Conoscere e Curare il Cuore 2016

LA GENETICA PER PREDIRE IL RISCHIO DI MORTE IMPROVVISA

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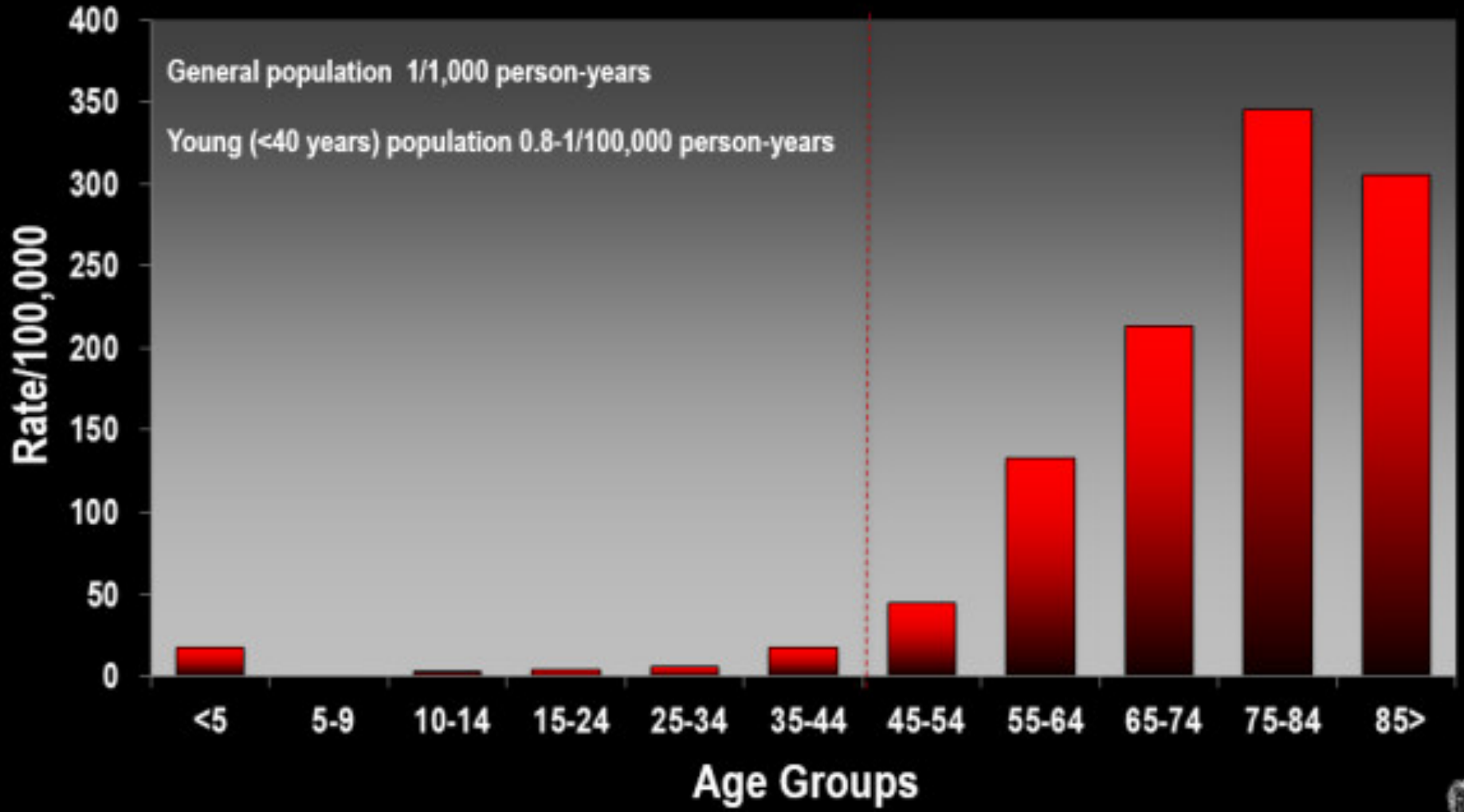
Azienda Ospedaliero - Universitaria di Parma

Annual incidence of SCD by age-group



Modified by Maron BJ et al., Circulation 2009 119;1085-1092

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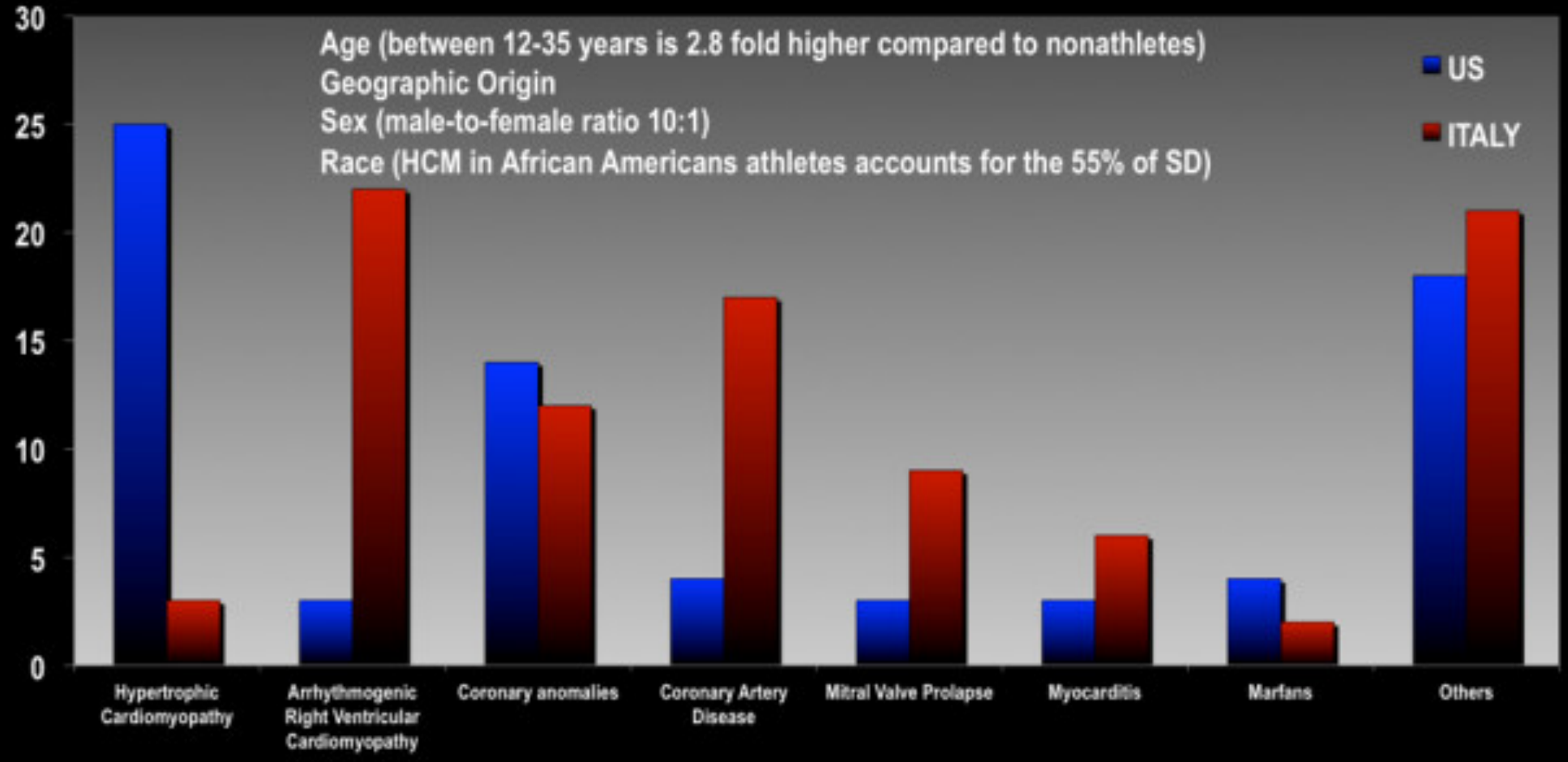
Parma

Incidence of SCD Athletes



Modified by Maron BJ et al., Circulation 2009 119;1085-1092

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Usefulness of Cardiovascular Genetic

- Intermediate Phenotype
- Risk stratification of well known phenotype
- Molecular Autopsy
- Family Screening

Intermediate Phenotype

LA STAMPA

07/11/2003

IL NUOTATORE NOVARESE E' STATO BLOCCATO PER IL SOSPETTO DI UNA GRAVE PATOLOGIA CARDIACA

Le paure di Fioravanti «Ditemi che cosa ho»

«Voglio solo sapere qual è la mia malattia?»

Usefulness of Cardiovascular Genetic

- Intermediate Phenotype
- **Risk stratification of well known phenotype**
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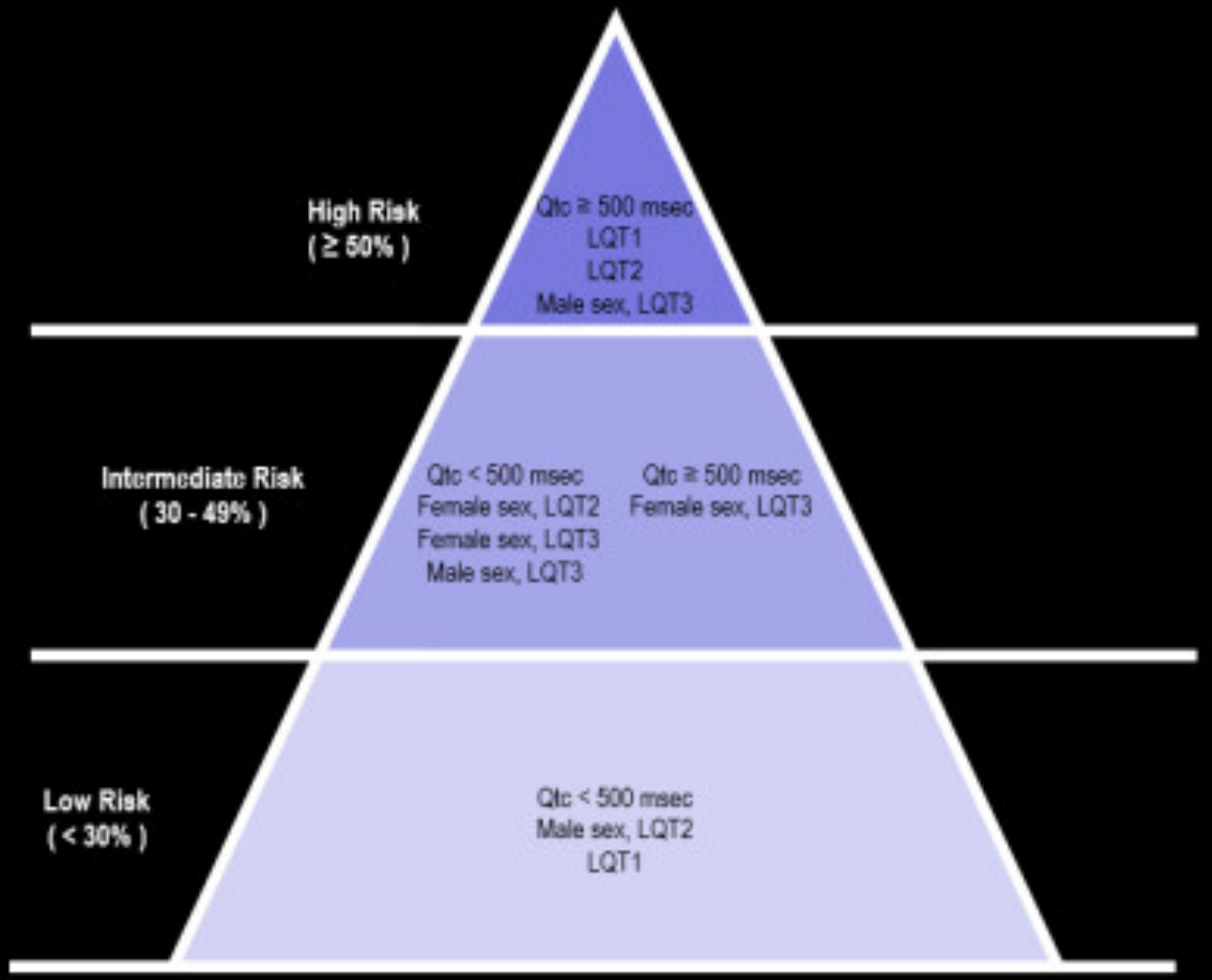
Risk stratification in well known phenotype

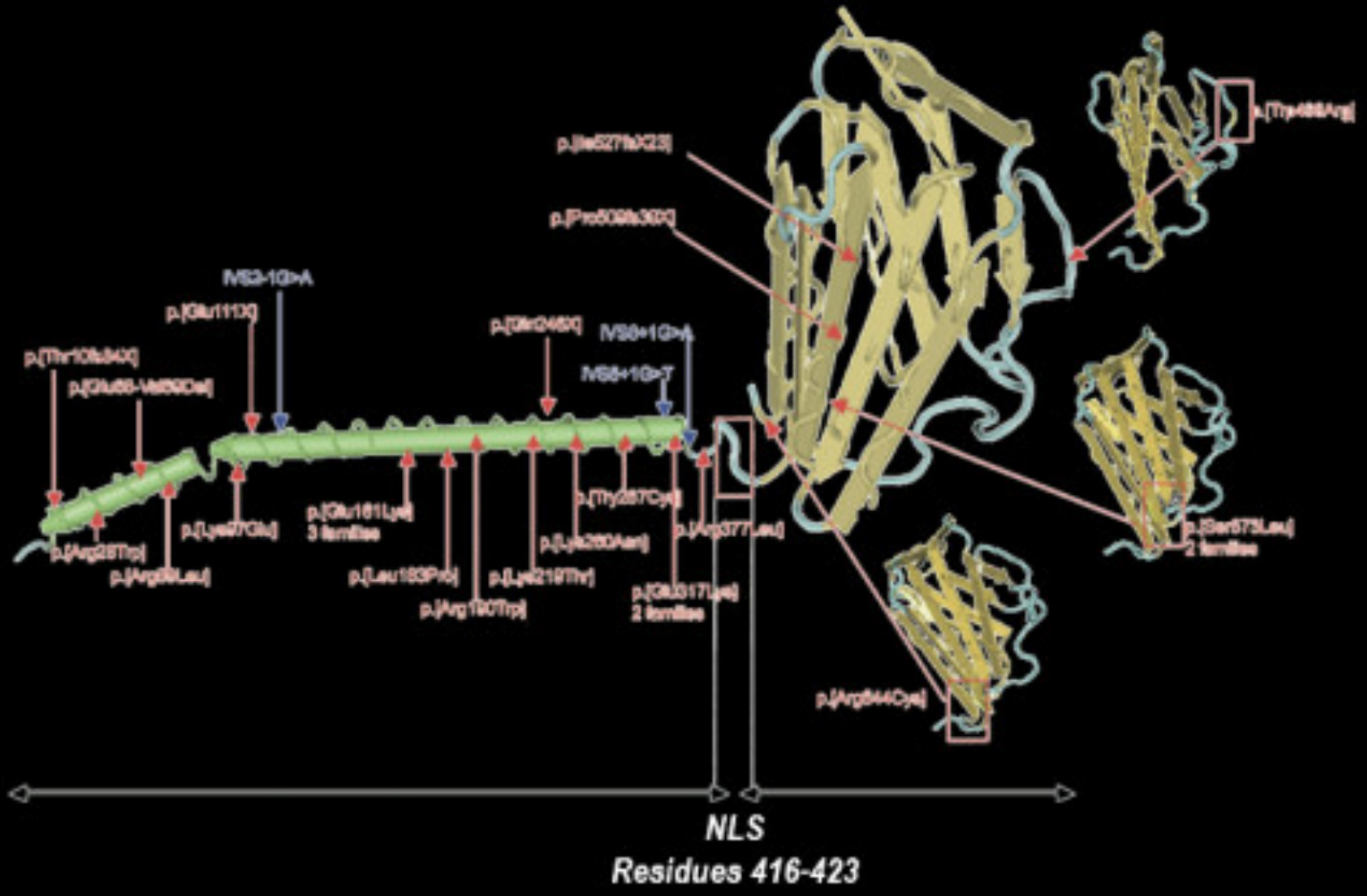
LQTc Syndrome



Priori SG et al., N Engl J Med 2003;348:1866-74

Risk stratification in well known phenotype

Laminophaties



Pasotti et al., Jacc 2008 Vol 52, No. 15;2052-2060

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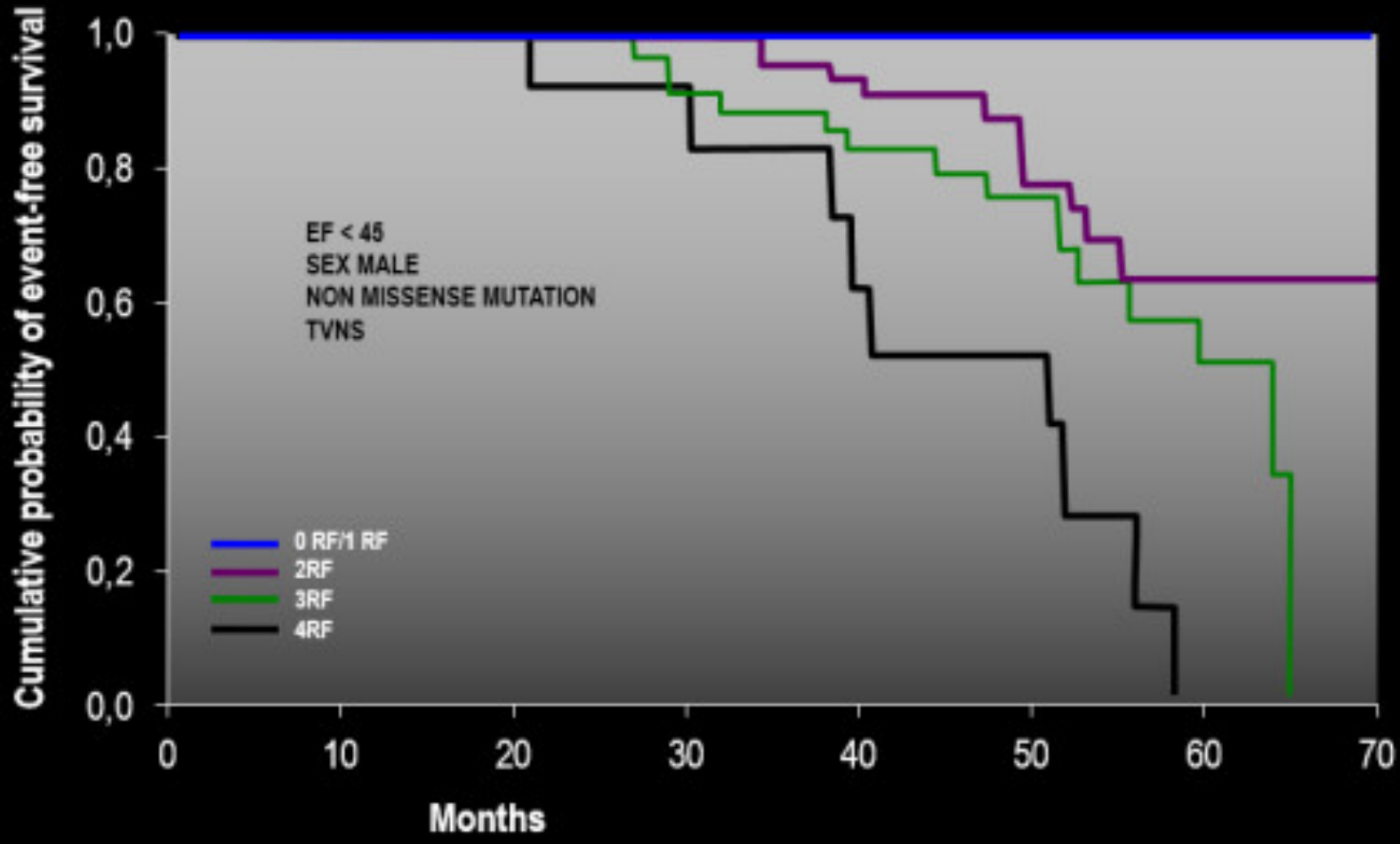
Risk stratification in well known phenotype

Laminophaties



Charron et al., Arrhythm Electrophysiol Rev. 2012 Sep; 1(1):22-8.

Usefulness of Cardiovascular Genetic

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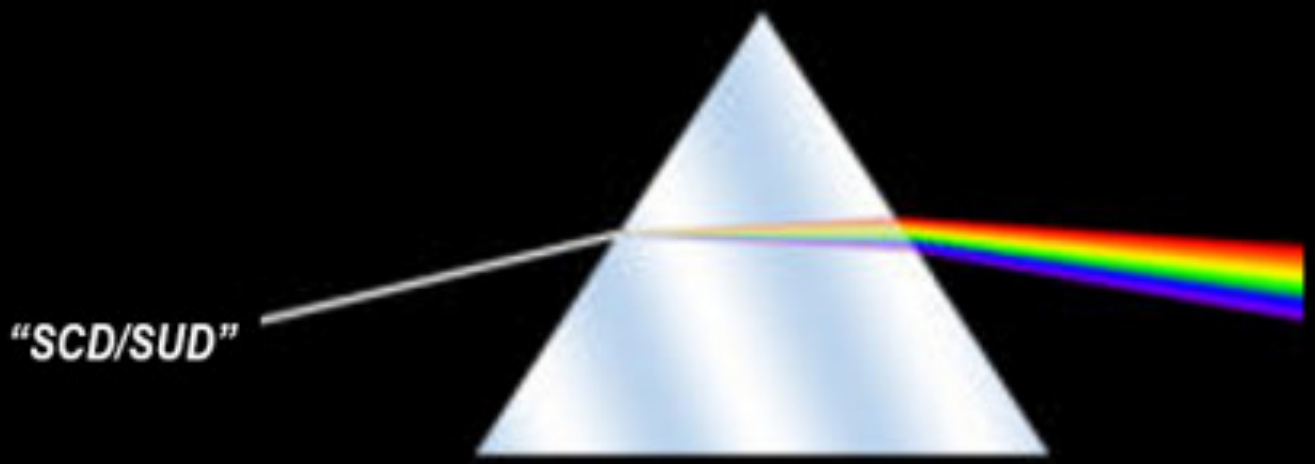
- Family Screening

Molecular Autopsy



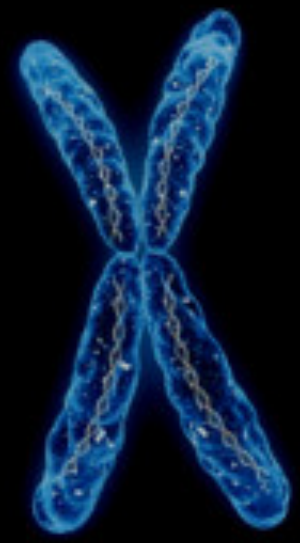
LQT/SQT
ARVC/D
CPVT
HCM
BS
CMD
FH
OTHERS….

Morphologically pre- symptomatic

Next generation sequencing

Exome sequencing

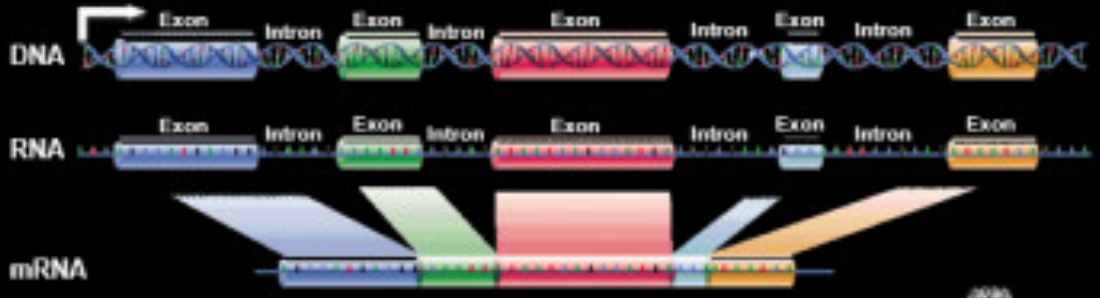
The exome (the protein-coding region of the human genome) represents less than 2% of the genetic code, but contains ˜85% of known disease-related variants



46 Chromosomes

>3 billions base pairs

More than 20.000 genes coding for proteins



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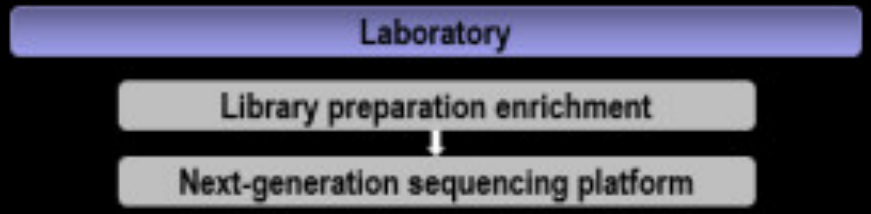
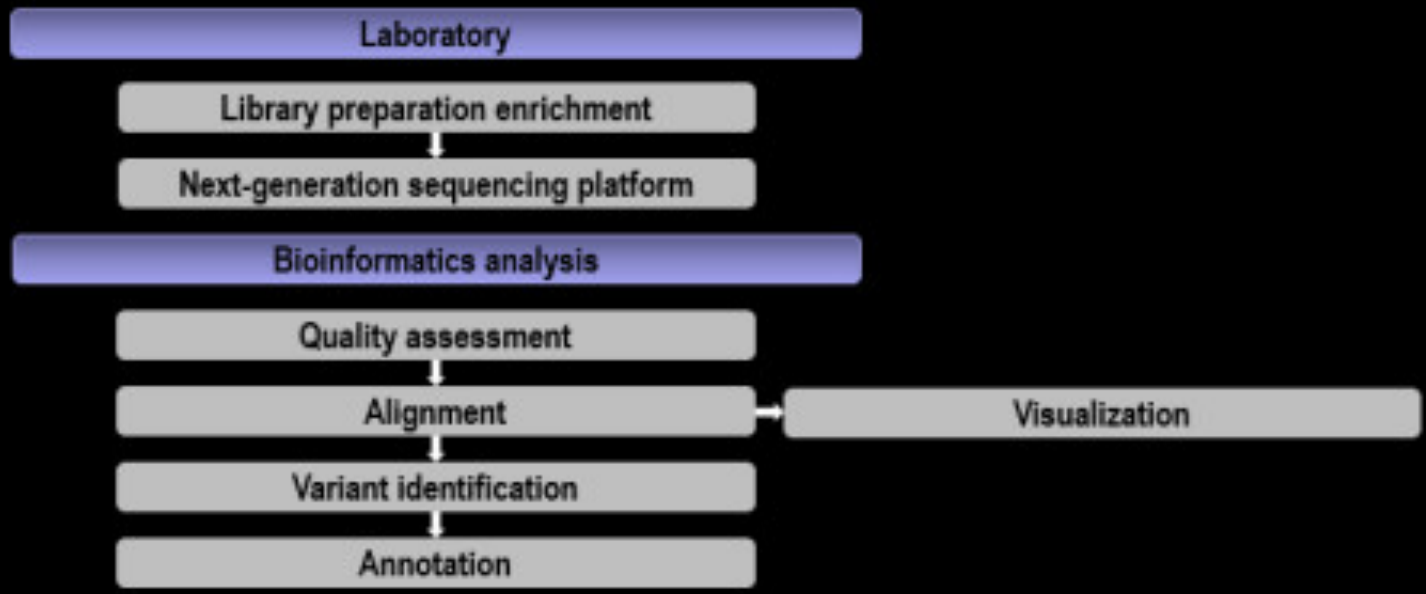
Next generation sequencing

Flow chart



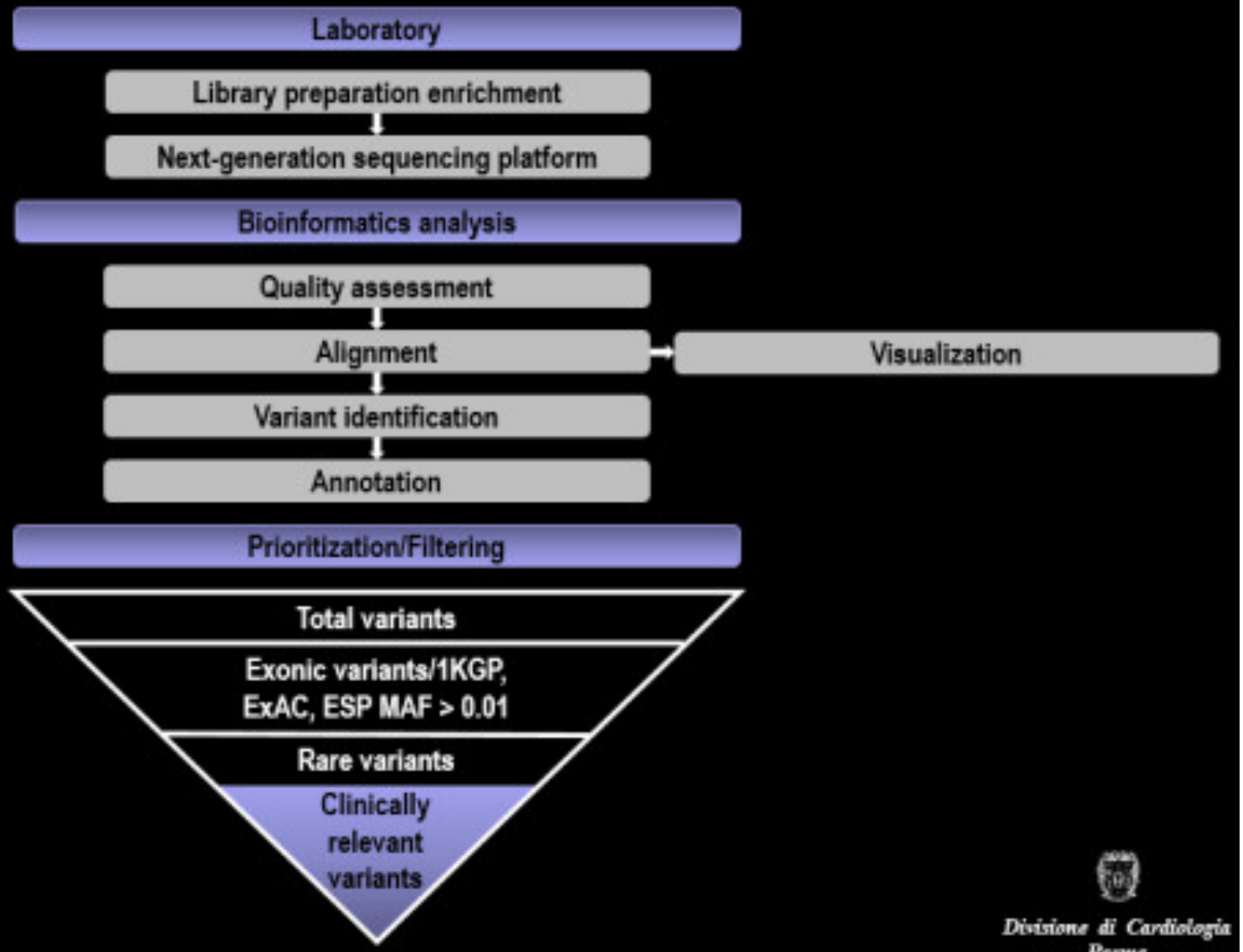
Next generation sequencing

Flow chart



Next generation sequencing

Flow chart



Next generation sequencing

Flow chart

Pathogenic

Likely pathogenic

Variant of unknown significance

Benign

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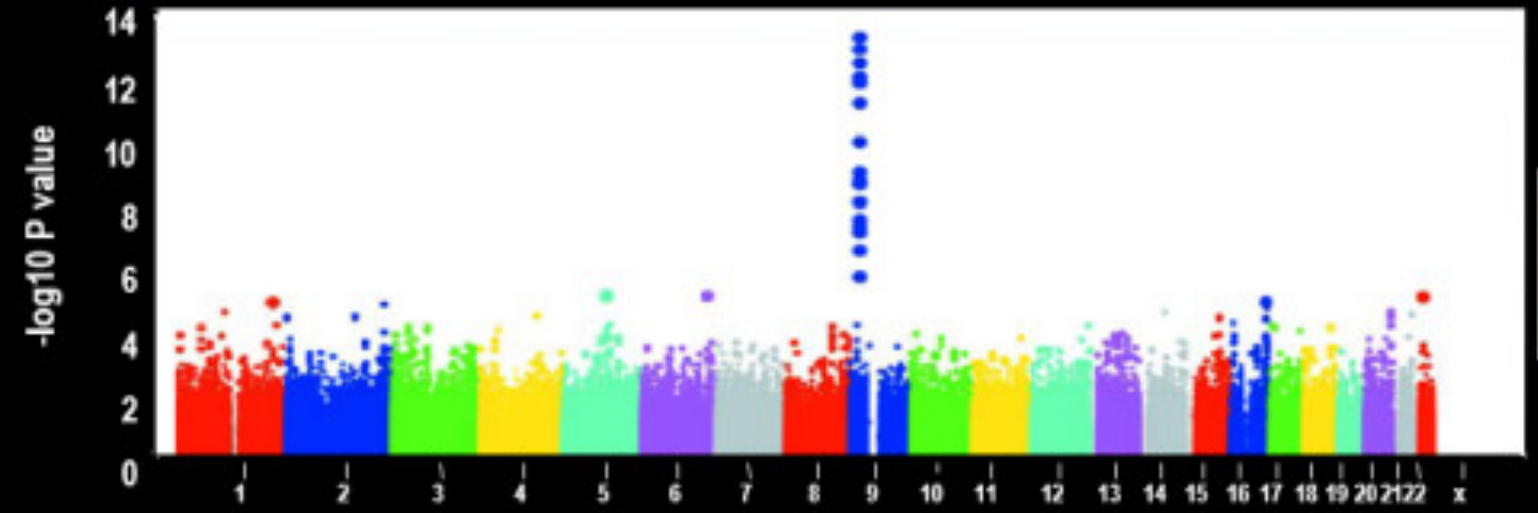
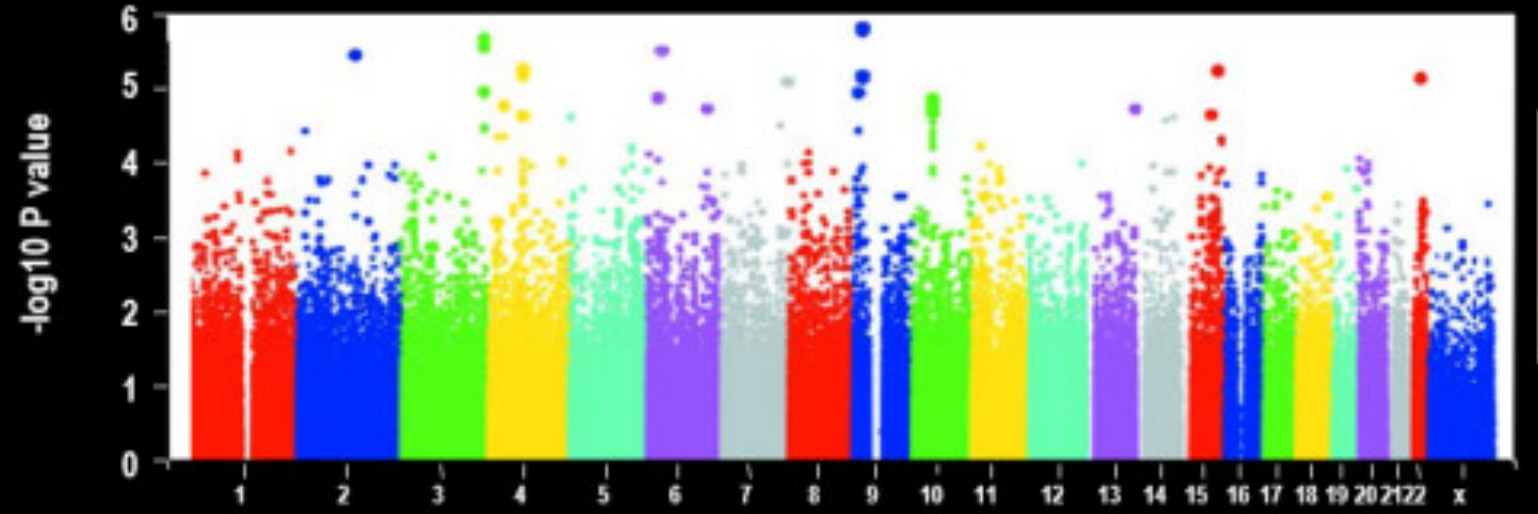
Genome wide association study

Chr 9 genetic variants and risk of MI



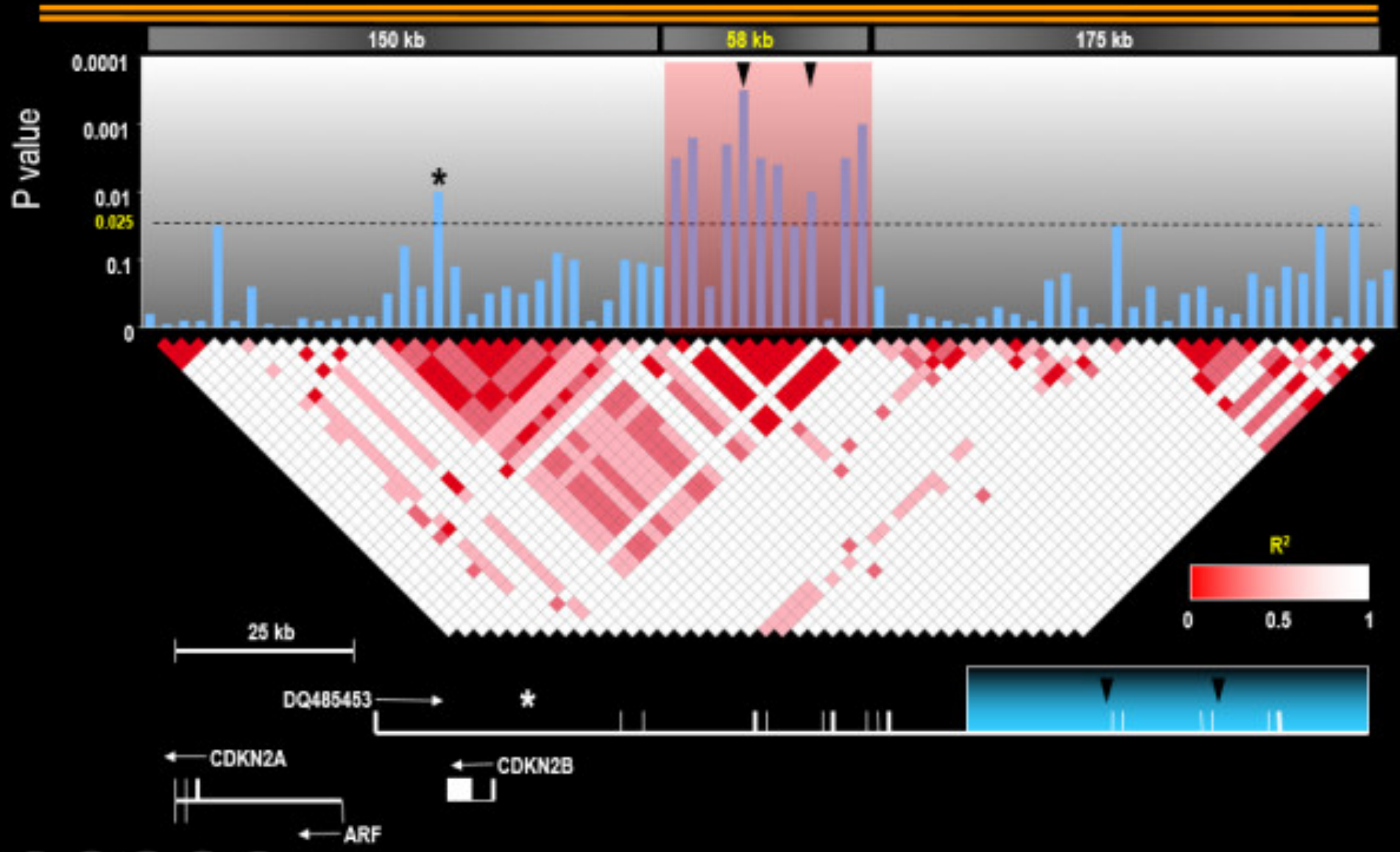
A
WTCCC study



B
German MI Family study

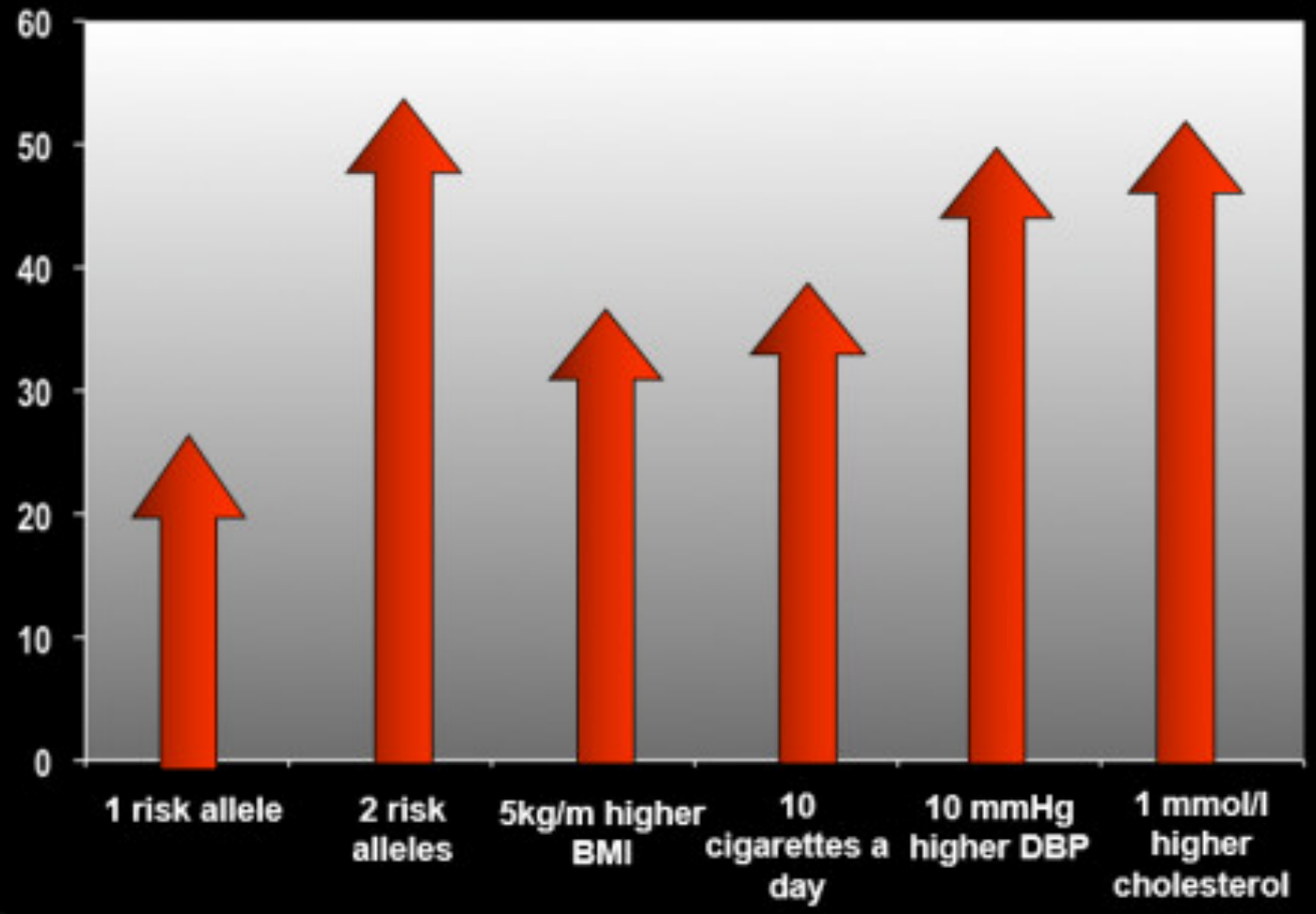
Samani N J et al. N Engl J Med 2007; 357:443-53

9p21.3 chromosomal region



McPherson R. et al. Science 2007; 316: 1488-9

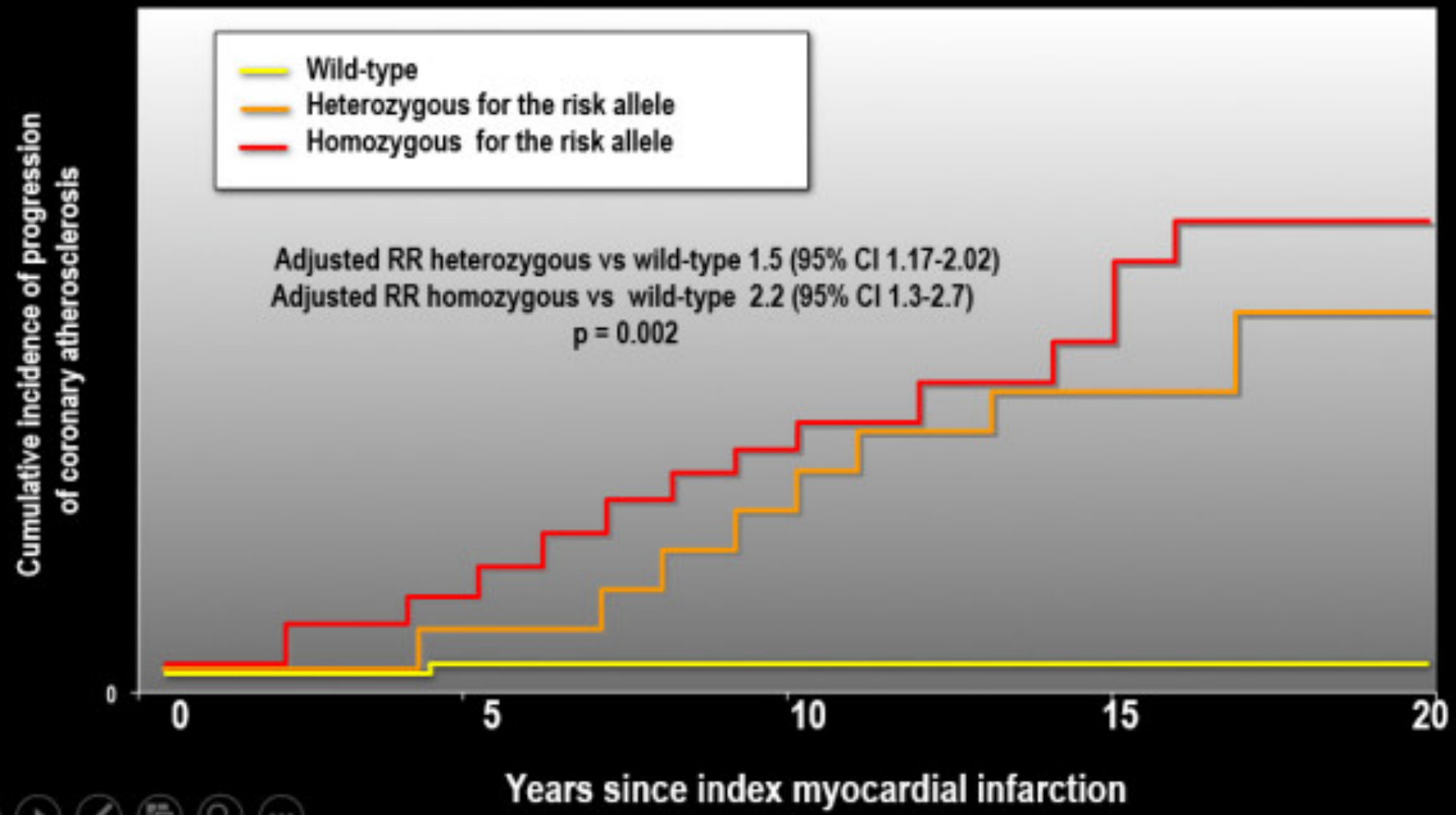
Risk of chromosome 9p21 locus compared with conventional risk factors



9p21.3 genetic variants in early-onset myocardial infarction

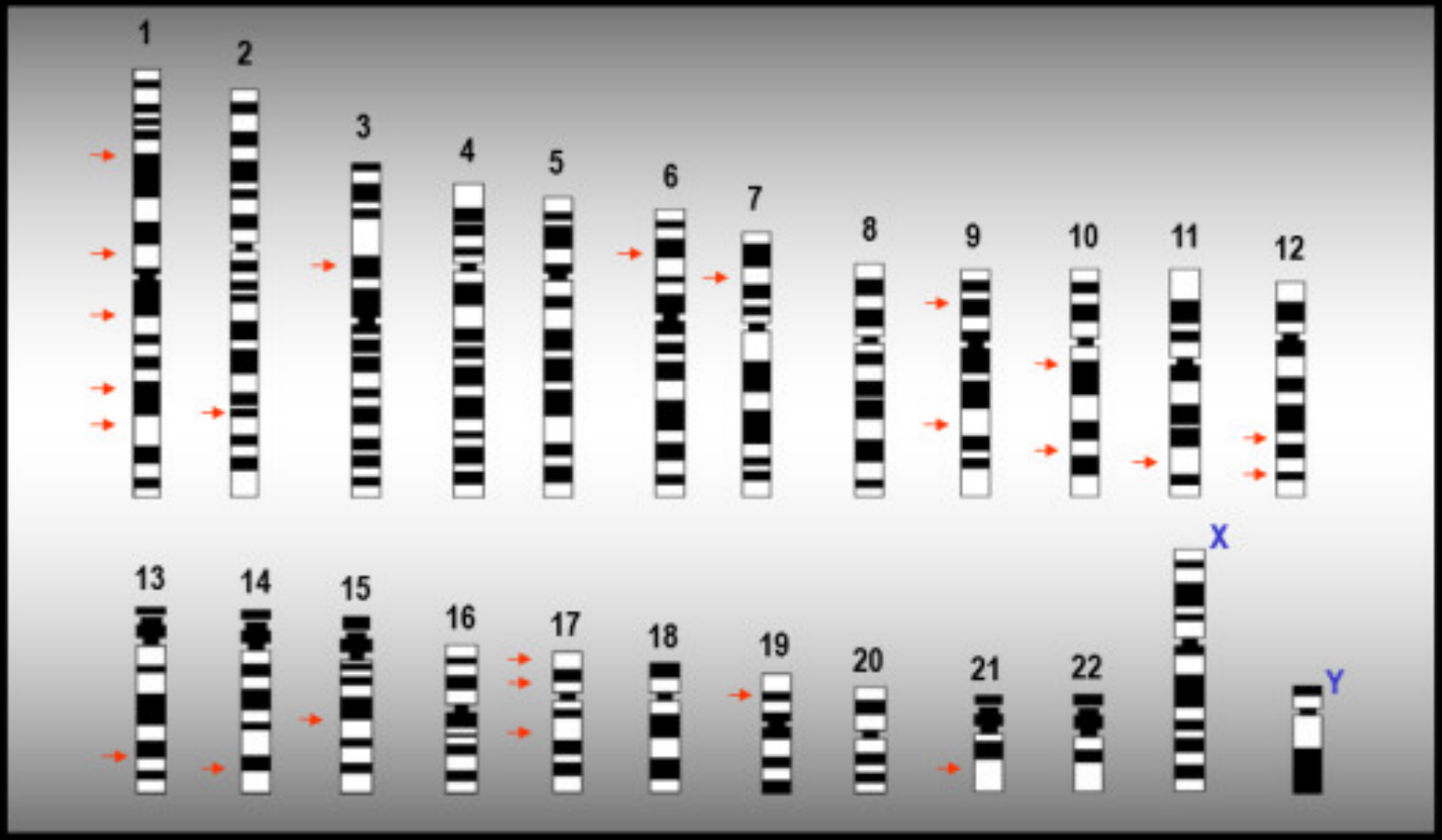
Angiographic endpoint

rs1333040

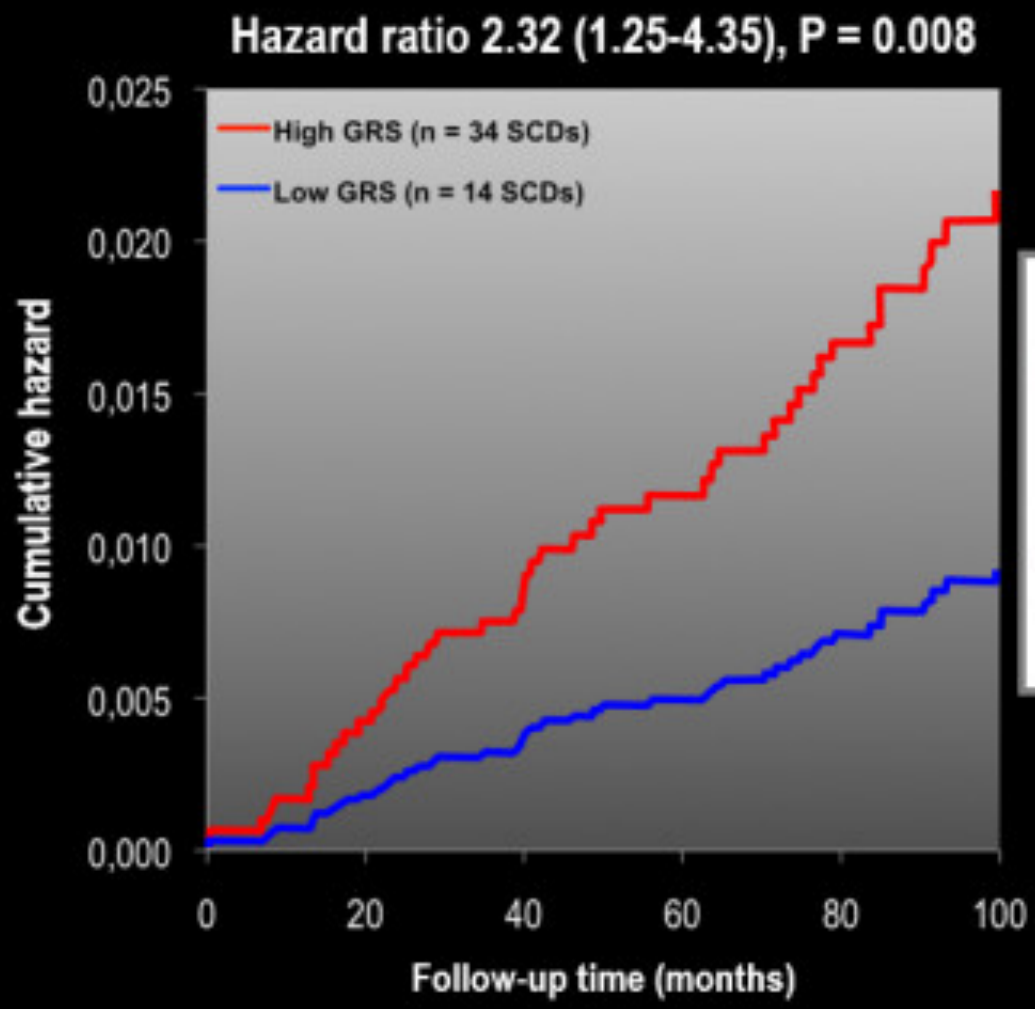


Ardissino D. et al., JACC 2011; Vol 58 4:426-34

Chromosomal location of coronary artery disease genes



Cardiovascular genetic
Genetic Risk Score



European Heart Journal Advance Access published April 23, 2015

European Heart Journal
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CLINICAL RESEARCH
Coronary artery disease

Predicting sudden cardiac death using common genetic risk variants for coronary artery disease

Jussi A. Hernesniemi[1,2*], Leo-Pekka Lyytikäinen[1], Niku Oksala[1,3], Ilkka Seppälä[1], Marcus E. Kleber[4], Nina Mononen[1], Winfried März[4,5,6], Jussi Mikkelsson[7,8], Tanja Pessi[7,9], Anne-Mari Louhelainen[7], Mika Martiskainen[7], Kjell Nikus[10], Norman Klopp[11,12], Melanie Waldenberger[11,12], Thomas Illig[11,12,14], Mika Kähönen[15], Reijo Laaksonen[1], Pekka J. Karhunen[7†], and Terho Lehtimäki[1†]

Hernesniemi J.A. et al. EHJ 2015 36(26):1669-75

TAKE HOME MESSAGES

- La genetica cardiovascolare, essendo applicabile precocemente nella vita, è uno strumento potenzialmente ideale per prevenire la morte improvvisa
- La traduzione pratica di questa potenzialità è oggi possibile in clinica ma resta ancora tecnicamente molto complessa
- Occorre fare riferimento ad un team multidisciplinare con competenze ultraspecialistiche (Cardiologo, Genetista, Psicologo)
- La genetica della SCD applicata alla cardiopatia ischemica rappresenta il futuro