



New Developments (and Challenges) in HTA

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The University of Melbourne
The Royal Melbourne Hospital



- consultant to government
- consultant to industry
- hospital clinician: general internal
medicine and clinical pharmacology



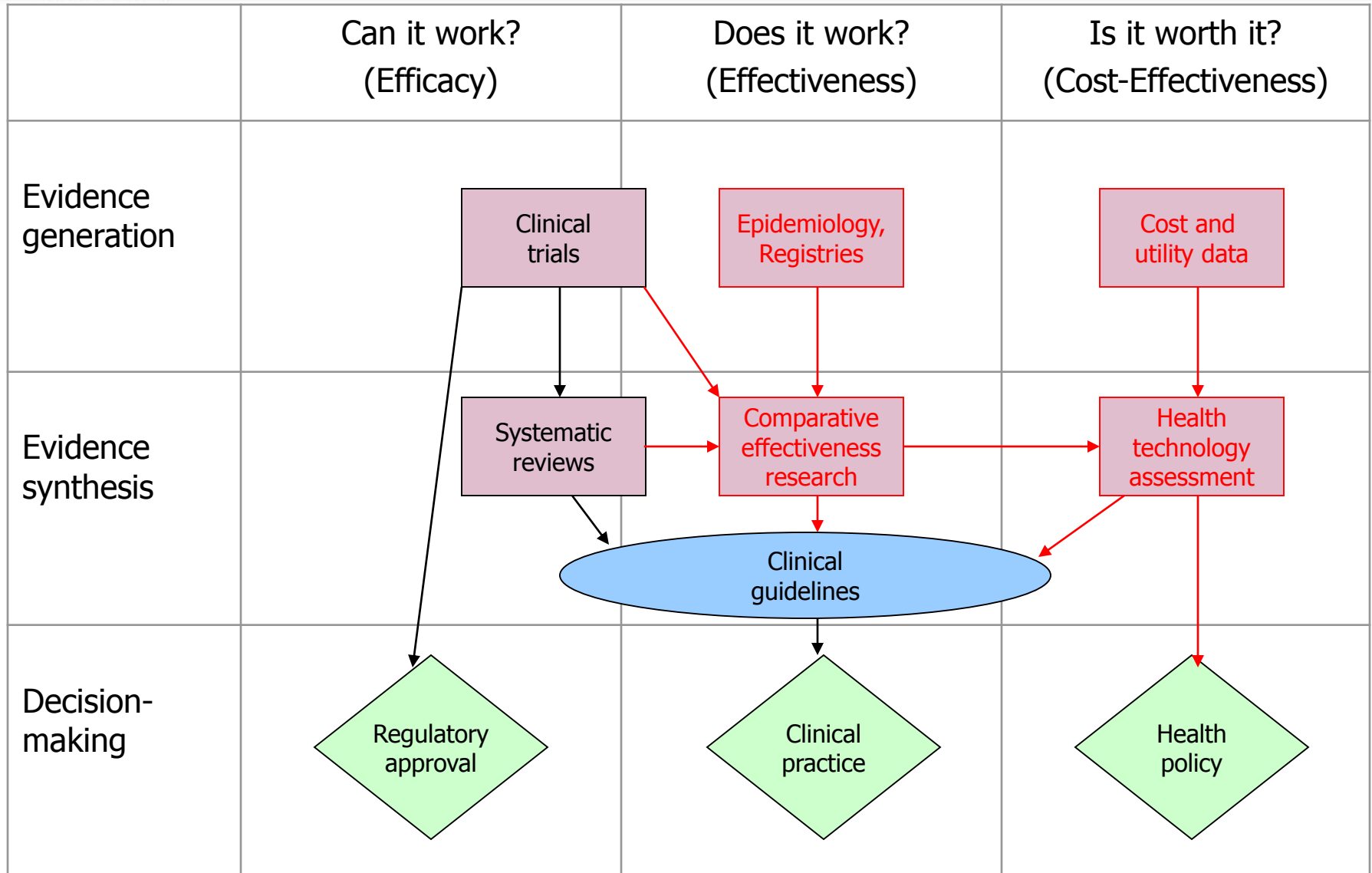
- need for 'real-world evidence'
- determining relative efficacies
- limiting uncertainty



'Real World Evidence'



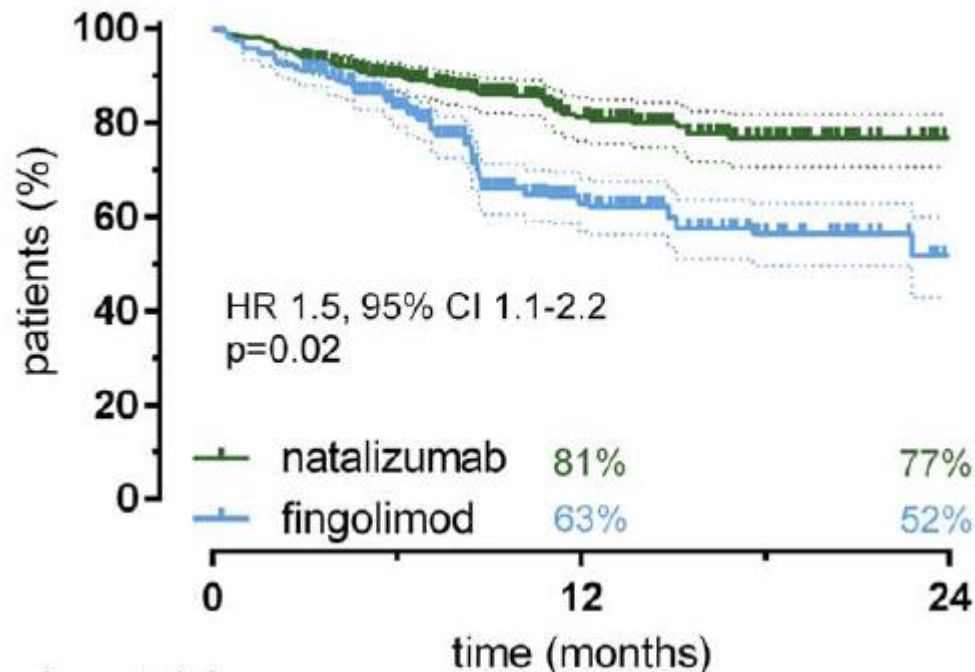
Evidence-Based Practice





- clinical registries
- meta-data, including data linkage
- post-policy evaluation
- patient-relevant outcomes

Switch to Natalizumab versus Fingolimod in Active Relapsing–Remitting Multiple Sclerosis





OPEN  ACCESS Freely available online

 **PLOS** | ONE

Real-World Efficiency of Pharmacogenetic Screening for Carbamazepine-Induced Severe Cutaneous Adverse Reactions

Zhibin Chen^{1,2}, Danny Liew^{1,2,3}, Patrick Kwan^{1,4,5*}

Chen et al. *PLOS One* 2014

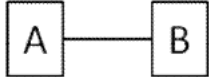

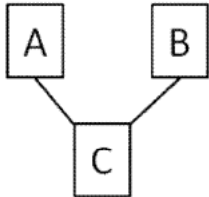
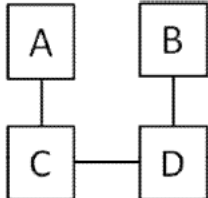
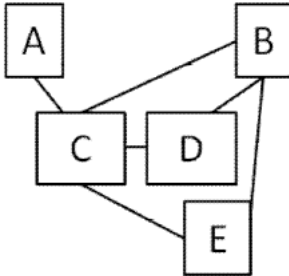


Determining Relative Efficacies



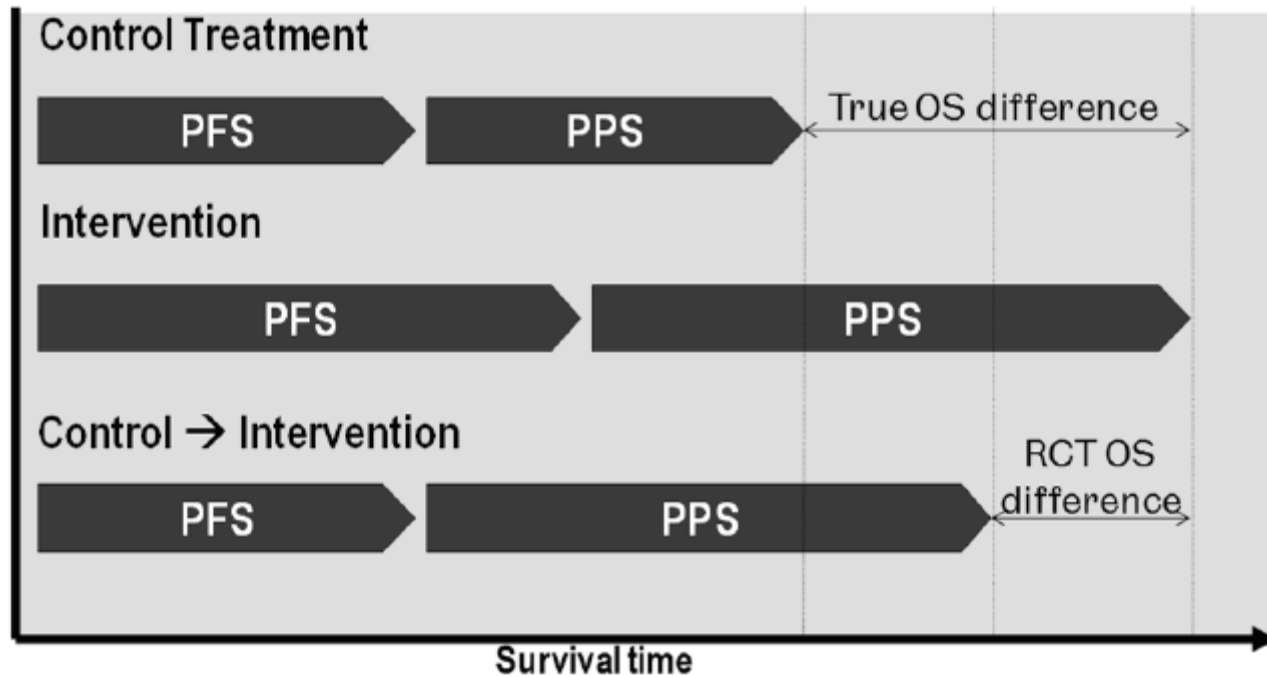
- absence of head-to-head data
- multiple comparators
- treatment switching in clinical trials

Comparisons

	a) Head to head clinical trial
	b) Naïve direct comparison
	c) Adjusted indirect comparison with a common comparator
	d) Multiple adjusted indirect comparisons
	e) Mixed treatment comparison



Treatment Switching in Clinical Trials



Notes: PFS = Progression Free Survival; PPS = Post Progression Survival; OS = Overall Survival; RCT = Randomised Controlled Trial



Adjusting Survival Time Estimates to Account for Treatment Switching in Randomized Controlled Trials—an Economic Evaluation Context: Methods, Limitations, and Recommendations

*Nicholas R. Latimer, PhD, Keith R. Abrams, PhD, Paul C. Lambert, PhD,
Michael J. Crowther, MSc, Allan J. Wailoo, PhD, James P. Morden, MSc,
Ron L. Akehurst, MSc, Michael J. Campbell, PhD*

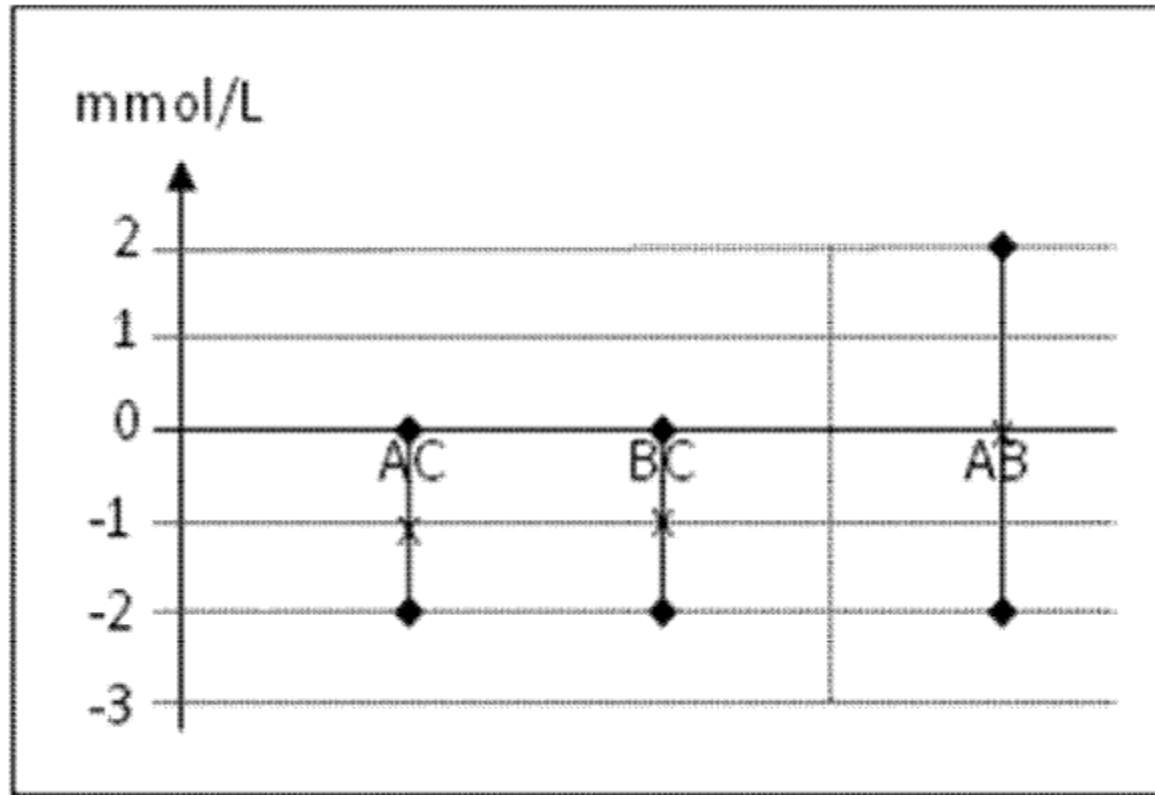


Dealing with Uncertainty



- simplifying comparisons
- managed entry schemes

Uncertainty in Indirect Comparisons





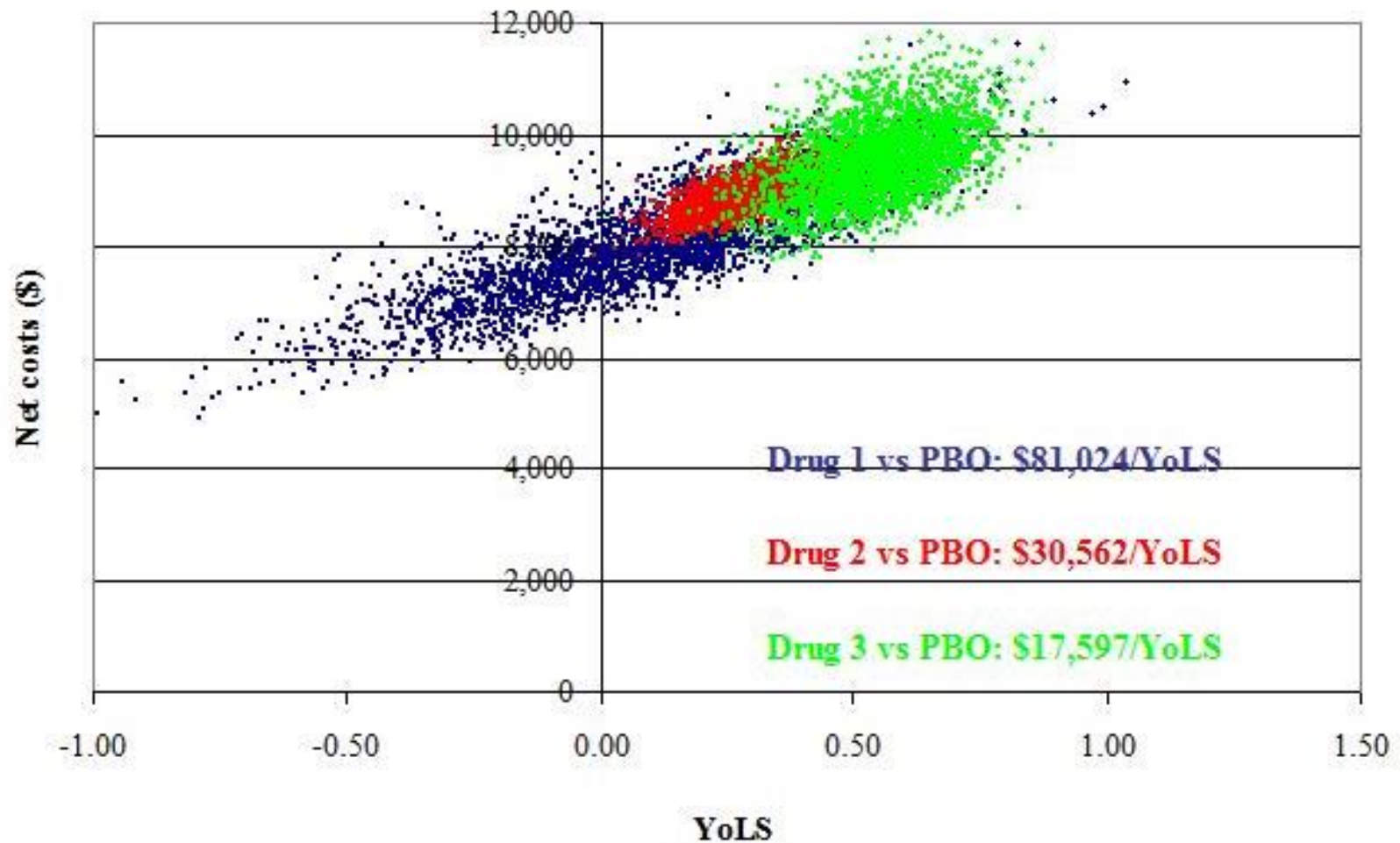
- Bayesian statistical principles
- use all available data - direct and indirect
- less uncertainty compared to adjusted indirect comparisons

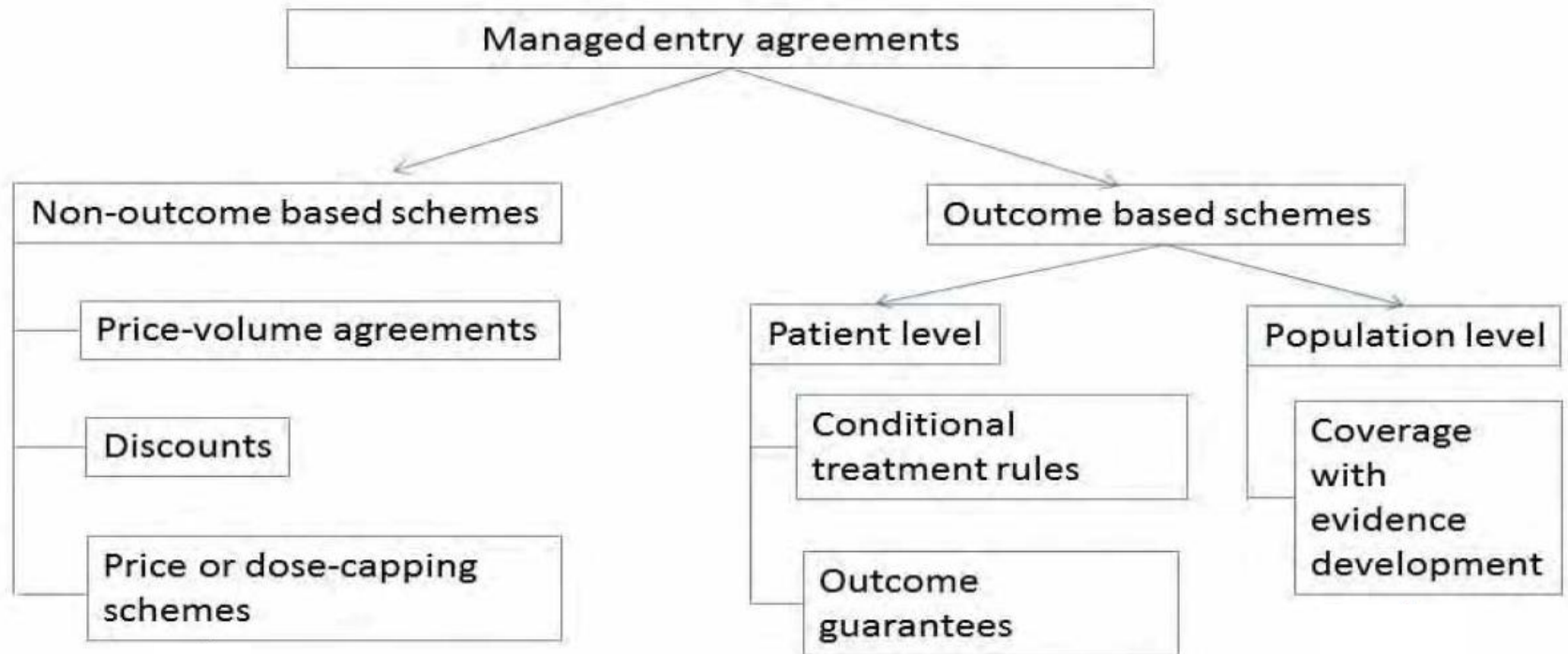
	RR	LL 95%CI	UL 95%CI
Non-fatal MI			
Drug1 vs PBO (RCT1)	0.56	0.40	0.77
Drug2 vs PBO (RCT2)	0.62	0.55	0.71
Drug3 vs PBO (RCT3)	0.59	0.42	0.83
Overall mortality			
Drug1 vs PBO (RCT1)	0.96	0.76	1.21
Drug2 vs PBO (RCT2)	0.88	0.82	0.94
Drug3 vs PBO (RCT3)	0.79	0.70	0.88



	RR	LL 95%CI	UL 95%CI
Non-fatal MI			
Drug1	(Ref)		
Drug2 vs Drug1	1.12	0.78	1.59
Drug3 vs Drug1	1.07	0.67	1.71
Overall mortality			
Drug1	(Ref)		
Drug2 vs Drug1	0.92	0.72	1.18
Drug3 vs Drug1	0.82	0.63	1.06

Results of CEA (prob sens analysis)







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