

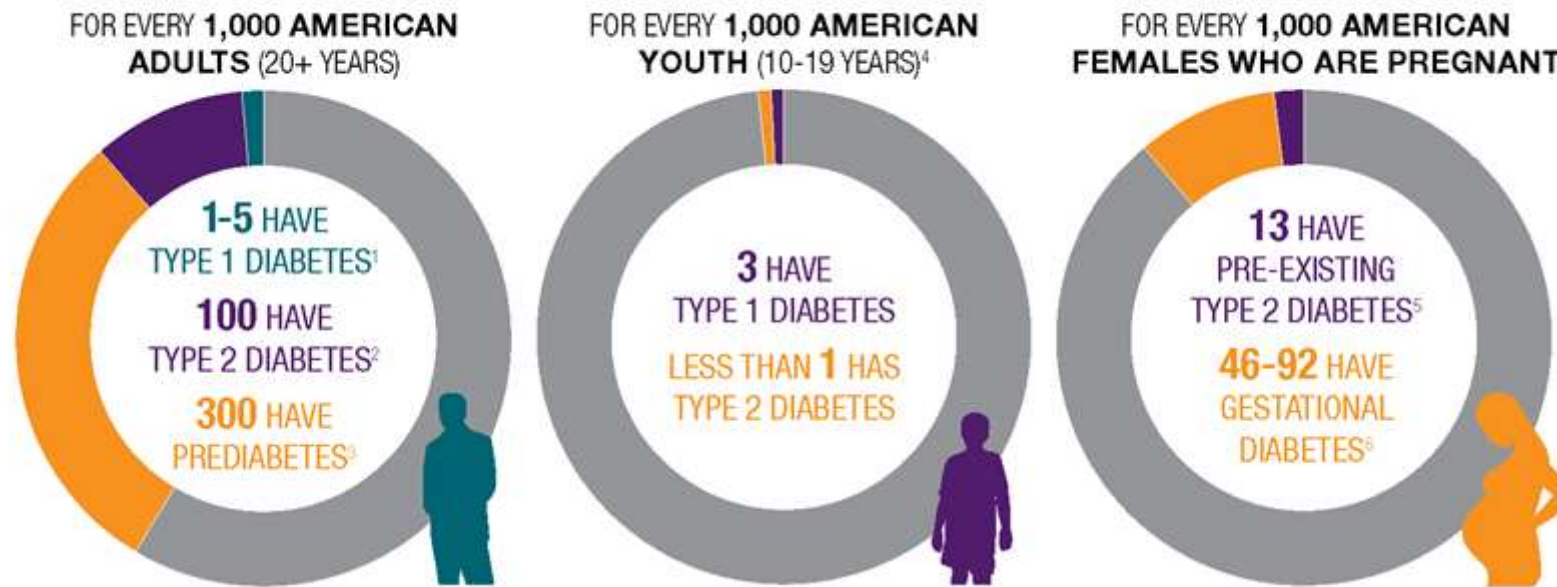
Évolution du traitement médicamenteux de l'adolescent avec un diabète de type 2

SLD 27.11.2024

Marianne Becker, endocrinologue et diabétologue pédiatrique, CHL

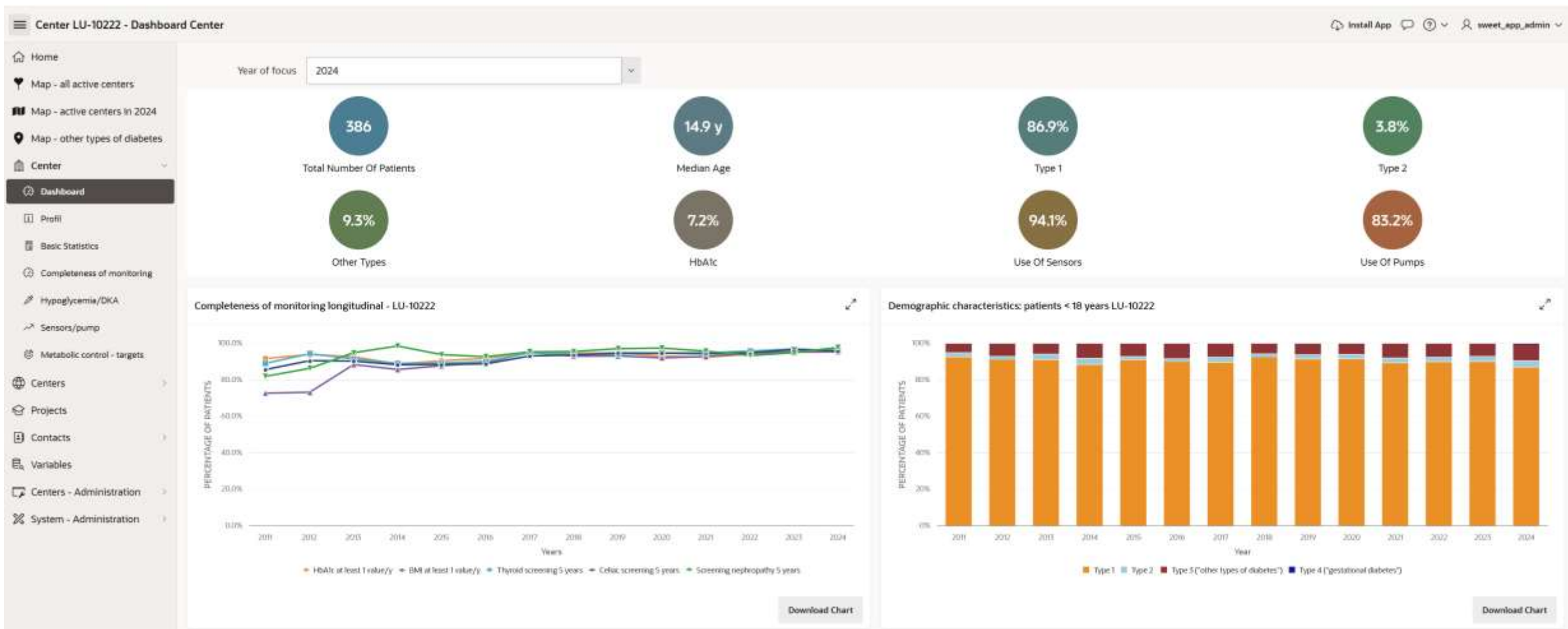
Incidence diabetes

OVER 29 MILLION AMERICANS HAVE DIABETES



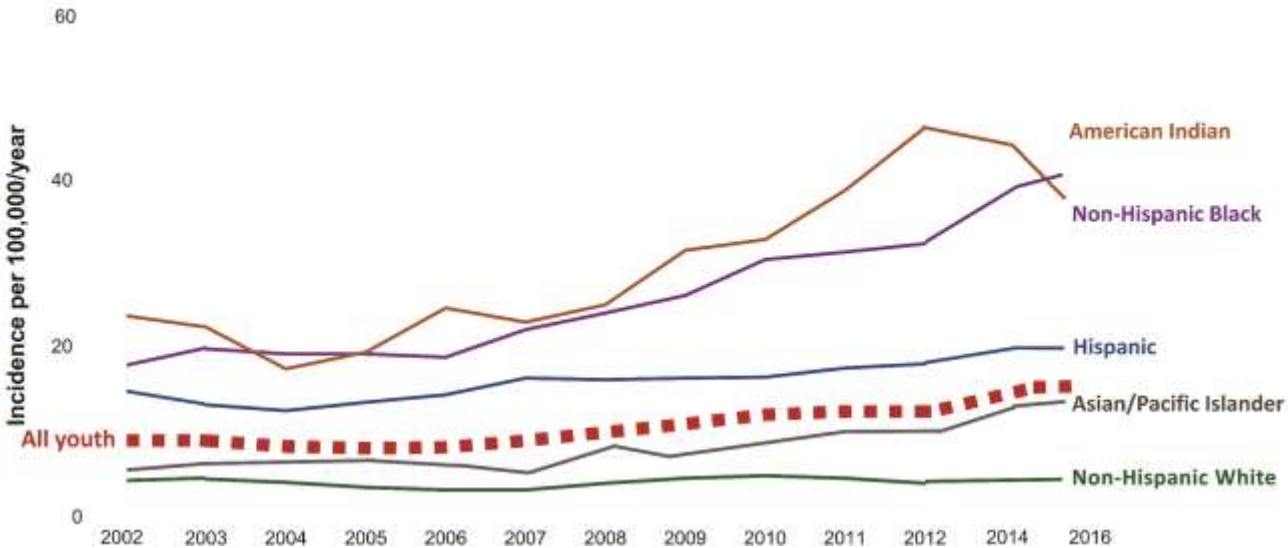
<https://endocrinenews.endocrine.org/society-publishes-resource-featuring-latest-diabetes-statistics/> 9/2015

Our center – data from the SWEET database



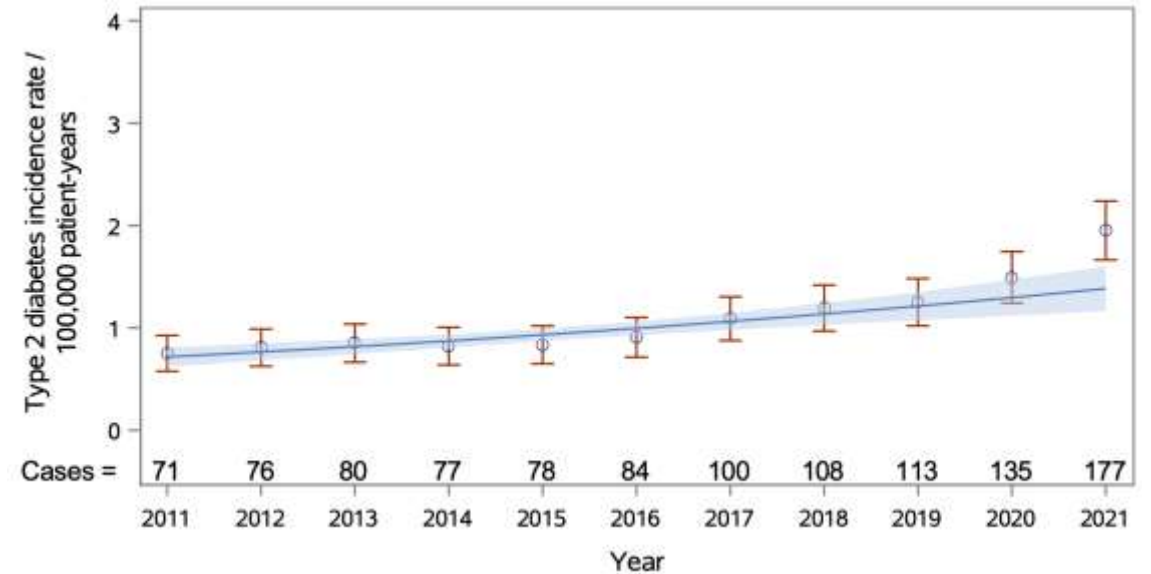
Incidence of type 2 diabetes in adolescents

Graphical abstract. Rising incidence of type 2 diabetes among multi-ethnic U.S. youth over the last two decades portends an awakening epidemic among children and adolescents worldwide



Data from the USA, adolescents < 20 years

Perng et al, Diabetes Care 2023;46(3):490–499

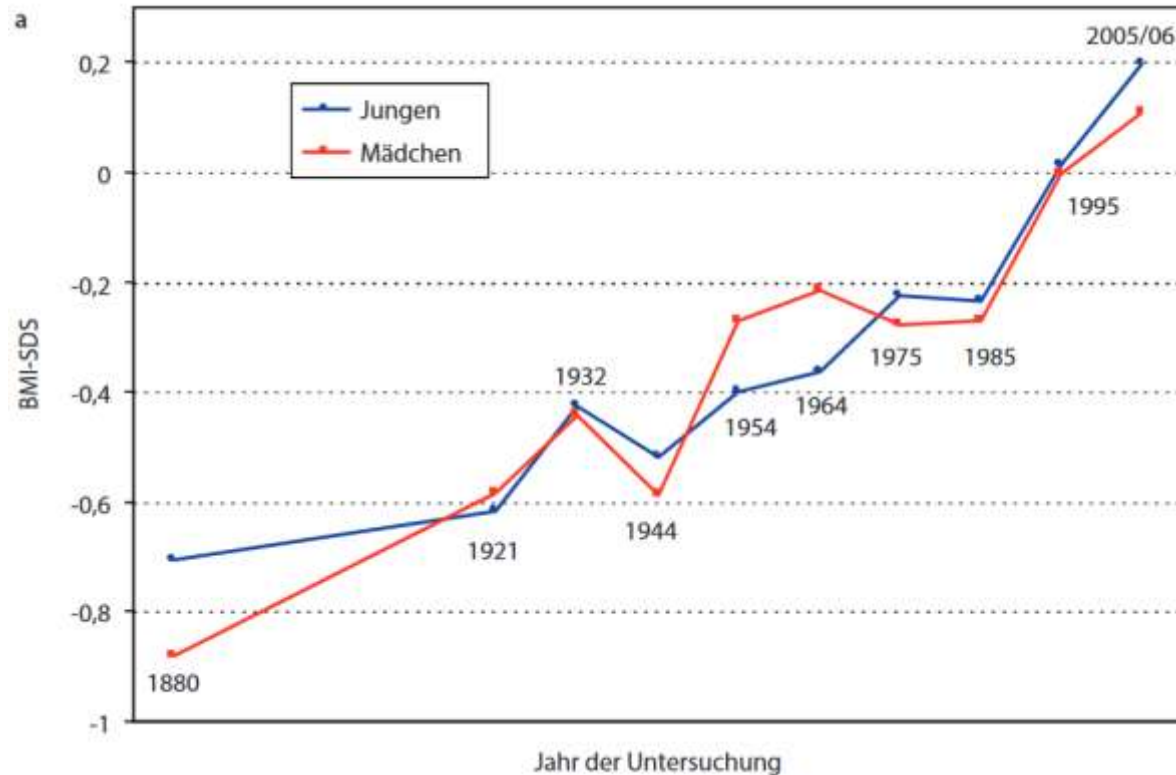


Data DPV (Germany, Austria, Switzerland, Luxembourg)
adolescents 6-18 years

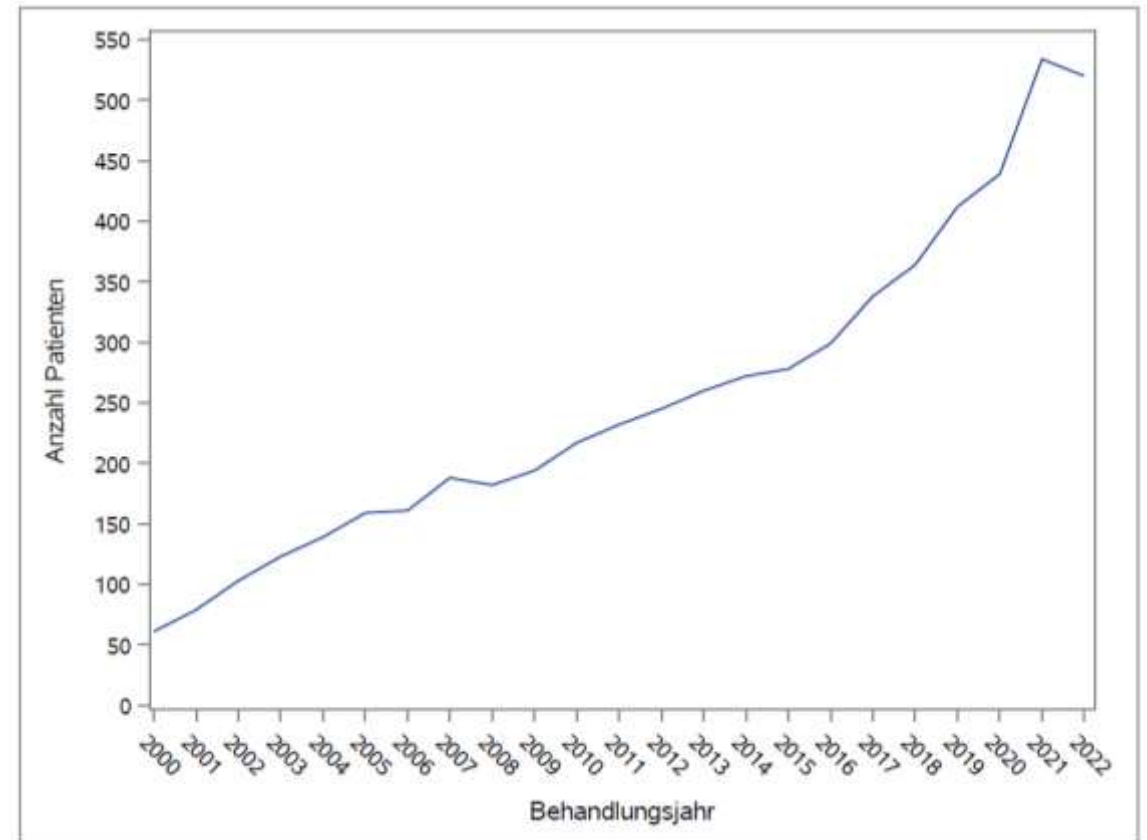
Denzer et al, Diabetes Care 2023;46(7):1379–1387

Type 2 diabetes and obesity

Obesity in children and adolescents



Number of reported case in DPV



Overweight and obesity in Luxembourg

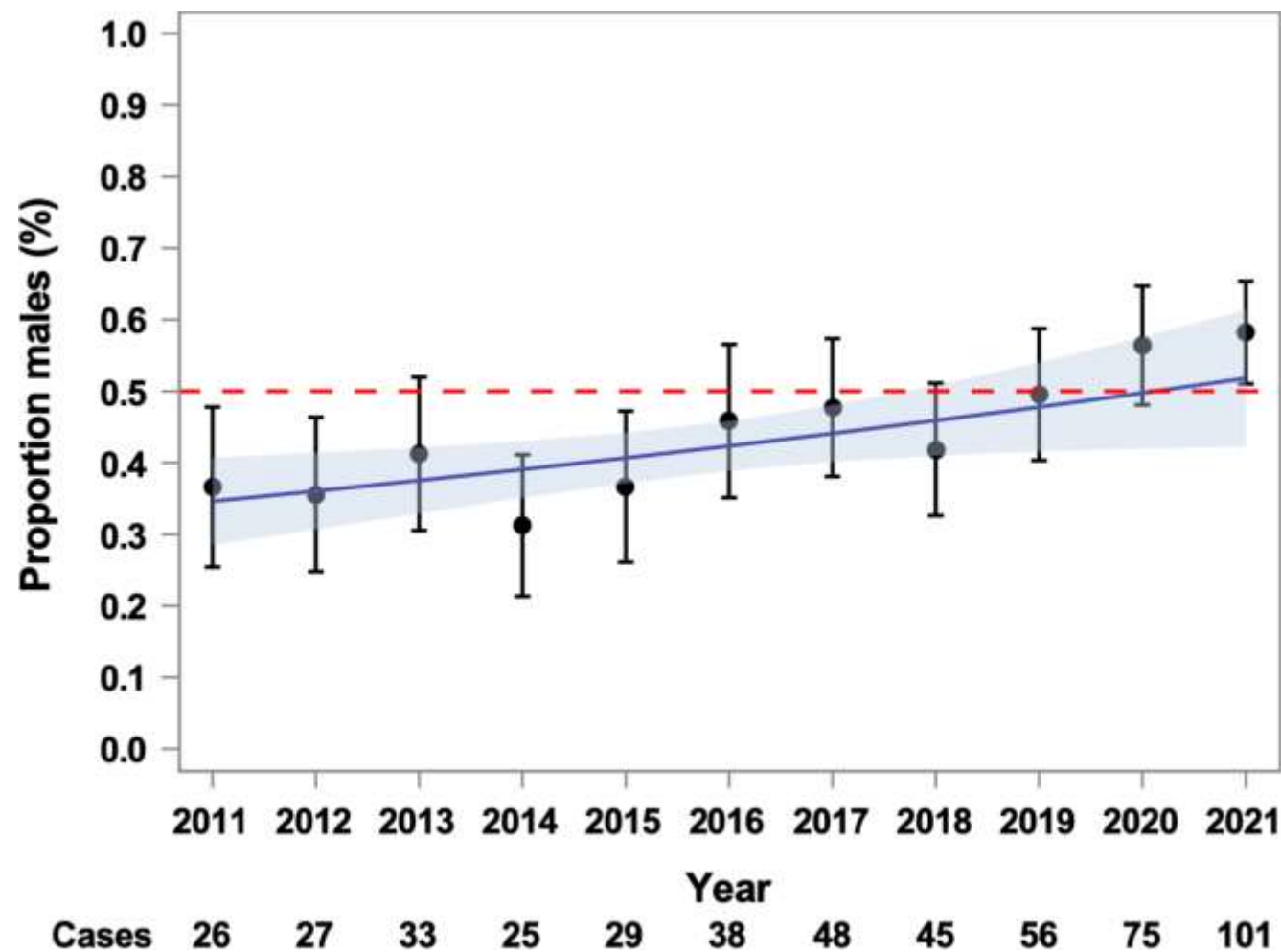
N = 1826	Median (P25/75/99)
Age [years]	10,17 (8,3/11,5)
Male[%]	51
BMI-SDS	0,26 (-0,55/1,23)
Total Cholesterol [mg/dl]	158 (141/174/230)
LDL-Cholesterol [mg/dl]	74 (61/89/139)
HDL-Cholesterol [mg/dl]	65 (56/75)

overweight (BMI-SDS 1 - ≤2) 19,5%

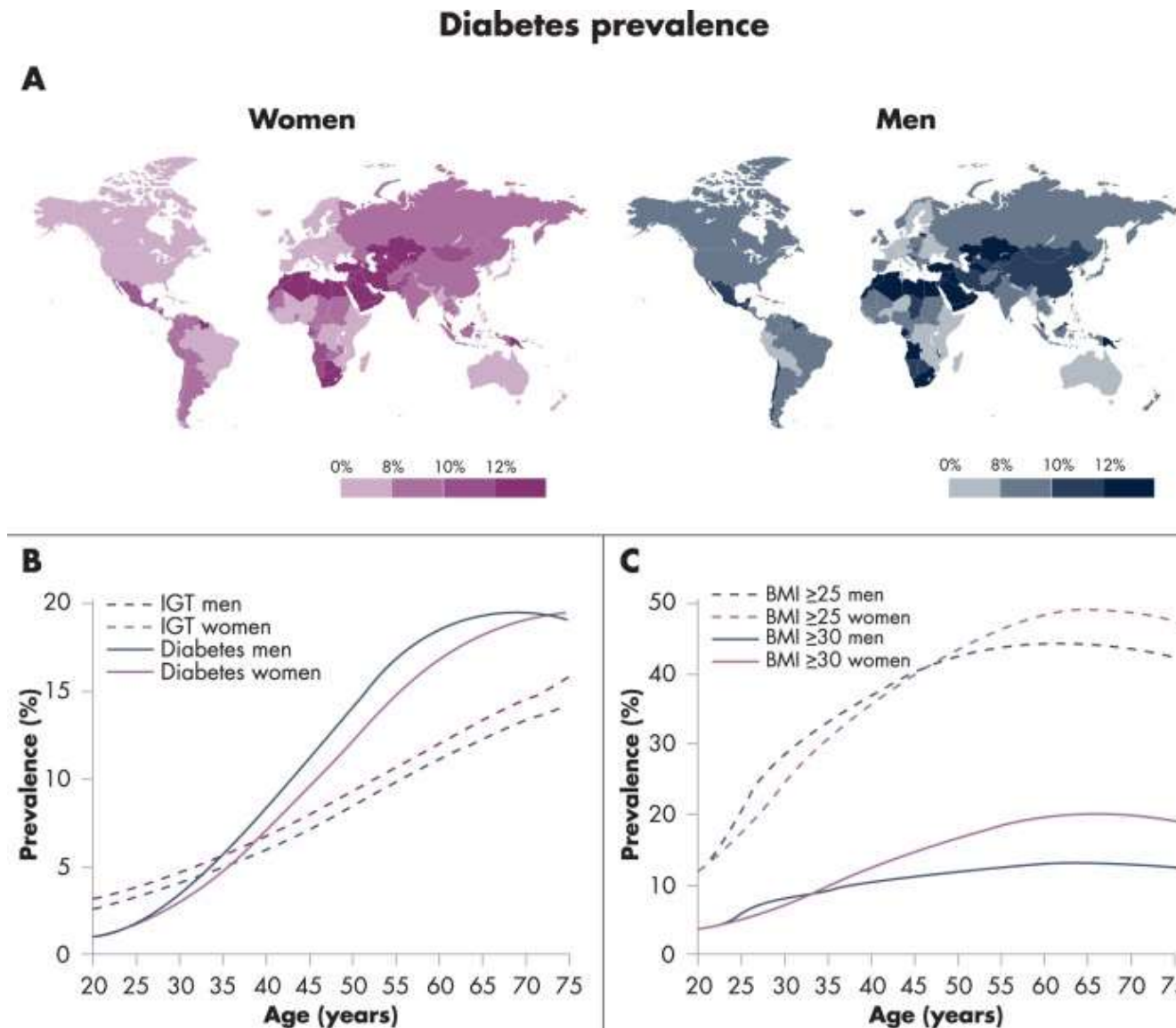
obesity (BMI-SDS >2) 10,5%

EARLIE data, unpublished

Type 2 diabetes incidence and sex ratio in youth



Type 2 diabetes and obesity prevalence and sex ratio in adults



Age > 25 years

Kautzky-Willer A et al,
Endocr Rev. 2016
Jun;37(3):278-316.

Type 2 diabetes in youth

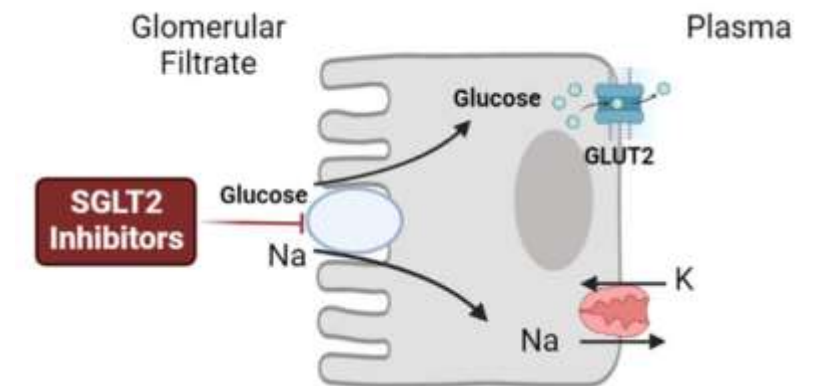
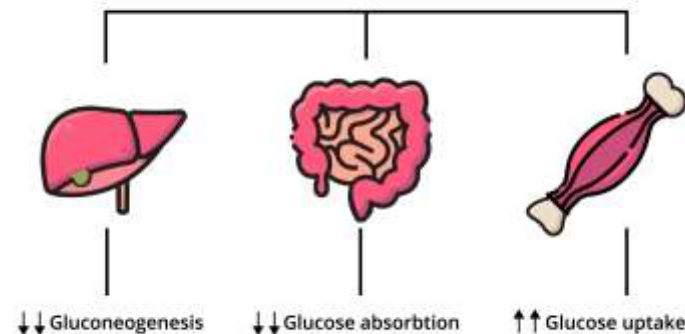
- Rare (T1D >>> T2D)
- Incidence increasing
- Incidence US (10/100.000) >> Europe (1/100.000)
- Girls > Boys, in adults: men > women

Treatment option for pediatric type 2 diabetes:

- 1) Lifestyle
- 2) OAD
 - Metformin
 - SGLT2 Inhibitors
- 3) GLP1 receptor agonists
- 4) Insulin

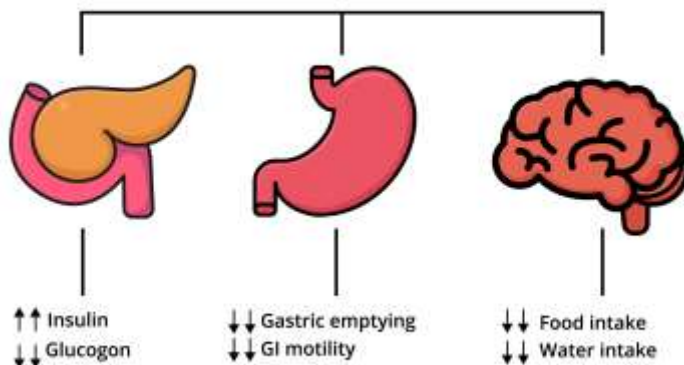


Metformin



Youssef, M. et al. *Int. J. Mol. Sci.* **2023**, *24*, 6039

GLP-1



Changes in pharmacotherapy

1) Lifestyle

2) OAD

- Metformin: **2001**
- SGLT2 Inhibitoren: **2021 dapagliflozin, 2023 empagliflozin**

3) GLP1 Rezeptor Agonisten Insulin: **2019 liraglutide, 2023 dulaglutide**

➔ New players since 2019:

- Did pharmacotherapy change?
- Did this change improve metabolic control and/or BMI?

RESEARCH LETTER

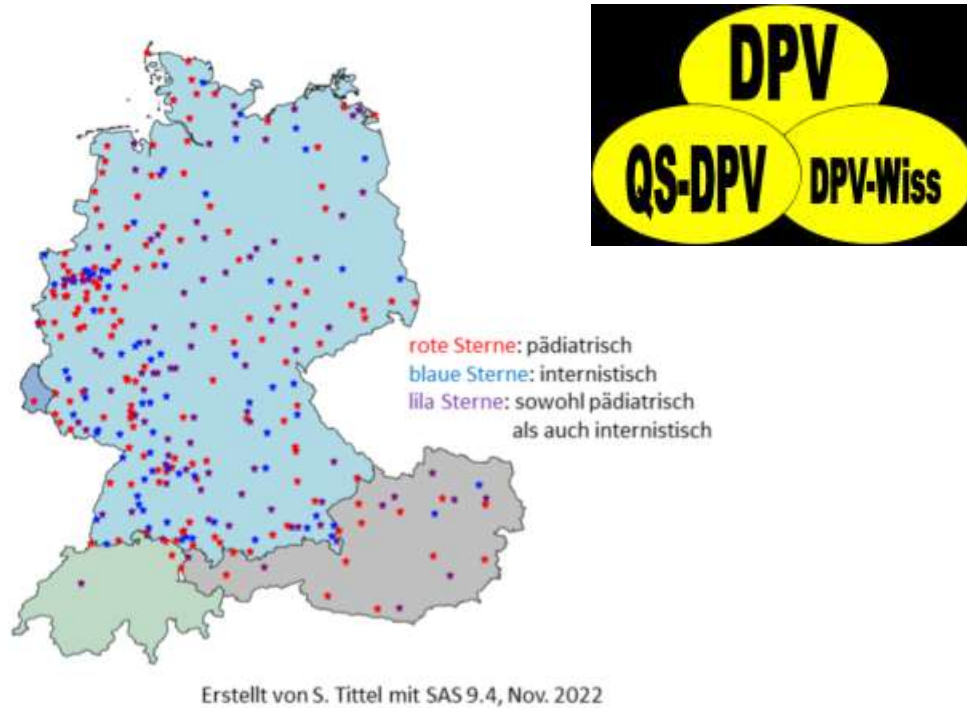
Trends in pharmacological management of paediatric patients with type 2 diabetes from 2000 to 2023 in German-speaking countries: Analysis based on the Diabetes Prospective Follow-up Registry

Susanna Wiegand MD, Marianne Becker MD , Stefanie Schmid MSc, Daniel Weghuber MD, Susann Weihrauch-Blüher MD, Thomas Reinehr MD, Rudolf Oeverink MD ... [See all authors](#) 

First published: 18 September 2024 | <https://doi.org/10.1111/dom.15930>

Susanna Wiegand and Marianne Becker contributed equally to this paper.

DPV-Karte: Orte mit teilnehmenden Einrichtungen



Cohorte

Inclusion criteria:

- Patients with T2D
- Diabetes onset before the age of 18
- Medical follow-up between 2000 and 2022

-> **2564** patients included

Data of 321 Diabetes centres included

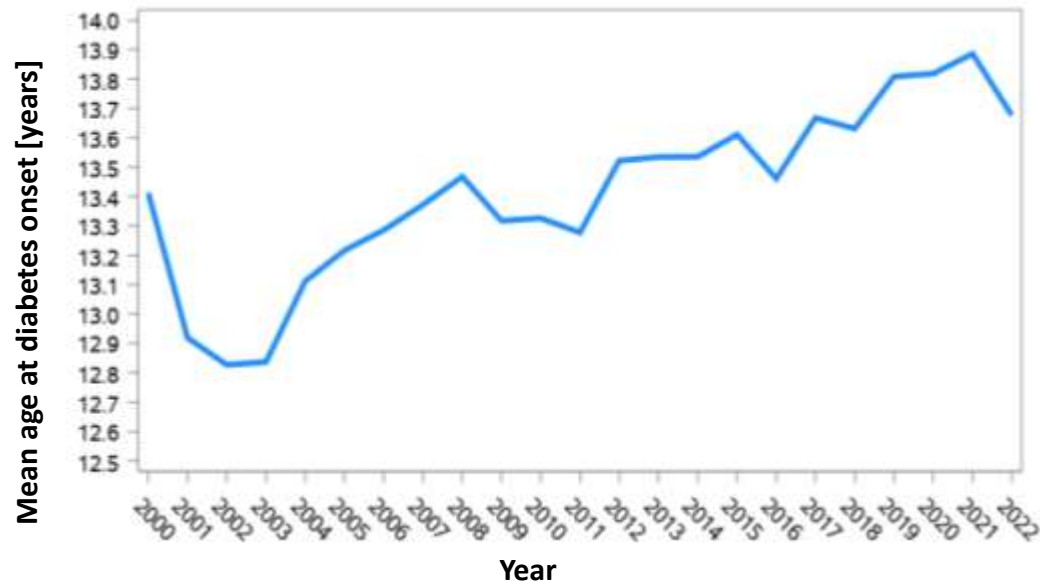


Characterisation of the cohorte:

2022:

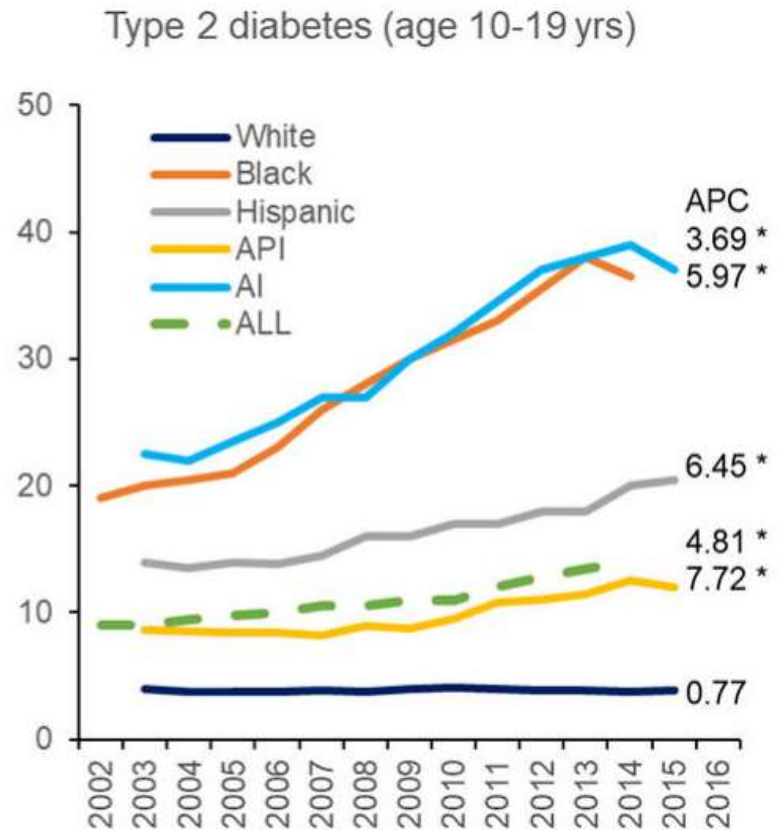
- Mean age 15.9 years
- Mean HbA1c at diabetes onset 7.8%
- Mean BMI SDS (German KIGGS data): 2.0
- 42% male
- 33% with a migration background

Age at diabetes onset

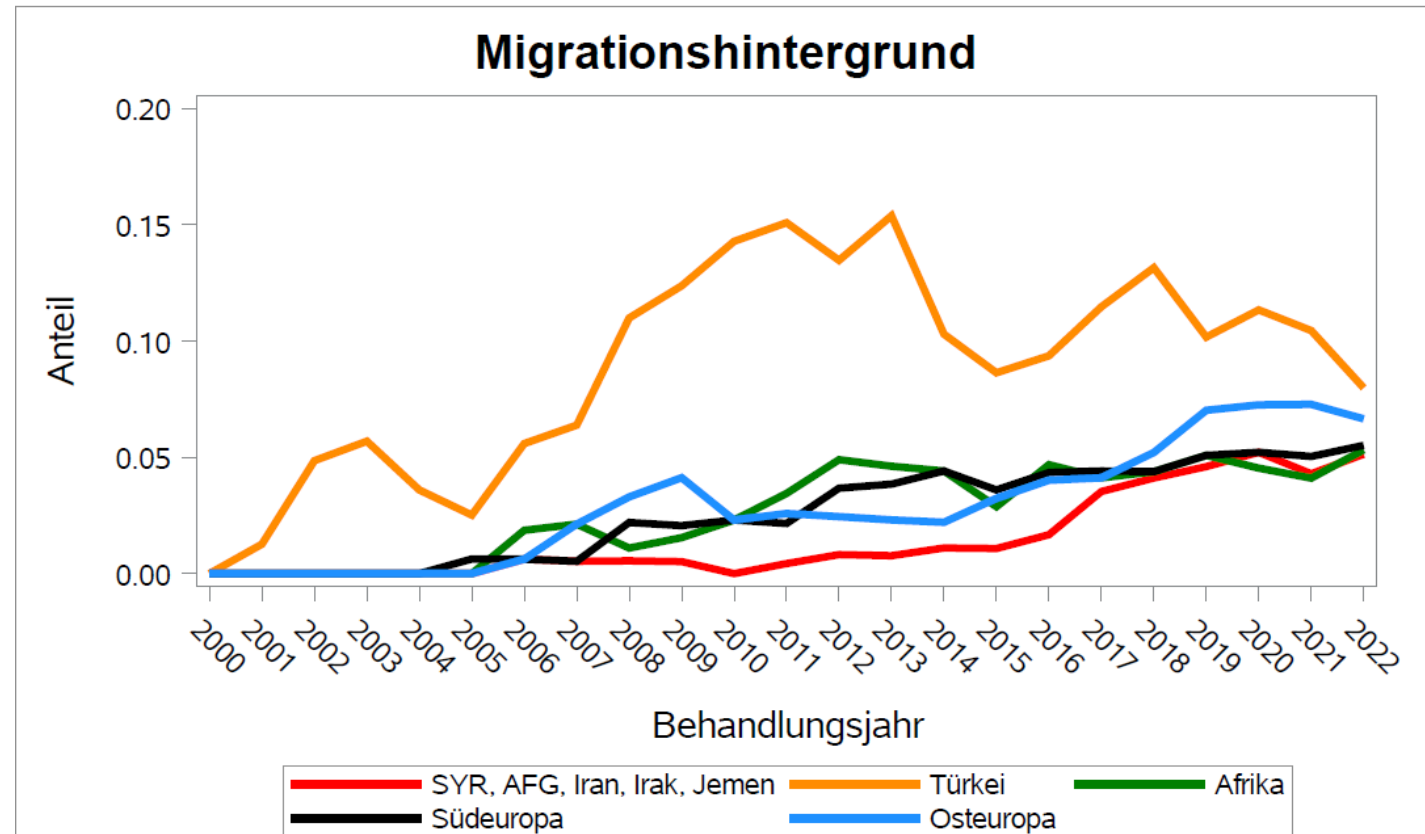


- Age at diabetes onset is increasing

Migration background:

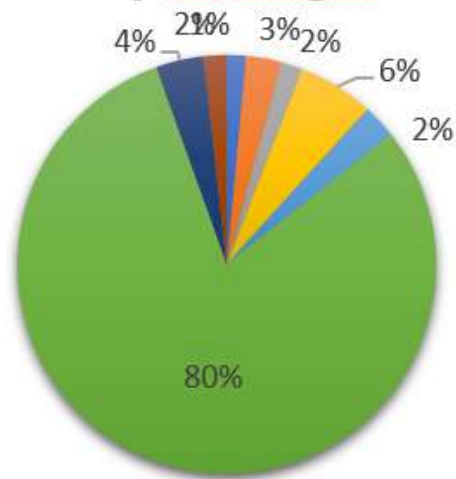


Dabelea, D. et al (2021), Twenty years of pediatric diabetes surveillance: what do we know and why it matters. Ann. N.Y. Acad. Sci., 1495: 99-120



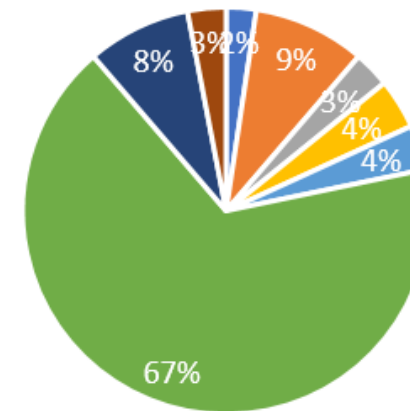
Migration background Type 1 vers Type 2 diabetes:

Country of origin T1D



■ Syria, Irak, Iran, Jemen ■ Turkey ■ Africa
■ Eastern Europe ■ Southern Europe ■ no migration background
■ Other ■ unknown

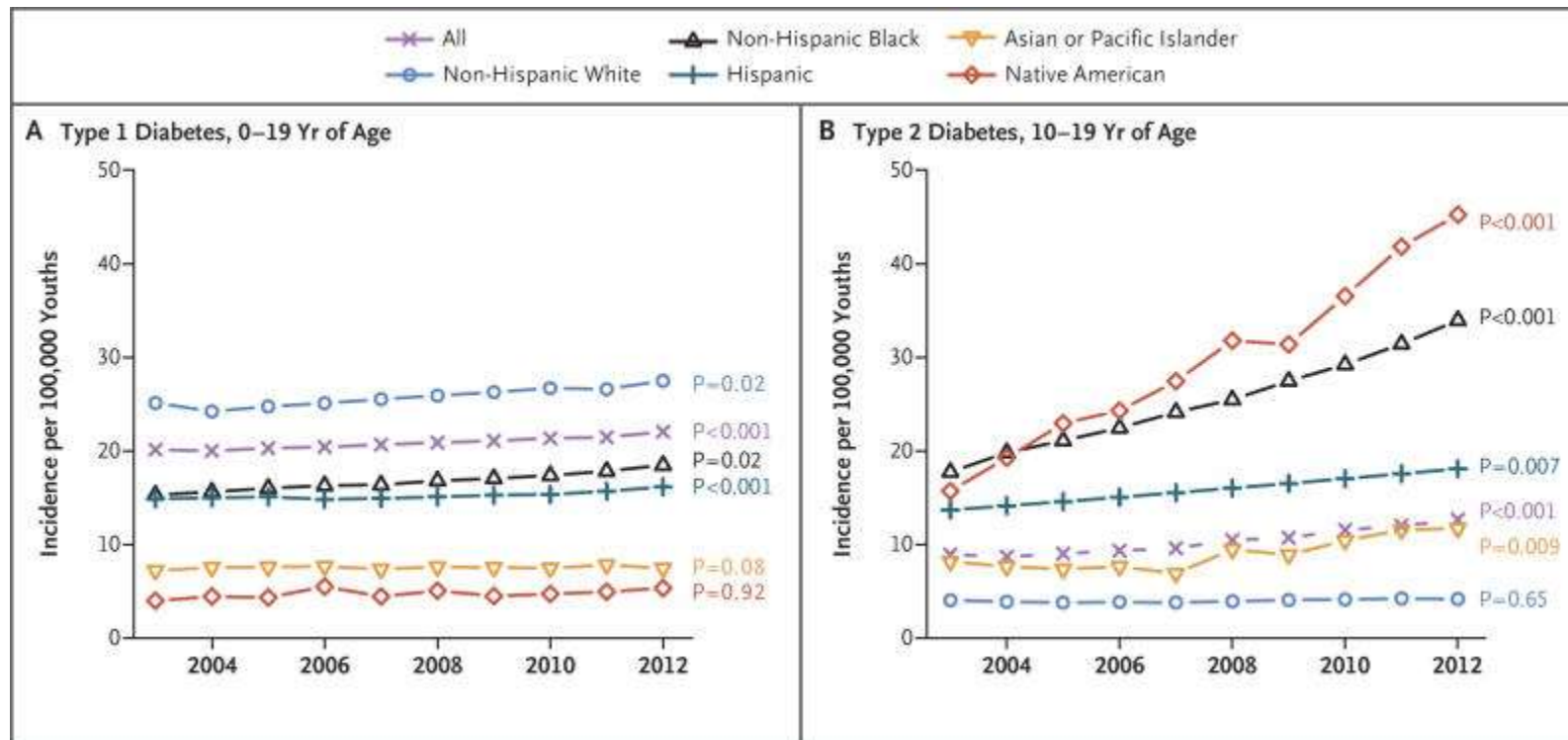
Country of origin T2D



■ Syria, Irak, Iran, Jemen ■ Turkey ■ Africa
■ Eastern Europe ■ Southern Europe ■ no migration background
■ Other ■ unknown

Data from DPV

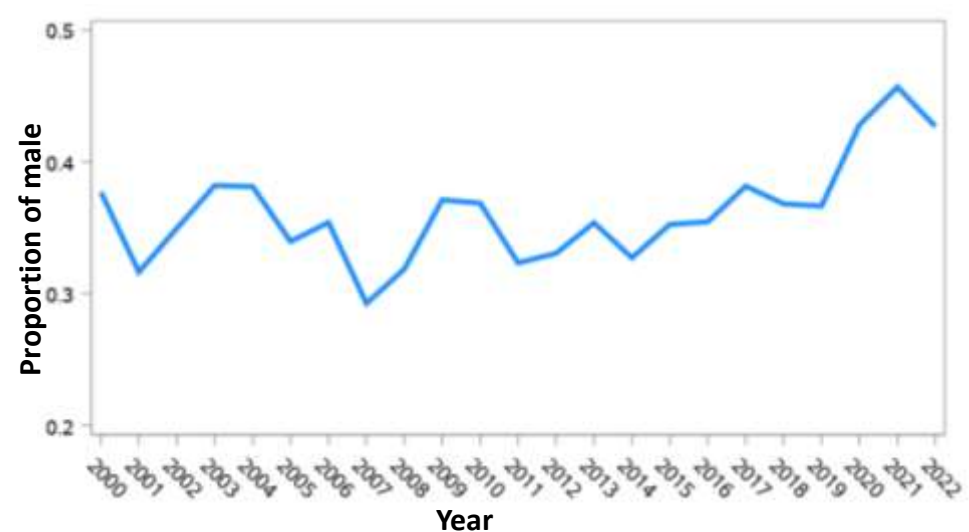
Incidence type 1 versus 2 diabetes depending on migration background



US data

Sex differences in our cohort

	Boys	Girls	p
percentage [%]	42	58	
Median age at diabetes onset [years]	14.7	13.9	<0.001
Median BMI SDS at diagnosis	2.3	2,1	<0.001
Median HbA1c at diagnosis	9.1	7.8	<0.001



Treatment in our cohort

Difference in gender:

	Girls	Boys	p-values
Mean insulin dosage [U/kg]	0.59	0.54	1.00
Initial insulin therapy [%]	9.34	16.45	0.00
Continuous insulin therapy [%]	28.34	26.36	1.00
Lifestyle only [%]	24.45	27.01	1.00
Monotherapy with OAD/GLP1a [%]	47.21	46.64	1.00
Combination insulin + OAD/GLP1a [%]	20.35	18.32	1.00
Insulin only [%]	7.99	8.04	1.00

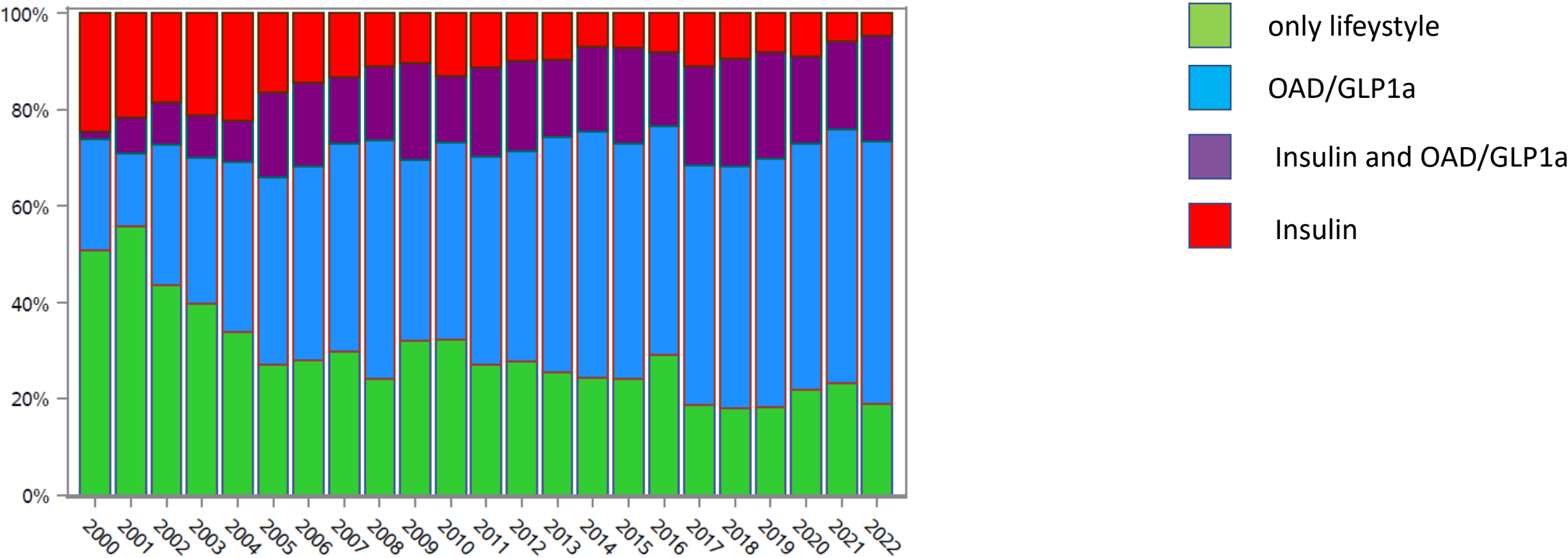
Treatment in our cohort

Differences depending on age:

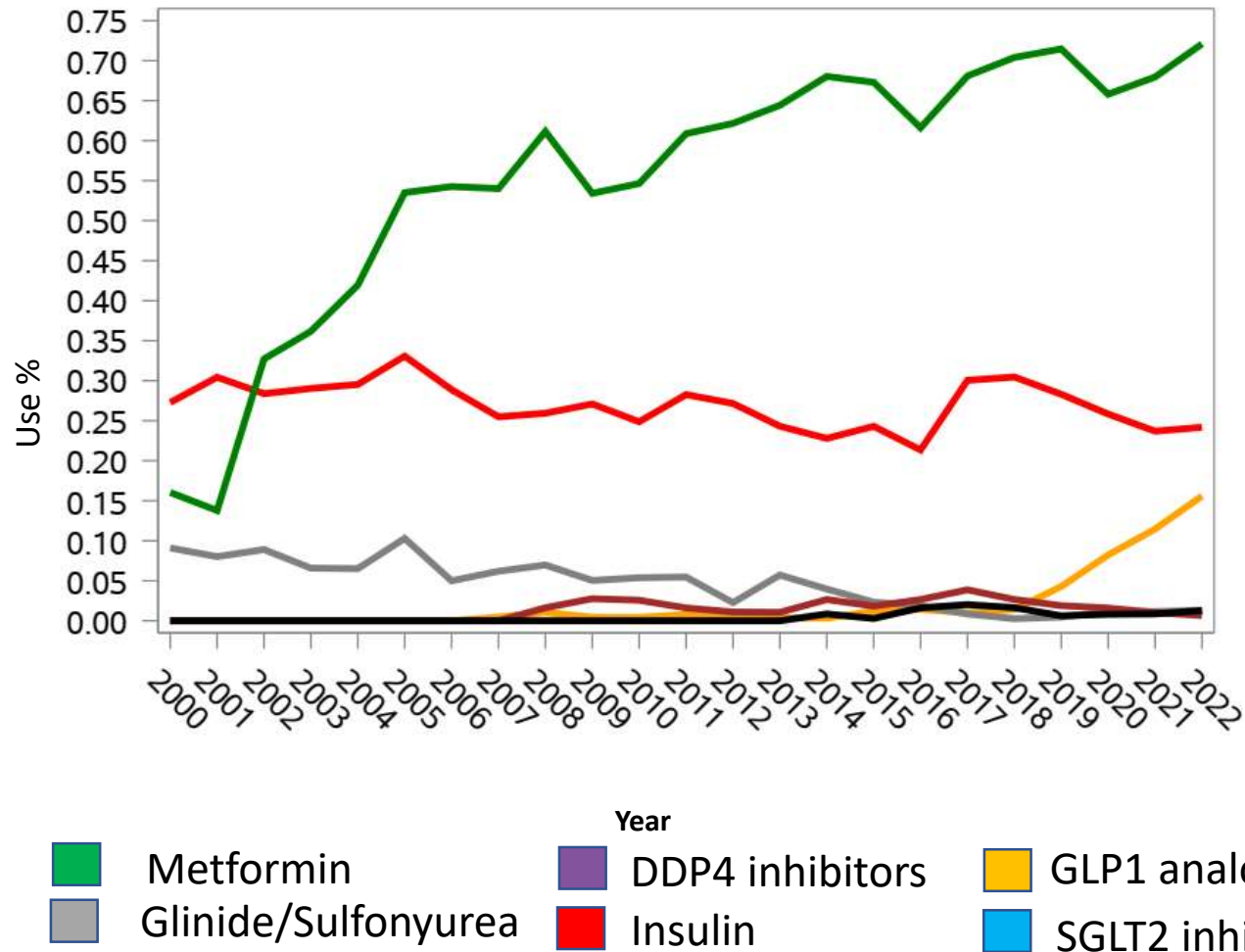
	6-11 years (n= 462)	12-18 years (n= 2102)	p-value
Mean insulin dose [U/kg]	0.7	0.53	0.00027
Initial insulin therapy [%]	5.23	13.86	0.00
Continuous insulin therapy [%]	36.64	25.95	0.00143
Lifestyle only [%]	31.15	24.29	0.0156
Monotherapy with OAD/GLP1a [%]	34.2	49.76	0.00
Combination Insulin + OAD/GLP1a [%]	23.53	18.62	0.08
Insulin monotherapy [%]	11.11	7.33	0.04149

-> Insulin and lifestyle for the younger ones

Changes in therapy 2000-2022:



Changes in therapy 2000-2022:



Approval for children:

Metformin 2001

GLP1 receptor agonists 2019

06/2019 EMA (Liraglutid)

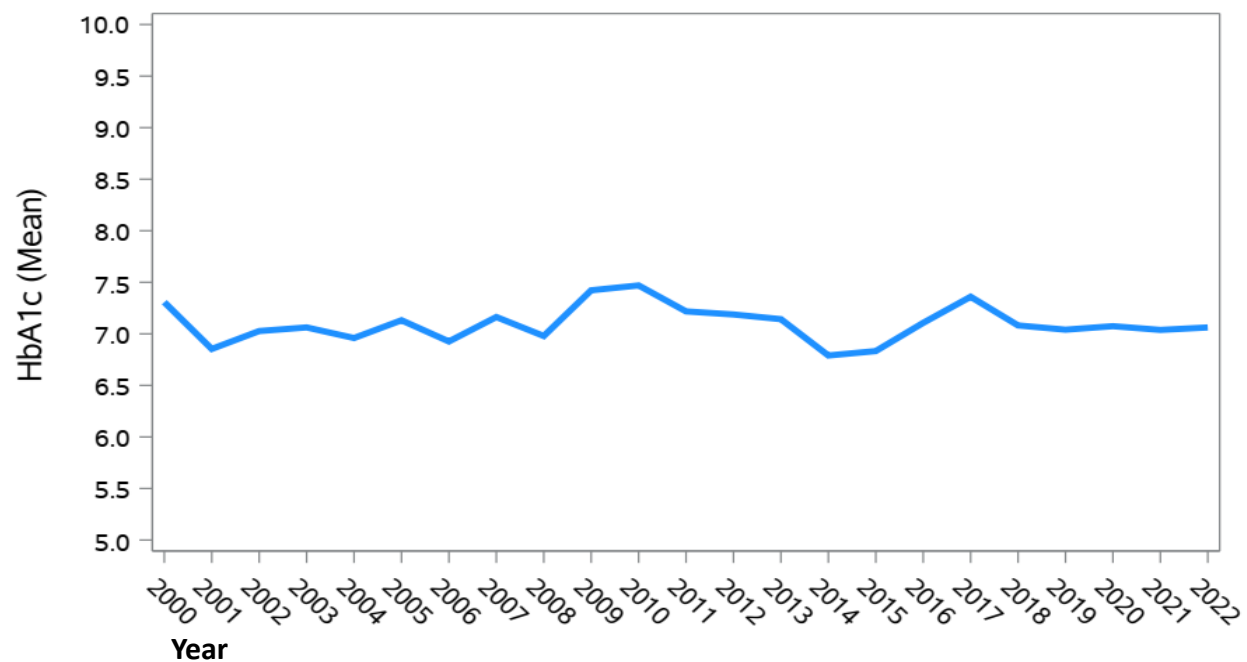
07/2019 FDA (Liraglutid)

SGLT2 inhibitors:

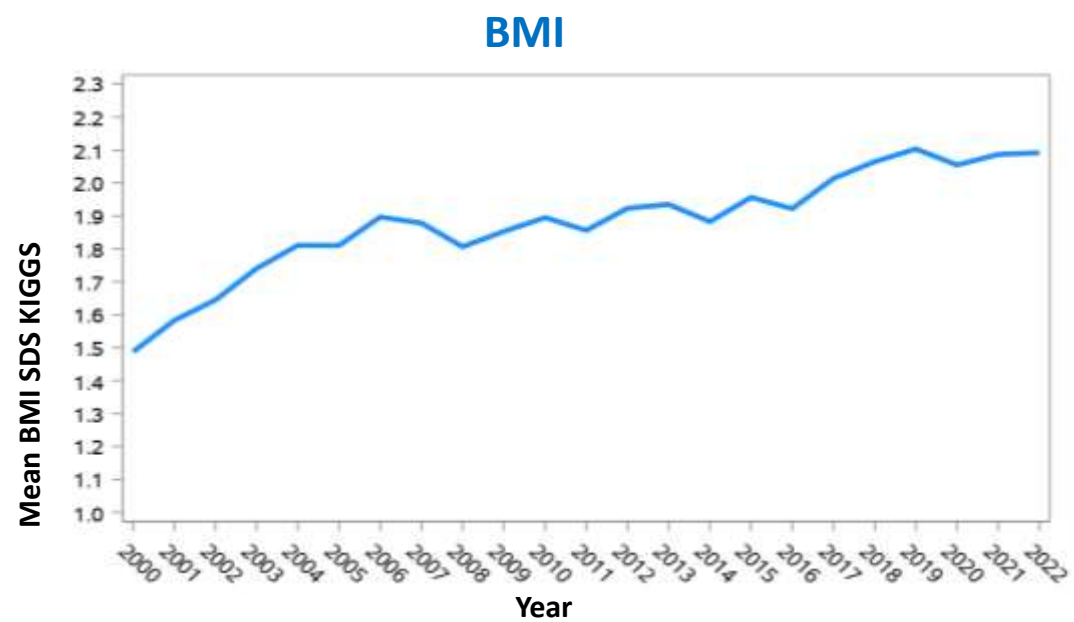
11/2021 EMA (Dapaglifozin)

06/2023 FDA (Empaglifozin)

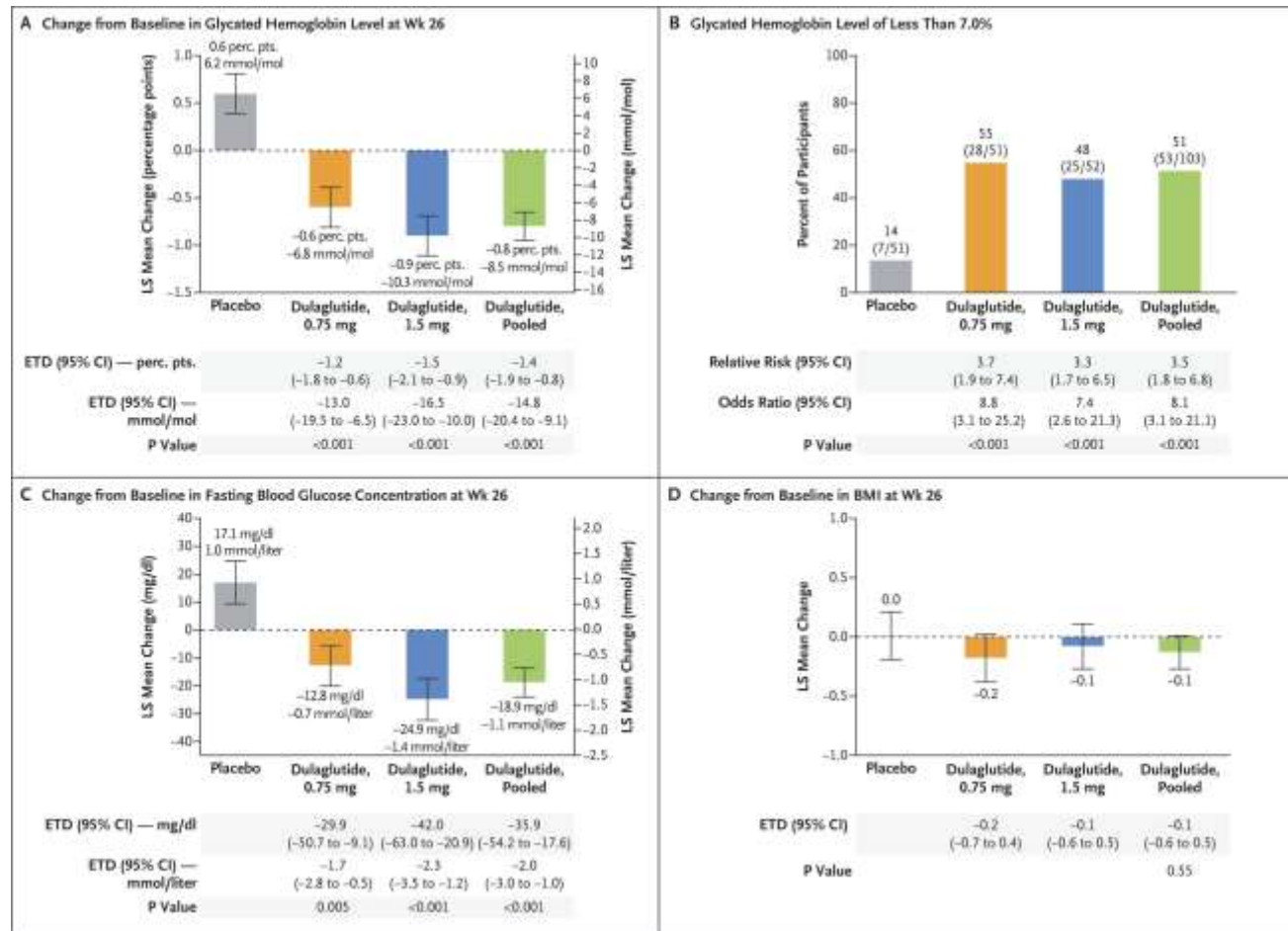
HbA1c level 2000-2022:



BMI Level 2000-2022:



-> Pharmacotherapy changed, but so far no effect on HbA1c nor BMI

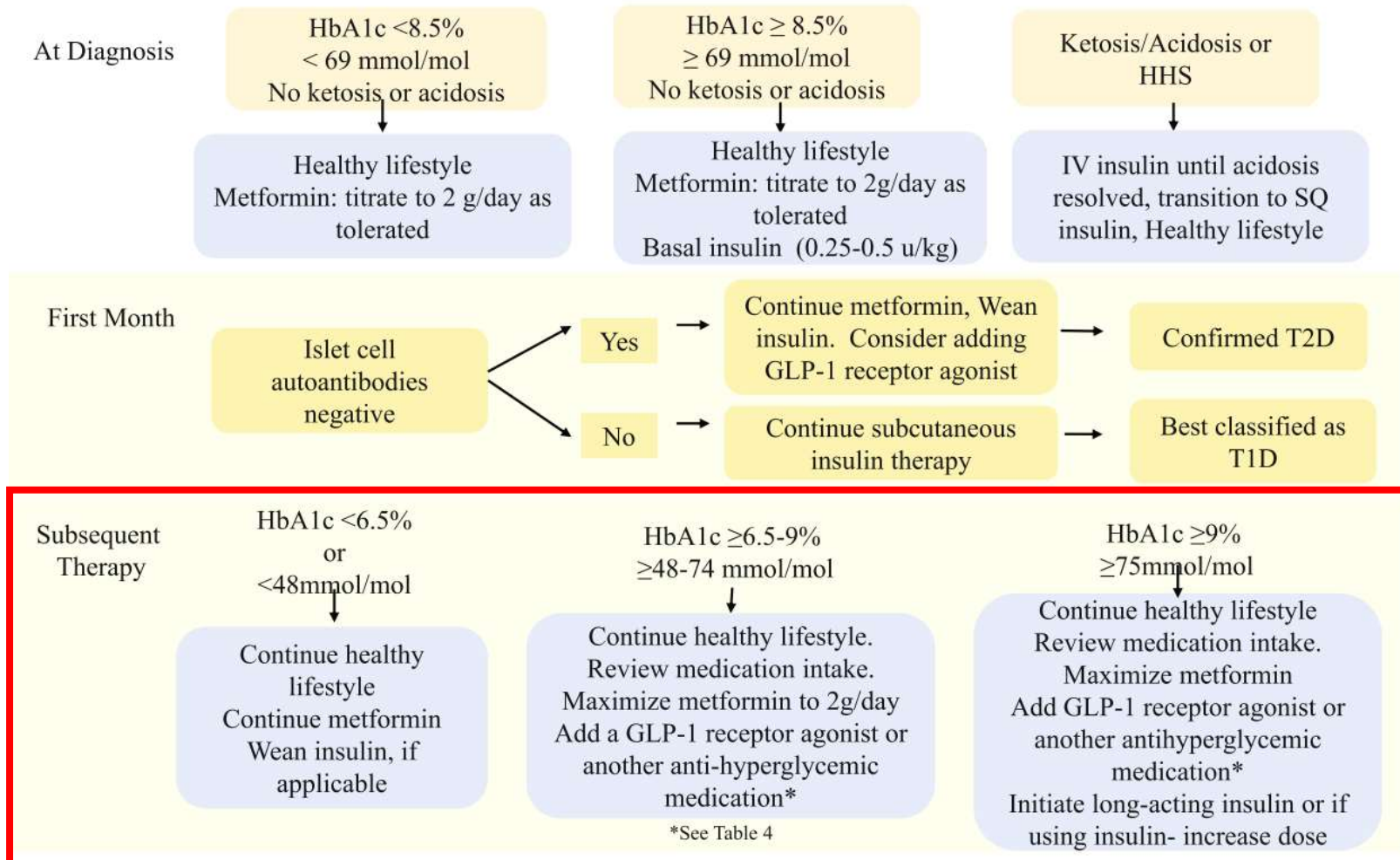


Hypothesis why no effect on BMI:

- dose max. 1,8 mg liraglutide for T2D, for weight loss: 1,2-3 mg

- Higher insuline resistance in youth compared to adults with T2D: higher resistance for the weight reducing effect?

Pediatric T2D treatment guidelines:



Shah AS et al. ISPAD Clinical Practice Consensus Guidelines 2022: Type 2 diabetes in children and adolescents. *Pediatr Diabetes*. 2022; 23(7):872-902.

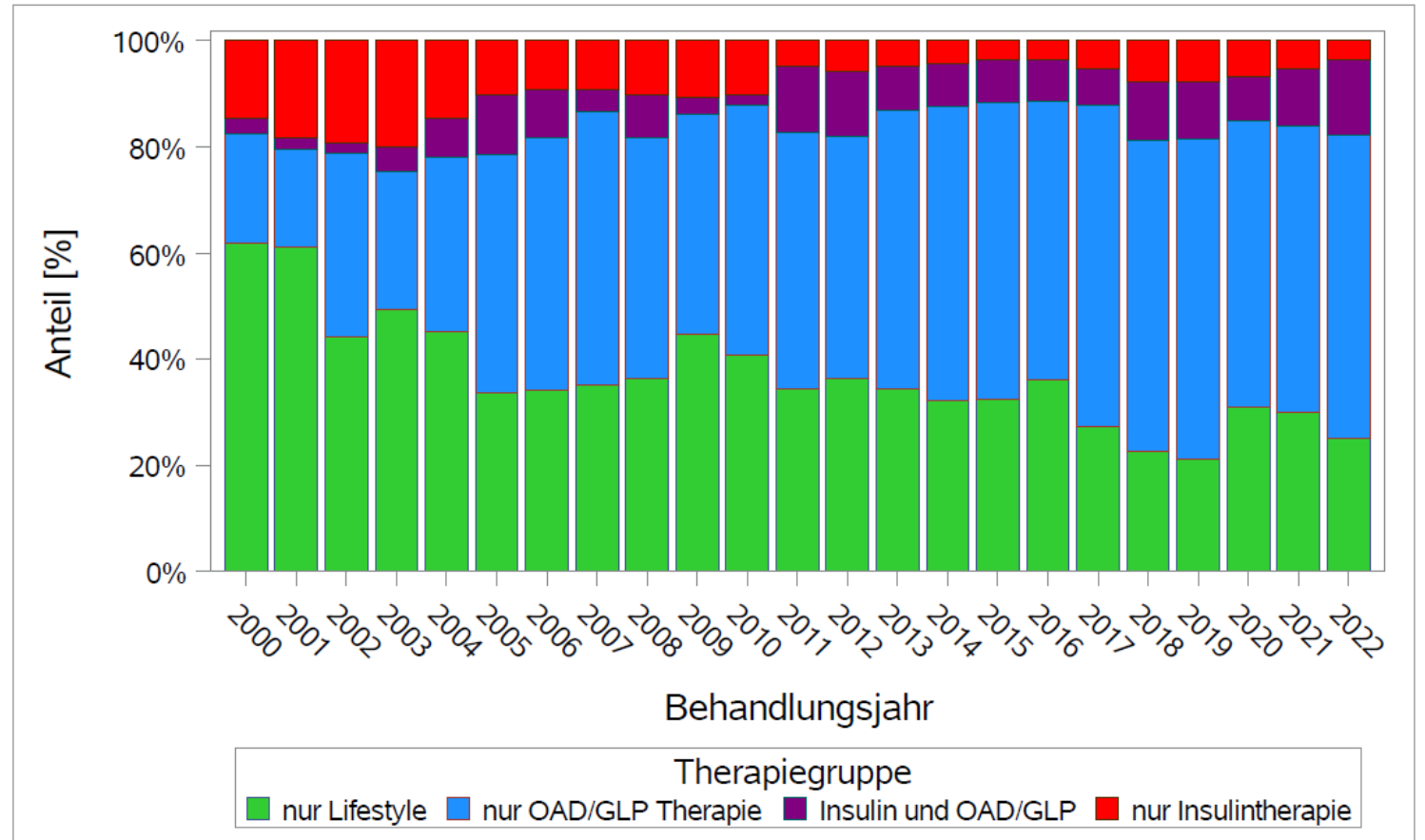
Pediatric T2D treatment guideline:

Subsequent
Therapy

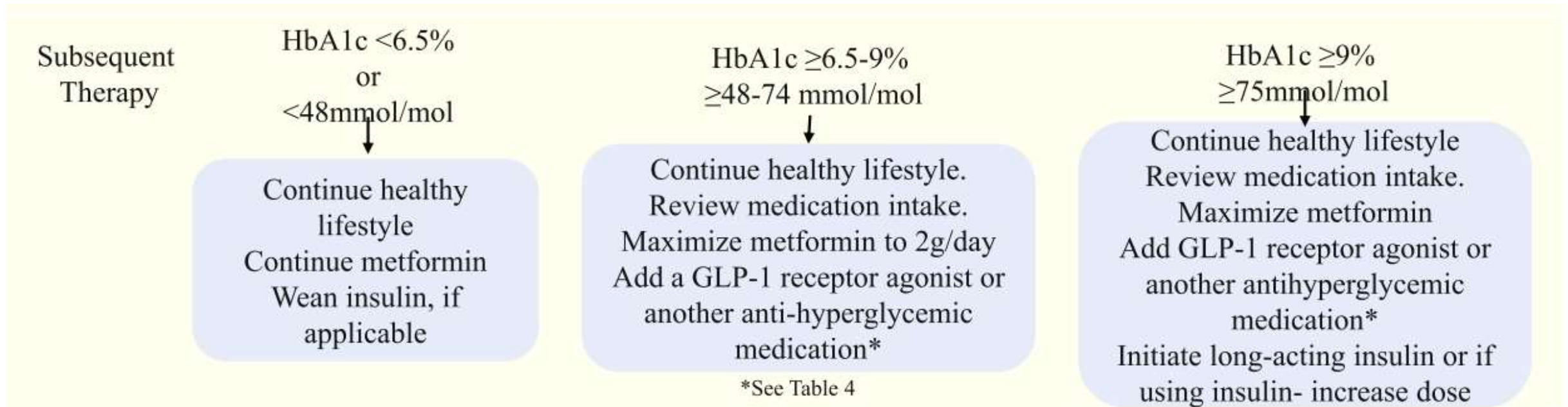
HbA1c <6.5%
or
<48mmol/mol

Continue healthy
lifestyle
Continue metformin
Wean insulin, if
applicable

HbA1c < 6.5 %



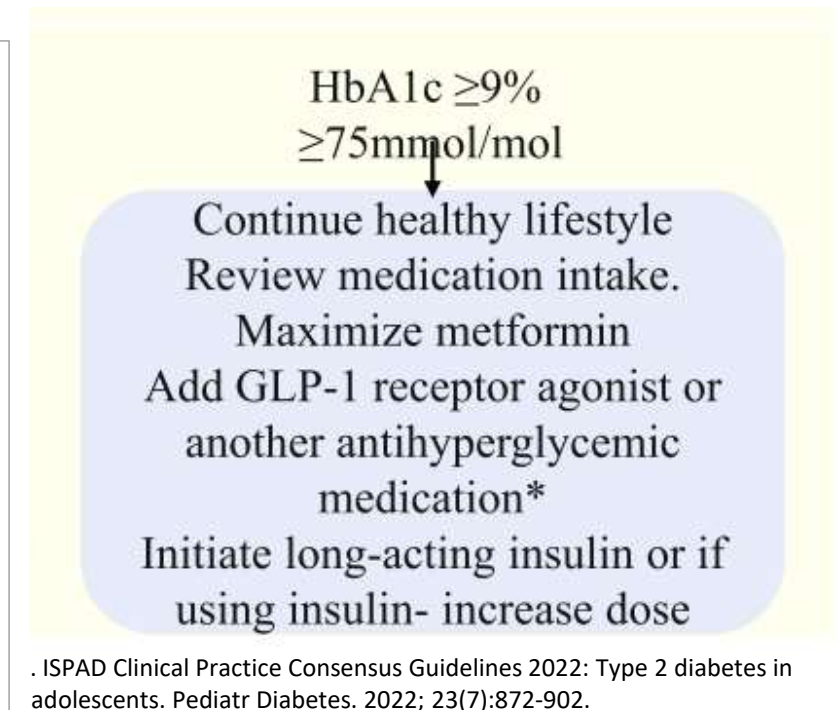
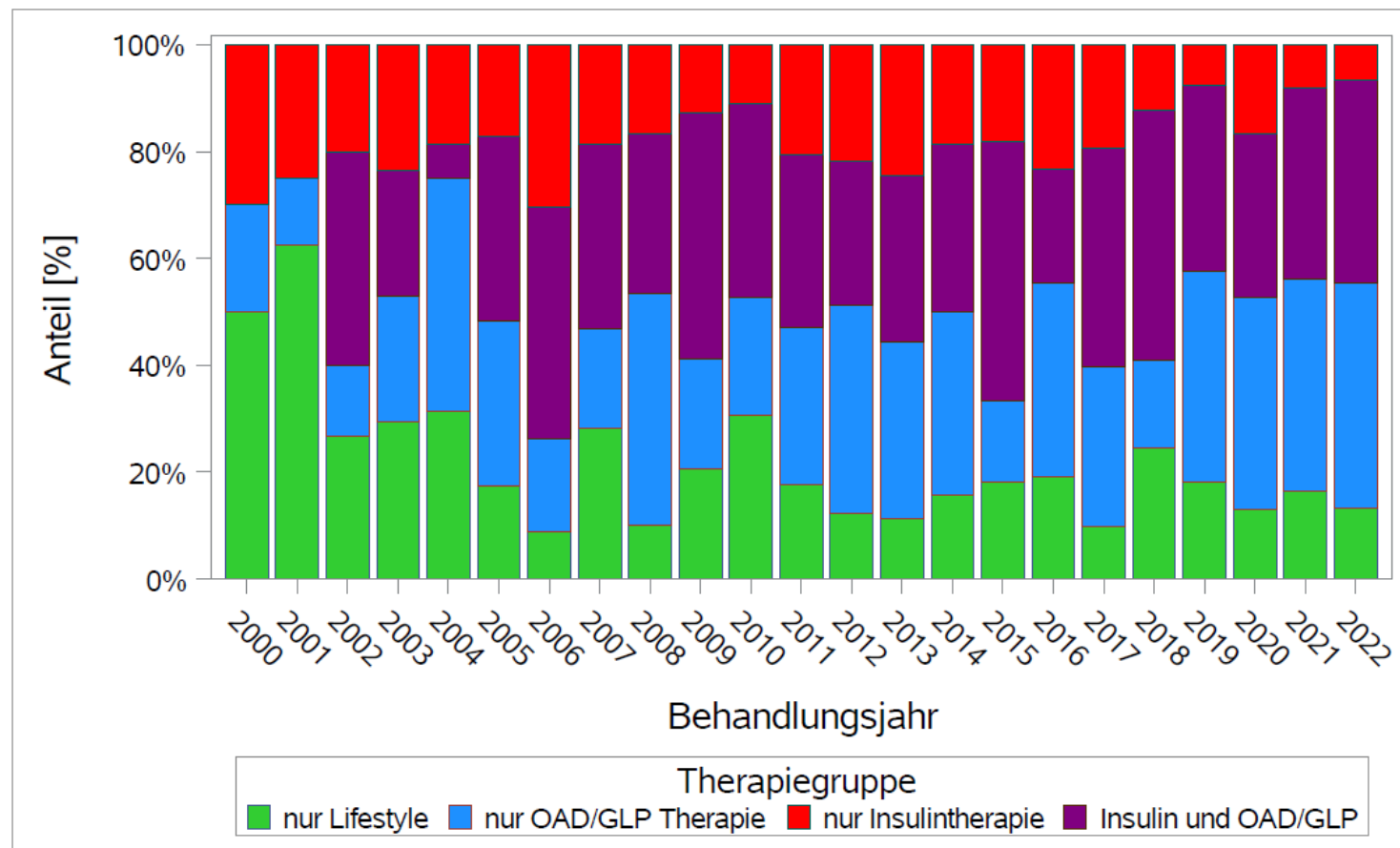
Pediatric T2D treatment guideline:



Shah AS et al. ISPAD Clinical Practice Consensus Guidelines 2022: Type 2 diabetes in children and adolescents. *Pediatr Diabetes*. 2022; 23(7):872-902.

Pediatric T2D treatment guideline:

HbA1c > 9 %



Conclusions:

- The **migration background of our** T2D cohort differs from migration background of T2D cohort from the US and from a DPV-T1D control cohort.
- **Pharmacological therapy** has changed from an exclusively lifestyle intervention or insulin monotherapy towards an increasing use of OAD/GLP1a (as monotherapy or in combination with insulin).
- However, while **HbA1c levels** of pediatric T2D patients remained stable during the past 22 years, patients became progressively more obese and were older at diabetes onset.
- The latest **ISPAD guideline** advises to accelerate the pharmacological therapy if HbA1c > 6.5%, and advises to avoid insulin monotherapy and if possible to stop insulin, is not yet always applied.

