Review of Decision-analytic Models in Chronic Myeloid Leukemia

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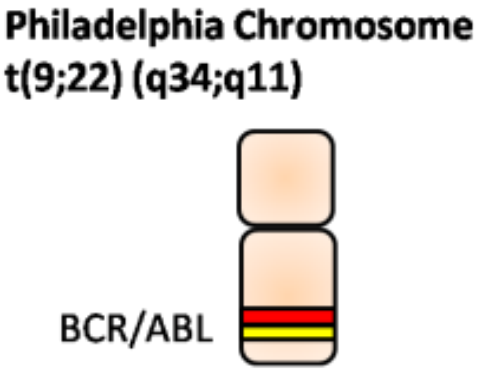
Overview

- Background CML, Decision Modeling, HTA
- Methods
- Results
- Limitations
- Conclusion

Background CML I

- Incidence: 1.6 cases per 100,000 adults
- Median age at diagnosis: 65 years
- Disease of hematopoietic stem cells,
  arising from a specific chromosomal aberration



- BCR-ABL transfusion gene encodes a tyrosine kinase (TK) that plays an important role in signal transduction and regulation of cell growth
- Current treatment options
  Tyrosine kinase inhibitors: Imatinib, Dasatinib, Nilotinib,
  Bone marrow/ stem cell transplantation,
  IFN-alpha, conventional chemotherapy

Sources: Hehlmann 2007, An 2010, Quintas-Cardama 2006, Baccarani 2009. Figure adapted from http://elbanet.ethz.ch/wikifarm/krebsvorlesung0607/index.php?n=Kurs.212

Background
Modeling and HTA in CML

- New treatment options (TKIs) revolutionized treatment and management of CML → rather chronic disease approach
- For prediction of long-term clinical effectiveness and quality-adjusted long-term outcomes: decision-analytic modeling and HTA
- Combination of evidence-based data of different areas: epidemiologic data, short-term effectiveness data, quality-of-life data, and costs
- Systematic and formal evaluation of the benefits, risks, and costs of promising innovative approaches

Objectives

Overview of published decision-analytic models evaluating different treatment strategies in chronic myeloid leukemia (CML):

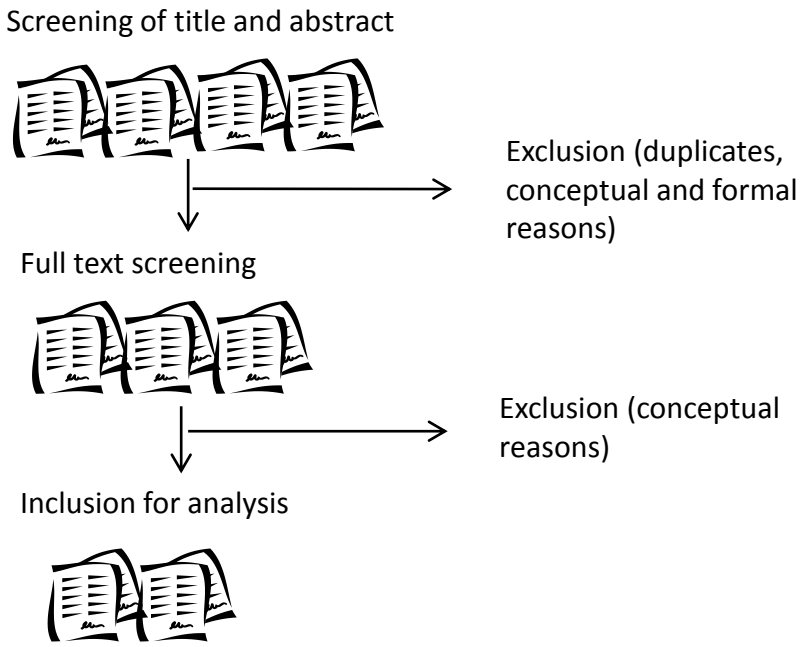
- To describe and analyze the structural and methodological approaches used and
- To derive recommendations for future CML models

Methods

Literature Search I

Systematic literature search in electronic databases:

- (Pre-)Medline
- EMBASE
- NHS EED
- EconLit
- Tufts CEA Registry



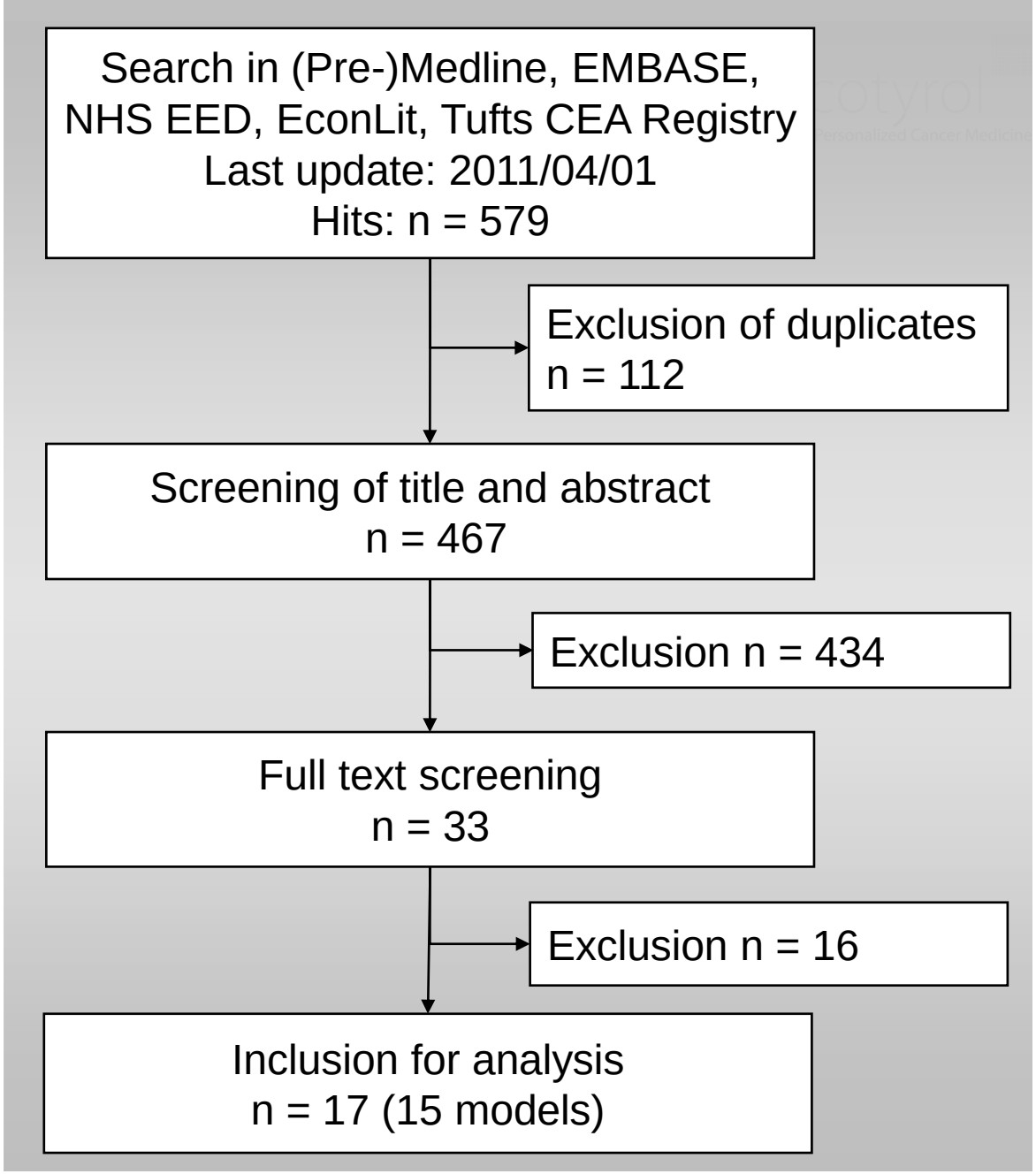
Literature Search II

Inclusion criteria

- Evaluation of treatment strategies in CML
- Decision-analytic model or any other type of mathematical healthcare model (AUC, DT, Markov models, microsimulation, DES…)
- Studies using models only as an illustration or in a tutorial were excluded
- Studies that only conducted economic evaluations along a clinical trial were excluded
- Only published studies as full-text were included in the review

Results

Flow Diagram Literature Search



Evaluated Treatment Alternatives

- Chemotherapy (e.g., hydroxyurea, busulfan, or other combination chemotherapy)
- Palliative care
- Interferon-alpha, interferon-alpha + cytarabine
- Bone marrow transplantation, stem cell transplantation
- Imatinib (1st generation TKI)
- Dasatinib (2nd generation TKI) (only as 2nd line tx)

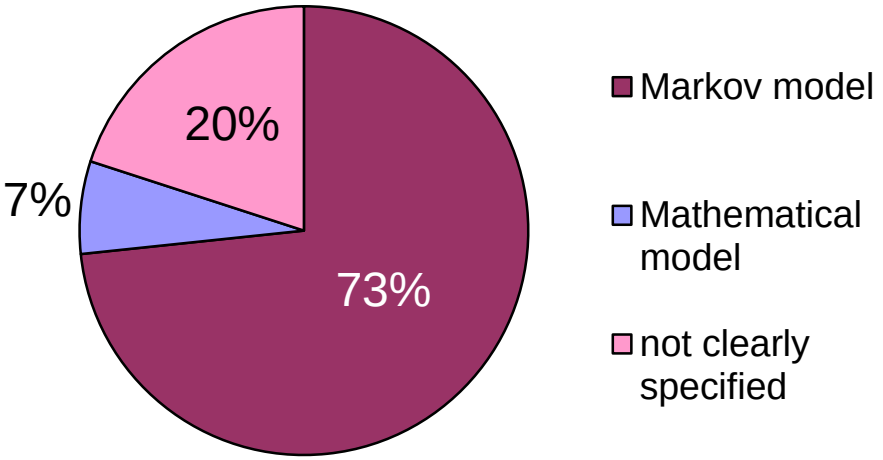
Economic Evaluation

- Most of the studies (n = 14) evaluated cost-effectiveness/ cost-utility ratio of the treatment alternatives
- One study did merely focus on the observed health effects

Health Outcomes

- Most studies (n = 13) reported a preference-based health outcome measure: quality-adjusted life years (QALYs)
- Two studies: only focus on survival without adjustment for quality

Modeling Approach



- Eleven studies chose a Markov model, whereas three of these explicitly stated to have used a combination of a decision tree (first 8 or 12 months) and a Markov model
- One study used a Gompertz model approach (referred to as mathematical model in the figure above)

Simulation Approach

- Not always described sufficiently
- Deterministic cohort simulation most frequent (n = 10)
- One study performed both:
  Markov cohort analysis and first-order Monte Carlo microsimulation

Time Horizon

- Time horizon ranged from 2 years to lifetime
- Eleven studies used a lifetime time horizon

Category	Variables	No.	%
Time Horizon	2 years	1	7
	5 years	2	13
	20 years	1	7
	Lifetime	11	73

Uncertainty Analysis

- All models conducted deterministic sensitivity analyses
- Four models reported a probabilistic sensitivity analysis

Personalized Medicine

- None of the models identified in the systematic literature review evaluated comprehensive personalized medicine strategies

Conclusions

Conclusions

- Several well-designed models for different CML treatment strategies
- Quality of reporting varied substantially
- Evaluations of novel treatment options such as second-generation TKIs underrepresented
- More subgroup evaluations for a more personalized decision making needed
- Lifetime time horizon due to chronic character of the disease necessary


Muito Obrigada
THANK YOU ☺
Vielen Dank