Obesità e Diabete Mellito di tipo1

Obesità e Diabete Mellito di tipo1

Angela Napoli

la prof./sa …Angela Napoli…. dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Il 4 marzo 2024 ‘World Obesity Day’, istituita nel 2015 dalla World Obesity Federation

***The Lancet* 2024 & Trend Mondiali** di **OBESITA’**
a pooled analysis of **3663 population-representative studies** with **222 million** children, adolescents, & adults, >190 paesi

nel 2022 il tasso di **OBESITÀ**

MONDO

⇒ tra le/i **BAMBINE/I** e le/gli **ADOLESCENTI : 4 volte superiore** a quello del **1990**.

⇒ Nelle persone **ADULTE** più che **raddoppiato** nelle **DONNE** e quasi **TRIPLICATO** negli **UOMINI**.
159 milioni di bambine/i e adolescenti **e 879 milioni di persone adulte** convivono con l’obesità

IN ITALIA

Popolazione Generale **18%**

Bambini e Ragazzi vs **Bambine** e **Ragazze**

12% vs **8%**

World Obesity Day March 4

Il 4 marzo 2024 ‘World Obesity Day’, istituita nel 2015 dalla World Obesity Federation

The Lancet studio sui **trend mondiali** di **OBESITA’,**
NCD Risk Factor Collaboration (**NCD-RisC**) and ‘**WHO**’

A LIVELLO GLOBALE

il **n° totale** di bambini/e, adolescenti e persone adulte con **obesità >un miliardo**

a partire dal 1990

vista anche ⇓ **% di persone sottopeso**

⇒ **l’obesità** la forma più comune di **MALNUTRIZIONE** al mondo

⇒ una delle **maggiori sfide per la salute pubblica a livello mondiale**

Obiettivi:

Sensibilizzare Cittadini e **Istituzioni** sull’impatto dell’obesità sullo stato di salute

Promuovere la **prevenzione** a livello **sociale**.

World Obesity Day March 4

Trends and cyclic variation in the incidence of childhood type 1 diabetes in two Italian regions over 33 years and during the COVID-19 pandemic

Incidence of **D1** in **Italian children** & **adolescents <15 yrs**
data collected over 33 years from two populations registries

A **4-year cycle** in the incidence showed
from 1989 to 2003

Increasing annual trend in **the incidence** of **3.6% per year**

from 2004 to 2019
Breakpoint followed by a **stable period**

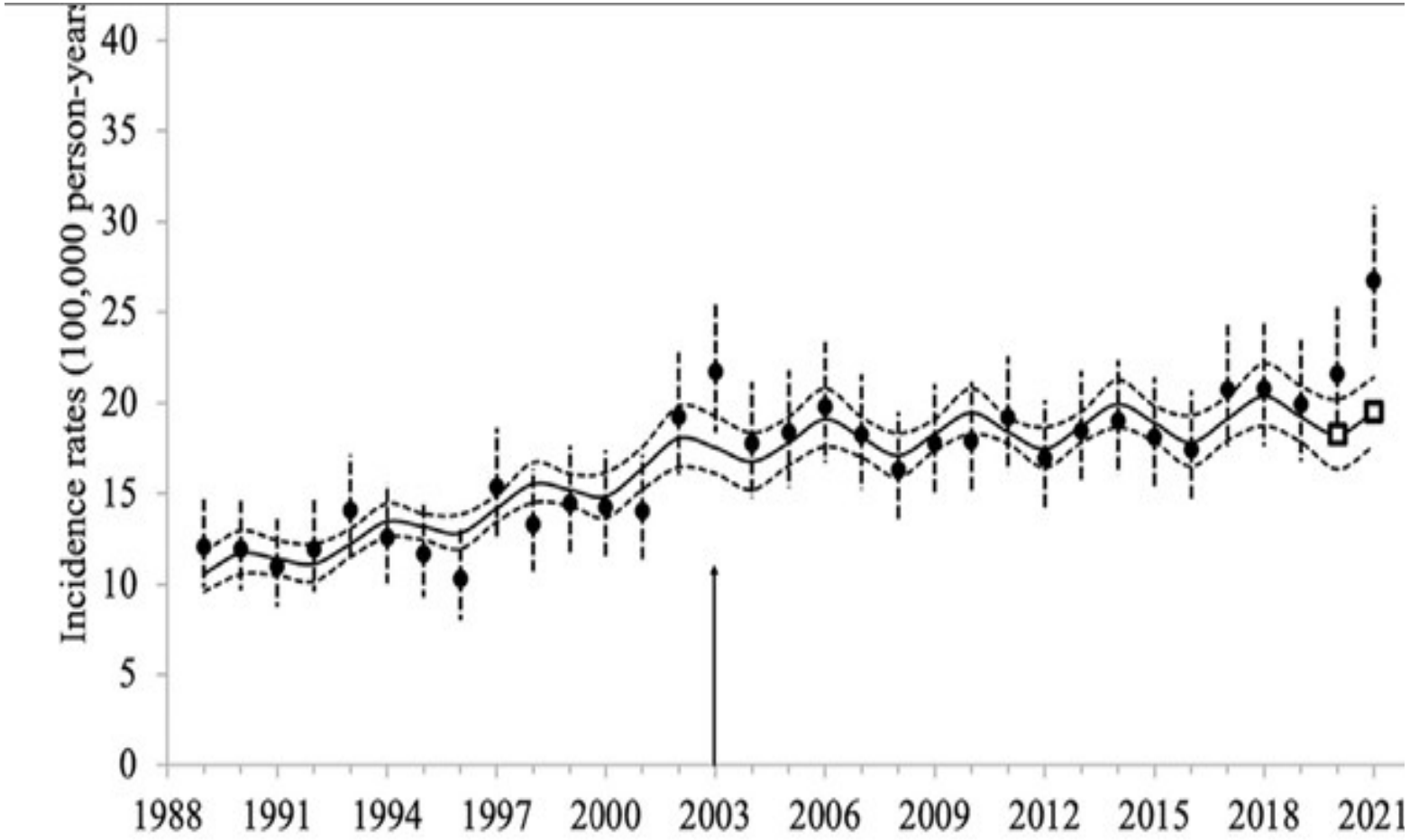
During the **second year** of **COVID-19 pandemic**
huge increase in the incidence of D1 reaching an unprencedented **rate** of **26.7/100.000 persons/ year**

These increases were **statistically significant in**
0.5-4 year old boys & **10-14 year old girls**

Diabetes Obes Metab 2023

Trends and cyclic variation in the incidence of childhood type 1 diabetes in two Italian regions over 33 years and during the COVID-19 pandemic

Rosaria Gesuita PhD[1,2] | Ivana Rabbone MD[3] | Vittorio Marconi MD[4] | Luisa De Sanctis MD[5] | Monica Marino RD[6] | Valentina Tiberi MD[6] | Antonio Iannilli MD[6] | Davide Tinti MD[5] | Lucia Favella PM[7] | Carlo Giorda MD[8] | Flavia Carle PhD[1,2] | Valentino Cherubini MD[6]



1989-2021

Circles & Dotted lines= Rates + 95% C.I./year

- **Solid Lines**= Incidence trend adjusted for sex and age class with a 4yr cyclic component
- **Dotted lines** 95% C.I. of the estimated incidence
- **Squares:** expected for 2020-2021
- **Arrow** : breakpoint year detected by the segmented regressin model

Diabetes Obes Metab 2023

Obesity in **Type1 Diabetes** in the World

The **SEARCH for Diabetes in Youth Study**
Overweight of Youth with T1D
22,1 %

'NHANES' National Health & Nutrition
of Youth without T1D
16.1%

T1D Exchange Registry (T1DX) & Prospective Diabetes Follow-up Registry
(Germany, Austria & U.S.) youth **2** to **18 yrs** with T1D for at least 1 year from,
↑body mass index (BMI) z scores
as compared with WHO international norms and respective country-specific national norms.

In the T1DX
The prevalence of obesity (BMI >95°percentile) **13,5 %** among Adolescents
↑ in Black/African American descent (**17.9%**) & Hispanic/Latino descent (**15.9%**) between 2011 - 2014.

In **Overweight/Obese Children**

T1D is diagnosed at **younger ages**, & obesity has been suggested to be an **accelerator** in the pathogenesis of T1D

Obesity is associated with **Insulin Resistance** and other **Cardiovascular Risk Factors** also in T1D patients.

In this regard, the **FinnDiane study** showed that **>over 40% of T1D** subjects had the diagnostic criteria for the Metabolic Syndrome

Betts P et al . Diabet Med. 2005 Feb;22(2):144-519.
Buzzetti R Diabetes Obes Metab. 2020 Jul;22(7):1009-101
Thorn LM et al (the FinnDiane study). Diabetes Care. 2005 Aug;28(8):2019-24.

Metabolic Aberrations, Insulin Resistance & Metabolic Syndrome

M.S. is another health outcome associated with both Obesity & T1D.

In the Pittsburgh EDC cohort (age 30.8 yrs)
M.S. prevalence in T1D

8 - 21% depending on the definition

⇑ Cardiovascular Disease, Nephropathy, & Death in T1D with MS

The Prevalence of **M.S.** in T1D (age 39.7 yrs), to be **31.9 %**
with an **Impaired Glucose Disposal Rate** as marker f **Insulin Resistance**.

Individuals with **Retinopathy** & **Neuropathy** had the **poorest estimated glucose disposal rate**, suggesting a **relationship** between **insulin sensitivity** & **microvascular complications**

Chillar´Estimated glucose disposal rate in assessment of the metabolic syndrome and microvascular complications in patients with type 1 diabetes. J Clin Endocrinol Metab. 2009;94(9):3530–3534
Pambianco G, The prediction of major outcomes of type 1 diabetes: a 12yr prospective evaluation of three separate definitions of the MS …. : the Pittsburgh Epidemiology of Diabetes Complications Study experience. Diabetes Care. 2007;30(5): 1248–1254..

Metabolic Aberrations, Insulin Resistance & Metabolic Syndrome

The Obese phenotype in T1D cannot be assumed to mirror what is expected from the literature in the general population & in people with T1D

However, **sex-differences in obesity** prevalence & its clinical consequences in adult T1D subjects have been **poorly investigated**

exhibits a unique phenotype & correlates with aberrant physiological endpoints regardless of body weight.

Age and sex-related characteristics of obesity in type 1 diabetic subjects: the Italian AMD Annals initiative

A. Giandalia[1], GT. Russo[1], P. Ruggeri[2], A. Giancaterini[3], E. Brun[4], M. Cristofaro[5], A. Bogazzi[6], MC. Rossi[7], G. Lucisano[7], A. Rocca[8], V. Manicardi[9], P. Di Bartolo[10], G. Di Cianni[11], C. Giuliani[12], A. Napoli[1] on behalf of the AMD Annals study group.

Aim

to analyze **potential age- and sex-related differences in the prevalence of obesity** and its association with **metabolic characteristics, cardiovascular risk factors** & **chronic complications**, in **adult** subjects with **T1D**, participating to the AMD Annals Initiative in Italy

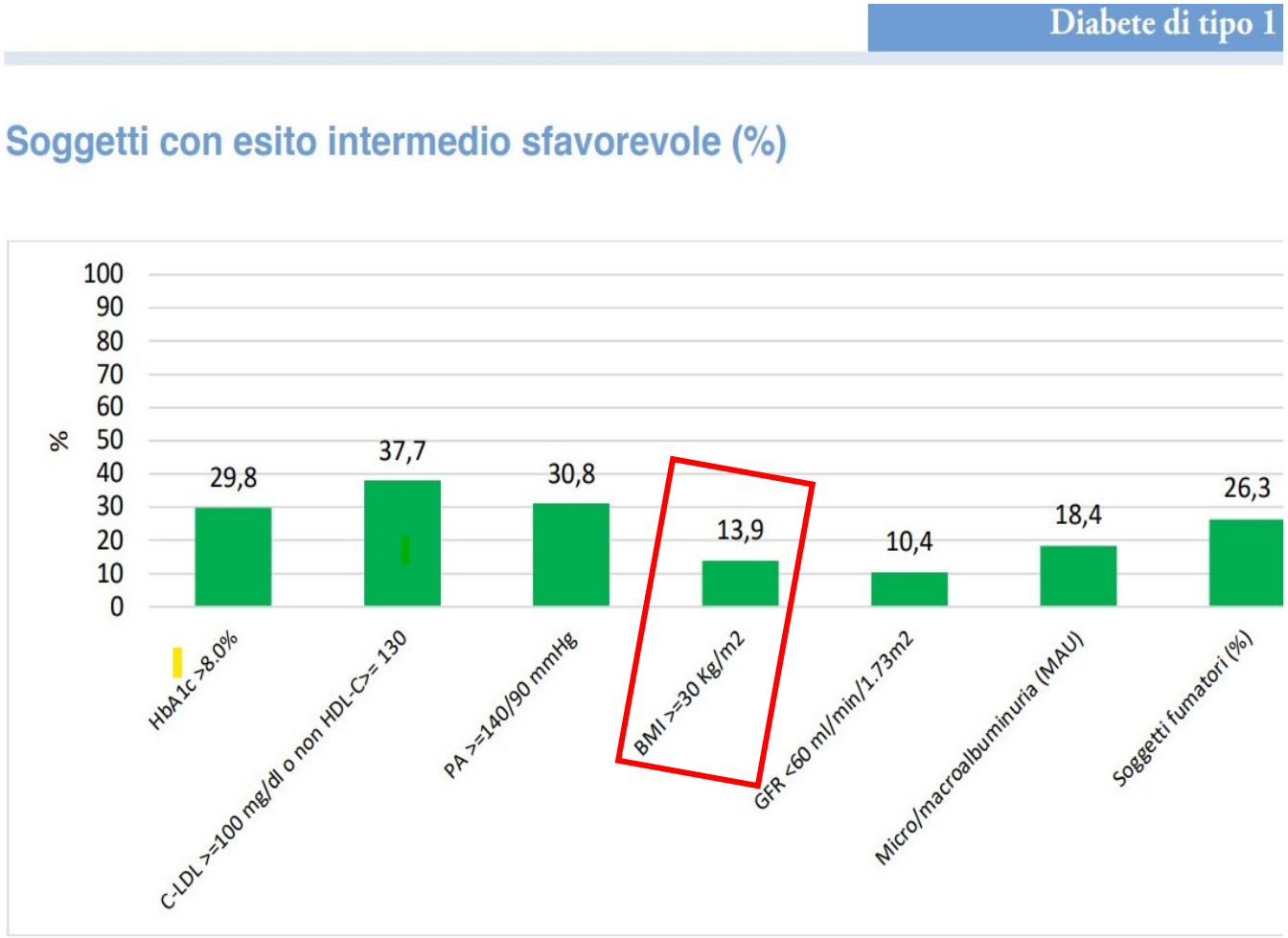
Methods:

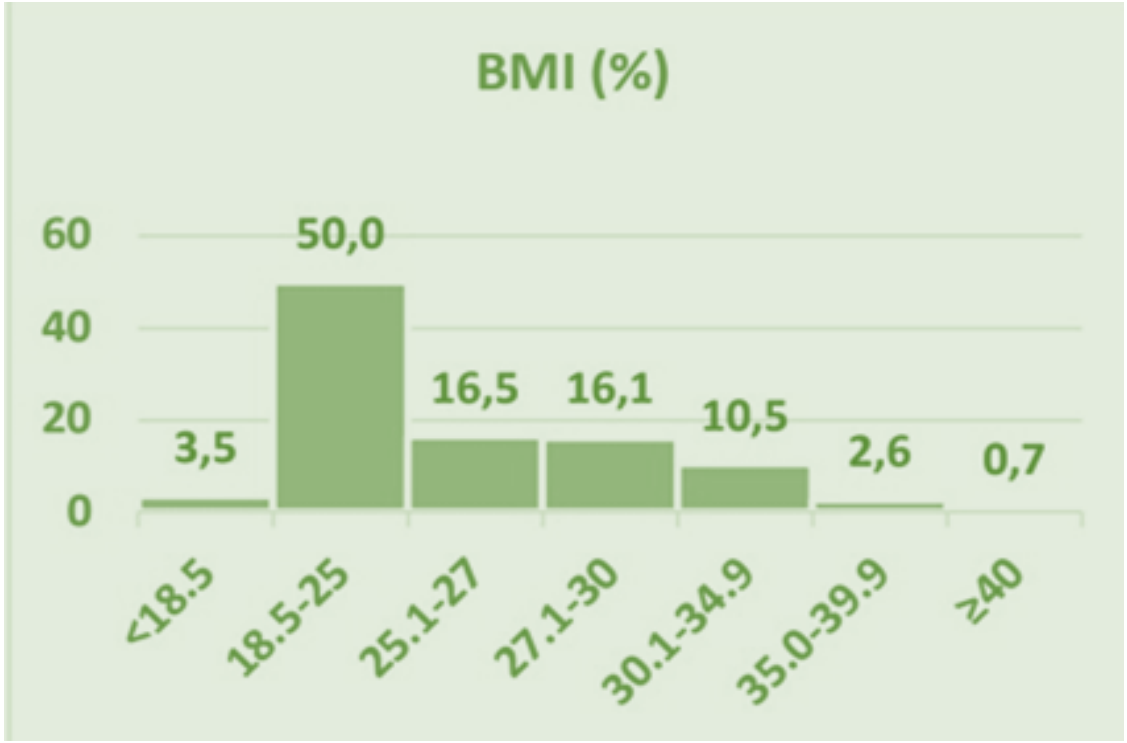
Centers share the same software for data extraction from electronic medical records (EMR)
Data are collected in a standardized format (**AMD Data File**).

Age and sex-related characteristics of obesity in type 1 diabetic subjects: the Italian AMD Annals initiative

n=**37.436** T1D subjects (**45.3% women**) from **282 Italian diabetes clinics** during **2019** (pre-pandemia)

Age **49.6 yrs,** BMI **28.6** kg/m^2





Annali 2023

Sex-related characteristics of obesity in T1D. JCEM2023

Obesity in **All** subjects with **Type1 Diabetes** in **Italy**

BMI ≥ 30Kg/m²	
2010	**11.9 %**
2022	**13.6**
2023:	**13.9**

Trend in crescita

Dal 2010 al 2020

un **incremento relativo** pari al **15,1%**

Annali 2023

Soglia minima raggiunta dai 'BEST PERFORMERS' pari al 25° centile della distribuzione

Gold Standard	HbA1c >8.0%	C-LDL >=100 mg/dl o non HDL-C>= 130 mg/dl	PA >=140/90 mmHg	BMI >=30 Kg/m²	GFR <60 ml/min/1,73 m²	Micro/ma-croalbumi-nuria (MAU)	Soggetti fu-matori (%)
25° *percen-tile*	25,0	32,5	21,5	11,9	6,2	11,1	22,7

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

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Obese Subjects irrespective of Sex

Older, with a **Longer Diabetes Duration**, ⇑ **HbA1c**, **Triglycerides**, **SBP**, **DBP**
Lower HDL-C levels
Less frequently Smokers

⇑ **Chronic Diabetes Complications**:
impaired renal function (eGFR<60 ml/min) obese vs non-obese subjects

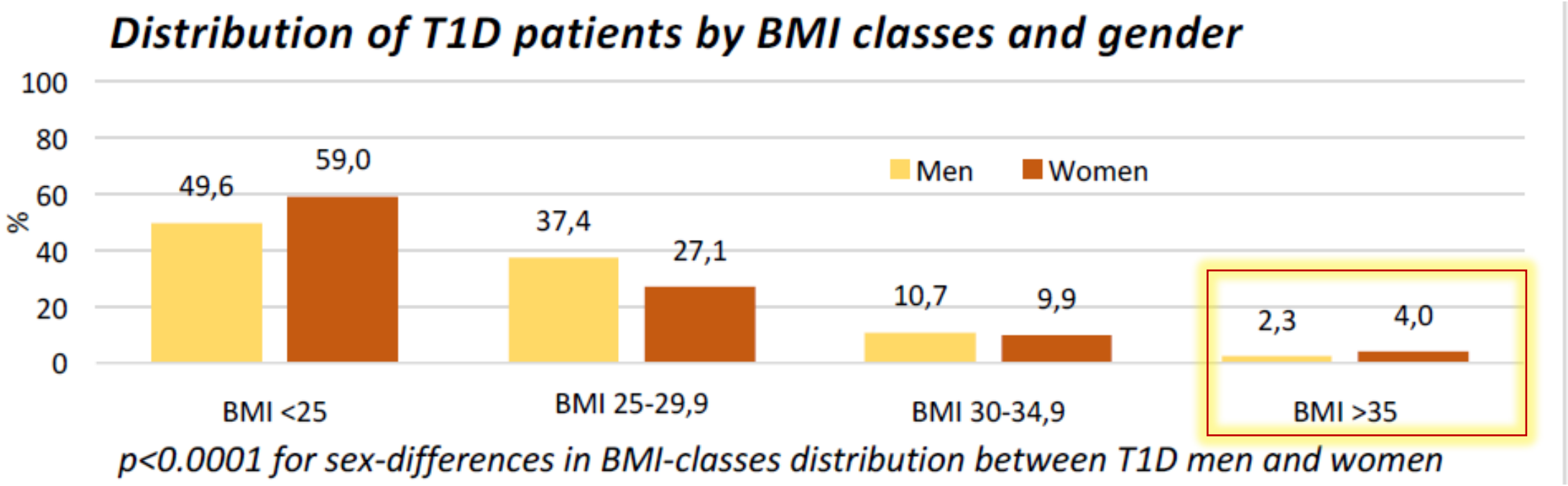
Sex-related characteristics of obesity in T1D. JCEM2023

Fig.1 BMI: Men vs Women: 25,5±4,1 vs 24,9±4,9 kg/m^2

Sex based BMI-classes distribution in **Men & Women** with **T1D** from the **AMD Annals Initiative**

Women **41.0%** Overweight/Obese

Men **50.4%** Overweight/Obese



The Obesity Rate: **13** vs **13.9%**

Severe Obesity (BMI ≥35 Kg/m^2) ⇑ **in Women**

BMI: Differenze di Genere nel DT1 dal 2011 al 2016

Annali 2012 **Annali 2023**

BMI >30	Donne	Uomini
2020	14	13.4

Italian General Population, the **prevalence of obesity** is overall **higher in Men:**

11.7% Men vs **10.3%** Women

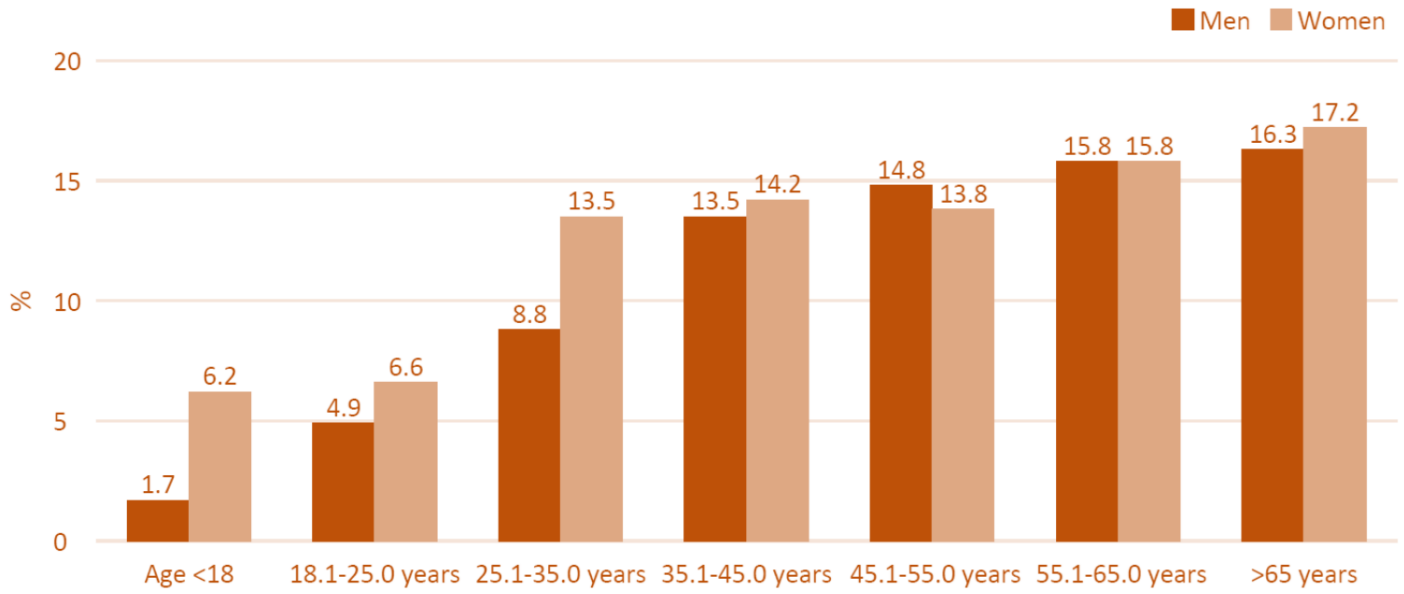
Incremento Relativo %

Maschi= 20,7% vs Femmine= 10,2%

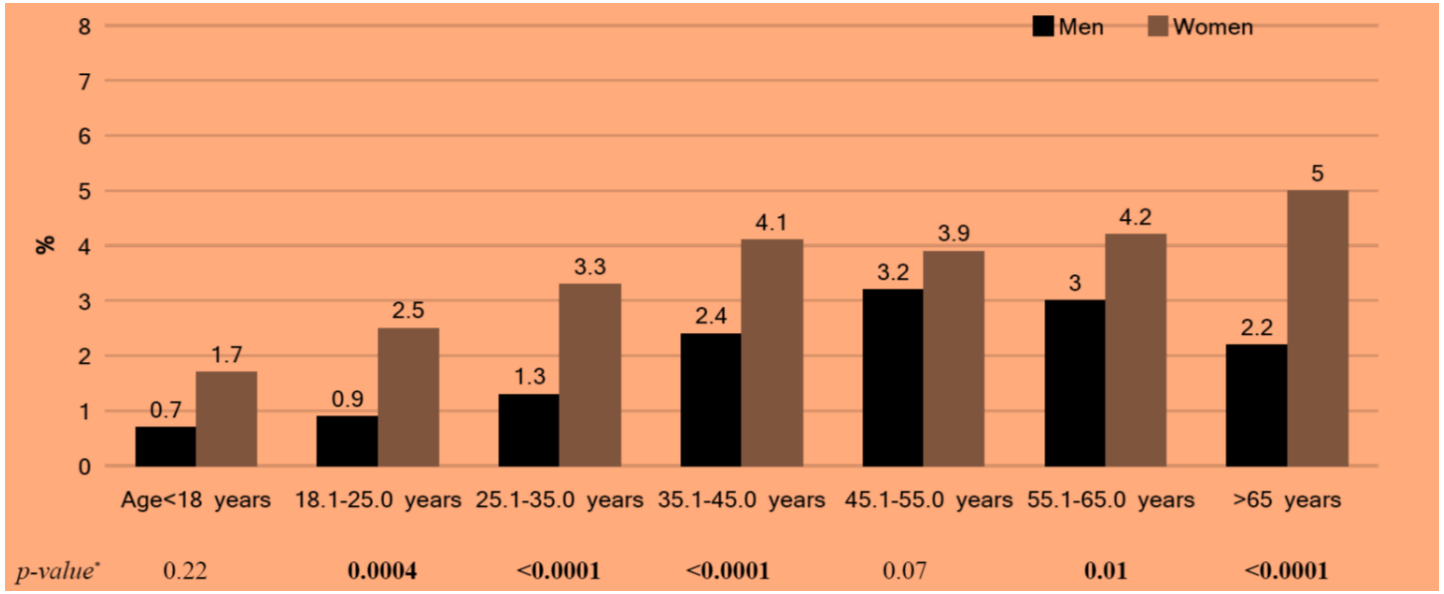
ISTAT. Indagine "Aspetti della vita quotidiana" . 2019

Fig2: Obesity & Severe Obesity in D1, according to Gender & Age-classes

BMI≥ 30Kg/m²



BMI≥ 35Kg/m²



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Obesity in T1D Subjects by Age and Sex

Overall, mean **BMI values increased with age in both sexes**,

Obesity prevalence ranged from

	Before the **age of 18yrs** ⇒⇒⇒⇒⇒⇒	**After** the **age of 65 yrs**
In Men	**1.7%**	**16.3%**
In Women	**6.2%**	**17.2%**

Severe Obesity

In Men	**0.7%**	**2.2%**
In Women	**1.7%**	**5.0%**

Population of **37.436 adults** with T1D (54.7% men, 45.3% women)

Sex -differences in clinical characteristics of non-obese and obese T1D

*p<0,05 **p<0,0001	NON-OBESE		OBESE	
	MEN	WOMEN	MEN	WOMEN
Age (yrs)	46.6±16.3	48.3±17.1**	51.3±14.1	52.1±15.9*
HbA1c (%)	7.7±1.3	7.8±1.3**	7.9±1.2	8.1±1.2**
Total cholesterol (mg/dl)	173.8±34.3	183.3±33.5**	173.1±37.9	182.1±35.8**
HDL cholesterol (mg/dl)	56.0±14.0	67.1±15.2**	49.1±12.3	58.9±14.8**
LDL cholesterol (mg/dl):	99.1±29.3	99.5±27.6	98.6±32.8	102.2±30.7**

D1 Obese Women compared to Men:

Older, Longer Diabetes Duration

Higher Values of **HbA1c**, **Total Cholesterol**, **LDL**- & **HDL-Cholesterol**

Population of **37.436 adults** with T1D (54.7% men, 45.3% women)

Sex -differences in clinical characteristics of non-obese and obese T1D

*p<0,05 **p<0,0001	NON-OBESE		OBESE	
	MEN	WOMEN	MEN	WOMEN
MAU (microalbumiuria) (%)	20.4	16.3**	27.8	21.8**
Retinopathy (%)	32.6	30.6*	47.1	43.9
CV events (%)	5.6	3.3**	9.9	6.1**

Chronic Diabetes Complications increase as BMI increase:

MAU, D.R. & CV: ⇓ **% *obese* Women** *vs obese Men* ⇑

eGFR<60 ml/min ⇑ **% *obese* Women** *vs obese Men*

NON OBESE MEN **vs** **OBESE MEN**

9.5 % 15.7 %

NON OBESE WOMEN **vs** **OBESE WOMEN**

10.9 % 17.8 %

*so that only **52% of obese T1D women show a eGFR ≥90 ml/min***

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In the **Italian General Population,** the prevalence of Obesity is overall **higher** in **Men**

In **D2 Severe obesity** is **more prevalent** among **Women + a higher mortality risk** than in men

in **D1, similar prevalence of obesity** in the **two sexes**

In **D1 Women** ⇑ %, in **all age groups**.

Unfavorable health outcomes/mortality associated with **Obesity** to further increase in case of severe obesity

41. Marlow AL et al *Adolescents with type 1 diabetes can achieve glycemic targets on intensive insulin therapy without excessive weight gain.*. Endocrinol Diabetes Metab. 2022 Jul;5(4):e352.
42. Alderisio A et al *Long-term body weight trajectories and metabolic control in type 1 diabetes patients on insulin pump or multiple daily injections: A 10-year retrospective controlled study.* Nutr Metab Cardiovasc Dis. 2019;29(10):1110-1117.
43. Rossi MC et al. BENCH-D Study Group. The complex interplay between clinical and person-centered diabetes outcomes in the two genders. Health Qual Life Outcomes. 2017 Feb6 21;15(1):41
44. Enzlin P, Mathieu C, Demyttenaere K. Gender differences in the psychological adjustment to type 1 diabetes mellitus: an explorative study. Patient Educ Couns. 2002 Oct-Nov;48(2):139-4545. Marlow AL, et al, Young children, adolescent girls and women with type 1 diabetes are more overweight and obese than reference populations, and this is associated with increased cardiovascular risk factors. Diabet Med. 2019 Nov;36(11):1487-1493.
46. Troncone A, et al Disordered eating behaviors in youths with type 1 diabetes during COVID-19 lockdown: an exploratory study. J Eat Disord. 2020 Dec 2;8(1):76.
47. Cosentino F,; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020 Jan 21 7;41(2):255-323.
48. Pintaudi B et al . Clinical profiles and quality of care of adults with type 1 diabetes according to their cardiovascular Risk: A Multicenter, Observational, retrospective study. Diabetes Res Clin Pract. 2021 Dec;182:109131
22. Russo G et al Age- and Gender-Related Differences in LDL-Cholesterol Management in Outpatients with Type 2 Diabetes Mellitus. Int J Endocrinol. 2015;2015:957105

Summary

Obesity

Data from our large cohort of **T1D** pts, **in line** with current data in **T1D worldwide**

3 recent **European studies** on adult T1D subjects with a **Obesity rate= 18%, 17%, & 15.3%**

sex difference: *data are* ***sparse & conflicting***

Severe Obesity (BMI>35 kg/m^2) in a nonnegligible **%** of **D1** subjects:

Italy: 3.3% vs **Catalonia 4.3%**

Age had an **impact** on % **Obesity** in **both Sexes**, reaching **17%** of the **T1D** population**>65 yrs old**

1 out **6 T1D** subjects

The same trend reported in **Catalonia**, where the obesity rate = **21%** of **T1D >40**yrs **old**

Polsky S, Ellis SL. Obesity, insulin resistance, and type 1 diabetes mellitus. Curr Opin Endocrinol Diabetes Obes. 2015

van Mark G, et al Patient and disease characteristics of adult patients with type 1 diabetes in Germany: an analysis of the DPV and DIVE databases. Ther Adv Endocrinol Metab. 2019

. DuBose SN, et al Obesity in Youth with Type 1 Diabetes in Germany, Austria, and the United States: Type 1 Diabetes Exchange Clinic Network and Diabetes Prospective Follow-up Registry. J Pediatr. 2015

OECD Health Statistics. [Online] 2020. https://www.oecd.org/els/health- systems/obesityandtheeconomicsofpreventionfitnotfat-italykeyfacts.htm

Da Genua IObesity and related comorbidities in a large population-based cohort of subjects with D1 in Catalonia Retrospective, cross-sectional study in Catalonia, Front Endocrinol (Lausanne). 2022

Lavens A, et al ; Belgian Group of Experts IQED and IQECAD. Effect of an Integrated, Multidisciplinary Nationwide Approach to Type 1 Diabetes Care on Metabolic Outcomes: An Observational Real-World Study . DTT, 2021

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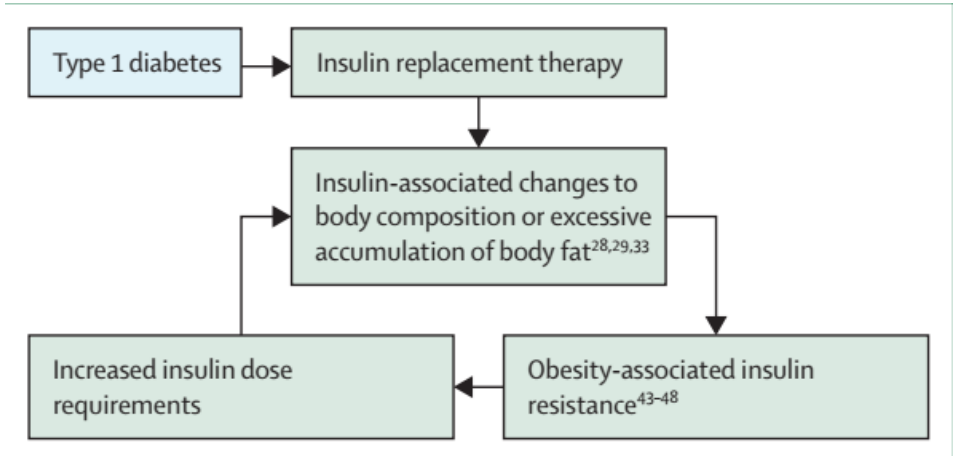
Theorical Drivers of weight gain in type 1D



- The **Intensification of insulin therapy** to achieve stringent glucose control often comes at the cost of **weight gain** both in **D1** & **D2**
- **Higher baseline HbA 1c** levels & **greater Decrements** in **HbA1c** during **intensive therapy** were **both** associated with a **greater increase** in **BMI**
- **Severe' hypo'** $\Rightarrow$ **more weight gain** *(defensive snacking, when exercising, or compensatory CHO intake)*
- An **improved Glycemic Status of glucose** $\equiv <$ **Renal Threshold (<glycosuria)** $\Uparrow$**conservation** of **ingested calories** & in part, $\Downarrow$ **daily energy expenditure**
- **Administer insulin peripherally**, **bypassing** effects **on the liver** & potentially **causes hyperinsulinaemia** & **fat accumulation** in **peripheral tissues**

Drivers of Weight Gain: Intensity/Mode of Treatment ? SEX/Gender?

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NO

Australian study in adolescents with **D1**, No increase of BMI-SDS with the implementation of insulin therapy with more intensive schemes (**MDI/CSII**).

Italian study showed **comparable body weight gain** over a **10-year follow-up** in **T1D** patients on **CSII** or **MDI**, **despite improved glycemic control** & **decreased insulin doses with CSII**.

The **higher rate** of **Severe Obesity in Women** than in men is **NOT** even **related to disparities in the use of adjunctive glucose-lowering therapies: Metformin, SGLT2i**, potentially reflecting the attempt to reduce weight &/or reach glucose targets in obese D1

YES

SEX/Gender

⇑ **%** of **severe obesity** observed in both D1 & D2 may involve **complex interactions** between biological (**sex**)- and nonbiological (**gender**)-related variables, many of which have **not** been **fully clarified**

Sex-related variables such as hormonal fluctuation through the life span, including **menopausal status** in women, sex differences in **Psychological factors**, **difficulty in adaptation** & **acceptation of the disease** &/or **depression** may be **more frequent in D1 women**

The role of **Eating Disorders** and **Parental Control** in **Younger Population** cannot be ruled out.

Controversy exists about the Optimal Route of Administration of Insulin replacement therapy.
Despite CSII **could** promote increased weight gain in people with D1, **No high-quality, prospective RCTs**.

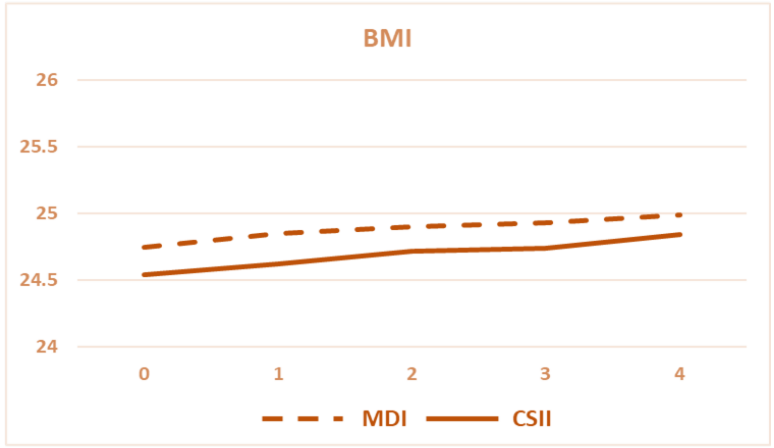
Artificial Pancreas systems **might ⇓ hypo frequency** by **better matching insulin administration to the glycaemic concentration**, **their use** is **currently low** and **no firm conclusions**

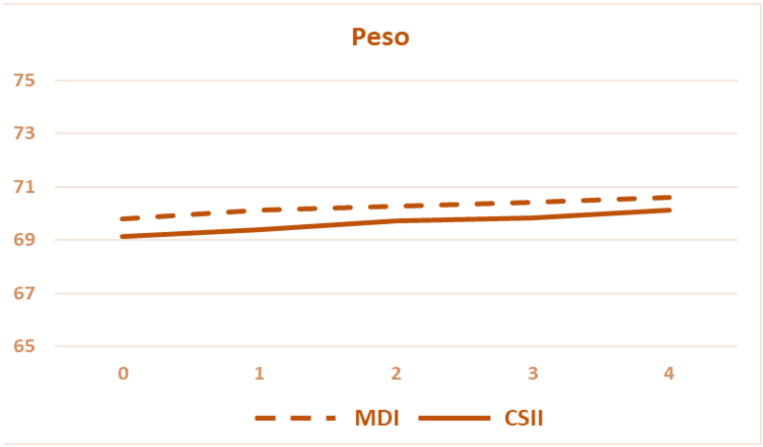
ANALISI LONGITUDINALE dei Soggetti con D1 in base a
TRATTAMENTO (Pumps vs MDI)
&
GENERE

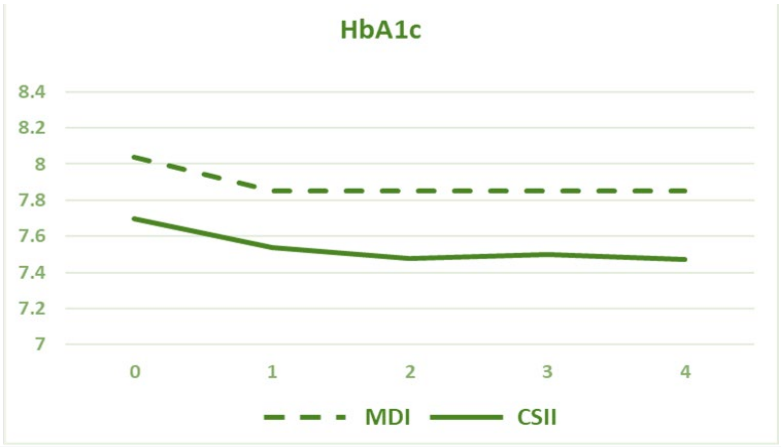
Analizzare le Traiettorie di Peso Corporeo, BMI e filtrato glomerulare (eGFR) in tutti i soggetti con D1 che abbiano intrapreso terapia con CSII nel periodo in esame vs. coloro che hanno continuato la terapia MDI

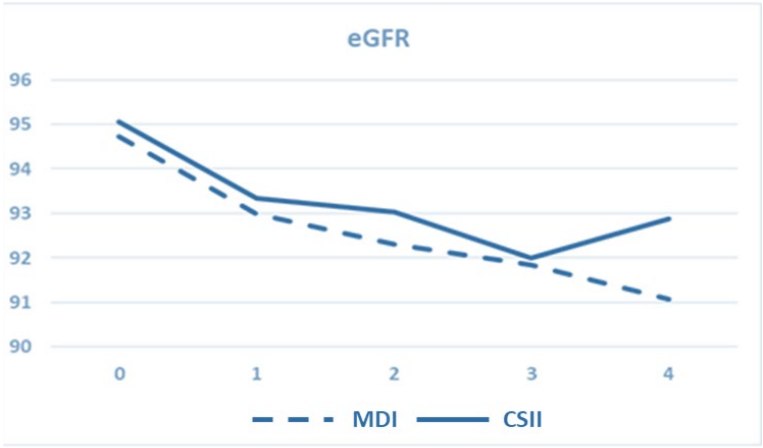
Analizzare le stesse traiettorie separatamente per maschi e femmine

Temporal Trend of BMI, Body weight, HBA1C, eGFR irrespective of Gender, by mode of Treatment: CSII vs MDI









The apparent **Weight Increase** of subjects on insulin pumps was rebutted by the statistical analysis of **BMI values** adjusted by the '**Propensity Score (PS) matching'**

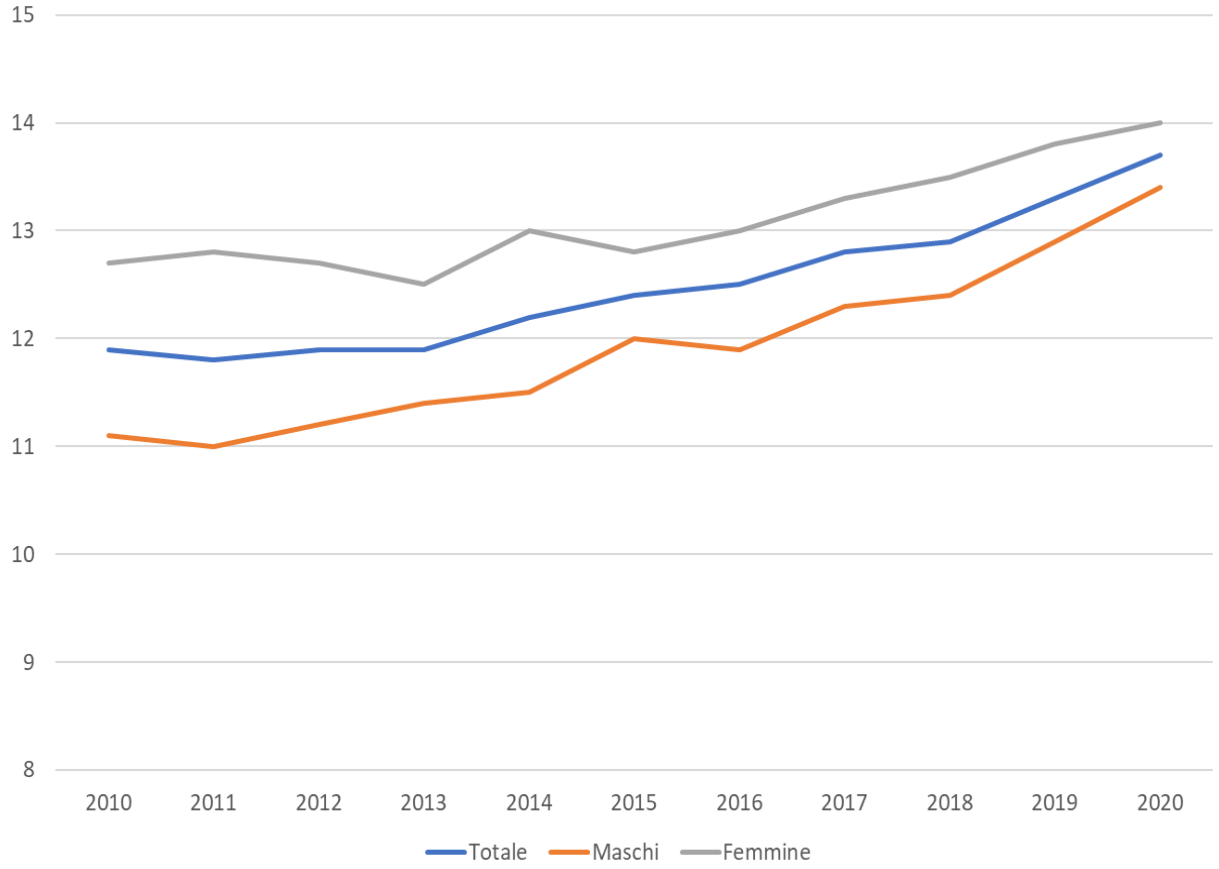
As regards the **kidney function**, the **eGFR decline** was less remarkable in pts who had started therapy with CSII

Dati aggiustati con 'Propensity Score (PS) matching' of ALL people irrespective of Gender on Pump therapy or MDI

After adjusting data for Sex, Age & Diabetes Duration through the 'Propensity Score (PS) matching':
In patients who **started** insulin treatment with **PUMPS**

- The **apparent** ⇑ **Weight Increase** was rebutted by the statistical analysis
- The **kidney function & eGFR decline** was less remarkable
- **Better metabolic profiles** (lower HbA1c and tryglicerides levels, higher HDL cholesterol values) **at baseline & longitudinally**
- **Favorable Health Indexes** (⇓ SBP levels, less smoking habit)
- **Less Micro** & **Macrovascular Complications** (⇓ Retinopathy & Cardiovascular events)
- with a **Less frequent use** of **Lipid-lowering** & **Antihypertensive drugs**

% OBESITA' (BMI ≥30 kg/m2) nel DIABETE tipo1: TREND TEMPORALE 2010 - 2020
Gender Perspective



Under a **Gender Perspective**, a **greater increase** in %**Obesity**

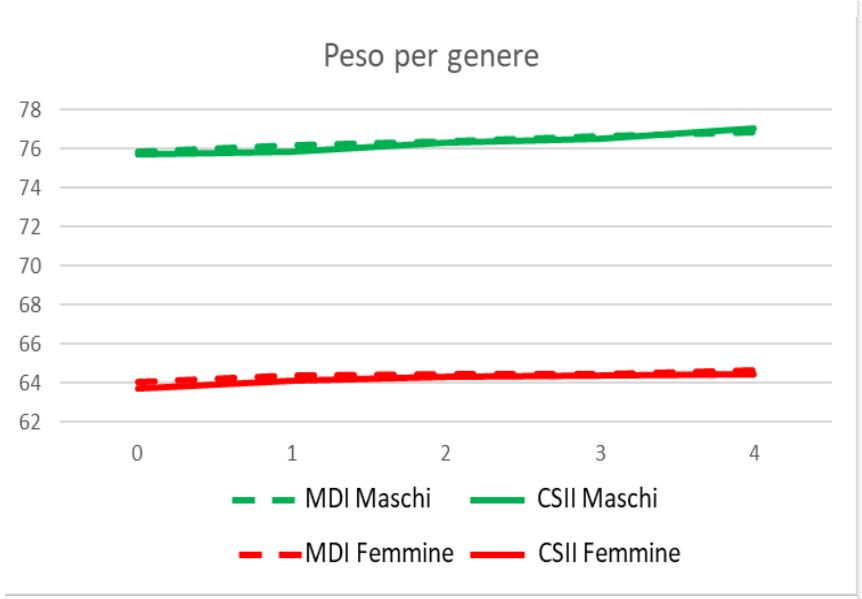
Men: from **11.1** to **13.4%** ≡ **20.7%** relative increase

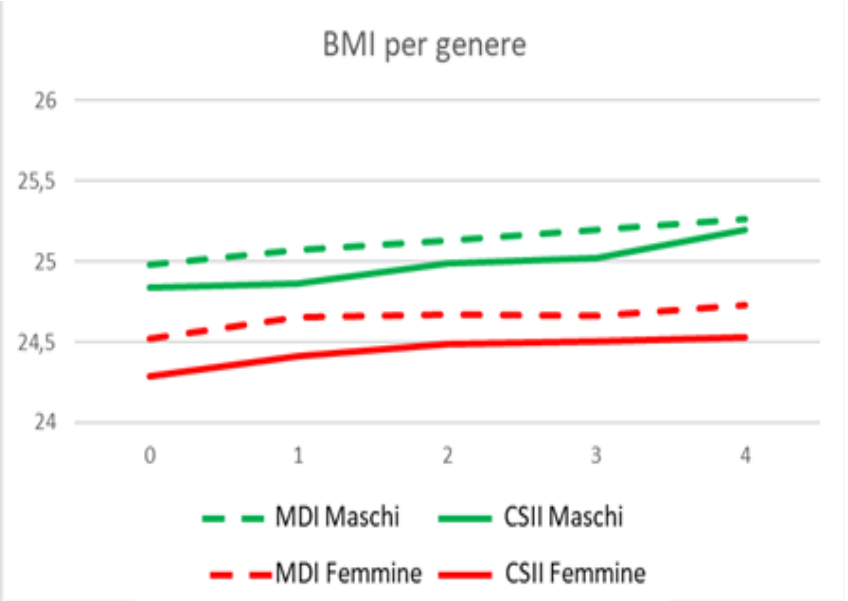
vs

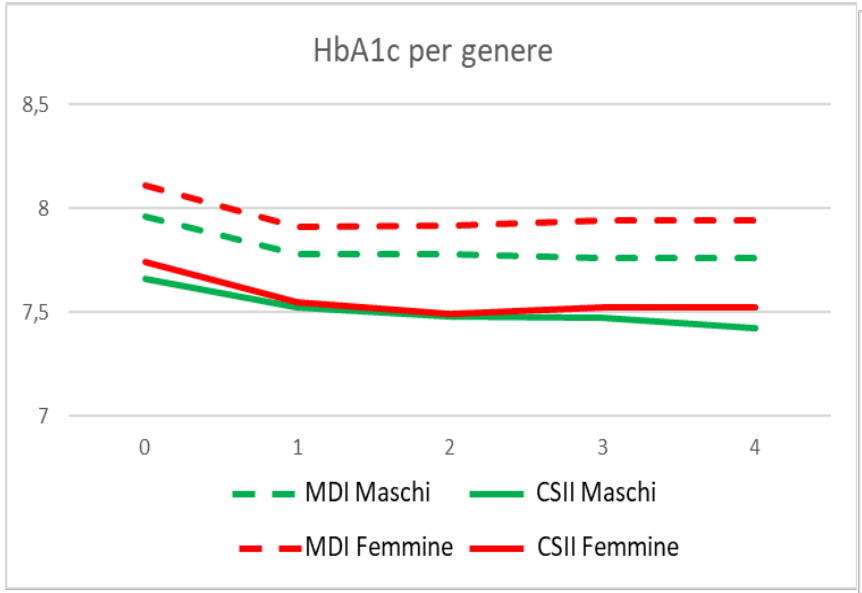
Women: from **12.7** to **14 .0%** ≡ **10.2%** relative increase

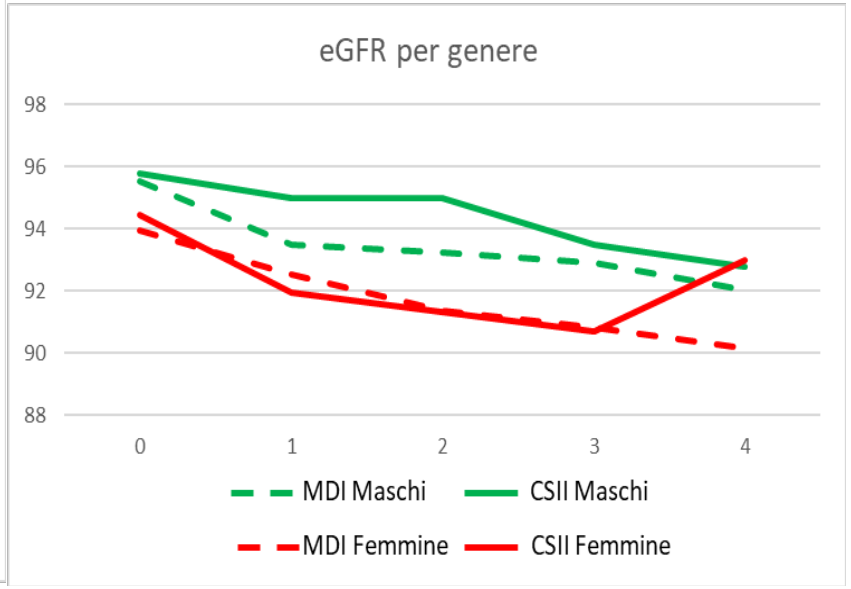
Notably**,** throughout the **ten year-observation period**, although the phenomenon had always been **more apparent** in **Women**,
the **GAP** with **Males narrowed progressively**
because of a **more rapid growth** of obesity among **males**

Trend of BMI, BODY weight, HBA1C, eGFR values over time for subjects who started therapy with CSII & in Controls who continued therapy with MDI, in relation to **Gender**

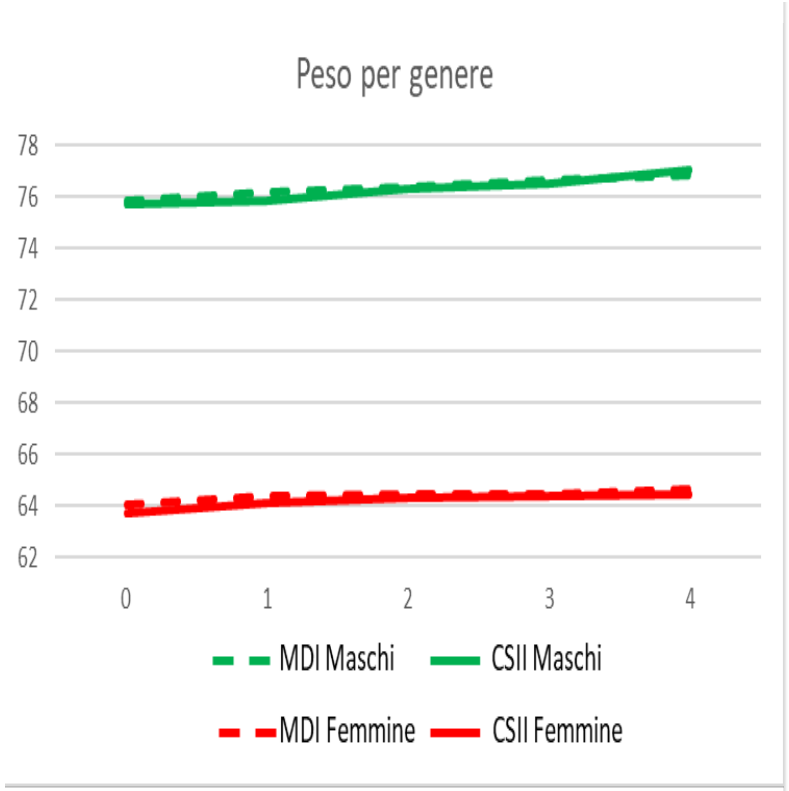


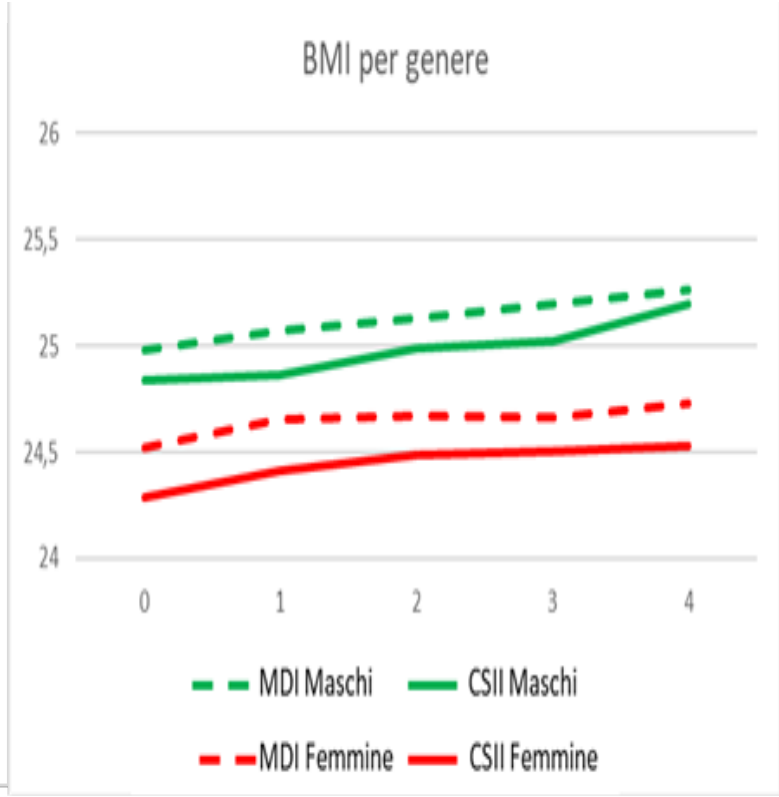






Trend of **BODY weight & BMI,** over time for subjects who started therapy with CSII & in Controls who continued with MDI in relation to **Gender**





PESO/BMI

MASCHI: Lievi incrementi con **MDI** & **CSII** * dal **2°**sem. in CSII vs dal **1°**sem. in MDI
Dopo 2aa dall'inizio della terapia con

Δ Peso (Kg)

CSII vs **MDI**
+1,34 vs **+1,01 kg**

A **12 mesi,** differenza*: **0,32 kg** (p=0,005)

Δ BMI (kg/m²)

CSII vs **MDI**
+0,36 vs **+0,28**

A **12 mesi, differenza*:** 0,09kg/m², (p=0,02).

FEMMINE: Lievi incrementi con **MDI** & **CSII** * dal 1° sem. in entrambi
Dopo 2aa dall'inizio della terapia

Peso (Kg)

Δ peso CSII vs **MDI**
+0,69 vs **+0,60Kg**

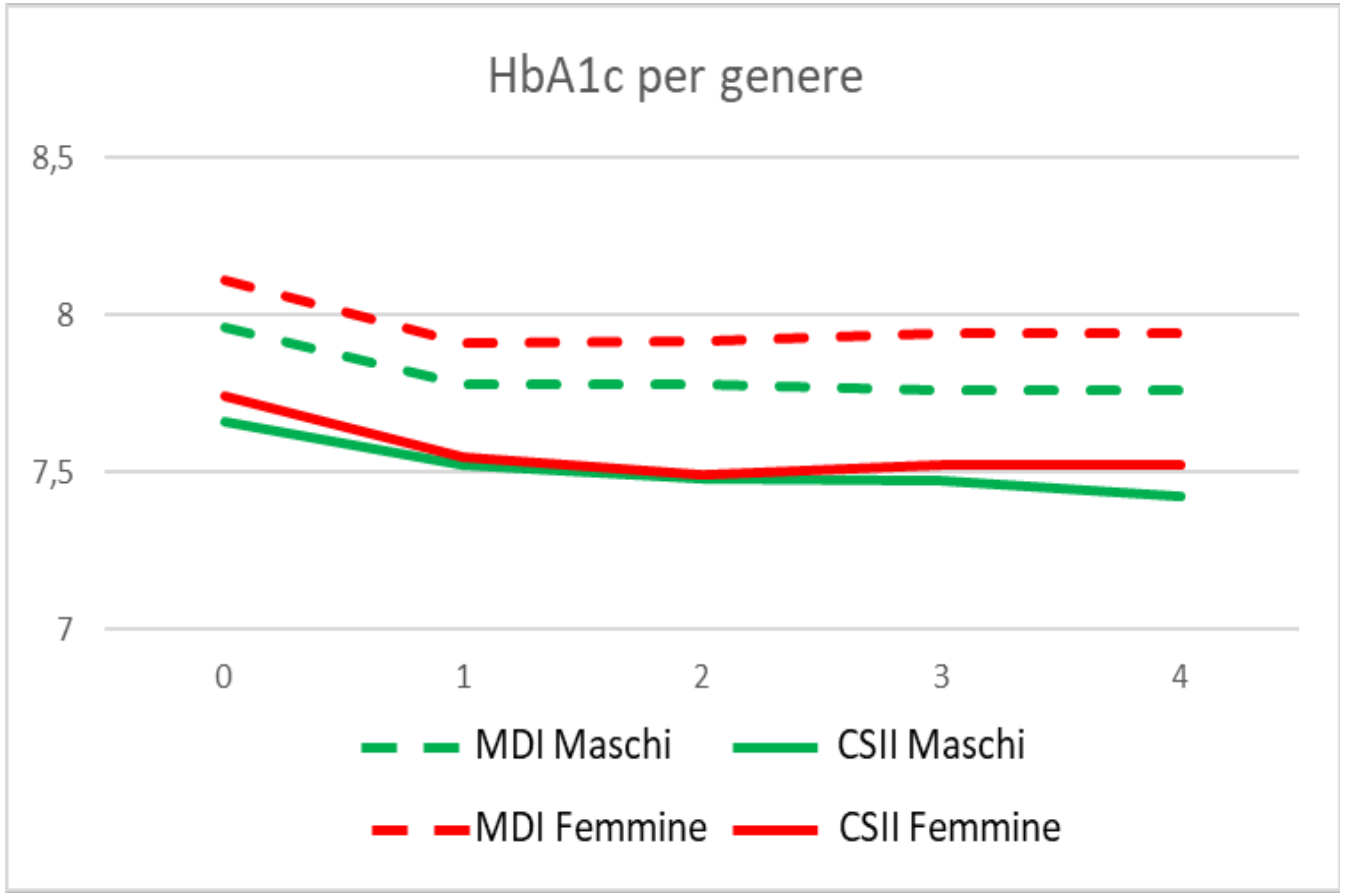
A **12 mesi, differenza:** 0.10kg(NS p=0,37)

Δ BMI CSII vs MDI

+ 0,24 vs **+0,21 kg/m²**

A **12 mesi, differenza ns**: 0,04 kg/m² (p=0,4)

Trend of **HBA1C** values over time for subjects who started therapy with CSII and in Controls who continued therapy with MDI in relation to Gender



HBA1C (%)

Maschi: Lievi ⇓ con **MDI** & **CSII** * dal **1°** sem

Dopo 2aa dall'inizio della terapia

⇓ **HBA1C CSII** vs **MDI**

-0.23 vs **-0,20%**

A **12 mesi, differenza:** NS *(p=0,31)*

Femmine: Lievi ⇓ con **MDI** & **CSII*** dal **1°**sem

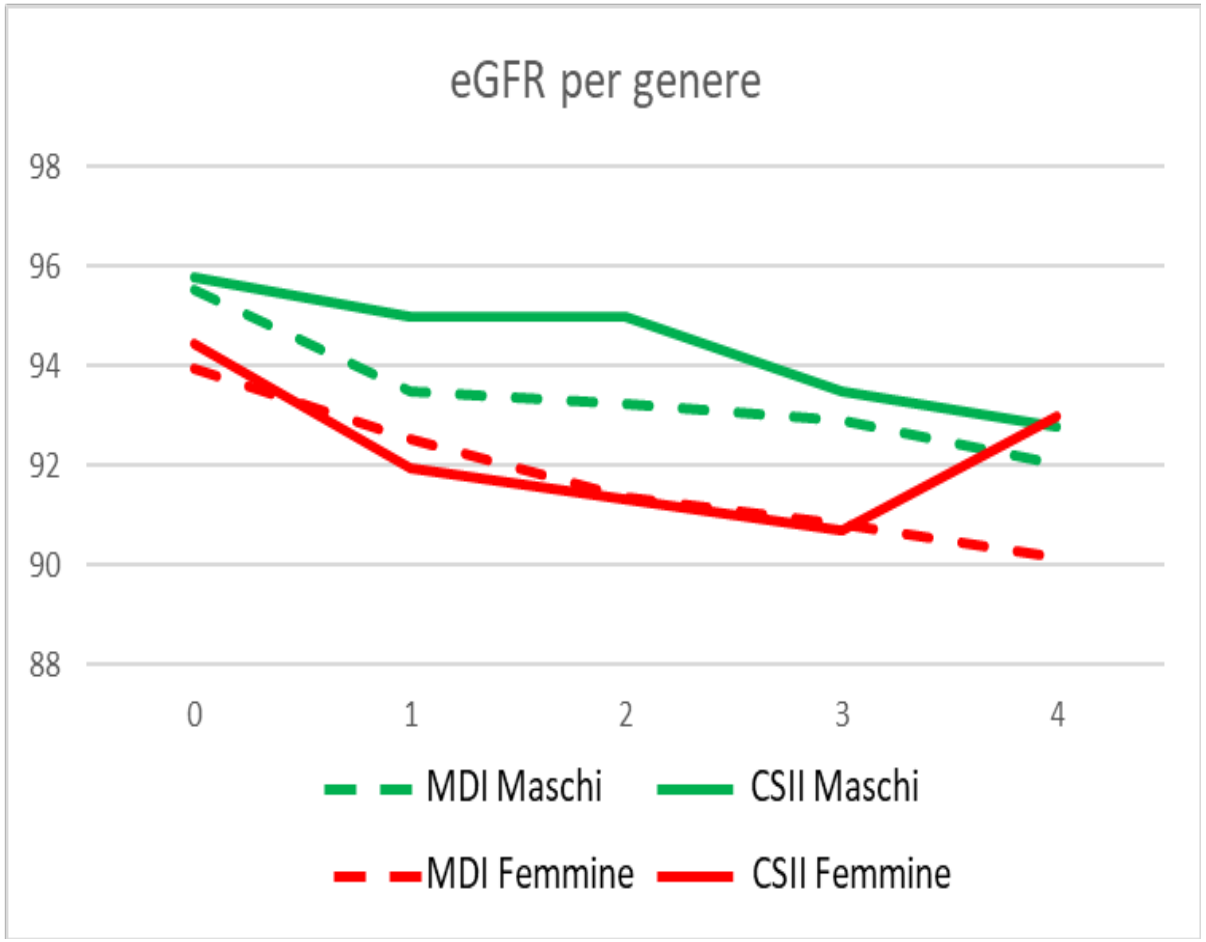
Dopo 2aa dall'inizio della terapia

⇓ **HBA1C CSII** vs **MDI**

-0.22 vs **-0,17%**

A **12 mesi, differenza :** NS *(p=0,1)*

Trend of **eGFR** values over time for subjects who started therapy with CSII & in Controls who continued therapy with MDI in relation to Gender



eGFR

Maschi:

Lievi ⇓ dal **1°**sem. con **MDI** & dal **3°**sem. **CSII**
Dopo 2aa dall'inizio della terapia
⇓ **eGFR CSII** vs **MDI**
-3.02 vs **-3.52** ml/min/1.73m^2
A **12 mesi, differenza: 0.50** NS (p=0,6)

Femmine:

Lievi ⇓ dal **1°**sem. con **MDI** & dal **3°**sem. **CSII**
Dopo 2aa dall'inizio della terapia
⇓ **eGFR CSII** vs **MDI**
-1.42 vs **-3.79** ml/min/1.73m^2
A **12 mesi, differenza*: 2.36** (p=0,007)

Cosa fare?

Diet and exercise

- Risk of hypoglycaemia might influence defensive snacking and exercise absenteeism
- Weight regain is likely with wavering commitment to treatment

Bariatric surgery

- Increased risk of hypoglycaemia and diabetic ketoacidosis
- Under-researched

Pharmaceuticals

- Restricted by market authorisations
- Require chronic use
- High cost and inadequate reimbursement
- Issues with tolerability
- SGLT inhibitors associated with diabetic ketoacidosis risk
- GLP-1 receptor agonists require additional injections

***Figure* 3: Schematic overview of issues associated with various approaches to weight management in people with type 1 diabetes**

SEMAGLUTIDE in 50 Overweight & Obese Pts vs 50 Controls with D1, Pilot Retrospective Study

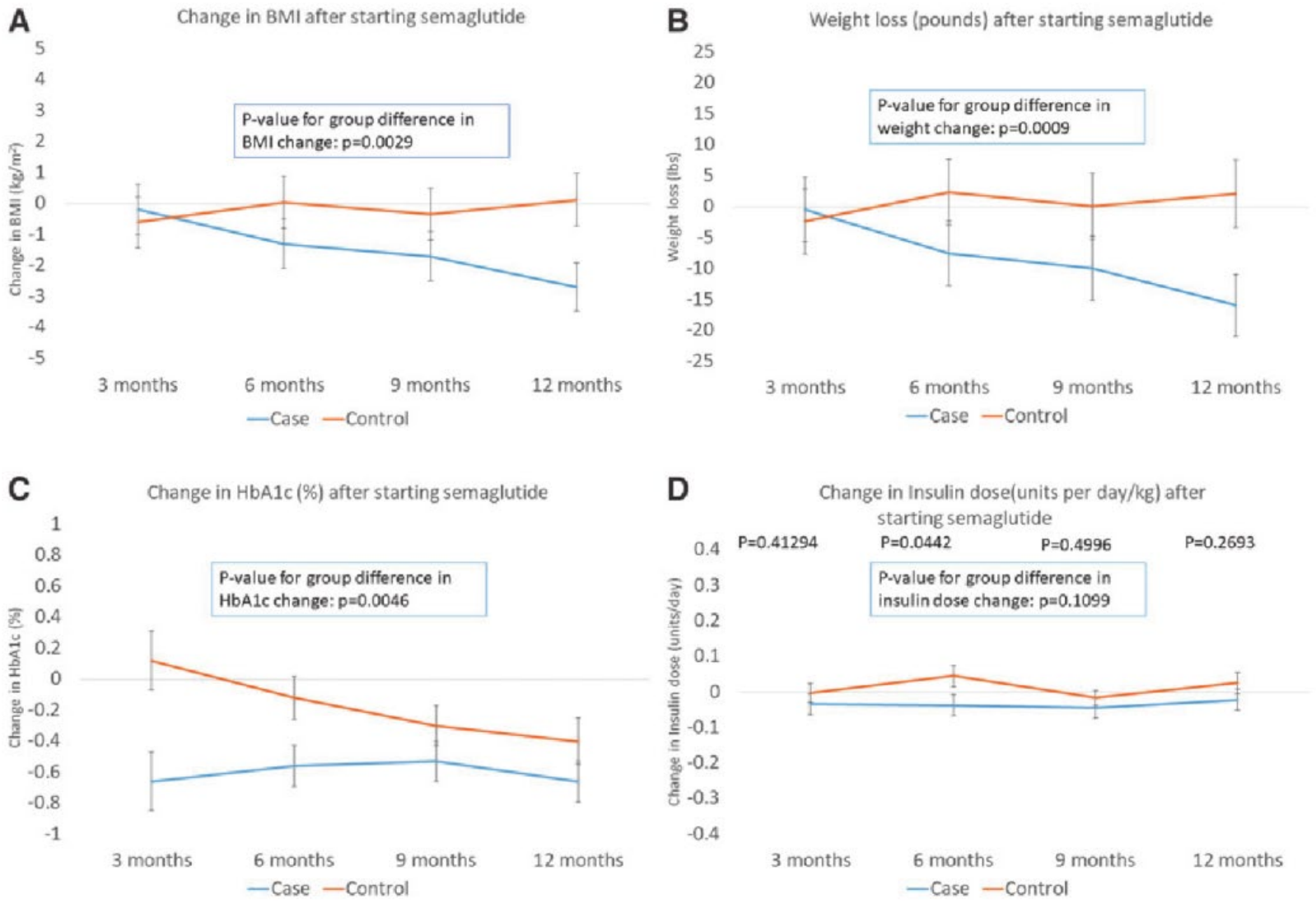


FIG. 1. **(A, B)** The changes in BMI and weight loss/gain in the semaglutide-treated subjects compared to the control group over 1 year. Total Daily Insulin dose was not different in the two group throughout out the year **(D)**. There was a significantly higher decline in HbA1c in the semaglutide group throughout the study period **(C)**. BMI, body mass index; HbA1c, glycosylated hemoglobin.

CGM metrics

TIR %	⇑ nel totale
TAR	non cambia
⇓ **TBR**	a 12 mesi
⇓ **SD**	nel totale e a 9 mesi
⇓ **CV**	nel totale e a 9 mesi

No Hospitalizations for **severe hypos** or **DKA**.

Satish Garg et al .Diabetes Technol Ther . 2024

Efficacy and Safety of Tirzepatide in Overweight and Obese Adult Patients with Type 1 Diabetes

Pilot (off label) study
Retrospective single-center real-world study on Adult pts with T1D

Cases: 62 OW/OB who were prescribed tirzepatide (treated group) & followed for 1 year out of 184 prescribed tirzepatide; *At least 3 months of use of tirzepatide was one of the inclusion criteria.*
Controls: 37 OW/OB computer frequency matched by age, d.duration, gender, BMI & glucose control

Results:

Cases vs **Controls**
Significantly larger ⇓ in **BMI** & **Weight** across **all time points**
⇓**HbA1c** in Cases, early as **3 months** & **sustained through a 1-year follow-up** (-0.67% at 1 year).
⇓ I**nsulin dose at 3 months** and **throughout the study period**
No Hospitalizations for **severe hypos** or **DKA**.
Improvement of '**CGM' METRICS:** mean glucose, TIR, TAR, SD & CV

Conclusions

tirzepatide facilitated a **18.5% weight loss** & improved glucose control in OW/OB D1pts at 1 yr.

Satish K Garg Diabetes Technol Ther . 2024 Jun;26(6):367-374.

Bariatric Surgery in people with type 1 diabetes

1) Retrospective study of 22 people in Belgium who previously had bariatric surgery
⇓ **BMI** & **Insulin Requirements**, but **No** improvement in **Glycaemic Control**

2) Retrospective study of 61 in Abu Dhabi
⇓ **BMI** of **9·2** kg/m² **at 6** mo & **11·4** kg/m² at **12** mo, ⇓ **HbA1c from 8·6%** to **7·8%**
only **3 reported cases of DKA**

3) A Swedish observational study
387 people who had Roux-en-Y Gastric Bypass vs **387** Controls with obesity,
matched for age, sex, BMI, & calendar yr of surgery
⇓ risk of **CD**, **Cardiovascular Death** & **Stroke** for the bypass group
No improvement in **Glycaemic control** and a ⇑ **risk for hypos**

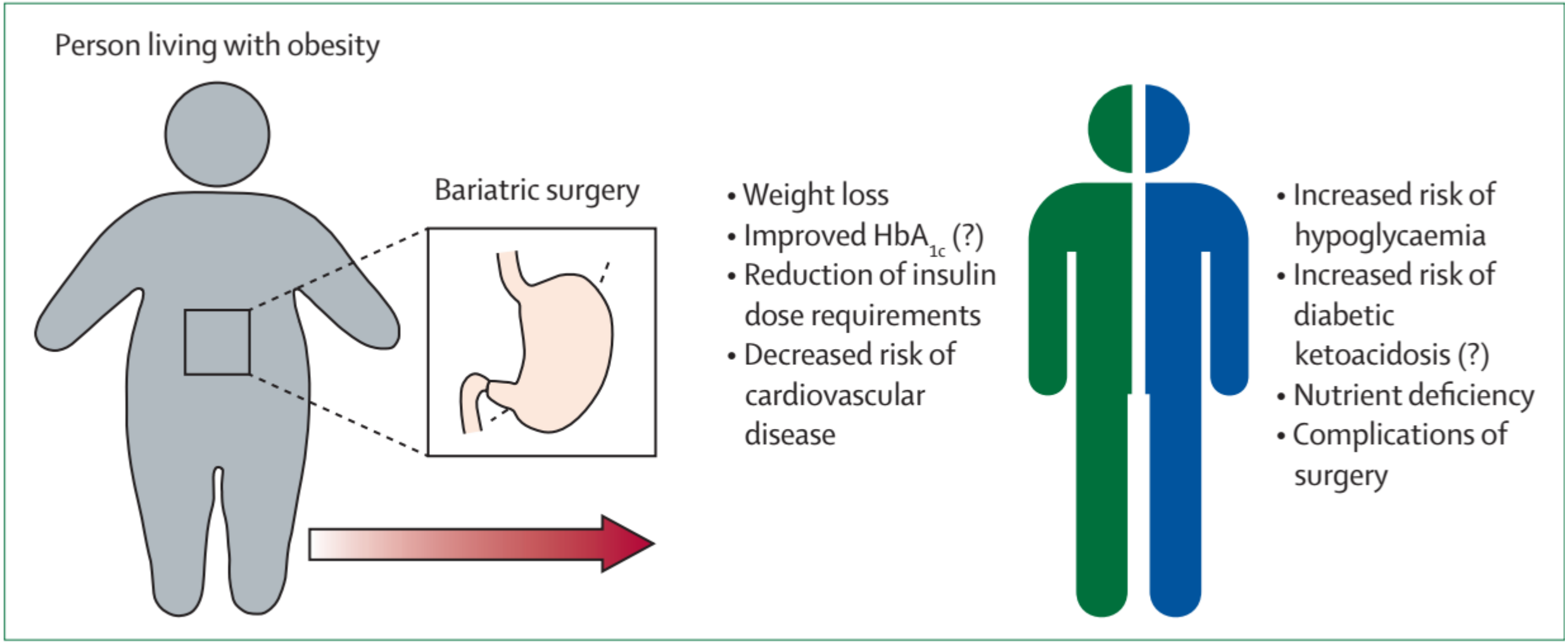
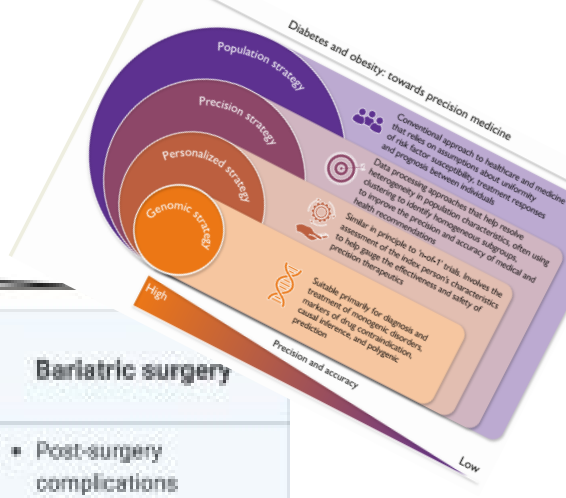


Figure 4: **Advantages and disadvantages of bariatric surgery in people living with type 1 diabetes**
Schematic overview of key benefits (green) and disadvantages (blue) of bariatric surgery.

Larger & Longer-term Studies are needed

The emergence of obesity in type 1 diabetes



Obesity in Type 1 Diabetes

	Interventions	Exercise therapy	Medical nutrition therapy	Adjunct Pharmacotherapies			Bariatric surgery
				GLP1-RA	Pramlintide	SGLT2 inhibitor	
Patient-centric level	Barriers	• Post-exercise hyperglycaemia • Nocturnal hypoglycaemia • Symptoms mimicking hypoglycaemia	• Fear of hypoglycaemia or emotional eating • Fluctuating blood glucose level	• Gastrointestinal adverse events • Symptomatic hypoglycaemic risk • Fear or burden of additional injections		• Diabetic ketoacidosis risk	• Post-surgery complications • Diabetic ketoacidosis risk • Symptomatic hypoglycaemic risk
	Strategies	• Continuous glucose monitoring • Closed-loop insulin pump therapy • Structured education training on carbohydrate consumption and insulin dosing	• Preferably low glycaemic index food • Nutritional and psychological counselling • Structured education on carbohydrate consumption and insulin dosing	• Begin with a low dose, gradually titrate • Tailored insulin dosing • Patient education on hypoglycaemia awareness • Individualised conversation and address concerns regarding the injection • Symptom-targetted therapy		• Stringent patient selection • Begin with a low dose, gradually titrate • Insulin dose adjustment • Home ketone measurement • Risk mitigation strategy (e.g., STICH protocol) • Healthcare provider and patient education	Limited evidence on risk mitigation

	Environmental and socioeconomic determinants	Health delivery framework	Diabetes technology	Clinical trials and regulatory processes	Sustainable evidence-based implementation
Systemic level	• Address social disparities • Evaluate food labelling regulations and nutrition access • Engage with food and media industries • Promote active environments • Improve policy coherence • Assess the effectiveness of implemented policies	• Combine the weight- and glucose-centric goals • Challenge misconceptions and stigma • Implement interdisciplinary care • Strengthen healthcare providers' competency in managing obesity and treatment risk • Clinical care pathway economic evaluation	• Promote digital inclusivity and literacy • Introduce reimbursement for social determinant-focused services • Safeguard data privacy • Validate data for accuracy, reliability and consistency • Advocate for user-centred design approach	• Scrutinise the pathways to facilitate regulatory approval • Promote international participation and funding opportunities • Improve trial access and empower patients through education • Evaluate the status of pharmacovigilance and cost-effective analysis	

REVIEW ARTICLE OPEN Clinical Research The emergence of obesity in type 1 diabetes Martin T. International Journal of Obesity

Obesità e Diabete Mellito di tipo1

Obesità e Diabete Mellito di tipo1

Grazie

Angela Napoli

Informare, guidare future iniziative volte a ridurre la prevalenza di obesità e promuovere uno stile di vita sano nelle società europee.

Health4EUkids: il ruolo dell'ISS e il lavoro sul WP4
Joint Action Europea Health4EUkids
il **C**entro **Na**zionale per la **P**revenzione delle malattie e la **P**romozione della **S**alute (**CNaPPS**) dell'**ISS**
il coordinamento del **WP4 "Trasferibilità e sostenibilità"**

4 macro aree esplicative:

- "Recommendation" **sintesi** delle conoscenze raccolte, prodotte e diffuse dai progetti
- "Policy" **accord**i, **dichiarazion**i o **alleanze** nate dall**'implementazione dei progetti**
- "Sustainability" **fattori** che **supportino la sostenibilità** della **buona pratica** o **l'utilizzo degli strumenti prodotti**, Il **termine del mandato** del singolo progetto implementato
- "Transferability/Scalability" **fasi essenziali per strategia** di **implementazione da trasferire** nelle **buona pratiche**.

⇒≡massima **attenzione** e **impegno** a livello delle **Politiche**, alla **costruzione di Database** di **Buone Pratiche**, alla costruzione di **Reti** e al **coinvolgimento Intersettoriale**, agli **interventi di Comunicazione** ed **Educazione**, al **contrasto** delle **Lacune** nella **ricerca** e all' **Equità** nella **Salute**