

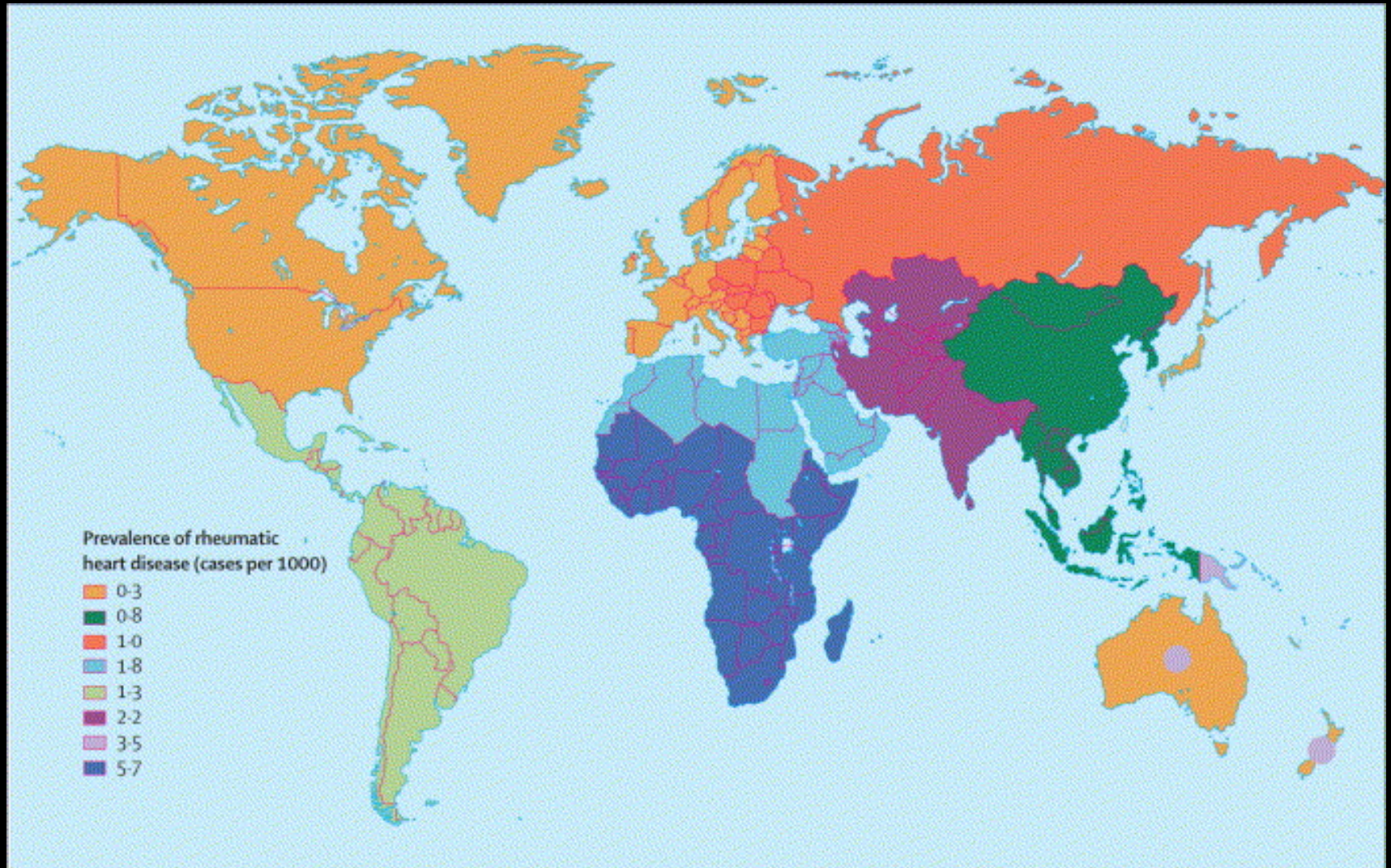
The RHDGen Network

Genetics of Rheumatic Heart Disease
(RHD)

The RHDGen Network

- Rationalé for RHDGen Network
- Proposed Activities
- Organisation
- Progress

Africa is the RHD Capital of the World



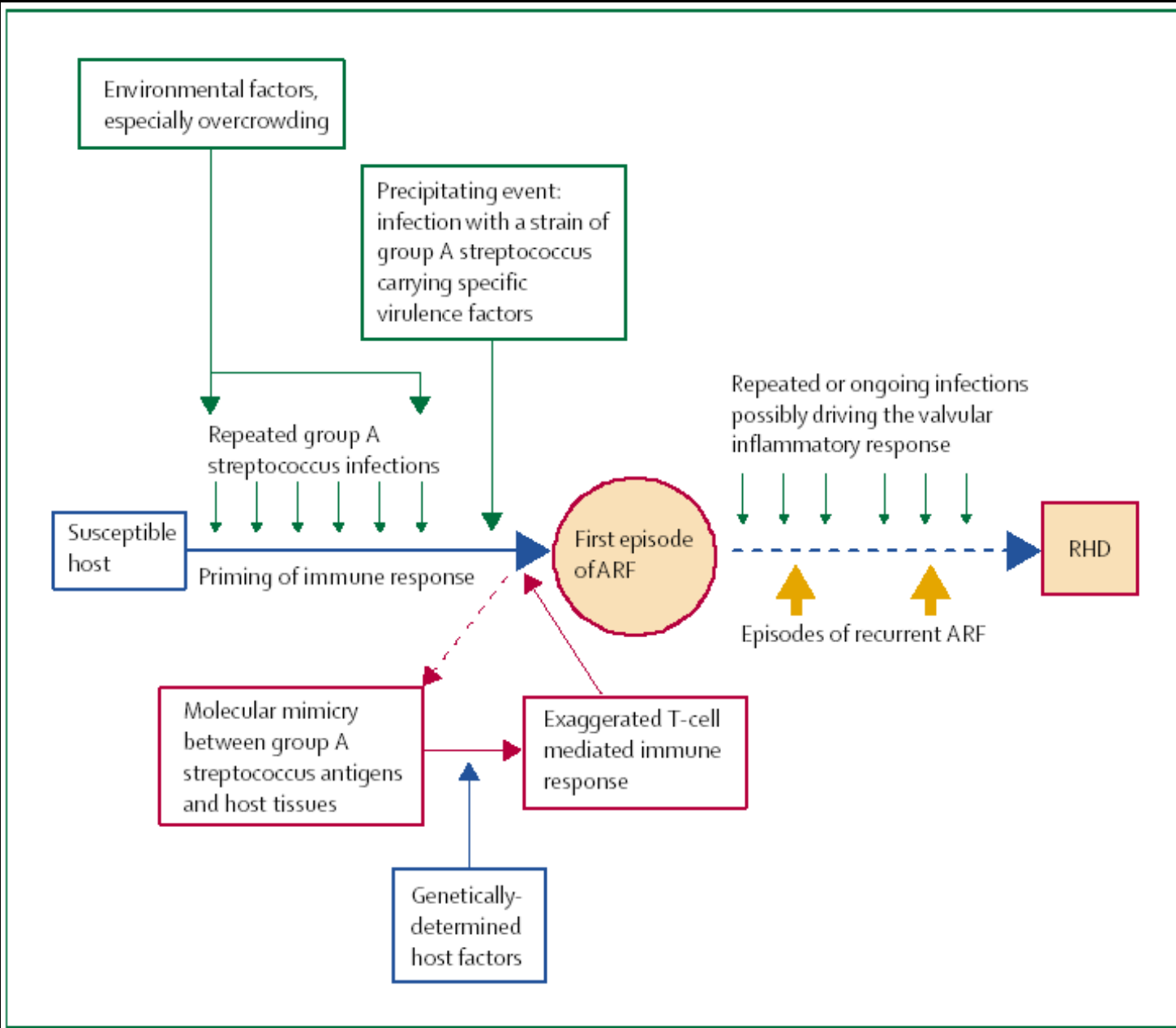
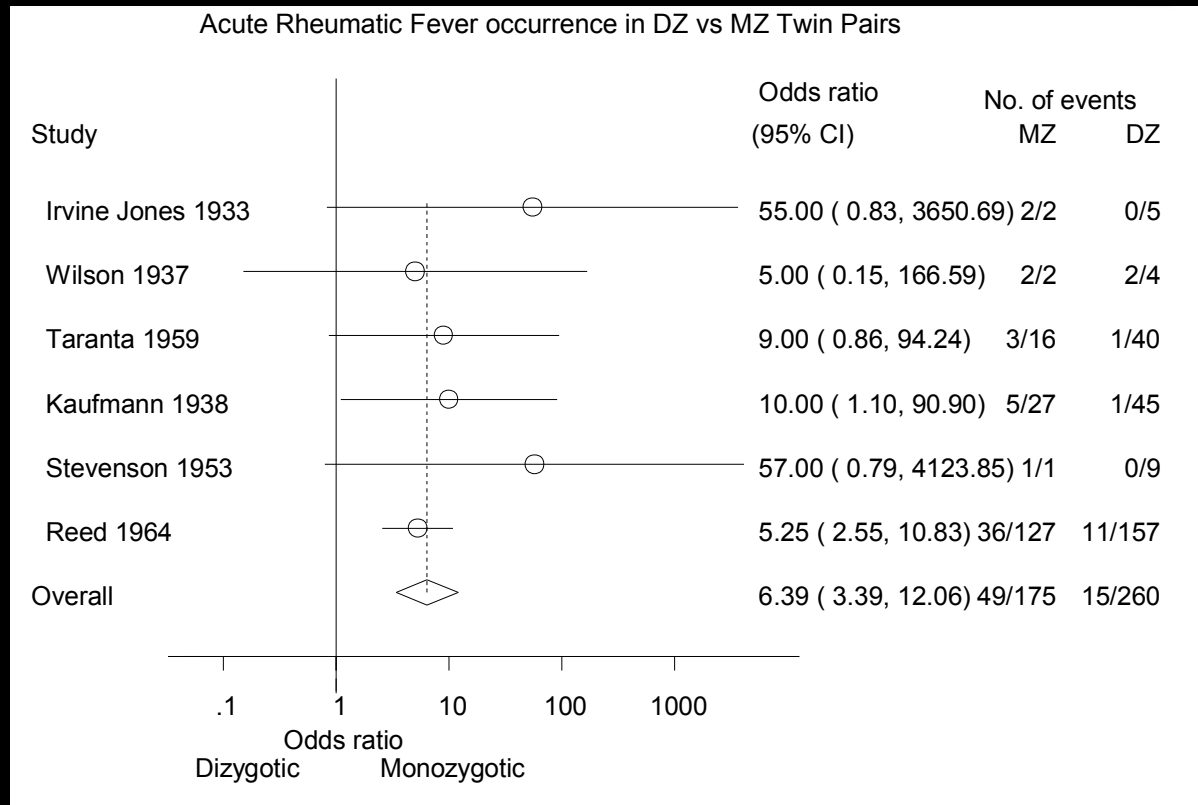


Figure 2: Pathogenetic pathway for ARF and RHD

Genetically determined host factors



Odds ratio of concordance for acute rheumatic fever according to type of zygosity in a random-effects synthesis of data from studies included in the meta-analysis.

Which genes are involved in increasing or decreasing your risks for developing RHD

Proposed activities

- To recruit 2,500 cases and 3,500 controls
 - Case-control (discovery of variants): 1500 cases and 1500 controls
 - Trio study (replication study) 1000 cases and 2000 controls
- To identify genetic variants affecting susceptibility and resistance to RHD
- To train a group of scientists and clinicians in genomic studies of multifactorial disease
- To build a network for phenotyping of RHD
- To address ethical, legal and social issues that are relevant to Africa

Genotyping strategy

- GWAS is the preferred strategy for detecting common variants that are associated with RHD: 'common variant, common disease' hypothesis (\$500 per sample)
- Whole genome sequencing would be ideal but the cost is prohibitive at this stage (\$4000 to \$5000 per sample)

Other scientific spin-offs

- Genetics of non-cardiac manifestations of acute rheumatic fever (ARF): Sydenham chorea, arthritis, skin changes
- Genetics of cardiovascular risk factors as quantitative traits: ECG and echo measurements, blood pressure, body size
- Opportunity for Immunology of ARF and RHD
- Platform for studies of ELSI

Progress

- Identification of the first 1,500 index cases is complete
- Standard operating procedures for the laboratory are being finalised
- Awaiting ethics committee approvals
- Start date for collection of DNA: 01 July 2013

Finally...

- We have already recruited 60% of probands required for the study
- The RHDGen Health Scholars Program will develop genomic teams of clinicians and scientists in 8 African countries
- RHDGen is a platform for the development of cardiovascular genetics in African populations