

**IMPACT OF COMMUNITY PHARMACIST
INTERVENTIONS TO MANAGE MEDICATION
ADHERENCE**

THESIS

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CERTIFICATE OF ORIGINAL AUTHORSHIP

I, Andrea Johanna Torres Robles declare that this thesis is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Discipline of Pharmacy, 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.

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Abstract

Background: As medication non-adherence continues to be a global public health problem, the development, evaluation and implementation of interventions to address this prevalent problem represent a key priority. Community pharmacists' role is evolving from the dispensing of medications to the provision of professional services aiming at improving patient outcomes. Pharmacists have, therefore, the potential to deliver interventions to manage medication adherence. Nonetheless, there is still a lack of evidence on the effect of community pharmacist-led interventions on medication adherence and clinical outcomes.

Objectives: To explore and evaluate the impact of medication adherence interventions undertaken by community pharmacists across different chronic diseases. This research aims to provide evidence on the efficacy and effectiveness of community pharmacist-led interventions in Australia and Spain on medication adherence to interventions and disease-specific outcomes.

Methods: Multiple methods were applied in this research. Chapter 2 presents a systematic review and network meta-analysis, following the PRISMA guidelines, comparing long term interventions on the impact on medication adherence across different chronic diseases. Chapter 3 describes a retrospective observational study evaluating the impact of a real-life practice intervention in Australia provided by community pharmacist to patients with chronic medications (rosuvastatin, desvenlafaxine, irbesartan). Chapter 4 present a cRCT to evaluate the impact of a medication adherence management service in a community pharmacy setting in Spain. Chapter 5 describes a sub-analysis of the cRCT including patients with asthma and COPD being prescribed inhaled medications. A multilevel regression model was used to measure the impact of the medication adherence management service on medication adherence and disease-specific clinical outcomes (Chapter 4) and inhaler technique (Chapter 5). Chapter 6 presents an effectiveness-implementation hybrid design evaluating the clinical impact of the medication adherence management service when translated to routine practice during an implementation study. For this

analysis, patients were classified in three groups: A) those allocated to the intervention group during the cRCT and continue during implementation, B) those allocated to the control group during the CRCT and continue during implementation, and C) new patients in the implementation study.

Results: Chapter 3 presents the impact of a real-life community pharmacist-led intervention in Australia. De-identified data of 2,530,562 patients and 3,328 Australian community pharmacies from 2014 to 2017 were contained in the database. A total of 1,805 pharmacies and 20,335 patients who met the inclusion criteria were included in the analysis, with an average age of 67 (SD: 11.76). Three months after the intervention was provided, there was an increase from 50.2% (SD: 30.1) to 66.9% (SD: 29.9) for rosuvastatin, from 50.8% (SD: 30.3) to 68% (SD: 29.3) for irbesartan and from 47.3% (SD: 28.4) to 66.3% (SD: 27.3) for desvenlafaxine, in adherence rates. Rates decreased over 12 months to 62.1% (SD: 32.0) (rosuvastatin), 62.4% (SD: 32.5) (irbesartan) and 58.1% (SD: 31.1) (desvenlafaxine).

The results of the cRCT are highlighted in Chapter 4. Patients (n=1,186) were recruited from 98 pharmacies and 87.5% (n=1,038) completed the six-month study. Compared to control patients, patients receiving the intervention had an Odds Ratio (OR) of 5.12 of being adherent at the end of the study. ORs for hypertension control, asthma control and COPD low clinical impact were 1.22 (95% CI: 0.78-1.91), 1.88 (95% CI: 1.05-3.36) and 2.01 (95% CI: 1.07-3.75), respectively, favouring the intervention group. For patients using inhaled medications (i.e. sub-analysis of patients suffering from asthma or COPD in the cRCT), the odds of improvement of patients with correct inhaler technique were 4.57 favouring the intervention group. The impact of the medication adherence management service resulted on an improvement on clinical outcomes (e.g. medication adherence and disease-specific outcomes) for all patients during the implementation study (i.e. routine-practice), with greater improvements observed on those patients who have not been exposed to the intervention before (groups B and C).

Conclusion: Community pharmacist-led interventions lead to an improvement in medication adherence and disease-specific clinical outcomes. A real-life intervention

in Australia resulted in the improvement of adherence after providing the intervention with an eventual decline on adherence rates post-intervention, highlighting the importance of continuous follow-up. To improve the effectiveness of this intervention, factors such as follow-up, fidelity measures and addition of other components to the intervention should be considered. These factors were considered when developing a medication adherence management service in Spain. This intervention resulted in the improvement of medication adherence and disease-specific outcomes under the cRCT (controlled environment) and the implementation study (real practice). The intervention also improved inhaler technique on patients suffering from asthma and COPD and contained multiple components (e.g. educational, attitudinal, technical), which have been found effective at improving medication adherence. The essential role that community pharmacists have in the management of medication adherence should be considered in the development of future interventions.

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Dissemination of Research

Peer-reviewed Publications

1. **Torres-Robles A**, Wiecek E, Tonin FS, Benrimoj SI, Fernandez-Llimos F, Garcia-Cardenas V. 'Comparison of Interventions to Improve Long-Term Medication Adherence Across Different Clinical Conditions: A Systematic Review With Network Meta-Analysis'. *Frontiers in pharmacology*. 2018;9:1454.
2. **Torres-Robles A**, Wiecek E, Cutler R, Drake B, Benrimoj SI, Fernandez-Llimos F, et al. 'Using Dispensing Data to Evaluate Adherence Implementation Rates in Community Pharmacy'. *Frontiers in pharmacology*. 2019;10:130.
3. **Torres-Robles A**, Benrimoj SI, Gastelurrutia MA, Martinez-Martinez F, Peiro T, Varas-Doval R, Perez-Escamilla B, Rogers K, Valverde-Merino MI, Garcia-Cardenas V. 'Effectiveness of a medication adherence management service in a community pharmacy setting. A cluster randomised controlled trial'. *BMJ Quality and Safety*. 2021 (**Accepted –Sent to production**)
4. **Torres-Robles A**, Benrimoj SI, Bosnic-Anticevich S, Gastelurrutia MA, Martinez-Martinez F, Peiro T, Varas-Doval R, Perez-Escamilla B, Rogers K, Valverde-Merino MI, Garcia-Cardenas V. 'Evaluation of a community pharmacist-led medication adherence management service on inhaler technique in patients with asthma and COPD: sub-analysis of a cluster randomised controlled trial'. 2021 (**To be submitted to "Journal of asthma"**)
5. **Torres-Robles A**, Benrimoj SI, Gastelurrutia MA, Martinez-Martinez F, Peiro T, Varas-Doval R, Perez-Escamilla B, Valverde-Merino MI, Zarzuelo MJ, Garcia-Cardenas V. 'Evaluation of the impact of a medication adherence management service on a community pharmacy setting during an effectiveness-implementation hybrid design'. 2021 (**To be submitted to "Journal of Health Services Research"**)

Conference proceedings

1. **Torres-Robles A**, Perez-Escamilla B, Valverde Merino M, Varas R, Peiro T, Martinez Martinez F, Benrimoj SI, Garcia-Cardenas V. A brief complex intervention to improve patients' beliefs and skills on inhaler use and its impact on clinical outcomes in COPD and asthma. European Society for Patient Adherence, Compliance and Persistence Conference, Portugal, 2019. (Oral presentation).
2. **Torres-Robles A**, Wiecek E, Drake B, Benrimoj SI, Fernandez-Llimos F, Garcia-Cardenas V. Big data techniques for measuring changes on medication implementation after an intervention provided by community pharmacists. European Society for Patient Adherence, Compliance and Persistence Conference, Ireland, 2018. (Oral presentation).
3. Tonin FS, Wiecek E, **Torres-Robles A**, Benrimoj SI, Fernandez-Llimos F, Garcia-Cardenas V. Impact of single and multiple component interventions to improve medication adherence: a network meta-analysis. European Society for Patient Adherence, Compliance and Persistence Conference, Ireland, 2018. (Oral presentation - Presented as second author).
4. **Torres-Robles A**, Benrimoj SI, Fernández-Llimós F, Tonin FS, Wiecek E, García Cárdenas V. [Comparisson of adherence interventions across disease states: A network meta-analysis]. II International Simpodader, Spain, 2018. (Poster presentation).
5. **Torres-Robles A**, Drake B, Benrimoj SI, Garcia-Cardenas V. Use of de-identified medication dispensing records to measure the effect of pharmacist intervention on medication adherence in a community pharmacy setting – 3 Minute Thesis Presentation. 1st International Conference Pharmacy Practice Research FIP, Portugal, 2018.

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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. Seven chapters are presented throughout the thesis, including copies of peer-reviewed publications as chapters of the manuscript. Spelling varies between US English and British English to meet journal requirements for manuscript submission. Andrea J Torres Robles is the primary author of each publication. Co-authors contributed to the conception, design of the work, data collection, data analysis, interpretation or critical revision of the manuscripts.

Chapter 1 includes the research overview, an overall rationale and the organisation and objectives of the thesis. Chapter 2 covers the contextual background of medication adherence interventions, including a systematic review and meta-analysis, highlighting the gaps and opportunities in practice.

Chapter 3 – 6 present evidence of the impact of community pharmacist-led interventions on medication adherence, addressing the specific objectives. Chapter 3 presents a retrospective analysis of the impact of a real-life intervention provided by community pharmacists in Australia. Chapter 4 describes a cRCT to evaluate the impact of a community pharmacist-led medication adherence management service in Spain, on medication adherence and disease-specific outcomes. Chapter 5 presents the impact of the intervention described in the cRCT on inhaler technique performance for patients with asthma and COPD. Chapter 6 presents the clinical effectiveness of the medication adherence management service during its implementation in routine-practice settings. Chapter 7 discusses the overall research, reflects on the strengths and limitations of the research work and provides recommendations for future research.

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Table of Contents

Abstract	iii
Dissemination of Research	vii
Acknowledgements	ix
Preface	xi
List of Figures	xv
List of Tables	xv
Abbreviations	xvi
Chapter 1	1
Synopsis	1
Research Overview	3
Rationale	5
Objectives	10
Chapter 2	12
Medication Adherence Interventions	12
The Concept of Medication Adherence	14
How to measure medication adherence	15
Interventions for improving medication adherence	17
Systematic Review and Network Meta-Analysis on adherence interventions	18
Medication adherence interventions in community pharmacies	30
Chapter 3	33
Using Dispensing Data to Evaluate Adherence Implementation Rates in Community Pharmacy	33
Chapter 4	45
Effectiveness of a medication adherence management service in a community pharmacy setting. A cluster randomised controlled trial	45
Chapter 5	72
Evaluation of the impact of a community pharmacist-led medication adherence management service on inhaler technique in patients with asthma and COPD	72
Chapter 6	96
Evaluation of a medication adherence management service in a community pharmacy setting: an effectiveness-implementation hybrid trial	96
Chapter 7	121
Discussion	121

Methodological reflections and limitations	132
Implications and recommendations for future research.....	134
Conclusions.....	136
References.....	139
Appendices.....	146
Authors' contributions.....	147
List of appendices	150

List of Figures

Figure 1. Thesis Structure	4
Figure 2. Medication Adherence Measures	17
Figure 1. Adherence management service intervention Overview	52
Figure 2. Study flowchart	57
Figure 3. Percentage of patients estimated from multilevel model of categorical outcomes. Intervention vs. Control group. Error bars represent 95% CIs.	59
Figure 1. Study Flowchart	92
Figure 2. Proportion of patients with Total correct inhaler technique estimated from multilevel model of categorical outcomes. Intervention vs. Control group. Error bars represent 95% CIs. (Visit 1 is equivalent to Baseline)	94
Figure 3. Proportion of patients with Critical correct inhaler technique estimated from multilevel model of categorical outcomes. Intervention vs. Control group. Error bars represent 95% CIs. (Visit 1 is equivalent to Baseline)	94
Figure 1. Flow of patients and pharmacies across Phases 1 and 2	117
Figure 2. Categorical outcomes for all groups during the phase 2.	119
Figure 3. Continuous outcomes for all groups during the phase 2.	119

List of Tables

Table 1. Baseline characteristics of study patients	57
Table 1. Patients' baseline characteristics.....	91
Table 2. Comparison of treatment vs control (reference) groups for main and secondary outcomes.....	93
Table 1. Service Outcomes	117
Table 2. Patients' baseline Characteristics	118

Abbreviations

ACQ	Asthma Control Questionnaire
ATC	Anatomical Therapeutical Chemical
BPL	Blood pressure Levels
CCQ	Clinical COPD Questionnaire
CFIR	Consolidate Framework for Implementation Research
CGOF	General Pharmaceutical Concil of Spain
CI	Confidence Intervals
CMG	Continuous measure of Medication Gaps
COF	Pharmacy Official Body (In Spain)
COPD	Chronic Obstructive Pulmonary Disease
cRCT	Cluster randomised controlled trial
DBP	Diastolic Blood Pressure
FISpH	Framework for the Implementation of Services in Pharmacy
MA	Medication Adherence
MPR	Medication Possession Ratio
NMA	Network Meta-Analysis
PCF	Practice Change Facilitators
PDC	Proportion of Days Covered

SBP	Systolic Blood Pressure
SD	Standard Deviation
WHO	World Health Organization

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