Slide 1: Conceptual, methodological, and ethical problems in communicating uncertainty in clinical evidence

Paul Han, MD, MA, MPH
Center for Outcomes Research and Evaluation
Maine Medical Center

Slide 2: Communicating uncertainty in clinical evidence: a growing need

• Growth of evidence-based medicine (EBM)
  o "[T]he conscientious, explicit, and judicious use of current best evidence in making decisions about individual patients."¹
• Rise of shared decision making (SDM) movement
• Increasing visibility of medical controversies

Slide 3: Why communicate uncertainty about clinical evidence?

• Scientific fidelity
• Psychological need
  o Information about uncertainty determines confidence in decision making in all domains of life
  o Propensity towards "overconfidence"
• Ethical mandate
  o Principle of patient autonomy

Slide 4: Problems in communicating uncertainty about clinical evidence

• Conceptual: What are we communicating?
  o Meaning and nature of uncertainty in clinical evidence
• Methodological: How should we communicate uncertainty?
  o Optimal approaches for representing and communicating uncertainty
• Ethical: Why should we communicate uncertainty, and what are the consequences?
  o Benefits and harms of communicating uncertainty in clinical practice

Slide 5: Uncertainty

• Main Entry: un·cer·tain·ty
• Pronunciation: -tən-ťə
• Function: noun
• Date: 14th century
  1: the quality or state of being uncertain  doubt
  2: something that is uncertain

• synonyms uncertainty doubt dubiety skepticism suspicion mistrust mean lack of sureness about someone or something. uncertainty may range from a falling short of certainty to an almost complete lack of conviction or knowledge especially about an outcome or result <assumed the role of manager without hesitation or uncertainty>. doubt suggests both uncertainty and inability to make a decision <plagued by doubts as to what to do>. dubiety stresses a wavering between conclusions <felt some dubiety about its practicality>. skepticism implies unwillingness to believe without conclusive evidence <an economic forecast greeted with skepticism>. suspicion stresses lack of faith in the truth, reality, fairness, or reliability of something or someone <regarded the stranger with suspicion>. mistrust implies a genuine doubt based upon suspicion <had a great mistrust of doctors>.

Metacognition: the conscious awareness of ignorance

**Slide 6: Uncertainty in medicine: a conceptual framework**

• Can distinguish different sources of uncertainty
  o Probability: indeterminacy of future outcomes, 1st order, “aleatory”
  o Ambiguity: indeterminacy of knowledge, 2nd order, “epistemic” uncertainty
  o Complexity: incomprehensibility of information

**Slide 7: Probability**

• Formal language of uncertainty
• Expression of indeterminacy/randomness
• Alternative interpretations
• Objective (frequentist) interpretation
  o Derivation/application: events repeated in time or space
  o Representation: rates (“natural frequencies”)  
• Subjective (Bayesian) interpretation
  o Derivation/application: personal belief, confidence in future events
  o Representation: percentages (“degree of belief”)

**Slide 8: Ambiguity**

• Decision theory construct
  o specific type of uncertainty: “2nd order” vs. “1st order,” “epistemic” vs. “aleatory”
• Lack of “reliability, credibility, adequacy” of information: “epistemic unreliability”

**Slide 9: Ambiguity: multiple sources and manifestations**

• Incomplete / missing information

- Amount or quality of available evidence
  - Questionable precision or accuracy
    - Wide confidence intervals
  - Questionable reliability
    - Inconsistent findings, reproducibility
    - Conflicting expert opinion

**Slide 10: Complexity**

- Features of information that make it difficult to understand
- Conditional probabilities, multiple risk factors, attributes, outcomes

**Slide 11: Sources of uncertainty in health care**

Diagram of examples and representations of different sources of uncertainty in the example of outcomes of breast cancer treatment

- Probability: 20% probability of benefit from treatment (*Indeterminacy of future outcome*)
- Ambiguity:
  - 10-30% probability of benefit from treatment (*Imprecision*)
  - Expert disagreement about benefits of treatment
  - (*Conflicting opinion/evidence*)
  - Insufficient scientific evidence of benefit (*Lack of information*)
- Complexity: 20% probability of long-term remission from treatment in patients with localized disease and HER2/neu-positive, estrogen-receptor positive, pre-menopausal, with no other comorbidities (*Multiplicity of causal factors and interpretive cues, conditional probabilities*)

**Slide 12: Uncertainty about clinical evidence: exemplars**

- Clinical prediction models (CPMs)
  - “...provide the evidence-based input for shared decision making, by providing estimates of *the individual probabilities* of risks and benefits...combine a number of characteristics (e.g., related to the patient, the disease, or treatment) to predict a diagnostic or therapeutic outcome.”
- Clinical practice guidelines (CPGs)
  - “…[are] systematically developed statements to assist practitioner and patient decisions about appropriate health care *for specific clinical circumstances.*”

**Slide 13: Uncertainty in CPMs**

(http://www.effectivehealthcare.ahrq.gov/index.cfm)
• Multiple sources, levels

**Slide 14: Uncertainty in CPGs: multiple sources, levels**

• Quality of evidence
  o Study design
  o Limiting factors
    ▪ Methodological limitations
    ▪ Inconsistency of results
    ▪ Indirectness of evidence
    ▪ Imprecision of results
    ▪ Publication bias
  o Effect size
• Strength of recommendations
  o Balance of desirable and undesirable effects
  o Patient/societal values
  o Economic costs

**Slide 15: Communicating uncertainty in clinical evidence: conceptual problems**

• Single-event probabilities: existence of probability at individual patient level
• Meaning of ambiguity: distinction from probability, importance in DM

**Slide 16: The problem of probability in clinical care**

• To use clinical evidence in patient care is to apply objective probabilities to individual patients and single events
• Conceptual problem: objective probability *does not exist* here
  o Idea of objective “single-event probability” logically incoherent
  o Objective (frequentist) vs. subjective (Bayesian) views of probability
• Fundamental irreducible uncertainty: indeterminacy (randomness)
  o No single, knowable “true” probability, “best” course of action for an individual patient

**Slide 17: The problem of ambiguity in clinical care**

• Idea of “low evidence” implies existence of distinct uncertainty beyond probability itself
  o Knight (1921) and Ellsberg (1961): “uncertainty about uncertainty”
• But from a pure subjectivist viewpoint: ambiguity *does not exist*
• Normatively, but not descriptively valid...
  o People do distinguish between risk and ambiguity (“ambiguity aversion”)

- Communicating ambiguity thus justified from descriptive standpoint
  - But leads to methodological problems...

**Slide 18: Communicating uncertainty in clinical evidence: methodological problems**

- Representing indeterminacy (randomness)
- Representing ambiguity
- Communicating uncertainty clinically

**Slide 19: Representing indeterminacy (randomness)**

- First-order, aleatory uncertainty
  - Represented by probability estimates
  - Quantitative, qualitative, visual representations
  - But conventional representations do not explicitly represent indeterminacy
- Important in domain of single-event probabilities
  - But difficult to understand
  - Non-quantifiable
  - Little prior work
- Emerging work on new qualitative, visual representations

**Slide 20: Representing indeterminacy in risk estimates: new approaches**

Two graphs illustrating the visual random static and visual random dynamic indeterminacy in risk estimates.

**Slide 21: Representing indeterminacy in risk estimates: new approaches**

- Limited evidence on effectiveness
  - No apparent effects on risk perceptions
  - Increase subjective uncertainty about risk but no other evidence on “understanding,” decision making
- Unknown outcomes, added value above communicating magnitude of probability estimates

**Slide 22: Representing ambiguity**

- Second-order, epistemic uncertainty
- In risk modeling: manifest by imprecision, represented by confidence intervals
  - Not often communicated to decision makers
  - Quantitative, qualitative, visual representations

• In clinical practice guidelines (CPGs): manifest by limited confidence in evidence, represented by quality ratings
  o Non-quantitative (verbal)
  o Emerging formal rating systems (USPSTF, GRADE, ACP)
• New representations, methodological problems
• Limited evidence

Slide 23: Representing ambiguity in risk estimates: NCI CCRAT
Two bars illustrating integrated textual and visual risk for developing colon cancer. One bar shows risk as a solid bar. The other shows risk as a blurred bar.

Slide 24: Representing ambiguity in clinical evidence: USPSTF

Slide 25: Methodological problems
• Separation of strength of recommendation (risk) vs. quality of evidence (ambiguity) important — at least psychologically
• Formal, explicit, parsimonious rating system a clear advance
• Yet methodologically problematic
  o Logically paradoxical ratings for cases of low evidence
  o Underlying conceptual problem: distinguishability of risk vs. ambiguity
• Lack of empirical evidence
  o Effectiveness and validity of ambiguity rating systems
  o Influence on judgment, decision making
  o Criteria for validation: expert consensus, but patient perspective also important, other criteria

Slide 16: Communicating uncertainty clinically
• Even more uncertainty...
• Patient decision support interventions (DeSIs) a natural possibility
  o Yet to be integrated in most existing decision aids
• But communicating uncertainty requires shared decision making
  o Construction of subjective confidence: not an exclusively scientific process
  o Interchange, not unidirectional information transfer from expert to layperson
• Physician-patient encounters
  o Optimal language, counseling techniques
• Implementation within processes of care

Slide 27: Communicating uncertainty in clinical evidence: ethical problems

- Patient autonomy
- Benefits and harms