Meta-modelling Markov Model Simulations for cost effectiveness analyses
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Motivation

Cost-Effectiveness studies...

..., it is recommended not to adopt particle therapy as standard treatment in NSCLC yet. More evidence is needed ...

[Grutters et al., The cost-effectiveness of particle therapy in non-small cell lung cancer: Exploring decision uncertainty and areas for future research, Cancer Treatment Reviews, 36, 6, 2010]

... and reporting guidelines

information about:
- Study Design
- Data Collection
- Analysis and interpretation of results

such as:
- effectiveness, quality, costing data
- details on modelling
- ...

[Drummond et al. Guidelines for authors and peer reviewers of economic submissions to the BMJ, BMJ 1996;313:275]
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Objective

To facilitate exchange, interpretation and re-use of Markov Model Simulations (MMS) by creating a candidate model sufficiently expressive to describe modelling assumptions, data input and computational specifications.
Markov Models in CEA

Markov Models

- model stochastic processes
- here: disease progress of a patient
- costs and utilities assigned to states and transitions
- probabilities assigned to transitions between states

### State Transition PayOff

1. **State**: 2
2. **Transition**: 0..*
3. **PayOff**: 0..*

### Diagram

- **Start**: $s_1$ (asymptomatic)
- **States**: $s_1$, $s_2$, $s_3$ (progressive disease, death)
- **Transitions**:
  - $p_{11}$
  - $p_{12}$
  - $p_{13}$
  - $p_{22}$
  - $p_{23}$
  - $p_{33} = 1$ (death)
Metamodel of Markov Model Simulations

Instance of Markov Model Simulation specifies
- simulation settings
- Markov Model instances (and thus Values) used in simulation
- results obtained by simulation

→ can serve as processing instruction for simulation programme and documentation of computed MMS

Markov Model Simulation
- simulation settings
e.g. halfCycle correction, initialAge, modalities,...
- results

Markov Model
- modalities
- payOff classes
- cycle duration

Values
- distribution of data
- source
- unit
- ...

Results
- results for individual markov model
- comparative results

State
- 2

Transition
- 1..*

PayOff
- 0..*
- 0..*
markovModelSimulation AnExampleSimulation {
  simulationSettings{
    simulationType : deterministic
    numberOfCycles {markovModel Grutters2010_1 : 1, markovModel Grutters2010_2 : 5}
    halfCycleCorrection : 1
    useModalities {modalityType proton, modalityType carbon}
    useMarkovModels {markovModel Grutters2010_1, markovModel Grutters2010_2}
    transfer {markovModel Grutters2010_1 : state State_treatmentDeath ->
      markovModel Grutters2010_2 : state State_death,
      ...
    }

    markovModel Grutters2010_1 {
      ...
    }

    markovModel Grutters2010_2 {
      ...
    }
  }
}

[Language Workbench Spoofax: http://strategoxt.org/Spoofax]

[example from:
markovModelSimulation AnExampleSimulation
simulationSettings {
  simulationType : deterministic
  halfCycleCorrection : 1
  useModalities : {modalityType proton, n}
  useMarkovModels : n
  transfer : markovModel Gruuters2010_1 ...
  ...
  ...
markovModel Gruuters2010_1 {
  ...
}
markovModel Gruuters2010_2 {
  ...
}

Visualisation of states and transitions used in this study, generated from the MMS description.

[Language Workbench Spoofax:
http://strategoxt.org/Spoofax]

[example from:
Acknowledgements

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Objective

- To facilitate exchange and re-use of Markov Model Simulations (MMS)

By creating candidate model sufficiently precise to describe modelling assumptions, data input and computational specifications.

Markov Models

Markov models (MM) are used to model candidate that evolve over time. They can be used to describe the progression of a patient, represented in number of mutually exclusive health states considered to clinically and economically important event states are connected by transition probabilities.

Features

- Values (MM input parameters) and Markov Model exist independently from Markov Model Simulations, this allows reuse of existing values and Markov Model instances.
- An instance of Markov Model Simulation provides the full model of the MM by specifying simulation settings, the Markov Model instance used in the simulation and the results obtained by the simulation.
- Thus, instances of Markov Model Simulations can serve as processing instructions for a simulation program and as documentation of computed MMS.

Language for MMS

Based on the meta-model, a language for MMS has been developed using the Spoofax Language Workbench [1]. The listing on the right shows an extract of the description of a published [3] cost-effectiveness study comparing radiotherapy modalities for non-small cell lung cancer in this language.

Data Model

An ontology-based model has been created to facilitate the exchange of MMS descriptions and to allow for the documentation of the simulation results.

Bibliography

[2] A meta-model for the description of Markov Model Simulations (MMS) studies for health economic evaluations has been developed. A first description language and data model has been implemented and tested on published MMS studies comparing radiotherapy modalities. Language and data model could be used for describing MMS to automated computing services as well as for reporting purposes where documentation of the modelling assumptions, simulation parameters and results is required. Testing on further cases is needed to improve the meta-model and to ensure its applicability to MMS studies in other medical areas.

Conclusion

- developed first candidate model for description of Markov Model Simulation studies
- implemented textual language and data model based on the candidate model, tested on published MMS
- could be used for describing MMS to automated computing services as well as for reporting purposes
- next... validation on further use cases, also beyond radiotherapy
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