Australian Regulatory Environment

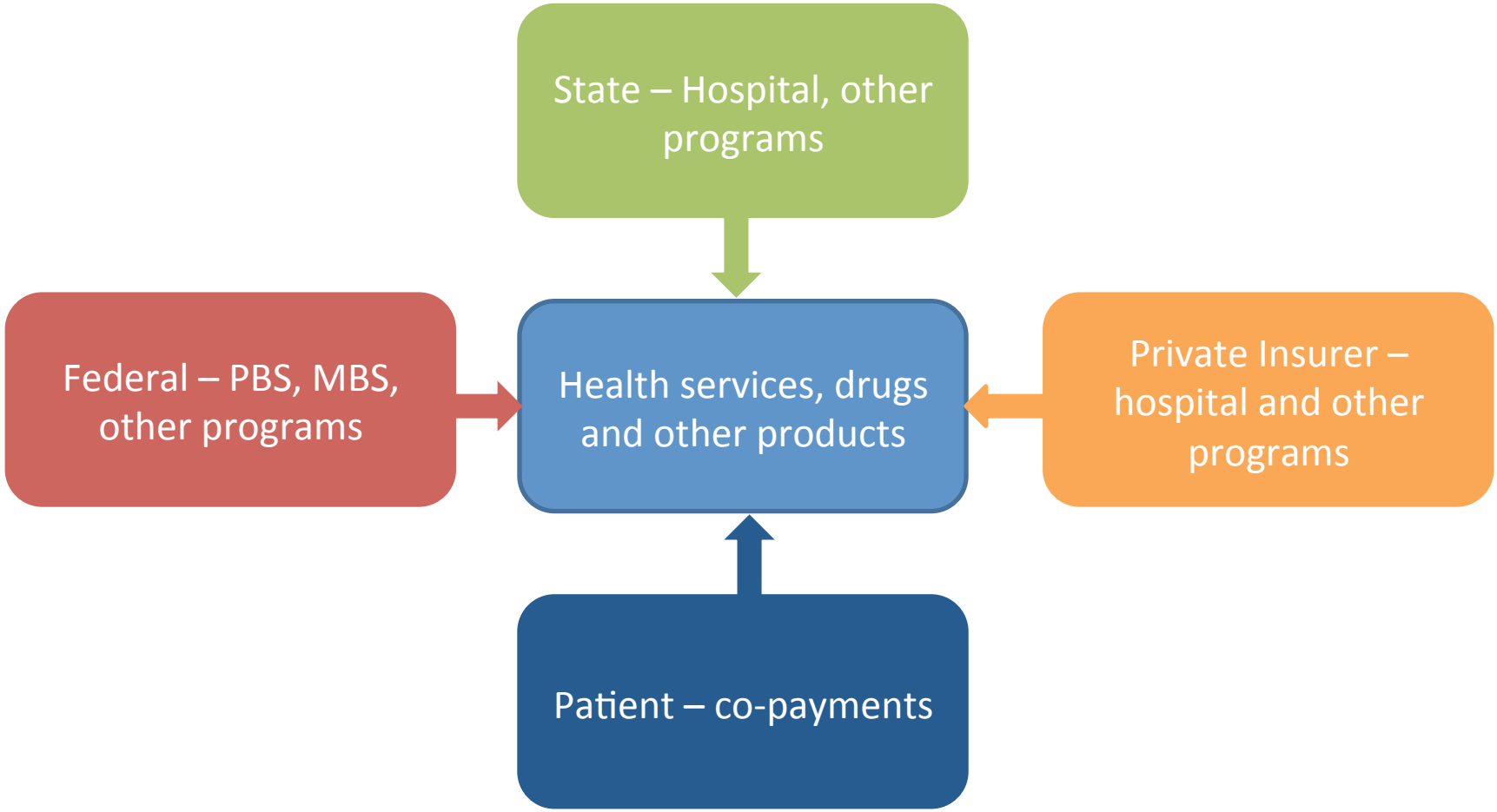
Geoff McColl

Pharmaceutical Benefits Advisory Committee

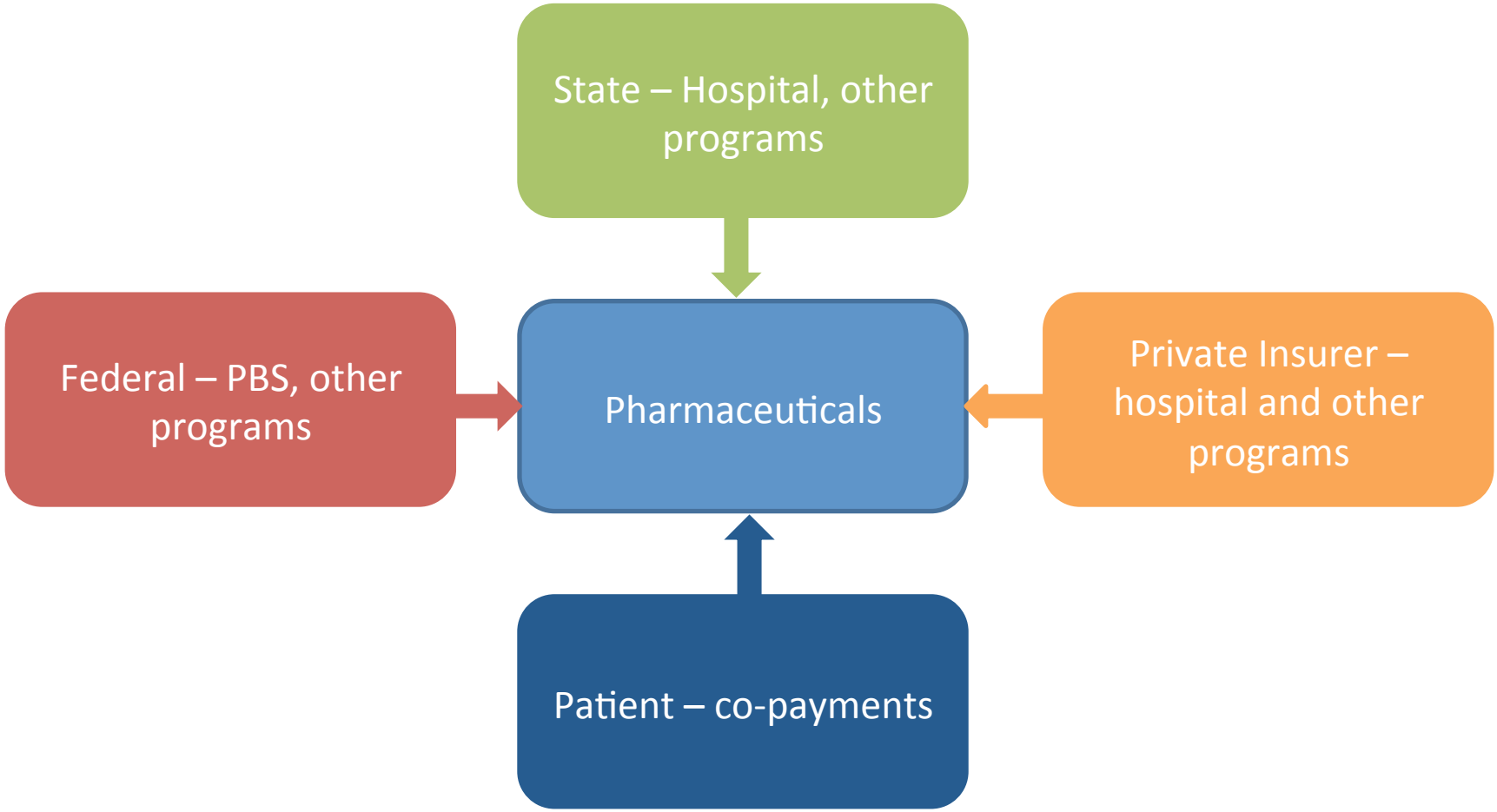
Agenda

- Australian health care regulatory and funding environment
- Pharmaceutical Benefits Advisory Committee (PBAC) processes
- Evidence and funding decisions – the future

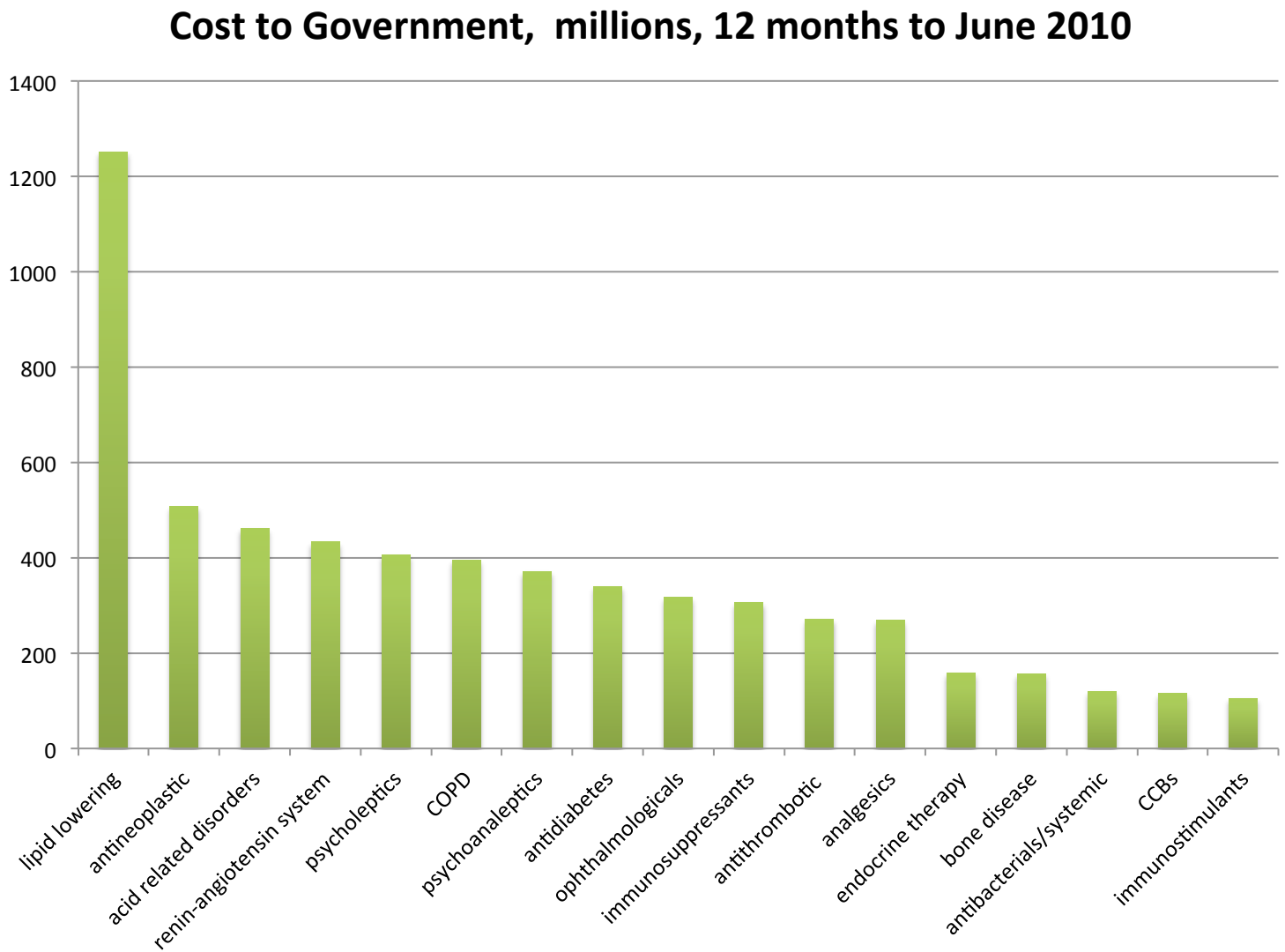
Australian Health Funding



Australian pharmaceutical funding

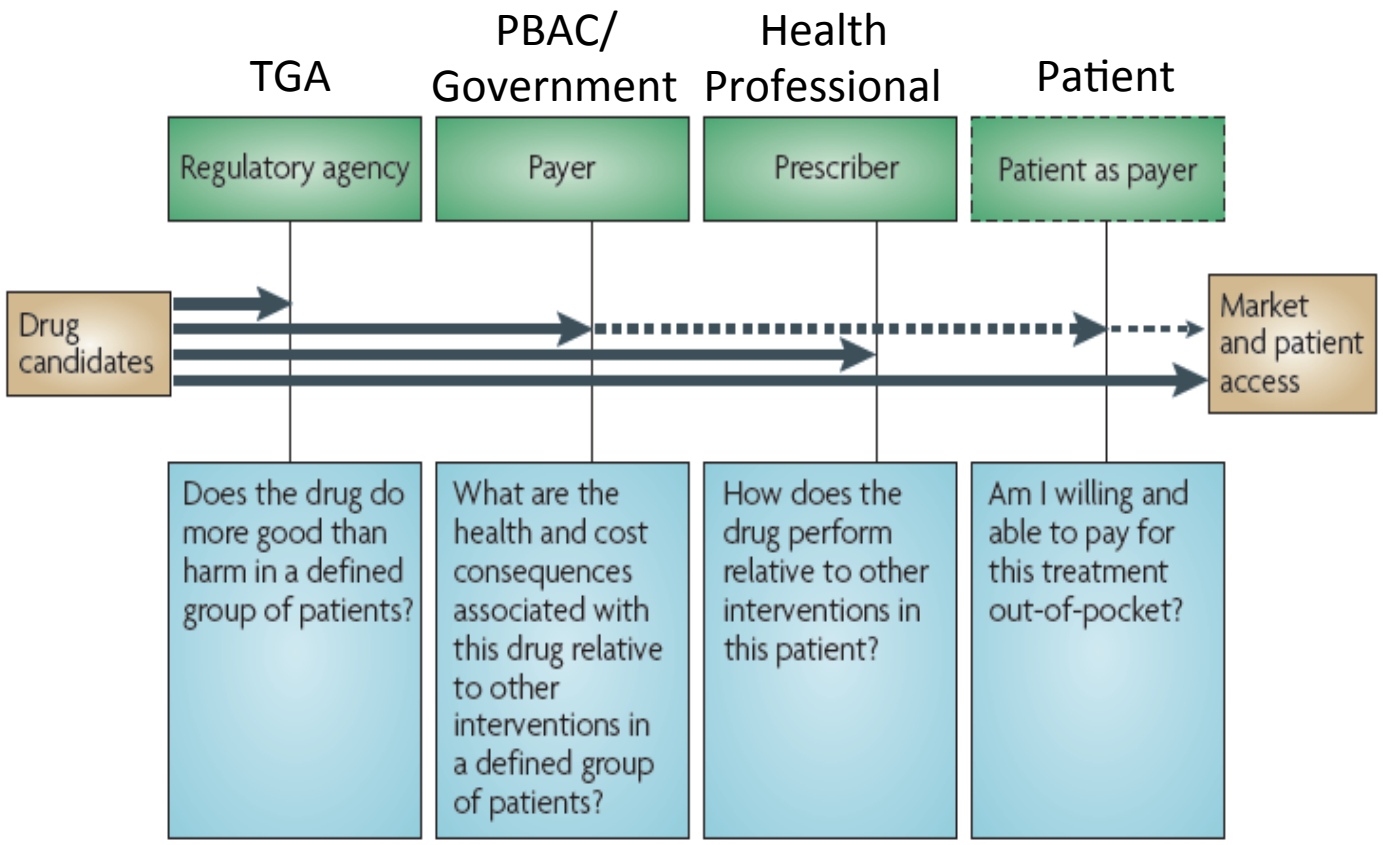


Pharmaceutical Benefits Scheme



Market Access

Eichler et al Nature Reviews 2011



PBS listing

- TGA
  - Reviews manufacture, safety and efficacy
- PBAC
  - Reviews comparative effectiveness
  - Reviews cost effectiveness
  - Reviews total cost (utilization and cost)
- PBPA
  - Negotiates price
- Approval by Minister/cabinet
- Listing on PBS

Pharmaceutical Benefits Advisory Committee (PBAC)

National Health Act

'…PBAC shall make recommendations to the Minister, from time to time as to the drugs and medicinal preparations which it considers should be made available as pharmaceutical benefits…

…the Committee shall give consideration to the effectiveness and cost of therapy involving the use of the drug, preparation or class, including by comparing the effectiveness and cost of that therapy with that of alternative therapies, whether or not involving the use of other drugs or preparations….'

[section 101(3),(3A), (3B), (3BA]

And also vaccines. [101(4B)]

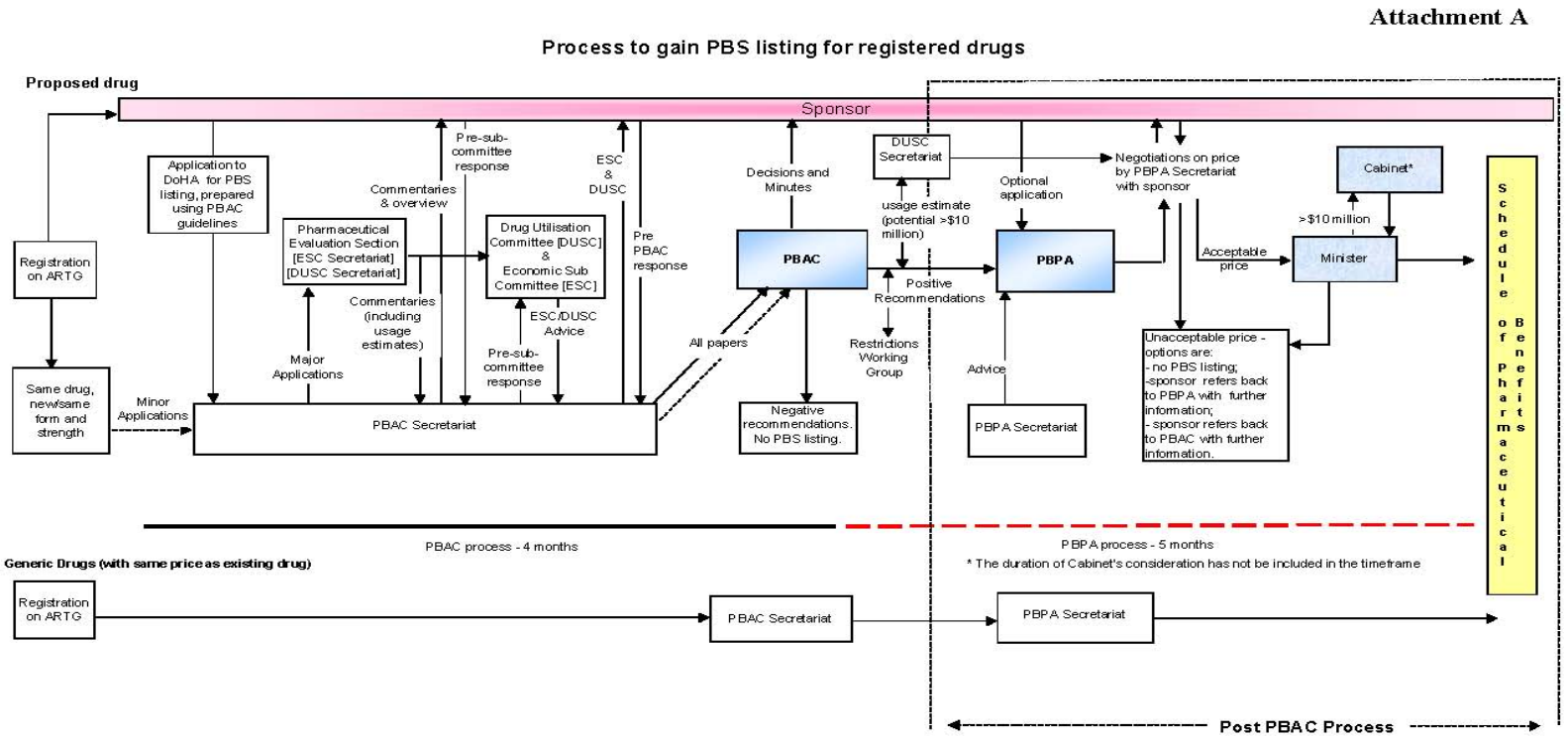
PBAC

- If a product is more costly, shall not recommend, unless it provides significant improvement in efficacy or reduction of toxicity for some patients [101(3B, (a))]
- Must specify whether drug or preparation should be treated as interchangeable on an individual patient basis – *therapeutic groups [101(3BA)]*
- Combination therapies (4AC)
  - Compliance
- Deletions
- Exemptions

PBAC

- Final decision – Section 85(2) (usually) , Minister declares.
- Generics (usually) – Secretariat/Department

PBAC processes



PBAC Data requirements

- Context – population, indication, comparator
- Comparative clinical trial evidence, based on systematic review methods – clinical claim for benefits and harms
- Basis for extrapolating clinical trials to Australian setting – considering generalisability, extrapolation, transformation
- Cost-effectiveness according to claim –
  - Equivalence = cost minimisation
  - Superiority = cost-effectiveness (cost-utility)
- Total budget impact/estimate of use
- Any other considerations (e.g equity, life-saving drugs, appropriate use)

Table 1 Assessment of Evidence of Cost per QALY Submissions to the PBAC 1994-2004

Data Item	Description	Scoring
Incremental cost per QALY	Incremental cost per additional QALY	$0,000[a]
Cost to government	Annual predicted additional financial cost to government of listing	$m
Clinical significance	Did the PBAC consider the size (point estimate) of the treatment effect to be clinically important	1 = Yes 0 = No
Precision of clinical evidence	Statistical reliability of the measure of the size of the treatment effect	$P \leq 0.05 = 1$ $P > 0.05 = 0$
Level of evidence	What is the level of the key clinical evidence presented to the PBAC?	Head-to-head RCT = 3 Indirect comparison RCT = 2 Nonrandomized = 1
Quality of studies	12-item checklist on selection and absence of bias in trial design and analysis[b]	High quality = 3 Moderate quality = 2 Low quality = 1
Relevance of evidence	Comparator and population in trial appropriate	1 = yes 0 = no
Life threatening	Condition associated with premature mortality (< 5 year survival)	1 = yes 0 = no
Economic model validity	Model structure	critically flawed = 1 some flaws but plausible = 2 reliable = 3
Modeled outcome	Translation of clinical outcomes to quality of life	critically flawed = 1 some flaws but plausible = 2 reliable = 3
Modeled cost	Cost estimates	critically flawed = 1 some flaws but plausible = 2 reliable = 3
No alternative acceptable therapy	Accepted placebo/standard care as comparator	Last line = 1 Not last line = 0
Uncertainty of cost per QALY	Upper limit in model sensitivity analysis	$0,000[a]
Previously considered	If the drug had been considered before for that indication	1 = Yes 0 = No

Harris AH et al, Medical Decision-Making, 2008:28:713-722.

Table 3 Probit Regression Model Results of Influences on Decision to Recommend Listing for Incremental Cost per QALY ($n = 103$)

Variable	Mean	Marginal Effect	
		(1)	(2)
Incremental cost per QALY ($0,000)	4.64 (3.59, 5.69)	–0.05 (0.00; –0.08, –0.03)	–0.06 (0.00; –0.10, –0.04)
Cost to government ($m)	17.28 (12.1, 22.4)	–0.01 (0.02; –0.01, –0.00)	–0.01 (0.02; –0.01, –0.00)
Clinical significance	0.50 (0.41, 0.60)	0.44 (0.00; 0.22, 0.66)	0.28 (0.00; 0.09, 0.47)
Precision of clinical evidence	0.75 (0.65, 0.85)	–0.12 (0.22; –0.32, 0.07)	
Level of evidence	2.79 (2.68, 2.89)	0.05 (0.46; –0.08, 0.19)	
Quality of studies	2.39 (2.26, 2.52)	0.04 (0.53; –0.09, 0.17)	
Relevance of evidence	0.56 (0.47, 0.66)	0.13 (0.09; –0.02, 0.28)	0.12 (0.12; –0.04, 0.28)
Life threatening	0.17 (0.09, 0.24)	0.37 (0.01; 0.10, 0.64)	0.44 (0.00; 0.18, 0.70)
Model validity	1.58 (1.44, 1.72)	0.02 (0.72; –0.08, 0.12)	
Modeled outcome	1.61 (1.48, 1.74)	0.09 (0.08; –0.01, 0.19)	
Modeled cost	2.19 (2.05, 2.34)	–0.09 (0.08; –0.20, 0.01)	
No alternative acceptable therapy	0.33 (0.24, 0.42)	–0.05 (0.59; –0.23, 0.13)	
Highest ICER ($0,000)	19.45 (11.30, 27.59)	0.002 (0.05; 0.00, 0.00)	0.002 (0.06; 0.00, 0.00)
Previously considered	0.63 (0.24, 0.42)	0.25 (0.00; 0.10, 0.40)	0.15 (0.02; 0.02, 0.28)
Previously considered Clinical significance	0.33 (0.24, 0.42)	–0.17 (0.06; –0.35, 0.01)	
Life threatening Clinical significance	0.12 (0.05, 0.18)	–0.22 (0.01; –0.38, –).06)	–0.23 (0.00; –0.38, –0.08)
Pseudo R^2		0.41	0.37

Harris AH et al, Medical Decision-Making, 2008:28:713-722.

PBAC decisions

Table 2 Characteristics of Data and Decisions on Submissions to PBAC 1994-2004

	QALYs	Life Years	QALYs or Life Years excl. both	All Cost-Effectiveness Analyses[a]	Non-Cost-Effectiveness Analysis[ab]	All Submissions[a]
Number	103	123	190[c]	340	462	802
Accept	31 (30%)	46 (37%)	62 (33%)	82 (24%)	212 (46%)	294 (37%)
Reject	48 (47%)	49 (40%)	85 (45%)	170 (50%)	128 (28%)	298 (37%)
Defer, withdrawn, request lower price	24 (23%)	28 (23%)	43 (22%)	88 (26%)	122 (26%)	210 (26%)
No alternate treatments available[d]	46 (47%)	14 (11%)	53 (28%)	117 (34%)	42 (9%)	159 (20%)
Previously considered	65 (63%)	74 (61%)	123 (64%)	198 (58%)	206 (45%)	404 (50%)

Harris AH et al, Medical Decision-Making, 2008:28:713-722.

PBAC decisions

- The following factors significantly influenced PBAC decisions
  - Clinical significance
  - Cost effectiveness
  - Cost to government
  - Severity of disease

Harris AH et al, Medical Decision-Making, 2008:28:713-722.

Current data issues with PBAC submissions

- Population in the trial vs PBS population
  - Subgroup analysis
- Comparison
  - Direct, based on randomised trial
  - Indirect, based on comparison via placebo or common comparator
- Outcomes
  - Surrogate vs clinical or patient relevant
  - Size of effect on outcomes – minimum clinically important difference
- Trial design
  - Early crossover or early stopping for benefit
- Cost effectiveness models
  - Utility conversion
  - Economic model structures and assumptions

How might pragmatic trials assist regulators/funders

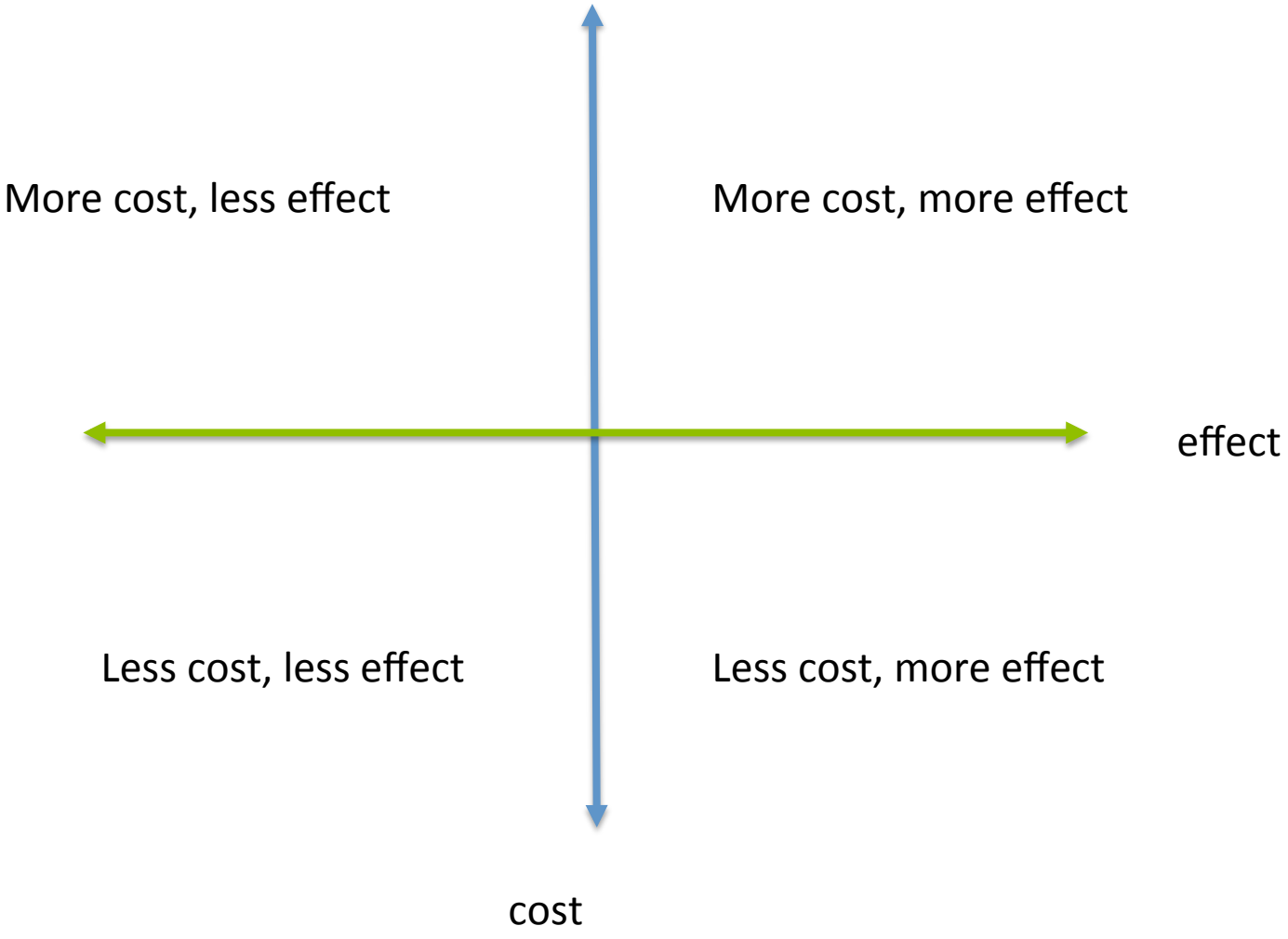
- Population in the trial vs PBS population
  - **Subgroup analysis**
- Comparison
  - Direct, based on randomised trial
  - **Indirect, based on comparison via placebo or common comparator**
- Outcomes
  - **Surrogate vs clinical or patient relevant**
  - **Size of effect on outcomes – minimum clinically important difference**
- Trial design
  - **Early crossover or early stopping for benefit**
- Cost effectiveness models
  - **Utility conversion**
  - Economic model structures and assumptions

Evidence and funding decisions – the future

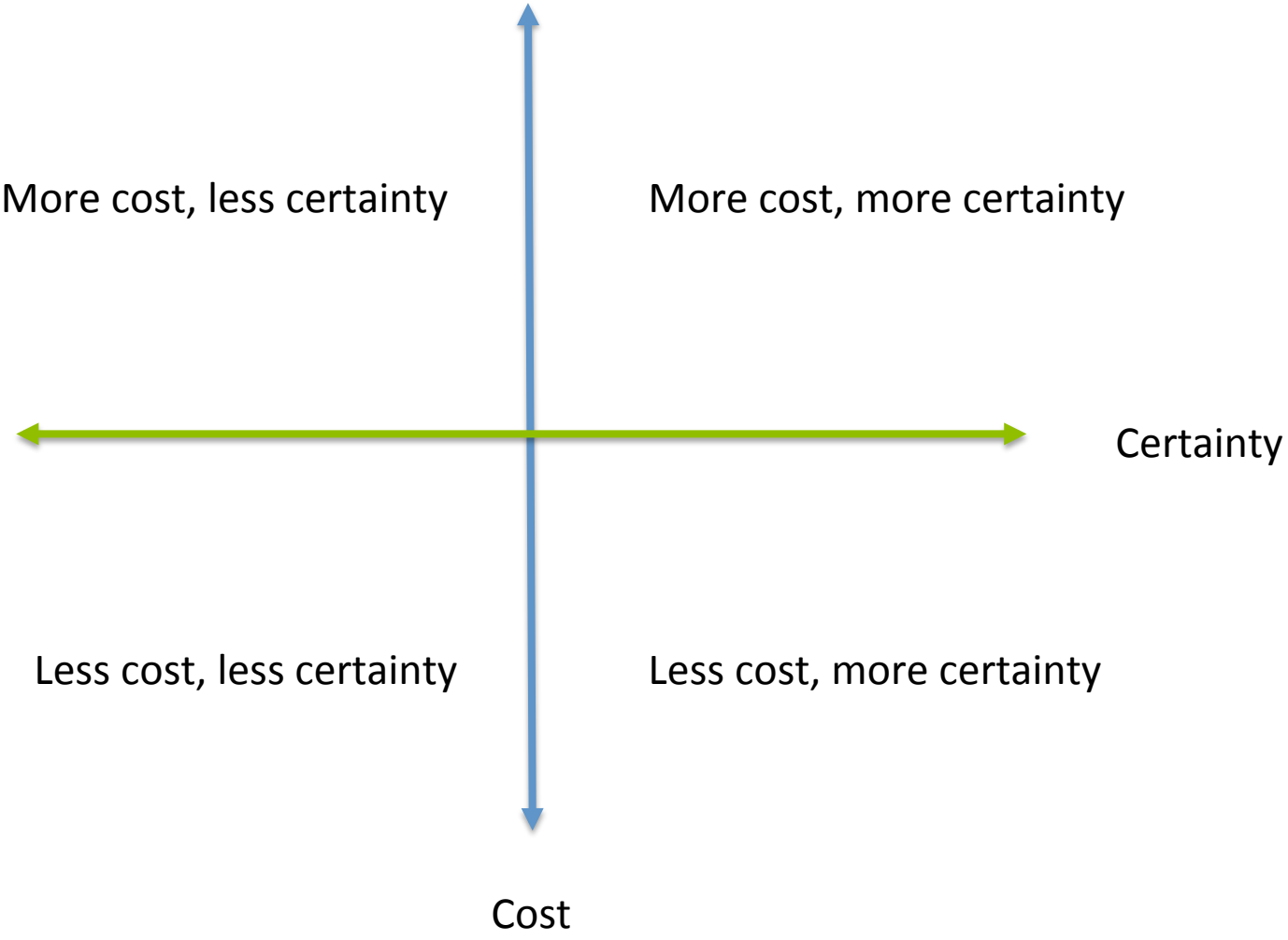
- Challenges
  - Personalised medicine – patho-physiological disease subgroups – genetic testing etc
  - New forms of evidence – pragmatic trials, naturalistic data
  - Costs of innovation (at a health system level)
  - Political factors

How might a regulator/funding agency approach new types of evidence?

Clinical claim and economics



Types of evidence and economics



Conclusions

- Regulators are likely to consider other forms of evidence in making funding decisions in the future
- The regulator will consider the rigor and uncertainty of new approaches
- Within a cost effectiveness framework there may be a trade off between uncertainty and price