EPIDEMIOLOGIA E INCIDENZA DI OBESITA', INSULINORESISTENZA E DIABETE TIPO 2 NELL'ETA' EVOLUTIVA

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Clinica Pediatrica - Centro Alta Specialità di Diabetologia
IRCCS Istituto G. Gaslini

Genova

CONGRESSO CONGIUNTO SID-AMD-SIEDP-SIE - ANIED-OSDI

"DIABETE ED OBESITA': SI PUO' INVERTIRE LA ROTTA?
Cosa abbiamo guadagnato e cosa abbiamo perso"

Genova (GE), 15 e 16 dicembre 2023

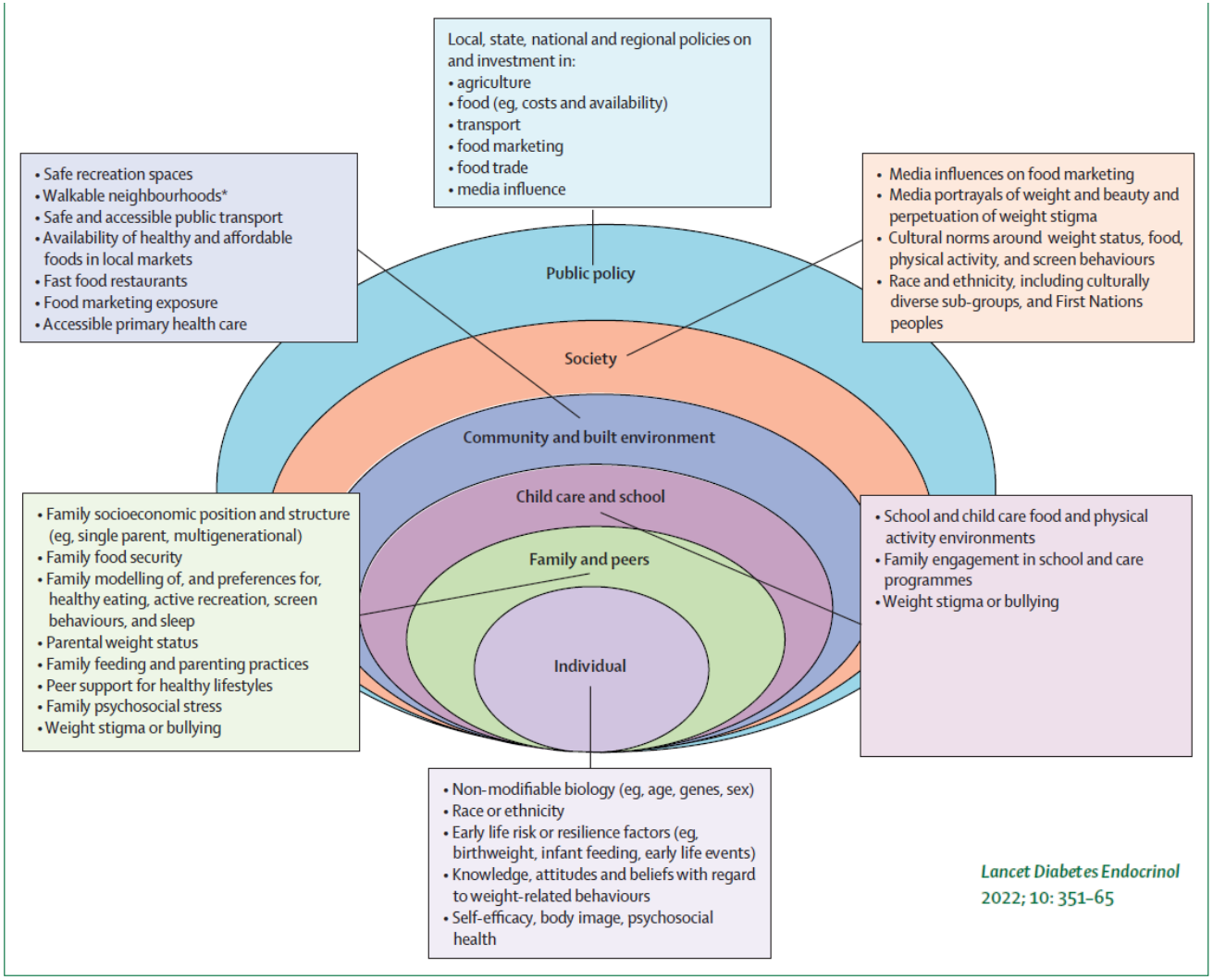
Il dr. Giuseppe d'Annunzio dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

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.).

OBESITA’

Eccessivo o anomalo accumulo di adipe che rappresenta un rischio per la salute (WHO)

Squilibrio tra consumo energetico e apporto calorico



Child and adolescent obesity

Natalie B. Lister[1,2], Louise A. Baur[1,3,4], Janine F. Felix[5,6], Andrew J. Hill[7], Claude Marcus[8], Thomas Reinehr[9], Carolyn Summerbell[10] & Martin Wabitsch[11]

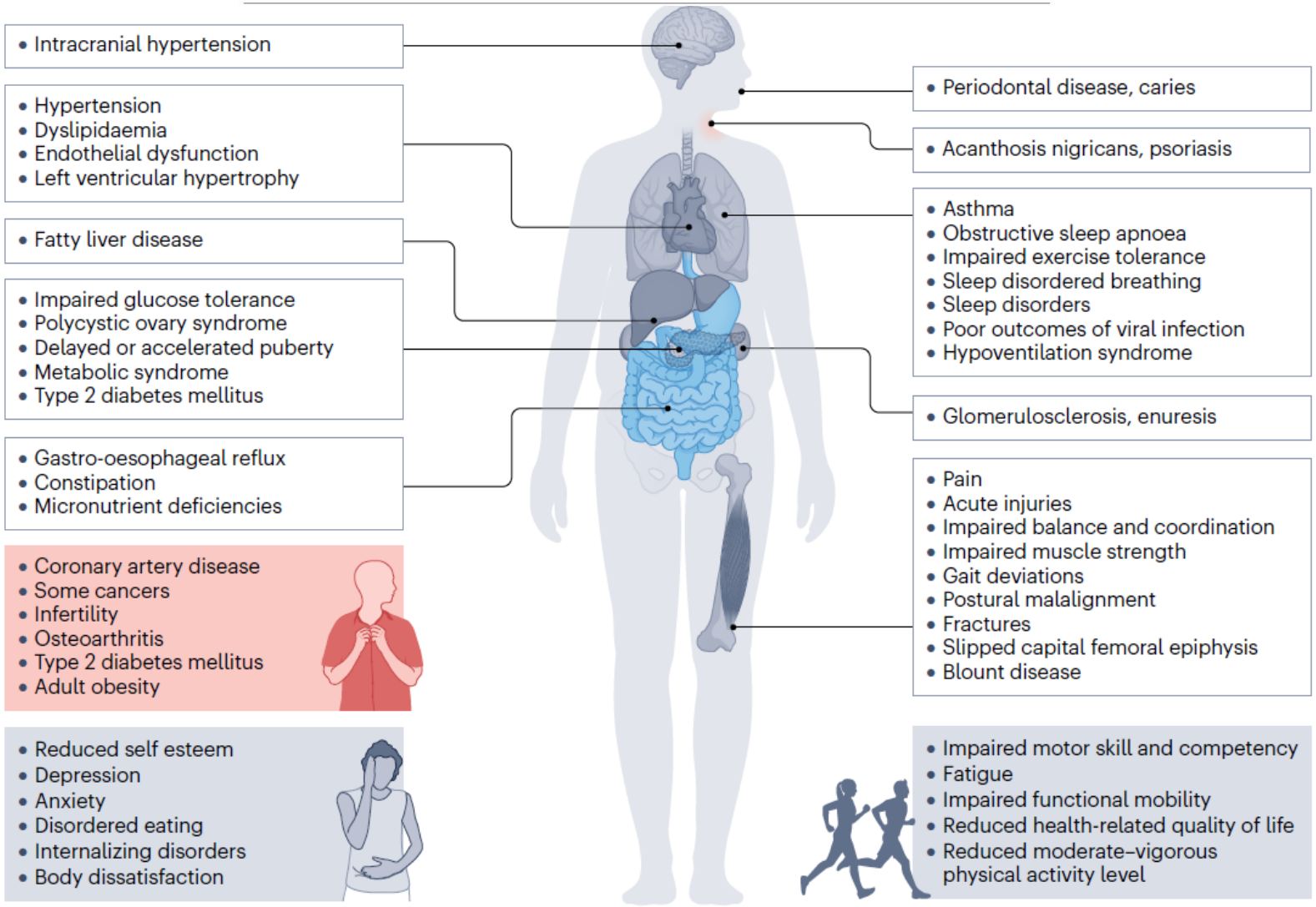


Fig. 2 | Childhood obesity comorbidities. Obesity in children and adolescents can be accompanied by various other pathologies. In addition, childhood obesity is associated with complications and disorders that manifest in adulthood (red box).

Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults

NCD Risk Factor Collaboration (NCD-RisC)*

Dal 1975 al 2016 prevalenza di obesità 5-19 anni

- **0.7-5.6 % femmine**
- **0.9-7.8% maschi**
- **Trend BMI stabilizzati in west Europa, regioni asiatiche di lingua inglese, paesi a più alto livello socioeconomico**
- **Trend BMI in aumento in sudest asiatico**
- **Prevalenza di obesità superiore al 20% in USA, Caraibi, Polinesia, Micronesia, Nordafrica,**

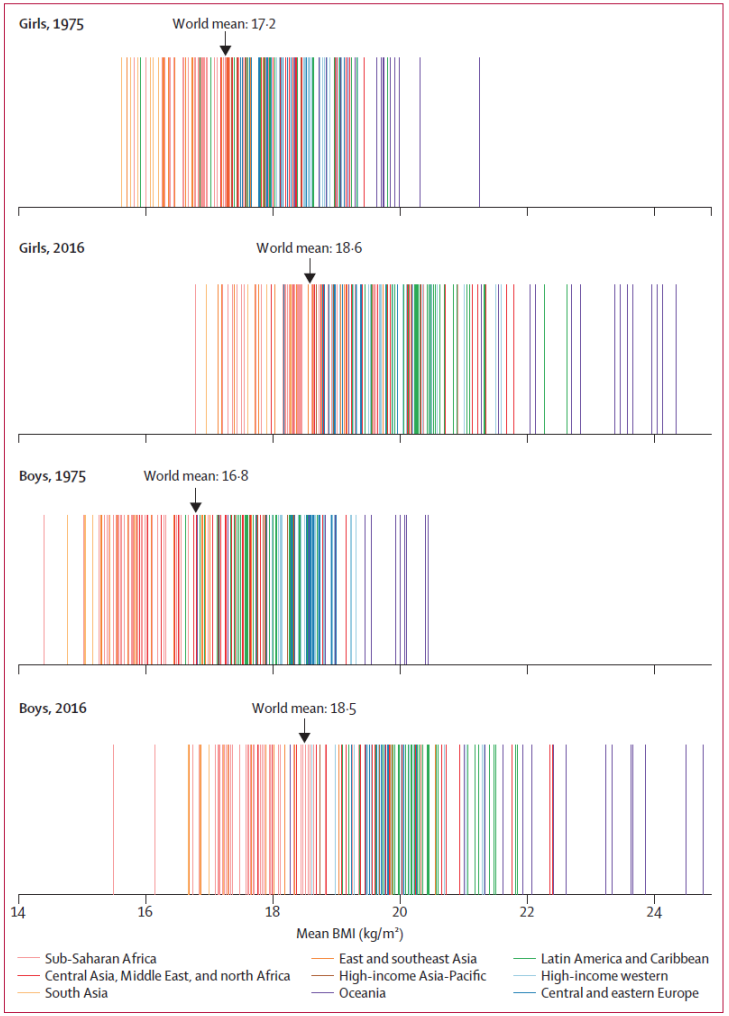


Figure 4: Age-standardised mean BMI in children and adolescents in 1975 and 2016
Each line shows one country. BMI=body-mass index.

Lancet 2017; 390: 2627–42

IN ITALIA….

Obesità e stili di vita dei bambini: OKkio alla SALUTE 2019

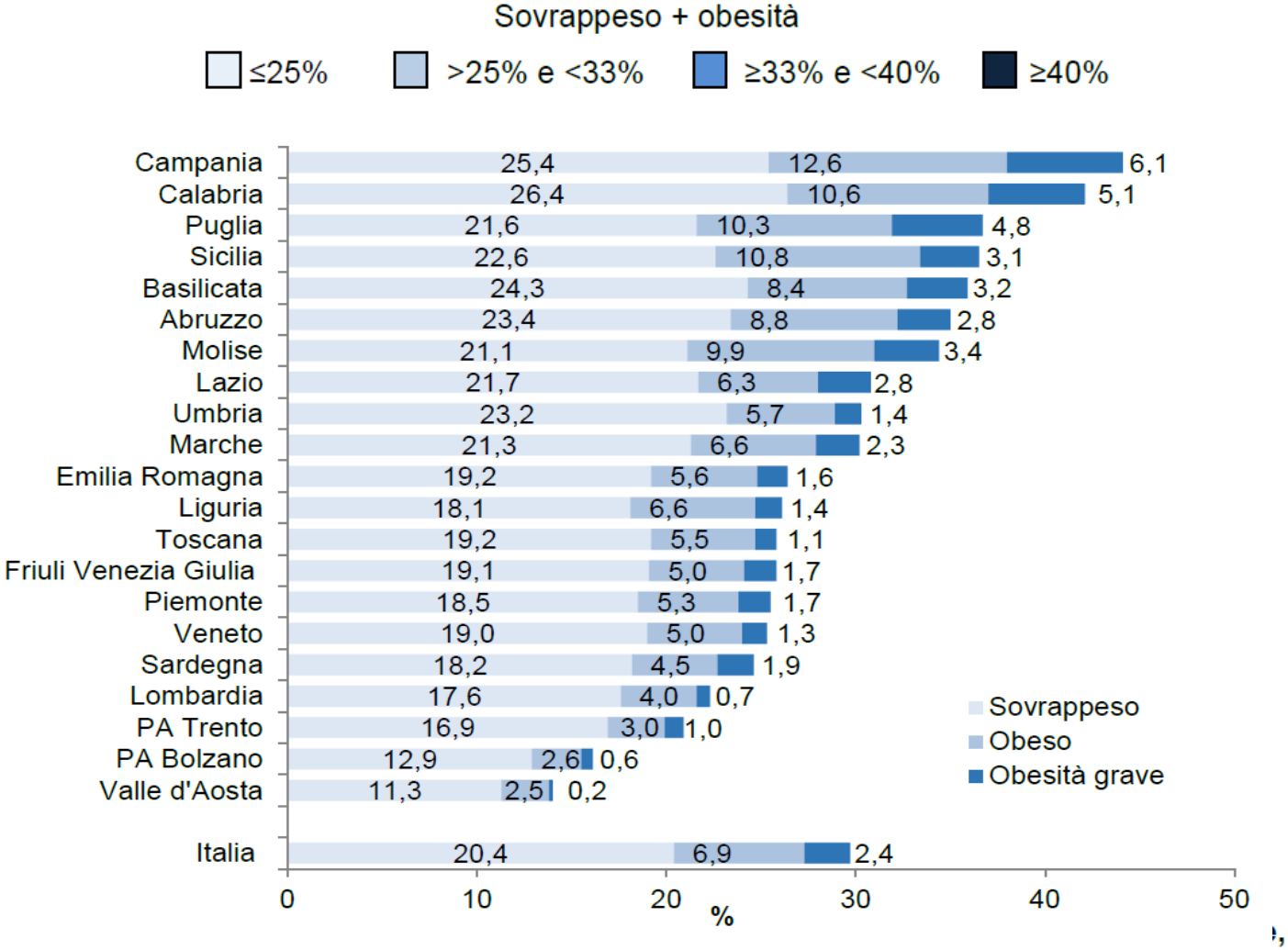
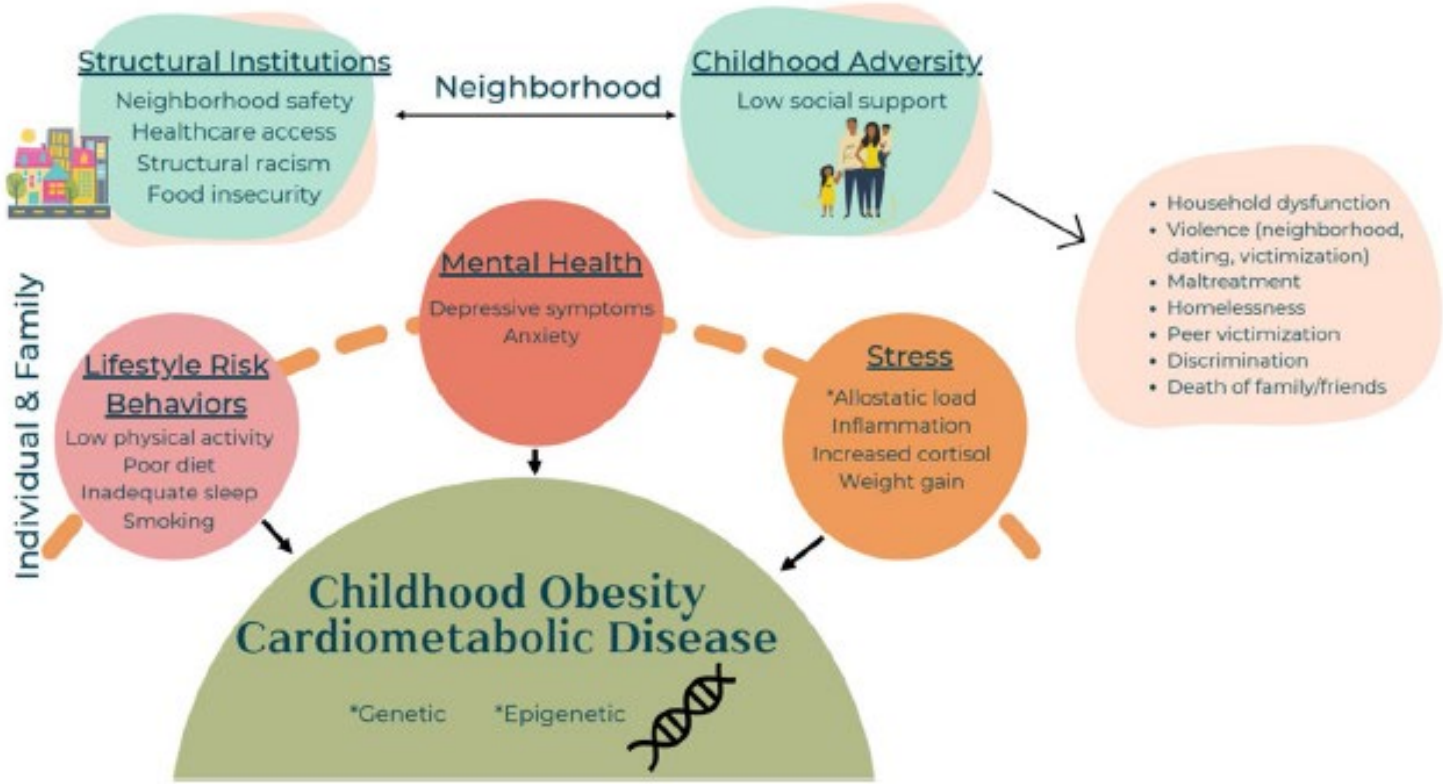


Figura 3. Sovrappeso e obesità (%) bambini di 8-9 anni per Regione. OKkio alla SALUTE, Italia 2019

Childhood Obesity and Cardiovascular Disease Risk

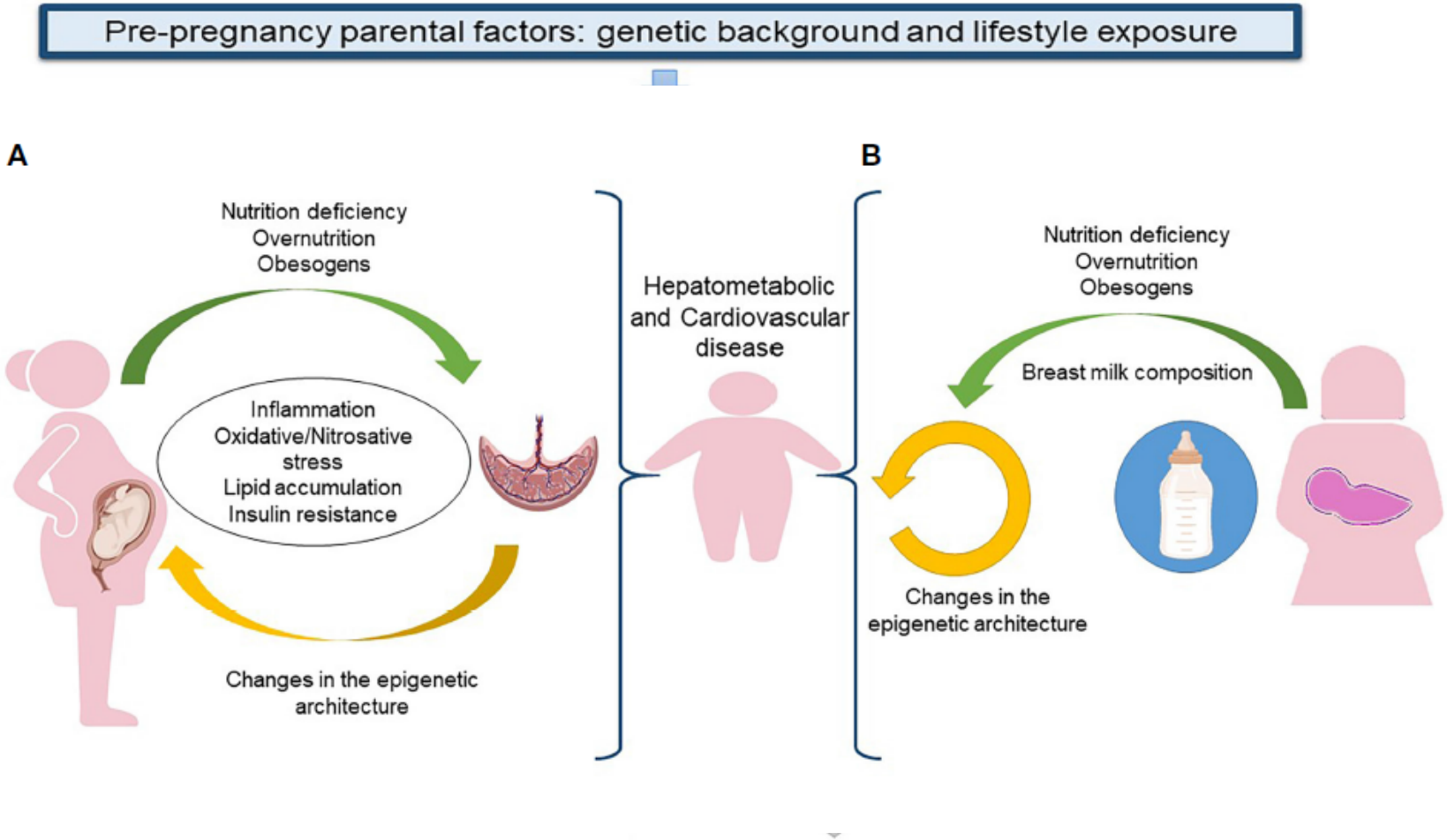
Stephanie T. Chung[1] · Andrea Krenek[1] · Sheela N. Magge[2]



Current Atherosclerosis Reports
https://doi.org/10.1007/s11883-023-01111-4

Genetics, epigenetics and transgenerational transmission of obesity in children

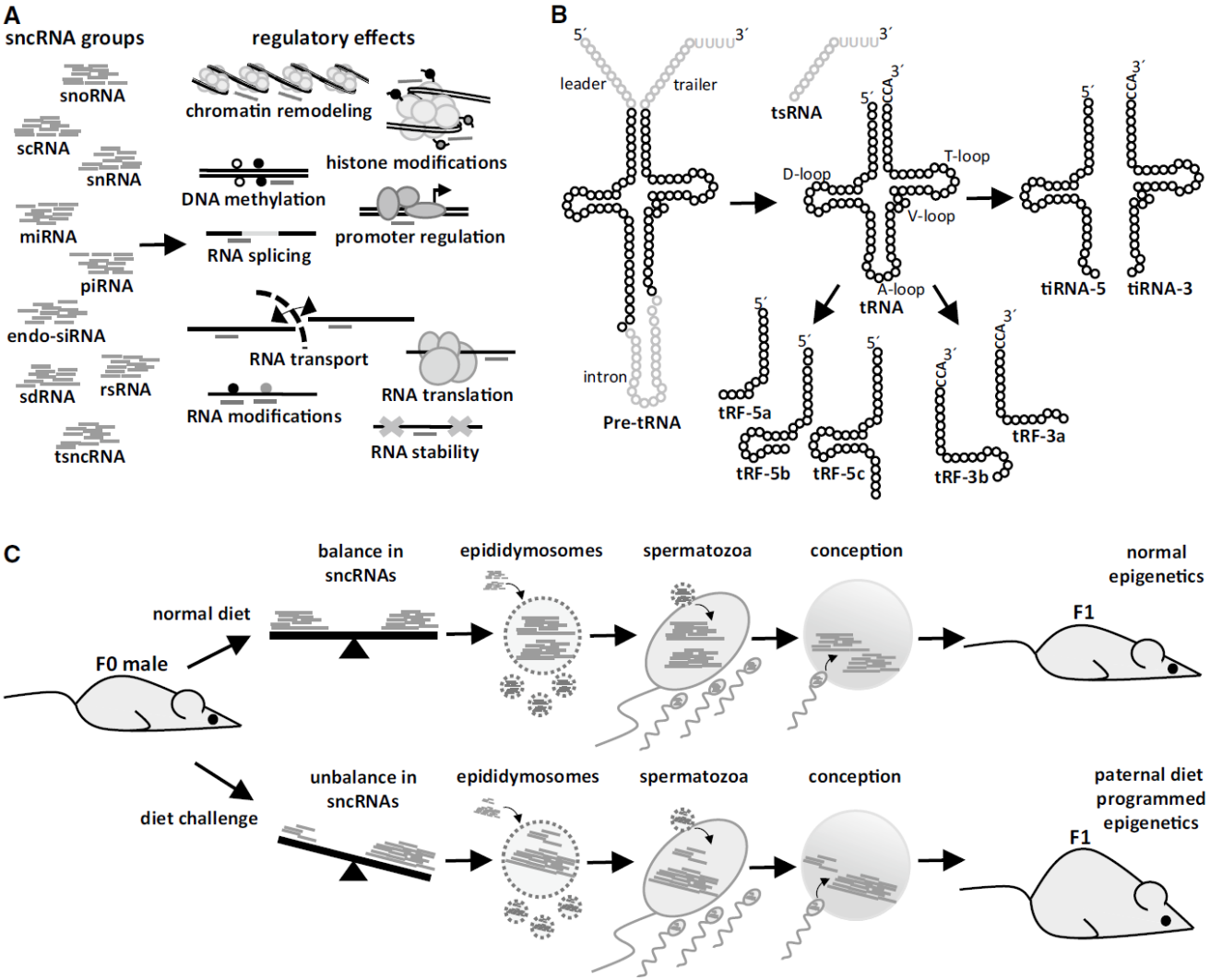
Nadia Panera[1†], Claudia Mandato[2*†], Annalisa Crudele[1], Sara Bertrando[3], Pietro Vajro[2] and Anna Alisi[1*]



10.3389/fendo.2022.1006008

The influence of paternal diet on sncRNA-mediated epigenetic inheritance

Line Katrine Klastrup[1] · Stine Thorhauge Bak[1] · Anders Lade Nielsen[1]



Molecular Genetics and Genomics (2019) 294:1–11

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 DECEMBER 6, 2007 VOL. 357 NO. 23

Childhood Body-Mass Index and the Risk of Coronary Heart Disease in Adulthood

Jennifer L. Baker, Ph.D., Lina W. Olsen, Ph.D., and Thorkild I.A. Sørensen, M.D., Dr.Med.Sci.

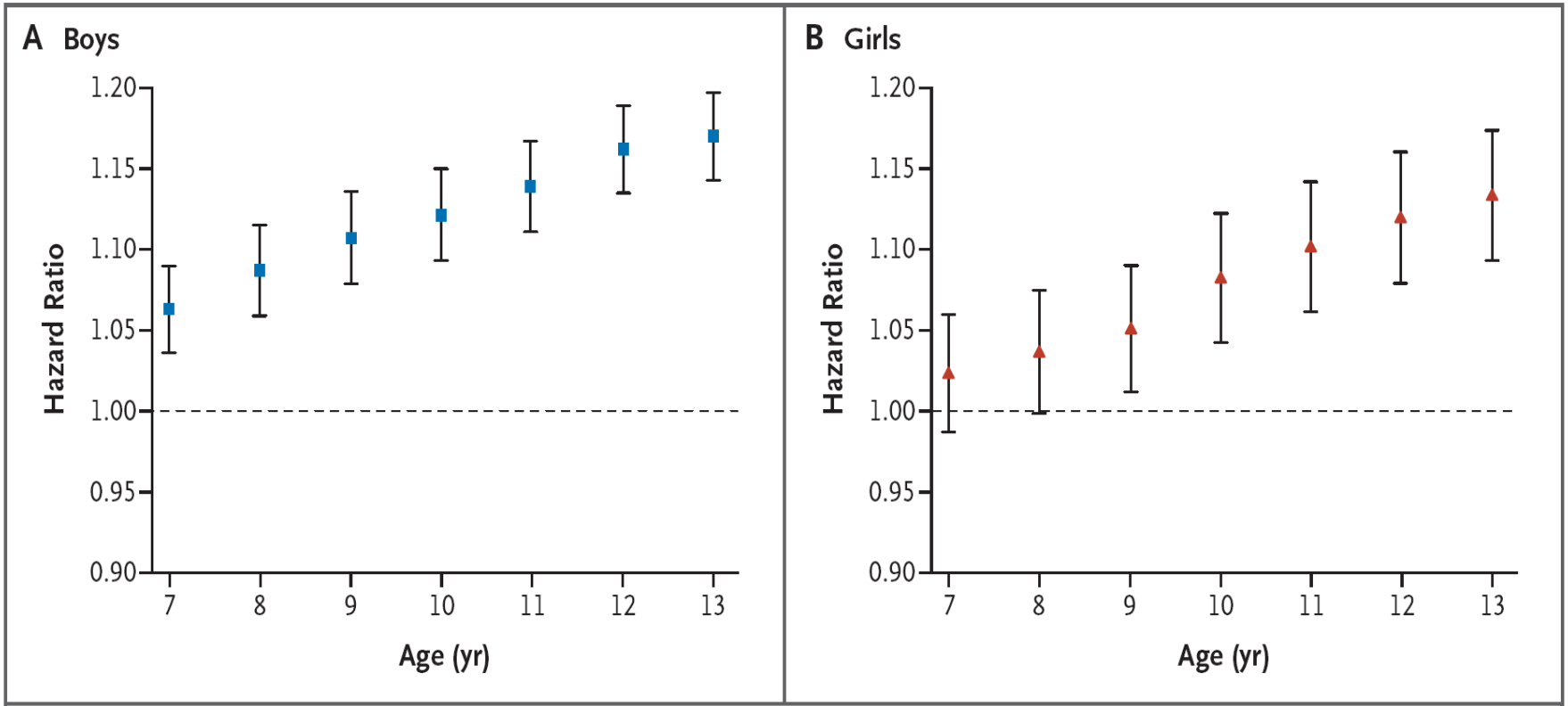


Figure 1. Body-Mass Index (BMI) in Childhood and the Risk of Coronary Heart Disease (CHD) in Adulthood.

The graphs depict the association between childhood BMI and the risk of having a CHD event (nonfatal or fatal) in adulthood. Hazard ratios and 95% confidence intervals are given for a 1-unit increase in BMI z score at each age from 7 to 13 years. The data are from 139,857 boys (Panel A) and 136,978 girls (Panel B) in the Copenhagen School Health Records Cohort. The associations were linear within each age, since trend tests resulted in the rejection of the alternative of nonlinearity modeled as a restricted cubic spline with five knots (all P values >0.15).

Laboratory assessment of cardiometabolic risk in overweight and obese children

Grazyna Sypniewska *

Department of Laboratory Medicine, Nicolaus Copernicus University, Collegium Medicum in Bydgoszcz, Sklodowskiej-Curie 9, 85-094 Bydgoszcz, Poland

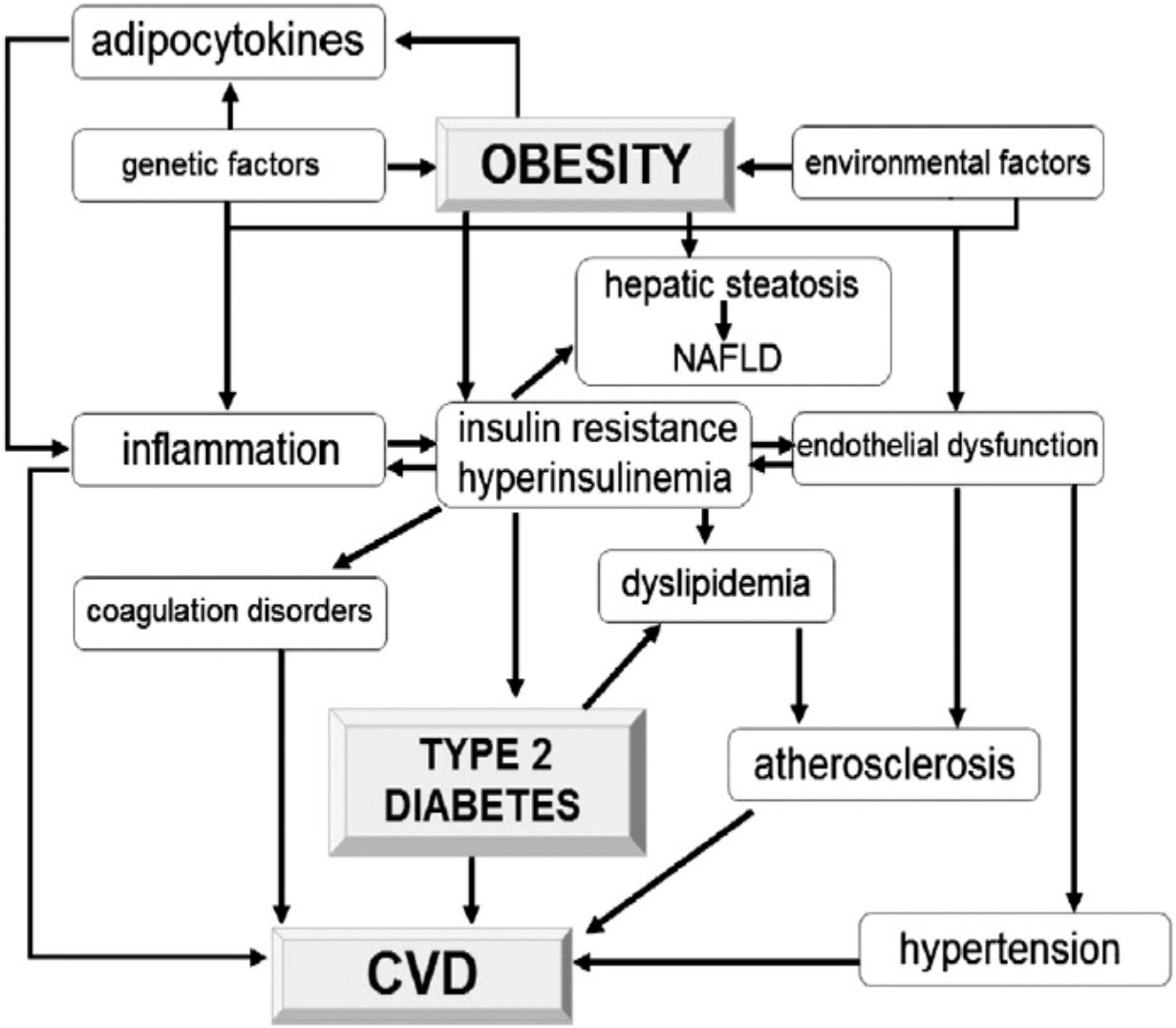


Fig. 1. Obesity related complications.

SINDROME METABOLICA

Descritta nel 1988 da Gerald Reaven :

associazione tra insulino- resistenza (IR), ipertensione, dislipidemia, ridotta tolleranza glucidica e altre anomalie metaboliche correlate a un incremento del rischio cardiovascolare in età adulta

SINDROME METABOLICA NELL'ADOLESCENTE

- **Prevalenza 2-4-8% all'età di 13-15-19 anni**
- **Cluster:**
  - **Alterazioni glicemia**
  - **Obesità: BMI > 90° Centile, Circonferenza vita**
  - **Insulino-resistenza (HOMA-IR, QUICKI, HOMA β%)**
  - **Alterazioni quadro lipidico**
    - **Trigliceridi <150 mg/dl; HDL >35 mg/dl; LDL <100 mg/dl**
  - **Ipertensione**
    - **Confronto con i Centili per la statura**
- **Familiarità**

International Journal of Obesity (2021) 45:12–24
https://doi.org/10.1038/s41366-020-00713-1

REVIEW ARTICLE

Pediatrics

The prevalence of pediatric metabolic syndrome—a critical look on the discrepancies between definitions and its clinical importance

Carolin Reisinger[1] · Benedicta N. Nkeh-Chungag[2] · Per Morten Fredriksen[3] · Nandu Goswami[1]

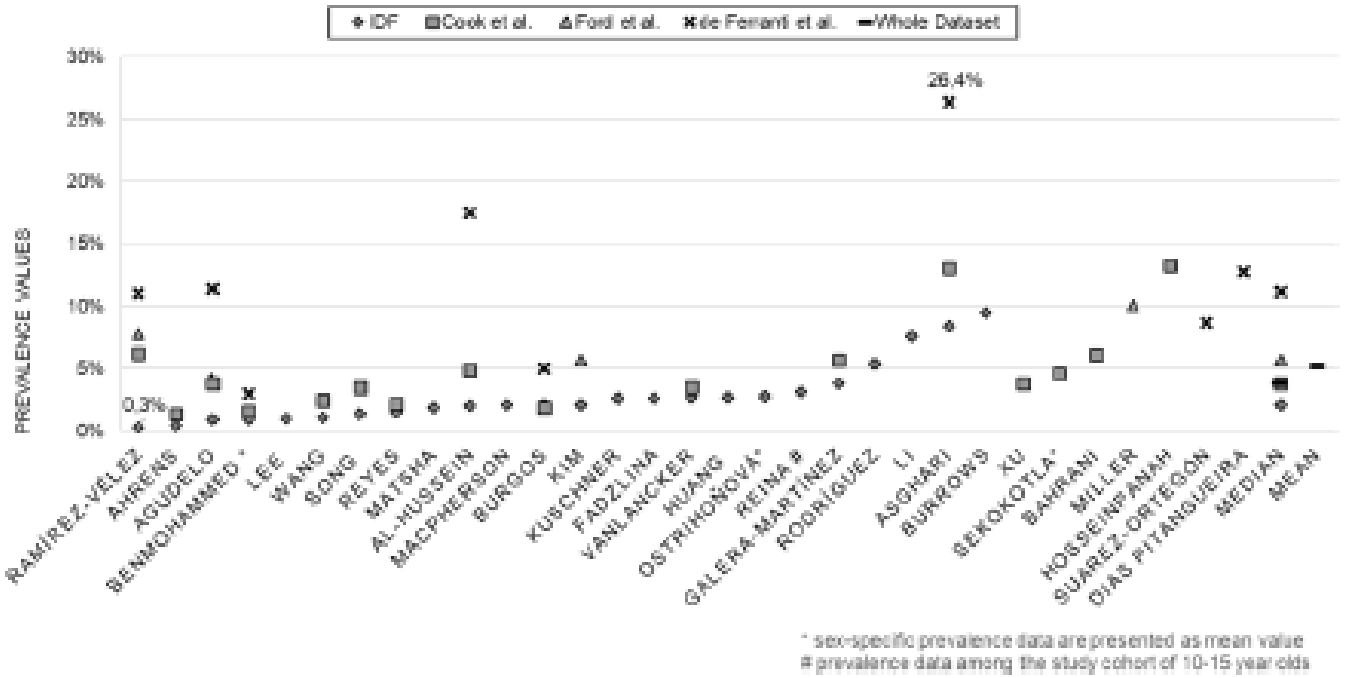


Fig. 2 Prevalence of metabolic syndrome based on the definitions from the IDF, Cook et al. [6], Ford et al. [26] and de Ferranti et al. [27]. Minimum: 0.3% in Colombia [32], maximum: 26.4% in Iran [33], mean value of the whole dataset: 5.2%, median value of the whole dataset: 3.8%.

International Journal of Obesity (2021) 45:12–24
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REVIEW ARTICLE

Pediatrics

The prevalence of pediatric metabolic syndrome—a critical look on the discrepancies between definitions and its clinical importance

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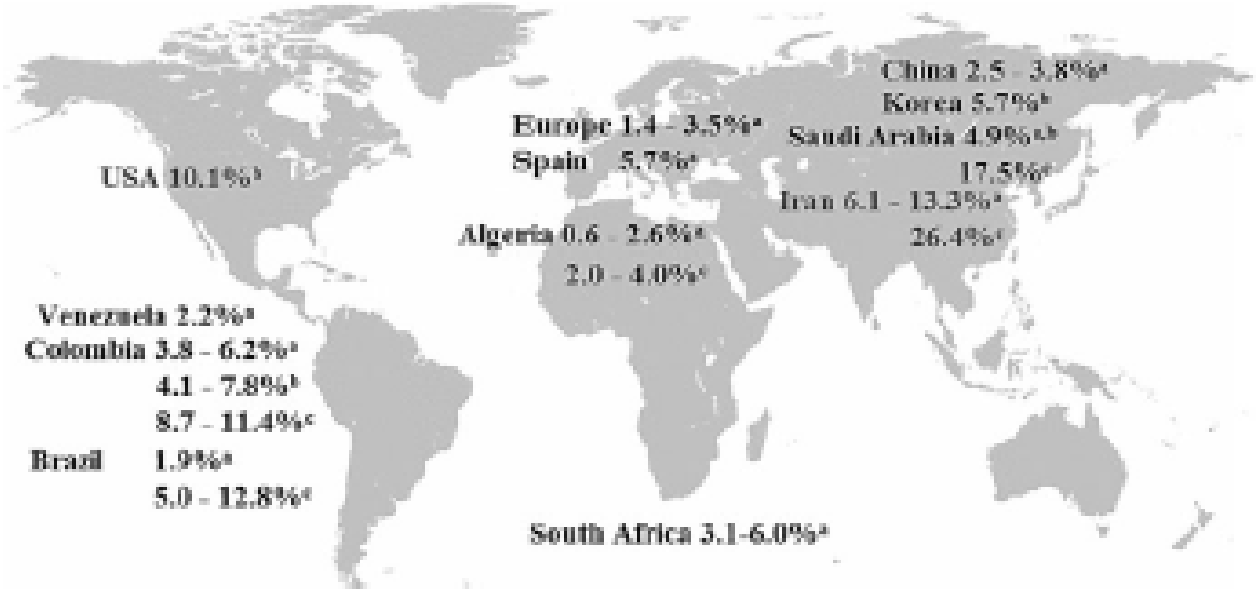
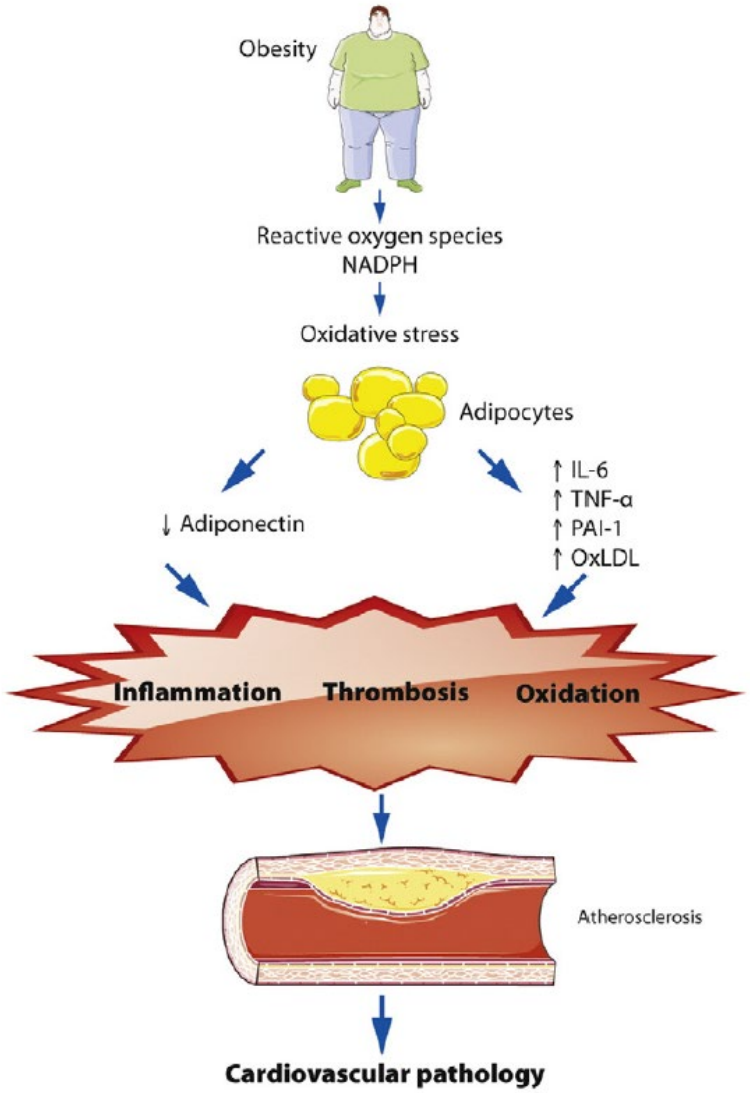


Fig. 4 Prevalence of metabolic syndrome in children and adolescents according to the definitions proposed by Cook et al. [6], Ford et al. [26], and de Ferranti et al. [27]. The prevalence is shown as a percentage range and is depicted for selected countries.

Pathophysiology of the metabolic syndrome

Emma McCracken, MRCP (UK) [a], Monica Monaghan, MBBCh, BAO, BSc, PhD, MRCP (UK) [b], Shiva Sreenivasan, FRCP Edin, FRCP [c,*]

- Positive family history[14]
- Smoking[15]
- Increasing age[16]
- Obesity[16]
- Low socioeconomic status[16]
- Mexican American ethnicity[16]
- Postmenopausal status[16]
- Physical inactivity[17]
- Sugary drink and soft drink consumption[18,19]
- Excessive alcohol consumption[20]
- Western dietary patterns[21]
- Low cardiorespiratory fitness[22]
- Excessive television watching[23]
- Use of antiretroviral drugs in human immunodeficiency virus infection[24]
- Atypical antipsychotic drug use (e.g. clozapine)[25]



Developmental origins of type 2 diabetes: Focus on epigenetics

Alexander Vaiserman[a,*], Oleh Lushchak[b]

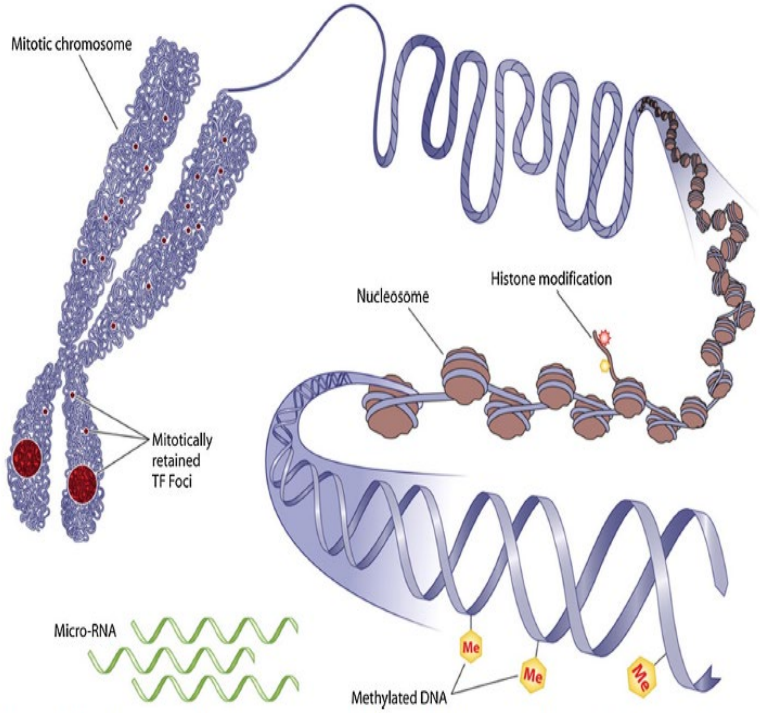


Fig. 2. Mechanisms of inheritable epigenetics. Mammalian gene expression is tightly controlled by genetic as well as epigenetic mechanisms. Epigenetics modifies the phenotype without altering the genotype of a cell. Shown here are some well-defined epigenetic mechanisms that include histone modifications, DNA methylation, and the noncoding RNA-mediated modulation of gene expression. Some of these mechanisms are inheritable through successive cell divisions and contribute to the maintenance of cellular phenotype. Recent studies show that the association of components of transcriptional regulatory machinery with target genes on mitotic chromosomes is a novel epigenetic mechanism that poises genes involved in key cellular processes, such as growth, proliferation, and lineage commitment, for expression in progeny cells. Fig. 2 and its legend are reproduced from Zaidi et al. (2010) with permission from the American Society for Microbiology.

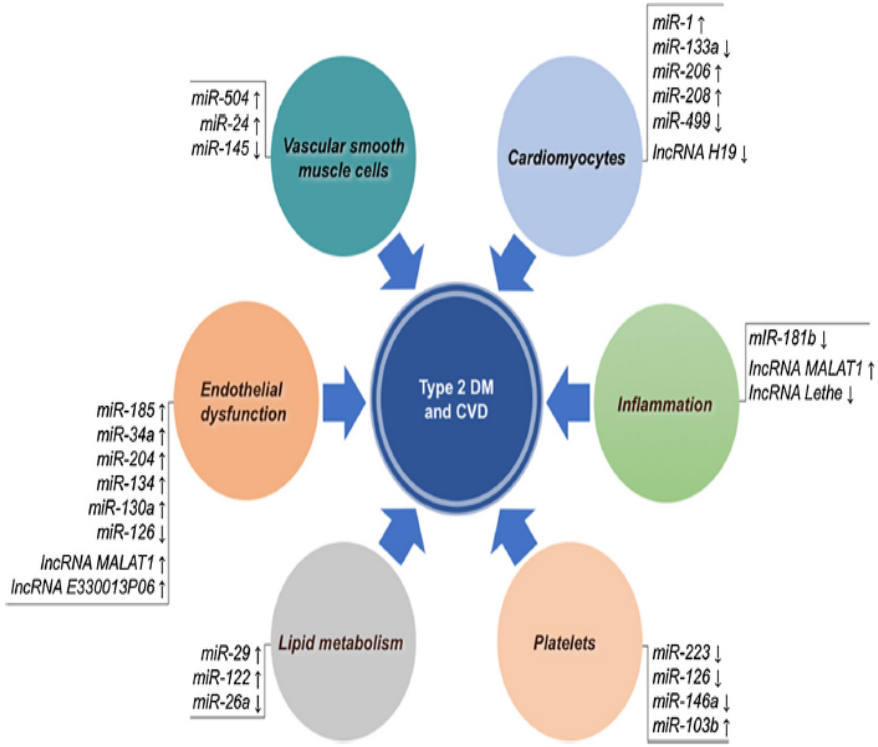


Fig. 3. Non-coding RNAs associated with both type 2 diabetes mellitus (DM) and cardiovascular disease (CVD). MicroRNAs (miRNAs) and long non-coding RNAs (lncRNAs) are grouped according to their main biological mechanism involved in atherosclerotic CVD. Arrows indicate overexpression (↑) or underexpression (↓). Fig. 3 and its legend are reproduced from De Rosa et al. (2018) with permission from the authors.

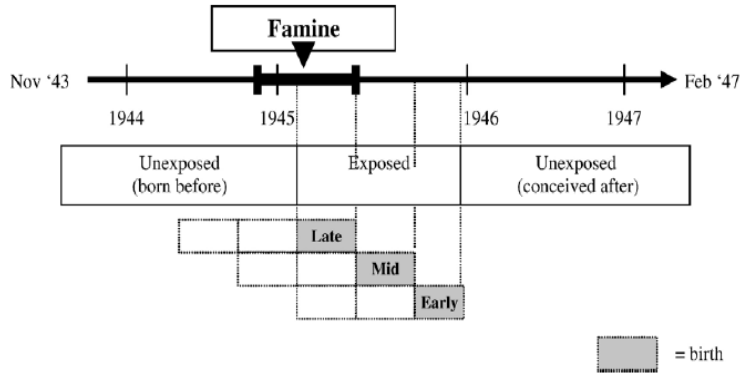
MODELLI UMANI DI DM2

- Gemelli monozigoti: stesso environment intrauterino, differente peso alla nascita → difetto di metilazione?
- Diabete gestazionale: rischio 3.7 volte > di DM2, < livelli di PPAR-γ, < espressione di adiponectina e resistina
- Ridotto apporto calorico materno: metilazione gene IGF2, IL10, LEP-MEG3, GNAS,
- Mese di nascita condiziona esposizione al sole, Vit. D, infezioni, melatonina:
  - Nascita gennaio-giugno: > rischio obesità
  - Nascita in autunno inverno: > ipometilazione gene LINE-1 → rischio di DM2
  - Gravidanza mesi caldi: > rischio diabete gestazionale

The Dutch famine and its long-term consequences for adult health

Tessa Roseboom *, Susanne de Rooij, Rebecca Painter

Department of Clinical Epidemiology Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam,



Exposure to famine		
In **late** gestation	In **mid** gestation	In **early** gestation
Glucose intolerance	Glucose intolerance	Glucose intolerance
	Microalbuminuria	Atherogenic lipid profile
	Obstructive airways disease	Altered blood coagulation
		Obesity (women only)
		Stress sensitivity
		Coronary heart disease
		Breast cancer

Figure 2 Long-term consequences of exposure to famine according to timing during gestation.

Early Human Development (2006) 82, 485–491

Youth-Onset Type 2 Diabetes: The Epidemiology of an Awakening Epidemic

Wei Perng,[1,2] Rebecca Conway,[1] Elizabeth Mayer-Davis,[3] and Dana Dabelea[1,2,4]

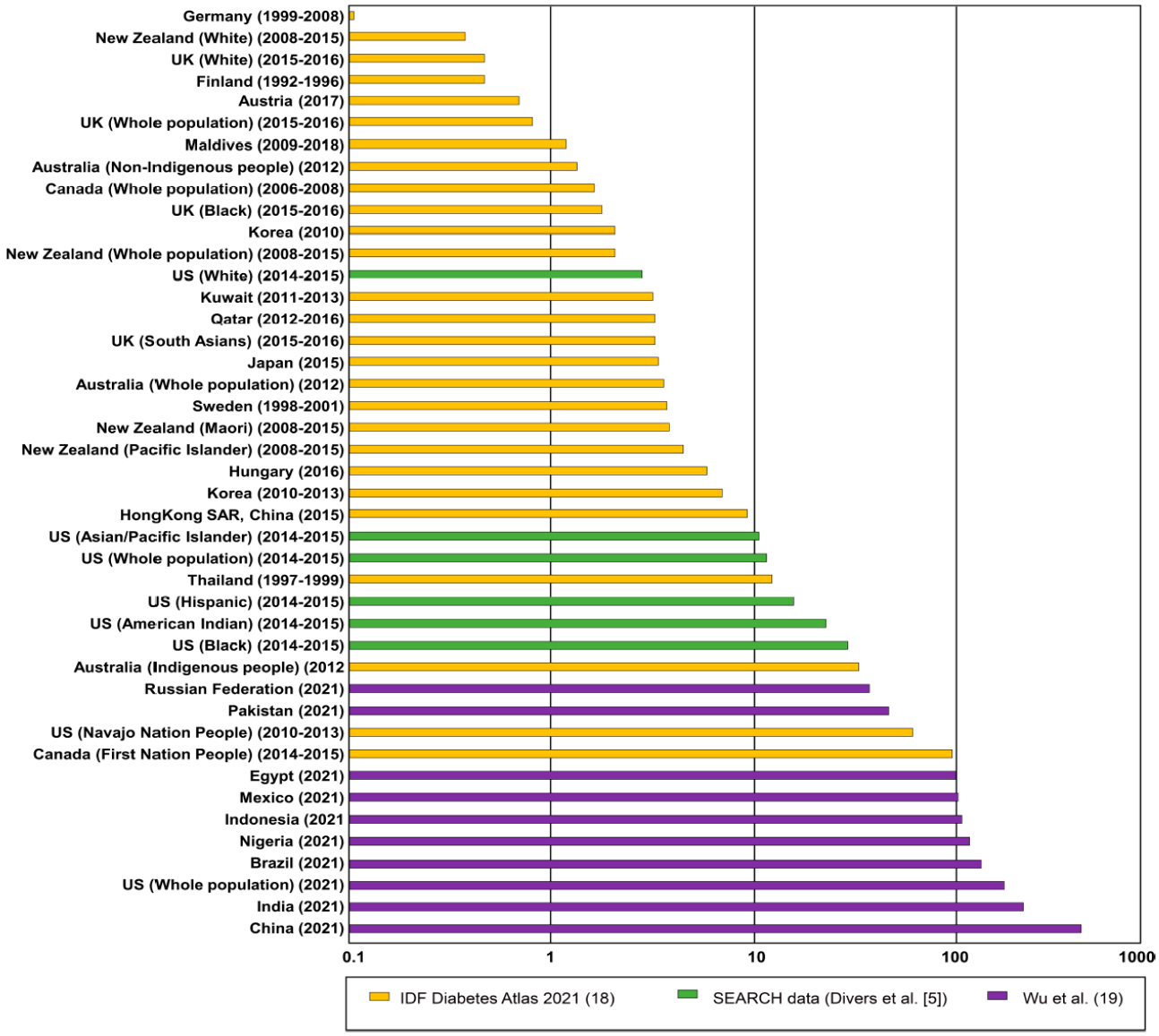
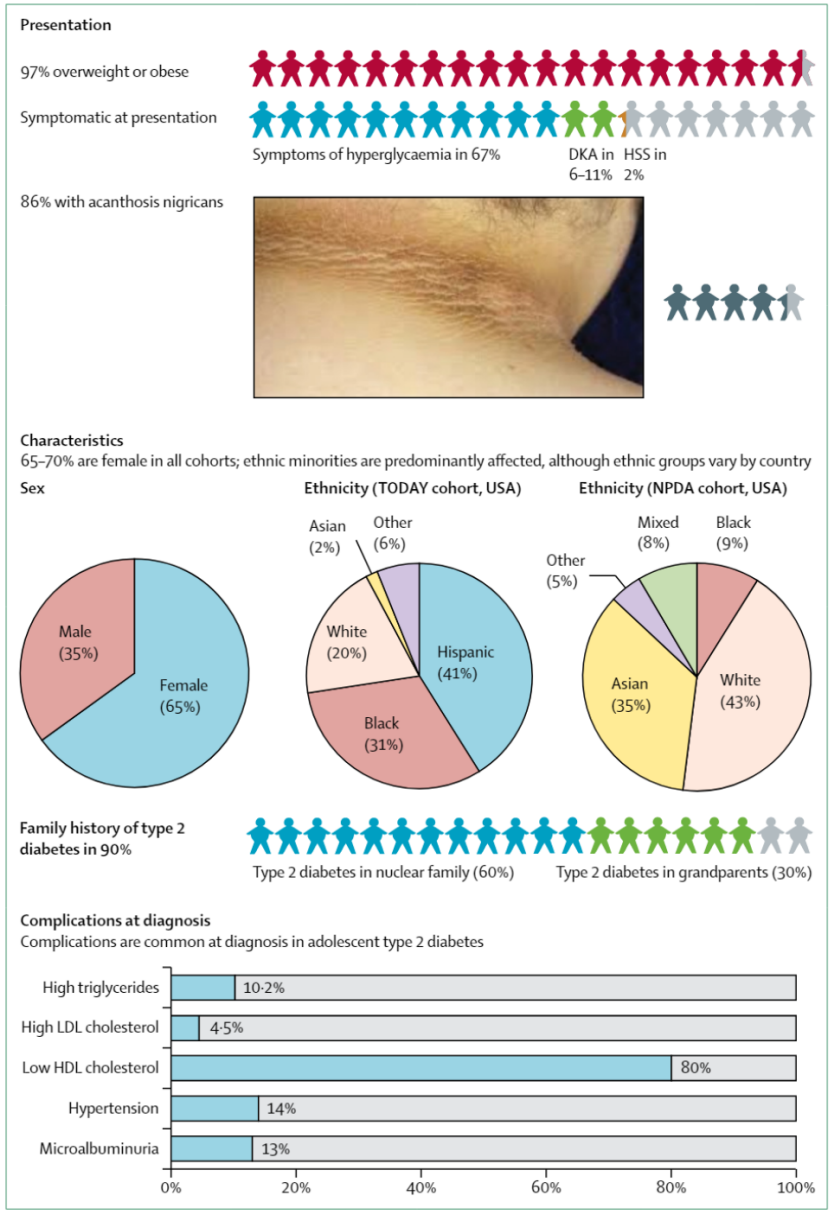


Figure 2—Global incidence of type 2 diabetes among children and adolescents (age <20 years), per 100,000.

Type 2 diabetes in adolescents: a severe phenotype posing major clinical challenges and public health burden

Russell Viner, Billy White, Deborah Christie



Lancet 2017; 389: 2252–60

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DOI: 10.1111/pedi.13409

ISPAD GUIDELINES

WILEY

ISPAD Clinical Practice Consensus Guidelines 2022: Type 2 diabetes in children and adolescents

Amy S. Shah[1] | Philip S. Zeitler[2] | Jencia Wong[3] | Alexia S. Pena[4] | Brandy Wicklow[5] | Silva Arslanian[6] | Nancy Chang[7] | Junfen Fu[8] | Preeti Dabadghao[9] | Orit Pinhas-Hamiel[10] | Tatsuhiko Urakami[11] | Maria E. Craig[12,13]

TABLE 1 Risk based screening for T2D in Children and Adolescents

Screening tests in youth should be considered after the onset of puberty or age 10 years, whichever is earlier, in youth with BMI≥85th percentile for age and sex with one or more of the following:
• Family history of T2D in the first- or second-degree relative.
• Race/ethnicity (Black, Native American, African, Latin American, Asian, Middle Eastern Pacific Islander, Australian Indigenous, Canadian First Nations).
• Signs of insulin resistance (acanthosis nigricans, HTN, dyslipidemia, polycystic ovary syndrome), low birth weight (small for gestational age) or high birth weight.
• Maternal history of T2D or gestational diabetes during the child's gestation.
• Current use of weight promoting atypical antipsychotic agents.[74–78]

TABLE 2 Diagnosis of pre-diabetes in Children and Adolescents

Diagnosis	Laboratory values
Impaired fasting glucose (IFG)	Fasting plasma glucose (FPG) 100–125 mg/dl (5.6–6.9 mmol/L)
Impaired glucose tolerance (IGT)	2-h plasma glucose is >140–199 mg/dl (7.8–11.0 mmol/L) after an OGTT (after 1.75 g/kg (max 75 g) anhydrous glucose dissolved in water).
Elevated A1c	HbA1c 5.7%–6.4% (39–47 mmol/mol) obtained from a laboratory based, diabetes control and complications trial (DCCT) aligned, National Glycohemoglobin Standardization Program certified methodology.

[a]Hyperglycaemic symptoms include polyuria, polydipsia, nocturia, unexplained weight loss and general fatigue. In the absence of

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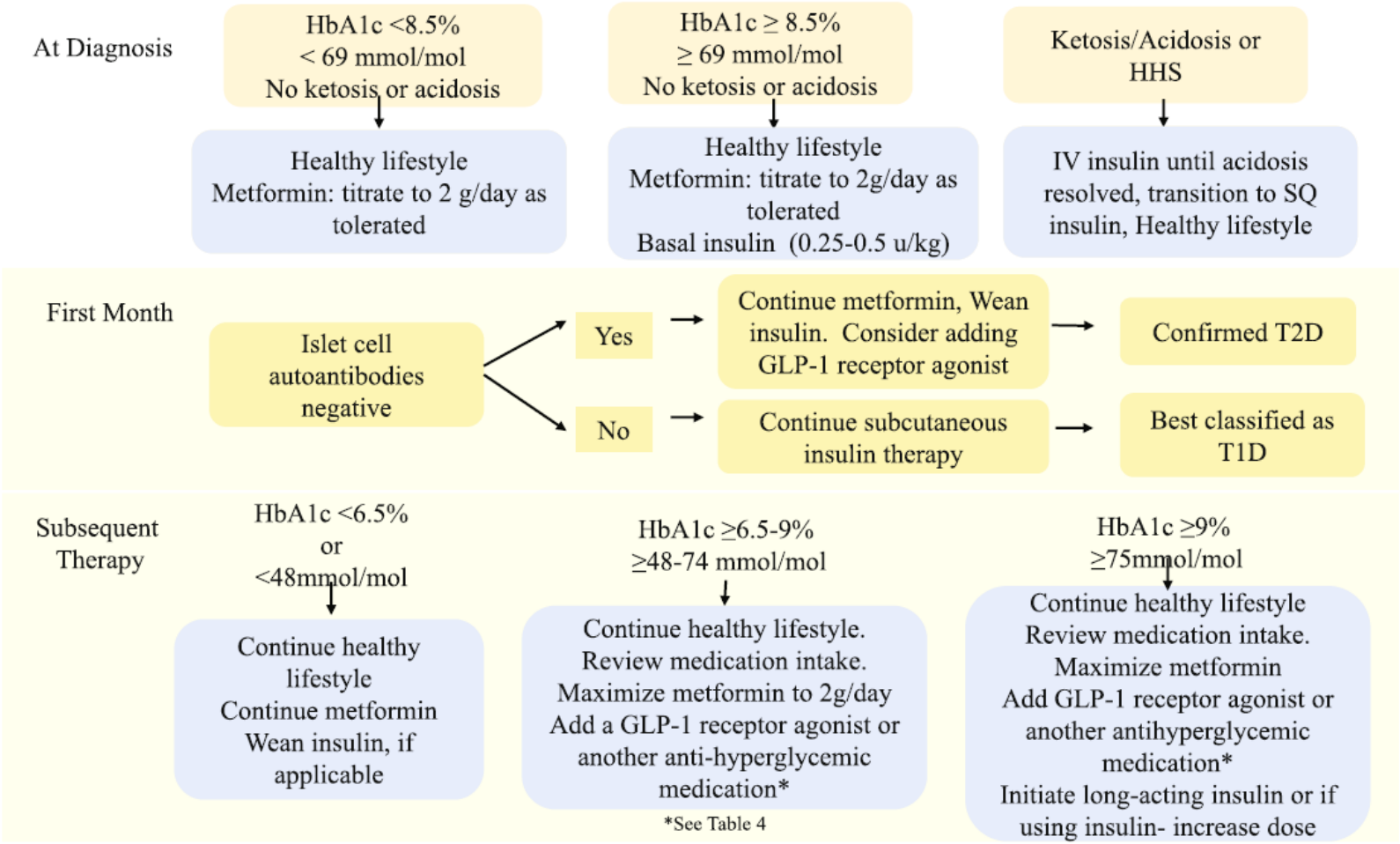
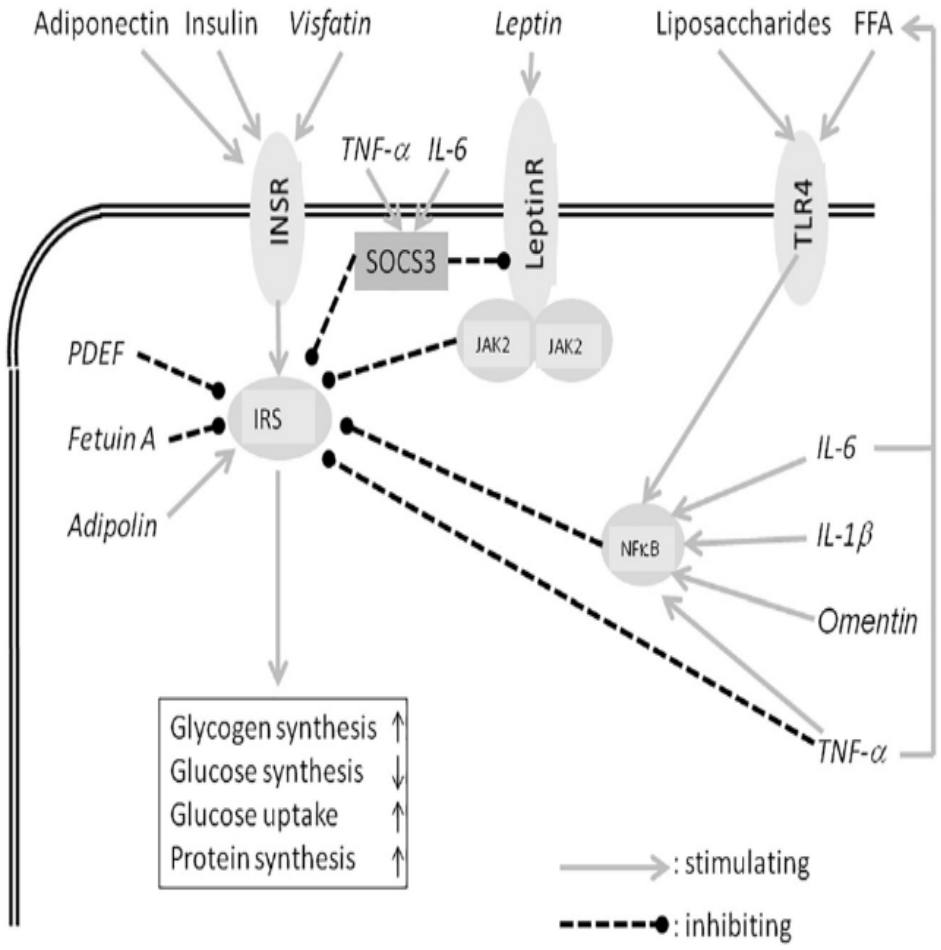


FIGURE 1 Management of T2D in Children and Adolescents. Initial management and subsequent therapy. Adapted from ADA Position Statement "Evaluation and Management of Youth-Onset Type 2 Diabetes". GLP-1, glucagon like peptide-1.

Inflammatory markers in children and adolescents with type 2 diabetes mellitus

Thomas Reinehr



Clinica Chimica Acta 496 (2019) 100–107

The changing face of diabetes in youth: lessons learned from studies of type 2 diabetes

Tamara S. Hannon[1] and Silva A. Arslanian[2]

Table 3. Complications and cardiovascular risk in youth T2D in the TODAY trial at baseline and follow- up[158,159,161]

	Prevalence (%)
Hypertension	
Baseline	11.6
End of study	33.8
Microalbuminuria	
Baseline	6.3
End of study	16.6
LDL ≥130 mg/dL or LLM	
Baseline	4.5
Month 36	10.7
Triglycerides ≥150 mg/dL or LLM	
Baseline	21.0
Month 36	23.3
hsCRP > 0.3 mg/dL	
Baseline	41.2
Month 36	46.3
Retinopathy	
At diabetes duration of 4.9 ± 1.5 year	13.7

LLM, lipid-lowering medication.

Ann. N.Y. Acad. Sci. 1353 (2015) 113–137 © 2015

Global burden of type 2 diabetes in adolescents and young adults, 1990-2019: systematic analysis of the Global Burden of Disease Study 2019

Jinchi Xie,[1,2] Maoqing Wang,[3] Zhiping Long,[1] Hua Ning,[3] Jingkuo Li,[1] Yukun Cao,[1] Yunfei Liao,[4] Gang Liu,[5] Fan Wang,[1] An Pan[2]

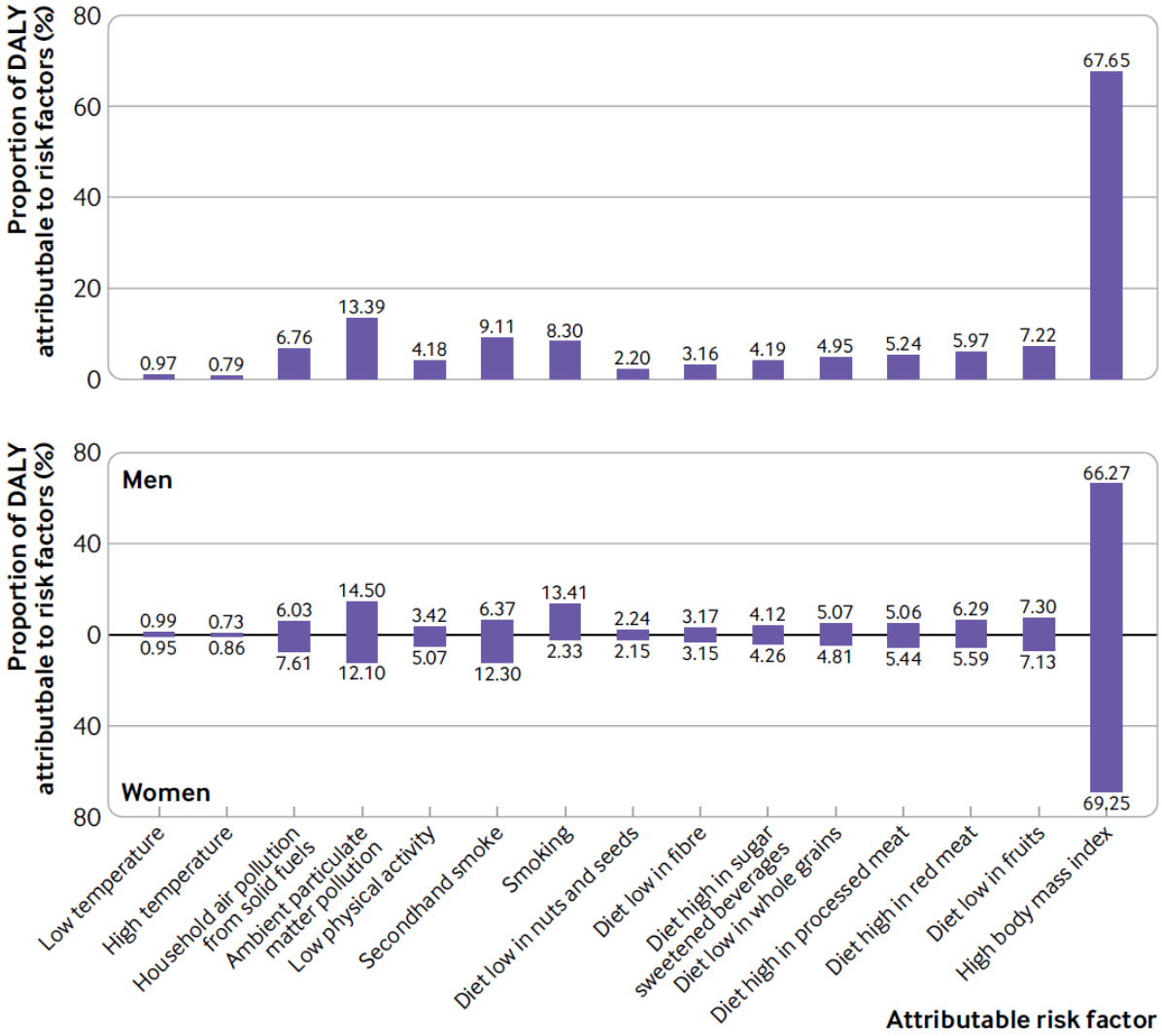


Fig 5 | Proportion of early onset type 2 diabetes disability adjusted life years (DALY) attributable to 15 risk factors globally (top) and classified by sex (bottom) in 2019

N Engl J Med. 2021 July 29; 385(5): 416–426. doi:10.1056/NEJMoa2100165.

Long-Term Complications in Youth-Onset Type 2 Diabetes

TODAY Study Group*

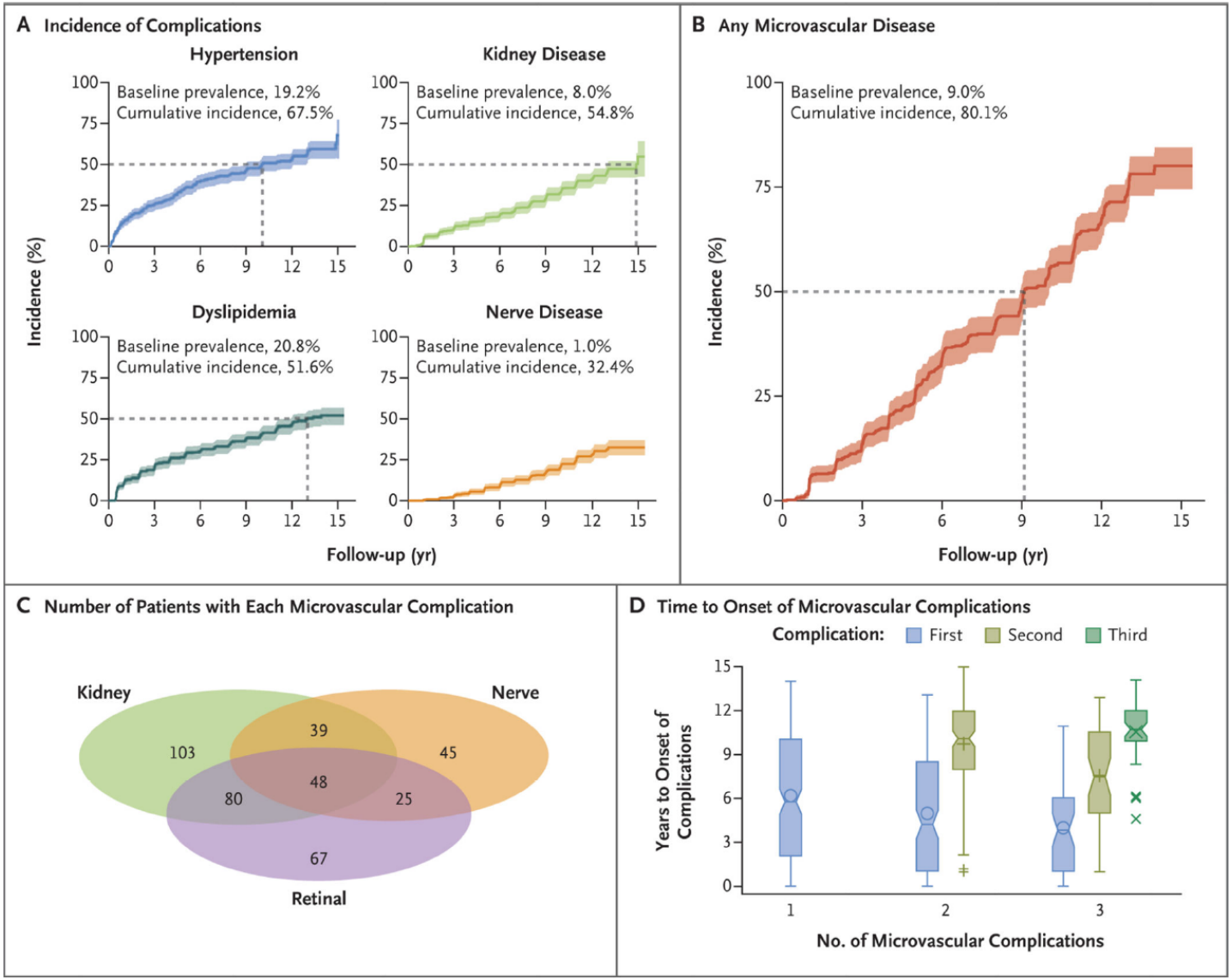


Figure 2. Diabetes-Related Complications That Occurred during the Study.

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Reparto e DH

GRAZIE PER L'ATTENZIONE