The Healthcare Utility of Diagnostic Whole-Genome Sequencing

**Problem Statement**: WGS is now incredibly affordable, yet not transparent in its utility to human life and healthcare.

**Goal**: One can formulate reasonable models that investigate if WGS has utility and at what price points.

**Simplifying assumptions**:

* + Mendelian phenotypes. Phenotypes caused by independent, high penetrance loci. Accommodations for autosomal recessive, autosomal dominant, and x-linked recessive loci.
  + People are drawn from a representative average population.
  + Genes that are already known (known severity, penetrance, expressivity).
  + Age-related onset of disease is explicitly modeled.
  + Cost of medical treatment is proportional to severity of disease.
  + Non-invasive diagnostic tests are preferred to invasive diagnostic tests.

**Relaxing the assumptions**:

* + Consider semi-Mendelian phenotypes: maintain independence assumption, allow for variable penetrance and expressivity.
  + Consider local populations enriched or under-enriched for disease alleles.
  + Consider model of increasing information about genes over time (modified exponential or S-curve)
  + Consider effects of age-related expressivity

**Methodology**: a set of assumed curves, integro-differential equations, solved by quadrature or numerical simulation. See e.g. Murphy&Topel (2005), <http://www.nber.org/papers/w11405>

**Big Question**: What year did/does WGS (alternatively WES) become a rational financial choice?

**Differences from Previous Work**: Previous work on the utility of WGS has addressed utility from the patient’s point of view [Lupo *et al (*2016), Sanderson *et al* (2016)] or has focused on semi-quantitive arguments based on empirical experience [van El *et al (*2013); Berg, Khoury, Evans (2011); Christensen *et al* (2015), Sanderson, Schadt (2016)]. This paper complements the existing literature by exploring alternative models where WGS or WES make more or less economic sense as the future unfolds.