

The Singapore Diabetes Prevention Program Cost-effectiveness Analysis Revisited: Proper Methods

Overturn Previous Conclusions

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Introduction and Objectives

A 2014 Singapore Cost-Effectiveness Analysis (CEA) from a healthcare system perspective claimed that Metformin and Lifestyle modification treatments were cost-effective for patients classified as having Pre-Diabetes. However, Incremental Cost-Effectiveness Ratios (ICERs) were calculated incorrectly, comparing all treatment alternatives to a common (Placebo) alternative.

Our main objective is to reproduce, correct and extend that analysis, using correct ICER calculation methods and to indicate the extent of losses when incorrectly implementing treatments that are not cost-effective.

We recalculated the Singapore CEA Incremental Costeffectiveness Ratios (ICERs) using the same input data and the same model as the original work (a one period (3-year) decision tree) but correcting the method to calculate the ICERs, eliminating dominated alternatives. The non-dominated alternatives were then considered to calculate the costeffectiveness of interventions and results compared with the Singapore cost-effectiveness analysis (CEA) conclusions. We also simplify the original model, indicating its equivalence to the more complex original work. We expand the deterministic analysis using the NLCs (Net Loss Curves) analysis to validate the results and indicate the costs of errors in conclusions.

The original analysis examined two perspectives: healthcare system and societal. We analyze only the healthcare system perspective because the same incorrect methodology and same questionable parameter data were applied in both perspectives and we want to demonstrate, only the differences of applying the correct methodology and measure the effect of implementing incorrect conclusions.

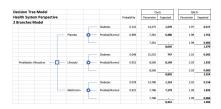


Fig 1. New Decision Tree Model, simplifying the original model.

Methods

We reproduced original costs, effects and (incorrectly calculated) ICERs in the original analysis. ICERs were then calculated correctly, using textbook methods (Drummond, Sculpher, Claxton, Stoddart, & Torrance, 2015; Glick, Doshi, Sonnad, & Polsky, 2015; Neumann, Sanders, Russell, Siegel, & Ganiats, 2017). The analysis was also expanded, using Net Loss Curves (Alarid-Escudero, Enns, Kuntz, Michaud, & Jalal, 2019; Simon Eckermann, 2017; S. Eckermann, Briggs, & Willan, 2008), showing the extent of losses in implementing any but the optimal treatment.

- 1. Produce a new decision tree model- two branched (Figure 1), using the same data from the Singapore study model input parameters to confirm the same results in the three branched model that included a possibility of a pre-diabetes patient returning to normal glucose levels with the same cost and effects as remaining in a pre-diabetes health state. The additional complexity of the original 3-branched decision tree was unnecessary as the third branch was irrelevant, given the assumptions employed.
- Calculate ICERs correctly, using the values of costs and QALYs obtained from the new two-branch model to compare with the published ICERs.
- 3. Evaluate the cost-effectiveness of the interventions graphically using and the Cost Disutility plane (C-DU Plane) Eckermann analysis (Simon Eckermann, 2017). This construct allows us to evaluate the technical and economic efficiency and inefficiency. This graphical method could have clarified that the original published analysis was in error.
- 4. Include the Expected Loss Curves in the analysis to illustrate graphically the magnitude of loss associated with adopting inefficient alternatives. This analysis indicates the costs of the error associated with using metformin instead of lifestyle modification, given that it is only the latter that is cost-effective.

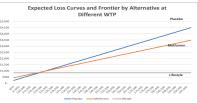


Fig 3. Expected Loss Curves and Net Loss Frontier

Results

When rerunning the Singapore model, the reproduction of the cost and QALY numbers showed that results were consistent with the original work. However, the only ICER relevant to report is Lifestyle vs. Placebo (\$18,778 per QALY); the Metformin alternative is weakly dominated by the combination of Lifestyle and Placebo. The cost-disutility plane demonstrated graphically that the only cost-effective alternative is lifestyle- under the proposed WTP (Figure 2). The expected net loss from implementing Metformin over the optimal Lifestyle is \$1.036 per patient at a WTP value of \$50,000 (Table 2 and Figure 3). This may be scaled up to a population level by multiplying that by the number of discounted total pre-diabetes patients over time who could be influenced by such a decision. Table 2 also indicates efficiencies of the treatments based on Eckermann, Placebo and Lifestyle are technically efficient (on the cost-effectiveness frontier: blue line in Figure 2): Metformin is not. Metformin has a technical inefficiency of 0.0418, indicating that an equiproportional reduction in cost and disutility of 4.18% would be needed to make it technically efficient. Three alternative WTP values are explored in Table 2 and Figure 2 that indicate the degree of economic efficiency (EE) of any but the optimal treatment. At a WTP of \$100,000/QALY, Lifestyle is optimal (EE = 1): Placebo and Metformin fall short with EE values of 0.1878 and 0.2427. These values indicate that to achieve the economic efficiency of lifestyle at that WTP, equiproportional reductions in cost and disutility of 81.22 and 75.73 percent would be needed (1-EE values in percent).

Intervention	Cost US\$	QALY	ICER vs. NME1		ICER vs. NME2	NME2
Placebo	8,050	1.979				
Metformin	8,331	1.992	21,615			
Lifestyle	8,895	2.024	17,625	(*)	18,778	Placebo (**)
NME1: is the NME2: is the (*) Metformin	most effective	e intervention	, not weakly			

Table 1. Correct calculation of ICERs from a health system perspective - using the appropriate method, taking out the consideration the dominated alternatives.

Conclusions

The Singapore DPP CEA main conclusions were that both the Lifestyle and Metformin interventions were cost-effective. We demonstrated that this claim of dual cost-effective treatments was incorrect, under the healthcare system perspective. This incorrect conclusion resulted from an inappropriate comparison of all alternatives to a common Placebo alternative. The expected Net Loss Curves demonstrated the high costs of investing in an alternative that is not cost-effective.

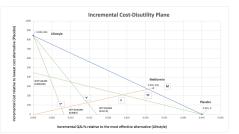


Fig 2. Incremental Cost-disutility Plane.

	Placebo (Point P)	Metformin (Point M)	Lifestyle (Point L)	
QALYs	1.979	1.992	2.024	
Costs	\$8,050	\$8,331	\$8,895	
Change in DU vs. Lifestyle (greatest QALYs)	0.045	0.032	0.000	
Change in Cost vs. Placebo (least costly)	\$0	\$281	\$845	
TE*	1	0.9582	1	
TI = DOD	0	0.0418	0	
EE WTP=\$10,000	1	0.7488	0.5325	
EE WTP=\$50,000	0.3756	0.4492	1	
EE WTP=\$100,000	0.1878	0.2427	1	
Expected Loss (WTP=\$10,000)	\$450	\$601	\$845	
Expected Loss (WTP=\$50,000)	\$2,250	\$1,881	\$845	
Expected Loss (WTP=\$100,000)	\$4,500	\$3,481	\$845	
Net Loss (WTP=\$10,000)	\$0	\$151	\$395	
Net Loss (WTP=\$50,000)	\$1,405	\$1,036	\$0	
Net Loss (WTP=\$100,000)	\$3,655	\$2,636	\$0	

Table 2. Eckermann Analyses: Technical and Economic Efficiencies and Net Losses.