Quantitative Reasoning in Evidence-Based Medicine

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Why this topic ?

- How we, as health care professionals, make CAUSAL INFERENCE ?
  - Patient with perforated duodenal ulcer, the surgery **saved** his/her life
  - Patient with AMI, emergency PTCA **saved** his/her life
  - Asymptomatic patient with hypercholesterolemia, long term statin use **prevented** AMI or stroke

A causes B ?

- What **evidence** do we need to draw causal inference ?

- What **hypothesis/belief** do we use when we make the inference ?
  - Deterministic ?
  - Stochastic / Probabilistic ?

Deterministic vs. Stochastic

- Clinical events are probably deterministic in nature, but the occurrence of these events can be described, surprisingly well, with probabilistic methods

- Unfortunately, health providers have to communicate with patients in deterministic terms

Clinical events deterministic or stochastic ?

- Up to 1/3 of all patients on ACE inhibitors suffer from dry cough
- A handful of patients had Stevens-Johnson Syndrome
- Some patients took cisapride and erythromycin and developed life-threatening arrhythmia

NEJM 2000;342:42-9. Looking Back on the Millennium in Medicine

- Elucidation of Human Anatomy and Physiology
- Discovery of Cells and Their Substructures
- Elucidation of the Chemistry of Life
- **Application of Statistics to Medicine**
- Development of Anesthesia
- Discovery of the Relation of Microbes to Disease
- Elucidation of Inheritance and Genetics
- Knowledge of the Immune System
- Development of Body Imaging
- Discovery of Antimicrobial Agents
- Development of Molecular Pharmacotherapy

Quantitative Reasoning in Medicine

- Three levels of lies
  - Lies
  - Damn lies
  - Statistics

- Batting average in baseball and
  Treating patients in medicine as examples

Batting average of baseball players

- Manny Ramirez of the Boston Red Sox
  - 0.325 in 2003
  - How likely he will go 0-for-4 three games in a row ? 0.009
- Joseph Chan of West Newton minor league
  - 0.09 in 2003
  - How likely he will go 1-for-3 in the next game ? 0.23

Mr. Ramirez's betting average

- 2003 154/569 (0.325)
- Career (1993 – 2003) 1,384/5,004 (0.617)
- He won't be fired if he hits 0-4 in three consecutive games
- Shall we lose faith in a C/T regimen with a 32.5% response rate if 12 consecutive cancer patients do not respond ?

Joseph Chan's batting

- One game in 2003, 1/3 = 0.333
- You will not hire him because he had a batting average (for one game) similar to that of Manny Ramirez
- Would you trust a home-made regimen that seemed to work in two out of five patients ?

Why do we trust studies with large numbers ?

- Because point estimates of a proportion or a mean can be very misleading
- For Manny Ramirez, after first game in 2004

If he is	0/4, then	1,585/5,008 = 0.316
	1/4	1,586/5,008 = 0.317
	2/4	1,587/5,008 = 0.317
	3/4	1,588/5,008 = 0.317
	4/4	1,589/5,008 = 0.317

Why do we trust studies with large numbers ?

- Because point estimates of a proportion or a mean can be very misleading
- For Joseph Chan, after first game in 2004

If he is	0/3, then	1/14 = 0.071
	1/3	2/14 = 0.143
	2/3	3/14 = 0.214
	3/3	4/14 = 0.286

Dr. C seeing patients

- Dr. C just completed his residency training, he/she has used drug D on three patients
- Shall he/she rely on his/her experience with three patients ?
- What if he/she has experience with 30 patients ?
- 300 patients ? 3,000 patients ?

The problem with 3,000 patients

- Are they all the same ?
  - Of course not, they are different with respect to age, gender, severity of disease, comorbidity, co-medications, genetic make-up, life-style factors, …
- Manny Ramirez faced many different pitchers in 1,383 career major league games
  - Right handed vs. Left handed pitchers
  - Home games vs. Away games
  - Day games vs. Night games
  - ...

How to interpret my experience with 3,000 patients ?

- Stratify them into homogeneous catergories
  - Age and gender
  - Severity of disease (e.g. that for Heart Failure and Cancer Staging)
  - Comorbidity
  - …
- Most of the time, after stratification, there are not that many patients in each category
  - Need to learn from the literature

Quantitative reasoning for the next level

- The concept of contingency table

Outcome	Treatment/Exposure	
	+	–
Good	a	b
Bad	c	d

- Most of the time, we focus on “a” and “d” and forget about “b” and “c”

Quantitative reasoning for the next level

- In a deterministic world, there is no “b” or “c”
- Evaluation of treatment, prognostic factor, and risk factor, follow the “rule-out” process
  - Due to chance (random error) ?
  - Due to systematic error ?
  - Due to true effect ?

New treatment vs. Standard treatment

40% success rate 20% success rate

Good enough ?

- May be, may be not

4/10	= 40%	2/10 =	20%
40/100	= 40%	20/100 =	20%
400/1,000	= 40%	200/1,000 =	20%

Due to chance variation ? Or is the new treatment really better ?

Evaluation of literature in EBM

- Evaluate whether the outcome of interest is due to chance
- Evaluate whether the outcome of interest is due to systematic error (i.e. comparing apples and oranges)
  - Bias
  - Confounding

Training physicians in the 21st century

- Biological Mechanism, Clinical Skills, Quantitative Reasoning, Bioethics Principle, and Lifelong Learning Attitude are essential ingredients
- Lack of Quantitative Reasoning at all levels of clinical training
  - Solution : MPH concentration in Quantitative Methods or Master of Clinical Epidemiology