

# Medical Decision Making: Modelling Multiple Treatments

Eka Kristiana Baker

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# Signed Statement

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

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# Abstract

Every day, practicing physicians make life changing decisions for patients, based on data gathered from clinical trials. Treatment benefit data is primarily based on results from trials conducted on patients in a specific controlled setting; they usually have limited health issues other than the disease for which treatment is intended. Realistically, patients for whom treatment is intended, particularly older patients, will have multiple conditions, called comorbidities, which could affect the actual benefit of treatment. In this thesis, we create a model that can predict the lifetime benefit of treatment for a patient with multiple comorbidities.

Currently, there are very few articles in the literature that focus on calculating treatment benefit in the presence of comorbidities, and no known satisfying solutions to this problem. One approach involves using Markov models to track the progression of a singular disease over time, and using a ‘comorbidity index’ to account for the effect of multiple conditions on the calculated benefit. An advantage of this method is the simplicity in which it captures comorbidity in the calculation. However, it could be difficult to quantify the level of comorbidity in a patient using this scale, still leading to an inaccurate predicted benefit. Furthermore, using this method, the specific comorbidities are not modelled; instead, the index is used only to increase the rate of death for these patients.

Another approach in the literature considers each patient individually, taking note of all of their comorbidities and the ‘snapshot’ benefit values assigned to each one. Under the assumption of independence between conditions, these values are analysed to find a more accurate benefit value for treating one of more of the diseases

at once. However, this only allows us to calculate the benefit at a single point in time, rather than a lifetime benefit that Markov model approaches allow. Since benefits can change over time, a lifetime measure allows us to find a better approximation of the true benefit of treatment. Both of these methods demonstrate that when multiple comorbidities are taken into account, the reported benefit of treatment decreases.

We consider a combination of both of these approaches to calculate a more accurate benefit of individual treatment in the presence of multiple comorbidities, and also the benefit of multiple treatments simultaneously. In this method, we use Markov chains to model the progression of individual episodic diseases over time. We then combine the individual models to create a Markov model that can track multiple comorbidities simultaneously.

For two specific treatments (carotid endarterectomy for carotid artery stenosis, and coronary artery bypass graft surgery for coronary artery disease), we use this model to demonstrate that the benefit of treatment measured in the presence of another disease is less than the benefit measured in isolation.

We also prove theoretically that for sensible treatments, the sum of the individual benefits measured in isolation is always greater than the benefits measured in the presence of comorbidities. We show that the same is true for the risk of treatment, where the risk is defined as the iatrogenic loss of treatment and is measured in the same units as benefit. This result is due to the effect of comorbidity on the benefit of multiple treatments. We are also able to show that, even accounting for the effect of comorbidity on the individual treatments, the sum of the individual benefits in the presence of other treatments (the withdrawal benefits) is greater than the combined benefit of treating all diseases at once. This implies that there is also an interaction between the treatments, as well as the comorbidities.

However, there are still some drawbacks with this model. For simplicity, we assume that both treatments occur simultaneously at the beginning of the chain. For surgical treatments though, this is unrealistic, since surgery can take a toll

on the patient. Thus, there is room for further refinement of the current model, and opportunity to allow for various other types of diseases to be modelled as well. Further research into the trade-off between model complexity and computation time could also be conducted in the future.