

# Personal Background

- ▶ 1984-1990 NCSU (Advisor: Doug Nychka)
  - Nonparametric function estimation/corn nutrient uptake
  - Grad student rep – photocopy machine
  - beach trip & grad student Thanksgivings
  - Grad student Computer Lab
- ▶ 1990 NIEHS/NIH
- ▶ 1992 USDA/Food Safety & Inspection Service
- ▶ 1995 FDA/Center for Devices and Radiological Health
- ▶ 2014 Myraqa (*in vitro* diagnostics consulting co.)
- ▶ 2014 Illumina, Director of Biostatistics

# Medical (Diagnostic) Tests

Simple over the counter tests to highly complex assays

- ▶ Strep, Flu, Drugs of abuse
- ▶ Pregnancy
- ▶ Blood glucose, cholesterol, prothrombin (blood clotting) time
- ▶ Pulse oximeter, fetal monitors
- ▶ Optical coherence tomography (glaucoma)
- ▶ Mammography
- ▶ EEG for traumatic brain injury, EMG for carpal tunnel
- ▶ STDs, Pap & HPV
- ▶ Cancer tests
- ▶ Genetic mutations (germ line and somatic)

# Evaluation of an Assay/Diagnostic Test

Example Data: 220 Patients

		TRUTH	
		Diseased	Non-diseased
		+	-
New	+	44	1
Test	-	7	168
Total		51	169

**estimated sensitivity** =  $44/51$  or 86.3%

**estimated specificity** =  $168/169$  or 99.4%

# Evaluation of Tests

Evaluated in context of use (users, subjects and sample type)

- ▶ Clinical accuracy (2x2)
  - impact of covariates, homogeneity across patient groups, potential for bias
- ▶ Analytical Performance
  - Stability of sample/storage conditions
  - Stability of reagents/storage conditions
  - Limits of detection
  - Precision (sources of variability)
  - Trueness/bias
  - Interfering substances (endogenous and exogenous)
  - Matrix effects

Wide range of statistical methods: experimental design, mixed models & variance component analysis, measurement error regression, categorical data analyses, missing data methods and more...

# Consulting to Next Generation Sequencing (NGS)

- ▶ Illumina's HiSeqX Ten released in 2014 – sequence over 45 human genomes in a single day for \$1000
  - first human genome - 15 years to sequence and cost 3 billion dollars (*Science and Nature*, 2001)

## ***From research use to the clinic***

- ▶ New focus: Development and manufacturing of a clinical product
  - test for Cystic fibrosis (139 variant assay)
  - test tumor tissue for many possible mutations simultaneously in order to determine whether a cancer patient will respond to a particular drug therapy
  - test pregnant mother's blood to determine whether fetus has chromosomal abnormality

# NGS Test - hundred of components!

Mon 2	Tue 3	Wed 4	Thu 5	Fri



# Key Skills

- ▶ Learn - learn the science/subject matter
- ▶ Communicate/ask questions
- ▶ Think - identify the statistical question that is relevant to the scientific question at hand
  - question you are approached with is often not the one they really want to answer
- ▶ Problem solve
- ▶ Write clearly what you did, why, what you can conclude, and any assumptions you made along the way
  - for non statistical audience/ decision makers

*Help run the experiments you design!*

# Thank you NCSU Statistics!

