Clinical Validation (deCODE genetics)

- The genetic risk test for each disease is well-validated

- Each genetic marker has been replicated in 5 to 60 separate populations

- The relative risk is derived from several thousands of patients and tens of thousands of controls – much larger than the data used to support most FDA-approved diagnostics and drugs

- Markers are shown to be independent and are therefore combined by multiplying the risks together using a standard, validated method
Useful genetic risk tests for common disease – are we there yet?

- **Heart attack – deCODE MI (2 markers)**
  - 21% of the general population has 1.5 fold risk for early heart attack and 1.3 fold risk regardless of age of onset (comparable to risk conferred by LDL-cholesterol)

- **Prostate cancer – deCODE ProCa (8 markers)**
  - 10% of the general population has average 2 fold risk, 1% has 3 fold risk (lifetime risk 48%)

- **Breast cancer – deCODE BreastCa (8 markers)**
  - 5% of the general population has 2 fold risk, 1% 3 fold risk (lifetime risk of 36%)

- **Type 2 Diabetes - deCODE T2 (4-8 markers)**
  - 10% of prediabetic patients have two-fold risk for quickly progressing to type 2 diabetes (50 to 70% absolute risk within 3 to 4 years)

- **Atrial fibrillation – deCODE AF (2 markers)**
  - 25% of the general population has average two-fold risk of AF (1.5 to 3.6 fold)
  - Reveals that AF is a much greater cause for stroke than previously recognized
  - 150,000 stroke and TIAs per year may be due to undiagnosed AF - discharged on the wrong drug for secondary stroke prevention
  - Focusing extra cardiac monitoring on test-positive patients may save Medicare almost 1 Billion dollars after accounting for costs of tests

- **Glaucoma – deCODE Glaucoma (3 markers)**
  - 2.3 fold risk for more aggressive form of glaucoma leading to earlier blindness if unrecognized
A Case Study Demonstrating Usefulness of a Genetic Risk Test

- 48 year old white male in apparent good health,
  - His father diagnosed with localized prostate cancer at age 70
  - Patient with low normal PSA at age 42

- deCODE Prostate Cancer test results (8 markers combined)
  - Relative risk = 1.88 fold compared to general population risk for white males.
  - Calculated lifetime risk = 1.88 X 16% = 30%
  - Modestly higher risk for aggressive vs non-aggressive disease

- High risk prompted early serum PSA test by primary care
  - PSA was high normal at 2.5ng/ml

- High risk prompted referral to urologist

- High risk prompted urologist to perform ultrasound-guided biopsy
  - Positive for cancer in 3 out of 12 core biopsies – 15% volume
  - Intermediate grade tumor (Gleason score of 6)

- Surgery after negative workup for metastasis – likely cure