



Innovative Medicines Initiative

# Diabetes disease in its complexity

## Clinician's perspective

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# Speaker disclaimer

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C. Mathieu is or has been consultant for and KU Leuven has received research support or honoraria from: NovoNordisk, MSD, Eli Lilly, Sanofi, Novartis, AstraZeneca, BMS, Janssen Pharmaceuticals, Pfizer, Medtronic, Roche, Servier



# Goal of therapy in diabetes mellitus

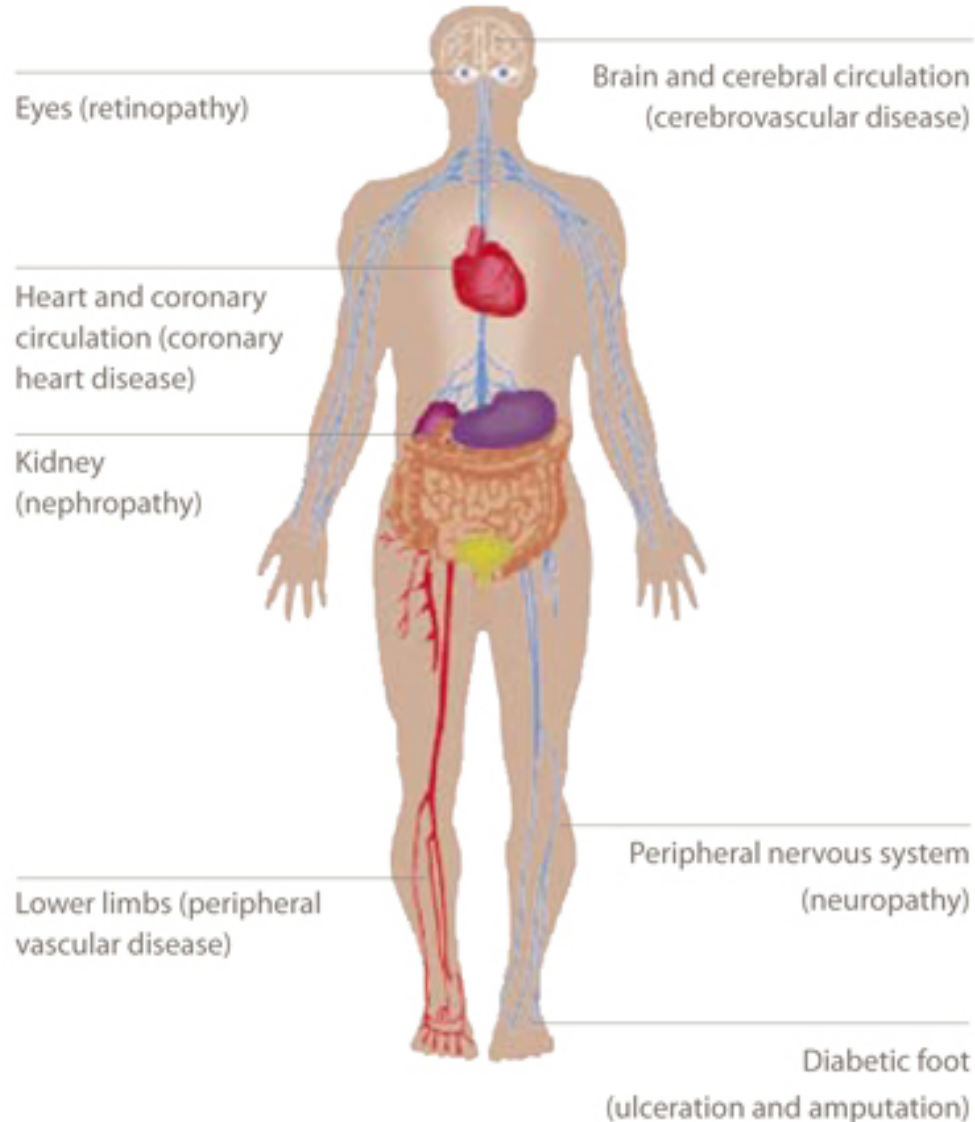
Quantity of life\*

and

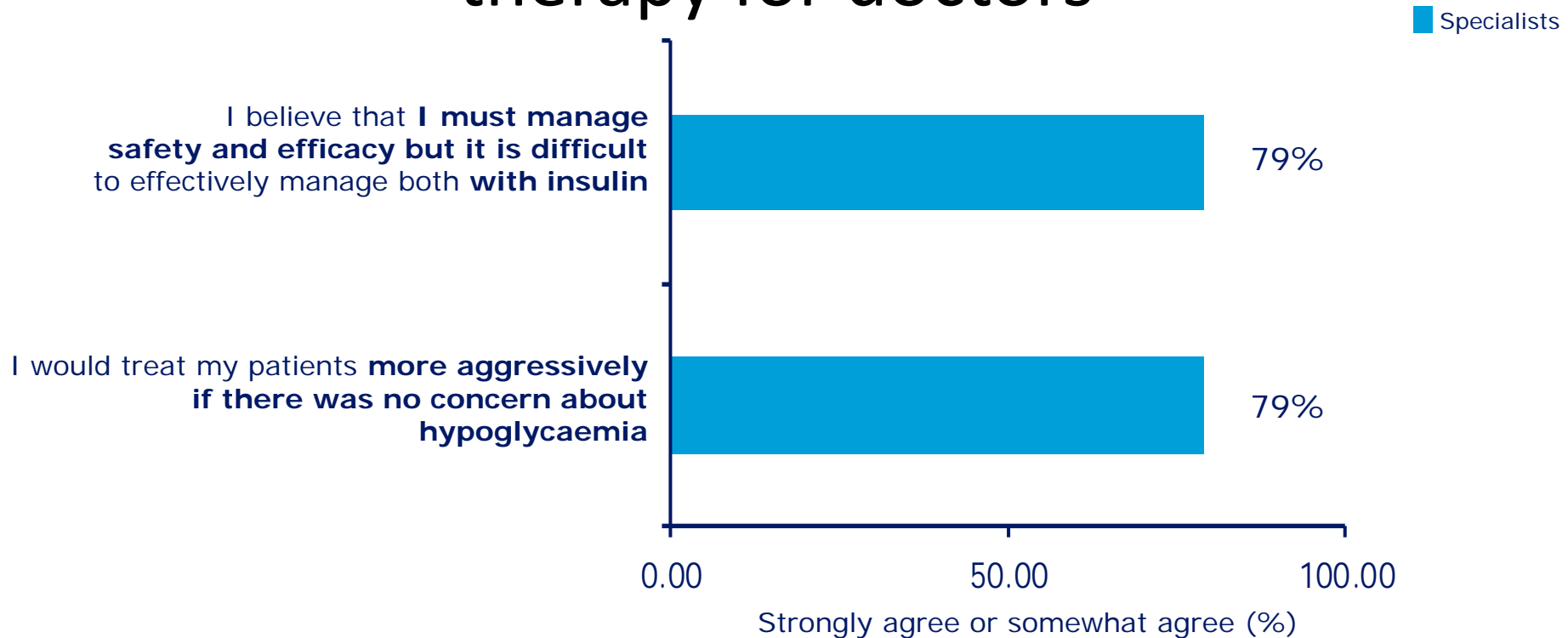
Quality of life\*

\*mainly determined by complications

# Diabetic complications



# GAPP™ study: Hypoglycemia as obstacle for therapy for doctors



## GAPP™

- A global internet survey of patient and physician beliefs regarding insulin therapy
- N= 1250 physicians

# Therapy of diabetes = risk factor management

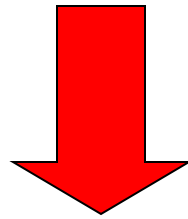
- Microvascular complications: Glycemic control
- Macrovascular complications:
  - Lifestyle
  - Weight
  - Blood pressure
  - Lipids
  - Glycemic control
  - ....
- Cancer risk

# Therapy of diabetes = risk factor management

- Microvascular complications: **Glycemic control**
- Macrovascular complications:
  - Lifestyle
  - Weight
  - Blood pressure
  - Lipids
  - **Glycemic control**
  - ....
- Cancer risk

# Type 1 diabetes

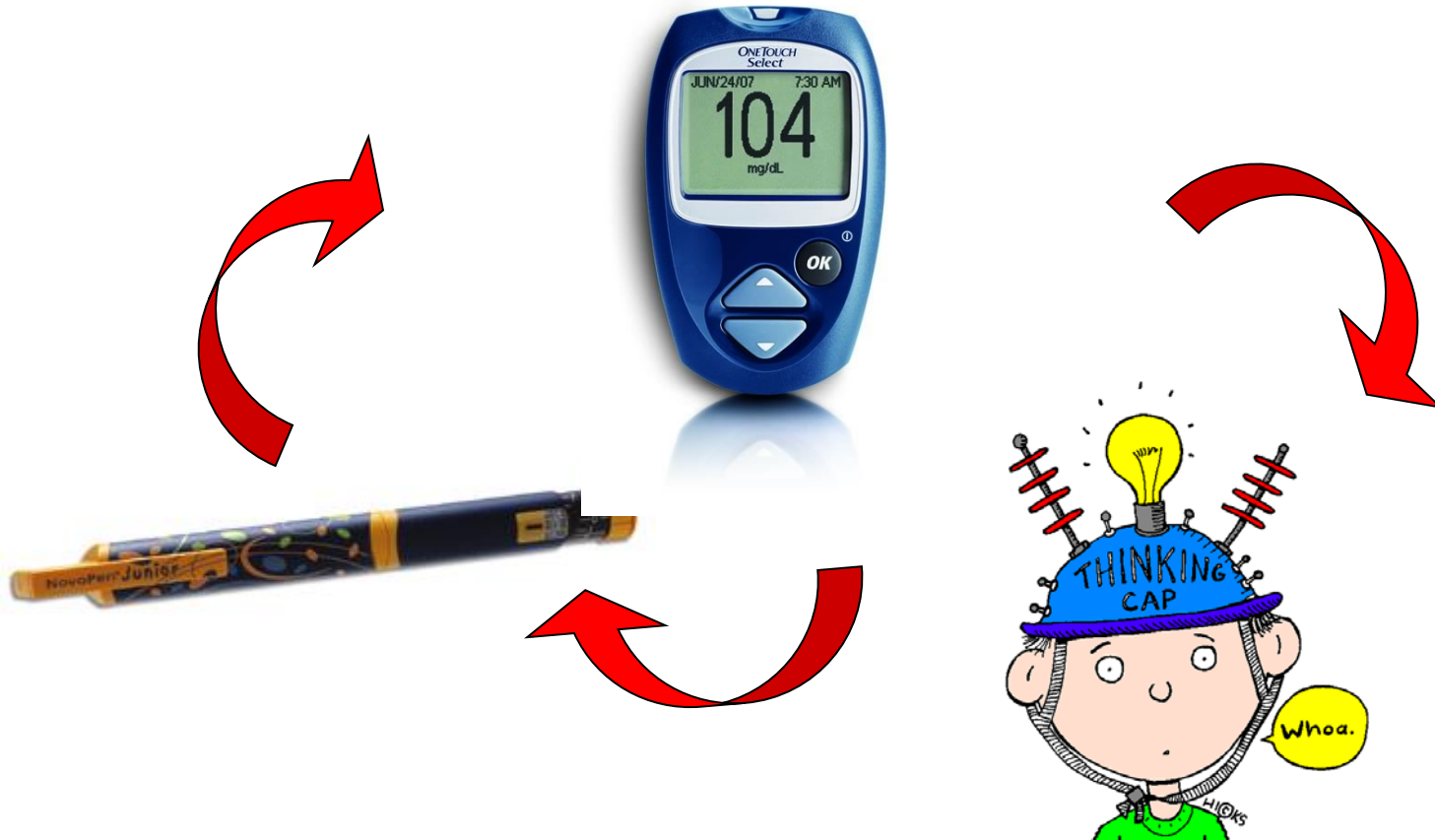
= Destruction of beta cells



Therapy: Replacement of all  
beta cell functions



# Replacing all beta-cell functions



# Type 1 diabetes: Tools

- Insulin
- Education and selfmonitoring of blood glucose
- Diet
- Lifestyle

# Tools

- Insulin
- Education and selfmonitoring of blood glucose
  - Diet
  - Lifestyle

# Achieving glycemic control

Insulin

Exercise

Stress



Nutrition

Stress

# Pathophysiology of T2DM

T2DM as a **Dual** Disease:

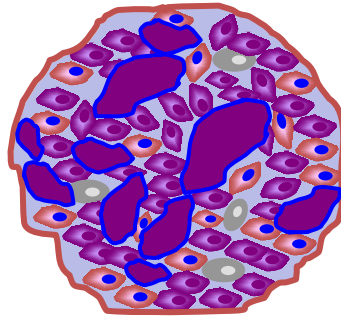
**β-Cell** Failure  
**Insulin** Resistance

# Hyperglycemia and CV risk

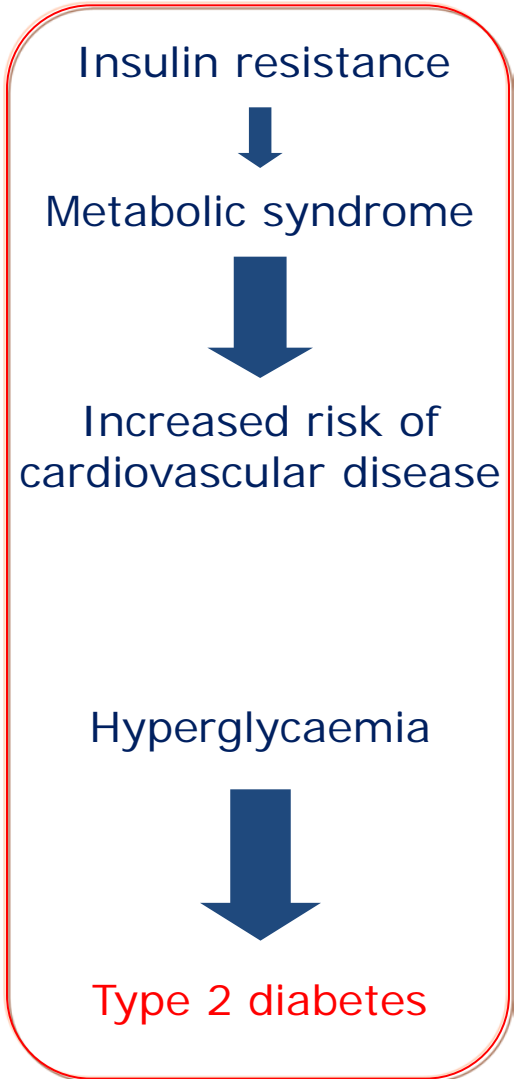
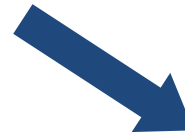
Unhealthy lifestyle and environmental factors



+



Failing beta-cells



# Type 2 diabetes and the heart

Lipids, blood pressure,  
coagulation, inflammation

Glucose

# Type 2 diabetes: Tools

- Glucose lowering agents
- Education and selfmonitoring of blood glucose
- Diet
- Lifestyle



# Type 2 diabetes: Tools

- Education
- Diet
- Lifestyle
- Multifactorial approach
  - Glucose lowering agents
  - Selfmonitoring of bloodglucose

# 'We live in interesting times'

**SmartCells, Inc.**  
**The Big Idea:**  
Insulin, Neurostimulation

**Smart<sup>®</sup> Insulin**, made based on **insulin** (the polypeptide hormone that stimulates insulin receptors, designed to "self" and "burst" apart, when a specified level of blood glucose activation occurs... and thus, it "time-releases" several doses of insulin "smartly" - all driven by glucose level changes - throughout a typical diabetic's day, or so it is hoped...

**Ordinary<sup>™</sup> Insulin Molecules**  
C21H39O6

**Acquired?**

**Transplanting Islet Cells**

1. Donor pancreas
2. Isletlets are isolated from the pancreas
3. Isletlets are cultured in the lab
4. Isletlets are implanted into the liver
5. Transplanted islets, increasing the beta cell mass

**Research Scope for Islet Transplantation**

**Before Camouflage**

- 1. Isletlet Isolation
- 2. Isletlet Culture
- 3. Isletlet Encapsulation
- 4. Isletlet Transplantation

**Genetically Engineered**

**Hydrogel Encapsulation**

**Heterotransplanted (BSCs + Islet Cells)**

**STOP DIABETES**

1. Express insulin islets, targeting the abdomen, facilitating maximum drug delivery to this area.
2. Dissolution of the isletlet results in the co-release of the drug and absorptive enhancer.
3. This physical site facilitates the absorption of the drug across the abdominal cell membrane and results in increase of bioavailability.

• Be it 30 years, even drug resistance is slowed. Try:  
• In-Oral, Insulin, Smart Single Drug System.  
• 300% more, together, breakthrough.

Glucose Monitor  
Control - Algorithm  
Insulin Pump

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# Current trends



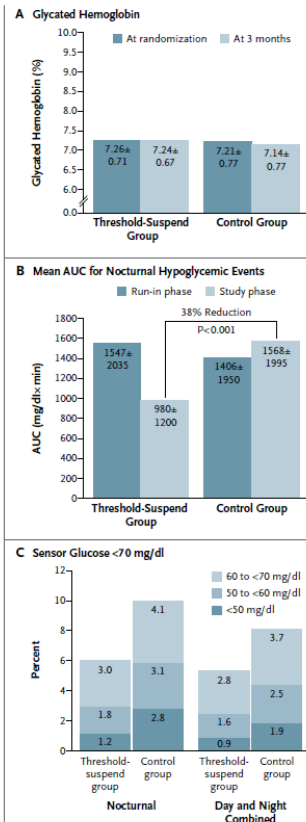
## ORIGINAL ARTICLE

# Threshold-Based Insulin-Pump Interruption for Reduction of Hypoglycemia

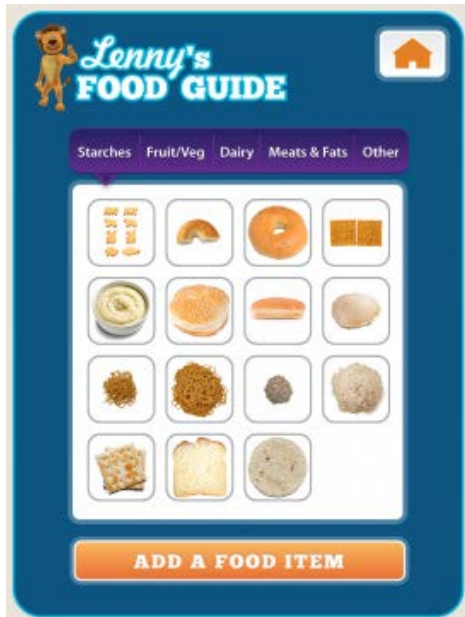
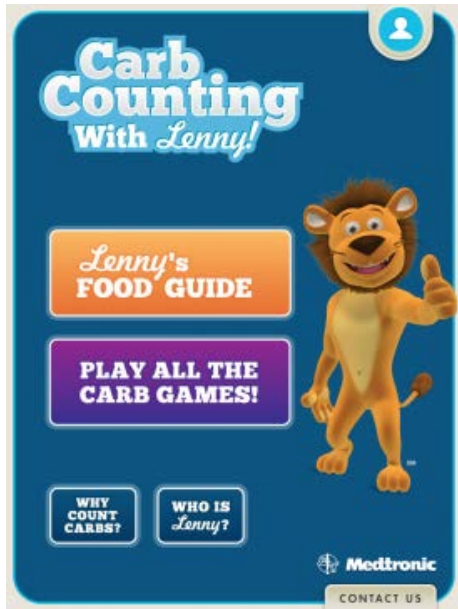
Richard M. Bergenstal, M.D., David C. Klonoff, M.D., Satish K. Garg, M.D., Bruce W. Bode, M.D., Melissa Meredith, M.D., Robert H. Slover, M.D., Andrew J. Ahmann, M.D., John B. Welsh, M.D., Ph.D., Scott W. Lee, M.D., and Francine R. Kaufman, M.D., for the ASPIRE In-Home Study Group\*

## Figure 2. Primary and Key Secondary End Points.

As shown in Panel A, the mean ( $\pm$ SD) changes in glycated hemoglobin concentrations during the study phase (the primary safety end point) were similar in the threshold-suspend and control groups ( $0.00\pm 0.44\%$  vs.  $-0.04\pm 0.42\%$ ; difference, 0.05 percentage points; 95% confidence interval [CI],  $-0.05$  to  $0.15$ ). As shown in Panel B, the mean area under the curve (AUC) for nocturnal hypoglycemic events during the study phase (the primary efficacy end point) was 37.5% lower in the threshold-suspend group than in the control group ( $P<0.001$ ). As shown in Panel C, the percentage of sensor glucose values that were less than 70 mg per deciliter was lower in the threshold-suspend group than in the control group, whether during nighttime hours (6.0% vs. 10.0%) or during day-time and nighttime hours combined (5.3% vs. 8.1%). The P value was less than 0.001 for each range in the panel. (See Table S2 in the Supplementary Appendix for the percentages of sensor glucose values in all ranges.) To convert values for glucose to millimoles per liter, multiply by 0.05551.



# Current trends





# Unmet needs

A clinician's point of view

=

A patient's point of view

# What is urgently needed?

- Understanding of diabetes management
  - Patients become experts—
    - Education tools
    - Calculation tools
- Access to diabetes specialists
- Labelling of foods
- Social hurdles
- **EDUCATION**



# EDUCATION





***"imagine if..."***

# Short term needs

- Achieving full control:
  - Less fluctuation of glycemia's:
    - Less hypo's
    - Less excursions after meals
  - Flat glycemic curves
- Less weight gain!
- No pain:
  - Injecting
  - Measuring blood glucose

Glucose sensitive insulins- no-hypo insulins  
Painless glucose values – Continuous values

# Short term needs

- Artificial pancreas: Intelligent pumps
  - Feedback
  - Closed loop
- Minipumps
- CHEAP

# Long term needs

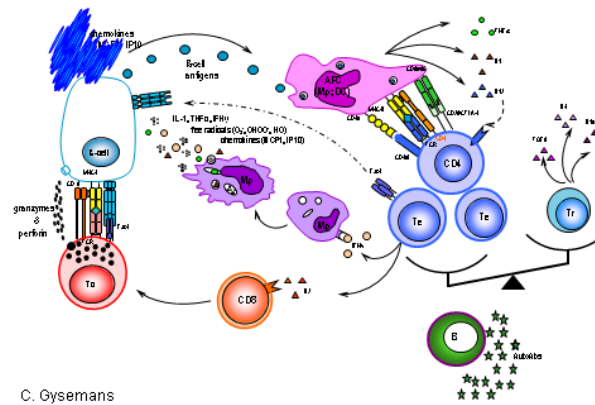
- Prediction
- Prevention
- Cure



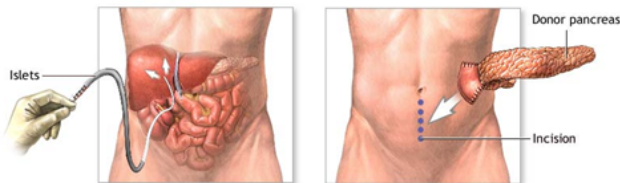
Natural immunomodulators as novel immunotherapies for Type 1 diabetes

[www.naimit.eu](http://www.naimit.eu)

## How are beta-cells destroyed in T1D?



## Type 1 diabetes



Cure

=

Replacement of pancreatic betacell

# Social unmet needs

- Awareness
- Access to endocrinologists



‘We live in interesting times’



Day of Affirmation Speech Robert F. Kennedy South Africa June 6th 1966