Increasing complexity of cancer care:
How displaced treatments impact efficiency, cost-effectiveness and equity

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A submitted thesis for a Doctor of Philosophy in Health Economics

at the Faculty of Business

University of Technology Sydney

2018

Certificate of Original Authorship

I, Philip Haywood, declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Business School at the University of Technology Sydney. This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

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27th October 2018

This research is supported by an Australian Government Research Training Program Scholarship.

The Elements of Cancer Care cohort study was approved by the Human Research Ethics Committee (University of New South Wales, approval number 07014).

Acknowledgments

This thesis is an outcome of a collective effort. I wish to thank my supervisors, Professor Rosalie Viney, Professor Marion Hass and Dr Melvin Chin, for their time and generosity in reading, discussing and challenging my work in this thesis. I would also like to thank Professor Jane Hall for her mentorship and introduction to the world of health economics. I wish to acknowledge the examiners of the thesis, Professor Stuart Peacock and Professor Andrew Roberts, whose critiques and comments improved the work contained in this thesis.

Robyn Ward, Sallie-Anne Pearson and Ben Daniels were responsible for the Elements of Cancer Care (EoCC) data which formed the basis of several chapters in this thesis. Robyn Ward was responsible for the oncologist's review. Alison Pearce conducted earlier work using the EoCC data. Thank you for these contributions. This research was supported by PhD grants from University of Technology Sydney, CHERE and the Translational Cancer Research Network (TCRN). The TCRN also provided conference funding to attend iHEA to present this work. Wendy Monaghan, Publications Editor (www.wendymonaghan.com.au), copy edited an early draft, with editorial intervention restricted to Standards D and E of the Australian Standards for Editing Practice, as stipulated by the Guidelines for Editing Research Theses.

This research would not have been possible without the participants in the Elements of Cancer Care cohort who gave up their time and consented to the use of their information. I would like to thank them as well. Research such as this thesis would not exist without contributions such as theirs.

Colleagues at the Centre for Health Economics Research and Evaluation (CHERE) - both past and present - provided advice, encouragement and distraction when necessary. Thank you Kees van Gool, Liz Chinchen, Kathleen Manipis, Serena Yu, Thomas Longden, Brendan Mulhern, Jody Church, Bonny Parkinson, Richard De Abreu Lourenco, Stephen Goodall, Paula Cronin and Margie Campbell amongst others. Thank you to the CHERE PhD group as well. I would also like to thank Dr Eric Haywood for reviewing the introductory chapters.

Most of all, I would like to thank my partner, Rachel. As well as Mum, Dad, Jim and Lyn. Thank you to my family and Rachel's family for their time, help and most of all their understanding. I could and would not have been able to finish this without all of you. I dedicate this work to the memory of Ben White, who sadly passed away during its completion.

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Abstract

Background

Medical technology is increasing the number of available treatments for cancer. For advanced cancer an increasing number of treatments can result in an increasing treatment sequence. Treatments are given one after another in a cycle of treatment, failure and then another treatment. Newly added treatments may not replace existing treatments. The movement of existing treatments into later lines of therapy is displacement.

Displacement poses challenges for economic evaluation. This thesis addresses three questions.

1. Does the displacement of a treatment alter its cost-effectiveness?
2. If the cost-effectiveness becomes less favourable can any resulting societal welfare loss be corrected by changing the price?
3. Can the required price change be calculated in Australia?

Methods

A theoretical framework is developed for displacement in cancer treatment. The implications of decision-making criteria and information gaps are assessed. Real-world data is used to estimate the number of treatments and lines of therapy received by patients, and costs of care. A systematic review and meta-analysis of randomised controlled trials which reported treatment outcomes of multiple lines of therapy is undertaken. The cost-effectiveness of displacing treatments for breast cancer, colorectal cancer and non-small cell lung cancer are modelled.

Results

The displacement of a treatment may result in dynamic and allocative inefficiencies. Real-world data showed 13-18% of participants received four or more lines of therapy. The mean health services cost of cancer care was approximately $4 000 per month. Displacement resulted in decreased effectiveness, an increased toxicity per unit time and reduced treatment length.

In the modelling, there was an increase in the incremental cost-effectiveness ratio with displacement. After displacement, reducing the price of cancer treatments by 32% was required to restore cost-effectiveness.

Conclusions

There is the potential for displacement in Australia. Displacement results in an increasing incremental cost-effectiveness ratio of a treatment. This can be corrected with price changes in most circumstances.

The Australian real-world data did not record all the treatments that were received by patients. Therefore, it is not able to be used to calculate the price changes that are required with displacement.

The addition of new treatments in Australia should consider the impact of displacement on currently subsidised treatments. A failure to do this results in biased assessments of the benefits and costs of new treatments. It will likely underestimate the cost and overestimate the benefit. Therefore, the potential for displacement should be considered in cancer treatment funding to ensure equity and cost-effectiveness.

Abbreviations

Abbreviation	Full-text
5-FU	5-fluorouracil
5-HT3	5-hydroxytryptamine 3 (receptor antagonist)
AC	a protocol consisting of doxorubicin and cyclophosphamide
ACIM	Australian Cancer Incidence and Mortality (Books)
AIC	Akaike information criterion
AIHW	Australian Institute of Health and Welfare
AR-DRG	Australian Refined Diagnosis Related Groups
ASM	additive separate model
ATC	Anatomical Therapeutic Chemical Classification System
AUD	Australian dollar
Aus.	Australian
BSC	best supportive care
C/E	cost-effectiveness
Ca	Cancer
Cet	Cetuximab
Cet+I	cetuximab and irinotecan
CHEERS	consolidated health economics reporting
CHeReL	Centre for Health Record Linkage
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
CPAP	Chemotherapy Pharmaceutical Access Program
CRC	colorectal cancer
CTCAE	common terminology criteria for adverse events
D	Docetaxel
DC	disease control
DEALE	Declining Exponential Approximation of Life Expectancy
DRG	Diagnostic Related Groups
ED	emergency department
EGFR	epithelial growth factor receptor
EM-CaP	Economic Models of Cancer Protocols research project
EoCC	Elements of Cancer Care
EQ-5D	European Quality of life-5 Dimensions
EViQ	Cancer Treatments Online
FEC	a protocol consisting of 5-fluorouracil, epirubicin and cyclophosphamide
FOCUS (trial)	fluorouracil, oxaliplatin, CPT11: use and sequencing
FOLFIRI	a protocol consisting of 5-fluorouracil, leucovorin and irinotecan
FOLFOX	a protocol consisting of 5-fluorouracil, leucovorin and oxaliplatin
G-CSF	granulocyte-colony stimulating factor

Gem	gemcitabine
Gem and Carbo	a protocol consisting of gemcitabine and carboplatin
HCD	high cost drug
HR	hazard ratio
HTA	Health Technology Assessment
HUI3	Health Utilities Index Mark 3
ICER	incremental cost-effectiveness ratio
IHPA	Independent Hospital Pricing Authority
IV	intravenous
KRAS	Kristen rat sarcoma
LYS	life year saved
MBS	Medical Benefits Schedule
Met	metastatic
MRC	Medical Research Council
N/A	not applicable
NCCN	National Comprehensive Cancer Network
NHCDC	National Hospital Costs Data Collection
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NICE	National Institute of Health and Clinical Excellence
NMB	net monetary benefit
NSCLC	non-small cell lung cancer
NSW	New South Wales
Onc	oncologist
OR	odds ratio
OR	overall response
OS	overall survival
P	price
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PFS	progression free survival
Pharm	pharmaceutical
PPP	purchasing power parity
PSA	probabilistic sensitivity analysis
Q	quantity
QALY	quality adjusted life years
QHES	Quality of Health Economics Studies
RCC	renal cell carcinoma
RCT	randomised controlled trial
RECIST	Response evaluation criteria in solid tumours
RPBS	Repatriation Schedule of Pharmaceutical Benefits
RR	relative risk

s100	section 100
SD	standard deviation
SPP	survival post-progression
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TGA	Therapeutic Goods Administration
TNM	Tumour Node Metastasis staging system
UK	United Kingdom
US(A)	United States of America
USD	United States of America dollars
XELIRI	a protocol consisting of irinotecan and capecitabine
XELOX	a protocol consisting of oxaliplatin and capecitabine

Symbols

Abbreviation	Full-text
$	dollar
%	per cent
g	gram
K	thousand
kg	kilogram
M	million
mg	milligram
mm	millimetre