Personalized Medicine in Cardiology –Rhythmology as an Example

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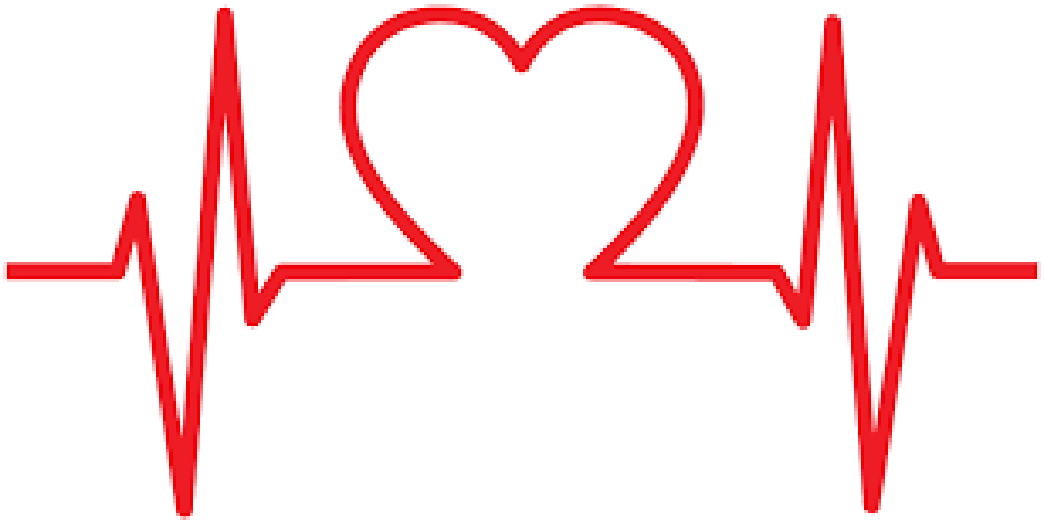
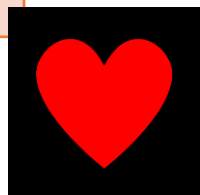


Levels of personalized medicine

- Biomarker based stratification (group building)
- Genome based information on disease related traits (including gender medicine)
- Assessement of individual disease risk
- Differential therapeutic interventions
- Unique individualized (private) therapy

essential prerequisite: Standardized detailed patient characteristics at baseline and during follow-up and outcomes



Potential benefits of personalized medicine

- Increased diagnostic and prognostic accuracy
- Increased sensitivity and early (presymptomatic) diagnosis allowing for early treatment options
- Increased prognostic accuracy (response to therapeutic interventions)
- Optimized therapeutic strategy
- Optimized follow-up and adjustments of therapeutic strategy

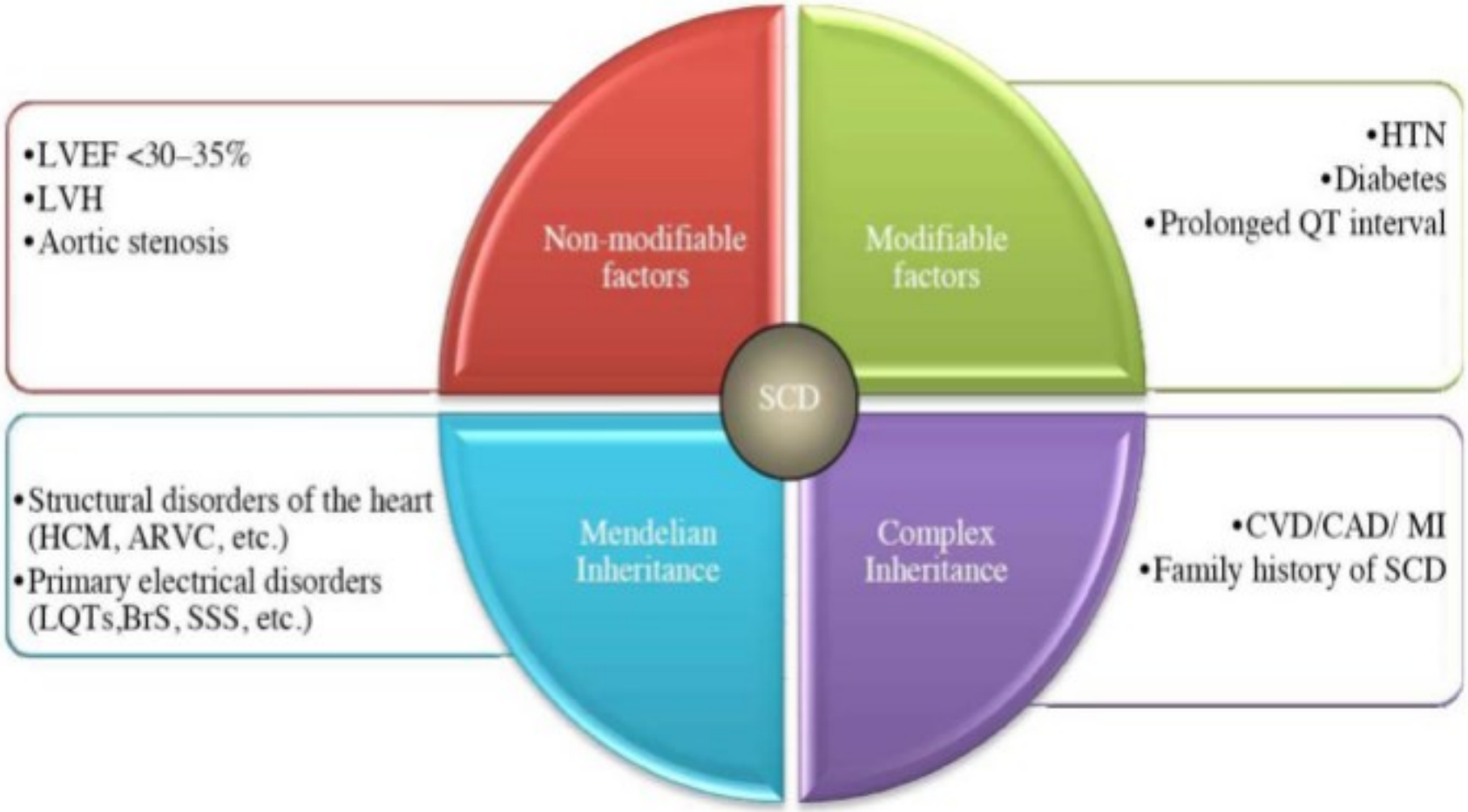
Need for large numbers to demonstrate superiority of Personalized medical care vs standard medical care

Cardiac Arrhythmias

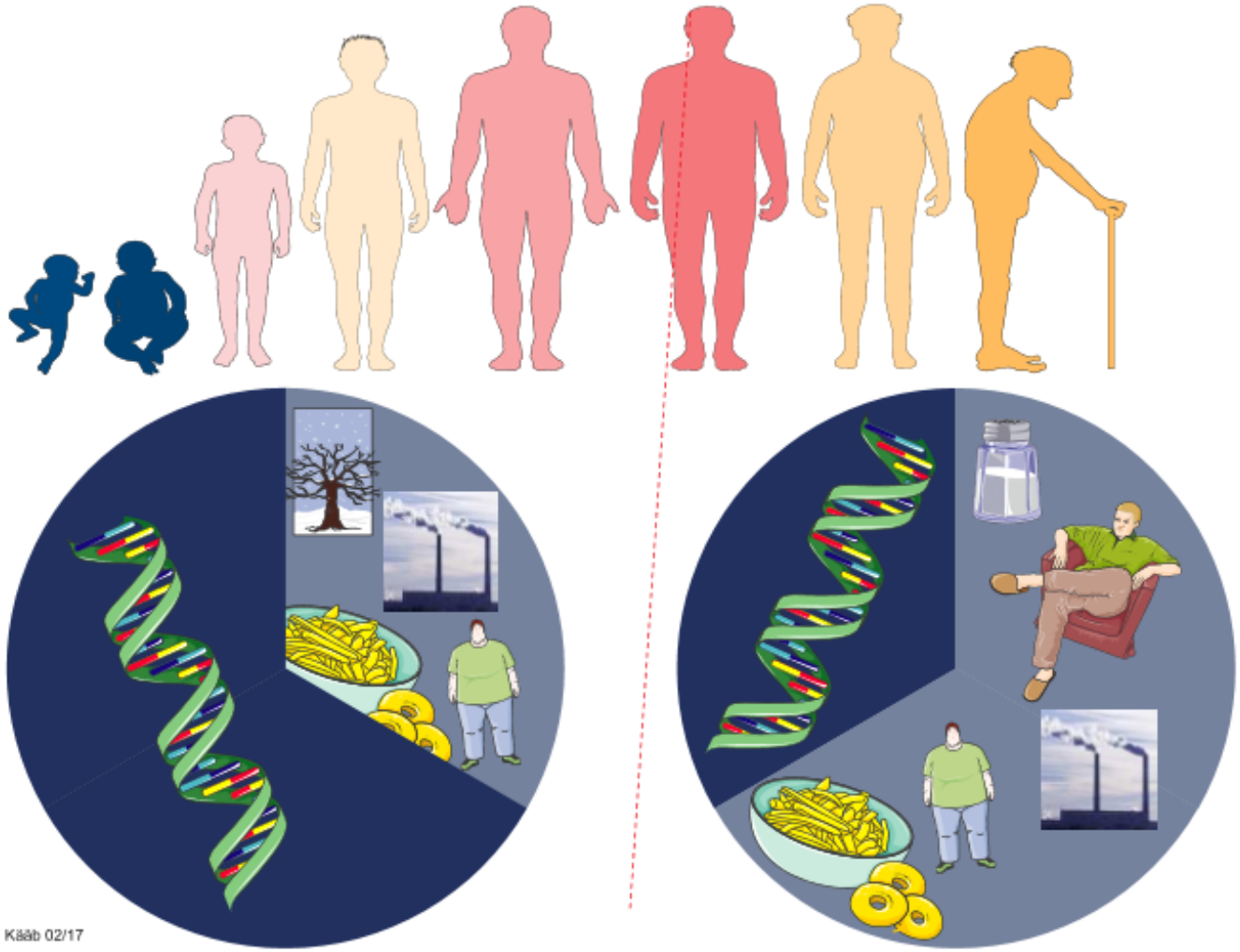
Biomarker assisted risk stratification and therapy in arrhythmias:

- Stratification ideally based on underlying pathophysiology should lead to more efficient therapy
- Biomarker are biological markers and signals that enable patient stratification in a qualitative and/or quantitative way (optimal sensitivity /specificity desirable)
- Biomarker to optimize risk stratification should demonstrate improved risk reduction, therapy and outcome

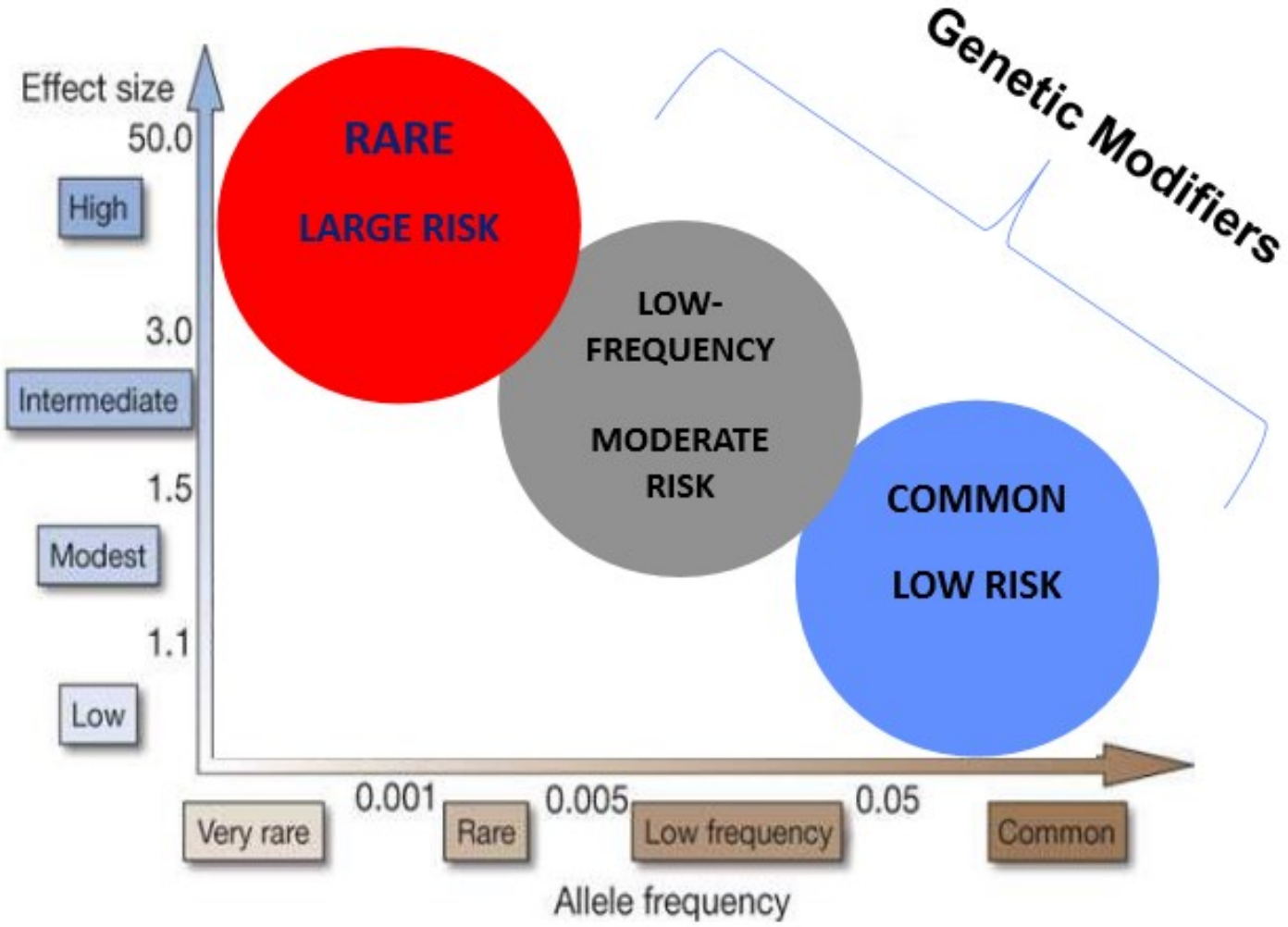
Risk stratification for sudden cardiac death



Genetic and environmental risk factors



Spectrum of genetic variants that occur in the general population



Biomarker based personalized medicine in cardiac arrhythmia management:

Examples:

- Genomics of ECG signals (focus on QT interval)
- Common genetic variants as modifiers in rare diseases (LQTS)
- Common genetic variants as modifiers in common diseases:

-serious adverse drug reaction: drug-induced LQTS

-Sudden Cardiac Death (SCD)

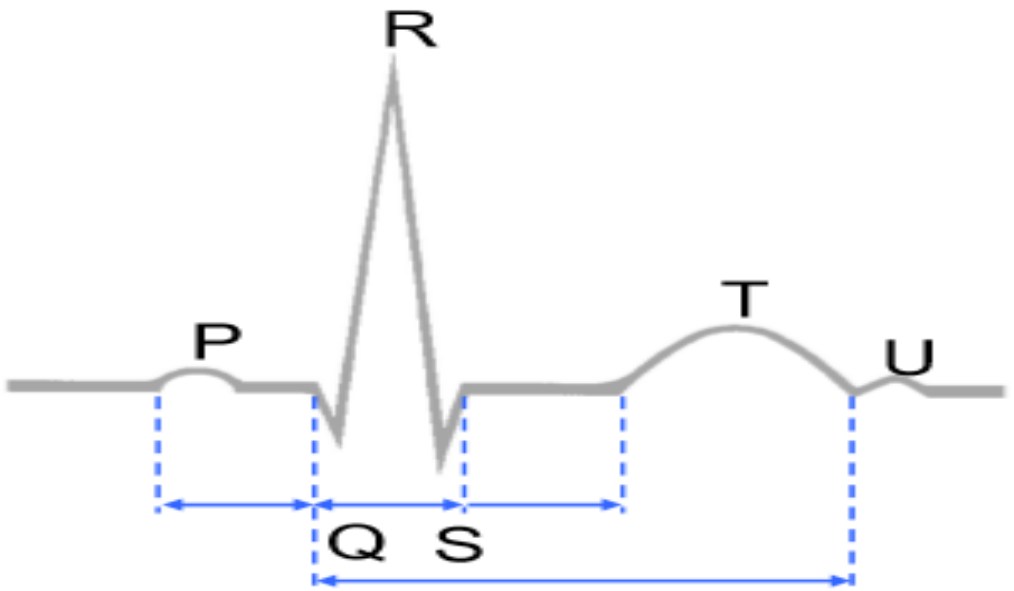
ECG-signals are quantitative and qualitative markers of myocardial electrical properties

quantitative

- RR-interval: sinus node function
- PR-interval: atrial conduction
- QRS-interval: ventricular conduction
- QT-interval: ventricular repolarization

qualitative

- Sinus rhythm+ /
- Early repolarization pattern



ECG-signals are heritable traits

- Silva CT, et al. Hum Gen (2015) 134:1211-1219
- Noseworthy PA, et al. JACC2011 Reinhard W, et al. Circ Cardiovasc Genet 2011
- Lubitz et al JAMA 2010; 304:2263-9.

Common Variants in Myocardial Ion Channel Genes Modify the QT Interval in the General Population

- Arne Pfeuferet al. Circulation Research. 2005;96:693-701