While geneticists have advanced the biology, population and clinical scientists have not done enough to assess its utility.

What is missing are mechanisms to evaluate the contribution of molecular genetics to the treatment and prevention of common disease, and translate this knowledge into practice.

Stages of Molecular Research:

Discovery to Application

1. Technology to sequence and genotype
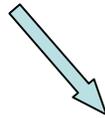
2. Localize susceptibility variants in the genome
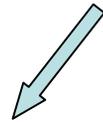
3. Define molecular mechanisms ?
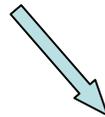
4. Clinical application ??????

Causal Process in Atherosclerosis
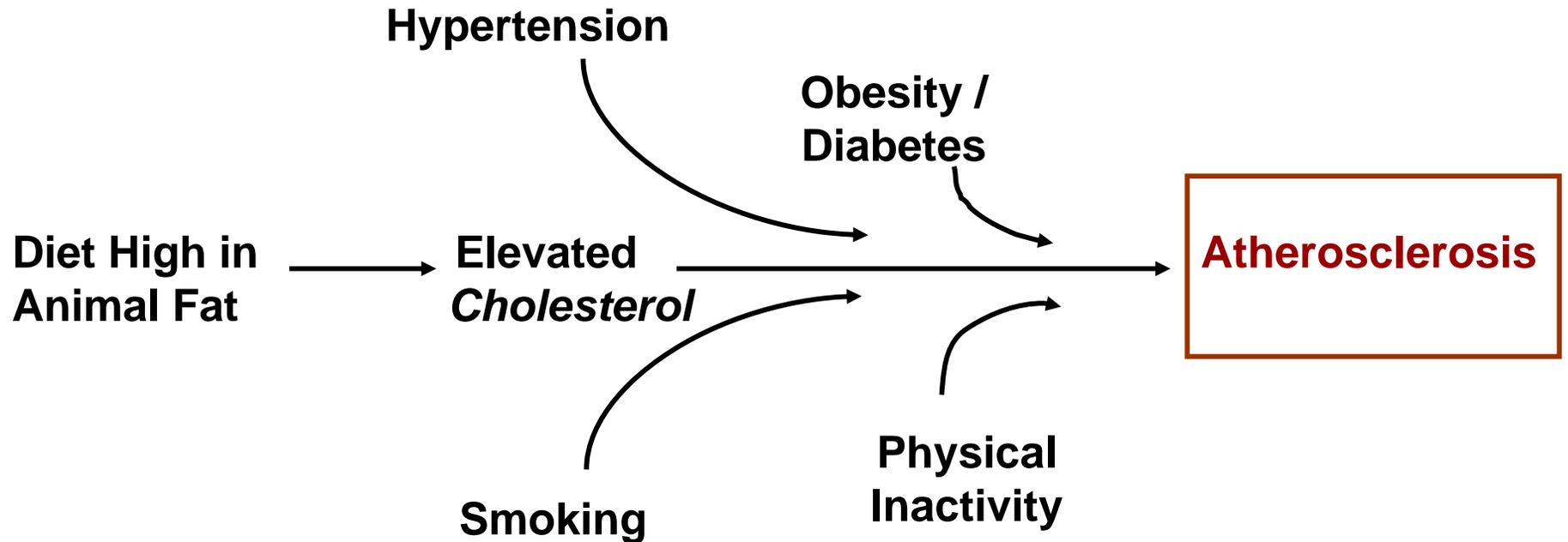
Risk stratification : Revisiting the High Risk vs. Population Strategy

Assumption:

Persons known to be at high risk will benefit from earlier, more intensive interventions, either through lifestyle or drugs.

Response:

Risk stratification has important limitations as a public health strategy. When both exposure and susceptibility are widespread, population-wide measures are often the most effective (e.g., smoking, cholesterol).

Likewise, the phenotype (eg, ↑ BP) is likely to be provide more information than the genotype.

Predicting Diabetes from Known Susceptibility Genes vs. Clinical Measurements

ROC for Information Provided by TCF7L2, PPARG, and CNJ11 Variants

ROC for Information Provided by BMI, FBG, Family Hx, BP, HDL
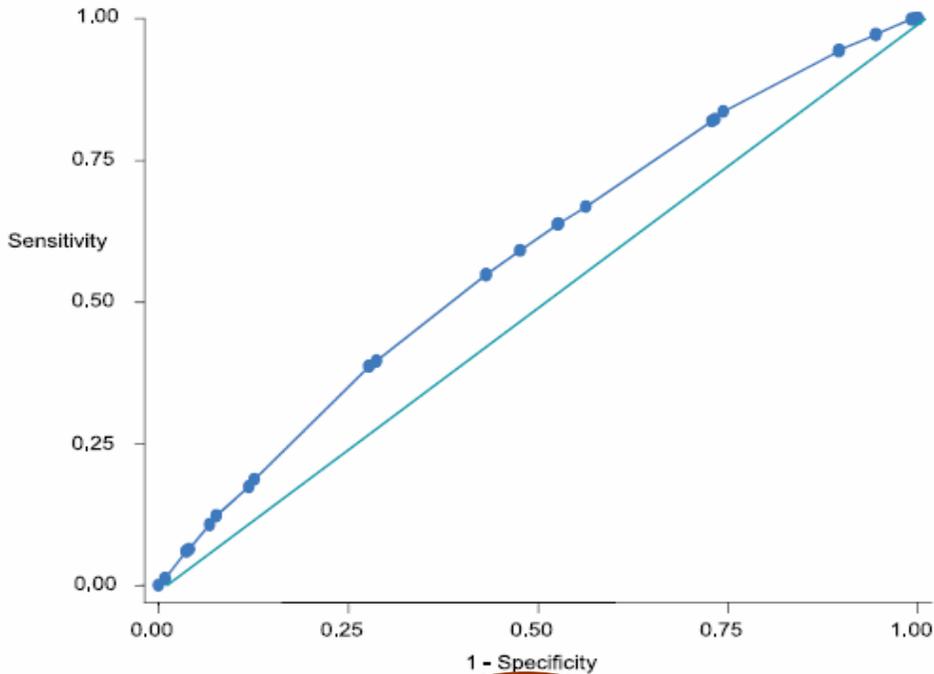
AUC = 0.58

AUC = 0.88

Weedon et al. PLoS Med 2006;3:1877
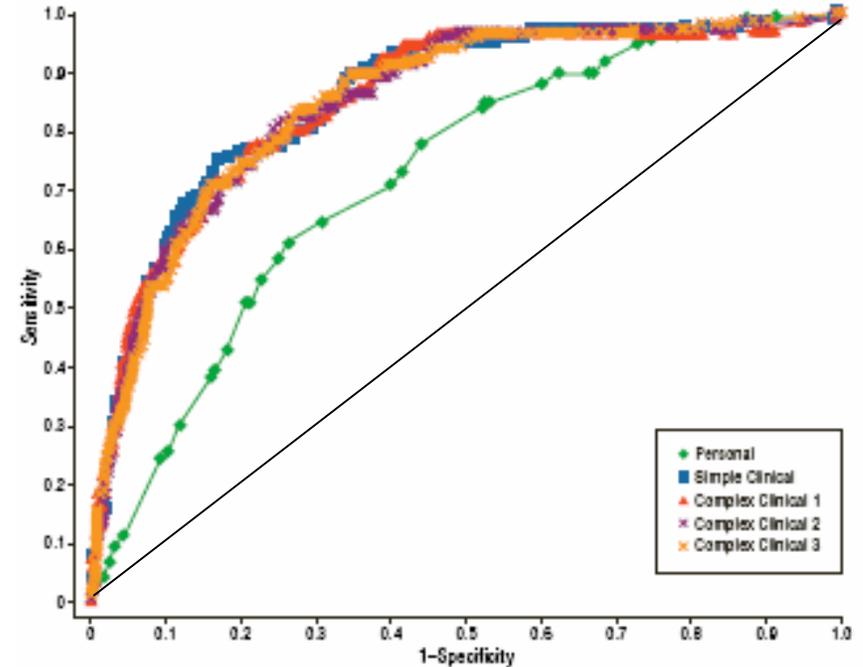
Wilson et al. Arch Int Med 2007;167:1068