

Il Diabete di Tipo 1: come sta cambiando l'epidemiologia e cosa ci suggeriscono le attuali Linee Guida

DIABETE TIPO 1

COME È CAMBIATO
IL TRATTAMENTO INSULINICO?

CATANIA | 24.25 MAGGIO 2019

AGOSTINO CONSOLI

DMSI & CeSI-MeT Università d'Annunzio – CHIETI
ITALY



Il Prof. Agostino Consoli dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Abbot, Astra Zeneca, Boheringer Ingelheim , Eli Lilly, Merck Sharp & Dhome, Menarini
Diagnostici, Novo-Nordisk, Sanofi-Aventis, Sigma-Tau, Takeda
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Diapositiva preparata da AGOSTINO CONSOLI e ceduta alla Società Italiana di Diabetologia.
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**Ringrazio sinceramente la SID per lo straordinario contributo alla mia
formazione culturale, scientifica e clinica.**

**Opinioni e giudizi espressi durante questa presentazione sono di mia esclusiva
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OUTLINE

- Epidemiology of T1DM (incidence, prevalence and temporal trends):
 - Results from large epidemiologic studies
- What can we learn from Epidemiology?
- Hypotheses explaining the increased incidence T1DM
- Take home message(s)

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Epidemiology of T1DM:

T1DM epidemiological projects:

- **DIAMOND**, Diabetes Mondial Project
- **EURODIAB**, The Epidemiology and Prevention
- **SEARCH**, The SEARCH for Diabetes in Youth

1990 – 1999

Child 1989 – 1994

112 Children 15 aa

43,014 US study

84 m Subjects < 20 aa

incidence and prevalence of diabetes in youth by age, sex, and race/ethnicity

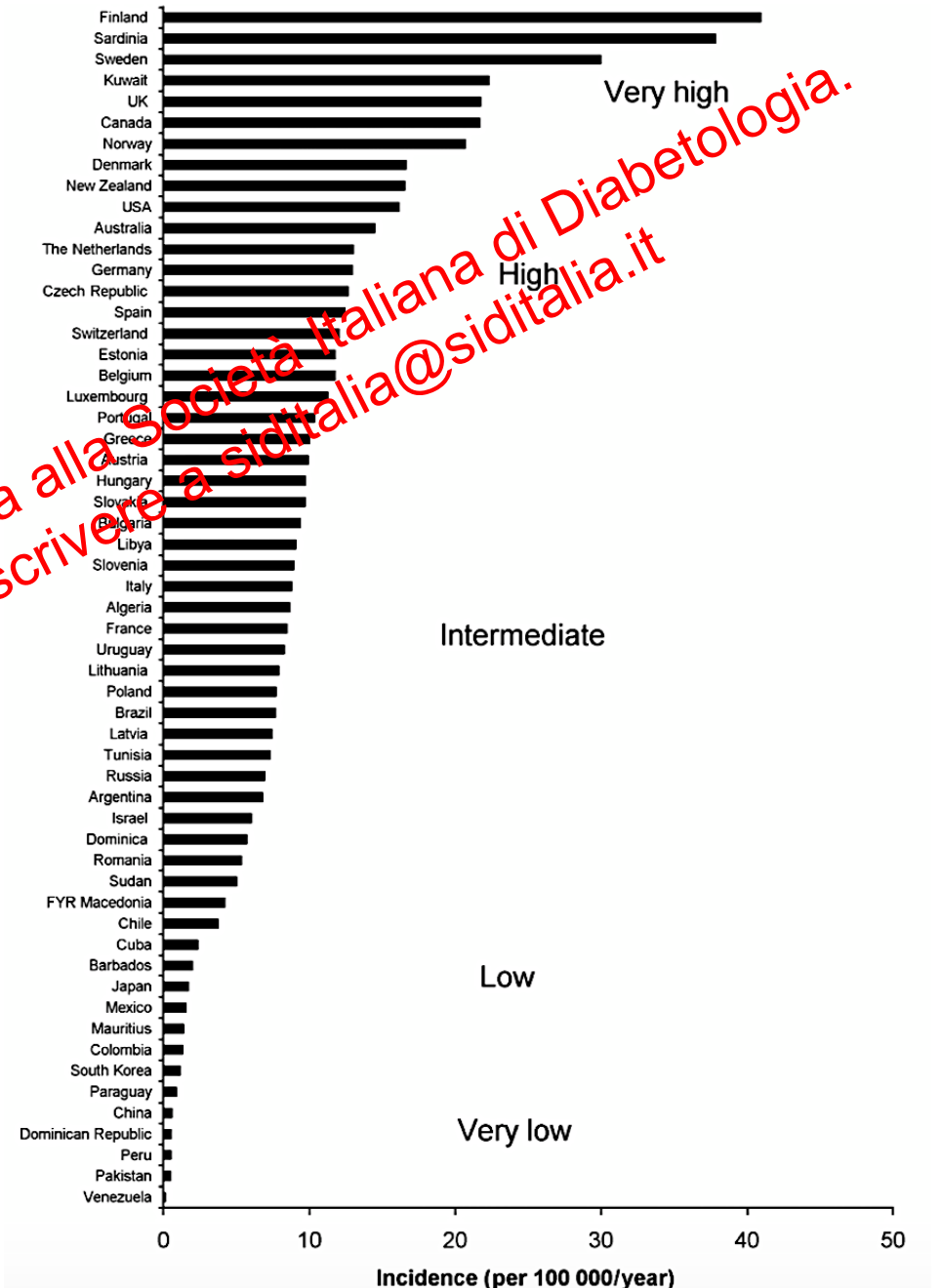
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Epidemiology of T1DM:

DIAMOND results

T1DM incidence varies tremendously among countries

- In most Asian populations:
 - <1 per 100.000/year
- In European populations:
 - From 4 per 100.000/year to 41 per 100.000/year
- In North American populations:
 - From 11 per 100.000/year to 25 per 100.000/year



Epidemiology of T1DM:

DIAMOND results

- The incidence increases with age
- No differences in age-group specific incidence between the genders

	Age group (years)	Risk ratio	95% CI
Boys*	0-4	1.00	
	5-9	1.52	(1.47; 1.58)
	10-14	1.94	(1.87; 2.01)
Girls	0-4	1.00	
	5-9	1.72	(1.66; 1.79)
	10-14	1.93	(1.86; 2.01)
Total†	0-4	1.00	
	5-9	1.62	(1.57; 1.66)
	10-14	1.94	(1.89; 1.98)

* Adjusted for centre.

† Adjusted for centre and sex.

Epidemiology of T1DM:

DIAMOND results

Continent	Total Age/ year*			0–4 years		5–9 years		10–14 years		P
	Trend %	95% CI	P	Trend %	95% CI	Trend %	95% CI	Trend %	95% CI	
Africa	3.0	(0.3; 5.8)	0.029	0.9	(–5.6; 7.4)	9.2	(3.8; 14.9)	0.6	(–3.0; 4.3)	0.154
Asia	4.0	(1.8; 6.2)	<0.001	1.3	(–3.5; 6.2)	5.0	(1.4; 8.8)	5.1	(1.8; 8.5)	0.238
Europe	3.2	(2.7; 3.6)	<0.001	4.7	(3.9; 5.6)	3.4	(2.7; 4.0)	2.2	(1.6; 2.8)	<0.001
North America	5.3	(3.3; 7.3)	<0.001	6.9	(2.4; 11.5)	4.7	(1.4; 8.1)	5.1	(2.3; 8.1)	0.674
South America	5.3	(2.8; 7.9)	<0.001	6.5	(1.2; 12.0)	9.2	(4.7; 13.9)	1.7	(–2.0; 5.6)	0.071
Central America and West Indies	–3.6	(–5.0; –2.1)	<0.001	–3.6	(–6.7; 0.3)	–4.2	(–6.5; –1.9)	–3.2	(–5.3; 1.0)	0.881
Oceania	3.2	(0.4; 6.9)	<0.001	11.1	(3.2; 19.6)	–0.6	(–6.4; 5.5)	2.1	(–3.3; 7.8)	0.042
All regions	2.8	(2.4; 3.2)	<0.001	4.0	(3.1; 4.9)	3.0	(2.4; 3.7)	2.1	(1.5; 2.7)	<0.001

The mean annual increase in incidence was **2.8 %** from 1990 to 1999:

Epidemiology of T1DM: EURODIAB results

Very wide range of incidence rates of T1DM within Europe

- From **3.2** cases per 100 000 per year in Macedonia to **40.2** cases per 100 000 in Finland
- High incidence rates in northern and north-western Europe and low in central, southern, and eastern Europe, except for Sardinia

Country	Region	Number of cases	Standardised incidence rate (95% CI) per 100 000*	Completeness of ascertainment (period)
Austria	Whole nation	753	9.1 (8.5–9.8)	99.7% (1991–94)
Belgium	Antwerp	112	11.6 (9.4–13.7)	98.7% (1989–94)
Bulgaria	Western	303	9.6 (8.5–10.7)	99.0% (1989–94)
	Eastern	218	6.8 (5.9–7.7)	99.0% (1989–94)
Croatia	Zagreb	83	6.8 (5.3–8.3)	100% (1989–94)
Czech Republic	Whole nation	1144	8.9 (8.3–9.4)	100% (1989–94)
Denmark	Four counties	221	10.0 (13.9–18.1)	99.2% (1991–94)
Estonia	Whole nation	206	10.3 (8.9–11.5)	100% (1989–94)
Finland	Two regions	425	40.2 (36.1–44.1)	100% (1992–93)
France	Four regions	837	5.5 (7.8–8.9)	99.0% (1991–94)
Germany	Düsseldorf	111	14.0 (11.4–16.6)	92.9% (1993–94)
	Baden-Württemberg	211	11.3 (10.6–12.0)	96.5% (1989–94)
Greece	Attica	333	9.5 (8.5–10.5)	100% (1993–94)
	Five northern regions	49	6.2 (4.5–8.0)	100% (1989–94)
Hungary	18 counties	822	8.9 (8.2–9.5)	99.6% (1989–94)
Iceland	Whole nation	52	13.5 (9.8–17.2)	100% (1989–94)
Israel	Whole nation	433	5.9 (5.3–6.4)	100% (1993)
Italy	Lombardia	530	7.0 (6.4–7.6)	NSSA
	Lazio	396	8.1 (7.3–8.9)	100% (1993–94)
	Sardinia	675	36.6 (33.9–39.4)	85.2% (1991–94)
	Eastern Sicily	150	11.4 (9.5–13.2)	98.3% (1991–94)
Latvia	Whole nation	221	6.6 (5.8–7.5)	99.7% (1993–94)
Lithuania	Whole nation	368	7.4 (6.6–8.1)	100% (1989–94)
Luxembourg	Whole nation	49	12.1 (8.7–15.5)	100% (1993–94)
Macedonia	Whole nation	93	3.2 (2.5–3.8)	100% (1989–94)
Netherlands	Five regions	421	13.0 (11.8–14.3)	95.9% (1991–94)
Norway	Eight counties	491	21.2 (19.3–23.1)	99.9% (1992–94)
Poland	Eight western provinces	542	6.7 (6.2–7.3)	100% (1991–94)
	Three cities	312	6.1 (5.4–6.8)	100% (1989–94)
	Gliwice	316	5.4 (4.8–6.0)	NSSA
	Bialystok§	31	5.5 (3.5–7.4)	100% (1994)
Portugal	Madeira	24	6.9 (4.1–9.6)	100% (1993–94)
	Portalegre	25	19.0 (11.5–26.5)	94.0% (1989–94)
	Algarve	51	13.6 (9.8–17.3)	85.1% (1991–94)
Romania	Bucharest	138	5.0 (4.1–5.8)	100% (1989–94)
Slovakia	Whole nation	656	8.4 (7.7–9.0)	100% (1989–94)
Slovenia	Whole nation	186	7.6 (6.5–8.7)	100% (1992–94)
Spain	Catalonia	839	12.3 (11.4–13.1)	98.4% (1991–94)
Sweden	Stockholm county	451	25.8 (23.4–28.2)	100% (1993–94)
Switzerland	Whole nation	353	7.9 (7.1–8.7)	NSSA
United Kingdom	Northern Ireland	462	19.6 (17.8–21.4)	98.6% (1989–94)
	Oxford	542	17.6 (16.1–19.1)	NSSA
	Leicester	169	15.9 (13.5–18.3)	100% (1989–93)
	Leeds	668	15.7 (14.5–16.9)	97.6% (1989–94)

NSSA=no secondary source of ascertainment. *Standardised for age and sex. †1993–94 only. ‡1989–93 only. §1994 only. ||1991–94 only.

Table 1: **Summary registration information for 44 EURODIAB centres**

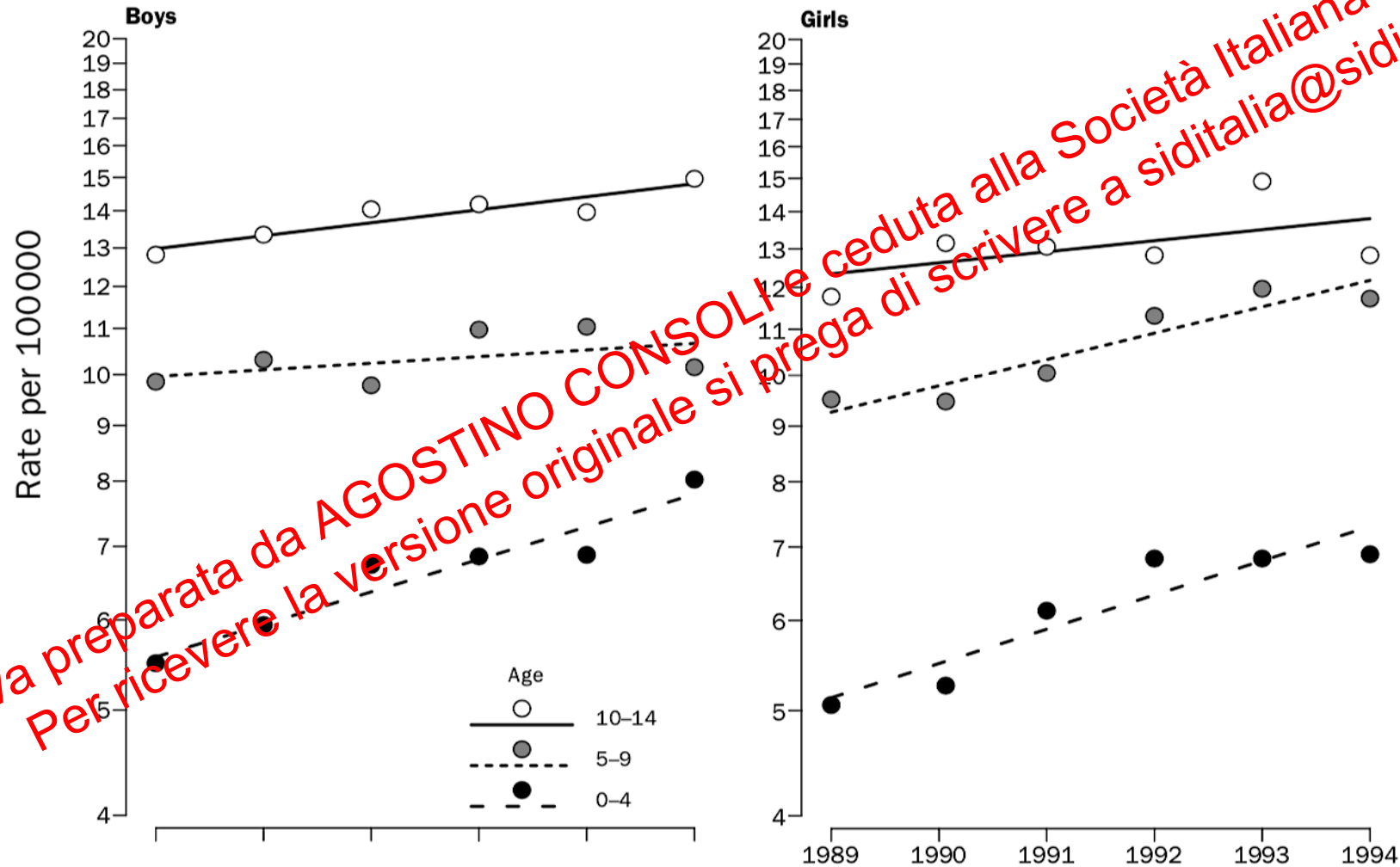
Epidemiology of T1DM: EURODIAB results

- The mean annual increase in incidence was:
 - 3.2 % from 1989 to 1999
 - 3.9 % from 1999 to 2003
- More rapid in some central European countries

Country	Risk ratio (95% CI) per year	p
Austria	1.08 (1.03–1.12)	0.0005
Belgium	1.10 (0.99–1.23)	0.09
Bulgaria (two centres)	1.05 (1.00–1.10)	0.06
Croatia	1.03 (0.91–1.17)	0.68
Czech Republic	1.08 (1.04–1.12)	0.0001
Denmark	0.91 (0.84–0.99)	0.02
Estonia	0.94 (0.96–1.12)	0.36
Finland	0.99 (0.93–1.04)	0.62
France	1.04 (1.00–1.09)	0.04
Germany	1.07 (1.03–1.10)	0.0004
Greece (two centres)	0.98 (0.93–1.04)	0.57
Hungary	1.07 (1.03–1.12)	0.0006
Iceland	0.99 (0.84–1.16)	0.88
Italy (three centres)	1.01 (0.97–1.04)	0.69
Italy (Sardinia)	1.01 (0.96–1.05)	0.78
Latvia	0.98 (0.90–1.05)	0.53
Lithuania	1.00 (0.94–1.06)	0.91
Luxembourg	1.04 (0.88–1.22)	0.68
Macedonia	1.01 (0.90–1.14)	0.84
Netherlands	1.02 (0.97–1.08)	0.47
Norway	0.99 (0.94–1.04)	0.67
Poland (three centres)	1.06 (1.03–1.10)	0.0006
Portugal (three centres)	1.13 (1.01–1.27)	0.04
Romania	1.03 (0.93–1.14)	0.57
Slovakia	1.09 (1.04–1.14)	0.0003
Slovenia	1.01 (0.93–1.10)	0.86
Spain	1.00 (0.96–1.04)	0.96
Sweden	1.03 (0.98–1.09)	0.25
United Kingdom (four centres)	1.02 (0.99–1.05)	0.14

Account has been taken of changes in age/sex structure of population.

Epidemiology of T1DM: EURODIAB results



Epidemiology of T1DM: SEARCH results

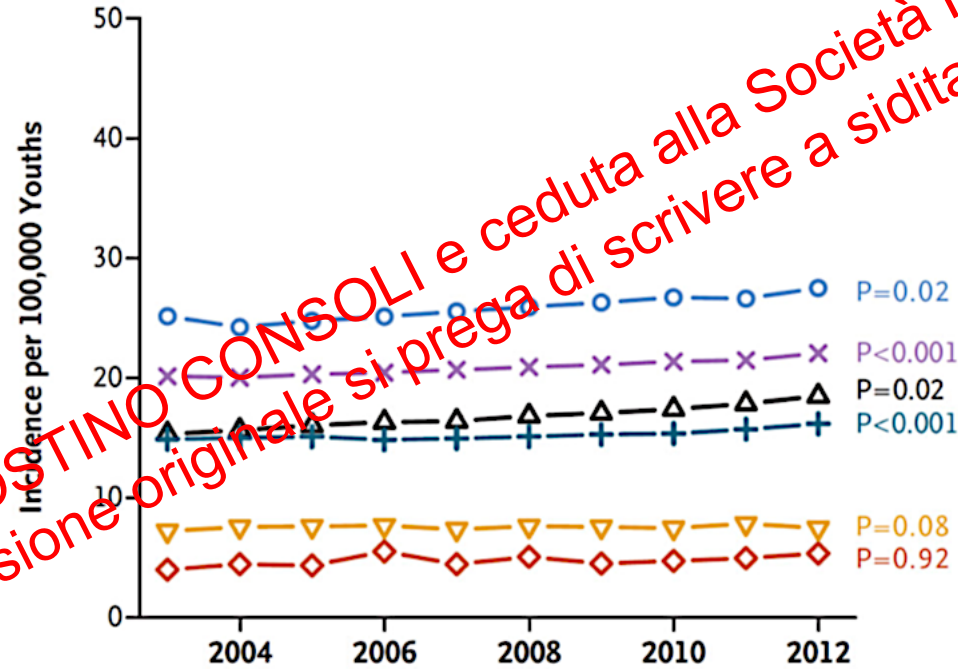
- Overall unadjusted estimated incidence rates of type 1 diabetes increased by **1.4%** annually from 2002 to 2012
- After adjustment for age, sex and race/ethnic group --> **1.8%**

Table 2. Type 1 Diabetes Incidence Rates, with the Use of 2-Year Moving Averages.*

Subgroup	Year										Unadjusted Model		Adjusted Model†	
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Annual Increase (95% CI) %	P Value	Annual Increase (95% CI) %	P Value
<i>no. of cases/100,000 youths/yr</i>														
All participants	19.5	19.1	19.9	20.8	21.4	22.0	22.0	20.4	20.5	21.7	1.4 (0.7 to 2.2)	0.03	1.8 (1.0 to 2.6)	<0.001
Age at diagnosis														
0–4 yr	16.5	16.1	14.6	14.6	14.3	14.2	14.6	16.4	14.0	14.9	–1.5 (–2.9 to –0.1)	0.03‡	–1.2 (–2.6 to 0.2)	0.10‡
5–9 yr	24.0	23.8	26.2	27.3	29.0	30.2	29.8	27.5	28.9	27.7	1.7 (0.0 to 3.4)	0.048	2.5 (1.1 to 3.9)	<0.001
10–14 yr	26.4	26.6	28.4	30.0	31.4	31.8	31.9	28.8	29.1	31.8	1.2 (–0.5 to 2.9)	0.17	2.1 (0.5 to 3.7)	0.009
15–19 yr	11.0	9.7	10.4	11.4	12.3	11.5	12.5	12.0	12.1	12.9	1.8 (0.2 to 3.4)	0.03‡	2.1 (0.5 to 3.6)	0.009‡
Sex														
Girls	19.5	19.1	19.3	19.7	20.7	21.6	21.6	19.7	19.5	19.9	0.7 (–0.9 to 2.3)	0.40	1.4 (0.3 to 2.5)	0.01
Boys	19.8	19.0	20.4	21.7	22.0	22.4	22.4	21.0	21.4	23.4	2.1 (0.7 to 3.5)	0.003	2.2 (1.3 to 3.1)	<0.001
Race or ethnic group														
Non-Hispanic white	23.9	23.5	24.2	25.2	26.3	27.4	27.5	25.4	25.3	27.0	0.8 (–0.5 to 2.2)	0.22	1.2 (0.2 to 2.2)	0.02
Non-Hispanic black	14.7	15.9	17.2	16.1	16.3	17.8	16.5	15.5	17.5	19.0	1.4 (–1.0 to 3.8)	0.27	2.2 (0.4 to 4.1)	0.02
Hispanic	13.7	12.2	13.9	16.1	16.4	16.1	16.9	16.2	15.2	14.8	3.7 (0.9 to 6.6)	0.009	4.2 (2.5 to 5.9)	<0.001
Asian or Pacific Islander	7.9	7.3	7.0	8.5	8.4	6.6	6.9	5.5	7.4	9.7	4.1 (–2.1 to 10.6)	0.20	3.7 (–0.5 to 8.1)	0.08
Native American	6.6	5.7	3.9	4.7	5.0	4.4	5.0	5.4	5.7	6.5	1.4 (–5.6 to 8.9)	0.71‡	0.4 (–6.5 to 7.7)	0.92
Study site														
South Carolina	16.8	16.6	17.7	17.6	18.8	20.4	19.9	19.1	19.0	18.6	1.4 (–0.4 to 3.3)	0.13	2.2 (0.6 to 3.8)	0.008
Ohio	24.7	27.1	25.0	23.3	23.8	24.4	24.2	25.1	25.8	26.1	0.7 (–0.9 to 2.3)	0.41‡	0.9 (–0.7 to 2.5)	0.27‡
Colorado	21.0	19.5	20.3	21.9	23.4	24.2	24.7	22.0	21.1	23.5	2.2 (–0.3 to 4.6)	0.08	1.6 (0.4 to 2.9)	0.01‡
California	14.5	13.9	16.5	18.0	17.4	16.4	16.7	16.8	16.1	16.4	0.9 (–1.4 to 3.2)	0.45	2.0 (0.2 to 3.8)	0.03
Washington	21.8	21.1	21.8	23.8	23.6	24.0	23.7	20.0	22.0	24.7	1.1 (–1.2 to 3.5)	0.36	1.5 (0.2 to 2.8)	0.02‡

Epidemiology of T1DM: SEARCH results

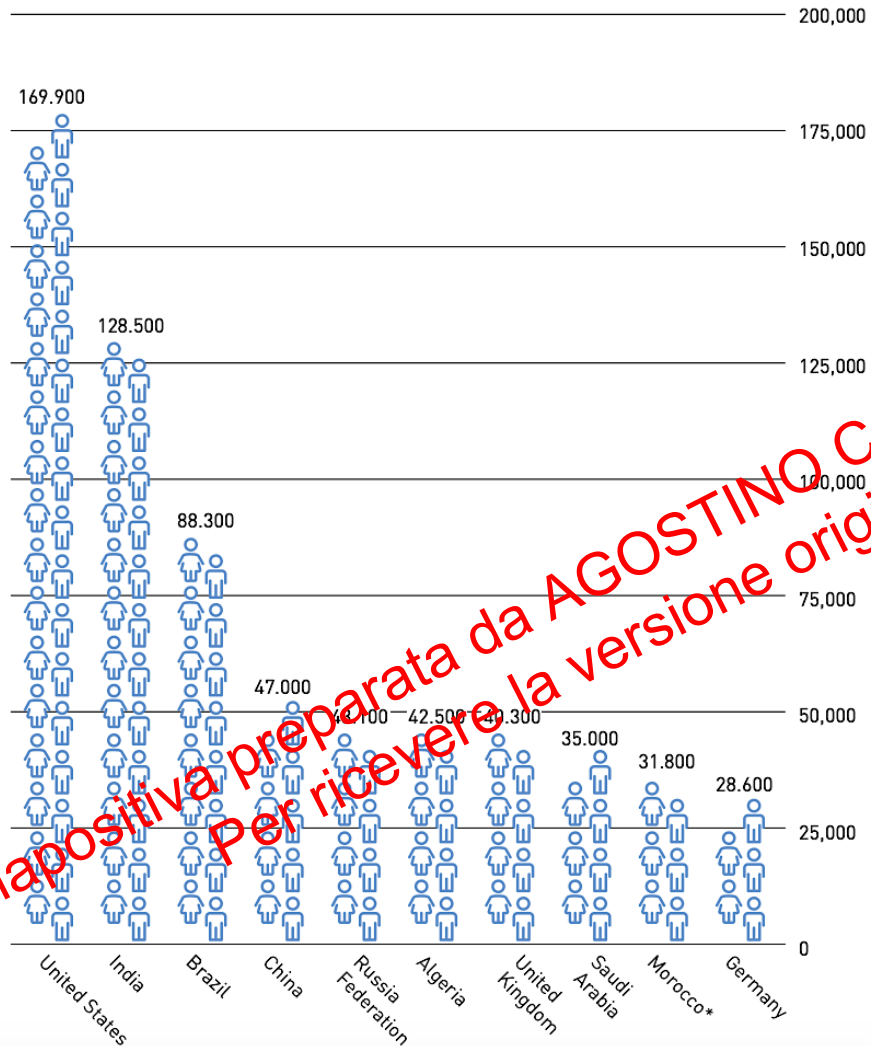
A Type 1 Diabetes, 0–19 Yr of Age



—x— All
—○— Non-Hispanic White
—△— Non-Hispanic Black
—+— Hispanic
—▽— Asian or Pacific Islander
—◇— Native American

Epidemiology of T1DM: IDF Atlas 2017

Top 10 countries for number of children and adolescents with type 1 diabetes (<20 years), 2017



75% of the children and adolescents with T1D

(<20 years) come from the top 3 countries"

Epidemiology of T1DM: IDF Atlas 2017

Table 3.16 Top 10 countries/territories for the incidence rates (per 100,000 population per year) with Type 1 diabetes (<20 years), 2017

Rank	Country	Incidence rates with type 1 diabetes
1	Finland	37.2
2	Kuwait	44.5
3	Sweden	39.5
4	Saudi Arabia	33.5
5	Norway	29.8
6	Algeria	26.0
6	Morocco	26.0
8	United Kingdom	25.9
9	Ireland	24.3
10	Denmark	23.0

*The data for Morocco is extrapolated from Algeria

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Incidence, prevalence, costs and quality of care of type 1 diabetes in Italy, age 0–29 years: The population-based CINECA-SID ARNO Observatory, 2002–2012

Table 1 Temporal trend in age- and sex-specific incidence of type 1 diabetes, age 0–29 years.

i. Males Incidence rates/100,000 (95% CI)				ii. Females Incidence rates/100,000 (95% CI)			
year	0–14 years	15–29 years	0–29 years	0–14 years	15–29 years	0–29 years	
2003	15.3 (11.3–20.8)	17.8 (13.7–23.1)	16.6 (13.6–20.3)	13.9 (9.9–19.1)	13.8 (10.2–18.5)	14.6 (11.7–18.3)	15.8 (13.0–19.3)
2004	19.4 (14.8–25.5)	16.2 (12.3–21.3)	17.7 (14.6–21.4)	19.0 (14.3–25.2)	11.6 (8.2–15.9)	19.2 (15.8–23.4)	13.9 (11.2–17.1)
2005	19.0 (14.8–22.5)	18.5 (14.5–23.5)	18.7 (15.7–22.3)	18.1 (13.9–23.6)	16.0 (12.1–20.5)	18.6 (15.5–22.3)	17.3 (14.4–20.6)
2006	14.4 (10.8–19.2)	15.2 (11.7–19.8)	14.8 (12.2–18.0)	13.6 (10.0–18.4)	18.5 (14.1–23.5)	14.0 (11.4–17.2)	16.7 (14.0–20.0)
2007	16.4 (12.6–21.4)	22.4 (18.0–27.8)	19.5 (16.5–23.1)	17.4 (13.3–22.6)	16.5 (12.5–21.0)	19.2 (16.1–22.8)	16.9 (14.0–20.4)
2008	16.4 (12.6–21.3)	22.6 (18.1–28.0)	19.6 (16.5–23.1)	13.6 (10.0–18.4)	14.7 (11.2–19.3)	14.2 (11.6–17.3)	15.0 (12.3–18.3)
2009	18.1 (14.3–22.9)	17.3 (13.7–21.8)	17.7 (15.0–20.8)	14.2 (10.9–18.7)	13.9 (10.7–18.0)	14.1 (11.7–17.0)	16.2 (13.6–19.4)
2010	17.8 (14.1–22.6)	20.1 (16.2–25.0)	19.0 (16.0–22.3)	16.2 (12.5–20.8)	18.2 (14.5–22.9)	17.2 (14.5–20.4)	17.0 (14.3–20.2)
2011	17.5 (13.4–21.9)	22.1 (18.2–26.0)	19.9 (17.1–23.0)	14.3 (11.1–18.6)	15.3 (12.1–19.4)	14.8 (12.4–17.7)	16.0 (13.5–18.9)
2012	15.7 (12.4–20.0)	19.2 (15.5–23.7)	17.5 (14.9–20.5)	13.7 (10.5–17.8)	14.2 (11.1–18.2)	13.9 (11.6–16.7)	14.7 (12.3–17.6)
P value*	0.91	0.66	0.28	0.33	0.55	0.57	0.57

* Cochran–Armitage test for trend.

ANNI 2003 - 2012

OVERALL RATE: 16.1/100.000 YA

MALES: 16.8

FEMALE 15.3

Age 0-14 : 15.8

Age 15-29: 16.3



Incidence, prevalence, costs and quality of care of type 1 diabetes in Italy, age 0–29 years: The population-based CINECA-SID ARNO Observatory, 2002–2012

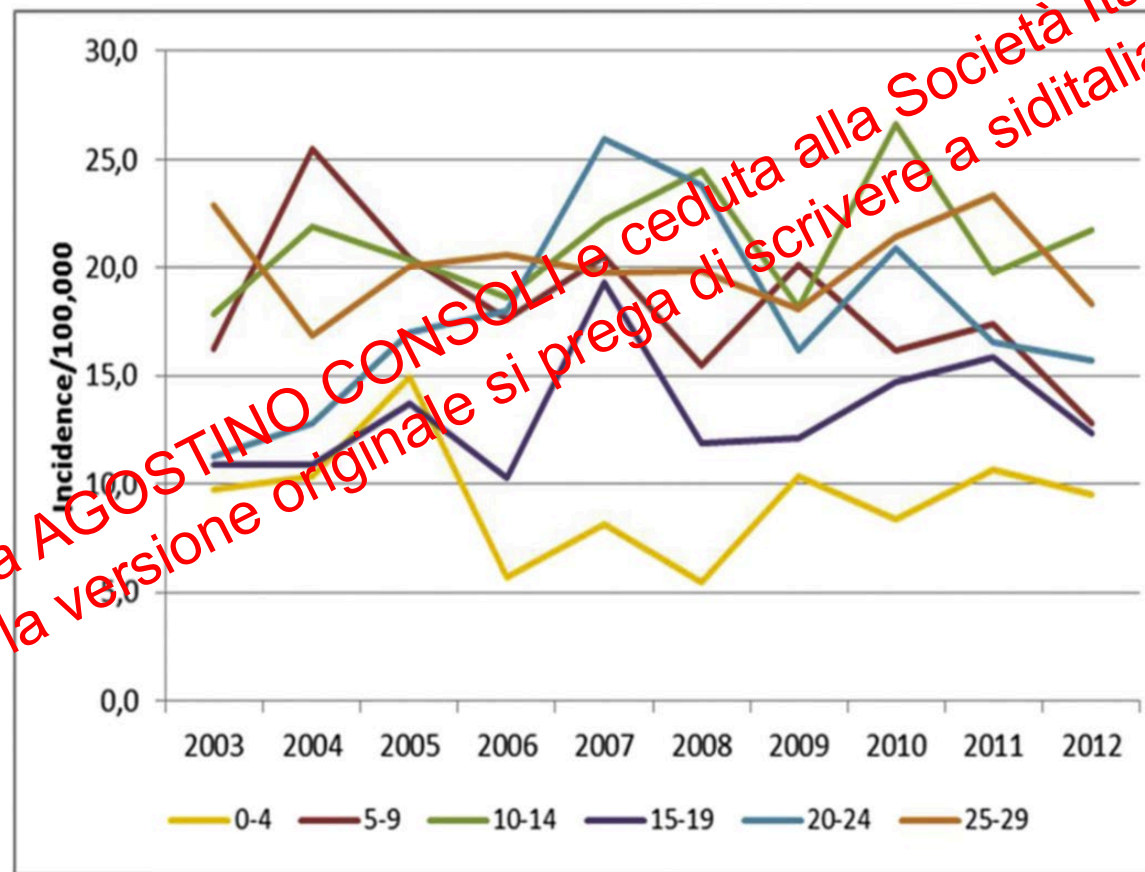


Figure 1 Incidence rates/100,000 person-years of type 1 diabetes by 5-year age group, 2003–2012, Italy.

Worldwide childhood type 1 diabetes incidence – what can we learn from epidemiology?

- Global and within-country variation:
 - Variation in genetic susceptibility
 - Environmental influences
 - Lifestyle factors
- Incidence increases from birth with a peak at puberty
- Rapid increase in the youngest (<5 years)
- No female bias
- Seasonality of onset, with a peak in winter

The changing epidemiology of type 1 diabetes: why is it going through the roof?

-THE HYGIENE HYPOTHESIS

-THE ROLE OF VIRUSES

-VITAMIN D DEFICIENCY

-EARLY LIFE FEEDING PATTERNS

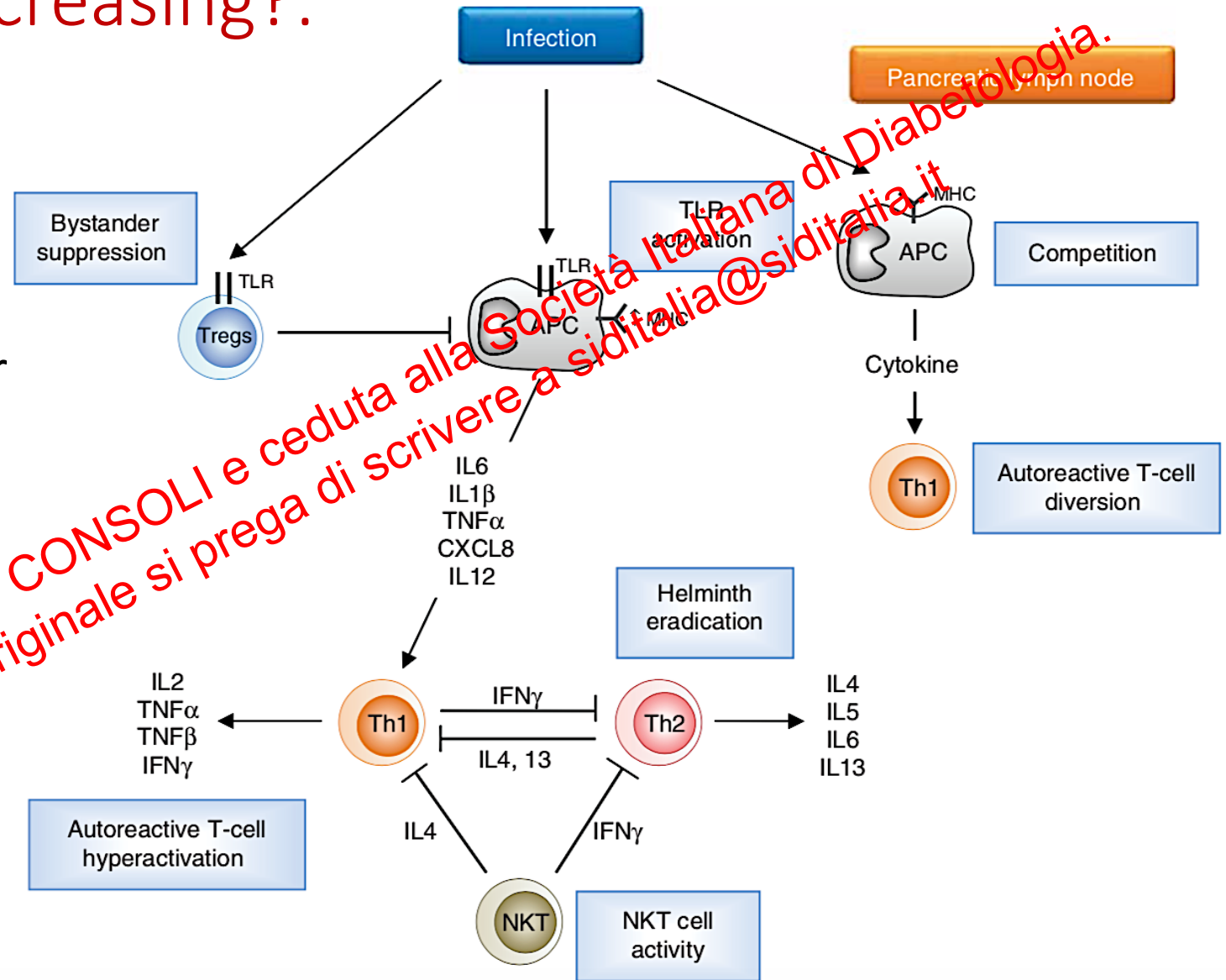
-GUT MICROBIOTA

-CHILDHOOD GROWTH PATTERNS.

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Why is type 1 diabetes increasing?: *The Hygiene hypothesis*

Reduced exposure to viruses or other infectious agents in early life may increase risk of T1D, due to an impairment in the maturation of the immune system



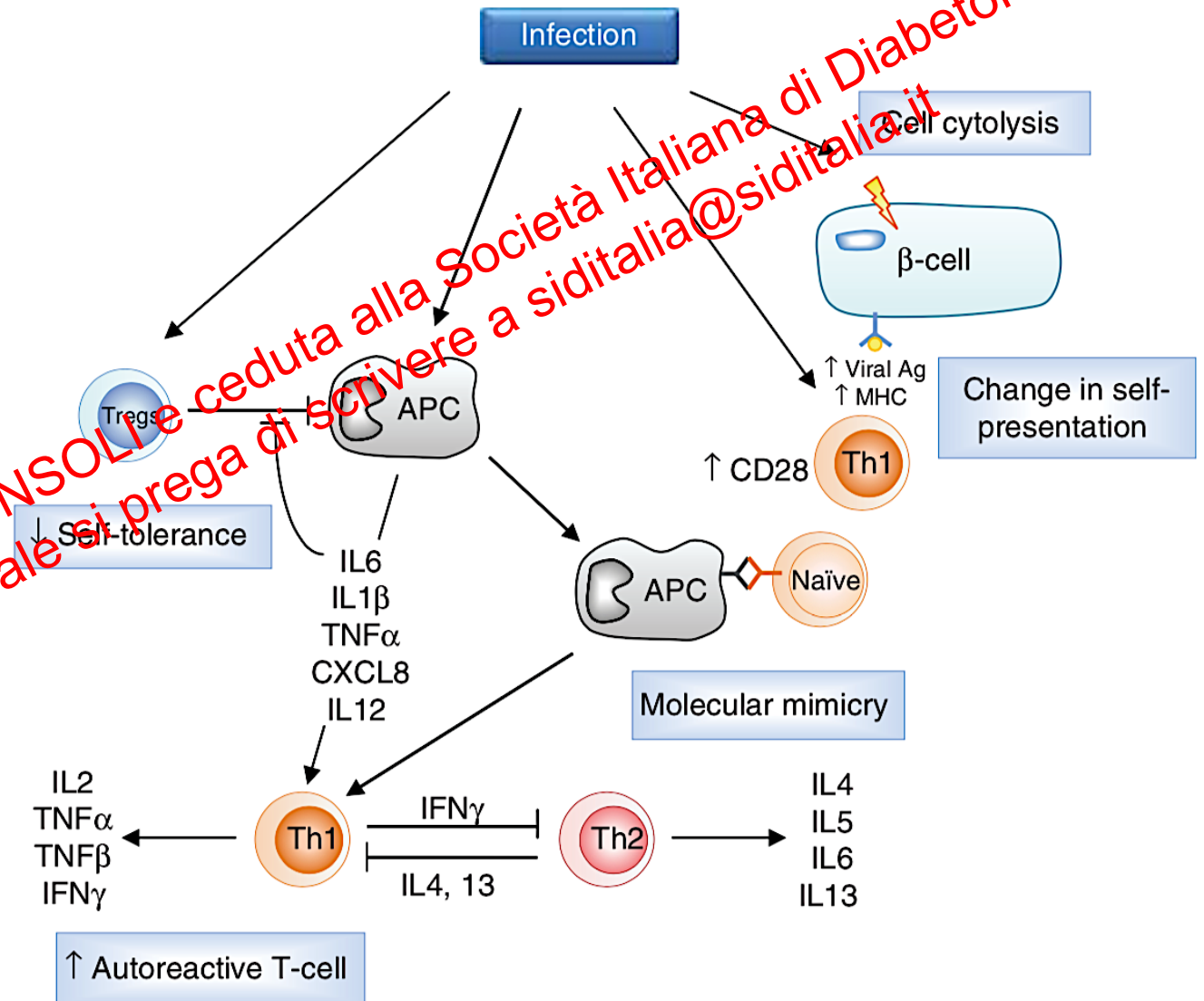
Why is type 1 diabetes increasing?:

The Viral hypothesis

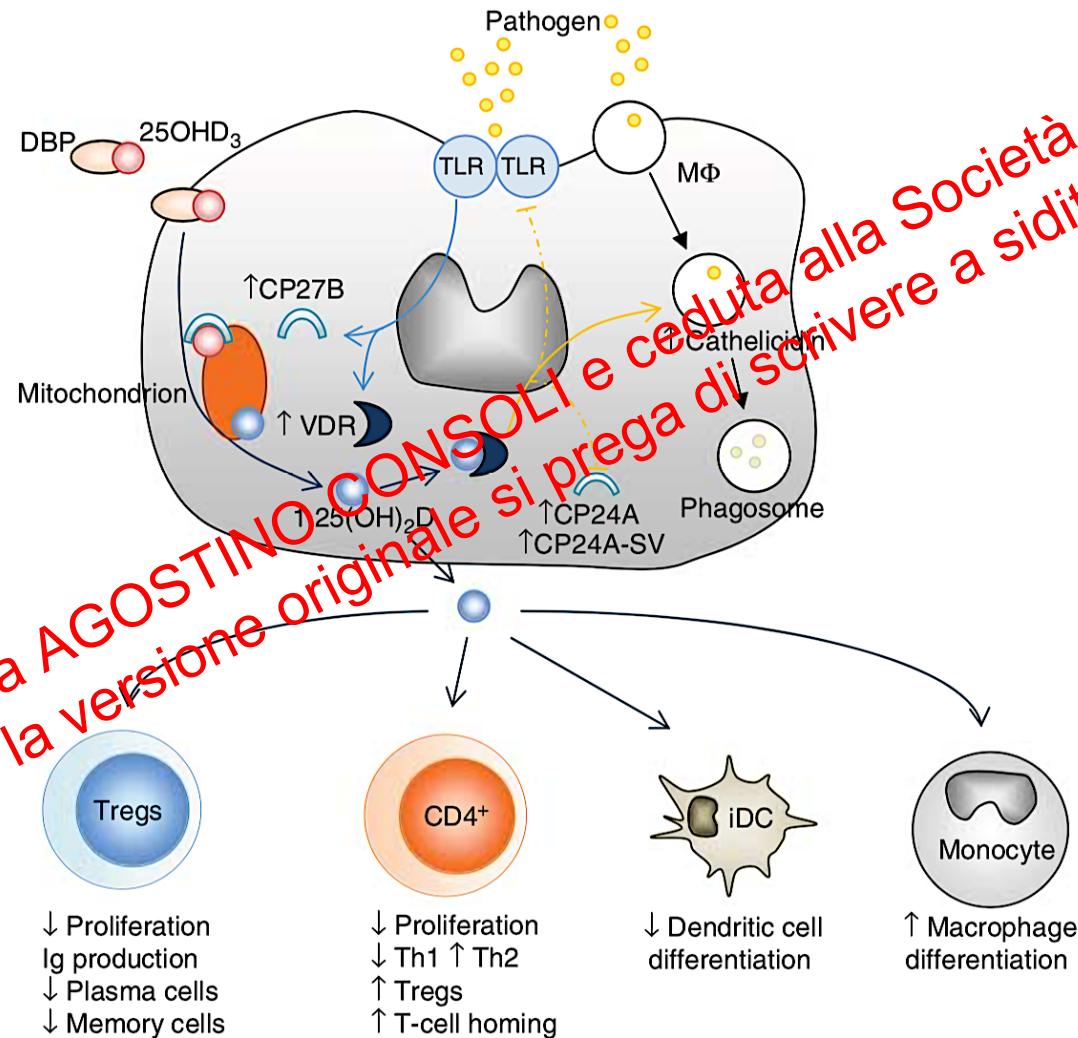
A variety of viruses including:

- Enterovirus
- rubella virus
- mumps virus
- Rotavirus
- Cytomegalovirus (CMV)

may initiate or accelerate the autoimmune process of type 1 diabetes



Why is type 1 diabetes increasing?: *The Vitamin D deficiency hypothesis*



Why is type 1 diabetes increasing?:

The Breast-feeding vs Cow's milk hypotheses

Breast milk hypothesis

- ↑ Oral tolerance – GHs and insulin
 - ↑ Protective effect by cytokines
-

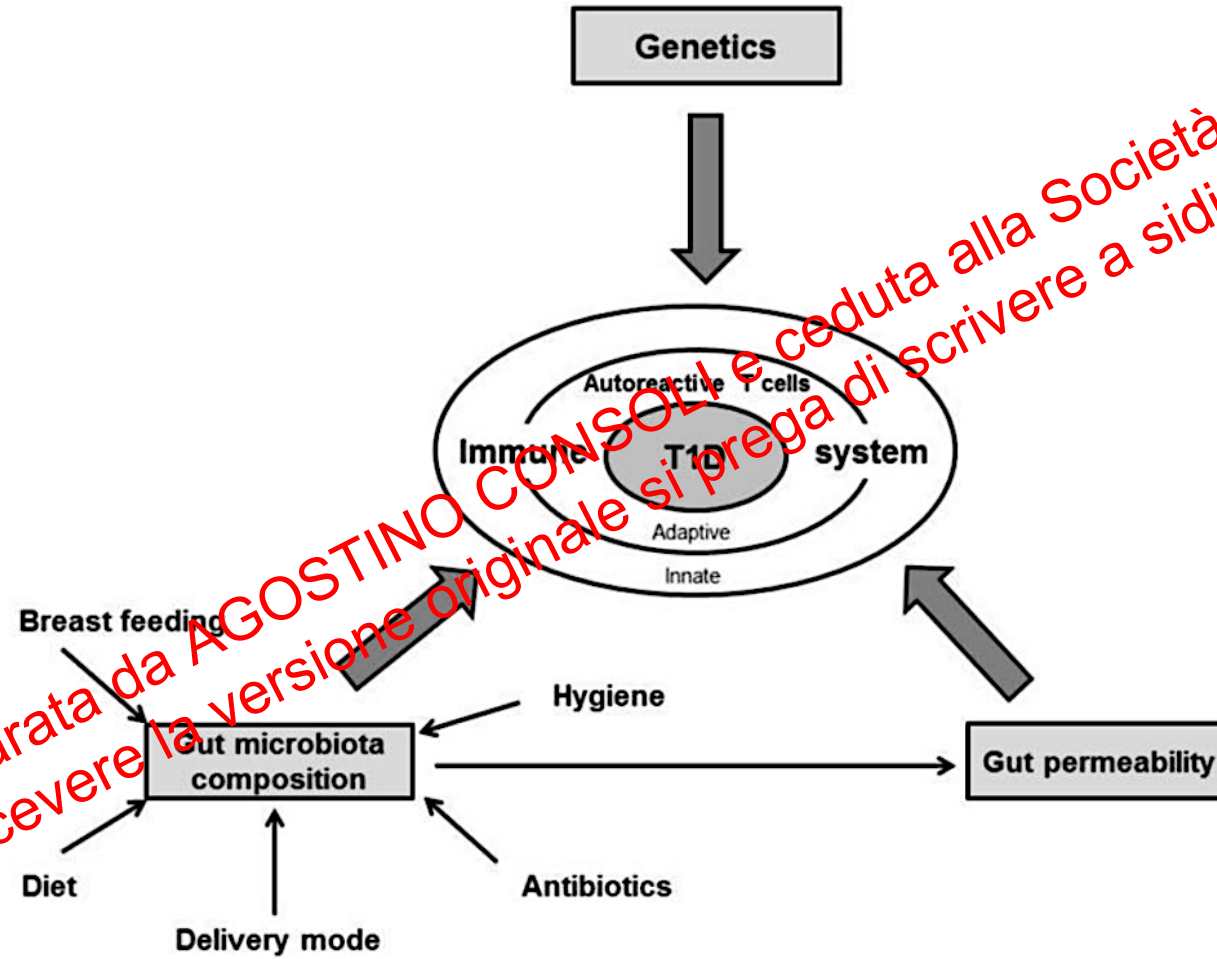
Cow's milk hypothesis

- ↓ Oral tolerance – caseins
-

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Why is type 1 diabetes increasing?:

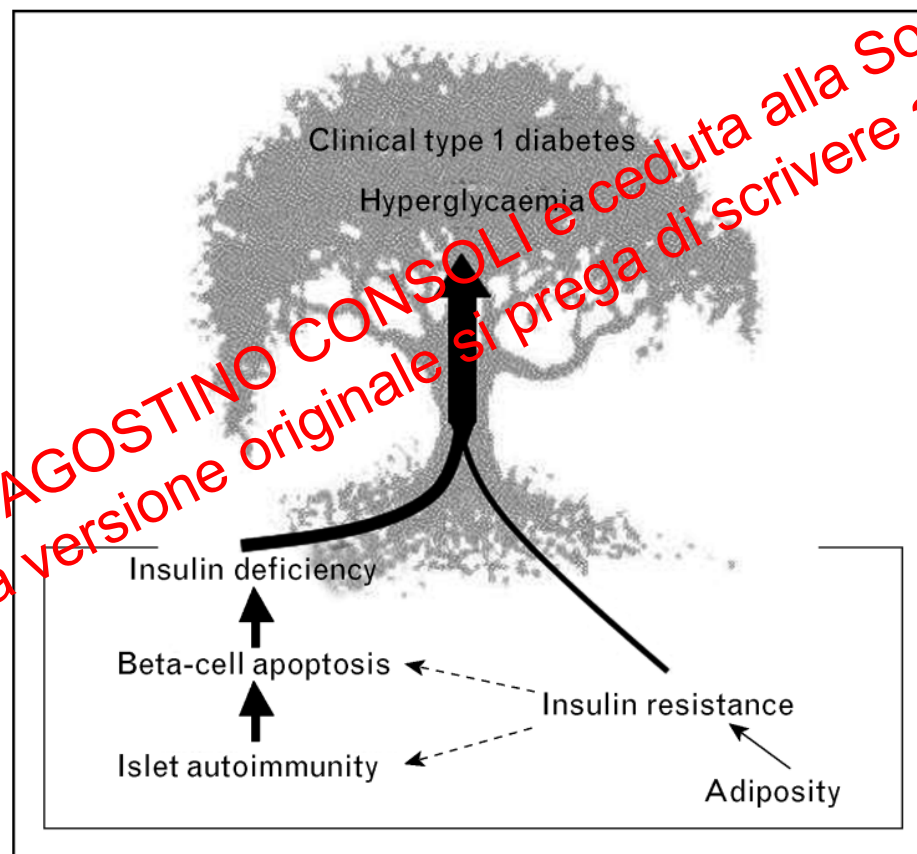
The Gut Microbiota hypothesis



Why is type 1 diabetes increasing?:

The Accelerator and Overload hypothesis

Figure 1 A summary of the established (solid line) and hypothetical (dashed line) role for insulin resistance in the pathogenesis of type 1 diabetes



Testing the Accelerator Hypothesis

Body size, β -cell function, and age at onset of type 1 (autoimmune) diabetes

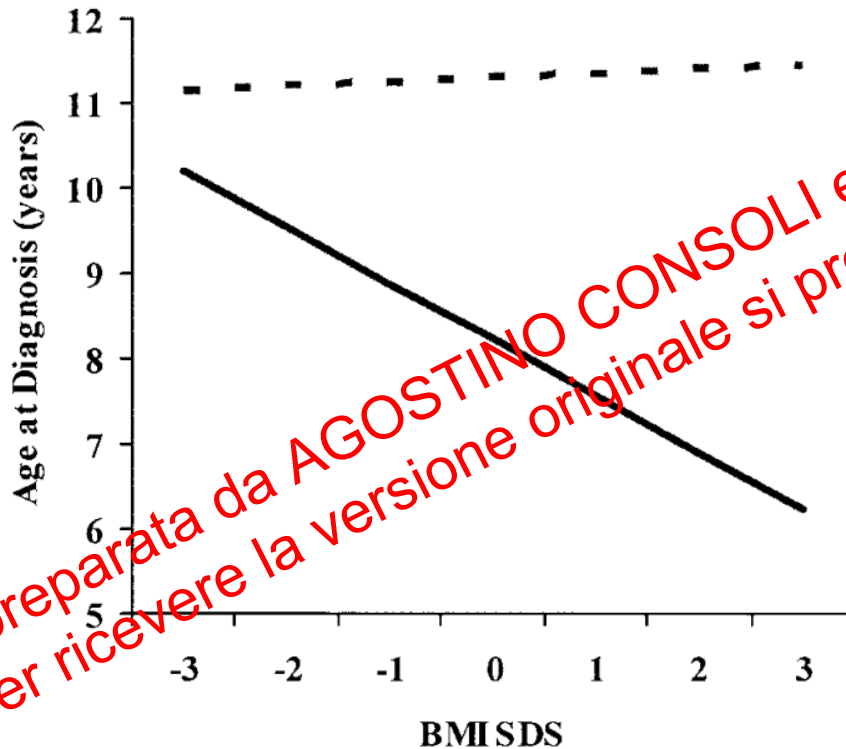
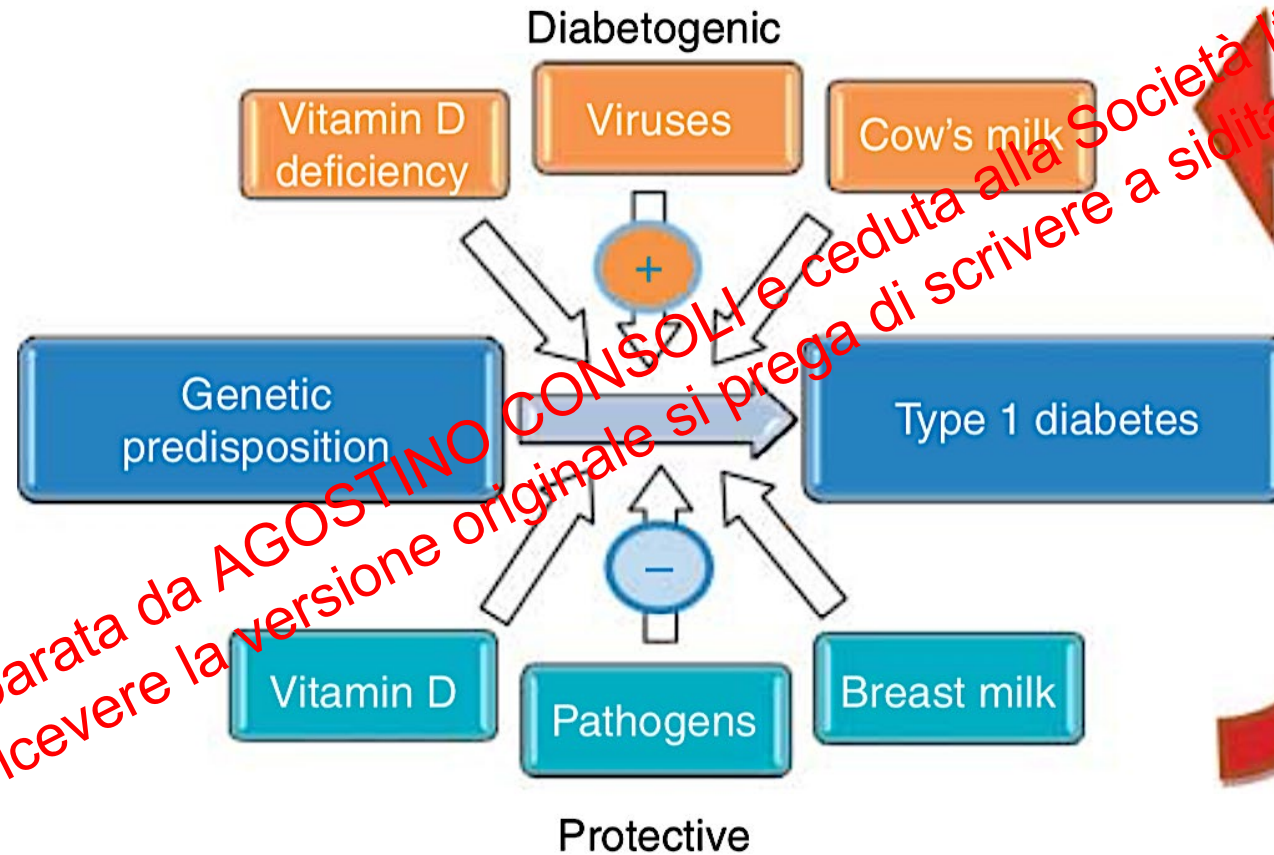


Figure 2—The relationship between BMI SDS and age at diagnosis of type 1 diabetes by FCP levels (below and above the median) from two multiple linear regression models, adjusted for sex, race/ethnicity, birth weight SDS, diabetes duration, and number of positive diabetes autoantibodies. FCP median is 0.5 ng/ml. $P < 0.0001$ for the interaction between BMI SDS and FCP on age at onset. - - -, FCP $\geq$ median; —, FCP $<$ median.

Why is type 1 diabetes increasing?: The “balance shift” model



What do the guidelines suggest?: *Screening*

Type 1 Diabetes in Children and Adolescents: A Position Statement by the American Diabetes Association

Jane L. Chiang,¹ David M. Maahs,² Katharine C. Garvey,³ Korey K. Hood,⁴ Lori M. Laffel,⁴ Stuart A. Weinzimer,⁵ Joseph I. Wolfsdorf,³ and Desmond Schatz⁶

Diabetes Care 2018;41:2026–2044 | <https://doi.org/10.2337/dci18-0023>

“Screening and Testing for Type 1 Diabetes in Asymptomatic Children with a panel of auto- antibodies is currently recommended only in the setting of research studies in first-degree family members of a proband with type 1 diabetes.”

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What do the guidelines suggest? *Distinguishing Diabetes Type*

Type 1 Diabetes in Children and Adolescents: A Position Statement by the American Diabetes Association

Jane L. Chiang,¹ David M. Maahs,²
Katharine C. Garvey,³ Korey K. Hood,²
Lori M. Laffel,⁴ Stuart A. Weinzierl,⁵
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Table 4—Characteristics of prevalent forms of primary diabetes in children and adolescents

	Type 1 diabetes	Type 2 diabetes	MODY*	Atypical diabetes**
Prevalence	~85%	~12%	~1–4%	≥10% in African American
Age at onset	Throughout childhood and adolescence	Puberty; rare <10 years	<25 years	Pubertal
Onset	Acute severe	Insidious to severe	Gradual	Acute severe
DKA at onset	~30%	~6%	Not typical	Common
Affected relative	5–10%	60–90%	50–90%	>75%
Female:male	1:1	1.1–1.8:1	1:1	Variable
Inheritance	Polygenic	Polygenic	Autosomal dominant	Autosomal dominant
HLA-DR3/4	Association	No association	No association	No association
Ethnicity	All, Caucasian at highest risk	All¶	All	African American/Asian
Insulin (C-peptide) secretion	Decreased/absent	Variable	Variably decreased	Variably decreased
Insulin sensitivity	Normal when controlled	Decreased	Normal	Normal
Insulin dependence	Permanent	Variable	Variable	Intermittent
Obesity	No†	>90%	Uncommon	Varies with population
Acanthosis nigricans	No	Common	No†	No†
Islet autoantibodies	Yes§	No	No	No

What do the guidelines suggest?: *Staging*

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Table 2—Staging of type 1 diabetes

	Stage 1	Stage 2	Stage 3
Stage	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• ≥ 2 autoantibodies • No IGT or IFG	• ≥ 2 autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or $\geq 10\%$ increase in A1C	• Clinical symptoms • Diabetes by standard criteria

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

What do the guidelines suggest?: *Treatment*

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“Most children with type 1 diabetes should be treated with intensive insulin regimens via either multiple daily injections of prandial insulin and basal insulin or continuous sub-cutaneous insulin infusion”

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Take home message(s):

- Epidemiological studies:
 - Show that the incidence of T1DM has been increasing by 2-5% worldwide
 - Have an important on-going role to investigate:
 - Causes
 - Clinical care
 - Prevention
 - Cure of T1DM

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