UTS UNIVERSITY OF TECHNOLOGY SYDNEY

Economic impact of medication non-adherence

Thesis

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Doctor of Philosophy

Graduate School of Health, Discipline of Pharmacy:
University of Technology Sydney

CERTIFICATE OF ORIGINAL AUTHORSHIP

I Rachelle Louise Cutler declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Graduate School of Health 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.

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

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Abstract

Background: Medication non-adherence is a global issue of major public health concern highlighted by the causal link between non-adherence, increased disease prevalence and health care resource use. Cost assessment of the economic burden lacks uniformity and consistency in determination. The use of a standardised methodology to determine the cost associated with medication non-adherence is required to facilitate international comparisons and demonstrate a reliable estimate of the magnitude of the problem on a global scale.

Objectives: To explore, analyse and estimate the economic impact of medication non-adherence. The research aimed to conceptualise and define a cost estimation framework to streamline the cost outcome indicators that are employed to evaluate the monetary burden linked to non-adherence. Additionally, a monetary estimate of the medication non-adherence burden in Australia was quantified whilst simultaneously exploring the potential role community pharmacists play in reducing the associated burden.

Methodology: A series of discrete studies were undertaken: (1) a systematic review of studies assessing the economic impact of medication non-adherence across disease groups; (2) development of a medication adherence cost estimation (MACE) framework through secondary analysis of the systematic review data; and (3) analysis of a large database of patient dispensing records appraising the cost of medication non-adherence in Australia and the cost saving effect community pharmacist led intervention had on adherence.

Results: The systematic review identified wide scoping cost variations reported across 79 studies, with lower levels of adherence associated with higher health care costs. Annual adjusted disease specific economic cost of non-adherence per person ranged from USD2015 $949- $44190 (chapter 3). Collation of outcomes resulted in the development of the MACE framework through identification of two core cost outcome indicators (direct and indirect costs), seven subcategories (hospital, primary

care, medical test, pharmacy, direct non-medical, societal and productivity costs) and 35 cost outcome indicator examples. The most utilised cost categories were hospital (68%, n=54), primary care (18%, n=15) and pharmacy costs (72%, n=57) (chapter 4). The national cost of medication non-adherence in Australia across hypertension, dyslipidaemia and depression was AUD2018 $10.4 billion. Community pharmacist led intervention was estimated to save the Australian health care system AUD2018 $1.9 billion annually. Application of the MACE framework post pharmacist intervention highlighted the greatest cost contributors to be associated with direct costs, particularly, outpatient expenses $2.1 billion, inpatient admissions $1.9 billion, prescription medications $1.8 billion and medical related expenses $1.6 billion (chapter 5).

Conclusion: Medication non-adherence is a costly burden placing financial drain on health care systems that has failed to be adequately prioritised by governments and health care organisations within national policy. The incorporated framework has been proposed to homogenise international measures and applied to the Australian landscape to demonstrate the scope of the problem and highlight the potential role of community pharmacists moving forward to counteract the rising economic encumbrance. The MACE framework facilitates the strengthening of adherence research and provides a strong foundation for evidence based costing studies to be incorporated into economic evaluations to aid decision making. Decision makers should seek to utilise pharmacists as an integrated member of the health care team to help curb the rising burden of medication non-adherence and generate cost savings to the health care system.

Dissemination of Research

Peer reviewed publications

1. **Cutler, R.L.**, Fernandez-Llimos, F., Frommer, M., Benrimoj, S.I. & Garcia-Cardenas, V. 2018, 'Economic impact of medication non-adherence by disease groups: a systematic review', *BMJ Open*, vol. 8, no. 1
2. **Cutler, R.L.**, Van der Linden, N., Benrimoj, S.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2019, 'An evidence based model to consolidate Medication Adherence Cost Estimation: the MACE framework', *Journal of Comparative Effectiveness Research,* vol, 8, no. 8, pp. 555-567.
3. **Cutler, R.L.**, Torres-Robles, A., Wiecek, E., Drake, B., Van der Linden, N., Benrimoj, S.I. & Garcia-Cardenas, V. 2019, 'Pharmacist led medication non-adherence intervention: reducing the economic burden placed on the Australian health care system', *Patient Preference and Adherence,* vol. 13, pp. 853
4. Torres-Robles, A., Wiecek, E., **Cutler, R.L.,** Drake, B., Benrimoj, S.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2019, 'Using dispensing data to evaluate adherence implementation rates from a community pharmacy program', *Frontiers in Pharmacology,* vol. 10, pp. 130

Conference proceedings

1. **Cutler, R.L.,** Garcia-Cardenas, V. and Benrimoj, S.I. 2015, 'A poor state of affairs- Overview of the current worldwide non-adherence crisis', International Pharmaceutical Federation 75th International congress, Dusseldorf, Germany, 2015
2. Garcia-Cardenas, V., Zeater, S., **Cutler, R.L.** and Benrimoj, S.I. 2015, 'Implementation of an adherence service in a community pharmacy setting- The Aim High project', International Pharmaceutical Federation 75th International congress, Dusseldorf, Germany, 2015

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Preface

This thesis is presented in fulfilment of the doctoral degree (Doctor of Philosophy) requirements of the University of Technology Sydney, Australia.

The thesis is structured as a PhD by compilation. Chapter 1 contains a research overview and general disposition of the thesis. An outline of the overall rationale, objectives and organisation of the thesis is included. Chapter 2 provides the background and reasoning for the topic. Chapters 3-5 comprise the sequential results including a systematic review outlining the economic impact of medication non-adherence across disease groups, development of the medication adherence cost estimation framework and a national estimate of the cost of medication non-adherence in Australia. The chapters have been structured as research articles containing all corresponding references, figures, tables and appendices related to the research activity. This is followed by Chapter 6, which discusses the results, summarises the contribution of work and provides recommendations for future research.

Rachelle L. Cutler is the primary author of each publication. Additionally, co-authors contributed to the conception or design of the work, data collection, data analysis and interpretation, or revision of the manuscripts.

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Abbreviations

A	adherent
AbC	absenteeism costs
AC	ancillary costs
ACC	acute care costs
AGRTP	Australian Government Research Training Program
ArC	arrest costs
BHIC	behavioural health inpatient costs
CAD	Canadian dollar
CHF	chronic heart failure
Com	commercial patients
DKK	Danish krone
EDC	emergency department visit costs
ESC	external services costs
EUR	Euro
FC	fracture costs
GBP	Great British Pound
HC	hospitalisation costs
IC	inpatient costs
InC	incarceration costs
InstC	institutional costs
IntC	interdisciplinary costs

IQR	interquartile range
KRW	South Korean won
LA	low adherence
LC	laboratory costs
MA	moderate adherence
MACE	medication adherence cost estimation
MBS	Medicare Benefits Schedule
MC	medical costs
Med	Medicare supplemental patients
MPR	medication possession ratio
MSC	medical services costs
MTC	medical test costs
NA	non-adherent
NC	non-compliance
NE	no exposure
NEHI	the New England Healthcare Institute
NP	non-persistent
NPC	non-pharmacy costs
OC	outpatient costs
OECD	Organisation for Economic Cooperation and Development
OtC	other costs
OtPC	other pharmacy costs
P	persistent

PAC	psychiatric assessment costs
PBS	Pharmaceutical Benefits Scheme
PC	pharmacy costs
PCC	primary care costs
PDC	proportion of days covered
POC	physician office visit costs
PPP	purchasing power parities
PrC	presenteeism costs
PRISMA	preferred reporting items for systematic reviews and meta-analyses
PTOC	paid time off costs
RC	radiology costs
SC	services costs
STDC	short term disability costs
T	turbulent
TC	total costs
TCMC	targeted case management costs
THC	total healthcare costs
TPC	total productivity costs
US	United States
USD	United States dollar
UTS	University of Technology Sydney
WCC	workers compensation costs
WHO	World Health Organisation