Trust, constraints and the counterfactual: Reframing the political economy of new drugs

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Abbreviations

AUSFTA	Australia–U.S. Free Trade Agreement
aICER	Average Incremental Cost Effectiveness Ratio
CABG	Coronary Artery Bypass Graft
CBA	Cost Benefit Analysis
CEA	Cost Effectiveness Analysis
CEA_i	Cost Effectiveness Analysis applied in conjunction with a threshold of i
COAG	Council of Australian Governments
CSIRO	Commonwealth Scientific and Industrial Research Organization
DTM	Decision Theoretic Model
EBM	Evidence Based Medicine
EVCI	Economic Value of Clinical Innovation
FCUSS	Finance Committee of the US Senate
FDA	Food and Drug Administration
FPP	Firm's preferred price (per effect of a new drug)
GDP	Gross Domestic Product
GTM	Game Theoretic Model
HTA/CEA	Health Technology Assessment/Cost Effectiveness Analysis
ICER	Incremental Cost Effectiveness Ratio
$IMER$	Incremental Manufacturing Cost Effectiveness Ratio
IMS Health	Not an abbreviation but the name of a pharmaceutical data company
$IPER$	Incremental Price Effectiveness Ratio
ITA	International Trade Administration (US Government)
maxWTP	maximum Willingness To Pay
MRI	Magnetic Resonance Imaging
NB	Net Benefit
NICE	National Institute for Health and Clinical Excellence
NME	New Molecular Entity
NPV	Net Present Value
npvPH	Net present value of the population's health
OECD	Organisation for Economic Cooperation and Development
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PEA	Price Effectiveness Analysis
PEND	Political Economy of New Drugs
Pharma	The pharmaceutical industry
PhRMA	Pharmaceutical Researcher and Manufacturers of America
PPP	Purchaser's Preferred Price
QALY	Quality Adjusted Life Year
R&D	Research and Development
RCT	Randomised Controlled Trial
TGA	Therapeutic Goods Administration
WHO	World Health Organisation

Glossaries

Table 1 Glossary of Characters

Character	Definition	Reference
Firm	The capitalised "Firm" refers to a player in a Game. It is introduced in Game 1, Chapter 8 and it features in Games 2 and 3 in Chapters 9 and 10 respectively. It is capitalised, as is the convention in Game theory models. It has specific production functions and markets.	First use of "Firm" is Section 3.2 Examples of published pharma-economic games p. 116
firm	A firm with a small "f" is a pharmaceutical firm with no specific cost function who participates in the reimbursement process, invests in R&D and lobbies for higher prices. Its objective function is profit maximisation.	
Institution	The capitalised "Institution" refers to a specific institution that is a player in a Game. In these Games the Institution needs to consider how to respond to a threat from Pharma or a specific Firm. It has specific rules it must play by.	First use of "Institution" is in Game 1, Chapter 8, p. 112
institution	And institution with a small "i" is the collective term for the regulators involved in decisions about new drugs. The institutions of interest in this thesis are those that work in countries that use cost effectiveness analysis to make decisions about the reimbursement of new drugs, have universal health care schemes and constrained budgets.	The country such an institution works in is described in Section 2.1 p. 21
Reimburser	The Reimburser is the key character in this thesis. She is not an economist and not a clinician. She is bureaucrat who works with a clear objective function: to maximise the health gains possible from this and future budgets.	First use of Reimburser and Health Economic Adviser is in Chapter 3 p. 45
Health Economic Adviser	The Health Economic Adviser is the second character in this thesis. His task is to take the problems presented to him by the Reimburser and apply economic theory to solve them.	
Pharma	Pharma is the name given to the pharmaceutical industry, particularly those firms that invests in R&D.	
Displacer	The Displacer's job description is to "find savings" in order to allow for the additional costs of programs such as the drug budget to be financed. He may or may not be able to find the least cost effective of existing programs and if he does he cannot always displace them. In most cases, he cannot displace patented health technologies.	The Displacer's first appearance is in Chapter 6, p. 98.
Social Decision Maker	Drummond et al (2005) refer to three types of Analysts: A, B and C. Analyst C takes the position that the role of the economic analyst is to provide information on a "wide range of costs and consequences and present them in a way that helps health care decision makers form a better judgement". (p. 18) The Social Decision Maker referred to in this thesis is the person in receipt of this information. He is not an economist. He is probably a clinician. He may have a preference for method of production, specifically, he may prefer to use a new drug rather than an existing drug, even if it is no more effective, because he values "newness".	The Social Decision Maker is introduced in the Conclusion Section 3.3 p. 190

Table 2 Glossary of Phrases

Phrases	Definition
Universal health care	The term universal health care is used to distinguish between the health care schemes in counties such as the US and other developed countries such as Canada, Australia, New Zealand, England, Scotland, Denmark, Sweden, Finland, Norway and the Netherlands. The latter counties have not achieved equitable access to a minimum level of care for all patients and significant disparities in utilisation and health outcomes remain. In Australia, the gap in access to health care for Indigenous Australian compared to non-Indigenous Australians contributes to the significant 20 year gap in life expectancy at birth for males.
New drug price	New drug price refers to the phenomena of new drug price as the focus of heated debate. It refers to all new drugs, not a specific new drug.
Political economy of new drugs	The political economy of new drugs (PEND) is the economic expression of the heated debate about how the surplus associated with a new drug's innovation should be allocated across consumers, institutional purchasers and firms via the price mechanisms.
Policy narrative	The policy narrative is the story that surrounds the development and implementation of a policy, such as how to regulate the price of new drugs. It could be a simple cause and effect narrative and may or may not make reference to evidence.
Evidence based policy narrative	The evidence based narrative is a term I use to describe a policy narrative that is populated by multiple references to empirical evidence but not evidence that justifies the actual policy choice. For example, reference to the burden of disease associated with a condition to justify a policy to screen for a condition, with no reference to the evidence of the effectiveness of that program in reducing that burden of disease.
New drug **New NME**	The new drug or new NME has recently been approved for prescribing by the FDA or TGA and now prices are being negotiated. Evidence of incremental cost and effect are available.
Future drug **Future NME**	The future drug is one that has not yet completed phase 3 trials or the molecule has not even been discovered. Evidence of incremental cost and effect is not available.
Future population's health	One of the objectives of the conventional political economy of new drugs is to identify the health of a future population with or without additional future drugs. Of course it is by and large today's population, just older, and with different medical technologies.
Present value of population's future health	The present value of the population's future health is the PV of expected life time health of a population in the future – not just the health in one year.
Net present value population's health	This is the previous concept less the loss in health effects today as a consequence of higher prices today and hence less health today.

Table 3 Glossary of prices and costs in price effectiveness analysis

FPP	The firm's preferred price is the price that the firm offers a new drug at and also a price that the firm justifies as the price that should be used.
PPP	The purchaser's preferred price is the price that a purchaser believes maximises the objectives, whatever these are. The purchaser might be making a "mistake"
$IPER, f$	The incremental price effectiveness ratio is arithmetically identical to the ICER but price is recognised as endogenous and a function of the choice of the decision threshold rather than as exogenous.

$IMER$, c	The incremental cost to the firm of producing the incremental health effect compared to the previous drug.
$I\pi ER$	The incremental economic rent to the firm on the incremental health effect.

Table 4 Notation and parameters

Parameter	Description
β_c	The health shadow price: the aICER of the most cost effective strategy to increase the population's health where this strategy will typically include a combination of financing and expenditure. It is a function of the economic context, c, which includes the amount of resources that need to be displaced in order to finance a new drug, the prevailing prices of inputs and the existing degree of inefficiency in the health budget.
n	The aICER of the most cost effective program or technology in expansion or adoption.
m	The aICER of the most cost effective program or technology in contraction or disinvestment.
d	The aICER of the program or technology that is displaced to finance the additional costs of the new drug.
r	The conventionally measured rate of return on new drugs.
c	The $IMER$ in algebraic form. Can vary across drugs.
ΔL^P	The additional life years experienced by patients from a new drug or new drugs.
$\mathcal{R}$	The investment in R&D by the firm.
e	One alternative expression of return on R&D, incorporating the budget constraint.
f	The algebraic expression of the IPER at which the firm offers a new drug.
ω	The share of additional economic rent from higher prices that is allocated to new drug R&D.
H	The investment by public sector research groups I pharmaceutical R&D.
λ	The conventional shadow price of the budget constraint defined by relaxing the budget constraint by one unit.
ΔC^P	The incremental cost to the health budget of the new drug at the given price.
ΔE	The net increase in the health of the population due to any cause or combination of causes
The following are all net changes in health to a specific group of patients as a consequence of a specific action or strategy (two actions)	
ΔE^{A}	(A) reallocation from least to most cost effective of existing programs.
ΔE^{D}	(D) displacing the program that
ΔE^{M}	(M) expanding or contracting the least cost effective program.
ΔE^{N}	(N) expanding or contracting the most cost effective program

Parameter	Description
ΔE^{P}	(P) from the adoption of a new drug
ΔE^{R}	(R) from the strategy of reimbursement (the net effect of the new drug and the services displaced to finance it.
ΔE^{T}	(T) the most cost effective alternative strategy to reimbursement.
$NEBh^{R}$	Net economic benefit of the decision to reimburse, expressed in health units.
$EVCI$	The economic value of clinical innovation
$\beta_c{}^{a}$	The health shadow price corresponding to the alternative strategy set which comprises all possible opportunities to reallocate.
$\beta_c{}^{v}$	As above but corresponding to all investment strategies.
μ	The parameter that defines the increased productivity of a program if there is an investment in improving its technical efficiency.
λ_e^B	The shadow price of the budget constrain (B) defined in expansion (e)
$\lambda_{e\|c}^B$	The shadow price of the budget constraint (B) defined in expansion (e), given previous contraction (c).
$CEAi$	Cost effective analysis applied to inform reimbursement decision, using a threshold of i to correspond to either a NB or an ICER metric
$ICERi$	The conventional ICER compared to a threshold of i
NBi	The conventional net benefit calculated using i
A	The best alternative strategy to reimbursement that is a reallocation (contraction of least cost effective to financing of most cost effective)
R	The strategy of Reimbursement, which comprises adoption and financing. (Not to be confused with $\mathcal{R}$, which is the amount invested into R&D)
T	The best alternative strategy to Reimbursement

Abstract

This thesis uses an applied game theoretic framework to address the following question: *What is the population health maximising decision threshold price for a new drug?* This threshold accommodates: strategic behaviour; inefficiencies in the health care system; budget constraints; suboptimality of displacement to finance the additional cost of new drugs; failure of markets to develop evidence of unpatented services; and the relationship between drug price and future innovation and health.

A framework (price effectiveness analysis, PEA) for the analysis of the reimbursement process as a strategic interaction is proposed and tested. PEA uses the results of cost effectiveness analyses as inputs in a model that derives the population health outcomes of reimbursement: the net health effect of i) adoption of the new drug; and ii) displacement to finance its additional costs.

The first result is that the health shadow price, β_c, is the population health maximising decision threshold, under the conditions of a fixed and allocatively inefficient budget:

$$\beta_c = \left(\frac{1}{n} - \frac{1}{m} + \frac{1}{d}\right)^{-1}$$

where n is the most cost effective of existing programs in expansion or adoption; m is the least cost effective in contraction, and d is the average ICER of services displaced to finance the additional costs of the new drug at the offer price. Allocative inefficiency is characterised by m-n and suboptimality of displacement by m-d.

The second result is that there are restrictive conditions under which there is an incentive for a rational institution to pay a price above β_c to take into account the relationship between price and future innovation. However, if these conditions are met, the firm will prefer to raise funds through the capital market rather than contract with an institution.

Currently, reimbursing institutions provide an incentive to develop evidence of the cost and effect of patented health technologies. Adopting β_c as the new drug decision threshold places a value on evidence of the least and most cost effective services, regardless of whether they are being proposed for reimbursement. Hence, the market's failure to provide evidence of unpatentable and unpatented health services is addressed and the health gains possible from a budget increased.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Brita Anna Kollontai Pekarsky 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.

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Brita Anna Kollontai Pekarsky

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Dedications

Professor Gavin Mooney

1943 - 2012

tietäjä

Dr. John A Vernon

1968 - 2012

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In 1980 I realised after one month at University of Adelaide that engineering was not where my heart lay, despite my passion for maths, computers and optimisation problems. **Bob Wallace** was a good friend and one of Australia's first academic health economists. He suggested I might like economics and he was right; economics was a perfect fit for me. For the next ten years Bob discussed economics with me on afternoons too numerous to count. When he retired, he gave me his copies of Penguin Readings in Health Economics and Cost Benefit Analysis (old school and very cool). I referred to these texts many times during this PhD.

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butter the edges of the bread first and the middle will look after itself

"No love lost"

Warsaw (Joy Division), Salford, 1977

(Trust)

"You want it all ... but you can't have it."

Faith No More, Sausalito, 1989

(Constraints)

"America's health care system is second only to Japan, Canada, Sweden, Great Britain, well ... all of Europe. But you can thank your lucky stars we don't live in Paraguay!"

Homer Simpson, Springfield, 1992

(The Counterfactual)

Benjamin Franklin once remarked, "In this world nothing can be said to be certain, except death and taxes." Spokespersons for the pharmaceutical industry might be inclined to argue that the benefit-generating capability of prescription drugs also belongs in this exclusive category. They could make a compelling case: ***recent studies suggest*** that pharmaceutical products increase longevity, improve quality of life, and often result in medical cost savings.

C. Giaccotto, R. Santerre and J.A. Vernon, 2005

(The political economy of new drugs)