



The Progetto CUORE

THE PREDICTION OF CORONARY HEART DISEASE

THE ITALIAN RISK COEFFICIENTS

Preliminary Results

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**The *Progetto CUORE* - Cohort Component is
a major collaborative longitudinal CVD study in Italy**

Collaborating Centres and Principal Investigators

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- ✓ **DATA CENTRE**
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Background

- ✓ **Global cardiovascular risk score**
- ✓ **Recommended predictive coefficients derived from the Framingham Study or the PROCAM Study**
- ✓ **Limitations:**
 - **Lacking of “more recent” risk factors**
 - **Lacking of more detailed values of RFs**
 - **Lacking of interactions between FRs**
 - **Derived from selected (high-risk) populations**

The *Progetto CUORE* Cohort Component Aims

- ✓ **To estimate CHD and Stroke predictive coefficients for the Italian population**
- ✓ **To assess the additional contribution of other risk factors: like socio-economic status, physical activity, working conditions**
- ✓ **To establish a common standardised database and DNA banks to assess the genetic contribution in nested case-control or case-cohort studies**

Methods - Cohorts Description

Cohort name	Centre	Sampling Frame	Baseline		Length F-up years	Sample Size			
			Age range	SP		Men		Women	
					N	PY	N	PY	
Monica Latina		PB	25-64	1982-87	15	852	11,615	871	12,291
Matiss 83-1		PB	20-69	1983-84	15	1,365	17,906	1,029	13,901
Matiss 83-2		PB	20-69	1983-84	15	353	5,183	901	13,209
Matiss 87-1		PB	20-69	1986-87	12	862	9,028	767	8,368
Matiss 87-2	Rome	PB	20-70	1986-87	12	432	5,007	833	9,657
Matiss 93		PB	20-77	1993-95	4	970	4,374	1,000	3,908
Roma-NFR ^o		F	55-76	1989-90	9	1,855	15,575	-	-
Roma-FINE		PB	65-84	1985-85	11	682	6,491	-	-
ATENA ^o	Naples	PB	30-69	1993-97	4	-	-	5,062	18,765
Friuli MONICA 1		PB	25-64	1986-86	14	942	12,694	938	12,942
Friuli MONICA 2	Udine	PB	25-64	1989-89	11	922	9,729	922	9,980
Friuli MONICA 3		PB	25-64	1994-94	6	891	5,239	895	5,295
Hemostatic Study		PB	45-64	1995-96	4	200	822	200	883
Brianza MONICA 1		PB	25-64	1986-87	12	818	9,566	841	10,094
Brianza MONICA 2		PB	25-64	1989-90	9	804	7,206	795	7,232
Brianza MONICA 3	Brianza	PB	25-64	1993-94	5	810	3,838	864	4,104
PAMELA 91		PB	25-74	1990-93	7	1,032	7,155	1,012	7,257
Milano SEMM 94 ^o		F	20-64	1992-96	4	2,601	9,514	5,270	24,275
Casteggio 84		PB	20-59	1984-84	15	267	3,796	288	4,175
All cohort			20-84	1982-97	8	16,658	144,736	22,488	166,337

^ PB= Population Based ; F = Factory Based o Spontaneous sampling

The CUORE Project – Preliminary Result

ESC WG Epid & Prev, Taormina – April 2002

Methods – Baseline measurements

- ✓ **7 cohorts are MONICA surveys undergoing MONICA quality control procedures, other cohorts investigated with the similar methods by the same MONICA teams**
- ✓ **All data pooled in a unique database, according to the EU MORGAM international standards and quality requirements**
- ✓ **Examined CHD RFs**
 - Age and gender**
 - Systolic Blood Pressure (mean of two consecutive measures)**
 - Total Cholesterol and HDL Cholesterol measurements**
 - Cigarette smoking (current smokers vs past or never)**
 - Body Mass Index (BMI)**
 - Diabetes mellitus (reported history at baseline)**

Methods – Mortality follow-up

End	31.12.98 for all cohorts				
Type	<ul style="list-style-type: none">• Active follow-up (16 cohorts)• Record linkage - mortality databases (3 cohorts)• Telephone interviews (2 cohorts)				
Coverage	<ul style="list-style-type: none">• Country (7 cohorts)• Region (6 cohorts)• Province (6 cohorts)				
Causes of Death	<table><tr><td>Information</td><td><ul style="list-style-type: none">• Death Certificates (18 cohorts)• ICD codes (1 cohort)</td></tr><tr><td>Codes</td><td><ul style="list-style-type: none">• ICD IX (18 cohorts)• ICD X (1 cohort), converted</td></tr></table>	Information	<ul style="list-style-type: none">• Death Certificates (18 cohorts)• ICD codes (1 cohort)	Codes	<ul style="list-style-type: none">• ICD IX (18 cohorts)• ICD X (1 cohort), converted
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Codes	<ul style="list-style-type: none">• ICD IX (18 cohorts)• ICD X (1 cohort), converted				
Census status	F-up concluded for all cohorts				
End point	ICD IX 410-414 codes				

Methods – Major Coronary Event follow-up

End **31.12.98 for all cohorts**

- Type**
- **Record linkage - HDD regional databases (19 cohorts)**
 - **Re-screenings (7 cohorts)**
 - **Postal questionnaire (6 cohorts)**
 - **Telephone interviews (9 cohorts)**

Suspected codes (ICD IX codes)

- **Fatal Events**

Underline CD: 410-414, 798, 799

and 250, 428, 440 if 410-414 in other CD

- **Non Fatal Events**

410-412, 36.0-9

Methods – Major Coronary Event follow-up

- | | |
|----------------------|---|
| Validation | <ul style="list-style-type: none">• Acute coronary events validated according to MONICA criteria |
| Census status | <ul style="list-style-type: none">• F-up concluded for 10 cohorts• F-up advanced for 5 cohorts• F-up ongoing for 4 cohorts (excluded) |
| End point | <ul style="list-style-type: none">• Validated Coronary Deaths (89)• Non fatal Definite MIs (148)• Non fatal Possible MIs (123)• Non fatal Silent MIs (32)• Coronary Bypass & PTCA (51) |

Methods – Comparison Exp vs Obs Deaths

	Mortality	Men			Women		
		Expected	Observed	Ob/Ex	Expected	Observed	Ob/Ex
All cohort	All Causes	1930	1399	0.72	700	504	0.72
19 cohort	CVD (390-459)	690	526	0.76	218	160	0.73
39,146 subject	CHD (410-414)	304	239	0.79	69	45	0.65
311,074 py	Cancer (140-208)	752	573	0.76	305	222	0.73
DNA available	All Causes	443	317	0.72	353	154	0.44
10 cohort	CVD (390-459)	144	101	0.70	106	47	0.44
18,713 subject	CHD (410-414)	69	54	0.78	34	14	0.41
128,793 py	Cancer (140-208)	186	157	0.84	158	70	0.44
DNA not available	All Causes	1487	1082	0.73	347	350	1.01
9 cohort	CVD (390-459)	546	425	0.78	112	113	1.01
20,433 subject	CHD (410-414)	234	185	0.79	35	31	0.89
182,281 py	Cancer (140-208)	566	416	0.73	147	152	1.03

Methods – Possible reasons of O vs E differences

- ✓ **Artefacts: non-appropriate age-specific rates**
- ✓ **Lost to follow-up (< 2%)**
- ✓ **Adopted Procedures**
 - active follow-up
 - record linkage techniques
- ✓ **Self-selection of participants at baseline:
in the PAMELA Study,
risk of death among non-responder
double than among responders**

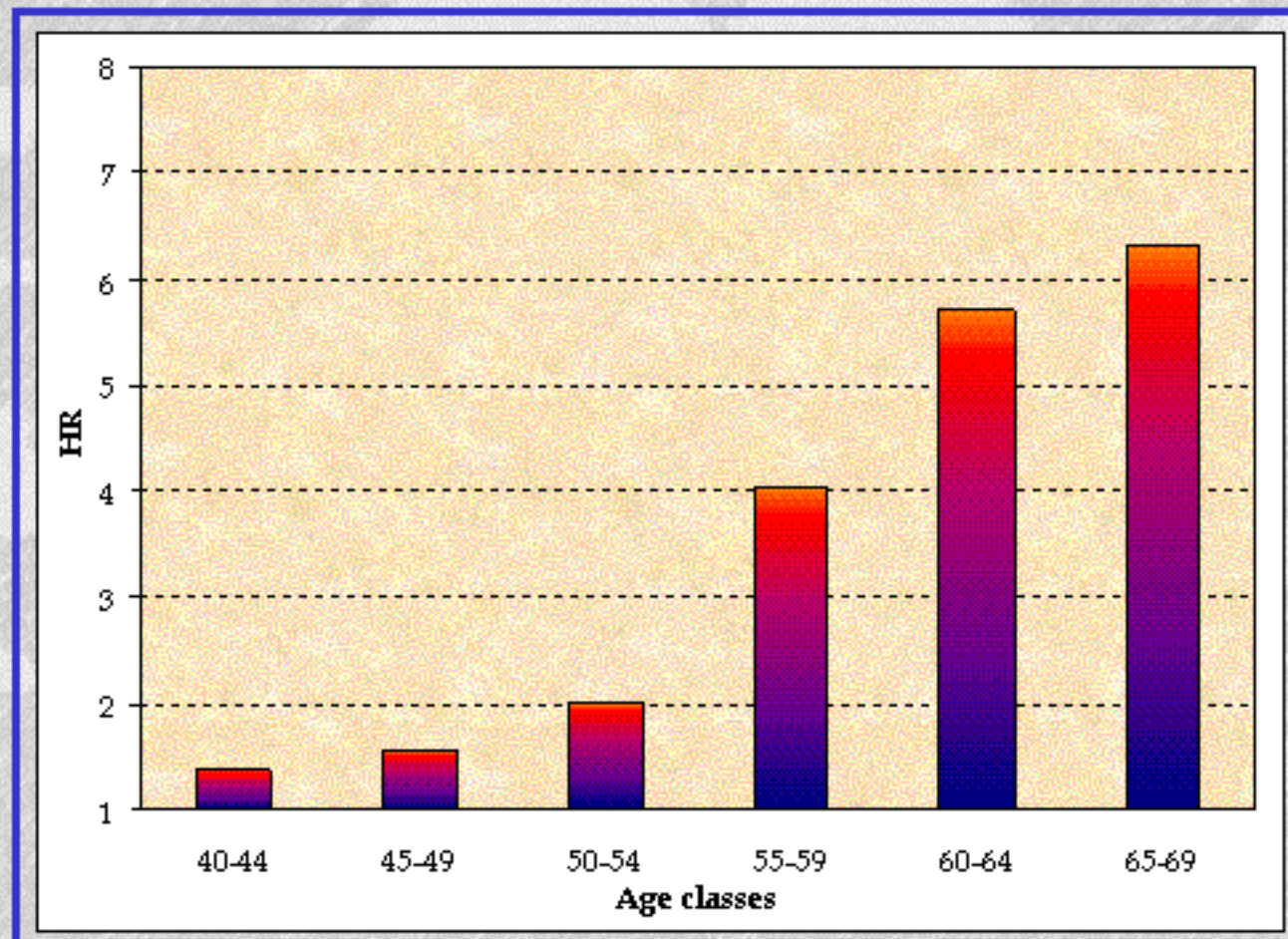
Results – Data included in the Analyses

Endpoints	CHD Deaths		Coronary Events	
	Men	Women	Men	Women
Cohorts included	16		12	
Age range (years)	35-74		35-69	
N. subjects	12,552	16,457	9,135	15,874
Median F-up (years)	8.82	5.08	7.61	4.91
n. events	234	43	341	115
Risk Factors				
Age (years)	52.6	-	49.7	48.9
SBP (mm Hg)	139.4	-	137.2	133.6
TC (mmol/l)	5.84	-	5.79	5.82
BMI (Kg/mt ²)	26.7	-	26.8	26.9
Smokers (%)	37.1	-	38.3	26.4
HDL-C (mmol/l)	-	-	1.29	1.55
Diabetes (%)	-	-	3.2	2.6
MI at baseline (%)	-	-	2.1	0.5

Assessing individual RF - **Age**

Multivariate-Adjusted HR - Major Coronary Event

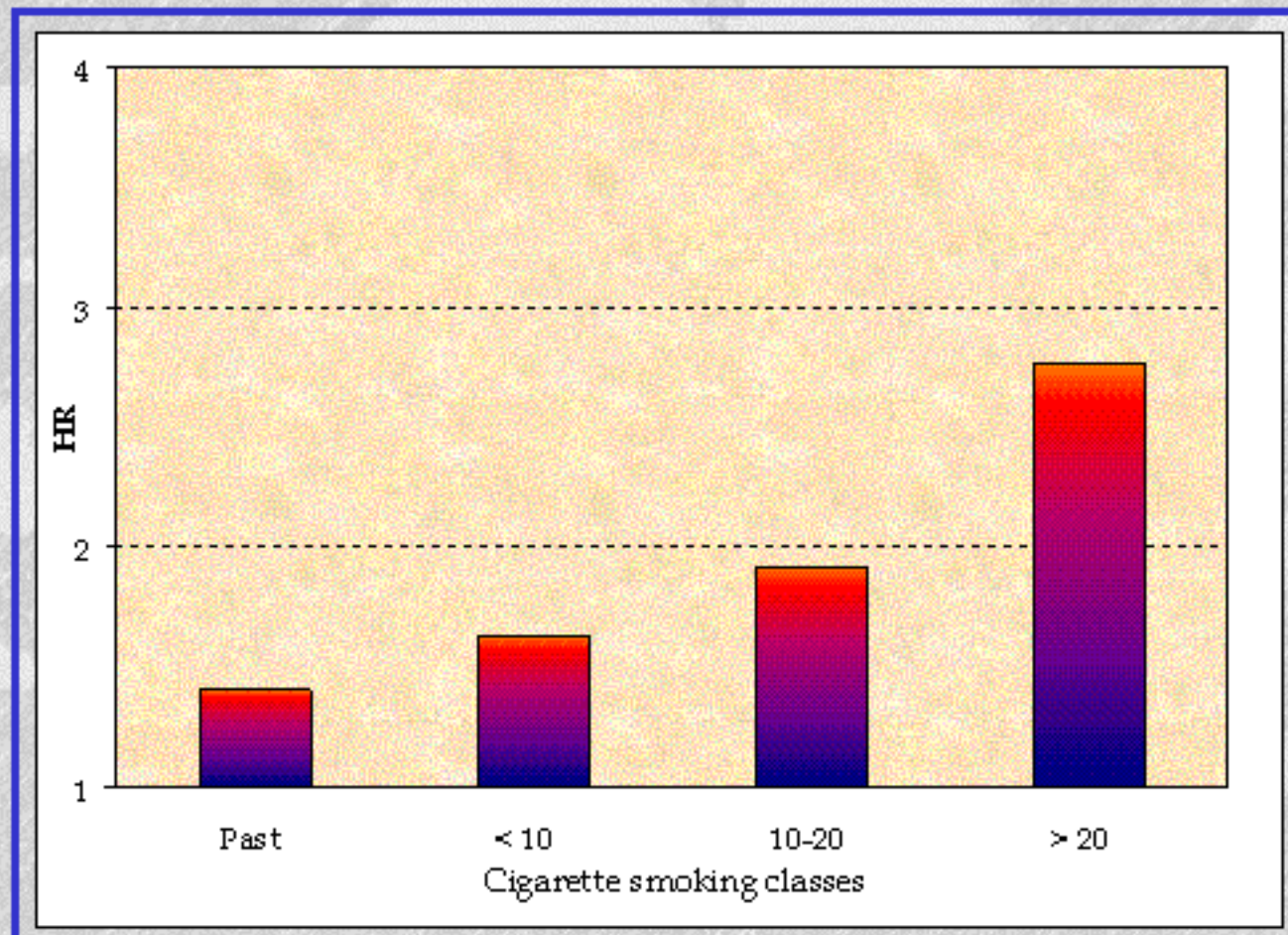
Men, 35-69 years



Assessing individual RF – **Cigarette smoking**

Multivariate-Adjusted HR - Major Coronary Event

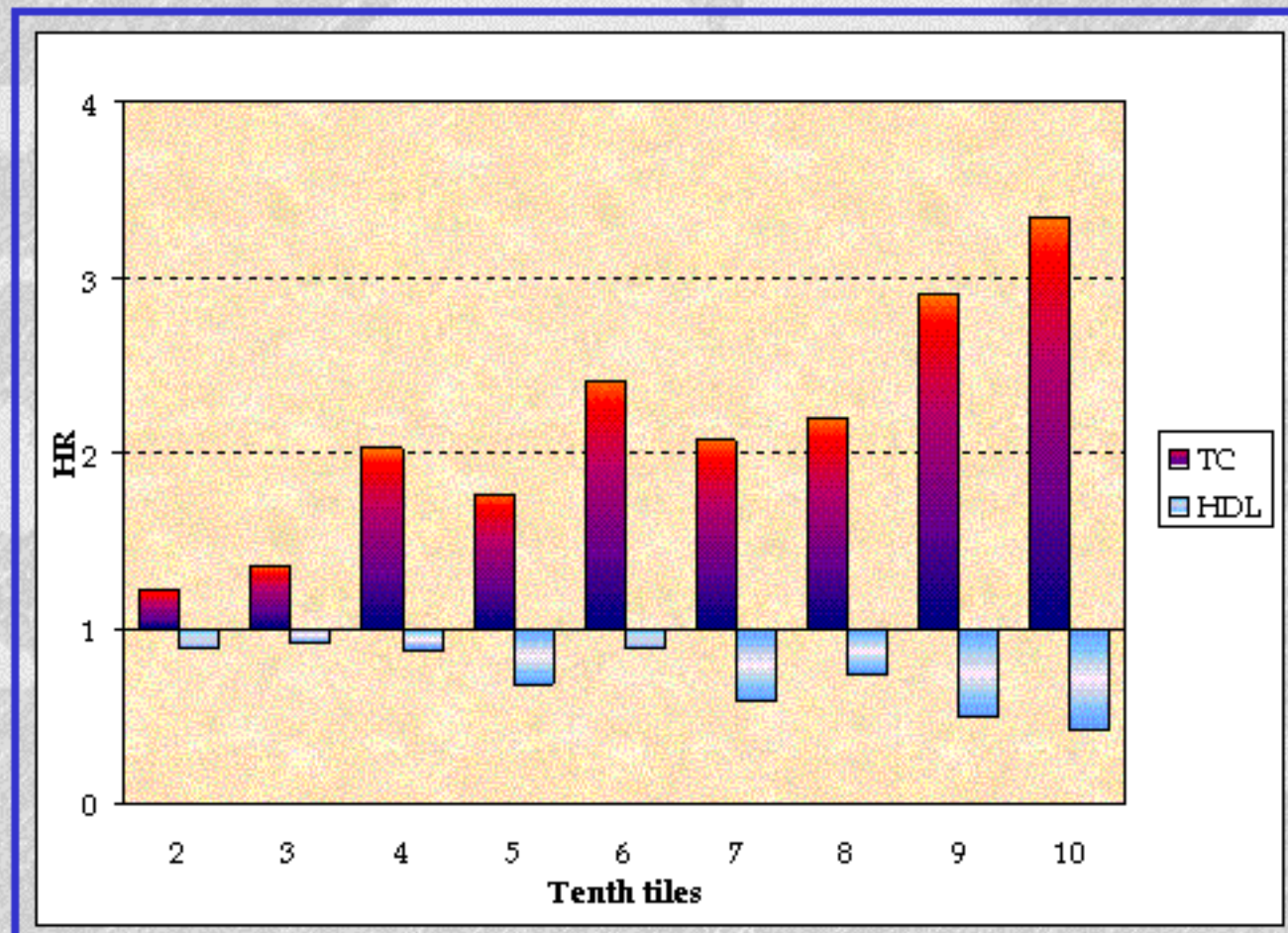
Men, 35-69 years



Assessing individual RF – TC and HDL-C

Multivariate-Adjusted HR - Major Coronary Event

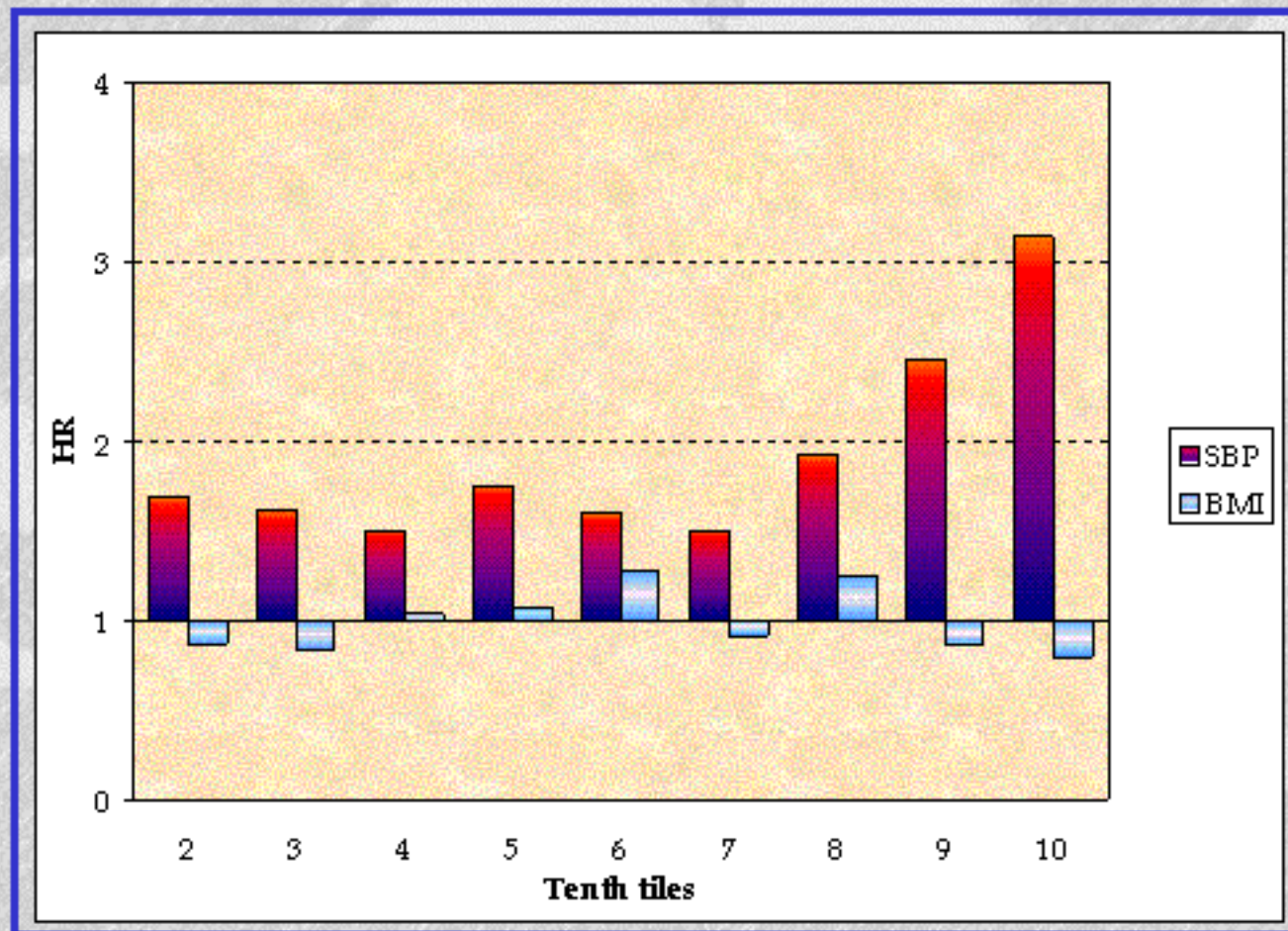
Men, 35-69 years



Assessing individual RF – **SBP** and **BMI**

Multivariate-Adjusted HR - Major Coronary Event

Men, 35-69 years



Conclusions – CHD Death, Men 35-74 years

- ✓ **9-year CHD Death predictive coefficients for standard RFs - Age, SBP, TC, SMK, BMI are reported**
- ✓ **CUORE estimates of risk coefficients for SBP and BMI (not significant predictor) are of the same magnitude of other studies**
- ✓ **CUORE estimates of risk coefficients for Cigarette Smoking and Total Cholesterol are smaller than the ones reported by other European and American studies**
- ✓ **The inclusion of older subjects may explain part of such differences**

Conclusions – Major CE, Men 35-69 years

- ✓ **7.5-year CE predictive equations calculated for 35-69 years old male Italians free of MI at baseline including in addition to standard RFs HDL cholesterol and Diabetes mellitus evidence that risk coefficients for**
 - **SBP remains stable**
 - **Cigarette smoking increases substantially**
 - **Total Cholesterol redoubles**
 - **BMI remains non statistically significant**
 - **HDL Cholesterol is a strong protective factor**
 - **Diabetes is an independent RF**

Conclusions – Major CE, Men 35-69 years

- ✓ **When the length of follow-up is taken into account, Diabetes seems to lose its predictive power after 10 year,**
- ✓ **Unexpectedly the coefficient of Cigarette Smoking increases for longer follow-up periods**
- ✓ **These results should be confirmed when all cohorts will be included in the analyses**

Conclusions – Major CE, Women 35-69 years

- ✓ **5-year CE predictive equations calculated for 35-69 years old female Italians free of MI at baseline are also reported**
- ✓ **In comparison to contemporary Men, estimates of Italian women's coefficients are**
 - **of the same magnitude for TC and HDL-C**
 - **increased for Age, Cigarette Smoking and SBP**
 - **non statistically significant for BMI**
 - **Diabetes is still an independent RF**
- ✓ **Also these preliminary results should be confirmed**