

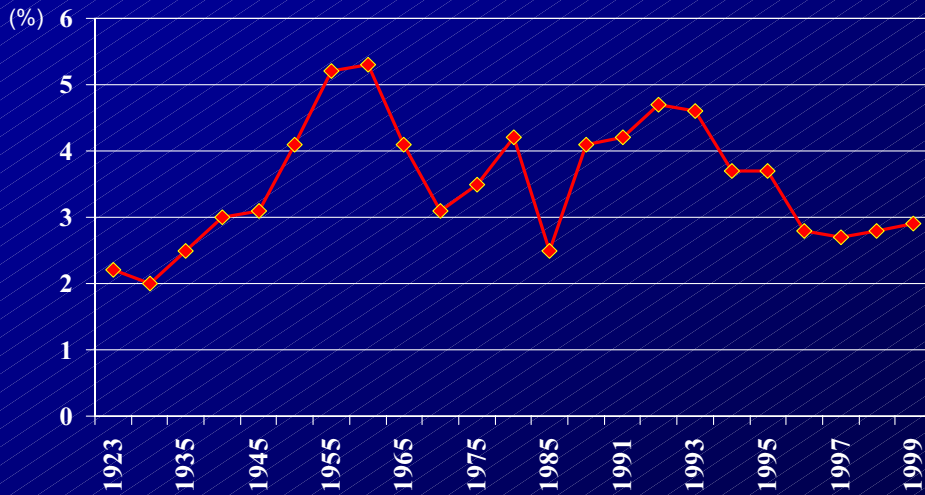
# DIABETES CARE IN TURKEY

Professor Ilhan Satman, M.D.  
Istanbul University  
Istanbul Faculty of Medicine  
Diabetes Division

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### Trends in Allocation of State Budget to Min. Health



### Provision and Financing of Public Health Services

#### Provision of services

Ministry of Health  
 University Hospitals  
 Military Hospitals  
 Municipalities  
 State Econom. Enterprises  
 Social Insurance Organizat.  
 Other Ministries

#### Funding

Min. Health  
 Higher Education Council  
 Min. Defense  
 Other Public Sectors  
 Compulsory insurance  
 Social Insurance Organization  
 Government Employees Retirem. Fund  
 Insur. Merchants, Artisans, Self-employ.

## Provision and Financing of Private Health Services

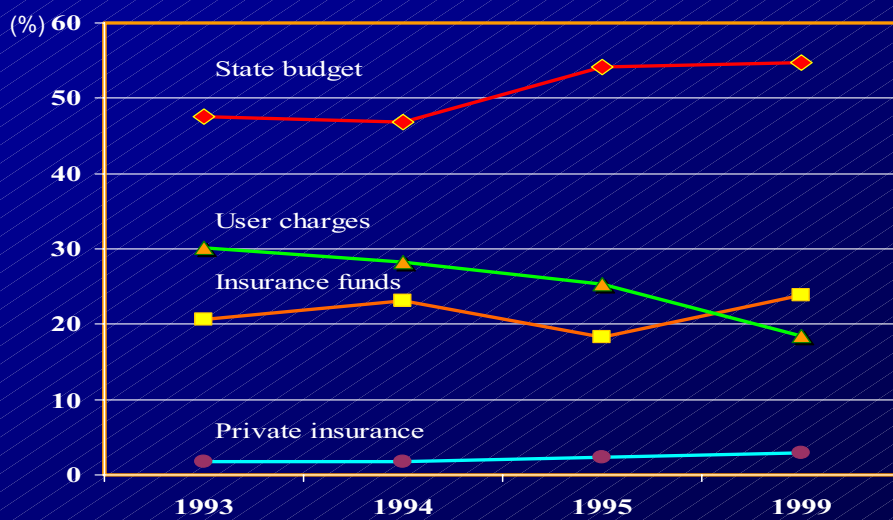
### Provision of services

Private Hospitals  
 Private Physicians  
 Private Pharmacists  
 Private Laboratories  
**Philanthropic**

### Funding

Private Insurance Funds  
 Out-of-pockets Payments  
 (User Charges)

## Aggregate Sources of Founding for Health Services



## Coverage of Health Insurance Programs

- Government programs cover 78.4% of the population. Rural and urban populations benefit equally. Due to economic reasons, some areas in the East and Southeast of the country used to be benefit less, but now the difference begin to decrease.
- Only 3% of the population is covered by private sector health insurance.
- 18.6% are user charges (out-of-pocket payments).

## Delivery of Health Care to Diabetics

- Most of the type 2 diabetics receive health care through secondary care units (State hospitals, Social Insurance System Hospitals and related Out-patient Clinics).
- Delivery of health care to type 1 diabetics is usually provided by Diabetes/Endocrinology Units of Teaching or University Hospitals.

## Diagnosis of Diabetes Mellitus

- Generally, diagnosis of diabetes is made in primary or secondary health care units by GPs or specialists.
- Type 1 patients are followed by pediatricians or internists.
- Type 2 patients are usually followed by internists.
- Complicated patients are referred to Diabetes or Endocrinology Units in Teaching or University Hosp, and consulted with diabetologist or endocrinologist.

## Availability of Facilities and Skilled Personnel

Diabetes centers are limited in number (58), most Teaching Hospitals have diabetes Out-patient Clinics.

<u>Skilled Personnel</u>	<u>Number</u>
Adult endocrinologist	206
Pediatric endocrinologist	53
Diabetologist	40
Diabetes nurse	108
Diabetes dietitian	61

## Childhood Diabetes: Prevalence

- **IDDM in school children (6-18 years) in Ankara**  
( Hatun&T Teziç, 1995)
 

Urban	0.22 (per 1000)
Rural	0.29
<hr/>	
General	0.27 (Girls: 0.32, Boys: 0.22)
- **Ro-CODEC (1995): IDDM (0-16 years) in Ankara**  
General 0.41 (per 1000)

## Childhood Diabetes: Incidence

- **Children&Adolescent Diabetes Working Group**  
522 Newly-onset IDDM in 1996-97  
(Girls: 54%, Boys: 46%)
 

Age group	Incidence (per 100.000/yr)
<hr/>	
0-14 years	2.8

## Turkey's Diabetes Epidemiology Survey (TURDEP 1997-1998)

Organized By

Istanbul Faculty of Medicine

Ministry of Health

State Institute of Statistics

(Supervised by WHO)

Satman I et al and TURDEP Group. Diabetes Care 2002; 25:1551-1556

### Screening Centers

Region	= 5
City	3x 5 = 15
County	6x15 = 90
District	3x90 = 270 (Urban)
Village	3x90 = 270 (Rural)
<hr/>	
Total	540 Centers

## Sample Size

Randomly assigned people, aged  $\geq 20$  yrs were invited

Urban  $3,457 \times 5 = 17,285 + 10\% = 19,013$

Rural  $1,825 \times 5 = 9,125 + 10\% = 10,037$

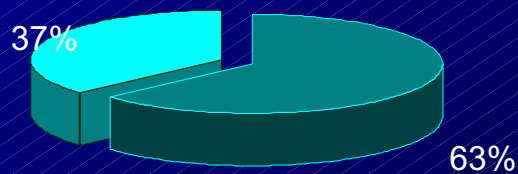
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Total 29,050

Average response rate: 85%

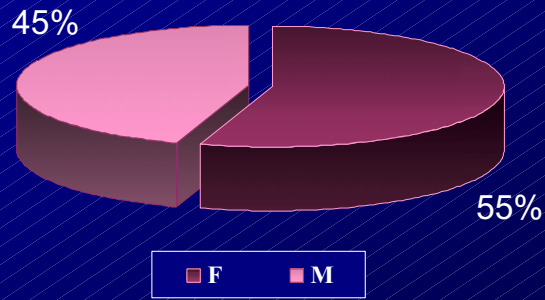
Urban 15,669 (82%) + Rural 9,119 (91%) = 24,788

## TURDEP By Settlements

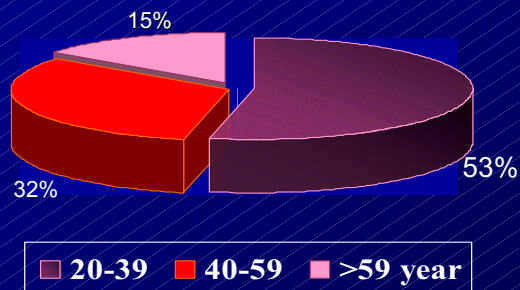




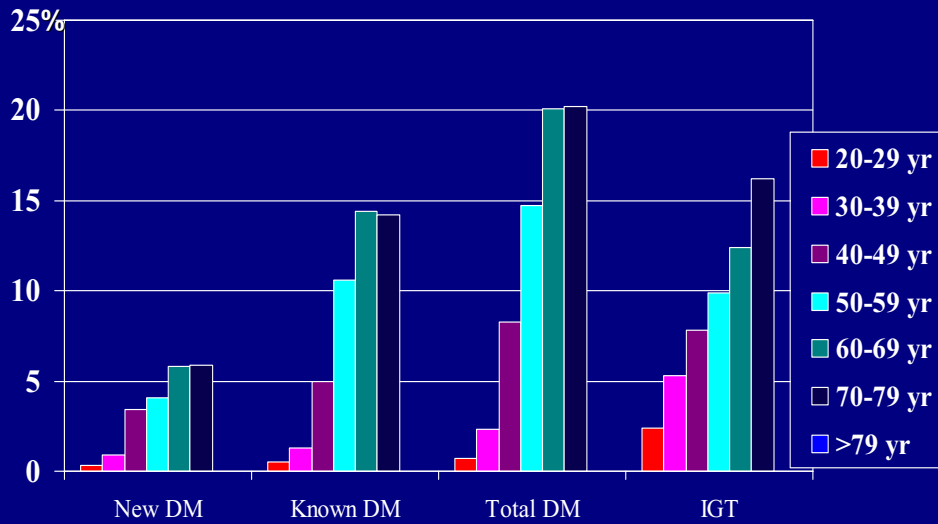
### TURDEP Sex Distributions



### General Age Distributions

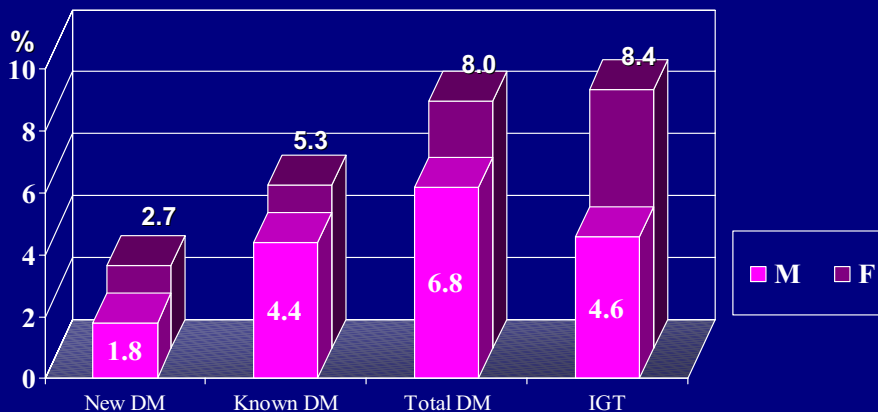


### Glucose Intolerance in Age Groups

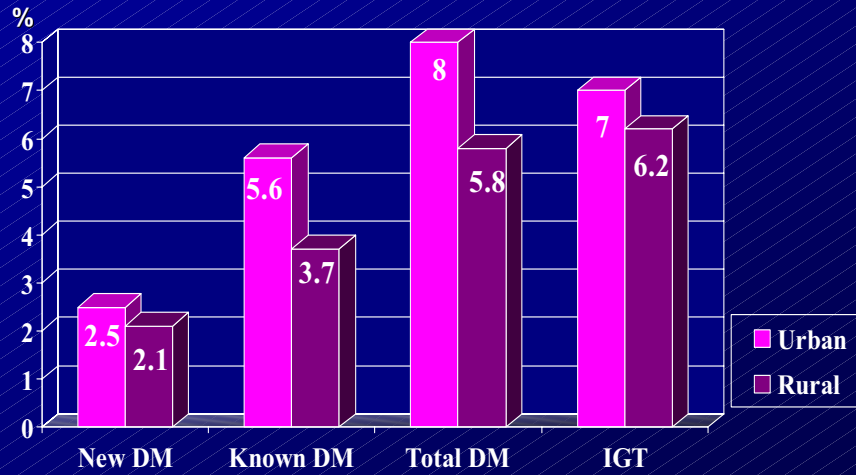


Satman I et al and TURDEP Group. Diabetes Care 2002; 25:1551-1556

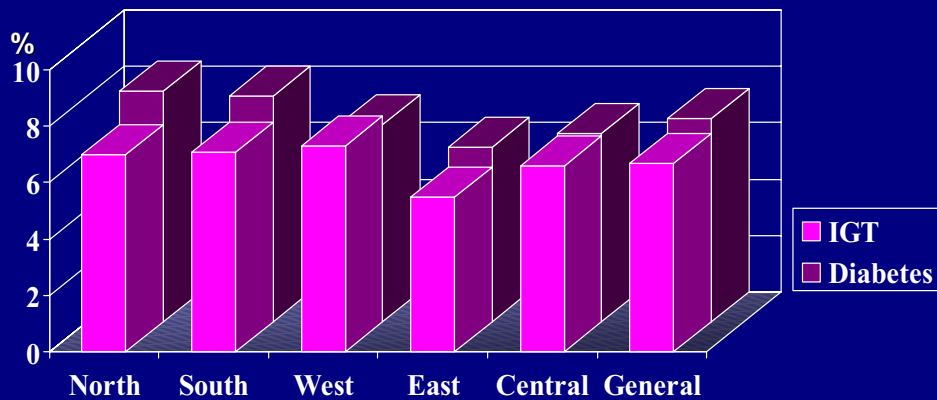
### Glucose Intolerance by Sex



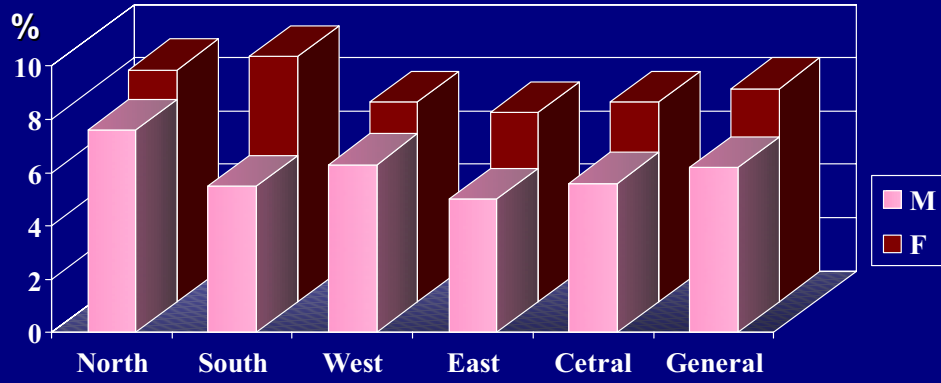
### Glucose Intolerance by Settlements



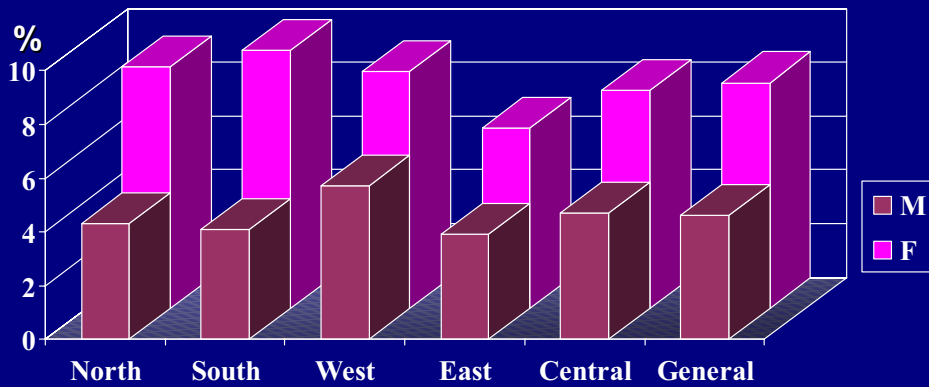
### Glucose Intolerance by Regions



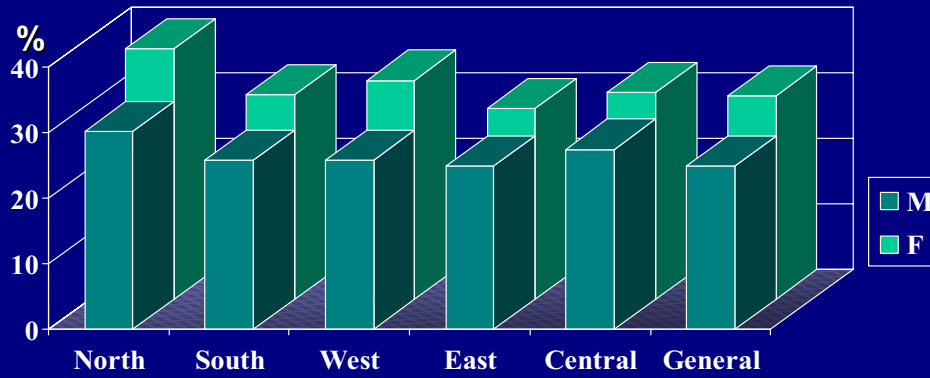
### Diabetes by Regions in Females and Males



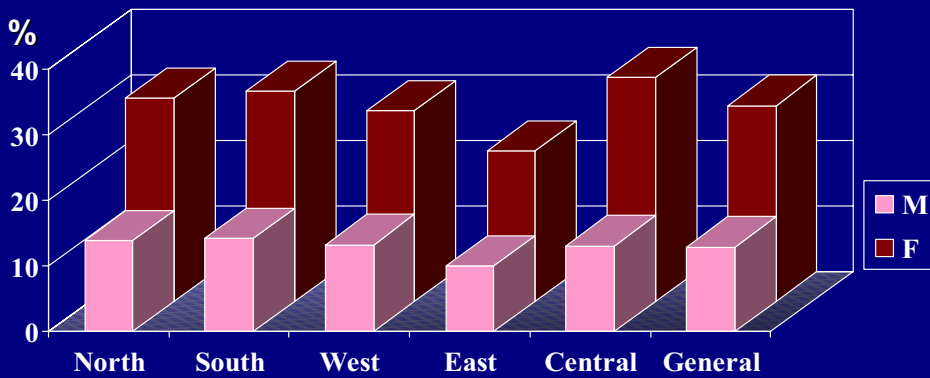
### IGT by Regions in Females and Males

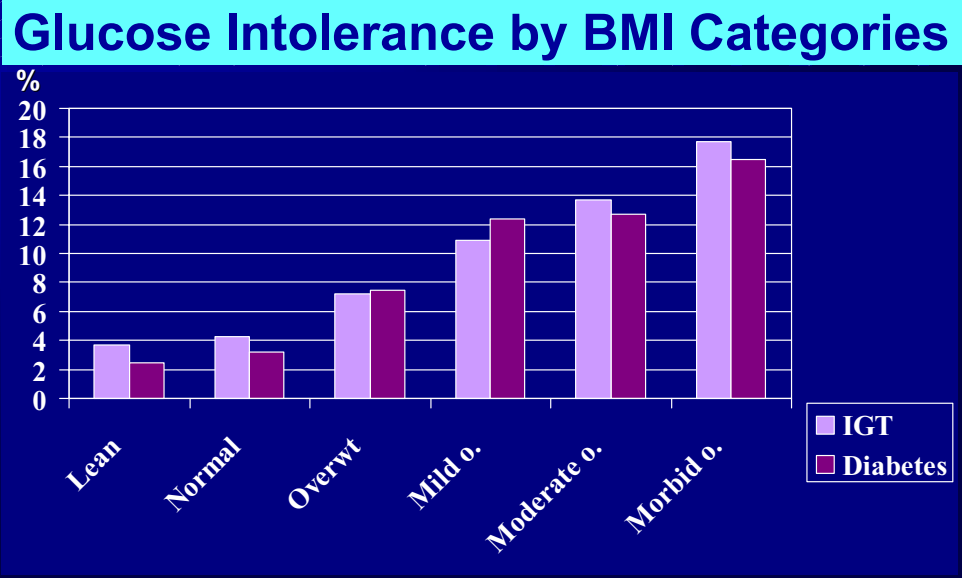


### Hypertension by Regions in Females and Males

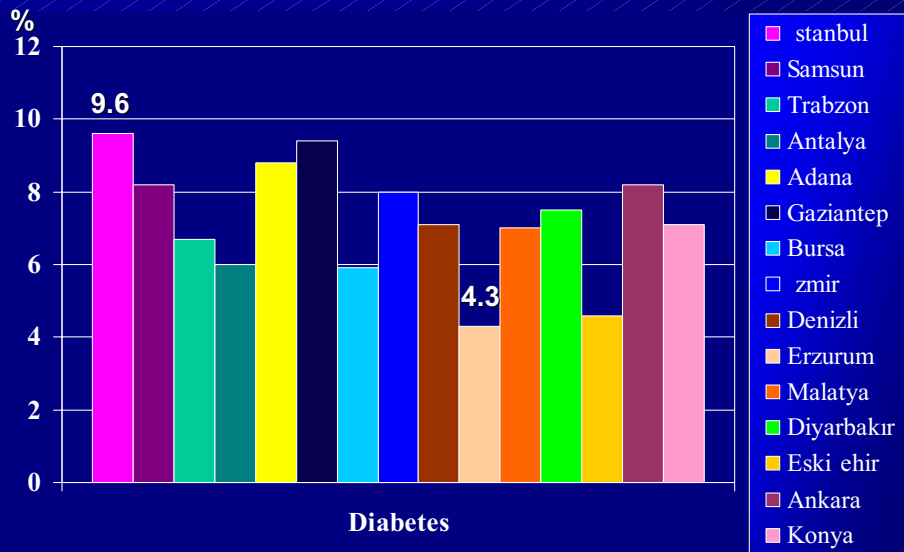


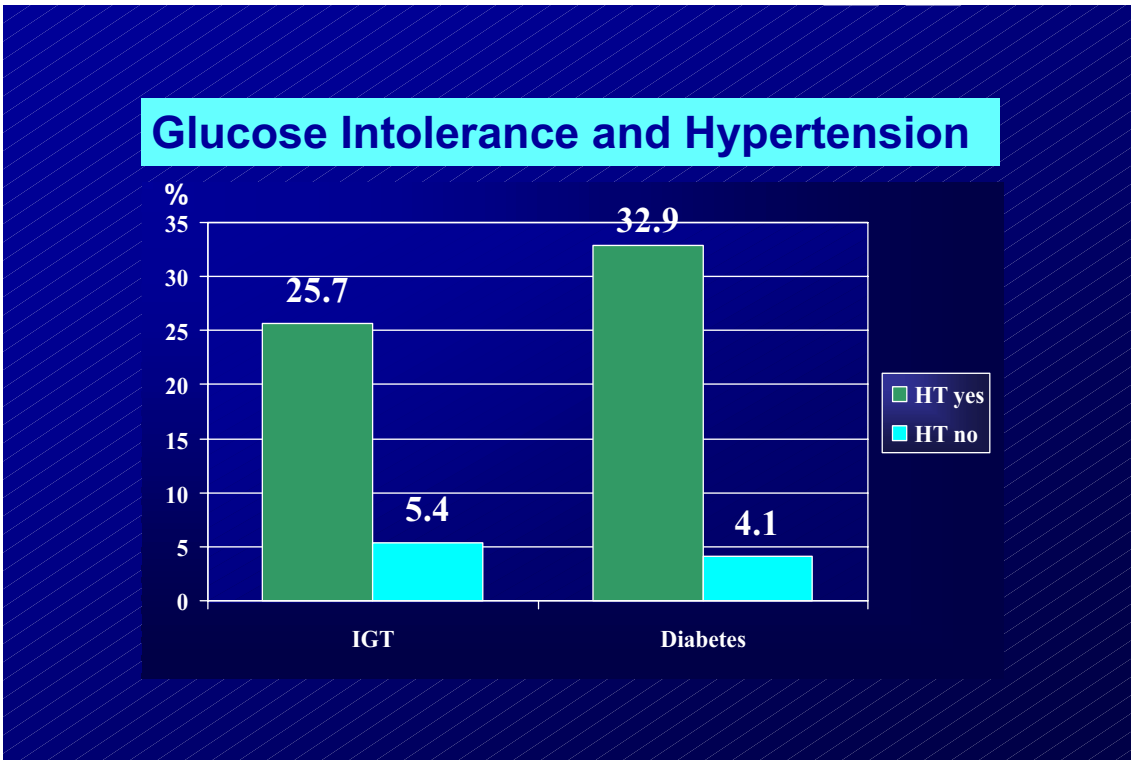
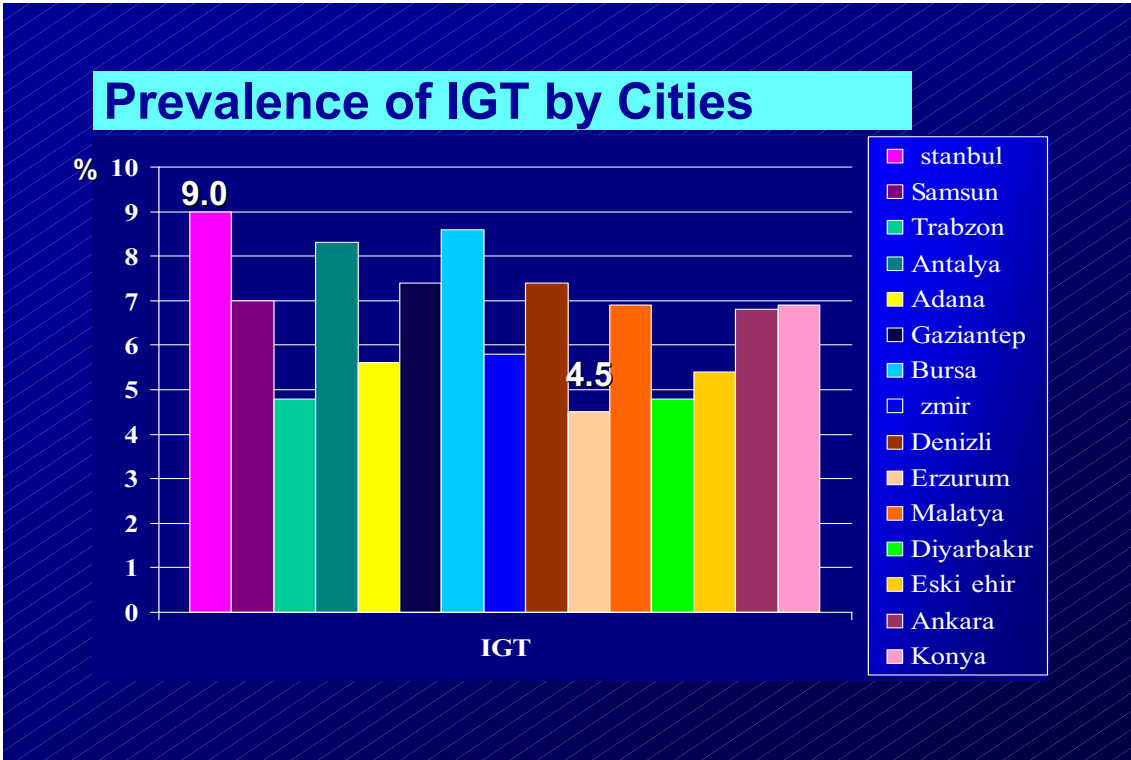
### Obesity by Regions in Females and Males





### Prevalence of Diabetes by Cities



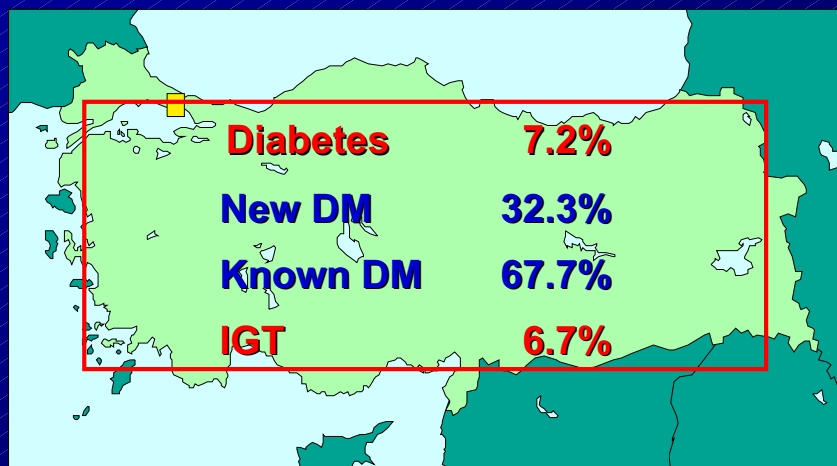


## Glucose Intolerance in Turkey

	New DM	Known DM	Total DM	IGT
Crude rate (%)	2.33	4.89	7.22	6.71
Standardized prevalence (%)				
World	2.52	5.36	7.88	7.00
Europe	2.80	6.09	8.90	7.58

Satman I et al and TURDEP Group. Diabetes Care 2002; 25:1551-1556

## TURDEP General Results



Satman I et al and TURDEP Group. Diabetes Care 2002; 25:1551-1556



## Results-I

TURDEP revealed that

- 2.6 millions of people with **DIABETES**  
(about 170,000 of whom with Type 1)
- 2.3 millions of people with **IGT**
- 11.4 millions of people with **HYPERTENSION**
- 7.6 millions of people with **OBESITY**

live in TURKEY.

## Results-II

According to TURDEP;

- Every one of third with **DIABETES** and
- Every one of two with **HYPERTENSION**

is not aware of his/her disease.

## Common Modes of Therapy in Type 1 Diabetes

- Conventional insulin therapy (24.1%):
  - 2 injections/day
    - \* human insulin
    - \* premixed rapid-acting analogs + NPY
- Intensive insulin therapy (%75.9) :
  - 4 injections/day (99%)
    - \* pre-meals short-acting + bedtime NPH insulin
    - \* pre-meals rapid-acting analogs + 1-2 times NPH/bedtime insulin glargine
  - SCII pump (31%)

## Diabetic Patient Education

- All diabetes centers, and diabetes units of Teaching or University Hospitals have “Diabetic Patient Education” or “Diabetes School” programs. Free sessions are open for public.
- Programs cover healthy nutrition, physical activity, self monitoring, prevention and early recognition of complications, avoidance of acute metabolic events, suspicion and emergency treatment of hypoglycemia, and diabetes management during special conditions.
- Self monitoring is routine and expenses are covered by the government for type 1 diabetes patients.

## Management of Diabetic Complications

- Most diabetes centers have consulting specialists belong to diabetes team (general/vascular surgeon, orthopedist, ophthalmologist, neurologist and nephrologist, obstetrician). Those who followed in primary or secondary care units are referred to these centers.
- Insulin is provided by the government for free for all type 1 patients.
- Laser photocoagulation, BP control with ACEI or ARB drugs, and renal replacement therapy are used whenever needed.

## Annual Cost of Diabetes in Turkey

Patient without complications	479 USD
Patient with complications	1397 USD

(The DiabCOST Study 1997)

## Management of Type 1 Diabetes at Istanbul University: Demographics

- n: 2300 (male 53%, female 47%)
- Age at diabetes onset:  $20.6 \pm 8.9$  yr (2-30 yr)  
0-15 year 21.3%, >15 year 78.7%
- Diabetes duration:  $7.5 \pm 6.9$  yr (0.1-39 yr)
- Family history of type 1 DM: 9%
- Mean HbA<sub>1c</sub>: Baseline  $9.7 \pm 2.6\%$ , Current  $8.1 \pm 1.9\%$
- Complications: Rp 17.2%, Nfp 6.2% (including microalbuminurea), Nrp 10%, HT 5.1%
- Comorbidities: Autoimmune thyroid d. 2.9% (mostly Hashimoto), celiac d. 1.4%, Addison d. 0.1%

## Management of Type 1 Diabetes at Istanbul University: Follow-up Program

- Initial visit: Medical history, complete physical examination, weight, height, BMI, pubertal stage, biochemistry, urine analysis, HbA<sub>1c</sub>, TSH, anti-GAD, ICA, C-peptide
- Follow-up visits: First year every month, then every 3 months (with Physical examination, body weight, BP)
- Follow-up investigations: HbA<sub>1c</sub>, urine, PP glucose
- Biochemistry, TSH annually, ECG after 20 yrs of age
- Microalbuminuria at onset, then annually
- Fundus: at onset, before puberty, then annually

## Management of Type 1 Diabetes at Istanbul University: Goals of Treatment

- HbA<sub>1c</sub> < 7%
- Pre-meal glucose 90-130 mg/dl
- BP <130/80 mmHg
- LDL-cholesterol <100 mg/dl
- HDL-cholesterol >40 mg/dl
- Triglycerides <150 mg/dl
- Microalbuminuria <30 mg/24hr

*Children and the Mediterranean*

*I Bambini nel Mediterraneo: Salute, Cultura e Assetto Urbano*

**"Diabetes mellitus and children in the Mediterranean"**

*Genova, January 8th, 2004*

## ***Epidemiology of childhood type 1 diabetes in the Mediterranean area***



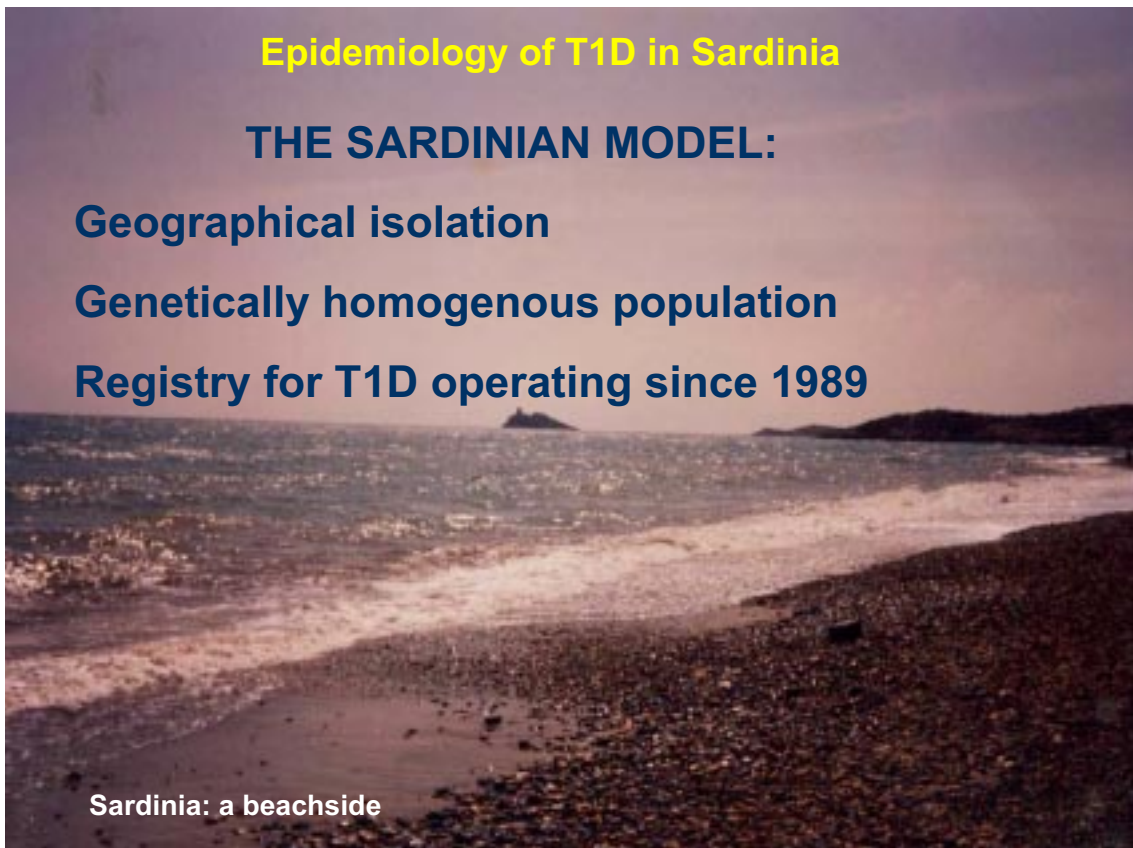
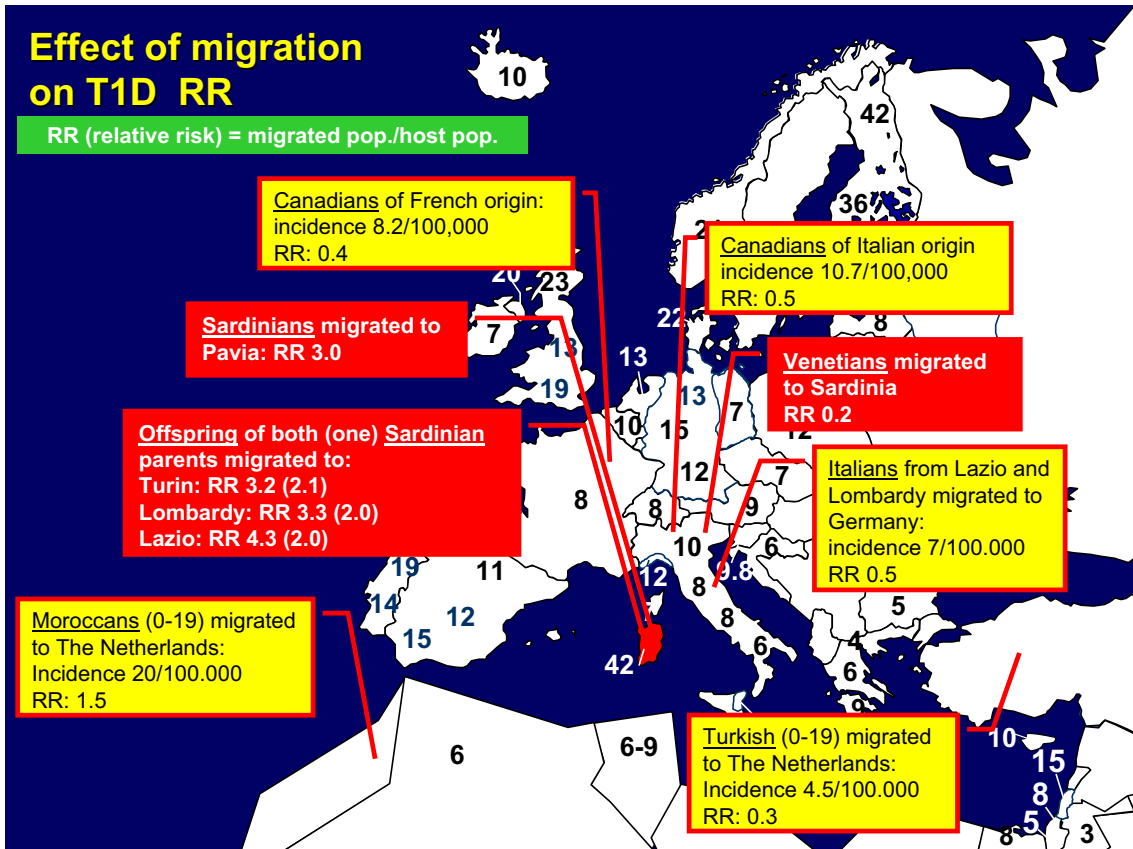
Marco Songini, Director  
Diabetes Unit - Azienda Ospedaliera "G. Brotzu"  
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Cagliari - Sardinia, Italy



### My talk for today:

- Overview on the epidemiology of T1D 0-14 in the Mediterranean area
- Epidemiology of T1D in Sardinia
- Epidemiology of pre-T1D
- Echological studies
- T1D and MS
- Conclusions







## Sardinian T1D Registry

T1D incidence (per 100,000) in Sardinia (1989-2002)  
age group 0-14 yrs (N = 1,576)

	SIR 0-14	0-4	5-9	10-14
Total	<u>41.7</u>	32.9	43.7	46.6
Males	47.6	35.9	48.4	55.7
Females	35.4	29.7	38.6	36.9
M/F	1.3	1.2	1.2	<u>1.5</u>
Cases (%)		22	35	<u>43</u>

Completeness = 91%

In Sardinia the prevalence of any DM 20-59yrs is 3.75% in M and 2.74% in F;  
M/F = 1.37; 16% were insulin treated (from Muntoni et al, 1988)

*Casu, Songini et al, submitted*

## Sardinian T1D Registry

Geographical distribution of T1D (0-14) RR

RR Alghero: 0.986 (0.979-0.993)

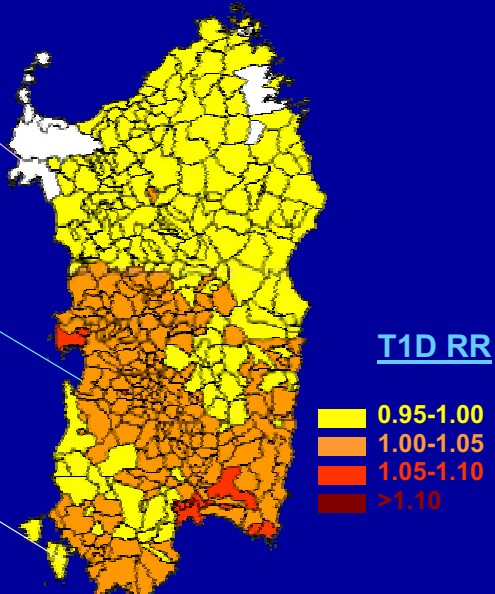
Incid. Catalonia : 11.5 (10.6-12.4)

RR Arborea: 0.2

Incid. Veneto 0-29: 10.9

RR Carloforte: 0.999 (0.996-1.00)

Incid. Liguria: 11.7 (7.6-16.2)

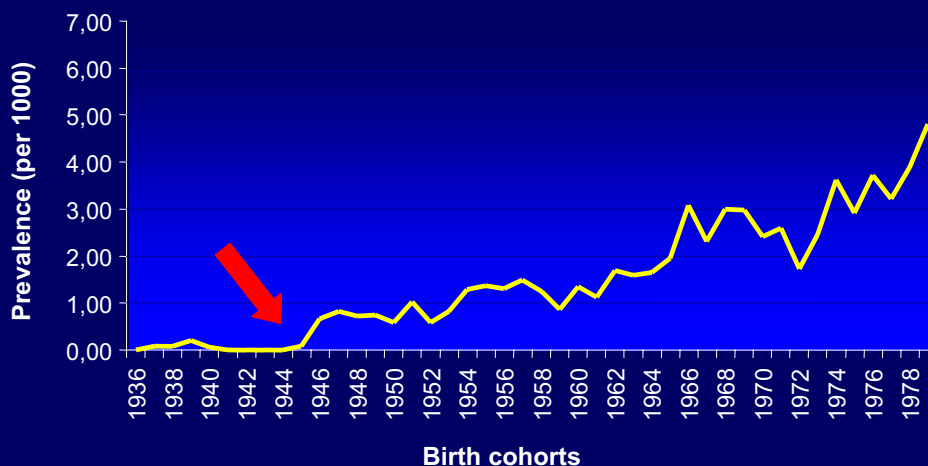


T1D Relative Risk 0-14 yrs (1989-99)

*Casu, Songini et al, submitted*

# The Sardinian Conscript T1D Registry

Secular trend of T1D in Sardinia  
(1936-78 birth cohorts)

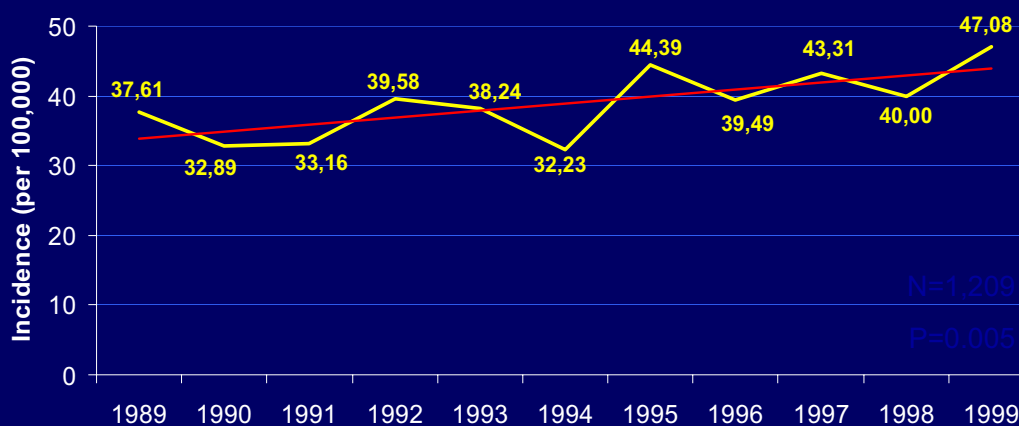


Male point prevalence at 18 years of age

*Casu, Songini et al, Pediatric Diabetes, in press*

# Sardinian T1D Registry

Temporal trend of T1D incidence 0-14 yrs (1989-1999)

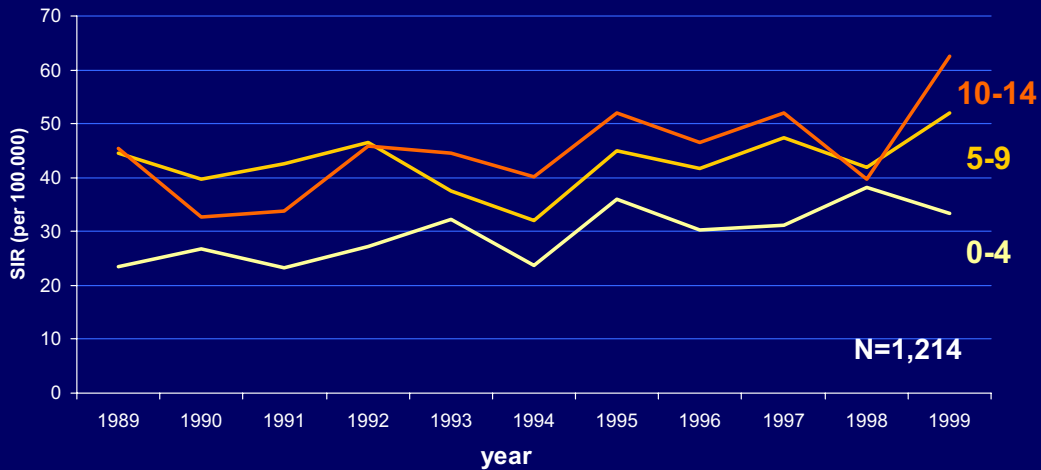


Yearly incr. incidence: **0.79** (Fin 0.67)  
 Yearly incr. rate: **2.8%** (Europe: 3.4%, WW 3%)  
 Predicted incidence rate year 2010 : **55** (Fin 50.2, China 1.7)

*Casu, Songini et al, submitted*

## Sardinian T1D Registry

Temporal trend of T1D incidence by age  
0-14 yrs (1989-1999)

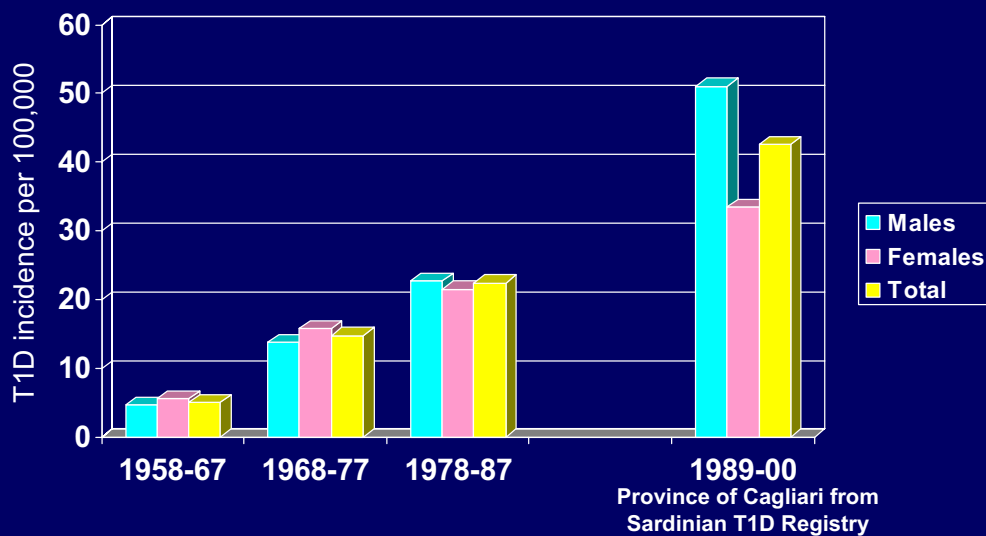


No significant difference in the increasing incidences among the age groups was found

Casu, Songini et al, submitted

## T1D incidence

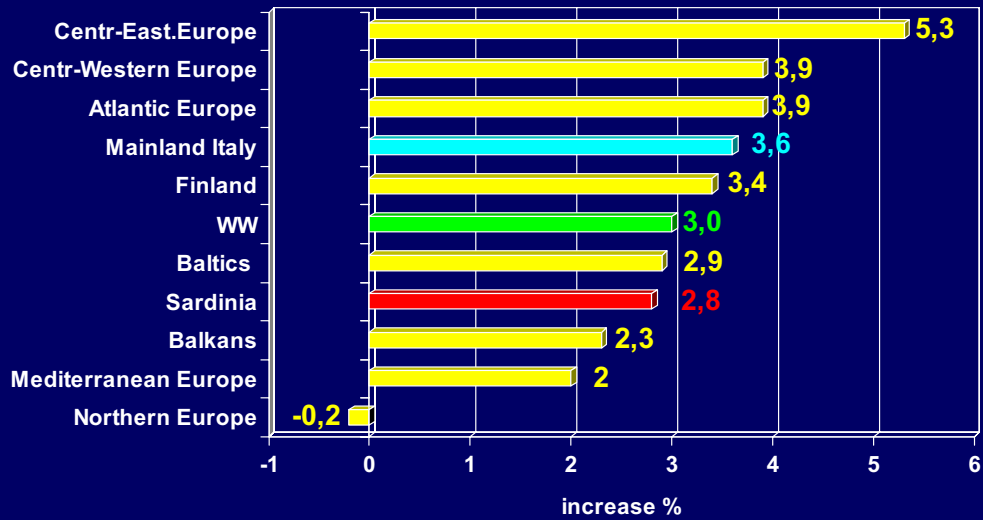
temporal trend: Cagliari province 0-14 yrs (1959-1987)



Modified from Paola Frongia, Paolo Pusceddu, Efisio Angius, personal communication

## Annual rate of increase of T1D incidence 0-14 years (1989-1998)

*The global incidence of childhood T1D will increase by 40% over 1998-2010!*



*Eurodiab Study Group 2001*

*RIDI Study Group, unpublished*

*Onkamo et al. 1999*

## Epidemiology of pre-T1D

(normal children found + for islet-related autoantibodies ICA,GADA,IA-2)



**Cagliari: main street**

## Prediction study-neonates

Prevalence of islet-related Abs among Sardinian newborns

### The Sardinian Newborn – IDDM Study (SNI)

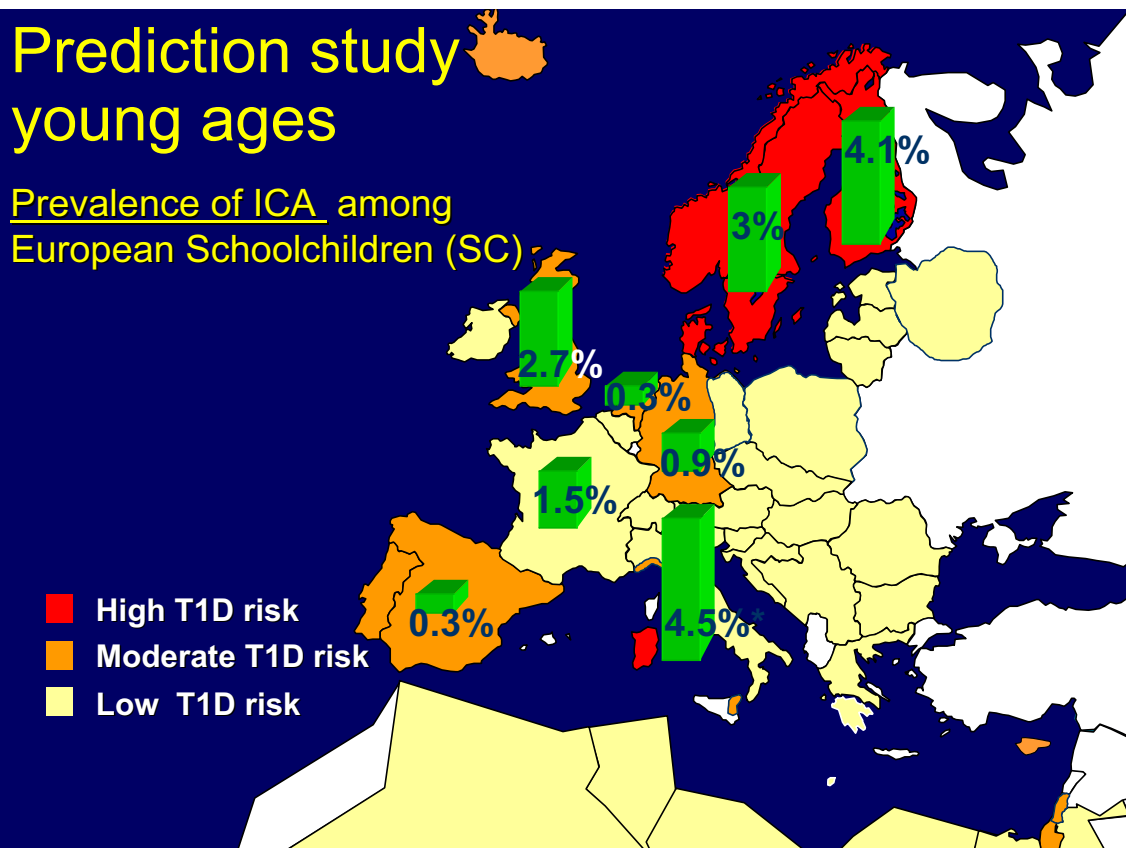
Unselected children aged 1:	2,959
• ICA $\geq$ 5 JDFu:	0.17%
• GADA $\geq$ 10 AU (98.5th percentile):	0.69%
• IA-2icA $\geq$ 4 AU (98.5th percentile):	1.38%

These results are comparable to those obtained from high risk selected population (*Finnish newborns, O. Simell et al. 1998*)

*Bottazzo, Songini, Casu, Cirillo et al. 1998*

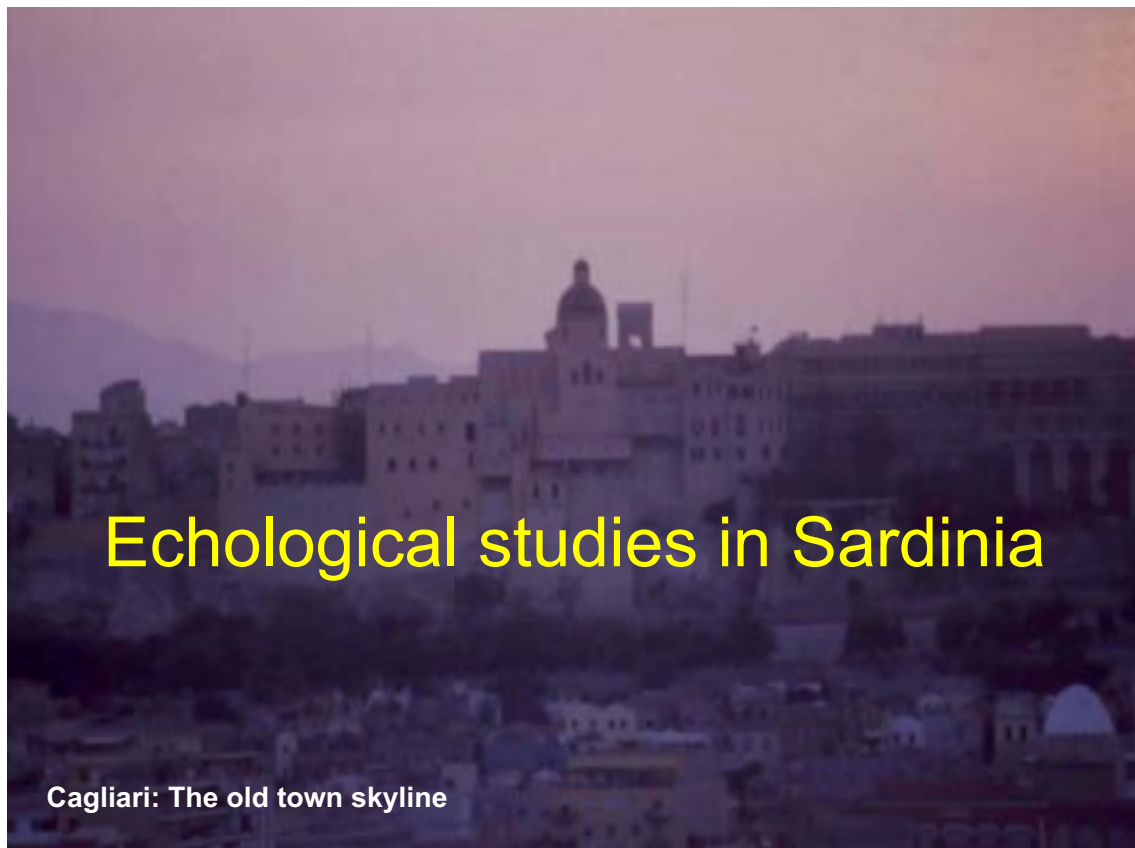
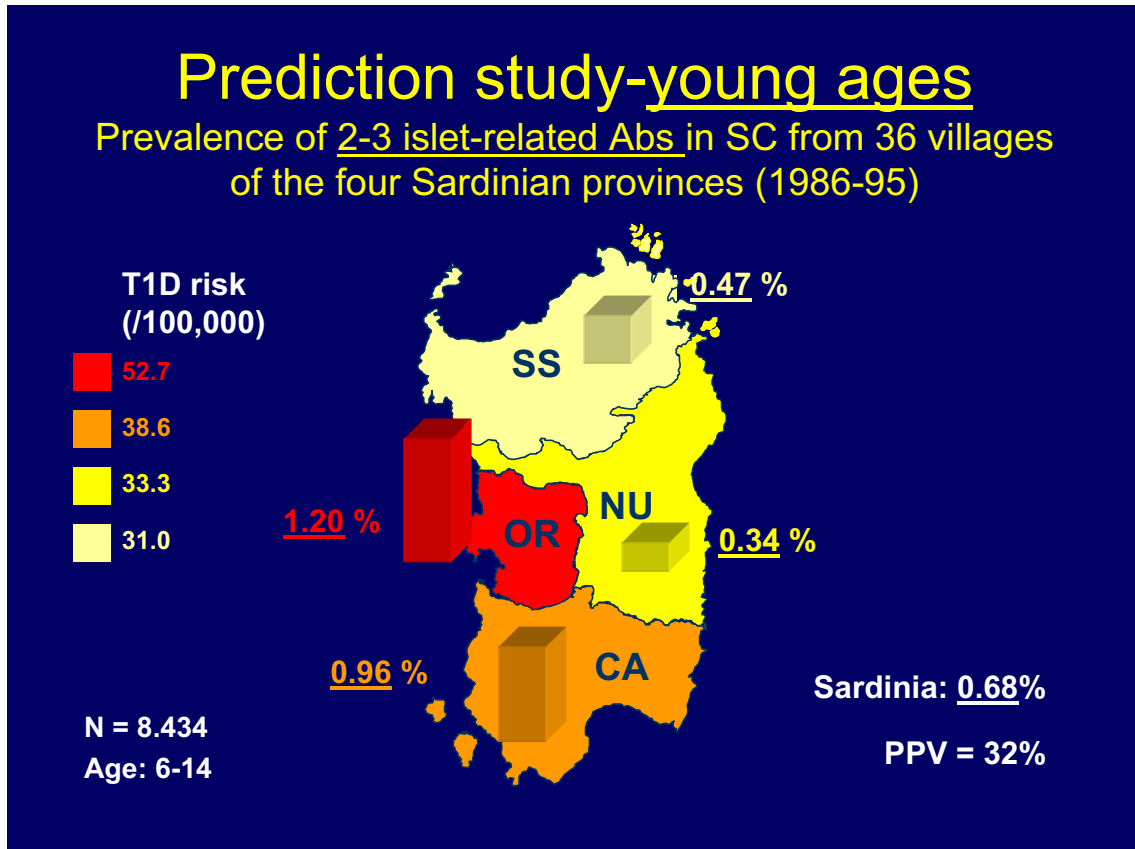
## Prediction study young ages

Prevalence of ICA among European Schoolchildren (SC)



E3

WORKSHOP III



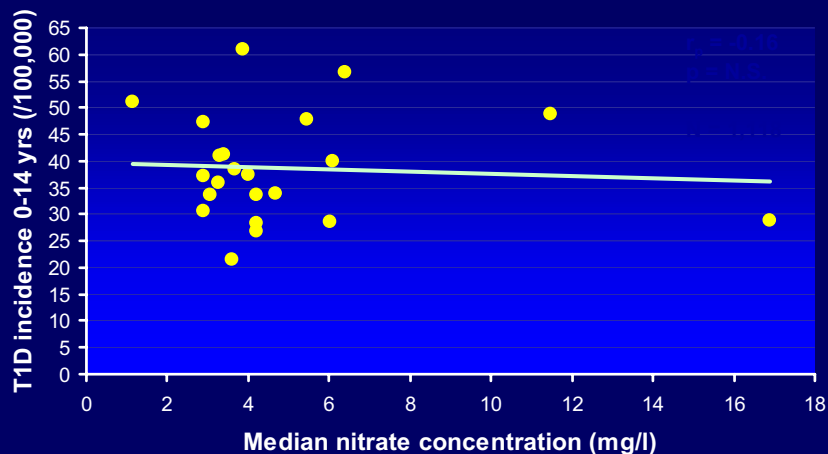
## Echological studies

### Correlation with T1D risk in Sardinia

§	Birth seasonality	YES
§	Onset seasonality	YES/NO
§	Temp, pop. density, urban/rural	NO
§	Average rainfall	NO
§	Latitude	NO
§	Time- and space-clustering	MILD
§	Overlap with: - malaria	NO
§	- talassemia	NO
§	- G6PD deficiency	NO
§	Nitrate intake (bottle and tap waters)	NO
§	Cow's and breast milk feeding	NO
§	Gross domestic product	NO
§	Coffee consumption	NO

## Echological studies

1) **No correlation between nitrate level in tap water and T1D incidence among the 21 Sardinian health districts (1989-98)**



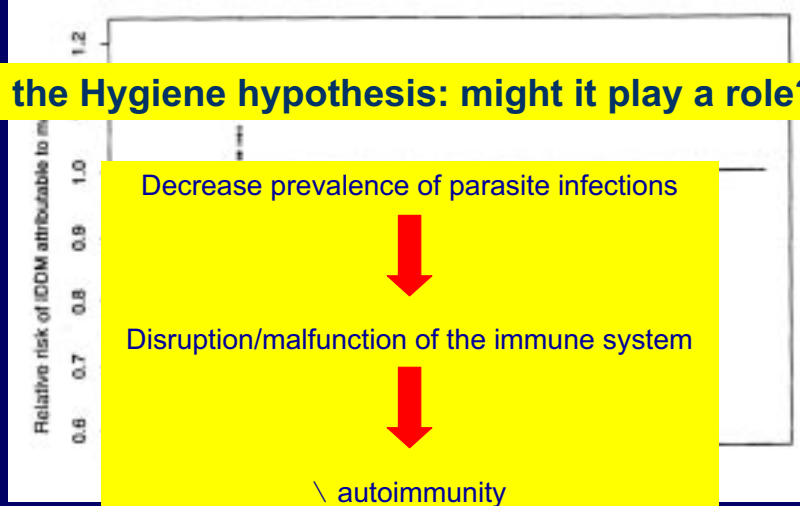
2) **No association between the consumption of bottled waters with different concentration of nitrates and the incidence of T1D**

Casu, Bottazzo, Songini et al. 2000

# Echological studies

## Malaria and T1D in Sardinia

the Hygiene hypothesis: might it play a role?

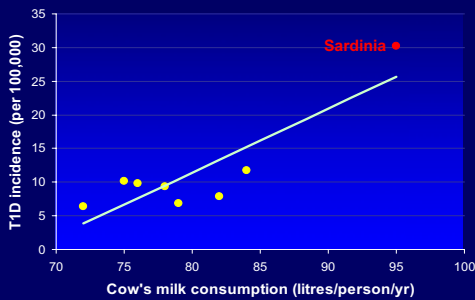


Relative risk of T1D due to past malaria in all Sardinian areas with low and high morbidity for malaria (Fermi, 1938)

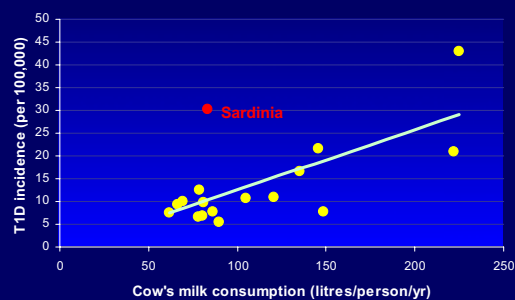
Songini, Bernardinelli, Bottazzo et al. 1998

# Echological studies

## Cow's milk consumption and T1D incidence



Italy



World

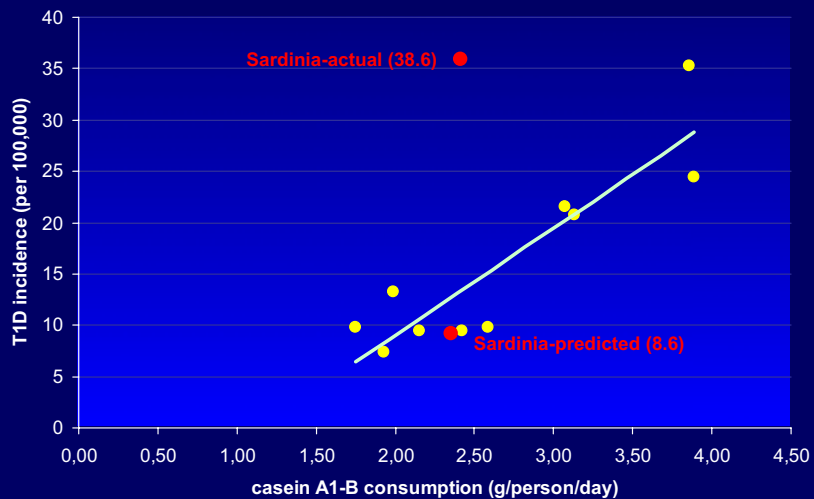
Fava et al. 1994  
Muntoni et al. 1994



## Echological studies

Cow's milk and T1D

$\eta$ -casein A1-B intake and T1D incidence



Elliott et al. 1999

Casu, Elliott, Bottazzo, Songini, et al. 2001

## Echological studies

Breast feeding in Sardinia

Influence of feeding habits on the risk of T1D in Sardinia

	T1D cases	Controls	OR (95% C.I.)
<b>Breast feeding</b>			
Yes	84	70	1 (ref. category)
No	16	30	0.41(0.19-0.91)

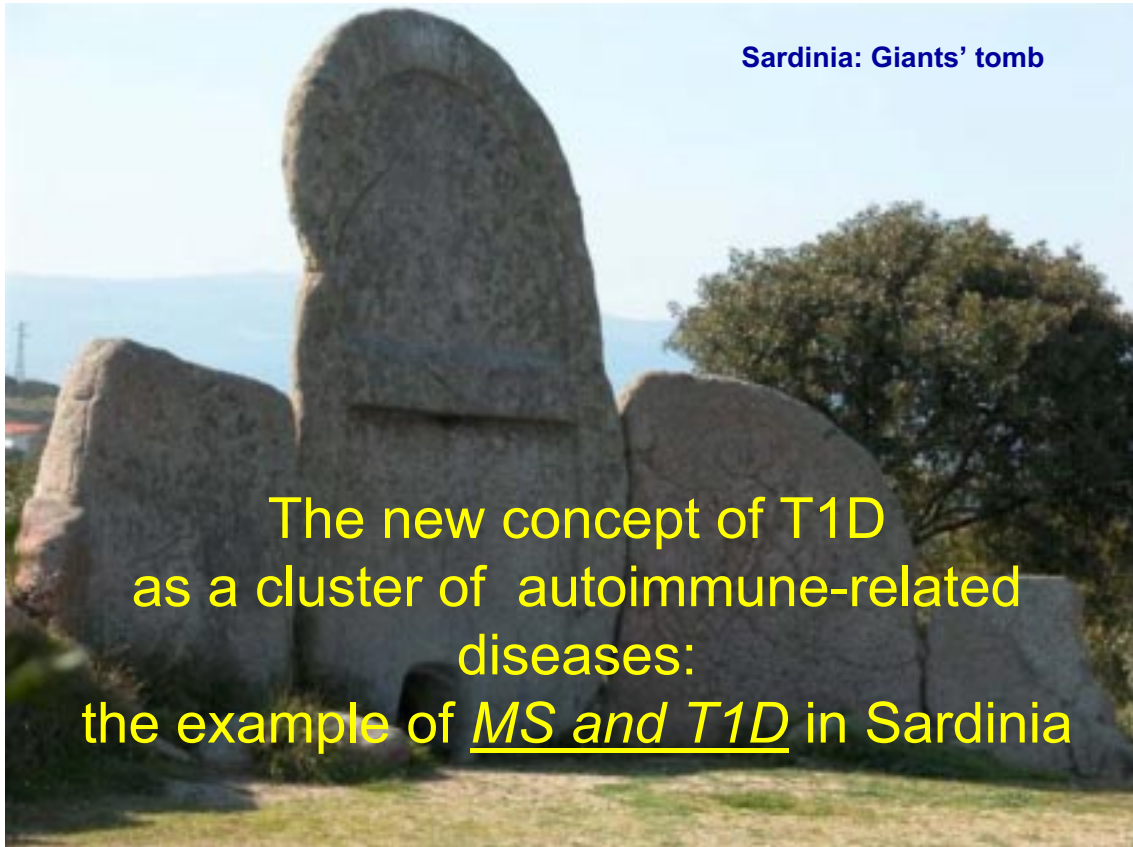
### The 'Accelerator' hypothesis

\ Body weight  
 \ insulin secretion  
 \ expression of betacell-autoantigens  
 ↓  
 betacell-autoimmunity

### High risk countries

Finland: \ body weight  
           \ T1D incidence  
 Sardinia: \ T1D incidence  
            \ body weight

Meloni et al. 1997



### Multiple Sclerosis (MS) and T1D in Sardinia

Population	Number	MS (Prev)	(95% C.I. )	Reference
<u>Sardinians (NW, all ages)</u>	270,000	<u>0.16 %</u>	(0.14-0.17)	Granieri et al. 2000
<u>Italians (all ages)</u>		0.05 %		Granieri et al. 1997
<u>Sardinian T1D adults (15-50 yrs)</u>	424	<u>0.47%</u>	(0.05-1.69)	Songini et al. (unpubl)
<u>Sardinian T1D schoolchildren</u>	650	<u>0.77%</u>	(0.25-1.79)	Chessa et al. (unpubl)

Population	Number	T1D (Prev)	(95% C.I. )	Reference
<u>Sardinian MS pts (9-65 yrs)</u>	1,053	<u>2.40%</u>	(1.54-3.49)	Marrosu et al. 2000
<u>Sardinian pop (20-59yr)</u>	6,255	<u>0.37%</u>	(0.22-0.52)	Muntoni et al. 1988

## Genetic association of MS with T1D

**In Northern Europeans: DRB1\*1501-DQB1\*0602 (DR2)\***

*\*Protective for T1D then T1D and MS occur together very rarely*

**In Sardinians:**

**DRB1\*0301-DQB1\*0201 (DR3)\***

**DRB1\*0405-DQB1\*0301 (DR4)\***

*\*Also predisposing to T1D, DR2 is very rare then T1D and MS may coexist*

*Marrosu et al. 2000*

## MS with T1D: together at last (Allegheny County, US)

Characteristics	T1D		Siblings†		Parents†	
	Males (n=148)	Females (n=149)	Males (n=143)	Females (n=187)	Males (n=84)	Females (n=140)
Age (yrs)	41.4	42.6	42.4	42.3	69.0	67.2
Duration T1D (yrs)	35.2	35.4	----	----	----	----
Observed MS prev.	0%	2.0%	0%	0.5%	0%	0%
Expected MS prev.	n/a	0.1%	n/a	0.1%	n/a	n/a
Relative increased risk of MS	n/a	20fold*	n/a	5 fold	n/a	n/a

\*p<0.01  
† unaffected with T1D  
n/a non applicable

*Dorman JS, Songini M et al. Diabetes Care, november 2003*

## Conclusions...



## To sum up (1)

- T1D has started to rise around the middle of the 20th century and keeps increasing ww in younger ages mainly in low risk countries (catch-up phenomenon)
- Whether it's an earlier presentation or a true increase it's not clear yet
- Sardinia is confirmed to be a hot spot for clinical T1D and islet-related autoimmunity, as for some other autoimmune-related diseases (CD, MS, not TD)
- An increasing T1D incidence in the Island has been found rising dramatically since the years 60' as in other countries
- No defined geographical clustering for T1D was found across the island

## To sum up (2)

- The combination of more than 1 islet-related autoantibody (rather than which) is the best predictor for the development of T1D in the Sardinian background population (SC)
- None of the classical ecological variables considered so far has shown any firm influence towards the etiopathogenesis of T1D in Sardinia; however other variables need to be further investigated
- Migrants data seems to support a different role of genetic vs environmental determinants
- There's still a long way in front of us to possibly prevent type 1 diabetes...

E3

WORKSHOP III

## *What we are doing now with the help of so many (1)*

- Trying to further improve the prediction of T1D in the general population by studying the immunological and genetic markers for T1D and other autoimmune diseases in Sardinian population and migrants and their relatives
- Investigating other putative environmental factors which can play a role towards the etiopathogenesis of T1D (e.g., chemicals, toxins, vaccinations, viral infections, etc.)

## What we are doing now... (2)

- Broadening the original investigation for T1D on the prevalence of others autoimmune diseases and to study their associations
- Comparing data from Sardinia and other areas by new collaborative studies(RIDI,TRIGR,ENDIT, SARDINIAN DIABFIN)
- Sensitizing Sardinian Health Authorities & population towards primary prevention of T1D and autoimmune diseases .....and by this way...
- improving the current care of diabetes in Sardinia!

## Acknowledgements

- Anthropology:** G. Vona (Sardinia-Italy)
- Other autoimmune diseases:**  
GF Bottazzo and coworkers (Rome-Italy)  
S. Mariotti and coworkers (Cagliari-Italy)  
T. Meloni and coworkers (Sardinia-Italy)  
M. Marrosu and coworkers (Sardinia-Italy)
- Epidemiology:** The Sardinian Epidemiology Study Group  
Eurodiab TIGER Study Group  
IDA Study Group  
RIDI Study Group  
Z. Laron, I. Askenazi (Israel)  
L. Bernardinelli and C. Pascutto (Pavia-Italy)  
P. Contu, L. Minerba (Cagliari-Italy)
- Genetic:** F. Cucca and coworkers (Sardinia-Italy)  
E.A.M. Gale and coworkers (UK)  
I. Loudianas (Sardinia-Italy)

# Acknowledgements

## Echological studies:

G.F. Bottazzo (Rome-Italy)  
M. Fadda (Sardinia-Italy)  
B. Elliot (New Zeland)  
P. Pozzilli (Rome-Italy)  
A. Contu, M. Carlini (Sardinia-Italy)

## Prediction Study:

G.F. Bottazzo & M. Locatelli (Rome- Italy)  
S. Carta, M. Sorcini, A. Olivieri (Rome-Italy)  
GF Bottazzo, A. Loviselli and the Sardinian Schoolchildren Study Group (Sardinia-Italy)  
GF Bottazzo,R. Cirillo and the Sardinian Newborn Study Group (Sardinia-Italy)  
A. Dolei, G. Delitala (Sardinia-Italy)  
M.T. Tenconi, G. Devoti (Pavia-Italy)  
The League of Sardinian Migrant Associations

## ASRIS (Association for Study and Research of IDDM in Sardinia):

M. Porceddu (secretary)  
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R. Pisano, A. Casu  
V. Cambuli  
VicePresident: M.Songini  
R. Cavallo

## R.A.S. (Regione Autonoma della Sardegna)

Italian Ministry of Healh, ADCT  
GPs&Pediaticians from Sardinia....and many more!

## European Union

National Institute of Health

*My Diabetes staff thanks you*

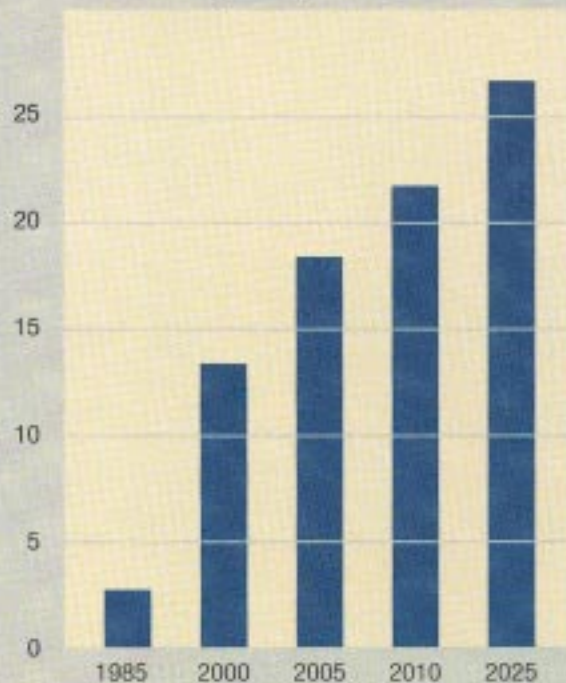


## Etiological classification of Diabetes Mellitus

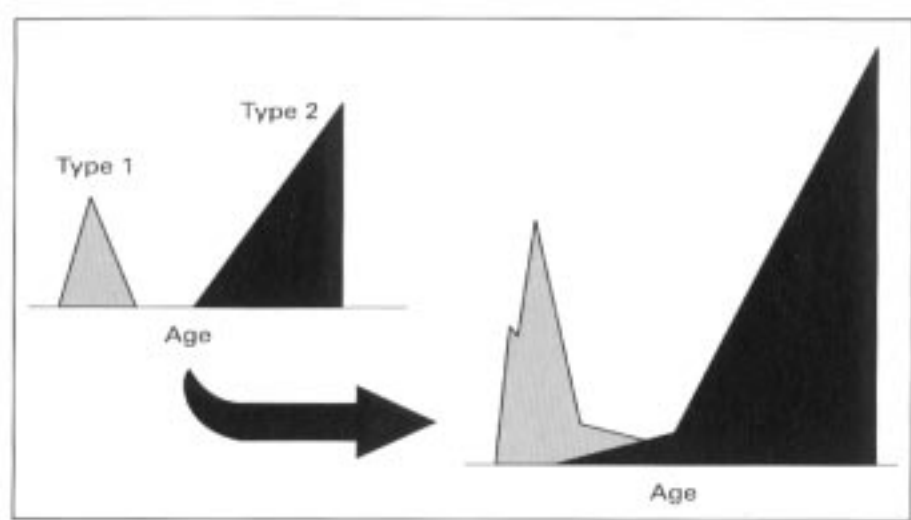
- I. Type 1 Diabetes
  - A. Immunological
  - B. Idiopathic
- II. Type 2 Diabetes
- III. Other specific types
- IV. Gestational Diabetes

*Expert Committee on the Diagnosis and Classification of  
Diabetes Mellitus, American Diabetes Association, 1999*

Global estimates of diabetes type 1  
1985 - 2025 (Million)





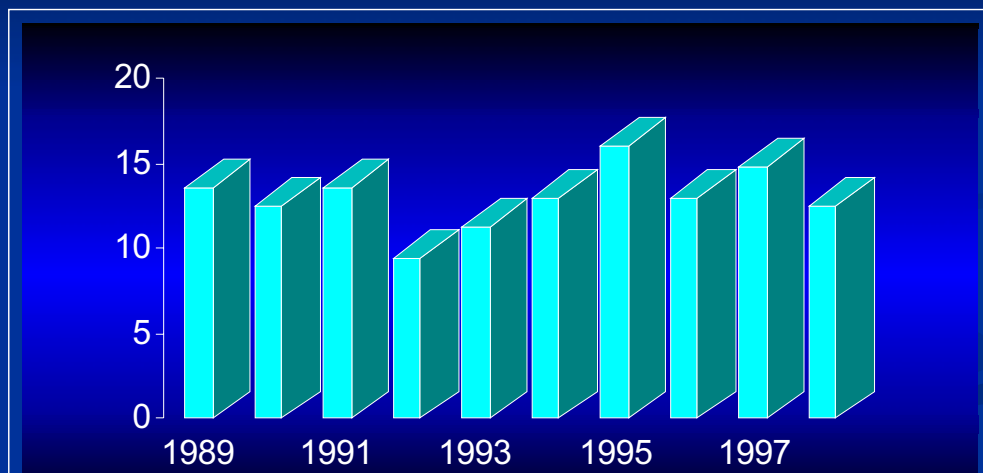


**Fig. 3.** The evolution of diabetes mellitus, showing the increased incidence in type 1 diabetes mellitus (with an early peak in under 5-year-old children and into adulthood) and type 2 diabetes, showing a very large increase with extension into adolescence and childhood.

Hom Res, 2002

**TYPE 1 DIABETES INCIDENCE IN LIGURIA REGION (0-14 yrs) FROM 1989 TO 1998**

*Distribution by year*



Diabetes Care  
2003