Treating Cardiovascular Disease: Optimization Models vs Risk-based Heuristics

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Cardiovascular Disease

- With more than half a million deaths in 2015, cardiovascular disease is the leading cause of death in America.
- Most common risk factors: blood pressure and cholesterol
- Traditional treatment approach: independent treatment of risk factors with one size fits all threshold based policy guidelines
- Our research objective is to develop clinical algorithms that can be used to improve treatment for the prevention of cardiovascular disease.

Markov Decision Process

Check the patient's risk profile → **Initiate a medication?**

Risk profile: SBP, TC, HDL, race, diabetes, smoking, age, risk calculator, gender

6 different medications are evaluated for their impact on reducing risk of CVD

- Objective: to maximize quality adjusted life years (QALY)
- Pill burdens considered instead of monetary costs.
- Each continuous risk factor discretized into 4 states
- Decision epochs from age 40 to age 74.
- Mayo clinic electronic records are used to fit a linear model for 3 risk factors and effect of medications on targeted risk factor.
- Framingham and ACC/AHA CVD risk calculators are used for assessing 10 year risk of developing CVD.
- Solution method: backward induction for finite horizon MDP
- Boundary condition: life expectancy after 75 years normalized for CVD risk profile at 75
- Important assumptions: only one medication initiated at a time and 100% adherence to medications

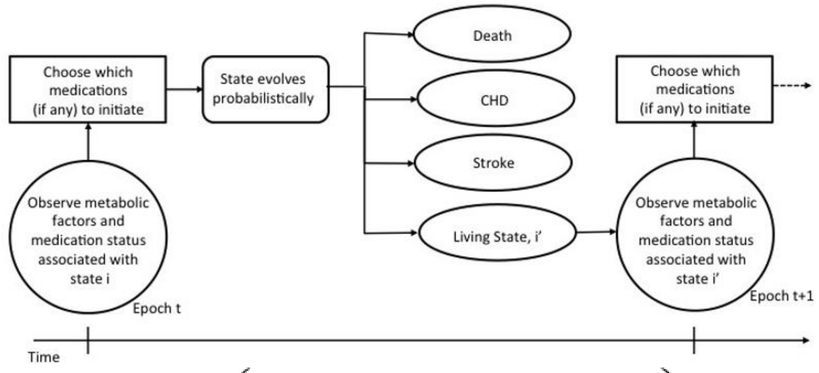
Risk Heuristic

- Uses a greedy approach to minimize CVD risk by choosing the medication change that most effectively reduces 10-year-risk at each epoch

Research Questions

- How do MDP and Risk Heuristic compare to current treatment guidelines in terms of expected life years and medication years?
- Does the MDP results follow a control limit policy?

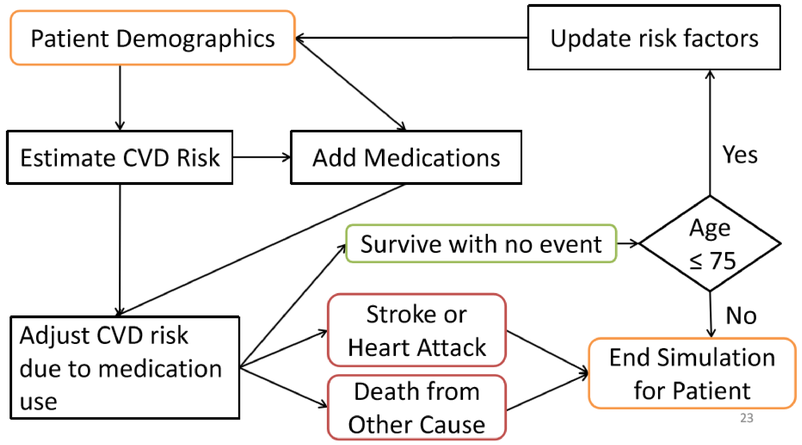
Decision making Process for MDP



$$V_t^*(\mathbf{s}) = \max_{a_t \in A(\mathbf{s})} \left\{ r_t^{a_t}(\mathbf{s}) + \lambda \sum_{\mathbf{j} \in S} p_t(\mathbf{j}|\mathbf{s}, a_t) V_{t+1}^*(\mathbf{j}) \right\}$$

$$a_t^*(\mathbf{s}) \in \arg\max_{a_t \in A(\mathbf{s})} \left\{ r_t^{a_t}(\mathbf{s}) + \lambda \sum_{\mathbf{j} \in S} p_t(\mathbf{j}|\mathbf{s}, a_t) V_{t+1}^*(\mathbf{j}) \right\}$$

Simulation Model



For $t = 40, \ldots, 74$:

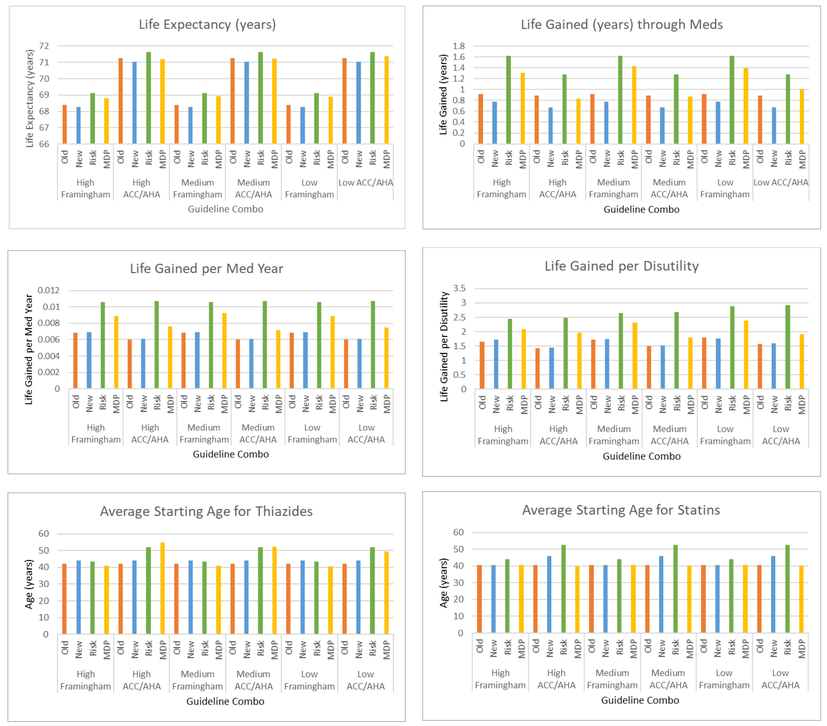
- Calculate patient's CVD Risk, $CVD(x_t, \mathcal{M}_t)$
- If $CVD(x_t, \mathcal{M}_t) > c$, start the medication m :

$$m \in \underset{m_i \in \mathcal{M} \setminus \mathcal{M}_t}{\operatorname{argmin}} \; CVD(x_t, \mathcal{M}_t \cup \{m_i\})$$

Current Guidelines

- Old Guidelines: JNC7 for SBP and ATP3 for cholesterol
- New Guidelines: JNC8 for SBP and ATP4 for cholesterol
- SBP guidelines use threshold of SBP at which to begin treatment
- Cholesterol guidelines use lipid profile along with general risk profile to begin treatment

Results



- Old Guidelines (JNC7, ATP3)
- New Guidelines (JNC8, ATP4)
- Risk Heuristic
- MDP

Conclusions

- Risk Heuristic (RH) performs best followed by MDP across all performance metrics for all combinations of risk calculators and disutilities
- Framingham risk calculator leads to lower life expectancies in CVD simulation due to overestimation of CVD risk compared to ACC/AHA risk calculator
- MDP and RH increase life expectancy by introducing medications earlier
- MDP and RH outperform old and new "one-size-fits-all" guidelines in terms of life gained relative to medication burden

Future Scope

- Establishing the generalizability of Risk Heuristic and MDP through larger and more diverse data set
- Incorporating lifestyle changes as part of treatment regimen to better reflect medical practices
- Developing a decision support system for medical professionals to use to evaluate alternative guidelines