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# **International Task Force for Prevention Of Coronary Heart Disease**



## *Coronary heart disease and stroke: Risk factors and global risk*

### *Slide Kit 1*

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PROCAM  
(**P**rospective **C**ardiovascular **M**ünster Heart Study)

## **Design and principal results**

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Slide 1:

## PROCAM (Münster Heart Study): Recruitment Area



The **Prospective Cardiovascular Münster** (PROCAM) Study (also known as the Münster Heart Study) was initiated in 1978 by the Institute of Arteriosclerosis Research at the University of Münster. In several waves of recruitment, more than 30.000 participants aged between 16 and 65 years were recruited from among the employees of 52 large companies and the public service in Münster and the northern Ruhr area, the area shaded on the slide. All participants are in continuing long term follow-up for heart disease, stroke and mortality.

Slide 2:

## **PROCAM (Münster Heart Study): Design**



### *PROCAM (Münster Heart Study): Design*



- \* beginning of the study 1978
- \* approximately 30.000 volunteers (one third women, two thirds men)
- \* age range 16 to 65 years
- \* employees of 52 large companies and the public service in Münster and the Northern Ruhr Area
- \* rate of participation on average 60%
  
- \* examination and interview by physician (standardized questionnaires)
- \* measurement of blood pressure and anthropometric data
- \* resting electrocardiogram
- \* case history and family history
- \* collection of blood sample after 12-hour fast (>30 laboratory parameters)
  
- \* examination carried out during paid working hours
- \* all findings were reported to the participant's general practitioner
- \* the investigators neither carried out nor arranged for any intervention
  
- \* questionnaires were sent to the participants every 2 years for follow-up
- \* examination repeated after 6 to 7 years

This slide shows the main characteristics of the PROCAM Study.

Slide 3:

## **PROCAM (Münster Heart Study): Outcome**



The slide features a dark blue background with yellow text. At the top, there are two small images: a building on the left and a heart rate monitor on the right. The title 'PROCAM (Münster Heart Study): Outcome' is centered at the top. Below the title, a red horizontal line separates it from the main content. The content consists of several bullet points, each starting with a yellow asterisk. The text is organized into a list of study characteristics, event counts, and survival statistics.

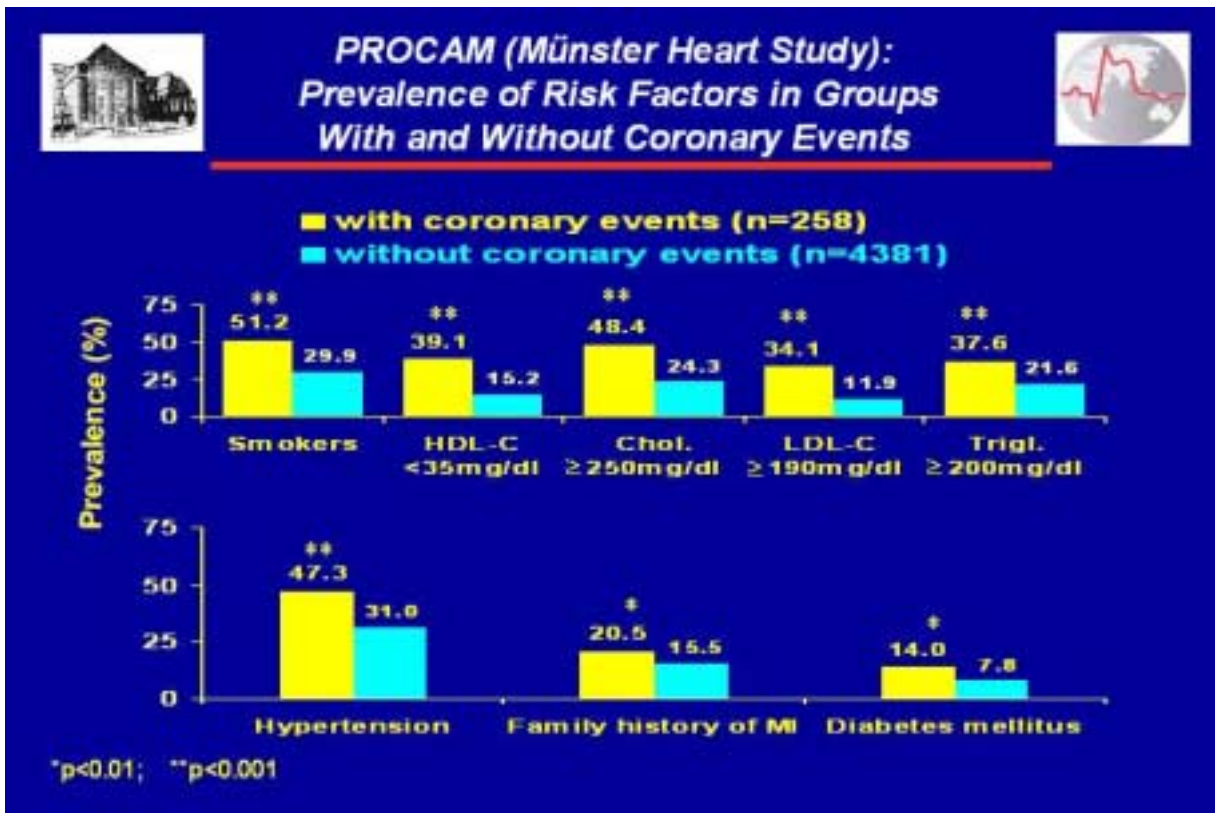
**PROCAM  
(Münster Heart Study):  
Outcome**

- \* 4,849 men aged between 40 and 65 years
- \* no prior history of myocardial infarction or stroke
- \* fixed follow-up period of 8 years
- \* 258 definite coronary events:
  - 28 sudden cardiac deaths
  - 49 fatal myocardial infarctions (MI)
  - 181 definite nonfatal MI
- \* 48 cerebrovascular events:
  - 41 non-fatal cerebrovascular events
  - 7 fatal strokes
- \* 161 deaths of non-coronary or cerebrovascular origin:
  - 79 cancer
  - 14 suspected coronary deaths
  - 8 other diseases of the circulatory system
  - 28 other diseases
  - 32 accidental or violent deaths
- \* 4,381 men survived 8 years without definite nonfatal MI or stroke

In the PROCAM Study only the cohort of 4849 men aged 40-65 years included a sufficient number of coronary events for valid statistical analysis on 8-year follow-up. The outcome characteristics of this cohort are shown on this slide. 4381 men survived 8 years without definite nonfatal MI or stroke, 258 definite coronary events occurred. Thus, the total size of this cohort is 4639 (258 plus 4381) men. LDL-cholesterol was not determined in 138 men with triglyceride levels above 400 mg/dL, 12 of whom had coronary events. Thus for figures including data on LDL-cholesterol, the total size of the cohort was 4501 and the number of coronary events was 246.

Slide 4:

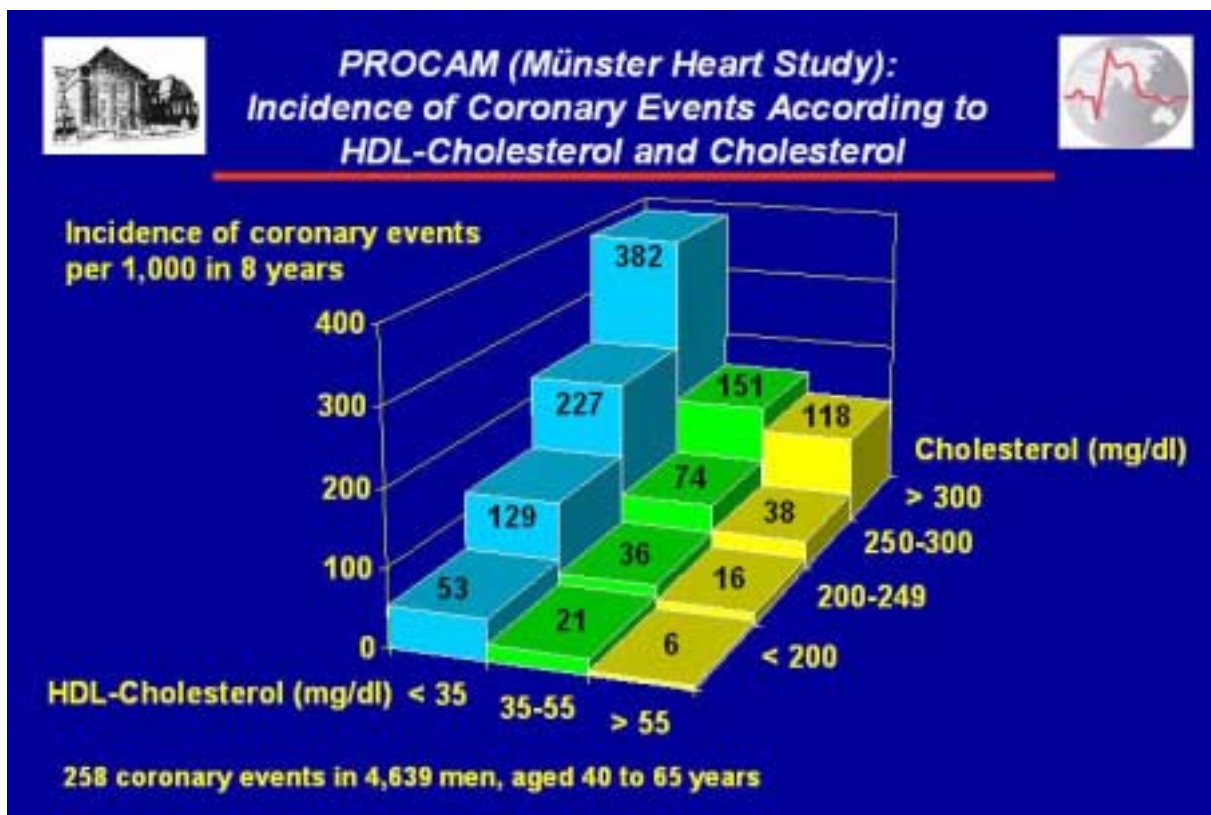
## PROCAM (Münster Heart Study): Prevalence of Risk Factors in Groups With and Without Coronary Events



In the cohort of 4639 men aged 40 to 65 years in PROCAM, 258 developed a coronary event (fatal or nonfatal myocardial infarction, sudden cardiac death) within 8 years of follow-up. As shown on this slide, each of the classic risk factors was between 50% and three times more common in men with a coronary event than in those without such an event.

Slide 5:

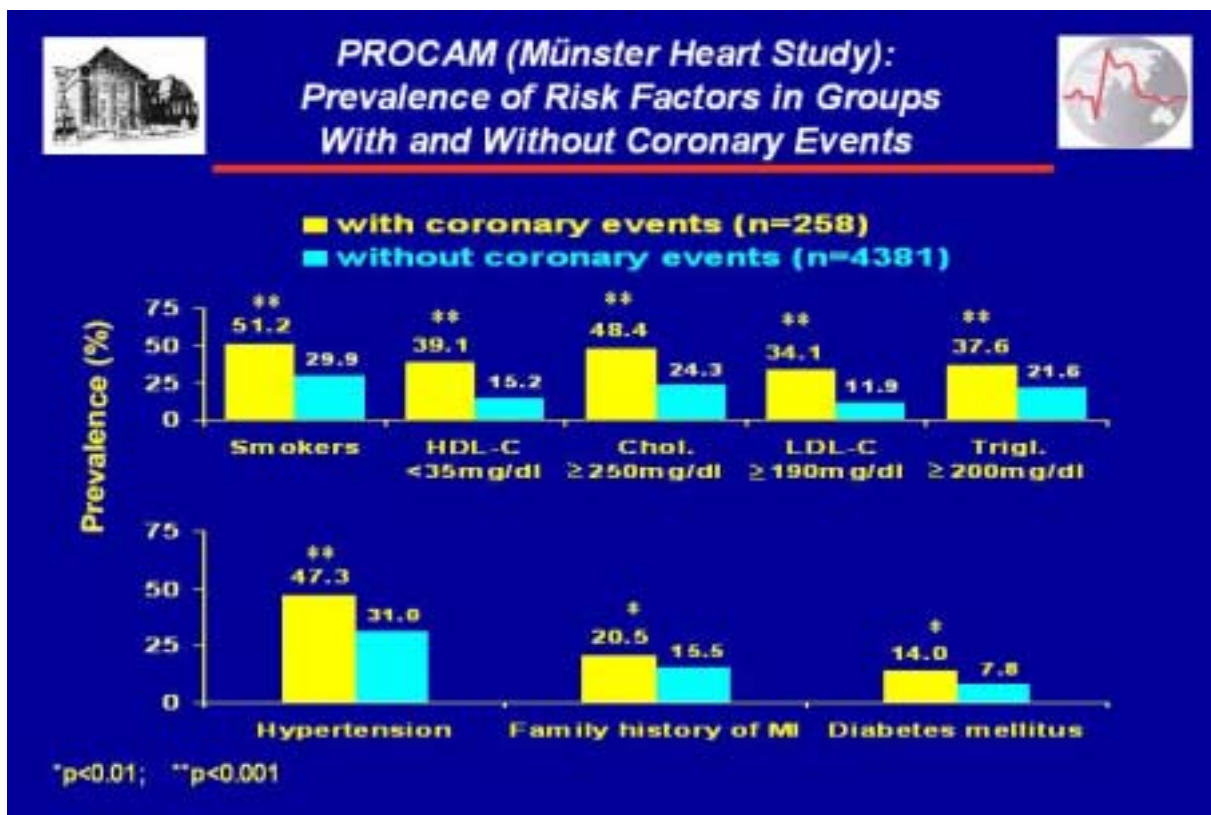
## PROCAM (Münster Heart Study): Incidence of Coronary Events According to HDL-Cholesterol and Cholesterol



Perhaps the most important result to emerge from PROCAM and other prospective epidemiological studies of coronary heart disease risk factors is the realization that risk factors do not act in isolation, but in synergistic interaction with other risk factors. That is to say, individual risk factors interact in a multiplicative rather than an additive fashion. This is illustrated in this slide which shows the interaction between total cholesterol and HDL-cholesterol. Risk increases dramatically, from only 6 per 1000 in 8 years among men with a total cholesterol below 200 mg/dL and an HDL-cholesterol above 55 mg/dL at entry into the PROCAM Study to a striking 382 per 1000 among men with a cholesterol above 300 mg/dL and an HDL-cholesterol below 35 mg/dL. This represents a more than 60-fold differential in risk.

Slide 6:

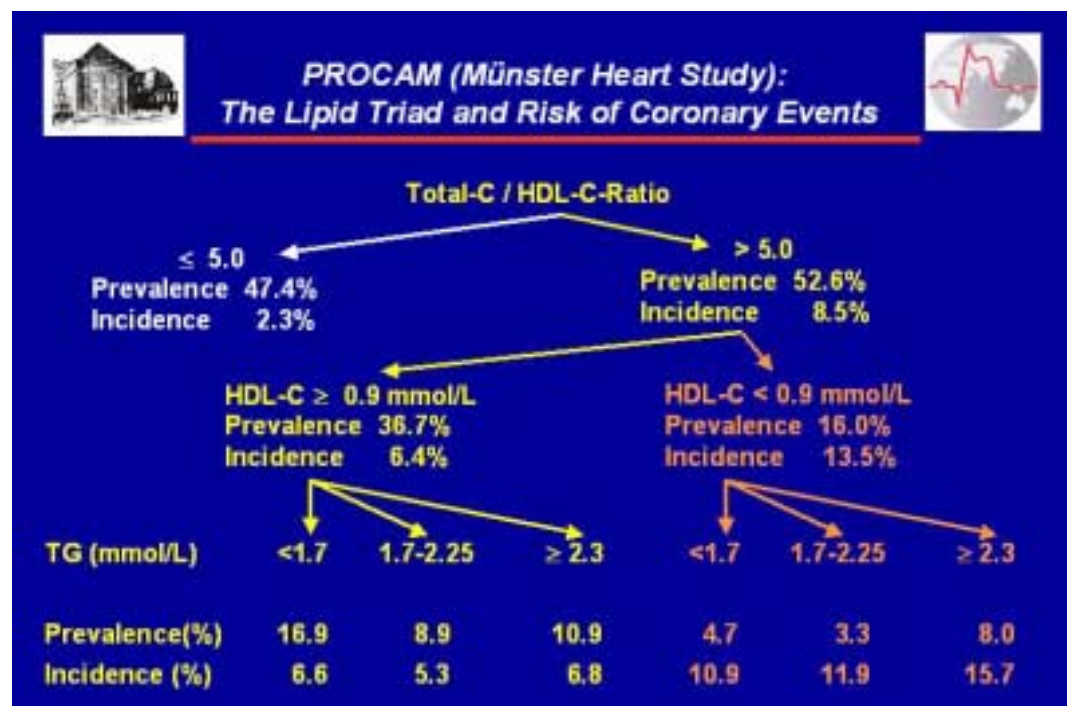
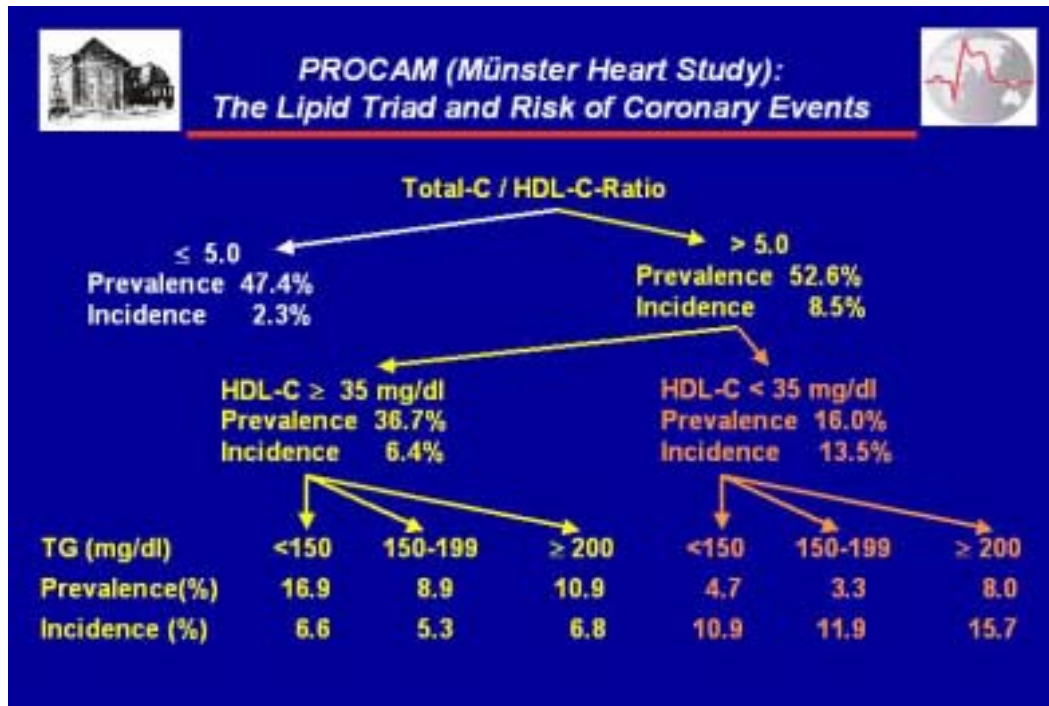
## PROCAM (Münster Heart Study): Prevalence of Risk Factors in Groups With and Without Coronary Events



In the cohort of 4639 men aged 40 to 65 years in PROCAM, 258 developed a coronary event (fatal or nonfatal myocardial infarction, sudden cardiac death) within 8 years of follow-up. As shown on this slide, each of the classic risk factors was between 50% and three times more common in men with a coronary event than in those without such an event.

Slide 7:

**PROCAM (Münster Heart Study):  
 The Lipid Triad and Risk of Coronary Events**

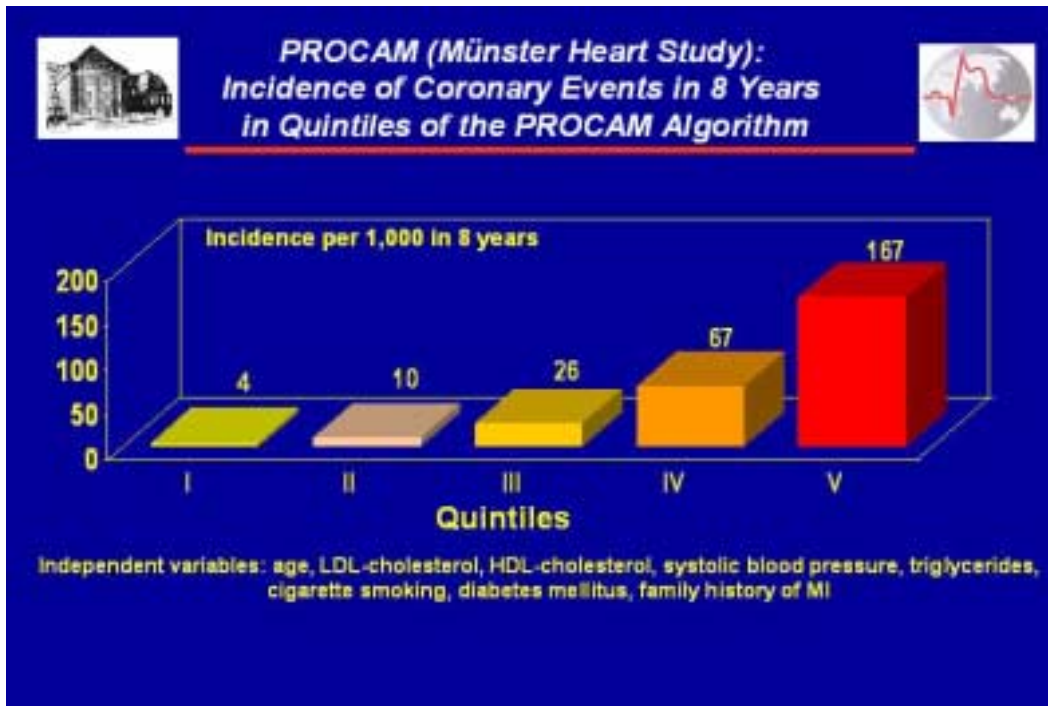


In recent years, much attention has been devoted to the so-called metabolic syndrome, a complex comprising insulin resistance, obesity, hypertension, and dyslipidemia. One of the most commonly observed defects in this condition is the combination of moderately raised total cholesterol, low HDL-cholesterol, and hypertriglyceridemia (Lipid Triad). When the cohort of men aged 40 to 65 in PROCAM was segregated using a total to HDL-cholesterol ratio of 5 as a cut-off (the median in the population, see slide 5), and then further segregated according to the HDL-cholesterol and triglyceride levels, a striking gradient of risk was observed, ranging from 6.6% among men with an HDL-cholesterol above 35 mg/dL (0.9 mmol/L) and a triglyceride level of below 150 mg/dL (1.7 mmol/L) to 15.7% among men with an HDL-cholesterol below 35 mg/dL (0.9 mmol/L) and a triglyceride level above 150 mg/dL (2.3 mmol/L).

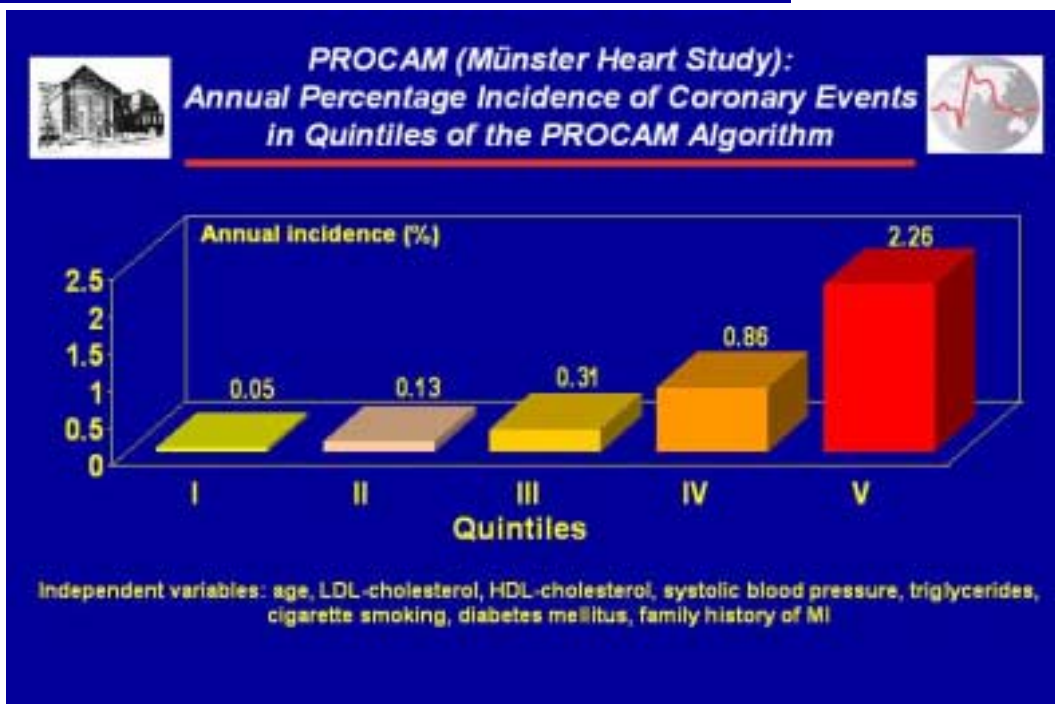
Slide 7a (on Top) shows these data in mg/dl, slide 7b (bottom) in mmol/L.

Slide 8:

## PROCAM (Münster Heart Study): Incidence of Coronary Events in 8 Years in Quintiles of the PROCAM Algorithm



If the results of the PROCAM Study had to be summed up in one slide, this would be it. What this slide shows is the incidence of coronary events occurring within 8 years of follow-up in men aged 40 to 65 in PROCAM, divided into fifths (quintiles) using a multiple logistic function derived from more than 50 variables measured in each man. The 8 variables listed here each make an independent contribution to risk. Taken together, they allow a more than 40-fold stratification of risk between the lowest and the highest quintile. Slide 8b shows the same results expressed on a per year basis.



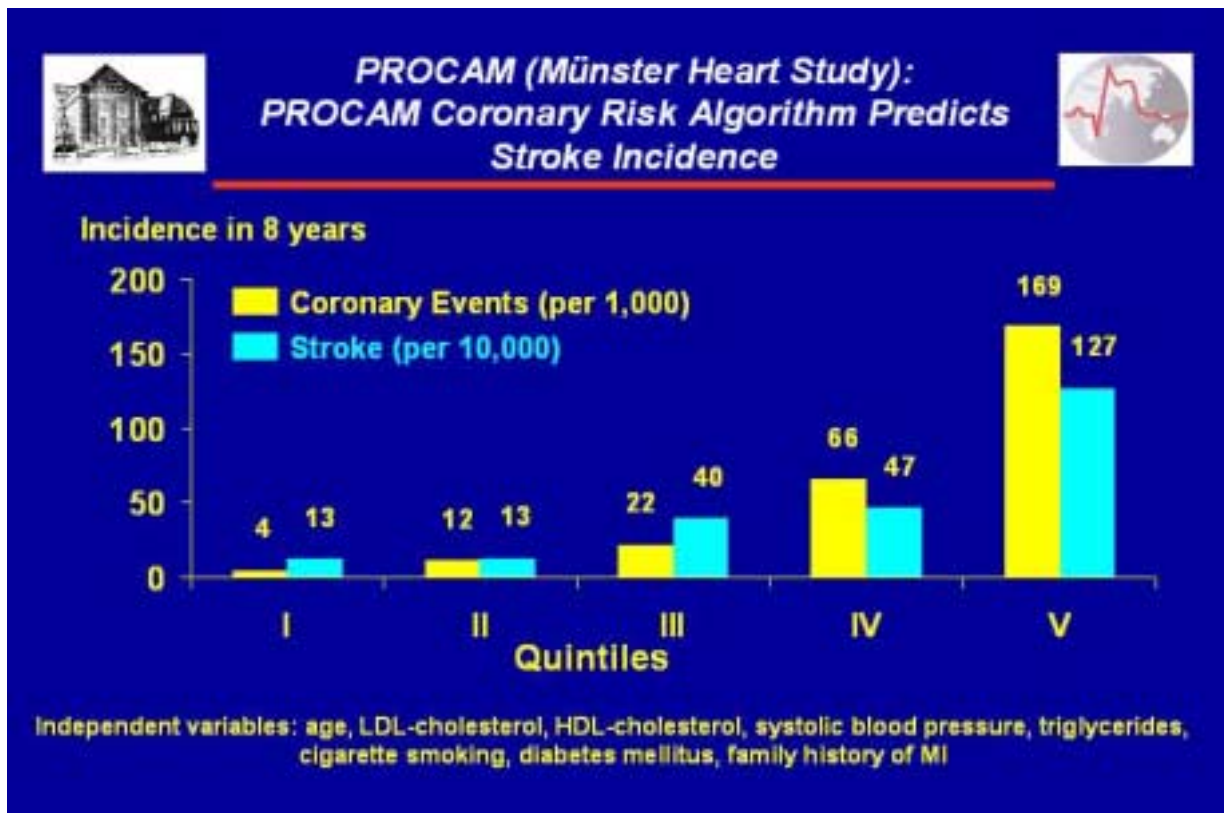
Slide 8b shows the same results expressed on a per year basis. The mean annual risk in each quintile is as follows:

- quintile 1: 0.05 %
- quintile 2: 0.13 %
- quintile 3: 0.31 %
- quintile 4: 0.86 %
- quintile 5: 2.26 %

Allocation of your patients to these quintiles can be performed using the interactive program on this Website [www.chd-taskforce.com/risk-english.htm](http://www.chd-taskforce.com/risk-english.htm)

Slide 9:


## PROCAM (Münster Heart Study): PROCAM Coronary Risk Algorithm Predicts Stroke Incidence




An important result of the PROCAM Study was the finding that the risk algorithm for coronary events also identified those men at high risk for stroke. As shown on this slide, the rate of increase in risk across the quintiles of the PROCAM algorithm was similar for coronary and cerebrovascular disease.

Slide 10:

## **PROCAM (Münster Heart Study): Risk Factors Included In Standard PROCAM Algorithm and Neural Network Analysis**



*PROCAM (Münster Heart Study):  
Risk Factors Included In Standard PROCAM Algorithm  
and Neural Network Analysis*



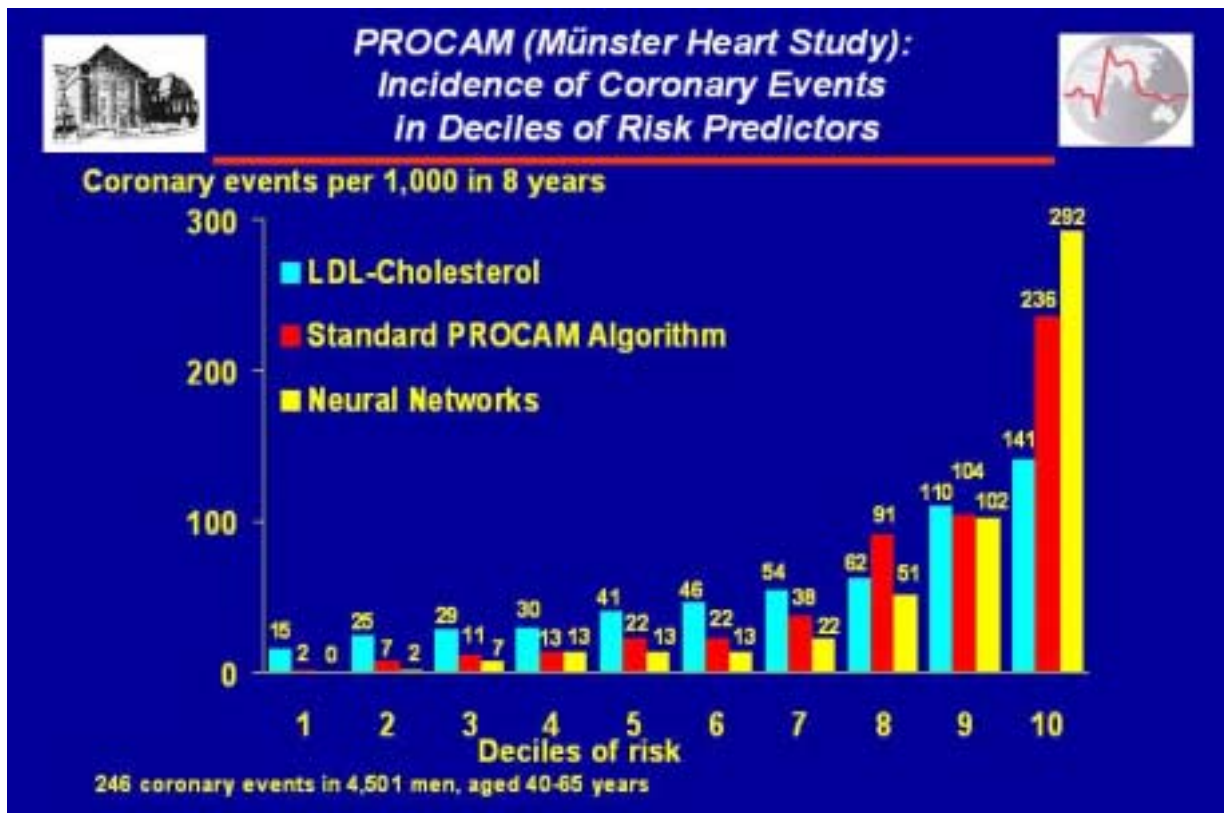
<b>Neural Networks</b>	<b>Standard PROCAM Algorithm</b>
<b>Age</b>	<b>Age</b>
<b>Systolic and Diastolic Blood Pressure</b>	<b>Systolic Blood Pressure</b>
<b>Antihypertensive Treatment</b>	
<b>HDL-C and LDL-C</b>	<b>HDL-C and LDL-C</b>
<b>Triglycerides</b>	<b>Triglycerides</b>
<b>No. of cigarettes/day</b>	<b>Cigarette Smoking (yes/no)</b>
<b>Diabetes, Fasting Blood Glucose</b>	<b>Diabetes (yes/no)</b>
<b>Body Mass Index</b>	
<b>Family History of MI</b>	<b>Family History of MI</b>

The Future of Risk Analysis:

A most promising approach to risk prediction is the use of neural networks to detect and exploit complex, non-linear interactions between risk variables. In the PROCAM Study, such neural network analysis allowed utilization of several variables which are shown on this slide.

Slide 11:

## PROCAM (Münster Heart Study): Incidence of Coronary Events In Deciles of Risk Predictors

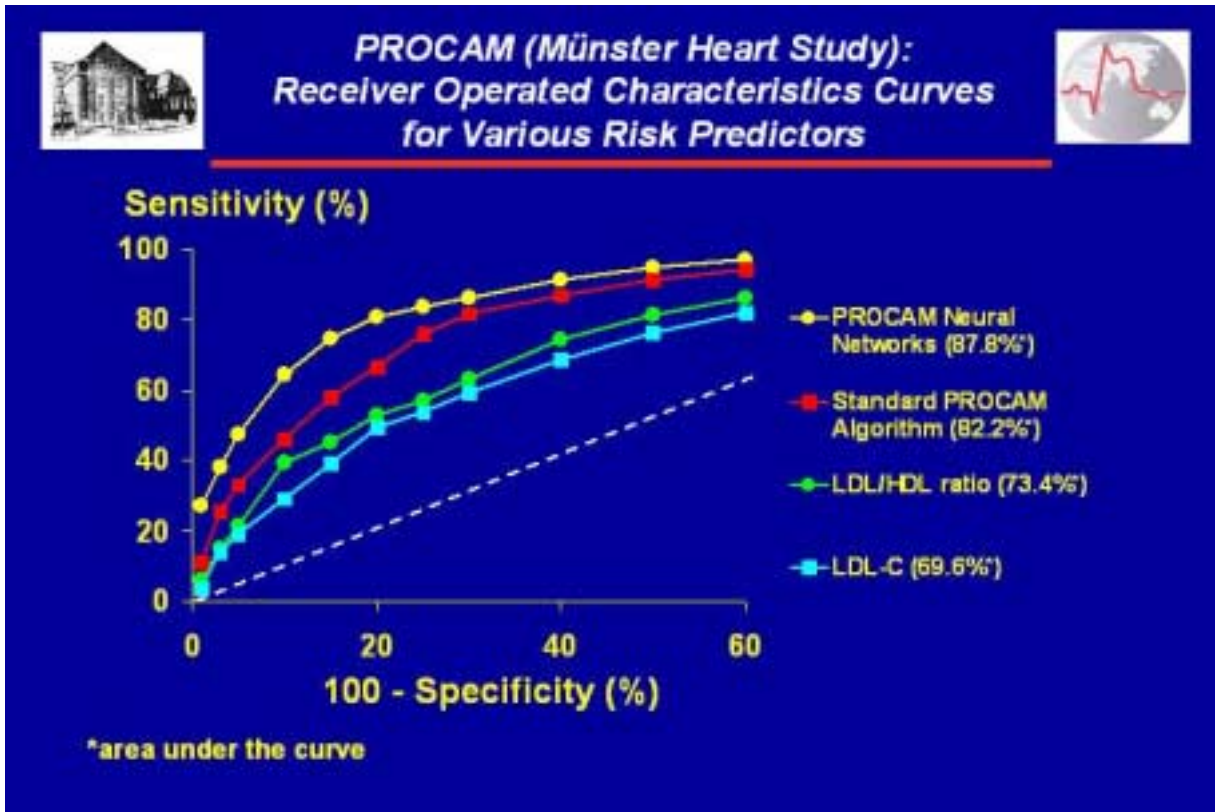


Improvement of Risk Prediction using Neural Networks:

As shown by the PROCAM Study, a logistic regression model (standard PROCAM algorithm) using 8 variables significantly improves risk prediction compared to a single risk factor such as LDL-cholesterol. Neural network improves the ability to predict risk even further. As shown in this slide, neural network analysis allocates a greater proportion of coronary events to the highest decile of risk.

Slide 12:

## PROCAM (Münster Heart Study): Receiver Operated Characteristics Curves for Various Risk Predictors



Perhaps the best measure of the performance of a predictive function is the area under receiver operated characteristics (ROC)-curves. A test which perfectly discriminates between affected and non-affected individuals passes through the top left hand corner of the graph (area under curve 100%). A test with no discriminatory power follows the dashed line shown on this slide (area under curve 50%) The better a test, the more the ROC-curve deviates from this line. As can be seen on this slide the area under the ROC-curve is significantly greater with neural network analysis compared to the standard PROCAM algorithm or single risk factors.