

**Economic Evaluation of
Pharmacist-led Medication Review
in the Primary Health Care
Centres in Chile**

Thesis

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2020

Doctor of Philosophy
Graduate School of Health, Discipline of Pharmacy:
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CERTIFICATE OF ORIGINAL AUTHORSHIP

I Antonio Osvaldo Ahumada Canale 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.

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Abstract

Background: Cardiovascular diseases (CVD) pose a burden on healthcare systems. There is evidence that pharmacist-led medication review with follow-up (MRF) improves therapeutic goal achievement in CVD risk factors, such as hypertension, type 2 diabetes mellitus and dyslipidaemia.

Objectives: To evaluate the economic impact of MRF added to Chilean primary care in CVD risk factors, by assessing the cost-effectiveness in older adults.

Methodology: A systematic review was conducted to evaluate the economic evaluations of pharmacist-led MRF in outpatients with CVD risk factors. Recommendations were generated to design a cluster randomised controlled trial (cRCT).

A cRCT was conducted in public primary care centres (clusters) in Chile to study the effect of MRF added to usual care compared to usual care alone. Older adults with five or more prescriptions, moderate or high CVD risk and enrolled in a primary care CVD prevention program were included. The intervention had three components: Pharmacists' training, MRF, and a practice change facilitator. Patients were followed-up for a year. For the economic analysis, health-related quality of life (HRQoL) was measured and was used to estimate quality-adjusted life-years (QALYs). Costs were evaluated from the public third-party payer perspective and were measured as 2019 United States dollars (USD). A cost-effectiveness threshold of 16,207 USD was used.

A trial-based cost-utility analysis was performed. Costs and QALYs were estimated through a multilevel model that accounted for clustering and covariates, while missing data was addressed using multiple imputation. Uncertainty was evaluated through a non-parametric bootstrapping. As a second analysis, a state-transition microsimulation model was developed to extrapolate outcomes

to a lifetime time horizon. Patient-level data was used to derive the model's probabilities. Deterministic and probabilistic sensitivity analyses were performed.

Results: Eleven studies were included in the systematic review. Eight found the intervention to be cost effective, while two found it to be dominant. Both, the trial-based and model analyses deemed the intervention as cost-effective. Incremental cost-effectiveness ratios of \$434/QALY and \$751/QALY respectively, were found. The trial-based analysis found increased dominant iterations when patients with more than nine medications were evaluated. In the model, a difference between groups of 5.9% in CVD mortality was observed. Sensitivity analyses showed either cost-effectiveness or dominance.

Conclusion: International evidence shows that MRF was value for money in outpatient settings. An adapted MRF method was deemed as a cost-effective addition to primary care in Chile with low uncertainty. Formal implementation should be considered by policy makers.

Dissemination of Research

Peer-reviewed publications

1. **Ahumada-Canale A**, Quirland C, Martinez-Mardones FJ, Plaza-Plaza JC, Benrimoj S, Garcia-Cardenas V. Economic evaluations of pharmacist-led medication review in outpatients with hypertension, type 2 diabetes mellitus, and dyslipidaemia: a systematic review. *Eur J Heal Econ*; 2019; 20(7): 1103–16.
2. **Ahumada-Canale A**, Vargas C., Martinez-Mardones FJ, Plaza-Plaza JC, Benrimoj S, Garcia-Cardenas V. Cost-utility Analysis of a Medication Review for Cardiovascular Outcomes: A Microsimulation Model. (SUBMITTED TO VALUE IN HEALTH (VIH-2020-0114))
3. **Ahumada-Canale A**, Vargas C., Balmaceda C. Martinez-Mardones FJ, Plaza-Plaza JC, Benrimoj S, Garcia-Cardenas V. Medication Review with follow-up for Cardiovascular Outcomes: A Trial based Cost-utility Analysis. (SUBMITTED TO CIRCULATION (CIRCULATIONAHA/2020/046444))
4. Martínez-Mardones F, Fernandez-Llimos F, Benrimoj SI, **Ahumada-Canale A**, Plaza-Plaza JC, S Tonin F, et al. Systematic review and meta-analysis of medication reviews conducted by pharmacists on cardiovascular diseases risk factors in ambulatory care. *J Am Heart Assoc*. 2019; 8(22):e013627.
5. Martínez-Mardones F, Benrimoj SI, **Ahumada-Canale A**, Plaza-Plaza JC, Garcia-Cardenas V. Clinical impact of medication reviews with follow-up in cardiovascular older patients in primary care: the Polaris trial, a cluster-randomized controlled trial. (UNDER REVIEW IN CIRC CARDIOVASC QUAL OUTCOME (CIRCCQO/2020/006575)).

6. Martínez-Mardones F, Benrimoj SI, **Ahumada-Canale A**, Plaza-Plaza JC, Venegas-Araneda P, Garcia-Cardenas V. Medication reviews with follow up on older patients with chronic kidney disease and cardiovascular risk factors: a cluster randomized controlled trial. (UNDER REVIEW IN EUR HEART J (EURHEARTJ-D-20-00680))

Authorship on national clinical guidelines

1. **Ahumada-Canale, A.**, Martínez-Mardones, F.J., Plaza-Plaza, Valdés, C. Manual for conducting medication reviews with follow-up in primary care centres, 2019. Web source: <https://www.sccoquimbo.cl%2Fgob-cl%2Fdocumentos%2Ffiles%2Finred%2Ffarmacia%2F28-05-2018%2FAtencion%2520Farmaceutica%2520y%2520SFT%2520en%2520APS%25202018.pdf&usg=AOvVaw1TAA8qfegTMfI0vakLlznd>
2. **Ahumada-Canale, A.**, Martínez-Mardones, F.J., Plaza-Plaza. Technical guidelines for the implementation of medication reviews in primary care. Chilean Ministry of Health, 2018. Web source: http://quimica.uc.cl/images/noticias/2019/2019_07_12_MANUAL-SEGUIMIENTO-FARMACO-TERAPEUTICO1_compressed.pdf

Conferences proceedings

1. 11th Health Services and Policy Research Conference by the Health Services Research Association of Australia & New Zealand. December 4-6 2019, Auckland, New Zealand. Oral presentation. Cost-utility analysis of pharmacist-led medication review in primary care patients with hypertension, type 2 diabetes mellitus and dyslipidaemia . **Ahumada-Canale A**, Martínez-Mardones FJ, Plaza-Plaza JC, Benrimoj S, Garcia-Cardenas V.
2. 2^o *Simpodader Internacional*. June 29 – 30th, 2018. Granada, Spain. Poster.

Economic Evaluations of Pharmacist-led Medication Review in Cardiovascular Diseases
Risk Factors: Systematic Review.

Ahumada-Canale A, Quirland C, Martinez-Mardones FJ, Plaza-Plaza JC, Benrimoj S,
Garcia-Cardenas V.

3. 1st International Conference Pharmacy practice research: postgraduate students,
postdoctoral fellows and supervisor's symposium conference organised by the International
Pharmaceutical Federation special interest group on pharmacy practice research. June 25 –
27th, 2018, Lisbon, Portugal. Three-minute thesis presentation.

Pharmacist-led Medication Review with follow-up on elderly patients in cardiovascular
disease risk factors using polypharmacy: A pilot study.

Antonio Ahumada, José Plaza-Plaza, Shalom Benrimoj, Victoria García-Cárdenas.

4. XXXIII Public Health Conference of the University of Chile. January 10-12th, 2018,
Santiago, Chile. Poster.

A pilot study of a pharmacist-led medication review with follow-up program in older adults
with polypharmacy of a cardiovascular prevention program in Chilean primary care.

Ahumada-Canale A, Martinez-Mardones FJ, Vielma C, Ebensperger R, Plaza-Plaza JC,
Benrimoj S, Garcia-Cardenas V.

Invited presentations

1. A pilot study of a pharmacist-led medication review with follow-up program in older adults
with polypharmacy of a cardiovascular prevention program in Chilean primary care. 1st San
Bernardo Municipality Health Scientific Meeting. August 31st, 2018. Santiago Chile.
2. Pharmacist-led Medication Review with Follow-up: The Polaris Trial. Public Health
Institute Annual Meeting. November 30th, 2017. Santiago, Chile.

3. Pharmacist-led Medication Review with Follow-up: The Polaris Trial 1st Valparaiso and San Antonio Health Service Administration Pharmacist Meeting. October 22nd, 2018. El Tabo, Chile

Acknowledgements

This research was possible with the support of the Graduate School of Health from the University of Technology Sydney (UTS), through the International Research Scholarship (UTS IRS), UTS Presidents Scholarships (UTSP) and higher degree by research yearly allowance. In addition, the UTS Faculty of Health provided funding for training purposes. Finally, The Faculty of *Química y de Farmacia* from the *Pontificia Universidad Católica de Chile* provided their facilities for pharmacists training and funding for research materials.

This research was possible thanks to the guidance, enthusiastic encouragement and useful feedback of my supervisors, Prof Shalom (Charlie) Benrimoj, Dr Victoria García-Cárdenas, Dr Cristian Plaza-Plaza and Prof Kylie Williams. I would like to express my deep gratitude to Constanza Vargas for mentoring me in the field of health technology assessment and to Carlos Balmaceda and Camila Quirland, which contributed with their expertise as well. In addition, I would like to acknowledge my research partner Francisco, for his devotion to the pharmacy profession and public health that allowed us to reach the objectives.

The Polaris trial was supported by the Chilean Ministry of Health and the Eastern, South-Eastern, South and Western Metropolitan Health Services Administrations. Municipalities of Puente Alto, La Granja, Pudahuel, San Bernardo, Vitacura, Ñuñoa and Quinta Normal participated in our trial. This project was possible thanks to health authorities and pharmacists of those institutions. Their motivation to strive with the ultimate end of helping patients who need it most was the engine that powered this research.

Finally, to my wife Fabiola, thank you for your unconditional love, support and patience along this journey. To my parents that allowed me to be where I am today, teaching me the values and principles to find my way through life. To my colleagues, especially Carmen and Elyssa, for always

being there and sharing my enthusiasm in research. To my life-long friends, Silvana, Paz, Felipe V, Felipe F, Héctor, Cristian and Francisco. Despite the distance, you have been as present and supportive as always in my life.

Preface

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

This document was structured as a thesis by compilation. Chapter 1 presents a synopsis describing the general approach of this thesis and research. Chapter 2 provides the background for cardiovascular diseases' clinical and economic impact, particularly in Chile. Medication review with follow-up is proposed as a clinically effective strategy to address cardiovascular risk factors. Chapter 3 introduces the basic concepts of economic evaluations in healthcare and contains a published systematic review of pharmacist-led medication review conducted in outpatients with cardiovascular risk factors such as, hypertension, type 2 diabetes mellitus and dyslipidaemia. This study frames the current state of cost-effectiveness analyses in the area, and a quality assessment to provided recommendations for future research. Chapter 4 describes the methods of the Polaris trial, a cluster randomised controlled study that included older adults with cardiovascular risk factors in Chilean primary care. This trial was a collaboration between UTS, the Pontifical Catholic University of Chile, and the Chilean government. A description of the Polaris method of MRF is presented. Chapter 5 and 6 contain submitted papers of a trial-based cost-effectiveness analysis and a decision-analytic model, using the Polaris trial results. Chapter 7 discuss the research outputs, explores limitations of each study, addresses transferability to other settings and proposes future directions. Chapter 8 presents conclusions arising from this research.

Antonio Osvaldo Ahumada Canale is the primary author of the publications. Co-authors contributed to the conception or design of the work, data collection, data analysis and interpretation, and/or revision of the manuscripts.

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Abbreviations

ADR: adverse drug reactions

CAD: Canadian dollar

CI: confidence interval

CKD: chronic kidney disease

cRCT: cluster randomised control trial

CVD: cardiovascular diseases

DBP: diastolic blood pressure

DALY: disability-adjusted life-years

DLP: dyslipidaemias

EQ5D: EuroQoL-5D

EU: European Union

FONASA: *Fondo Nacional de Salud*

GP: general practitioner

HbA1c: glycated haemoglobin

HDL: high density lipoprotein

HF: heart failure

HTN: hypertension

HRQoL: health-related quality of life

ICC: intra-class correlation

ICER: incremental cost-effectiveness ratio

IHD: ischaemic heart disease

ISAPRE: *Institución de Salud Previsional*

LDL: low-density lipoprotein

LMICs: Low and middle-income countries

MRF: medication review with follow-up

MTM: medication therapy management

NCDs: non-communicable diseases

OR: odds ratio

PAHO: Pan American Health Association

PCNE: Pharmaceutical Care Network Europe

PCF: practice change facilitator

PI: prediction interval

PUC: *Pontificia Universidad Católica de Chile*

PW: Pharmacotherapy workup

QALYs: quality-adjusted life-years

RCT: randomised controlled trial

RN: registered nurse

SBP: systolic blood pressure

T2DM: type 2 diabetes mellitus

TC: total cholesterol

TG: triglycerides

TIDieR: template for intervention description and replication

UTS: University of Technology Sydney

USD: United States dollars