Use Case 2: Phenotype Classification
Call Notes 2/10/2020

Notes from today's discussion
1. What do we mean by phenotype?
   a. Captured by Jana from discussion: 'objectively observable or measurable characteristics' for which some (non-imaging) reference standard exists

   b. From draft White Paper: **Phenotype**: one or more observable physiological characteristics describing a person, e.g., a clinical state such as a presence or absence of disease, disease stage, etc.

   c. Additional possible definitions from Pat Cole's e-mail:
      i. The observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences. The expression of a specific trait, such as stature or blood type, based on genetic and environmental influences.

      ii. all the observable characteristics of an organism that result from the interaction of its genotype (total genetic inheritance) with the environment. Examples of observable characteristics include behaviour, biochemical properties, colour, shape, and size.

      iii. The term "phenotype" refers to the observable physical properties of an organism; these include the organism's appearance, development, and behavior. An organism's phenotype is determined by its genotype, which is the set of genes the organism carries, as well as by environmental influences upon these genes. Due to the influence of environmental factors, organisms with identical genotypes, such as identical twins, ultimately express nonidentical phenotypes because each organism encounters unique environmental influences as it develops. Examples of phenotypes include height, wing length, and hair color. Phenotypes also include observable characteristics that can be measured in the laboratory, such as levels of hormones or blood cells.

      iv. the physical and psychological characteristics of an organism from both genetics and environment, or a group of organisms having like traits. An example of **phenotype** is a group of organisms which are all affected in the same ways by nature and nurture

2. Phenotype classification does not require distinct categorical placement and can be polychotomous (i.e. 80% A, 10%B, 10%C)

3. General Discussion of validation deferred to the larger group:
   a. Terminology
      i. Development set vs. Test Set vs. Validation Set
      ii. Internal validation vs. External Validation
   b. Validation: in totality only or in totality after validation of the individual markers?
   c. How to combine uncertainty of the individual measurements—same combined score may have different precision profiles.
   d. Incremental value of each measurement: how to determine whether addition of a new parameter adds value /additional information?

Use Case 2: Phenotype Classification
Call Notes 2/10/2020

Topics for discussion next time
1. Phenotype definition (briefly)
2. Structure of the QIBA Profile claim for phenotype classification
   a. Method only or also supportable performance claim?
   b. discrimination of the model (i.e. identifies the phenotype correctly). Must exceed null (guessing) value. Can be illustrated by Predictiveness curve – by M. Pepe et al. use plaque characteristics model as example
   c. reproducibility of the score (and phenotype) from the model, where the score would map to a phenotype. Note that same score can have different precisions, depending on the underlying QIB values that generated the score.
   d. Calibration – can use a table instead of scaled metrics? Because predicted and truth are on the same measurement scale