From data to models: incorporating uncertainty into decision support systems

Wade P Smith, PhD
New York Oncology Hematology
Albany, NY 12206

Outline
- From data to information to models
- Some basic models
- Why do we model?
- Decision support

Probabilistic vs Mechanistic models
A mechanistic model uses fundamental physics to predict an outcome
An example: Monte Carlo dose calculation

A probabilistic model links probabilities of outcomes to initial states
An example: flipping a coin.
When probabilistic?

- No need to model the mechanism
- Mechanistic too difficult
- Not enough info to form a mechanistic model
- Looking for a mechanism

Frequentist and subjective probabilities

- Frequentist:
  - rolling dice
- Subjectivist:
  - will my sports team win?
  - Can be defined with a ‘bet’
Logistic Regression

$$P(x) = \frac{\exp(\beta_0 + \beta_1 x)}{1 + \exp(\beta_0 + \beta_1 x)}$$

Model Validation

Compare your model vs another data set

Discover that it doesn’t always work as well as you would like.

Need more variables:
Try a multivariate logistic regression, or a neural net.

Neural network

Modeling inspired by structure of neurons
Each node has a series of weighted inputs, the output ‘fires’ as a function of the weighted inputs.
Neural network

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Output = \( f(\sum_{i=1}^{n} weight_i \times input_i) \)

Neural network

Choose an output function.
Require large amounts of data to learn from
Somewhat of a black box – may make it difficult to learn mechanisms after validating the model.

Bayesian Model

- A directed acyclic graph that represents a set of variables
- Each node contains a set of states (a conditional probability table) for that variable
- Conditional probability tables contain the quantitative dependencies between variables
- Conditional probabilities can come from:
  - Mechanistic models (e.g. TCP)
  - Prospective clinical studies
  - Retrospective analysis
  - Physician beliefs (subjective probabilities)
Example Bayesian model

Example Bayesian model

Example Bayesian model
Example Bayesian model

P(advanced, SRS, cure, no side effect, MRI+) = 0.3 * 0.5 * 0.7 * 0.9 * 0.02

Diagnostic Reasoning

P(C1) = 0.50

E1 E2 C1 C2
0 0 0 0
1 1 1 1
0 1 0 1

P(C2|E2) = 0.67

We observe Effect 2

E1 E2 C1 C2
1 1 1 0
1 1 1 1
0 1 0 1
Diagnostic Reasoning

We observe Effect 2

We observe Effect 1

<table>
<thead>
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<th>E1</th>
<th>E2</th>
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<th>C2</th>
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Logical Reasoning
Reasoning under uncertainty

- The Partin tables predict the incidence of extra prostatic extension given PSA, Gleason Score, and Clinical Stage of the patient.
- Built using Logistic Regression
- Widely used

- How well does it perform on another data set?
- Is LR the best performing model?

Machine learning for improved pathological staging of prostate cancer: a performance comparison on a range of classifiers.
Regnier-Coudert O, McCall J, Lohman B, Lam T, McClinton S, N'dow J.

Model comparison using a different data set:
Logistic Regression,
Bayesian Network (3)
Neural Networks (2)
Random Forest
Support Vector Machine
k-nearest neighbors
Machine learning for improved pathological staging of prostate cancer: a performance comparison on a range of classifiers.
Regnier-Coudert O, McCall J, Lothian R, Lam T, McClinton S, N'dow J.

Using the 3 clinical variables from the Partin tables the simplest Bayesian Network (naïve Bayes) outperformed all of the other methods.

With the addition of 2 clinical variables, the Bayesian Networks which allow interdependencies between variables outperform

A decision aid for intensity-modulated radiation-therapy plan selection in prostate cancer based on a prognostic Bayesian network and a Markov model.
Quality Adjusted Life Expectancy (QALE)

• QALE combines life expectancy with quality of life for different possible outcomes

• Long-term prostate cancer health-states & utilities:
  − Full health: 1.0
  − Urinary difficulty (grade 1): 0.88
  − Bowel problems (grade 2): 0.71
  − Gr1 Urinary + Gr2 Bowel: 0.70
  − Distant metastasis: 0.25

• In this model there is time-discounting so that each year is valued less than the previous year

• A Markov Model is used to compute QALE

* S. T. Stewart, Med Care, 43 (2005) 347

• Comparison of earlier model prediction (x-marks) with results of a clinical study (solid dots) for Overall Survival and Metastasis-free survival.

• The model over predicts development of Mets.

* RTOG 92-02 (Horwitz JCO '08)
A prospective study comparing the predictions of doctors versus models for treatment outcome of lung cancer patients: A step toward individualized care and shared decision making.
Three goals:
Which point to choose on the ROC curve
When to order a PET
Which dose is optimal given the probability of disease (50 Gy or 66Gy)

Input to the model:
Probability of LN involvement for given disease location and staging.
Probability of LN involvement given a PET result (FP vs FN)
Probabilities of control from the literature
Utilities of health states

Original model differs from physician practice, which leads to a different model, and an understanding of practice.
Markov Model

Patients are in one of several health-states.

Patients have a probability to make transitions between states during each time-cycle.

The transition probabilities from:
- values from the literature
- life expectancy data for a healthy individual comes from the SSA.

A simplified graphical representation is shown at the right.

\[
QALE = \sum_s (\text{Time in state } s) \times (\text{Utility of state } s)
\]

Projected quality adjusted life expectancy (QALE) for Meningioma patients treated with IMRT or proton therapy.
Summary

- The value of model validation
- Many models lead to the need for decision support
- Thank you for your time