Modeling to assess value: Is it ready for prime time?

Fellow’s Day

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Potholes, pitfalls and precipices

- Lack of realism
- Weak inputs
- Faulty technique
- Inadequate uncertainty handling
- Insufficient validation
- Poor reporting
With Advanced Simulation

- Use all the data available to us
- Incorporate whatever new data become available, as they are generated
- Use individual’s values and examine the decision from his or her point of view.

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Example: A Fib

5 x more likely  

50% more deadly

1.4 x more disabling

systemic emboli
AF: a vexing problem

![Graph showing prevalence of AF with age]

- Older studies
- Newer studies

Prevalence (%)

Age (yrs)
Example: A Fib

5 x more likely

67%↓

50% more deadly

1.4 x more disabling

47% of time out of range

<1/2 use it

systemic emboli
Predictors unknown:
- stroke risk
- bleeding risk
- warfarin effect
Personalized medicine:
Atrial fibrillation and anticoagulation: from randomised trials to practice

J. Jaime Caro  Patti A. Groome  Kenneth M. Flegel
• bleeding risk
• warfarin effect
Decision 21st Century Style

- don’t adhere warfarin
- no AC
  - dabigatran
  - rivaroxaban
  - apixaban

Stroke:
- \( P_{\text{SI}/W} \)
- \( P_{\text{B1}/W} \)
- Nil
- MI

Bleed:
- \( V_S \)
- \( V_B \)
- \( V_N \)
- \( V_M \)

MI: 1-PS-PB

Graph:
- Log Hazard (PY)
- Time (days - log)

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For people who have atrial fibrillation (AFib) not caused by a heart valve problem, “product” is the first and only once-a-day prescription blood thinner proven to reduce the risk of AFib-related stroke with no routine blood monitoring, no dietary restrictions, and no regular dosage adjustments.
AF – Atrial Fibrillation
AC – Anticoagulant
CRNM – Clinically Relevant Non-major Bleeding
ICH – Intracranial Haemorrhage
HS – Haemorrhagic stroke
MI – Myocardial Infarction
SE – Systemic Embolism
Limitations

- This Markov model will not allow:
  - Modeling of stroke risk by CHADS2 or CHA2DS2-VASc
  - Detailed INR modeling
    - time spent in different INR ranges
  - Warfarin startup period + stabilization
  - Change in warfarin status (e.g., naïve to experienced to failure)
  - Updating CHADS2 scores after stroke event and age change
  - Event based adjustment of hazard rates (e.g., death)
  - Conditional event rates for subsequent events (e.g., stroke, bleed)
  - Modeling of treatment interruption, d/c or switching
  - Detailed modeling of resource use (e.g., treatment, MD visits, hospitalization and discharge)
  - Detailed modeling of hospital discharge
  - Capturing multiple events with competing risks
- Can’t capture treatment-specific inputs (e.g., mRS distributions linked to AC)
- Poor handling of complex competing risks
- Cumbersome to run multiple scenarios x VKA status
- No structural sensitivity analysis.
An attempt by industry – largely pharma – to justify the astronomical cost of their latest product!

- Combine unrelated studies together in a model to paint the best case
- Model population does not match the actual
- Lack of objective evidence, thus, likely bias in mfr models
- If direct costs still are not enough, add in indirect costs
- Use quality of life measures to lay a guilt trip on Managed Care
- Real world experience never meets model assumptions.
Can’t We Do Better?

Discrete Event Simulation
Modeling technique that conceptualizes the course of individuals in terms of the events they experience and the effect these have on current and future health, medical resource use, and other components.
DES for AF

START

Patients & Characteristics (e.g., age, gender, CHADS, WF status, baseline utility score)

Estimate baseline time to events: Stroke, systemic emboli, bleeding, MI, death

Cloning

Apply treatment efficacy: Update time to stroke, systemic emboli, bleeding, MI

Apixaban
No txt
Aspirin
Warfarin
Dabigatran
Rivaroxaban

Death?

Y

Model End?

N

Update event times

Process event:
Update age
Accumulate outcomes (costs, LYS, QALYs)
Record time of event
Count number of event
Assign subsequent care
Update utility score
Update treatment status
Update WF status

Determine next event & passage of time

Assign other treatment-related event times:
txt discontinuation, txt interruption, physician visit, change in LOC, change in WF status, INR monitoring

Exit
Limitations

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  - Conditional event rates for subsequent events (e.g., stroke, bleed)
  - Modeling of treatment interruption, d/c or switching
  - Detailed modeling of resource use (e.g., treatment, MD visits, hospitalization and discharge)
  - Detailed modeling of hospital discharge
  - Capturing multiple events with competing risks
- Can capture treatment-specific inputs (e.g., mRS distributions linked to AC)
- Full handling of complex competing risks
- Easy to run multiple scenarios by treatment status
- Yes structural sensitivity analysis.

Strengths

- This DES model will allow:

- Easy to run multiple scenarios by treatment status

McGill
With Advanced Simulation

Use all the data available to us.

Incorporate whatever new data become available, as they are generated.

Use individual's values and examine the decision from his or her point of view.

Truly pursue personalized medicine – even in health economics!