Effective Interventions and Patient Perceptions on the Management of Medication Adherence: a focus on mHealth

Thesis

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CERTIFICATE OF ORIGINAL AUTHORSHIP

I Elyssa Katlin Wiecek 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.

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Abstract

Background

Non-adherence to medications remains a global crisis with high prevalence causing worsening health outcomes, increased morbidity, and even death. Multiple dimensions affect the medication-taking process ranging from patient-related determinants to health system causes. Many interventions to improve adherence have seen disappointingly modest improvements with the most effective strategies including multiple components. These interventions are normally delivered as a package without the full understanding of what are the most effective components. The Digital Revolution has put mHealth (mobile health) at the forefront of new, emerging tools for improved adherence. An approximate 200 new mHealth apps are added to the market each day with 46% of patients adapting mobile technology to improve their health in the previous twelve months. While the technical tools within apps such as dosage reminders have been proven effective, other components such as rewards and gamification have yet to be evaluated. The variety of components being offered also warrants an exploration of the opinions of their users. Through understanding effectiveness by adherence outcomes and users' experiences within these mHealth offerings, a full understanding of their success and acceptability is possible.

Objectives

To explore, analyse and estimate the effect of interventions to improve medication adherence. This research aimed to gain a better understanding of the combination of components within effective interventions as well as evaluated an emerging mHealth tool, Perx Health. Simultaneously, beliefs, perceptions and experiences of users of the innovative mHealth intervention were explored to understand the acceptability and adoption of the technology.

Methodology

A series of discrete studies were undertaken: (1) a network meta-analysis of studies assessing the effectiveness of interventions and their components aimed at improving medication adherence; (2) evaluation of the impact of an innovative mHealth intervention, Perx, utilising multiple components on sustaining optimal adherence levels; and (3) analysis of users' beliefs, perceptions and experiences within the mHealth app for an understanding of the app's desirability and adoption as a tool to improve adherence.

Results

The network meta-analysis identified 249 studies evaluating interventions to improve adherence over multiple periods of time. Multicomponent interventions were found to the be the most effective interventions at improving adherence over 10 months, with education in combination with technical and attitudinal components (OR 0.49, 95% CrI 0.27-0.88) and rewards in combination with technical interventions having the most effective odds ratio (OR 0.03, 95% CrI 0.01-0.13) against standard of care. The Perx mHealth app utilising rewards, technical components, education and attitudinal components revealed high rates of adherence, average at 87.6% (SD 16.9%), above an optimal adherence threshold standard of 80%, over 6 months. An analysis of 6,296 user reviews of the mHealth app discovered a highly accepted and appreciated tool for aiding the management of medication adherence. Users reacted positively to reminder and reward components specifically, though expected improvements within technical functionality issues and the frequency of rewards.

Conclusion

Interventions to improve medication adherence have revealed modest improvements in effectiveness, with a continued need for multicomponent interventions to sustain adherence over 10 months. The evaluated mHealth intervention, Perx, utilising multiple components, including rewards, technical, education and attitudinal components, highlighted an intervention able to sustain optimal adherence rates over time. User reviews recognised a highly desirable and appreciated mHealth intervention in aiding the management of medication adherence. MHealth interventions should continue to

be innovated and adopted as helpful tools in improving medication adherence but must be evidence-based and evaluated for their effect on health outcomes.

Dissemination of Research

Peer reviewed publications

1. **Wiecek E**, Torres-Robles A, Cutler RL, Benrimoj SI, Garcia-Cardenas V 2020, 'Impact of a Multicomponent Digital Therapeutic Mobile App on Medication Adherence in Patients with Chronic Conditions: Retrospective Analysis', JMIR, vol. 22, no. 8.

2. Cutler, R.L., Torres-Robles, A, **Wiecek, E**, Drake, B., Van der Linden, N., Benrimoj, S.I.C. & 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, p. 853.

3. **Wiecek, E**, Tonin, F.S., Torres-Robles, A, Benrimoj, S.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2019, 'Temporal effectiveness of interventions to improve medication adherence: A network meta-analysis', PloS one, vol. 14, no. 3, p. e0213432.

4. Torres-Robles, A, **Wiecek, E,** Cutler, R., Drake, B., Benrimoj, S.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2019, 'Using Dispensing Data to Evaluate Adherence Implementation Rates in Community Pharmacy', Frontiers in Pharmacology, vol. 10, no. 130.

5. Torres-Robles, A, **Wiecek, E,** Tonin, F.S., Benrimoj, S.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2018, 'Comparison of Interventions to Improve Long-Term Medication Adherence Across Different Clinical Conditions: A Systematic Review With Network Meta-Analysis', Frontiers in Pharmacology, vol. 9, no. 1454.

6. Tonin, F.S., **Wiecek, E,** Torres-Robles, A., Pontarolo, R, Benrimoj, S.C.I., Fernandez-Llimos, F. & Garcia-Cardenas, V. 2019, 'An innovative and comprehensive technique to evaluate different measures of medication adherence: The network meta-analysis', Research in Social and Administrative Pharmacy, vol. 15, no. 4, pp. 358-65.

Conference proceedings

1. **Wiecek E**, Torres-Robles A, Cutler RL, Garcia-Cardenas V 2019, 'Gamifying medication adherence: retrospective analysis of a mobile application utilising gamification and incentives to improve adherence', Poster presented at the 23rd Annual International Society for Patient Medication Adherence.

2. Leite J, **Wiecek E,** Torres-Robles A, Cutler RL, Garcia-Cardenas V 2019, 'The effectiveness of using mobile applications to improve medication adherence: a systematic review', Poster presented at the 23rd Annual International Society for Patient Medication Adherence.

3. **Wiecek E,** Torres-Robles A, Cutler RL, Benrimoj, SI, Garcia-Cardenas V 2018, 'Evaluation of a community pharmacy medication adherence service: A study protocol', Poster presented at the 2nd Annual Simpodader Internacional.

4. **Wiecek E**, Benrimoj SI, Fernandez-Llimos F, Tonin FS, Torres Robles A, Garcia-Cardenas A 2018a, 'Comparing the efficacy of intervention strategies to enhance medication adherence: a network meta-analysis', Poster presented at the 1st Annual Pharmacy Practice Research: Postgraduat Students, Postdoctoral Fellows and Supervisors Symposium Conference Organised by the FIP Special Interest Group (SIG) on Pharmacy Practice Research.

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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 an outline of the overall rationale, objectives and organisation of the thesis. Chapter 2 provides the background and reasoning for the research. Chapters 3-5 comprise the results including a network meta-analysis assessing comparative effectiveness of interventions to improve medication adherence, evaluation of a mobile health app's impact on medication adherence and an exploration of user beliefs, perceptions and experiences using the aforementioned mobile health app. 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.

Elyssa K Wiecek 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

ABC Project Team: Ascertaining Barriers for Compliance

ADHD: Attention Deficit Hyperactivity Disorder

AI: artificial intelligence

BCT: Behaviour Change Techniques

BE FIT: The Behavioral Economics Framingham Incentive Trial

CDC: Centre for Disease Control

COREQ: Consolidated Criteria for Reporting Qualitative Research

CrI: Credibility Interval

DIC: Deviance Information Criterion

EMERGE: ESPACOMP Medication Adherence Reporting Guideline

HIV: Human Immunodeficiency Virus

HREC: Human Research Ethics Committee

IQR: Interquartile range

M-DOT: Mobile Direct Observation of Therapy

MAQ: Medication Adherence Questionnaire

MARS: Medication Adherence Report

MEMS: Medication Events Monitoring Systems

mHealth: Mobile Health

MMAS-4: Four-item Morisky Medication Adherence Scale

MMAS-8: Eight-item Morisky Medication Adherence Scale

MPR: Medication Possession Ratio

NICE: National Institute for Health and Care Excellence

OR: Odds Ratio

PDC: Proportion of Days Covered

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: International Prospective Register of Systematic Reviews

SD: Standard deviation

SOC: Standard of Care

SQL: Structured Query Language

STROBE: STrengthening the Reporting of OBservational Studies in Epidemiology

SUCRA: Surface Under the Cumulative Ranking Curve

WHO: World Health Organization

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