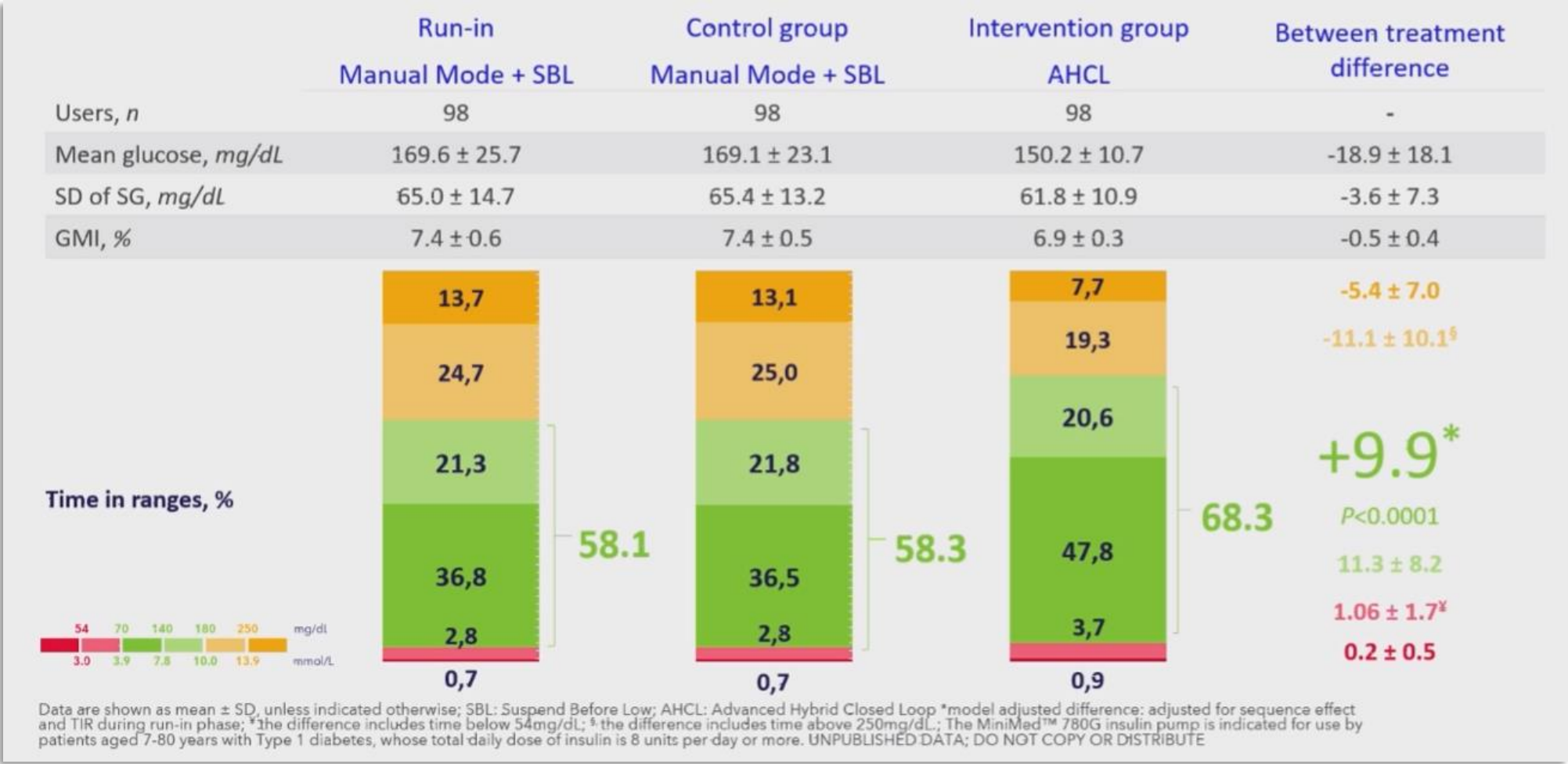
	Run-in Manual Mode + SBL	Control group Manual Mode + SBL	Intervention group AHCL
Time in AHCL, %	-	-	97.0 ± 3.99
Time in SBL, %	96.5 ± 17.6	98.96 ± 9.5	2.4 ± 2.8
Sensor use, %	96.2 ± 3.6	96.0 ± 4.0	96.3 ± 3.0
SMBG per day, <i>n</i>	5.7 ± 3.2	6.2 ± 3.2	1.7 ± 1.5

Data are shown as mean ± SD, unless indicated otherwise; SBL: Suspend Before Low; AHCL: Advanced Hybrid Closed Loop; The MiniMed™ 780G insulin pump is indicated for use by patients aged 7-80 years with Type 1 diabetes, whose total daily dose of insulin is 8 units per day or more.

SBL: suspendido antes de la baja; AHCL: circuito cerrado híbrido avanzado

Participantes con AHCL pasaron, en promedio, 2.4 h/día más en rango

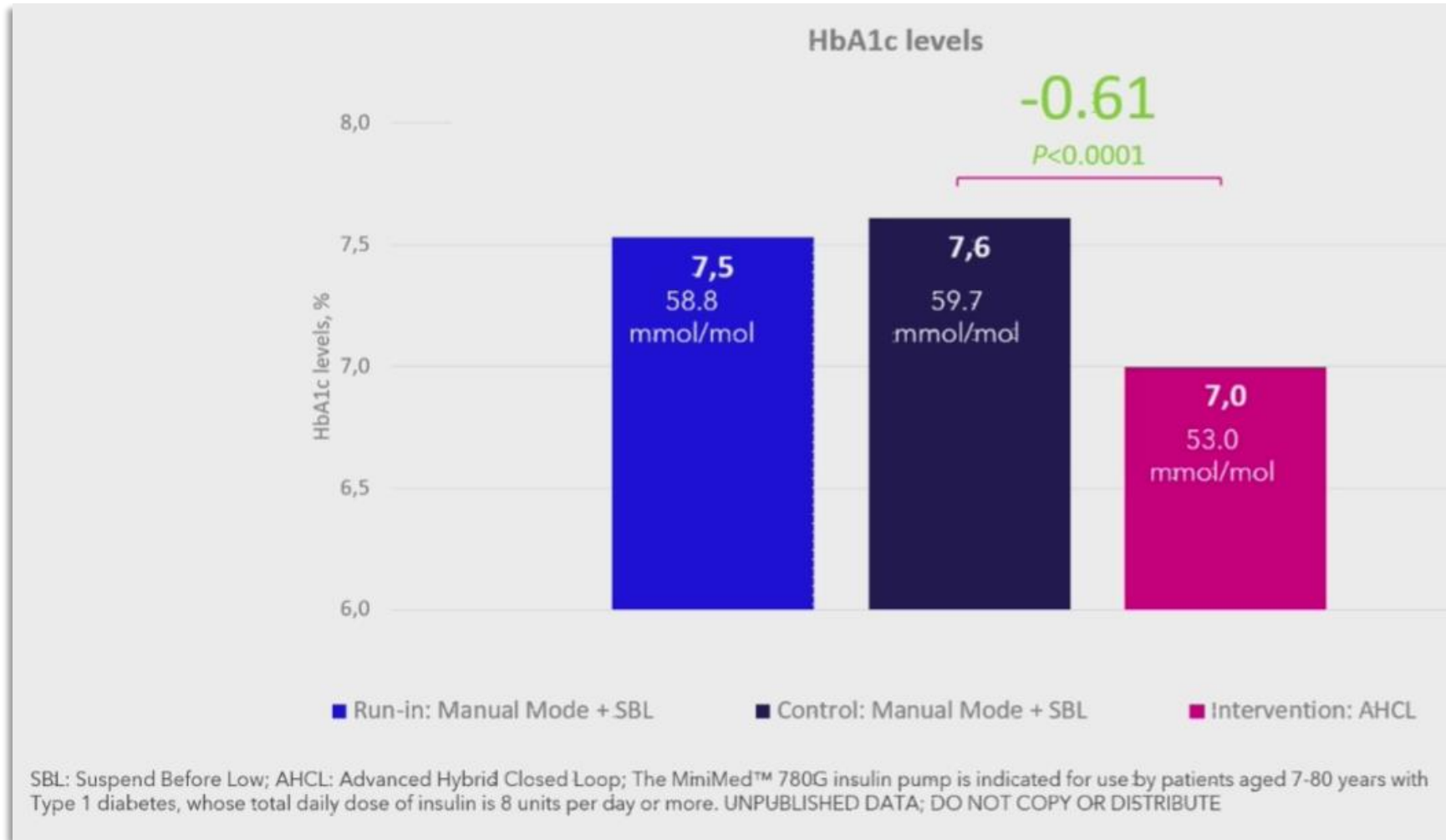
Con +10% de reducción de la hiperglucemia



SBL: suspendido antes de la baja; AHCL: circuito cerrado híbrido avanzado

La HbA1c mejoró con -0.6% con la terapia AHCL

Comparada con el grupo control con modo manual SBL



No hubo diferencias en TDD

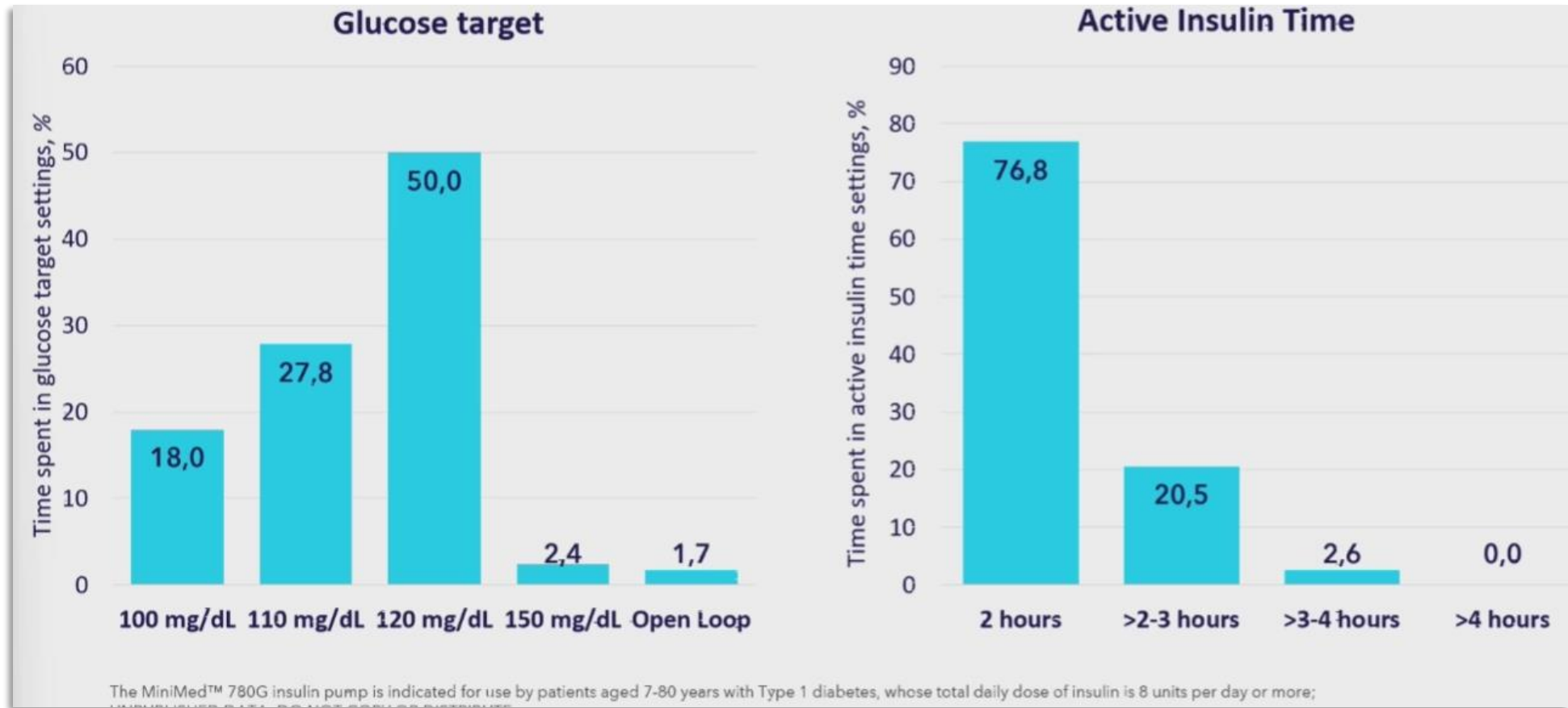
21.6% de bolos de insulina entregados automáticamente con el sistema AHCL



TDD: dosis total diaria; SBL: suspendido antes de la baja; AHCL: circuito cerrado híbrido avanzado

El protocolo de reducción de la glucosa fue basado en el TIR con riesgo de hipoglucemia

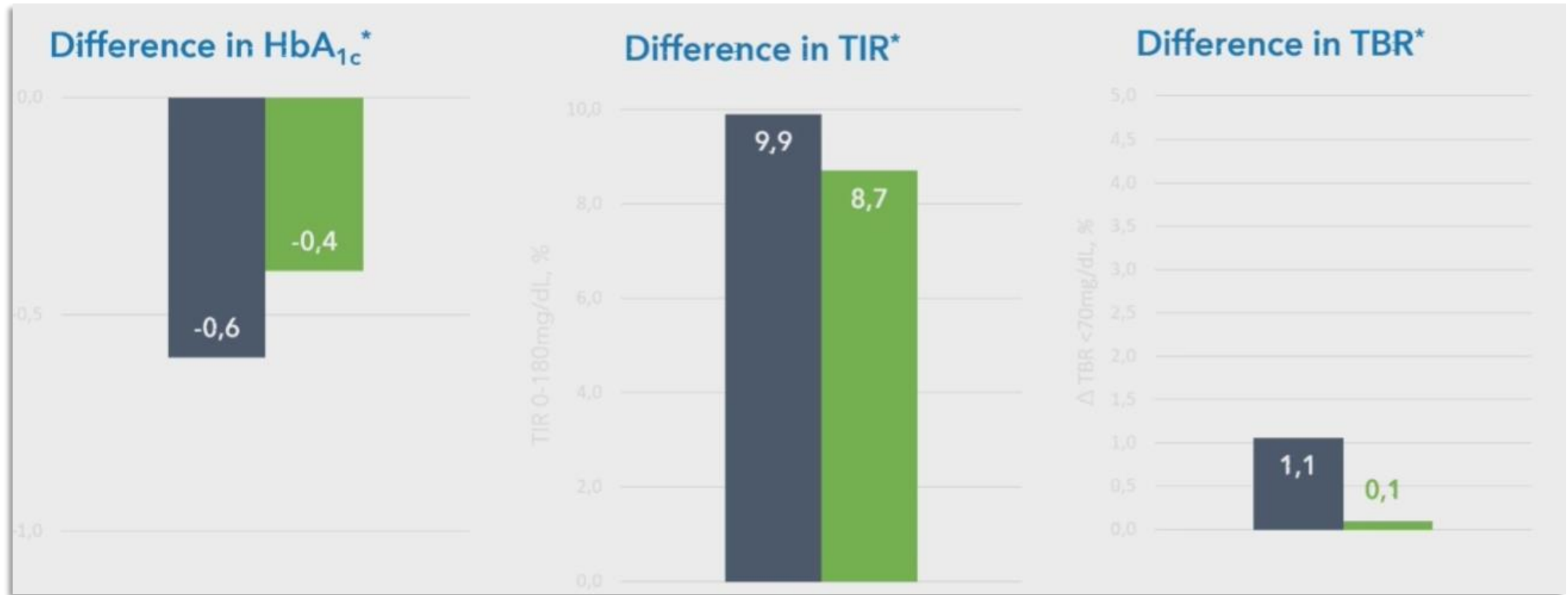
Con una glucemia de inicio de 120 mg/dL con la terapia AHCL



DATA NO PUBLICADA

TIR: tiempo en rango; AHCL: circuito cerrado híbrido avanzado

Resultados comparables entre los sistemas AID



■ MiniMed 780G system - LENNY
■ Closed-loop therapy with CamAPS FX2

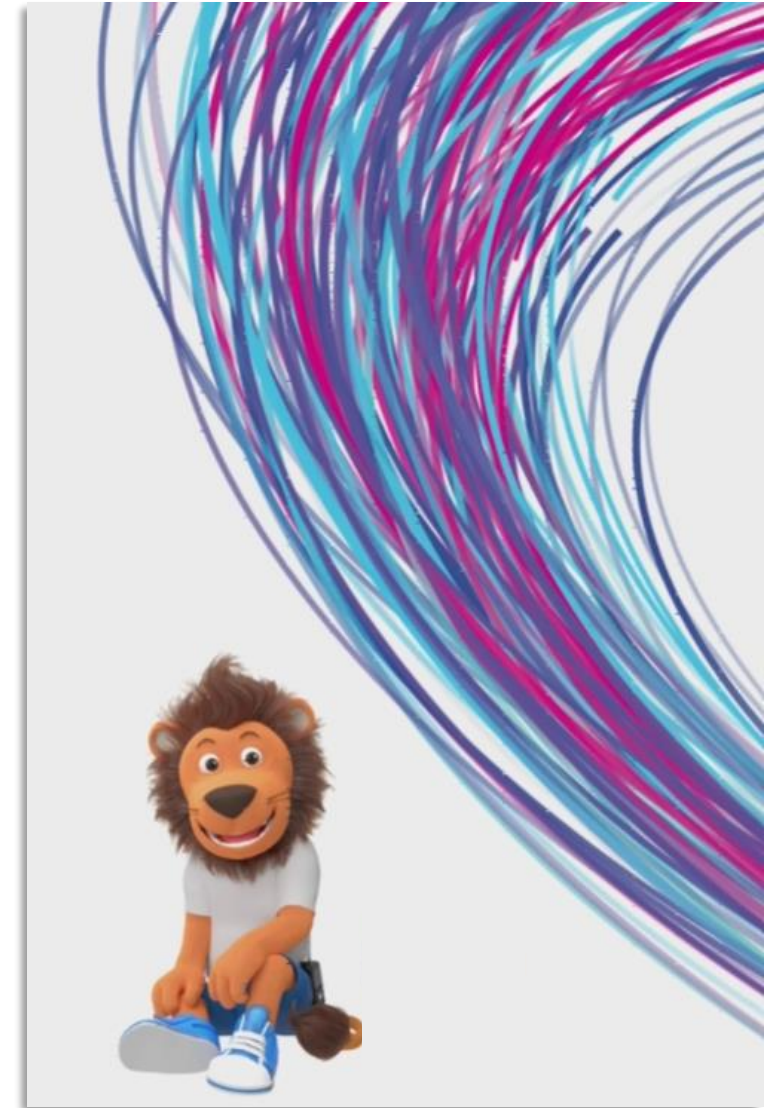
AID: infusión automatizada de insulina; TIR: tiempo en rango; TBR: tiempo bajo el rango

Superioridad de AID en registros recientes

Diabetes Care. 				
Demographic, Clinical, Management, and Outcome Characteristics of 8,004 Young Children With Type 1 Diabetes				
Jessica L. Sandy, Sascha R. Tittel, Saketh Rompicherla, Beate Karges, Steven James, Nicole Riales, Anthony G. Zimmerman, Elke Fröhlich-Reiterer, David M. Maahs, Stefanie Lanzinger, Maria E. Craig, and Osagie Ebekozien, on behalf of the Australasian Diabetes Data Network (ADDN), the T1D Exchanged Quality Improvement Collaborative (T1DX-QI), and the Prospective Diabetes Follow-Up Registry Initiative (DPV)				
	DPV	T1DX-QI	ADDN	P
Users, <i>n</i>	5,219	1,831	954	-
HbA1c, %	7.3 ± 0.9	8.0 ± 1.4	7.7 ± 1.2	<0.001
780G LENNY trial 7.0%				

Conclusiones

- ✓ *El estudio LENNY demostró que el uso del sistema MiniMed 780G en jóvenes de 2-6 años con $TDD \geq 6$ U es seguro y efectivo.*
- ✓ *MiniMed 780G mejoró los outcomes con +9.9% (+2.4h) en el TIR y –0.6% en la HbA1c.*
- ✓ *Familiares y cuidadores reportaron un mejor sueño y menos temor a la hipoglucemia.*



MENSAJES CLAVE



Resultados consistentes que se replican en distintos países y en diferentes poblaciones



Siendo factibles resultados uniformes surge la posibilidad de pensar en nuevas métricas cercanas a la normoglucemia



AID cambia paradigmas en relación a selección de “candidatos”, permitiendo mayor inclusión y beneficios para todos los usuarios



ISPAD's 50th Annual Conference

Lisbon, Portugal | October 16 - 19, 2024

GRACIAS POR SU ATENCIÓN
#ISPAD50



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¿Qué hay de nuevo en Diabetes 2?



ISPAD's 50th Annual Conference

Lisbon, Portugal | October 16 - 19, 2024

Adriana Roussos

Hospital de Niños Ricardo Gutiérrez, Buenos Aires



Adriana Roussos

- Médica pediatra, especialista en Nutrición.
- Jefa Sección Nutrición y Diabetes, Hospital de Niños R. Gutiérrez, CABA.
- Docente adscripta UBA, Pediatría.
- Docente de posgrado UBA, USAL, Barceló.

Conflictos de interés:

- No presento con respecto a esta disertación.

Diabetes 2 en jóvenes: Hoja de ruta

HACIA UN MEJOR CONTROL

MCG EN DT2

- Fundamento
- Evidencia
- Métricas

ACTUALIZACIÓN EN TRATAMIENTO

NUEVAS GUÍAS ISPAD

- Objetivos
- Tratamiento farmacológico

Objetivos glucémicos y métricas de MCG en DT2: hacia un Consenso

Tadej Battelino. Ljubljana (Eslovenia)

Jefe de Departamento de Endocrinología, Centro Médico Universitario de Ljubljana. Farmacólogo clínico. Profesor titular de Pediatría de la Facultad de Medicina de la Universidad de Ljubljana.



¿Por qué?

- Relación dosis-respuesta entre los niveles de glucemia y la ECVA, ERC, IC.

Honigberg MC y col. J Am Coll Cardiol. 2021; 78(5): 453-464.

- Relación dosis-respuesta entre los niveles de glucemia y capacidad cognitiva.

- Estructura cerebral y capacidades cognitivas.

Ranglani. Diabetes Obes metab 2023; 25:3136-3143.

- Demencia vascular y no vascular.

Celis-Morales. Diabetes Care 2022; 45:634-641.

La glucemia elevada es dañina, aún en el rango “normal”

Evidencia de MCG en DT2

Efectos del monitoreo continuo de glucosa sobre el control glucémico en pacientes con diabetes tipo 2 tratados con insulina basal. Estudio clínico aleatorizado

CON INSULINA

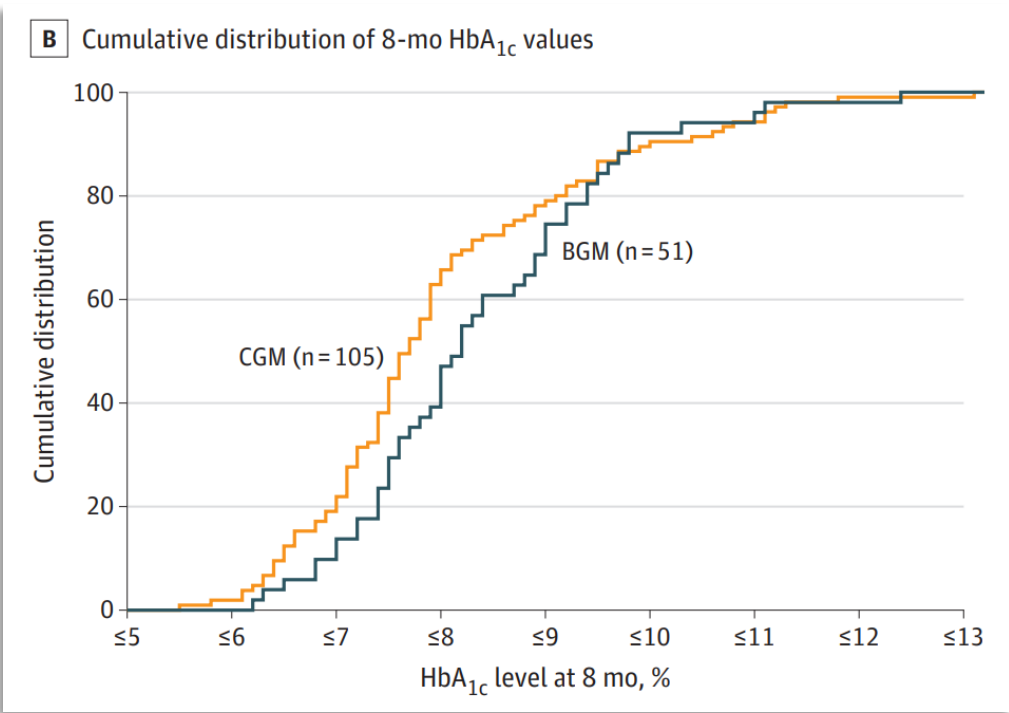
EAC, multicéntrico, EE.UU.

117 adultos con DT2

Insulina basal solamente, con o sin ADO

MCG: HbA1c significativamente menor

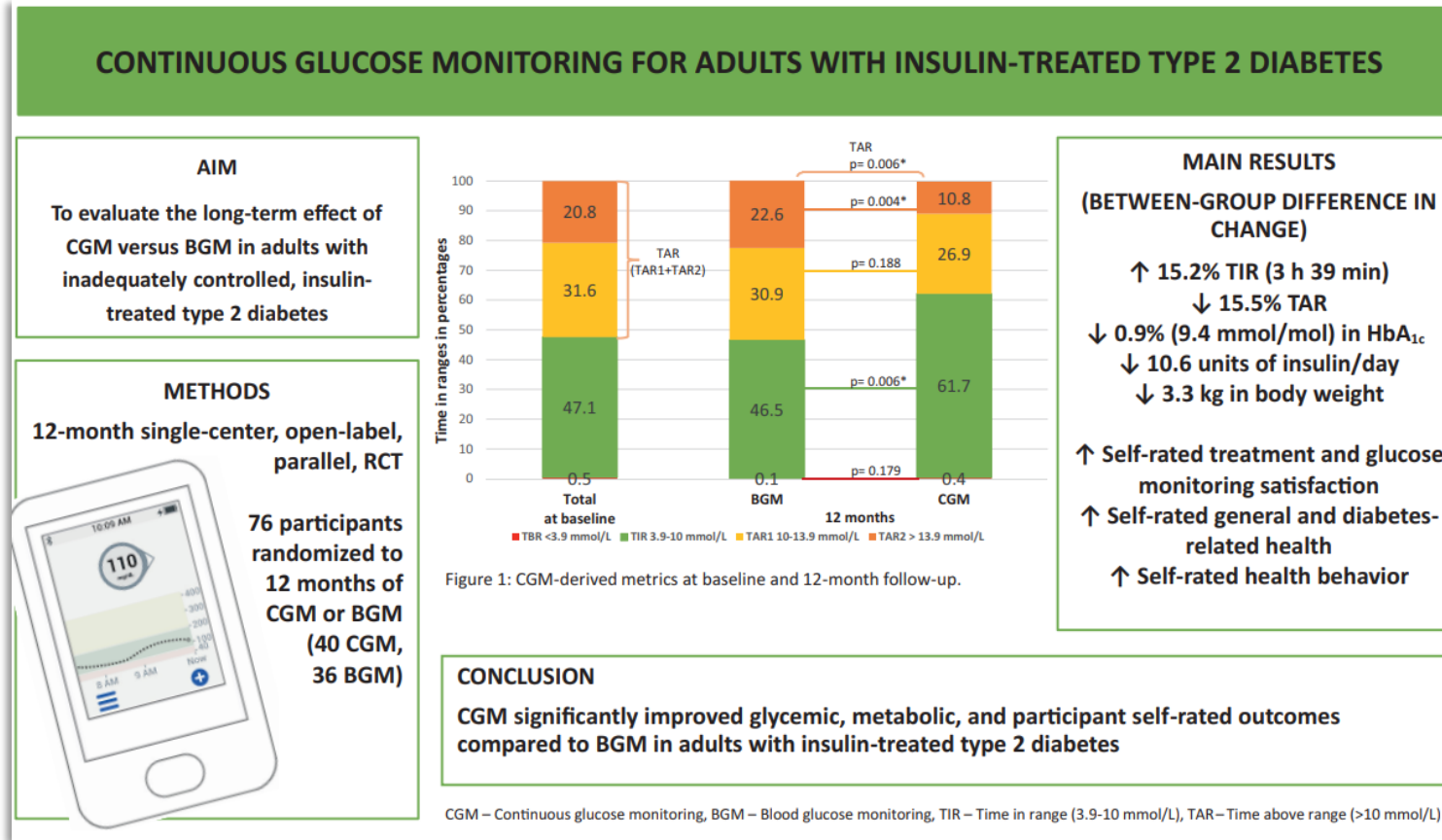
TIR significativamente mayor



	Baseline CGM	Baseline SBGM	8 mo CGM	8 mo SBGM	Diff.	p
N	114	59	93	53		
TIR (%)	40(26)	40(25)	59(25)	43(26)	15 (8-23)	<0.001
TAR > 250 (%)	26(22)	25(21)	11(11)	27(24)	-16 (21-11)	<0.001
Mean glucose (mg/dL)	209(48)	206(45)	179 (43)	206 (53)	-26 (41-12)	<0.001

Comparación de monitoreo continuo de glucosa con control de glucemia en adultos con diabetes tipo 2 insulinizados y con inadecuado control (Steno2Tech Study).

Estudio aleatorizado, controlado, de un centro a 12 meses



CON INSULINA

83% solo con basal

17% MDI

66% AR GLP-1

Péptido C presente

TIR: ↑ 15%

TBR: sin diferencia

DDT: ↓ 10,6U

Peso -3,3 kg

MDI: múltiples dosis de insulina; TIR: tiempo en rango;
TBR: tiempo bajo el rango; DDT: dosis total diaria

Cambios en el control glucémico a 24 semanas con el uso de monitoreo flash de glucosa en la vida real en pacientes de Europa con diabetes tipo 1 y 2 con diferentes niveles de control glucémico

TIR < 70	Basal-bolus			Basal			SIN INSULINA		
	Sensor 1	Sensor 12	Difference; p-value (95% CI)	Sensor 1	Sensor 12	Difference; p-value (95% CI)	Sensor 1	Sensor 12	Difference; p-value (95% CI)
Number of subjects	588	588		70	70		21	21	
Mean glucose (mmol/L)	10.1	9.4	−0.7; p < 0.0001 (−0.83 to −0.57)	10.4	9.5	−0.9; p = 0.0007 (−1.38 to −0.39)	9.9	8.7	−1.2; p = 0.02 (−2.21 to −0.24)
eHbA1c (%)	7.9	7.5	−0.4; p < 0.0001 (−0.52 to −0.36)	8.2	7.6	−0.55; p = 0.0007 (−0.87 to −0.24)	7.9	7.1	−0.77; p = 0.02 (−1.39 to −0.15)
eHbA1c (mmol/mol)	63.4	58.6	−4.8; p < 0.0001 (−5.66 to −3.9)	65.7	59.7	−6.1; p = 0.0007 (−9.46 to −2.66)	62.4	54.0	−8.41; p = 0.02 (−15.19 to −1.64)
TIR 3.9–10.0 mmol/L (%)	51.7	61.0	9.3; p < 0.0001 (7.84 to 10.77)	48.6	60.7	12.1; p < 0.0001 (6.63 to 17.5)	52.7	72.2	19.5; p = 0.003 (7.62 to 31.47)
CV (%)	31.0	30.0	−1; p < 0.0001 (−1.39 to −0.54)	30.3	29.2	−1.09; p = 0.11 (−2.44 to 0.25)	29.0	25.5	−3.5; p = 0.03 (−6.71 to −0.31)
Glucose SD (mmol/L)	55.6	50.5	−5.1; p < 0.0001 (−6 to −4.16)	55.7	50.1	−5.6; p = 0.001 (−9.02 to −2.27)	50.6	39.9	−10.7; p = 0.003 (−17.21 to −4.2)
Time < 3.0 mmol/L (%)	0.2	0.0	−0.27; p = 0.0006 (−0.43 to −0.12)	0.2	0.0	−0.3; p = 0.07 (−0.56 to 0.02)	0.1	0.0	−0.6; p = 0.13 (−1.33 to 0.19)
Time < 3.9 mmol/L (%)	0.9	0.7	−0.4; p = 0.006 (−0.76 to −0.13)	0.8	0.4	−0.5; p = 0.10 (−1.04 to 0.09)	0.7	0.0	−1.7; p = 0.13 (−3.99 to 0.55)
Time > 10.0 mmol/L (%)	46.3	37.2	−9.2; p < 0.0001 (−10.7 to −7.6)	49.7	37.6	−12.1; p < 0.0001 (−17.6 to −6.6)	45.3	27.0	−18.3; p = 0.006 (−30.7 to −5.9)

Impacto en el monitoreo flash de glucosa en personas con diabetes tipo 2 inadecuadamente controladas con terapia no insulínica antihiper glucémica (IMMEDIATE)

Estudio aleatorizado controlado

	isCGM + DSME	DSME
n	58	58
Age (y)	59.2 ± 9.6	57.6 ± 10.6
Duration of T2D (y)	9.2 ± 6.3	10.9 ± 5.9
Females, n (%)	21 (36.2)	21 (36.2)
HbA1c (%)	8.5 ± 1.0	8.7 ± 1.2
HbA1c (mmol/mol)	69 ± 11	72 ± 14
% TIR (70-180 mg/dl)	56.3 ± 26.4	57.5 ± 25.7
% TAR (> 180 mg/dl)	42.5 ± 27.4	40.2 ± 27.3
% TBR (< 70 mg/dl)	1.0 ± 2.7	1.4 ± 3.3
Mean glucose (mg/dl)	10.0 ± 2.8	9.7 ± 2.7
Weight (kg)	85.6 ± 1.0	85.5 ± 22.4
Body mass index (kg/m ²)	30.0 ± 6.1	29.8 ± 6.4
Waist circumference (cm)	102.6 ± 14.0 ^a	101.4 ± 16.7 ^a
Systolic blood pressure (mmHg)	127 ± 13	126 ± 17 ^b
Diastolic blood pressure (mmHg)	81 ± 10	81 ± 12
eGFR (ml/min/1.73m ²)	88.9 ± 19.5	89.8 ± 17.2
Number of non-insulin antihyperglycaemic therapies	2.6 ± 0.8	2.7 ± 1.0
Metformin, n (%)	58 (100.0)	56 (96.6)
Sulphonylurea, n (%)	32 (55.2)	25 (43.1)
SGLT2i, n (%)	20 (34.5)	25 (43.1)
DPP-4i, n (%)	25 (43.1)	27 (46.6)
GLP-1 RA, n (%)	16 (27.6)	20 (34.5)

	isCGM + DSME	DSME	Adjusted mean difference (95% CI)	Adjusted P value
n	51	48		
% TIR (3.9-10.0 mmol/L)	76.3 ± 17.4	65.6 ± 22.6	-9.9 (-17.3 to -2.5)	.009
% time in the tight glycaemic range (3.9-7.8 mmol/L)	50.3 ± 21.9	40.4 ± 23.1	-8.5 (-16.6 to -0.3)	.042
% TAR (> 10.0 mmol/L)	21.2 ± 18.1	30.7 ± 24.5	8.1 (0.5 to 15.7)	.037
% TBR (< 3.9 mmol/L)	1.9 ± 3.5	3.0 ± 6.5	1.3 (-0.8 to 3.3)	.218
% TBR level 2 (< 3.0 mmol/L)	0.6 ± 2.3	0.9 ± 3.1	0.3 (-0.8 to 1.4)	.553
Mean glucose (mmol/L)	8.1 ± 1.5	8.8 ± 2.4	0.6 (-0.2 to 1.3)	.123
SD (mmol/L)	2.2 ± 0.6	2.4 ± 0.6	0.2 (-0.1 to 0.4)	.113
CV (%)	27.3 ± 6.9	28.1 ± 7.1	0.7 (-2.2 to 3.5)	.650
Number of hypoglycaemic events	1 (0.0, 5.0)	0.5 (0.0, 5.3)		
Number of nocturnal hypoglycaemic events	0 (0.0, 2.5)	0 (0.0, 4.0)		
Number of level 2 hypoglycaemic events	0 (0.0, 1.0)	0 (0.0, 1.0)		

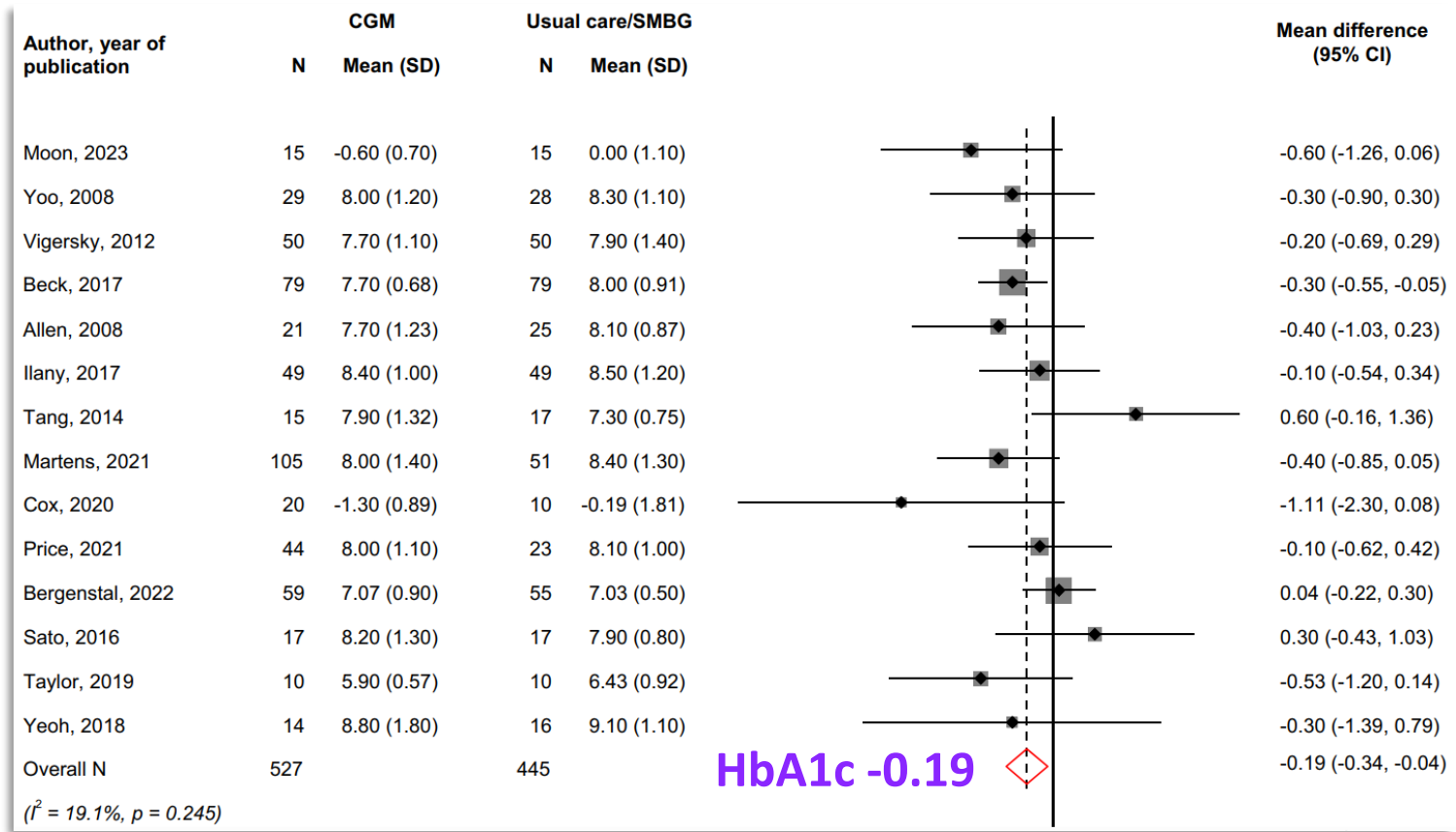
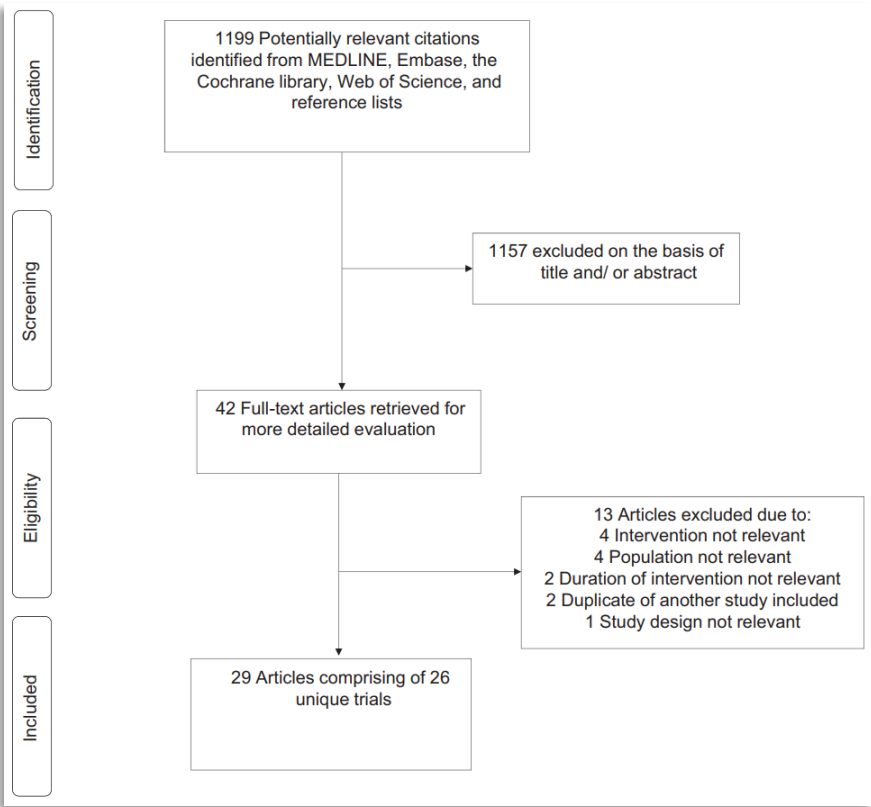
TIR: ↑ 10%

TIR: ↑ 8,5%

TBR: sin diferencia

Eficacia y seguridad en el monitoreo continuo de glucosa en pacientes con diabetes tipo 2.
Revisión - metaanálisis de evidencia internacional

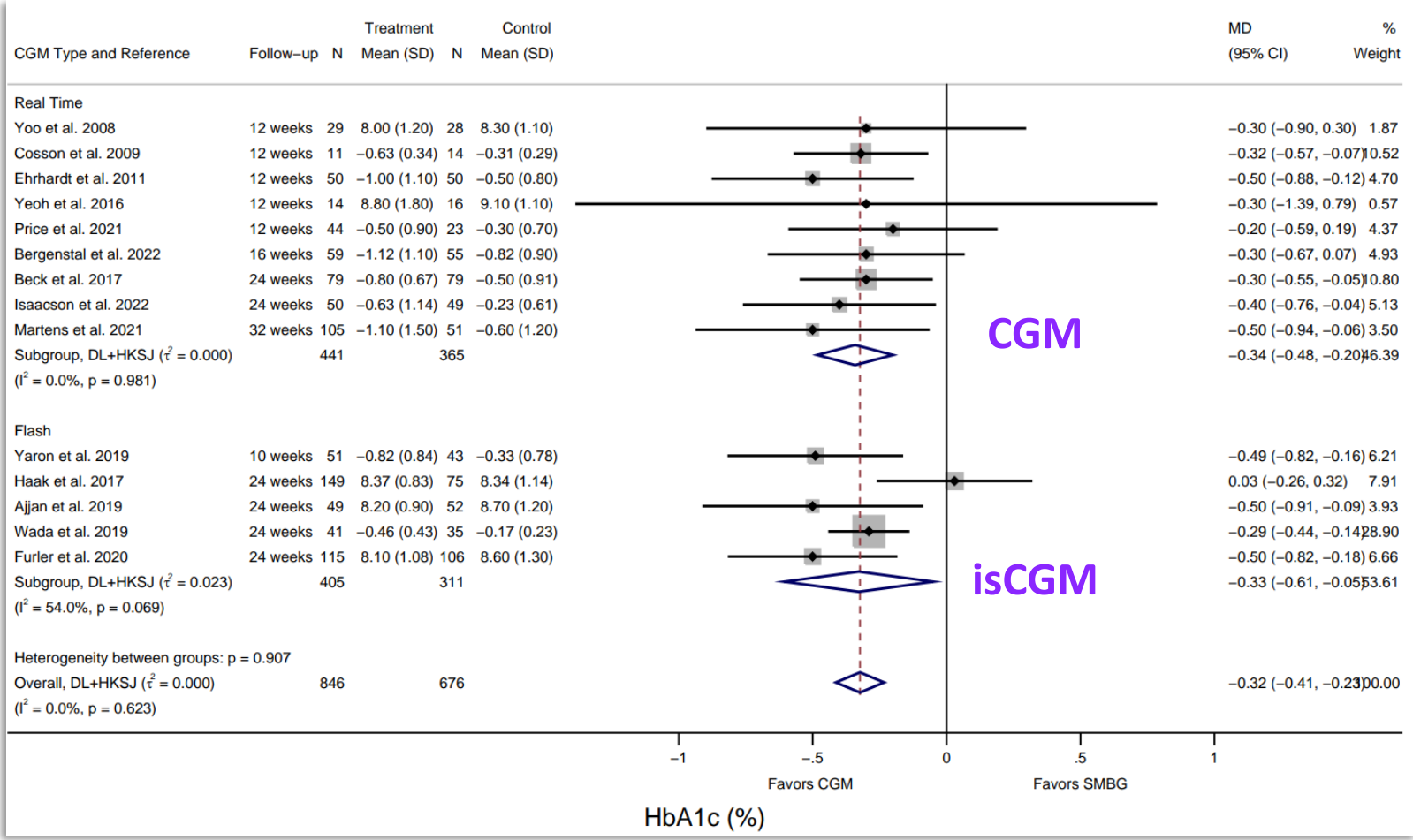
Reducción significativa en HbA1c
CGM vs usual/SMBG



CGM monitoreo continuo de glucosa; SMBG: automonitoreo de glucosa en sangre



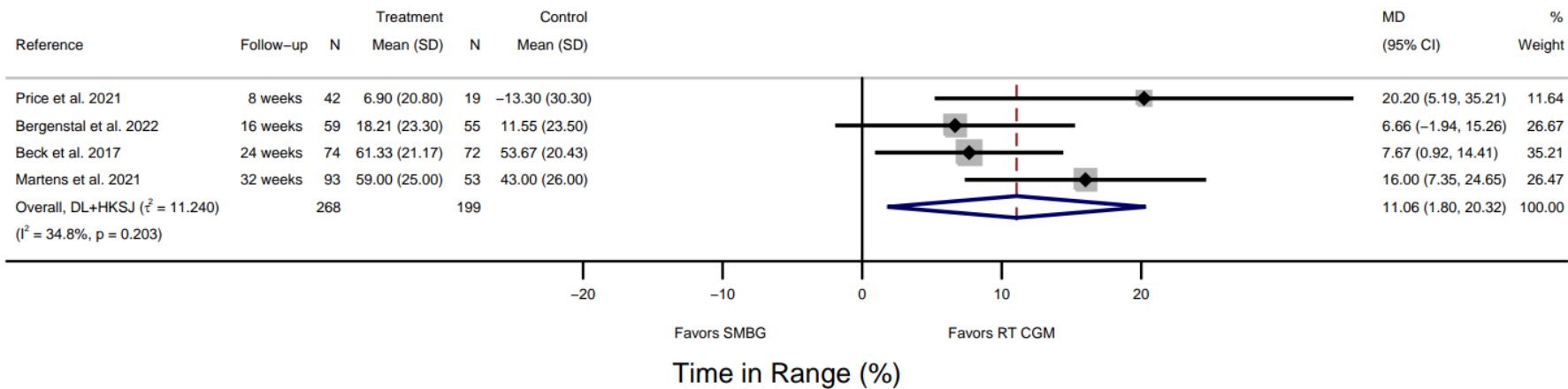
Efectividad del monitoreo continuo de glucosa sobre las métricas de control glucémico en pacientes con diabetes tipo 2. Revisión sistemática metaanálisis de estudios aleatorizados



HbA1c -0.3

A

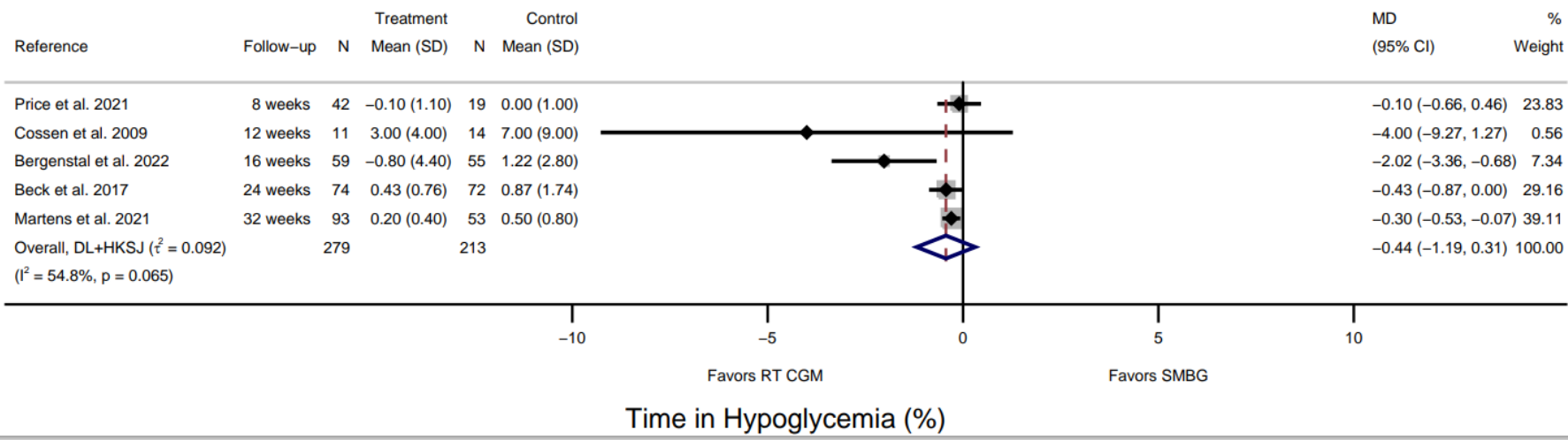
Change in Time in Range (70 to 180 mg/dL)



▲ TIR

C

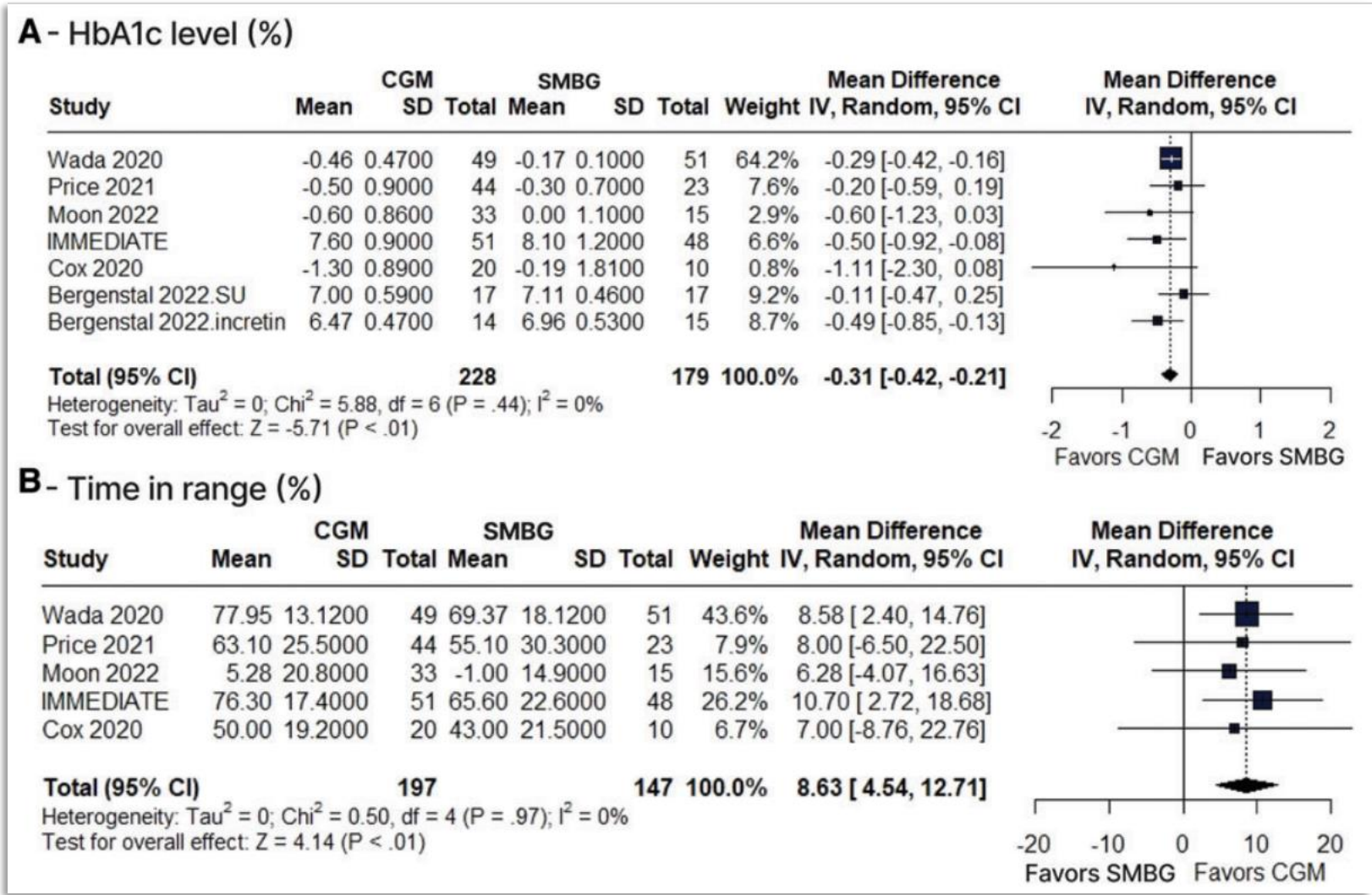
Change in Time in Hypoglycemia (<70 mg/dL)



▼ TBR

METANÁLISIS 3

Sistemas de monitoreo continuo de glucosa en pacientes con diabetes tipo 2 no insulinizados: revisión sistemática – metaanálisis de estudios aleatorizados

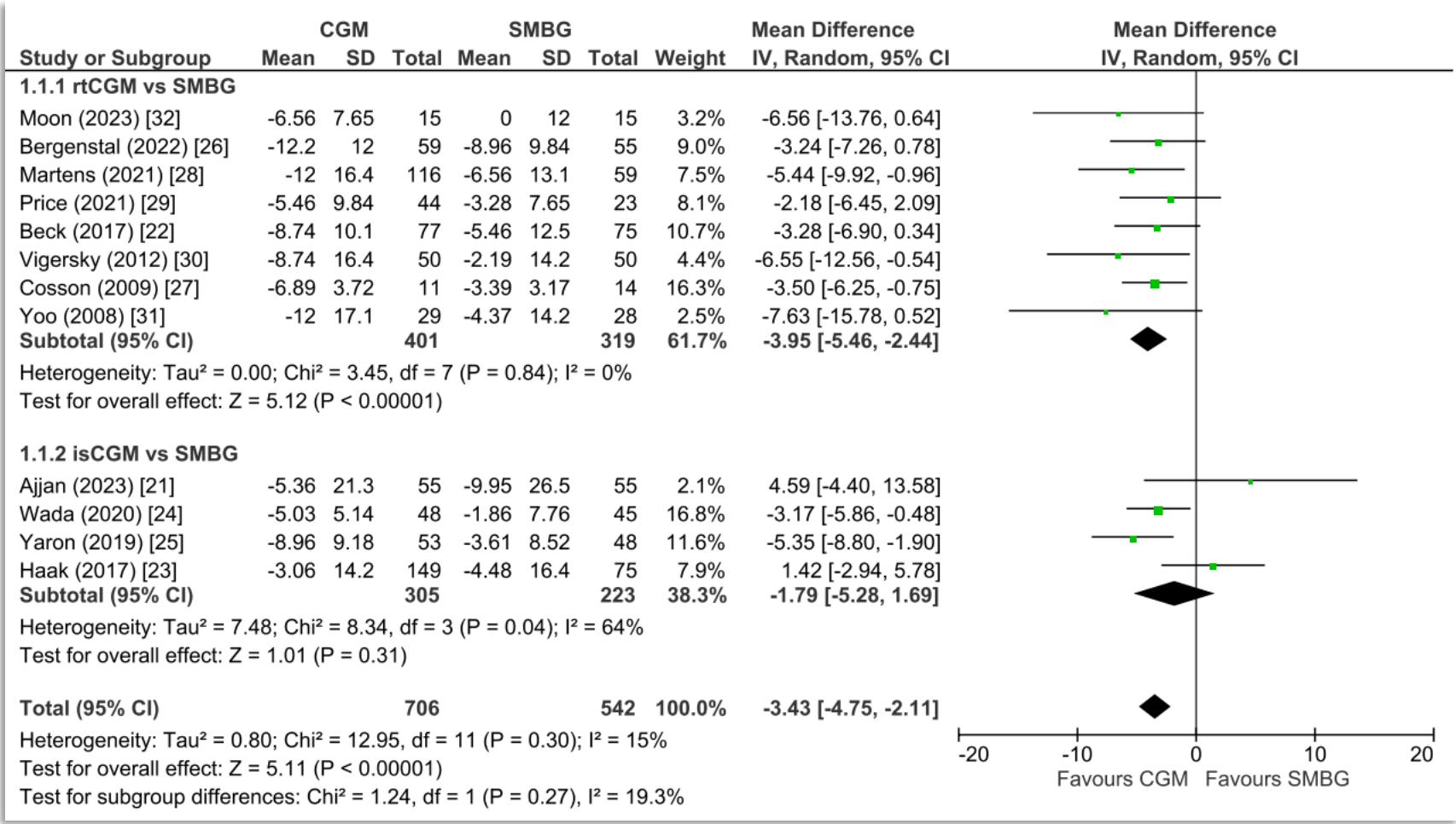


Hb A1c -0.31

TIR + 8.6



Monitoreo continuo de glucosa en pacientes adultos con diabetes tipo 2.
Revisión sistemática – metaanálisis



Hb A1c -0,31%
IC -4,75- -2,11
p<0,00001

Subgrupo sin
insulina: -0,29%
P=0,004

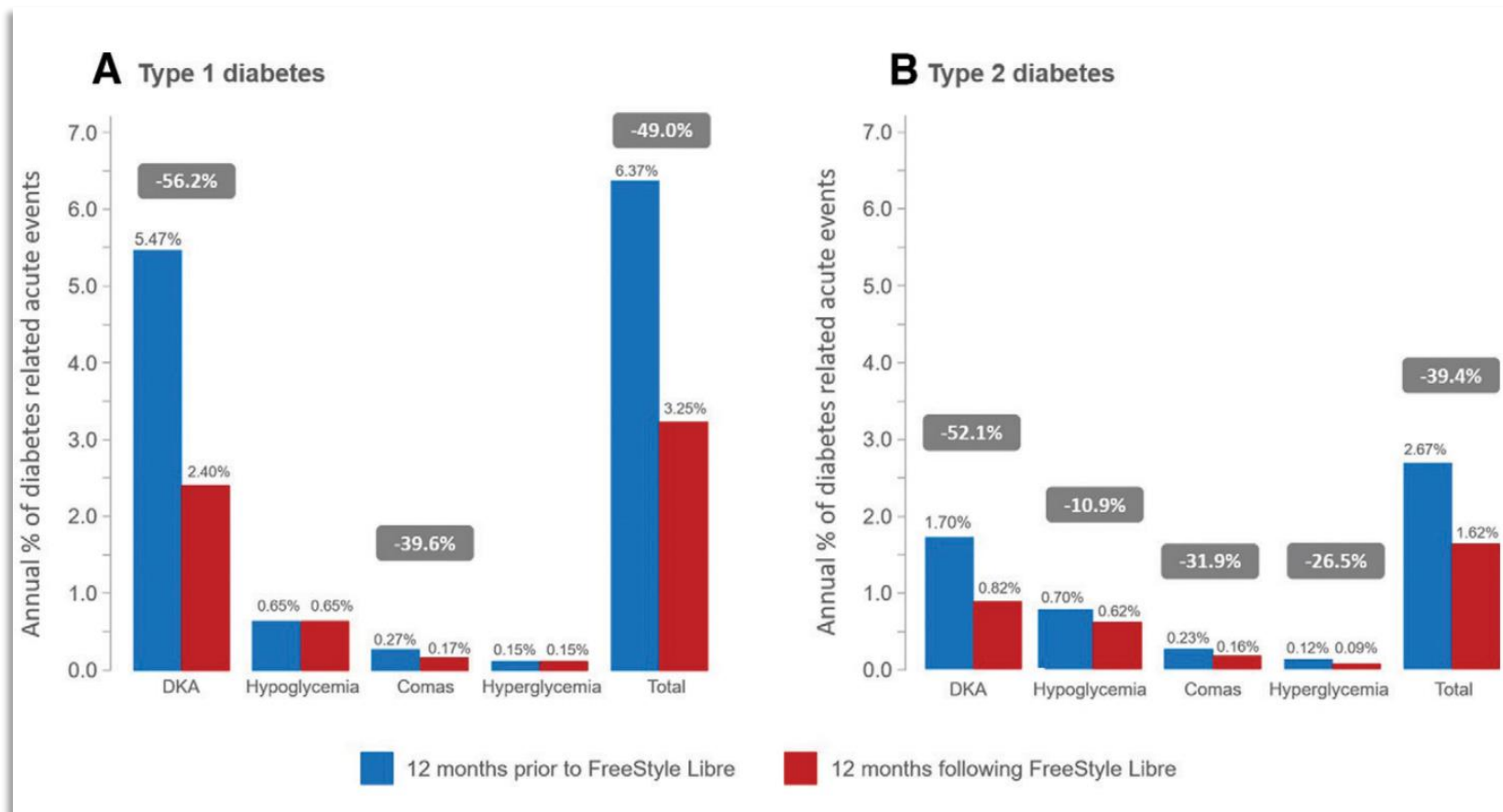
COSTO-EFECTIVIDAD

Caída marcada de las complicaciones agudas de la diabetes en pacientes con diabetes tipo 1 o tipo 2 luego del inicio del monitoreo flash de glucosa. Estudio RELIEF

74.011 individuos con DT1 o DT2.

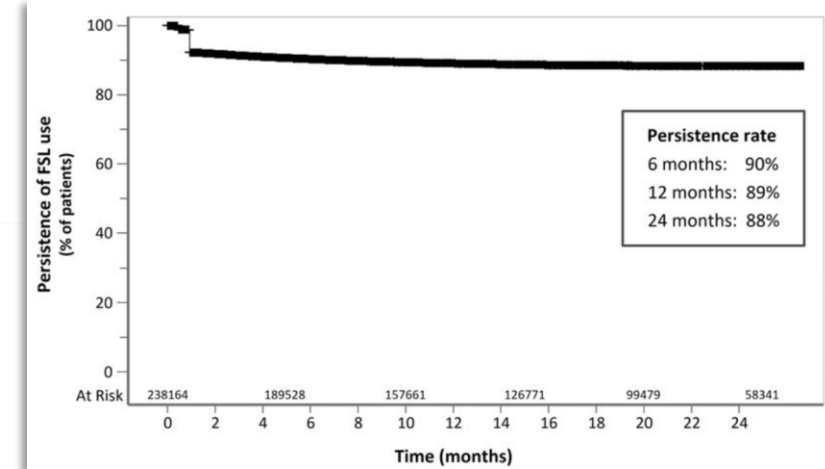
Usuarios de isCGM Libre identificados de la base de datos de reclamos de Francia.
Persistencia en el sistema a los 12 meses: 98,1%

-39,4% internaciones por complicaciones agudas en DT2



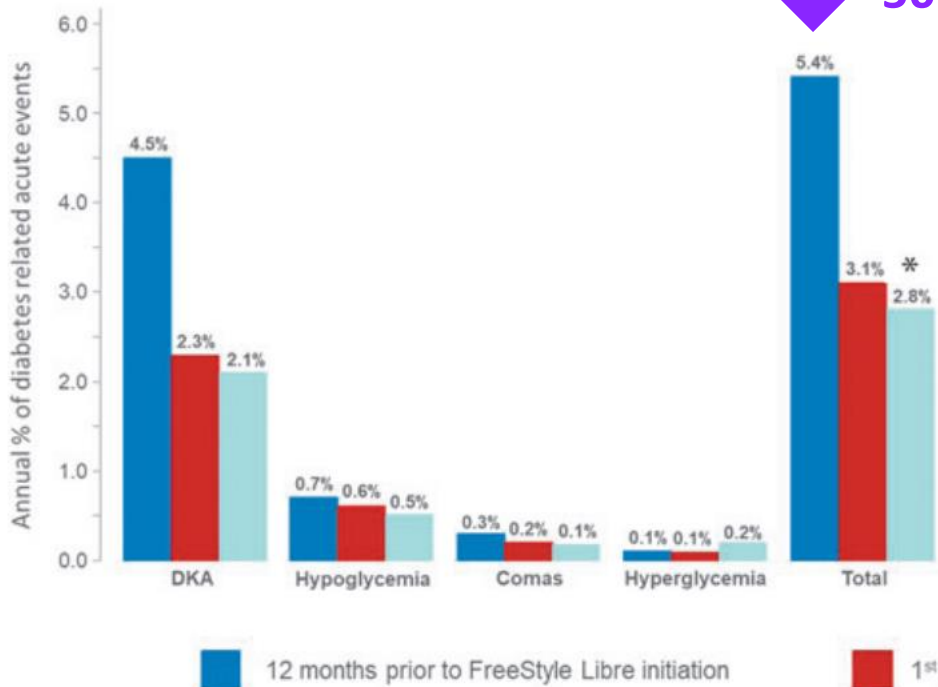
A 2 AÑOS...

Caída marcada de las complicaciones agudas de la diabetes con monitoreo flash de glucosa luego de 2 años de su inicio: análisis extendido del estudio RELIEF

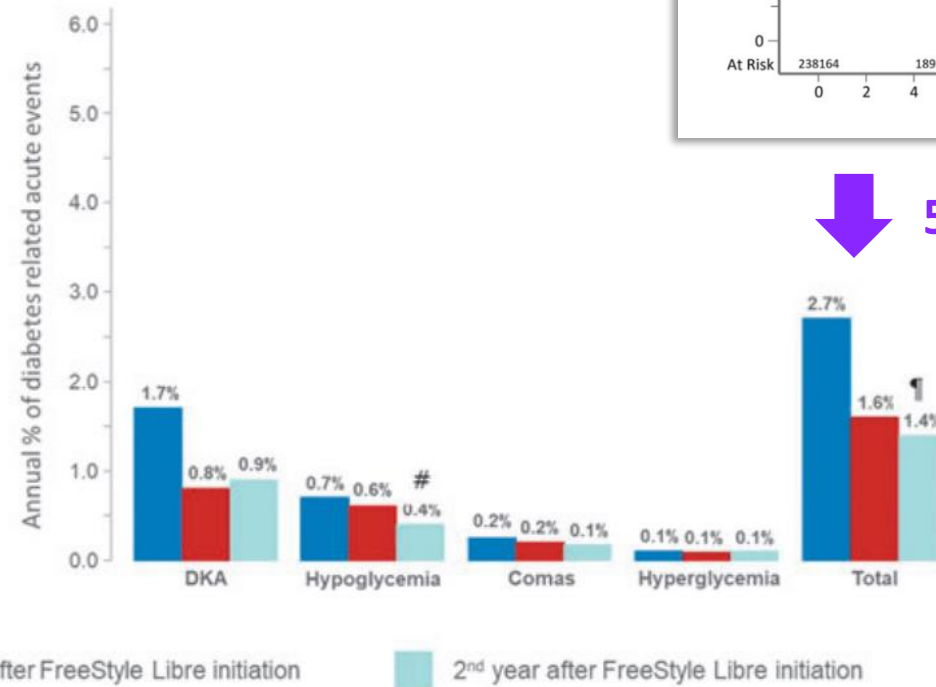


50 %

A Type 1 diabetes (n=31,446)

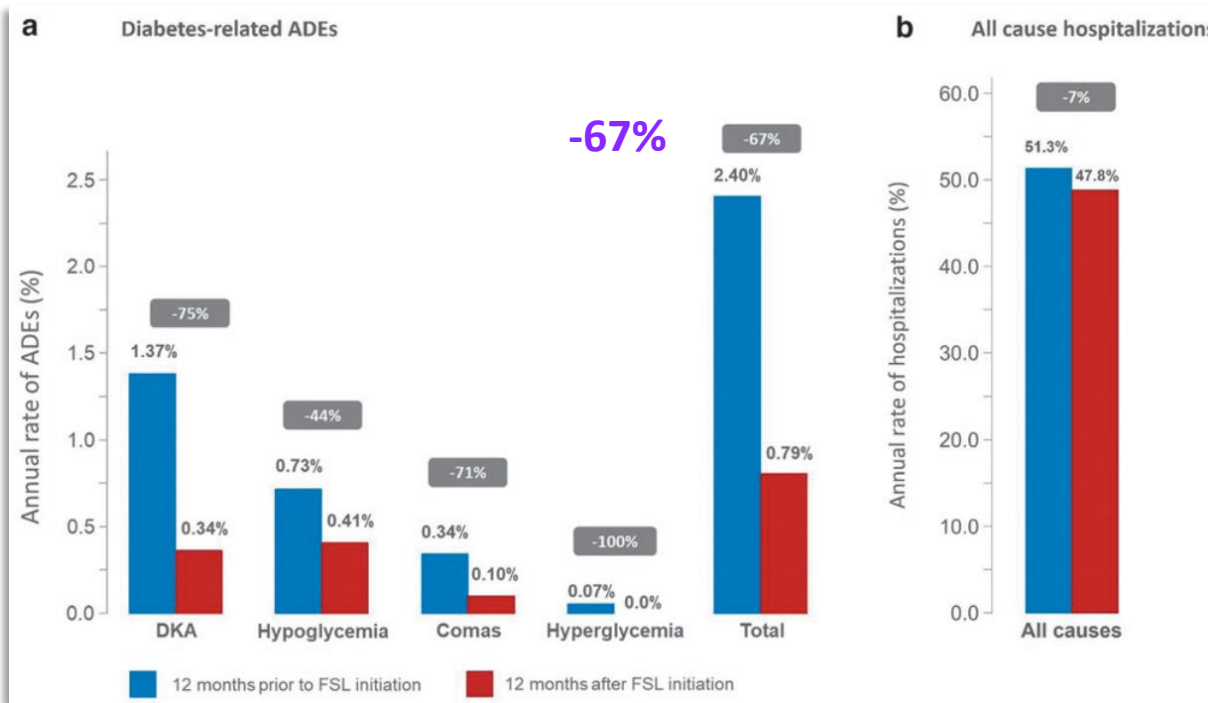


B Type 2 diabetes (n=41,027)

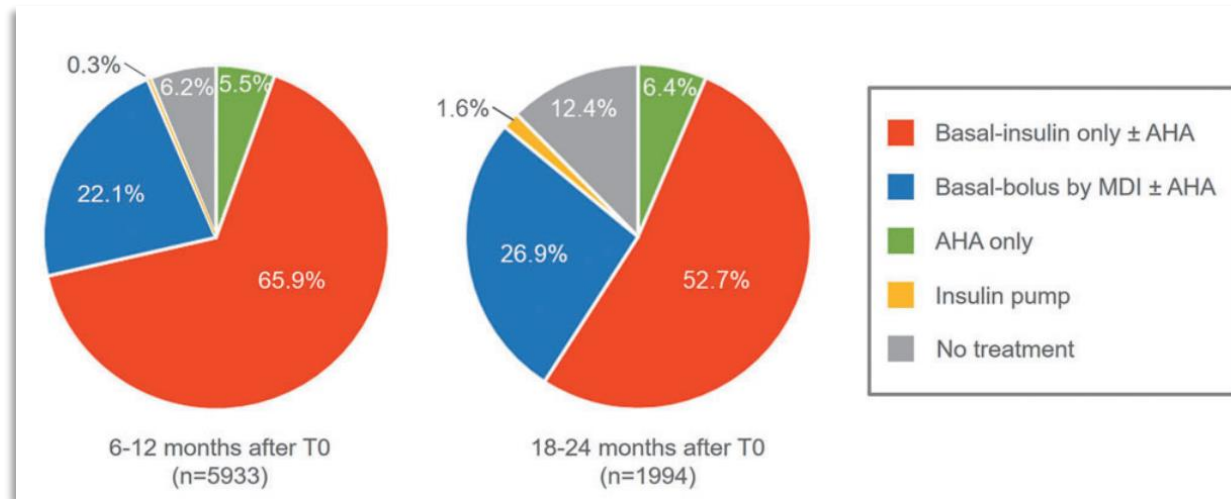


En DT2 con insulina basal...

Marcado descenso de las complicaciones agudas de la diabetes luego del inicio del dispositivo Libre Free Style en pacientes con diabetes tipo 2 con insulina basal en Francia

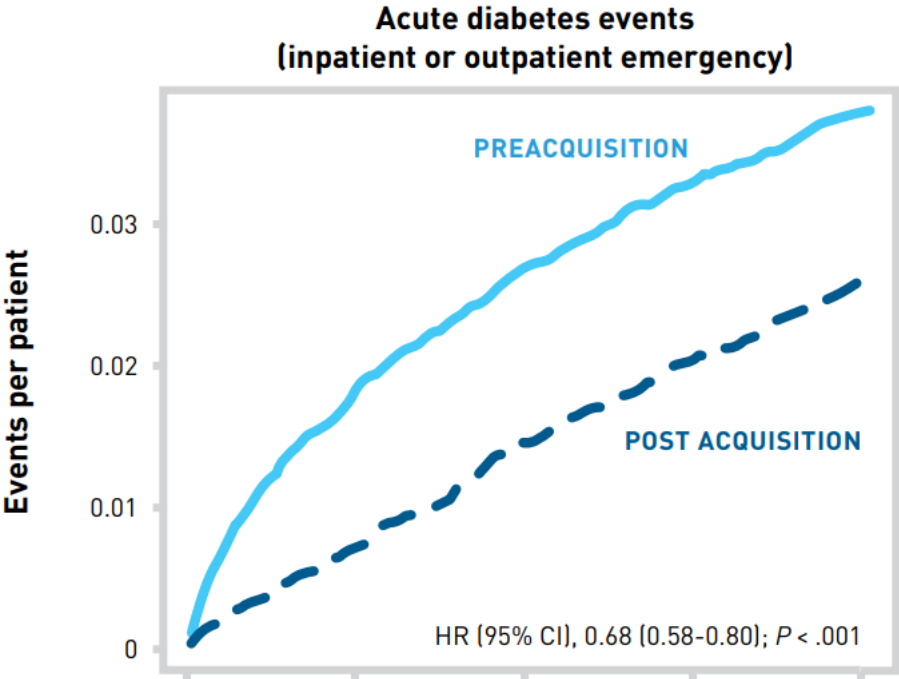


Intensificación de la terapia



Monitoreo continuo flash se asocia con reducción de los eventos durante el tratamiento no intensivo de la diabetes

Characteristic	Value
N	10,282
Follow-up in days, median (10%, 90% deciles)	171 (152, 182)
Age in years, mean (SD)	53.1 (9.6)
Aged 18-49 years	32.3%
Aged 50-64 years	62.5%
Aged ≥65 years	5.2%
Gender (male)	51.9%
Comorbidities	
Hypertension	80.6%
Obesity	55.6%
Pulmonary disease	24.5%
Depression	24.2%
Hypothyroid disease	21.5%
Anemia	19.2%
Liver disease	18.5%
MI or coronary artery disease	15.8%
Peripheral vascular disease	10.8%
Renal disease	9.6%
Heart failure	6.9%
Insulin usage status	
Insulin (basal/NPH/premixed)	38.7%
Noninsulin therapy	61.3%
Noninsulin diabetes medications	
Biguanide	71.2%
Sulfonylurea	30.4%
GLP1 agonist	30.3%
SGLT2 inhibitor	26.2%
DPP4 inhibitor	20.6%
TZD	7.4%
Meglitinides	1.6%
Alpha-glucosidase inhibitor	0.4%



DT2 con o sin
insulina

-32%

Days from index					
Pre-	0	-45	-90	-135	-180
Post	0	45	90	135	180
Patients at risk					
Pre-	10,282	10,282	10,282	10,282	10,282
Post	10,282	9983	9676	9355	9080



Monitoreo continuo de glucosa:

Facilita el manejo de la diabetes



Reduce costos



¿Predice mejor las complicaciones?

Un ejemplo...

Asociación entre control glucémico medido con monitoreo continuo de glucosa y marcadores urinarios de enfermedad renal en diabetes: Hyogo Diabetes Hypoglycemia Cognition Complications study

Table 1 Characteristics of the study participants

	T2DM			NDM (N= 39)	P
	Normo-albuminuria (N= 166)	Microalbuminuria (N= 58)	Macroalbuminuria (N= 21)		
Male, %	67.5	67.2	76.2	46.2	0.050
Age, years	68 (62–72)	68 (62–72)	71 (65–74)	71 (68–74)*	0.008
Duration of T2DM, years	11.5 (5.3–21.0)	12.5 (9.3–24.0)	17.0 (9.0–24.0)	0 (0–0)**	<0.001
BMI, kg/m ²	24.0 (21.9–25.7)	24.4 (23.0–27.7)	24.9 (22.4–27.6)	23.9 (22.1–26.1)	0.185
SBP, mmHg	126.0 (115.0–137.0)	129.0 (118.3–140.8)	138.0 (130.0–146.0)*	130.5 (121.5–139.0)	0.027
DBP, mmHg	75.0 (68.0–82.0)	78.0 (71.0–83.0)	75.0 (70.0–92.0)	78.0 (70.5–83.0)	0.319
UA, mg/dL	5.2 (4.4–6.1)	5.2 (4.5–6.1)	5.6 (5.2–6.7)	5.2 (4.8–6.1)	0.183
HbA1c, % [mmol/mol]	7.0 (6.6–7.5) [52]	7.2 (6.8–7.7) [55]	7.1 (6.4–7.8) [54]	5.9 (5.7–6.1) [40]**	<0.001
GMI, %	6.7 (6.2–7.1)	6.8 (6.3–7.3)	7.0 (6.2–8.0)	5.9 (5.7–6.0)**	<0.001
TIR, %	78.2 (69.2–87.6)	77.8 (61.6–88.2)	73.9 (41.7–87.4)	93.8 (91.1–97.4)**	<0.001

Un ejemplo...

Asociación entre control glucémico medido con monitoreo continuo de glucosa y marcadores urinarios de enfermedad renal en diabetes: Hyogo Diabetes Hypoglycemia Cognition Complications study

	Crude		Model 1		Model 2	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
UAlb/Cr						
HbA1c	1.424 (1.073–1.889)	0.014	1.125 (0.806–1.571)	0.490	1.127 (0.807–1.574)	0.483
GMI	1.710 (1.259–2.324)	0.014	1.484 (1.066–2.067)	0.019	1.485 (1.067–2.067)	0.019
TIR	0.980 (0.967–0.992)	0.002	0.985 (0.971–0.998)	0.029	0.985 (0.971–0.998)	0.029
TIT	0.981 (0.970–0.992)	<0.001	0.986 (0.974–0.998)	0.021	0.986 (0.974–0.998)	0.021
TAR	1.021 (1.009–1.034)	<0.001	1.015 (1.002–1.029)	0.028	1.015 (1.002–1.029)	0.028
TBR	0.974 (0.929–1.021)	0.275	0.989 (0.938–1.042)	0.677	0.988 (0.937–1.042)	0.665
SD	1.023 (1.003–1.042)	0.020	1.023 (1.000–1.046)	0.052	1.022 (1.000–1.046)	0.053
CV	0.998 (0.960–1.036)	0.907	1.007 (0.961–1.056)	0.760	1.007 (0.960–1.056)	0.776
GRI	1.013 (1.003–1.024)	0.012	1.012 (1.001–1.024)	0.037	1.012 (1.001–1.024)	0.038

TIR mantiene su valor predictivo
HbA1c lo pierde

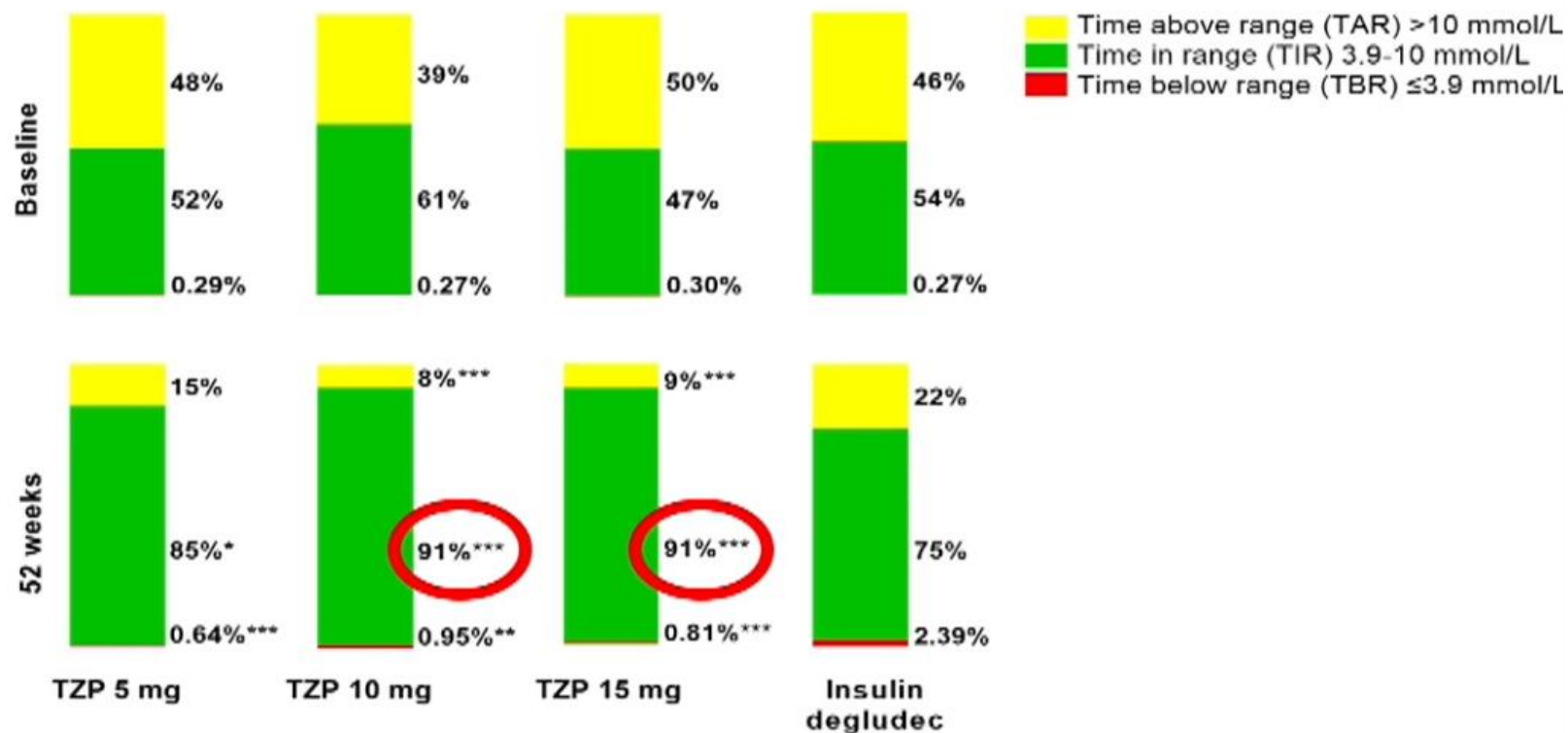
MCG: Los objetivos

MÉTRICAS: Tiempo de rango estrecho (TITR) en DT2

DT2 con agonista dual GLP-1 y GIP: tirzepatide
TIR: 70-180 mg/dl

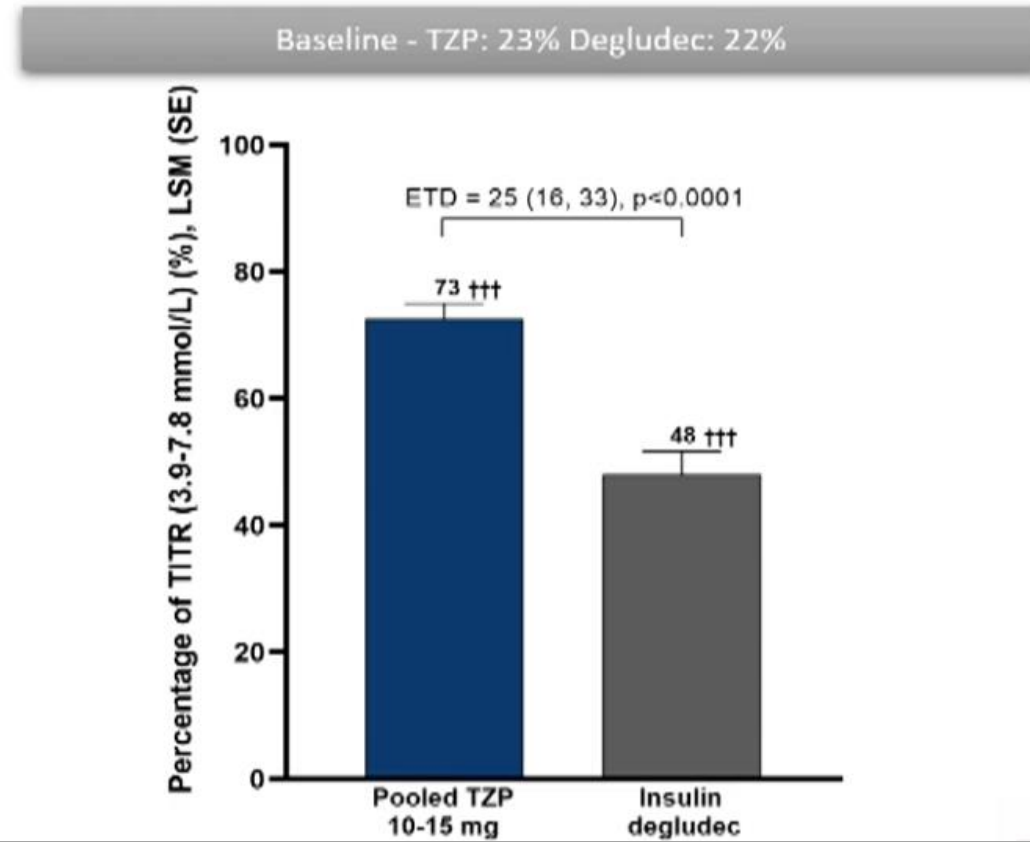
TIR >90%

Se necesita un
marcador más
ajustado



TITR: 71-140 mg/dl a las 52 semanas

TITR: 73%

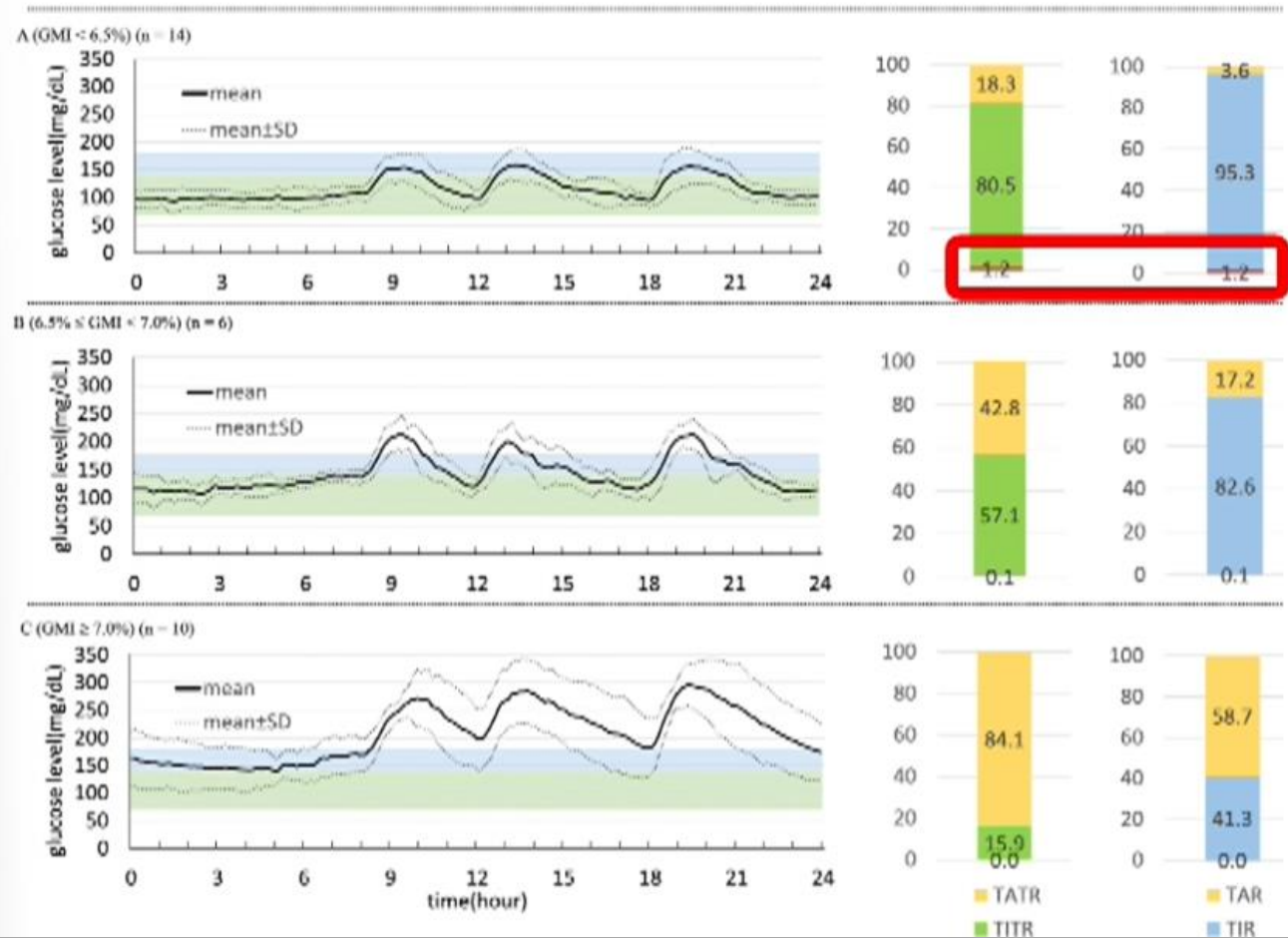


La pérdida inicial en DT2 corresponde al TITR

Exploring time in tight range targets (TITR) in drug-naïve Japanese individuals with type 2 diabetes

Published online: 19 March 2024

Mizuki Ishiguro¹ · Kiyotaka Ando² · Rimei Nishimura¹
Acta Diabetologica
<https://doi.org/10.1007/s00592-024-02247-8>



TITR/TIR	ΔTITR	ΔTIR
0.84	Comp.	Comp.
0.69	-23.4%	-12.7%
0.38	-64.6%	-54.0%

GMI
<6,5%

GMI 6,5%-
<7%

GMI 7% o
más



T1TR: nuevo objetivo para “control óptimo”
y potencialmente “remisión” de DT2

Perspectivas

Cambio de paradigma hacia el uso de MCG en DT2:

- En todos **al inicio**.
- **Uso continuo:** tratamiento con insulina o insulíntricos.
- **Uso intermitente:** pacientes sin insulina, cada 3 meses, para reforzar educación, evaluar cambios en el tratamiento, evaluar riesgo de complicaciones microvasculares.

Continuous glucose monitoring for the routine care of type 2 diabetes mellitus

Ramzi A. Ajjan¹, Tadej Battelino², Xavier Cos³, Stefano Del Prato⁴, Jean-Christophe Philips⁵, Laurent Meyer⁶, Jochen Seufert⁷ & Samuel Seidu⁸✉

¿En pediatría? Poca evidencia

Asegurarse de utilizar dispositivos de calidad (como MCG integrados avalados por FDA)

Consenso próximo a salir:

DT2 sin insulina:

¡No es la versión final!
no concluido

- Con resultados glucémicos subóptimos: MCG al menos 6 meses.
- Para todos, considerar uso intermitente durante 14 días, cada 3 meses.
- Objetivos: TIR >70%, TAR <25%, TMAR <5%, TBR <4%, salvo riesgo particular de hipoglucemias: objetivo individualizado.
- **Para el que alcanza un TIR >70%, sobre todo con expectativa de vida larga: TITR >50%**
- Es apropiado utilizar MCG en DT2 aun sin insulina si se sospecha hipoglucemia.
- Puede usarse el MCG para educación o como herramienta motivacional para mantener una concordancia terapéutica y apoyar intervenciones como mejoras en alimentación, actividad física y ejercicio.

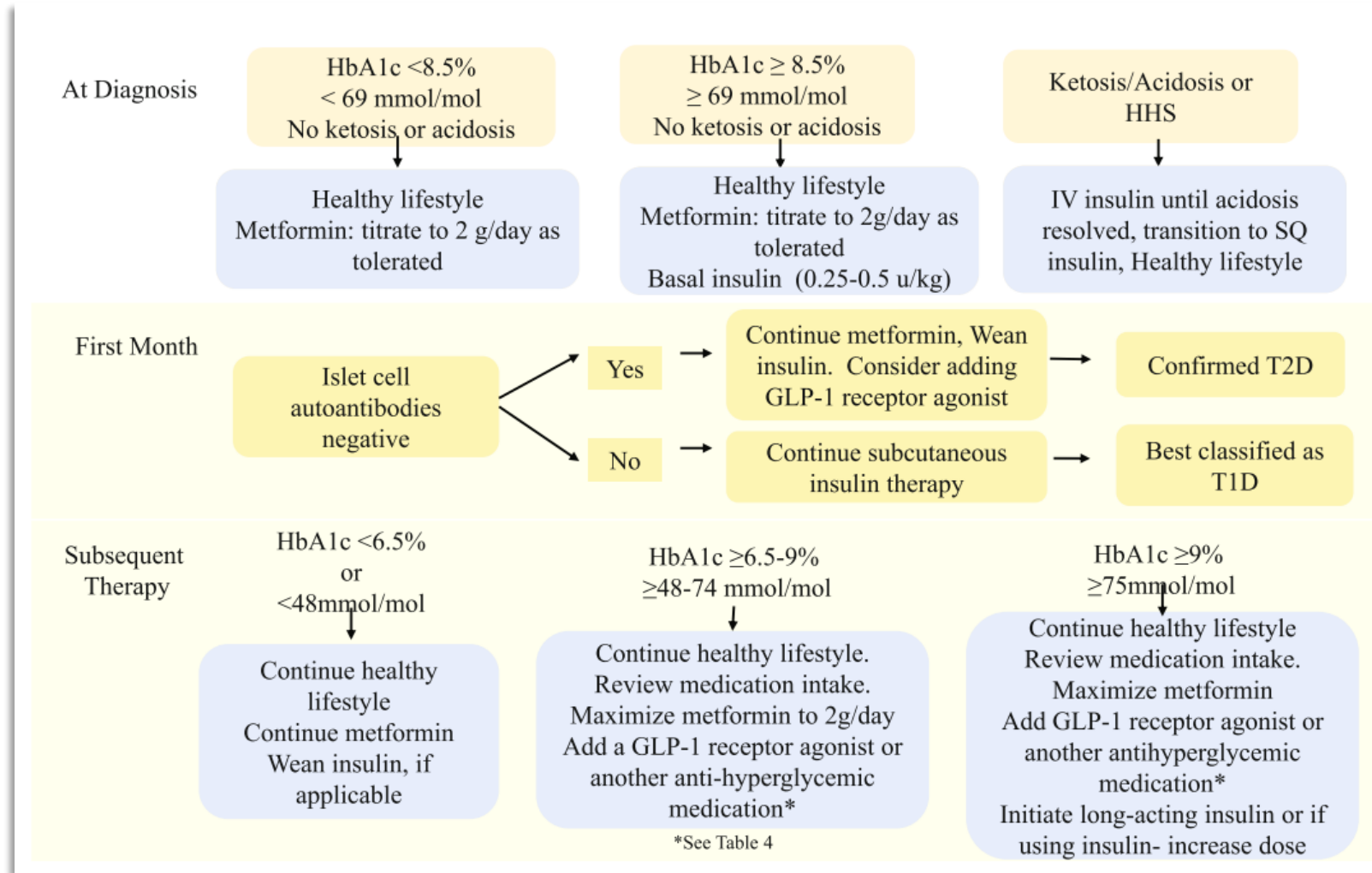
Rol de aGLP-1 e iSGLT2 en el tratamiento de la DT2 pediátrica

Amy Shah, Cincinnati, Ohio (EE.UU.)

Profesora de Pediatría, Universidad de Cincinnati.
Médica de la División Endocrinología del Hospital
de Niños de Cincinnati. Directora del Programa de
Dt2 en adolescentes.



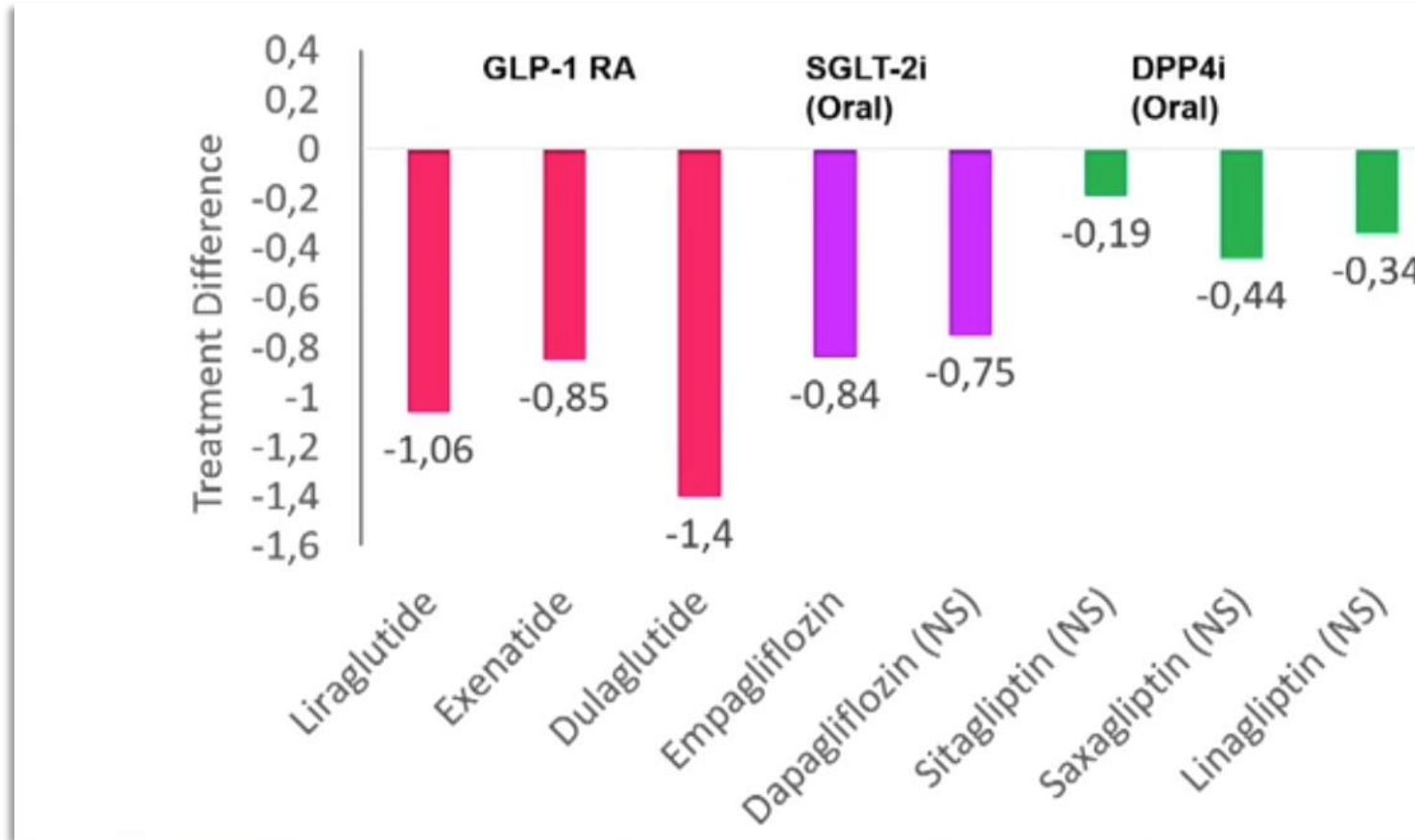
¿Qué cambiará en las guías ISPAD?



AR GLP-1e iSGLT-2: Resumen de evidencia en adultos

	AR GLP-1	iSGLT-2
Administración	Inyectable 1/d o 1/sem	Oral 1/d
Hb A1c %	↓0,7-1,7	↓0,3-1,2
Peso/IMC	↓2-5 kg	↓1,5-3 kg
TA sistólica	↓2-5 mm Hg	↓3-5 mm Hg
Lípidos	↓C-LDL, LDL pequeñas y densas , triglicéridos.	↓Triglicéridos, ↑C-HDL
Enfermedad renal	sí	sí
Enfermedad cardiovascular	ACV, eventos ateroscleróticos	Insuficiencia cardíaca
Eventos adversos	Gastrointestinales (náuseas, distensión, dolor abdominal)	Infección genital (común) CAD euglucémica
Costo	\$\$\$\$	\$\$\$

Estudios pediátricos GLP-1 e iSGLT2 DET HbA1c

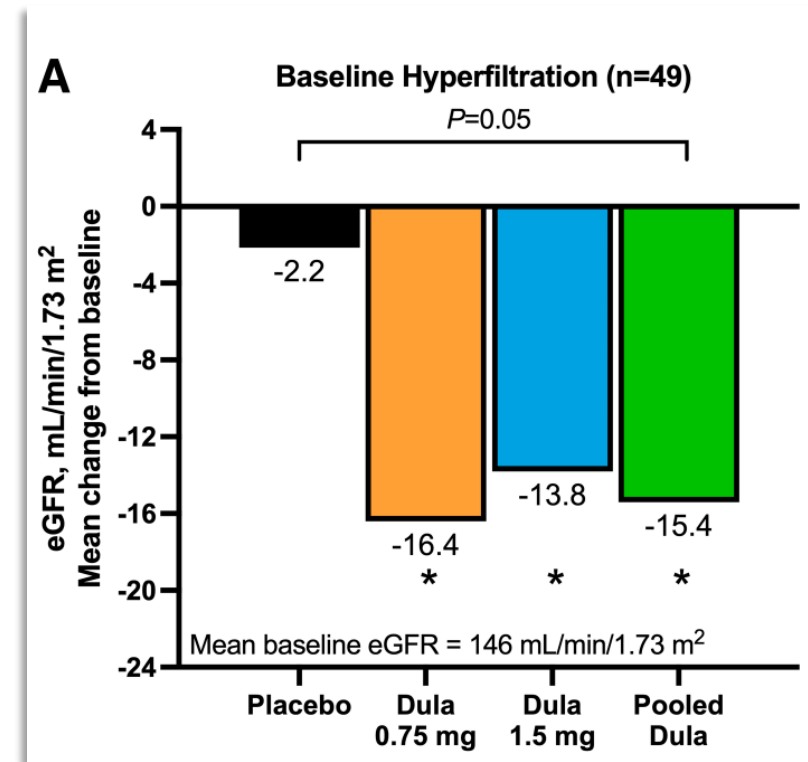


Tamborlane. N Engl J Med 2019; 381:637-646.
 Tamborlane . Diabetes Care 2022; 45(8): 1833-1840
 Arslanian N Engl J Med 2022; 4:387(5): 433-443

Laffel. Lancet Diabetes Endocrinol 2023; 11(3): 169-181.
 Tamborlane. Lancet Diabetes Endocrinol 2022; 10(5): 341-350.

Resultados secundarios

- Sin diferencia en peso, lípidos, HTA, complicaciones relacionadas a DT (no significativas o no estudiadas).
- **Dulaglutida:**
 - Mejoría en lípidos
 - Mejoría en hiperfiltración



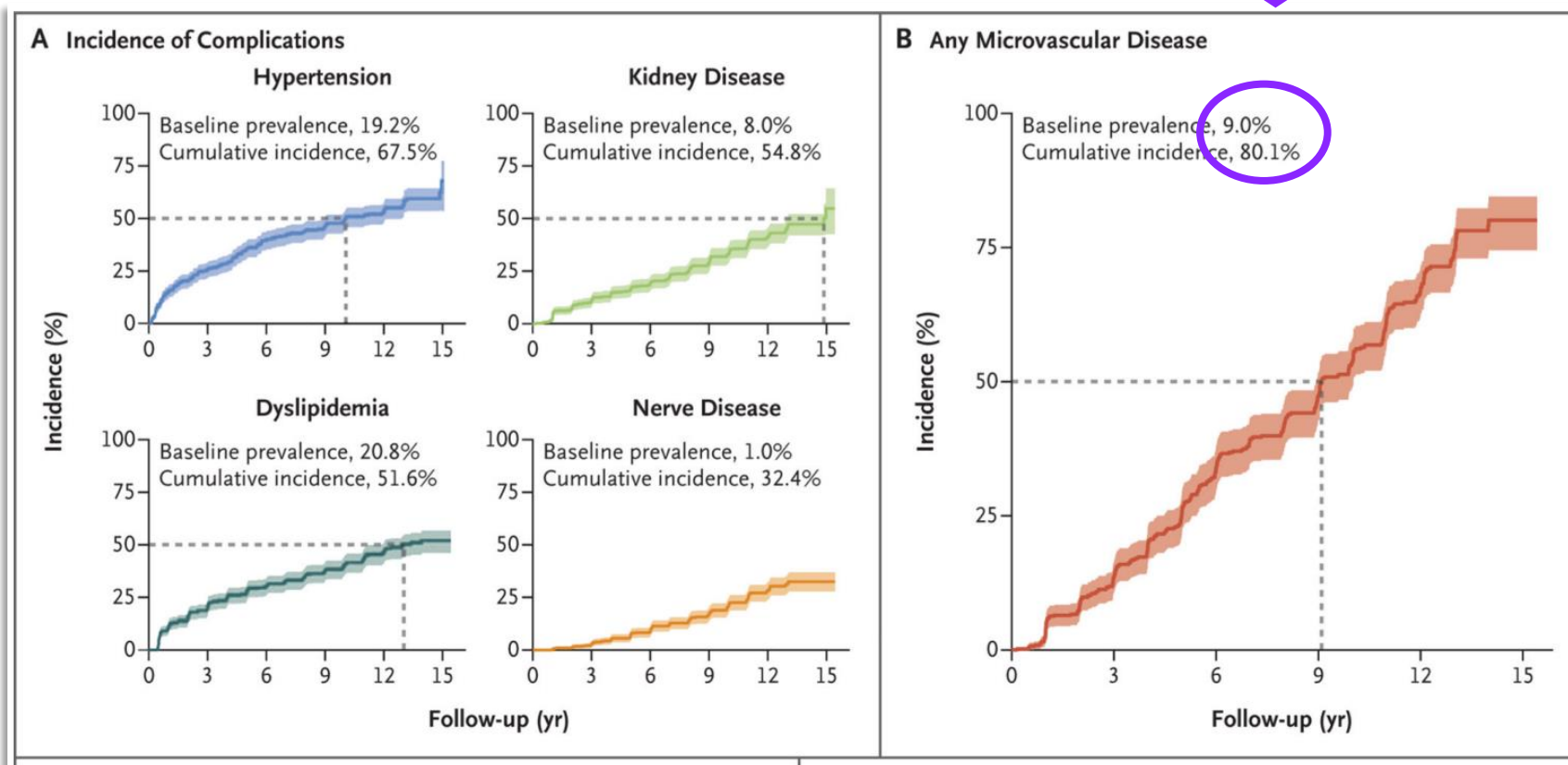
¿Por qué actualizar las guías?

- Metformina: falla 51,7% (media de seguimiento 3,8 años)
- Altas tasas de complicaciones

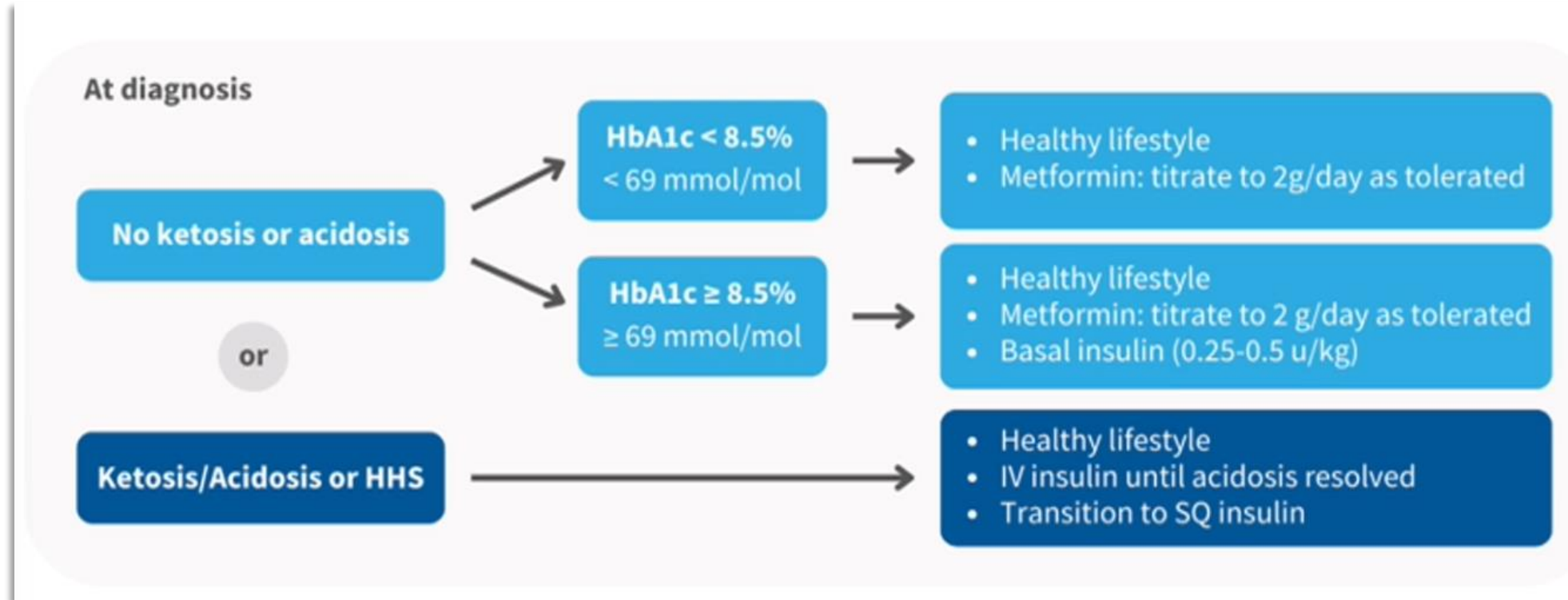
80%

Estudio TODAY

- Edad media: 26 años
- Tiempo medio desde el diagnóstico: 13 años



No cambia el manejo inicial



Metformina sigue siendo 1° línea: efectiva en el 50%, segura, económica

¿Qué cambia?

objetivo

Subsequent therapy

HbA1c <6.5
<48mmol/mol **



- Continue metformin
- Wean insulin, if applicable
- If on multiple meds, consider weaning

HbA1c ≥6.5%
≥48 mmol/mol

+

- Review medication adherence.
- Maximize metformin
- Stepwise: Add GLP-1 receptor agonist or SGLT-2 inhibitor***
- Consider initiation of long-acting insulin or if using insulin-increase dose
- Add prandial insulin if HbA1c targets are not met despite combination therapy



Continue
healthy
lifestyle

¿Cómo elegir la 2º medicación?

Preferencias individuales:

- Vía de administración
- Dosificación
- Efectos colaterales (ej GI, ITUs frecuentes)
- Grado de reducción de glucosa requerido
- Costos, cobertura, aprobación por la entidad regulatoria.
- Presencia de comorbilidades

¿AR GLP-1 o iSGLT2?

Consideración clínica	Terapia potencial
A1c elevada	AR GLP-1 o iSGLT2, >8,5%: insulina basal
Fobia a las agujas	iSGLT2
Dificultad para tragar comprimidos	AR GLP-1
Disminuir número de pastillas	Terapia combinada (metformina/empa)
Efectos adversos con metformina	iSGLT2
Dislipidemia	AR GLP-1 (Dulaglutida)
Anormalidades renales	AR GLP-1 (Dulaglutida), pero tal vez iSGLT2
Pérdida de peso	iSGLT2 o AR GLP-1?
MASLD	iSGLT2 o AR GLP-1?

¿Por qué no elegir uno primero?

- La respuesta es diferente que en adultos:
 - Tal vez se necesiten dosis más altas, estudios de mayor duración, enfocados no solo a la HbA1c, sino a otros resultados.
- Todavía hay muchas preguntas sin respuesta:
 - Capacidad de disminuir el deterioro de la célula beta.
 - Impacto en las comorbilidades/complicaciones relacionadas con la diabetes.
- Terapia combinada
- Nuevos agentes (terapias duales o triples)

Diabetes 2 en jóvenes: **RESUMEN**

HACIA UN MEJOR CONTROL

MCG EN DT2

- Fundamento
- Evidencia
- Métricas

ACTUALIZACIÓN EN TRATAMIENTO

NUEVAS GUÍAS ISPAD

- Objetivos
- Tratamiento farmacológico

Diabetes 2 en jóvenes: **RESUMEN**

**EL MCG DEBERÍA ESTAR
DISPONIBLE PARA LAS
PERSONAS CON DT2**

- Uso continuo
- Uso intermitente
- TITR

**OBJETIVO:
HbA1c <6,5%**

**FÁRMACOS DE 2º LÍNEA:
AR GLP-1 o iSGLT2**

Gracias por su atención



sanofi



ISPAD's 50th Annual Conference

Lisbon, Portugal | October 16 - 19, 2024

La educación a través de las distintas etapas de la diabetes

Florencia Grabois

- Médica pediatra
- Especialista en Nutrición Infantil UBA
- Docente de medicina Infantil UNCO
- Educadora Certificada en Diabetes UNSAM
- Hospital Provincial Neuquén
- Comité de Pediatría SAD
- Comité de Educación SAD

- **Conflictos de interés:**

Sanofi



Agenda

ESCUELA

Grupo de interés especial

Mejorando el tiempo escolar

Gun Forsander

ADOLESCENCIA

Empoderando adolescencias vía educación en diabetes y apoyo Transición

Steven James

SCREENING

Qué aprendimos sobre los programas de screening

Jéssica Melin

OTRAS CONDICIONES ASOCIADAS

Desafíos para el manejo de diabetes con otras condiciones asociadas

Eduardo Calliari

Grupo de interés especial

ESCUELA

Are Australian students with type 1 diabetes safe at school? A consumer perspective

Type selection

Preferred Presentation Type: Poster presentation

General data

Category: 4.b: Diabetes at School

Title

Title: Are Australian students with type 1 diabetes safe at school? A consumer perspective

Abstract text

Introduction: The death of an Australian student whilst in the custody of the school in 2019 has led to workplace safety regulators examining management of Type 1 Diabetes (T1D) in schools.

Objectives: To seek consumer views on safety concerns for students with T1D during school time and school-related activities.

Methods: Consumers were invited to partake of a deidentified on-line survey on school safety incidents in April 2024 using Typeform software. Participants were sourced from the community of Australia's largest independent consumer organization, the Type 1 Foundation. Results were quantified and qualitative responses about safety concerns were categorized by the authors into medical safety (risk of harm), workplace safety (lack of requisite training), discrimination (lack of equal opportunity) and negligence (lack of execution of duty of care). Qualitative responses could be classed on more than one category.

Results: 652 people responded from all Australian States comprising parents (84%), students (6%) and teachers (6%). 65% of respondents expressed safety concerns about a student with T1D. Of those reporting safety concerns, there was no significant State based difference nor significant differences between students attending a public school (64%), catholic school (66%) or independent school (56% $p=0.052$). The most common source of guidance for all respondents was the student's medical team (33%) followed by the national "Diabetes in Schools" program (26%). Qualitative responses of safety concerns were categorized by medical safety (69%), workplace safety (73%), discrimination (38%), and negligence (64%).

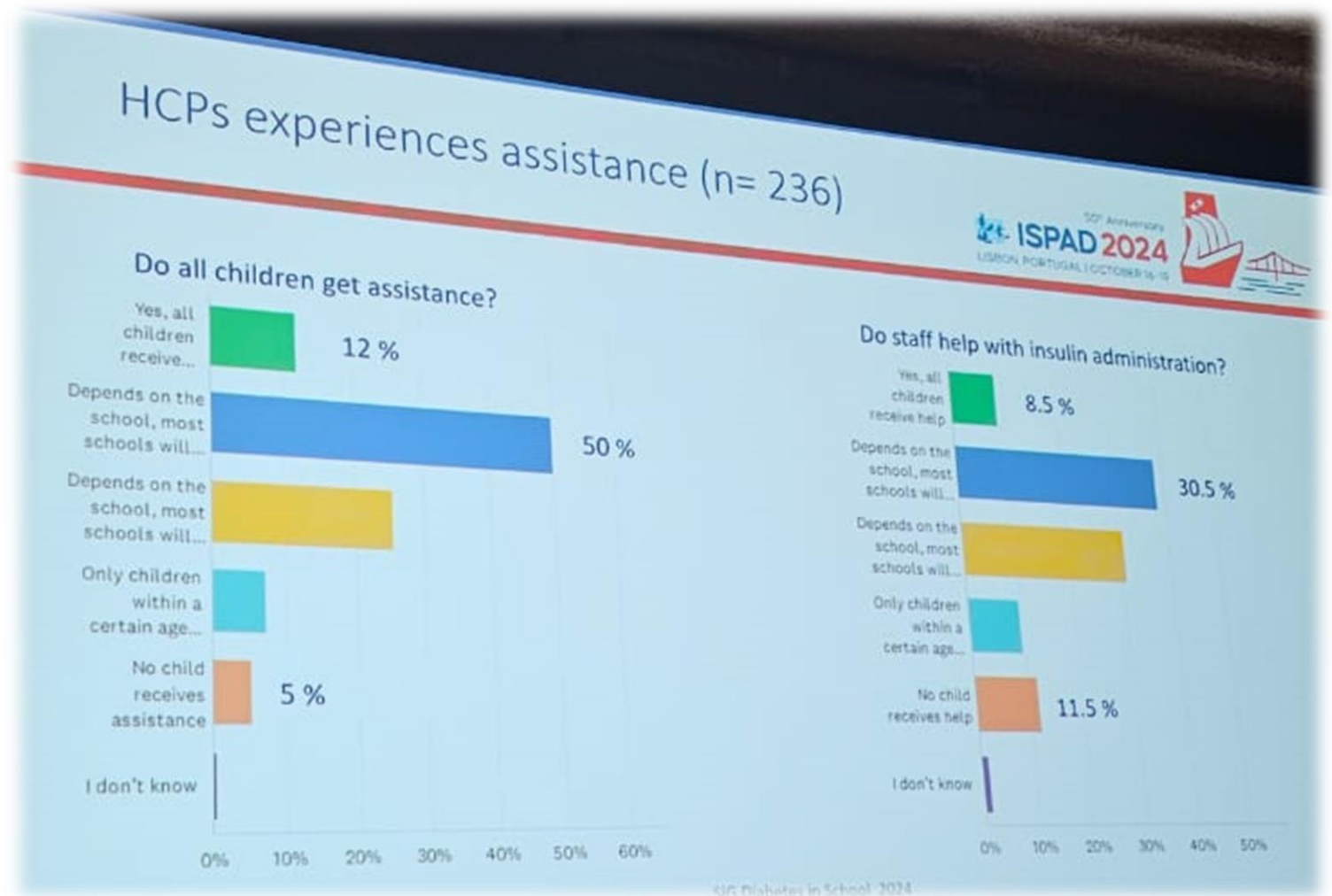
Conclusions: Consumers have significant concerns about safety of students with T1D in Australian schools, especially related to medical safety, compliance with workplace safety, duty of care and discrimination.

An Australian "comprehensive" national program for students with Type 1 Diabetes has failed to satisfactorily address safety issues.

Schools rely primarily on medical teams to advise school staff.

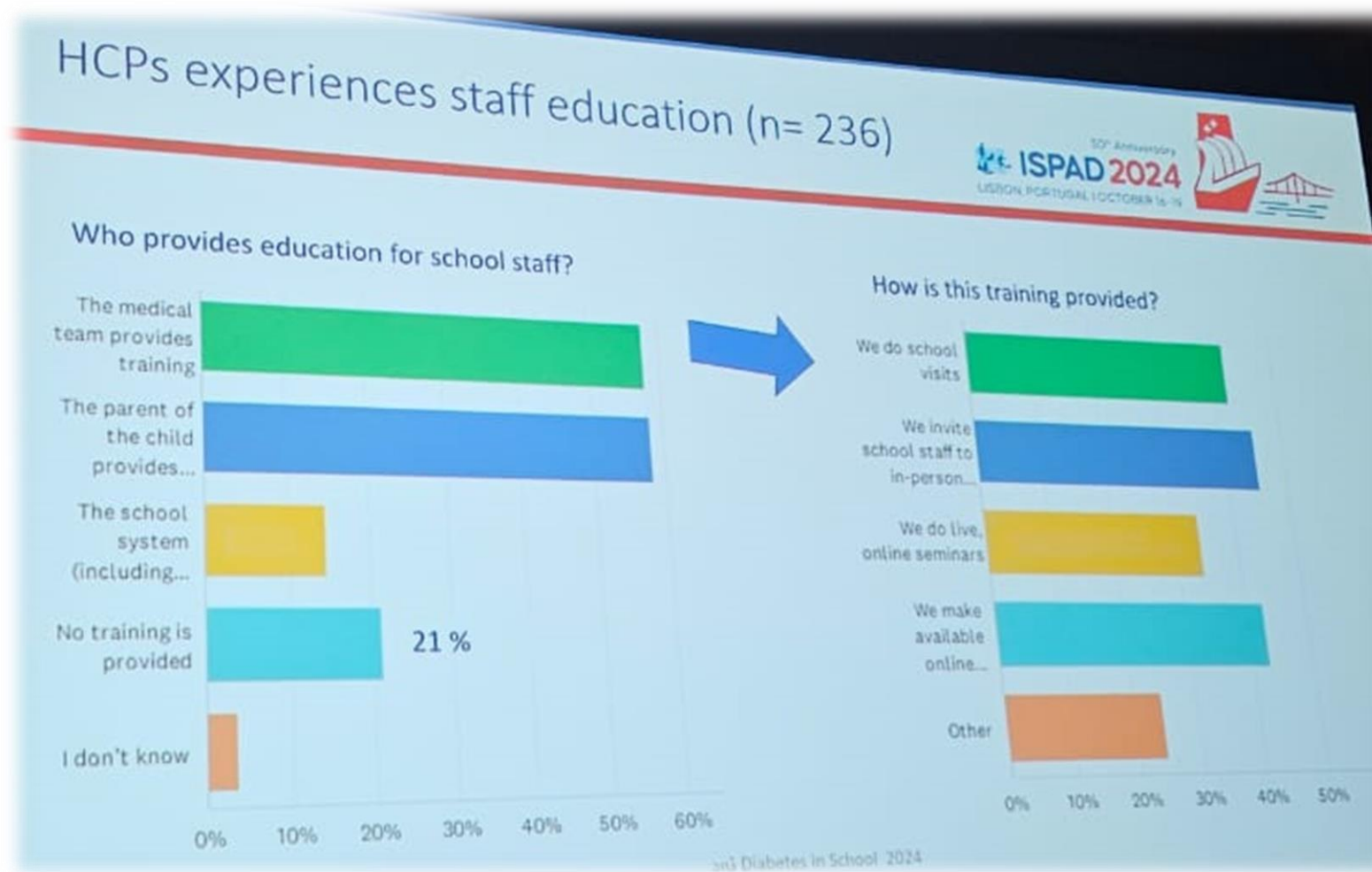
ESCUELA

Grupo de interés especial



ESCUELA

Grupo de interés especial



ESCUELA

Grupo de interés especial

JENIOUs-CwD diabetes in schools research project: a worldwide survey on type 1 diabetes (T1D) management in children and adolescents in schools

Type selection

Preferred Presentation Type: Oral presentation

General data

Category: 4.b: Diabetes at School

Title

Title: JENIOUs-CwD diabetes in schools research project: a worldwide survey on type 1 diabetes (T1D) management in children and adolescents in schools

Abstract text

Introduction: T1D management in schools is challenging and publications tend to be regional with a small number of participants.

Objectives: To assess the experiences of families of children and adolescents (C/A) with T1D during school time globally.

Methods: Cross-sectional online survey-based study. A 41-question Google Forms survey aimed at families of T1D C/A, supported by ISPAD-JENIOUS and the ISPAD Diabetes in Schools Special Interest Group. The questionnaire was developed in English, translated into 13 languages, and promoted through email and social media. The inclusion criteria were: 1) T1D 2) age below 19 years 3) school attendance. The countries were divided according to the UN geographic regions and the World Bank income classification.

Results: Preliminary data was collected from May/2023 to February/2024. There were 6,556 responses from 54 countries, 50%(n=3,304) from Europe, 37%(n=2483) Americas, 9%(n=595) Asia and 2% (n=165) Africa. High-income countries: 53%, upper-middle-income countries: 39%, lower-middle and low-income countries: 6%. Mean age(SD) was 10.7y(3.81); diabetes duration: 4.3y(3.4); females: 49.1%(n=3,223). Families reducing work hours because of diabetes: 52.8%; in children < 6 years: 63%. 50.4% reported reducing insulin dosage to avoid hypoglycemia, and 16% that the child misses school due to diabetes at least once a month. School support: 54.8% did not have someone at school responsible for diabetes care, and 48.1% did not have a diabetes management plan. Overall, 19.2% are dissatisfied with the school's support, and 49.4% think it can improve.

Conclusions: This is the largest study conducted worldwide to assess diabetes care in school settings. School personnel have limited knowledge about diabetes, and there is a high incidence of family members reducing work hours to assist their C/AwD at schools due to a lack of support. Our results revealed that there is an urgent need to improve diabetes management support in schools. These results can help develop strategies locally and internationally.

ESCUELA



Mejorando el tiempo escolar

MISIÓN DE LA ESCUELA PARA TODOS

- Aprender
- Estar seguros
- Jugar
- Acceso al agua
- Acceso a la comida

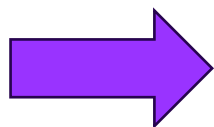
MISIÓN DE LA ESCUELA PARA UN NIÑO CON DBT

- Empoderar para que prosperen académica y socialmente y administren su salud

Más oportunidades

Declaración de posición sobre la diabetes tipo 1 en las escuelas 2024

- ✓ La educación es la adquisición de conocimientos y perspectivas sobre DT1
- ✓ El entrenamiento es el desarrollo de habilidades y la aplicación práctica de la educación en un estudiante con DM1
- ✓ La educación y el entrenamiento deben cumplir con los requisitos, estándares y regulaciones jurisdiccionales locales.



Plan de manejo
de diabetes

ISPAD International Society for Pediatric and Adolescent Diabetes  Student with Type 1 Diabetes Medical Orders (DMP) from Medical Team consented by Parent  School and Parent develop plan on how Medical Orders are implemented at school 				
School / Education authority are responsible for providing safe systems of work, including education and training of school personnel to ensure competency. EDUCATION is the gaining of knowledge and perspective about T1D. TRAINING is the skill development and practical application of the education on the student with T1D. Education and Training must comply with local jurisdictional requirements, standards and regulations.				
	Applicable to	School responsibilities	Content	ISPAD Recommendations
LEVEL 1 EDUCATION	All school personnel 	All school personnel have a duty of care to apply an appropriate urgent response to all students, including those with T1D. The duty is to: • Act immediately • Escalate to a person with training 	Foundational understanding of T1D and how it impacts students and families Recognition of signs, symptoms and urgency to treat: • Low glucose levels • High glucose levels if student unwell Who to contact for help	Level 1 Education (e-learning (other sources)) 
LEVEL 2 EDUCATION AND TRAINING	School personnel who interact directly with the student and are likely to need to respond immediately to medical events: • In the classroom and • During other school-based activities 	Schools have a duty: • To protect the health and safety of staff and students • To ensure staff are educated and trained Student has the right to: immediate access to a person with T1D specific first aid skills to keep them free from foreseeable harm 	Understanding details of the student's medical orders (Diabetes Management Plan); T1D specific first aid training according to student's Emergency Response Plan (Diabetes Action Plan) • How and when to initiate treatment for high or low glucose levels • Understanding when and where to call for additional assistance Knowledge of the impact of food and activity on glucose levels Education and training is specific to the needs of individual students	Complete: • Level 1 Education • Level 2 Education and Training course • T1D First Aid Training • Individualised Education and Training by parent (may be assisted by education from medical team) 
LEVEL 3 EDUCATION AND TRAINING	Complex care of the student with T1D must be undertaken by: • Authorized Health Professional (e.g. Nurse)  OR • Non-medical personnel with the appropriate: 1: Education that is student specific 2: Training that provides the authority as required in local jurisdiction 	Schools have a duty: • To provide safe systems of work and appropriate training for its personnel • To safely facilitate prescribed complex T1D medical care • To provide trained and authorised school personnel to provide complex medical care • To ensure informed parental consent 	Complex medical care includes: 1. Insulin administration 2. Other T1D medical interventions and interventions. Content of Level 3 Education and Training should be: • Informed by the student's medical orders (Diabetes Management Plan) • Individualised • Applicable on-campus and individualised for each off-campus activity	Complete: • Level 1 & Level 2 Education • T1D First Aid Training • Individualised Level 3 Education e-learning modules • Level 3 Training to authorise complex care • Individualised Education and Training by parent (may be assisted by education from medical team) 

Results

- 146 respondents (from across 29 countries); 52.1% of the study population hailed from high-income, 25.3% from upper-middle-income, and 22.6% from lower-middle and low-income countries
- 61.6% were people with diabetes, and 38.3% were adult carers of a person with diabetes
- People with diabetes were mainly female (54.1%), had a mean $\pm$ SD age of 18.5 $\pm$ 3.6 years, and were diagnosed at the age of 9.0 $\pm$ 4.4 years. 58.2% were receiving paediatric diabetes care
- 84.2% respondents had received education on managing diabetes independently
- 38.4% reported having received information about the transfer from pediatric to adult-based diabetes healthcare settings



International Society for Pediatric and Adolescent Diabetes, Oct. 2024, Lisbon, Portugal



SCREENING



¿Qué aprendimos sobre los programas de screening?

To screen or not to screen ???

The issue is what to do!! ” Mosse Philip

Pros & Cons of screening for Type 1 diabetes

- Educated families
- Early diagnosis
- Lower prevalence of DKA
- Feeling of satisfaction and reassurance
- Opportunity to participate in prevention studies



- Overprotection of the child
- Children treated as ill
- Negative impact on parent-child relationship
- Worry and anxiety

Ansiedad



- Longitudinal studies
- Children with high genetic risk
- 15 years follow-up
- Visit 2-4 times per year
- Islet autoantibody testing at each visit



- Screening study - Sweden
- Children from general population
- Age 2-14
- Home capillary test for autoantibodies for type 1 diabetes, celiac and autoimmune thyroid disease

Anxiety

- Increases after information about genetic risk and islet autoantibody positivity
- Decreases over time especially for those who remain negative for islet autoantibodies
- Difference between mothers and fathers
- Factors associated with anxiety:
 - First degree relative
 - Ethnic minority status
 - Low education level
 - Accurate risk perception of the child's T2D risk
 - Positive for islet autoantibodies

Ansiedad

Anxiety – after IA screening

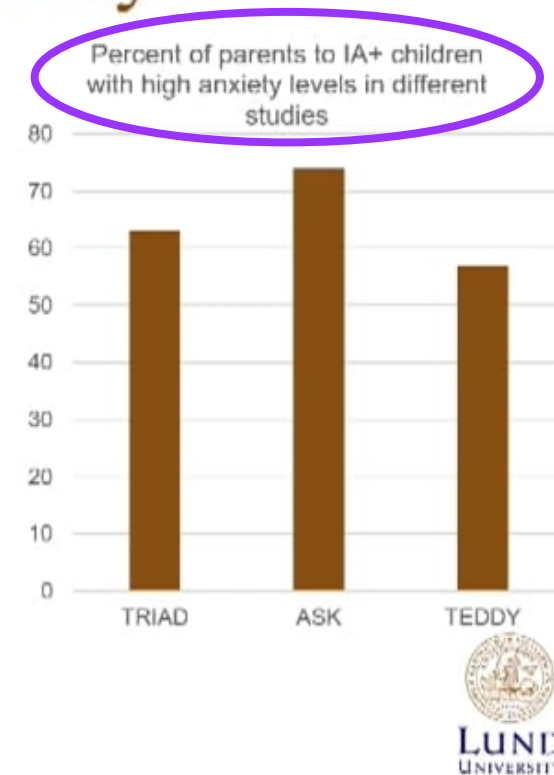
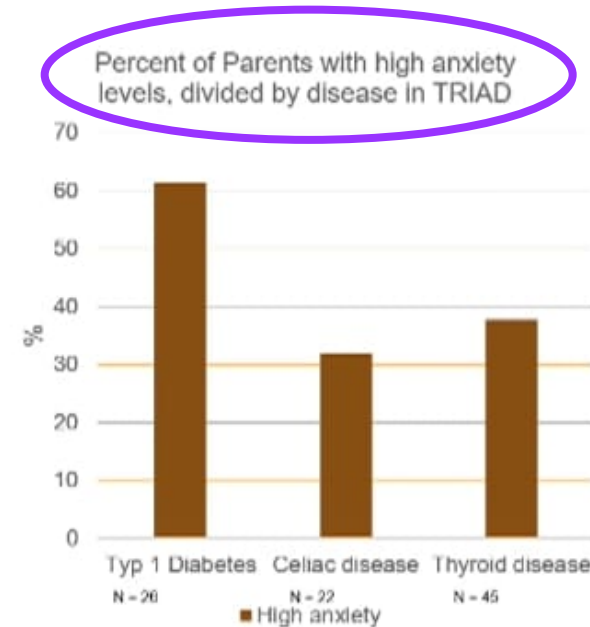
- **FRIDA** Screening in Germany, 2-6 years old children, between 2015-2019.
 - Increased PHQ-9 scores in mothers to IA+ children, declined after 1 year.
 - The PHQ-9 is a screening tool for depression (Ziegler, JAMA. 2020)
- **ASK**: Screening in Colorado, US.
 - Increased anxiety in parents to IA+ children at first follow-up visit. Remained elevated at visit 2 but started to trend down. (O'Donnell, Diabetes Care. 2023)



Ansiedad

- 6-item short form of the SAI
- Scores >40 – High anxiety
- T1D, Celiac and Thyroid disease
- 2 time-points
 - After information on results
 - After 1 year

Anxiety – TRIAD study

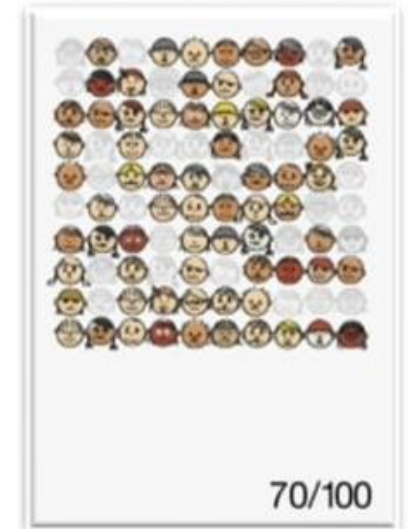


Risk communication

- Challenging!
- Underestimation is common
- Parents risk perception accuracy may decrease over time
- Important for retention and compliance

Strategies in TEDDY:

- Documented annual risk information
- Different materials and methods
- Ask questions
- Underestimation notification



“Percent - 70%”

“70 children out of 100 within 10 years”



- Time
- Staff consistency
- Information & Education
 - In different ways and format
 - Repeated
 - Ask questions



<http://www.teddy.lu.se/>

Strategies



CONDICIONES ASOCIADAS



Diabetes y otras condiciones asociadas

SME. DOWN

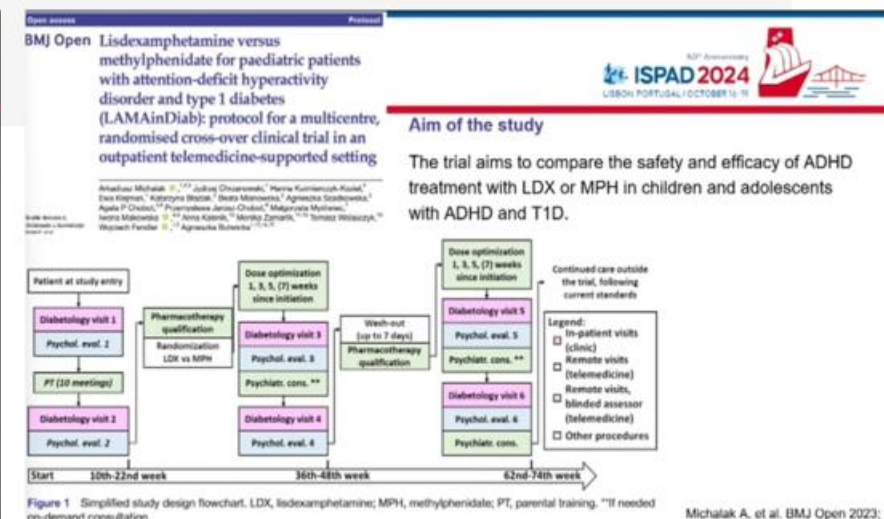
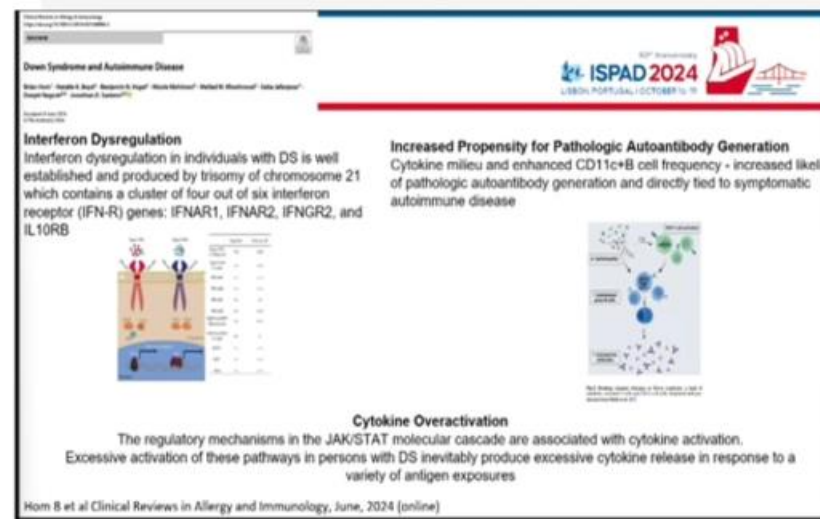
Diversos mecanismos genéticos asociados a su fisiopatología debido a la trisomía

ADHD

Distintos mecanismos debidos a la medicación

TEA

Impacto ambiental, genético
Medicación (risperidona)





Mensajes Clave

ESCUELA

SENDAS
PMD
Declaración de
posición sobre
DT1 en las
escuelas 2024

Gun
Forsander

ADOLESCENCIA

Falta evidencia
para poder
afrontar los
desafíos que
implica la
transición

Steven James

SCREENING

Los programas
de screening
deben incluir
educación y
apoyo al grupo
familiar

Jessica Melin

OTRAS CONDICIONES ASOCIADAS

T21
SDAH
TEA
Requieren
estrategias de
educación
individualizada

Eduardo
Calliari



Muchas Gracias

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Muchas gracias

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