Bridging the Gap between Physical and Mental Illness in Community Pharmacy (*PharMIbridge*): Randomised Controlled Trial

Statistical Analysis Plan Version 2.0

Title:

Bridging the Gap between Physical and Mental Illness in Community Pharmacy (*PharMIbridge*): Randomised Controlled Trial

Trial registration number: ACTRN12620000577910

Research Team:

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Table of Contents

i. Updates from previous version (v1)

i.i. Medication persistence cut-off value

The cut-off value for defining non-persistence was changed to 30 days delay in medication refills. Other processes involved in the primary outcome calculations illustrated in the SAP (section **4.1.1**) remained unchanged. The original cut-off value was adapted from a systematic review in which authors found studies had adopted various values for defining the medication non-persistence ranging from 14 – 120 days (Sattler, Lee, & Perri, 2013). Psychotropic medications such as antipsychotics, antidepressants, and mood stabilisers as well as medications for other long-term health conditions such as antithrombotic agents, and medications for diabetes, cardiovascular disease, and obstructive airway diseases, were included in this analysis. After comprehensive data preparation and curation, the preliminary descriptive analysis found the average days of supply of these prescriptions were around 34 days (**Table i**). Therefore, a 30-day refill gap was applied in defining medication persistence, which meant participants were approximately skipping a repeat prescription (refill), and would likely be classified as non-persistent with their medications.

Table I Average days of supply per medication group

Medication Group	**Number of Prescriptions**	**Days of Supply, Mean (SD)**
Antidepressants	4143	29 (8.4)
Antipsychotics	3930	34 (17.0)
Mood stabilisers	1541	53 (33.6) *
Antithrombotic agents	169	29 (1.0)
Medications used for diabetes	893	36 (17.5)
Medications used for cardiovascular diseases	3248	33 (12.3)
Medications used for obstructive airway diseases	307	31 (11.6)
All groups	14231	34 (18.1)

* standard pack sizes and Pharmaceutical Benefits Scheme quantities are larger for mood stabilisers than other medications of interest

i.ii. Analyses of secondary outcomes related to the linked hospital care data

A secondary outcome of the RCT is to examine differences in hospital admissions or emergency department visits between the intervention group and the comparator group. However, almost three quarters of participants had no record of hospital admissions and/or emergency department visits. The mixed-effects negative binomial models were not appropriate due to a lack of convergence and effective sample size. Mixed-effects logistic regression model was used to compare the difference in hospital admission between RCT groups. A mixed-effects negative binomial regression model was

further applied to explore the difference in the number of hospital admissions between RCT groups among those who had at least one hospital admission. The same analytic approach was applied to analyse the emergency department visit outcome and mental health-related hospital admission and emergency department visit outcomes. This approach was listed as potential analytical methods based on data suitability and assumptions in the original SAP.

i.iii. Data imputations for key outcomes as sensitivity analyses

Further to the initial SAP outlined in section 4, multiple imputations by chained equation were used to impute missing data for several key outcomes (adherence to psychotropic medications, health state utility, and K6 total score) as part of the sensitivity analyses to explore the impact of missing data. Data imputations were implemented separately by randomised treatment groups with the assumption that data were missing at random (Faria, Gomes, Epstein, & White, 2014). Sixty iterations were performed on these imputations and data were analysed using the imputed dataset with results collated according to Rubin's rules, which would reflect the variability within and across imputations (White et al., 2011). A user-contributed Stata program package (ICE) was used to implement the multiple imputations, which is flexible to impute different types of data.

Variables included in the equations were slightly different for the three outcomes. For the adherence to psychotropic medications outcome, approximately 13% of missing data at follow-up were imputed using the multiple imputations by chained equations, with age, sex, number of self-reported mental illnesses, number of self-reported physical health conditions, service completion status and baseline self-reported adherence to medications (RAM) score included in the equations.

For the health state utility, variables included in the equations were age, sex, level of education, employment status, number of self-reported mental illnesses, number of self-reported physical health conditions, self-reported general health, death indicator, and the baseline utility scores. And for the K6 total score, variables included in the equations were age, sex, level of education, employment status, number of self-reported mental illnesses, number of self-reported physical health conditions, self-reported general health, and the baseline K6 scores.

i.iv. Stratification of Kessler 6-item (K6) scale scores

The Kessler 10-item scale (K10) has been widely used in the Australia National Studies to assess the low, moderate, high and very high levels of psychological distress (Enticott et al., 2022). The K6 scale is comprised of six items selected from K10 which shows equivalent usefulness in terms of internal validity, measurement timeframe, and the assessment for psychological distress (Furukawa, Kessler, Slade, & Andrews, 2003). Four strata of scores (Low 6-9; Moderate 10-14; High 15-18; Very high 19-30) were used to define the four levels of psychological distress, which were generated and validated

from the normative data from the 2007 Australian National Survey of Mental Health and Wellbeing (Slade, Grove, & Burgess, 2011).

i.v. CONSORT flow diagram

The template for the Consolidated Standards of Reporting of Trials (CONSORT) flow diagram was erroneously omitted in v1 and has been added as Figure 5.1.

1. Study design

The *PharMIbridge* Randomised Controlled Trial (RCT) will evaluate the effectiveness of an individualised, pharmacist-led support service for people with severe and persistent mental illness (SPMI) focusing on adherence and the management of physical co-morbidities, compared to standard care involving a Medication Review Service (MedsCheck). Community pharmacies will be randomised using a 1:1 ratio, to either the Intervention Group (IG) or Comparator Group (CG) within four Australian regions (Australian Capital Territory (ACT), Hunter New England (HNE), Northern Sydney (NS), Regional Victoria (VIC)). All recruited pharmacy staff will receive Blended-Mental Health First Aid (BMHFA) training. Additionally, IG pharmacists will receive training on adherence, goal setting, motivational interviewing, managing physical health concerns and complex issues relating to psychotropic medication. Details on the study design of the *PharMIbridge* RCT are published elsewhere (Wheeler et al., 2020).

1.1 Purpose and scope

The purpose of this document is to minimise bias by defining and making publicly available our analysis approach prior to reviewing or analysing any trial data. The following statistical analysis plan (SAP) has been developed to inform the analysing and reporting of the main outcomes from the *PharMIbridge* RCT including our approach to expected protocol deviations, withdrawals, missing data, and loss to follow up. Outcomes considered in this SAP are the primary and key secondary outcomes that will inform both the main effectiveness findings of the trial and future Medical Services Advisory Committee (MSAC) applications. In this SAP, broad statistical analysis principles are outlined, primary and secondary trial outcomes are described, along with appropriate methods for statistical comparison. Other outcomes, such as those related to the *PharMIbridge* training program outcome and qualitative data analysis will be reported elsewhere. This SAP should not be taken as a comprehensive plan for all future analyses using RCT data.

2. Analysis principles

General analysis: Comparative analyses will allow for the clustered nature of the data and baseline values will be adjusted in the models. The cluster will be the community pharmacy and the analysing unit will be the individual consumer participant.

Stratified analysis: Stratified analyses will be conducted based on the metropolitan or non-metropolitan location of community pharmacies.

Intention-to-treat analysis: All analyses will be undertaken based on the 'intention-to-treat' principle, that is, participants' data will be analysed according to the group to which they were initially allocated (White et al., 2011).

Per-protocol analysis: Due to the impact of the novel coronavirus (COVID-19) pandemic, consumer participants may have not completed each data collection milestone within the targeted timeframe. For example, a 6-month review including a follow-up survey should be completed 6 months after the initial intervention/comparator service interview with the participating pharmacist. However, some consumer participants were unable to attend appointments as scheduled due to state-wide lockdowns and other factors associated with the pandemic such as social distancing. A per-protocol sample is defined if consumer participants who have completed the initial pharmacist intervention/comparator service interview within 8 weeks after completing the baseline survey, and if they have completed the 6-month follow-up survey within 16-32 weeks after the initial pharmacist intervention/comparator service interview. Participants, who have received extra medication management services, such as a home medicines review (HMR), will be excluded from the per-protocol analysis to eliminate potential contaminations between groups. Per-protocol analyses will be undertaken for the co-primary outcomes (subjective and objective measures of adherence) and several key secondary outcomes.

Exclusions: Data will be excluded if participants actively withdraw and request that their data are destroyed.

Presentation of results: Descriptive data will be summarised as mean (SD) or median (range or 25-75th percentile) for continuous variables and frequency (percentage) for categorical variables, respectively. Between-group comparisons will be calculated and presented with 95% confidence intervals wherever possible.

Level of significance: The statistical significance level will be set at less than 5%.

Statistical software: All analyses will be performed using Stata 17 (StataCorp) or SPSS Version 27 (IBMCorp).

3. Trial profile

The progress of clusters and individuals through phases of the trial will be presented in a flow diagram in accordance with the CONSORT extension statement for cluster trials (Campbell, Piaggio, Elbourne, & Altman, 2012). An outline of the flow diagram is presented in Figure 4.1.

3.1 Data sources and analysis samples

The data will be collected from a number of sources depending on the type of information collected and the availability of the data. There are six samples used in this analysis plan, which are defined below:

Baseline completion data sample: Consumer participants who consented to participate in the study and completed a baseline process, which included a baseline survey and an initial interview with the pharmacist, will be considered members of the baseline completion data sample.

Survey completion data sample: Consenting participants will be assessed at baseline and reassessed at the 6-month endpoint using online questionnaires. Consumer participants will be considered members of the survey completion data sample if they completed surveys at both the baseline and 6-month points.

Service completion data sample: Consumer participants allocated in different arms will receive relevant intervention and comparator services. Clinical implementation outcomes relating to these services will be recorded by participating pharmacists using a purpose-designed research module developed by Guild Link. Consumer participants will be considered members of the service completion data sample if they have completed at least the initial pharmacist interview for an intervention or comparator service.

Linked hospital data sample: All consented consumer participants' hospital admission and emergency department visit data in the relevant jurisdiction will be linked based on a participant's identifiers, including name, date of birth, sex, and current residence. Consumer participants who have completed the baseline process, and whose hospital data were provided by the relevant data linkage agencies will be considered members of the linked hospital data sample.

Linked MBS/PBS data sample: All consumer participants with a valid consent form for MBS and PBS data linkage will be linked for health care (MBS) and pharmaceutical utilisation (PBS) data through Service Australia. Consumer participants successfully linked to the MBS and PBS database will be considered members of the linked MBS/PBS data sample.

Pharmacy dispensing history data sample: Consumer participants with dispensing history records provided by Guild Care or participating pharmacies will be considered members of the pharmacy dispensing history data sample.

3.2 Cluster characteristics and baseline comparisons

Baseline completion data will be used to describe the characteristics of community pharmacies by the RCT groups. Between-group differences will be tested using Fisher's exact tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Details of the coding and analysis for each variable are listed below (Table 3.1).

Table 3.1 Pharmacy specific variables

Variables	Coding	Statistical analysis
Number of pharmacies	-	-
Participants recruited per pharmacy, median(IQR)	-	Wilcoxon rank-sum test
Location[a]	1=MMM1, 0=MMM2-7	Fisher's exact test
Pharmacy region [b]	1=ACT 2=HNE 3=NS 4=VIC	Fisher's exact test
Number of full-time pharmacists present	-	Wilcoxon rank-sum test

[a] *Remoteness based on the Modified Monash Model (MMM)*

[b] *ACT, Australian Capital Territory; HNE, Hunter New England; NS, Northern Sydney; VIC, Regional Victoria*

3.3 Consumer participants' characteristics and baseline comparisons

Baseline characteristics of participants will be presented by the RCT groups. Between-group differences will be tested using a mixed-effects linear regression if the dependant variable is continuous, mixed-effects logistic regression if the dependant variable is binary or mixed-effects ordered logistic regression if the dependant variable is ordinal. In each regression model, the RCT group will be entered as a fixed effect, and the pharmacy will be entered as a random intercept.

Baseline variables common to the intervention and comparator group, coding and proposed analyses are listed below (Table 3.2).

Table 3.2 Consumer participant-specific variables

Demographic characteristics		
Variables	**Coding**	**Statistical analysis**
Age	Number	Mixed-effects linear regression
Gender	1=Male 0=Female	Mixed-effects logistic regression
Country of birth	1=Australian 0=Other	Mixed-effects logistic regression
Indigenous identity	1=Aboriginal or Torres Strait Islander, 0=Not Aboriginal or Torres Strait Islander	Mixed-effects logistic regression
Language primarily spoken at home	1=English, 0=Other	Mixed-effects logistic regression
Employment status	1=Employed, 0=Unemployed, disability pension, or other	Mixed-effects logistic regression
Education status	1=Year 12 or under, 2=Certificate or diploma, 3=Undergraduate or graduate degree	Mixed-effects ordered logistic regression
Self-reported health characteristics		

Variables	Coding	Statistical analysis
Multiple mental illnesses diagnoses	1=More than one mental illness, 0=One mental illness	Mixed-effects logistic regression
Moderate/severe depression	1=Reported, 0=Not reported	Mixed-effects logistic regression
Moderate/severe anxiety disorder	1=Reported, 0=Not reported	Mixed-effects logistic regression
Bipolar disorder	1=Reported, 0=Not reported	Mixed-effects logistic regression
Schizophrenia/schizoaffective disorder	1=Reported, 0=Not reported	Mixed-effects logistic regression
Substance use disorder	1=Reported, 0=Not reported	Mixed-effects logistic regression
Post-traumatic stress disorder, PTSD	1=Reported, 0=Not reported	Mixed-effects logistic regression
Personality disorder	1=Reported, 0=Not reported	Mixed-effects logistic regression
Other mental illnesses	1=Reported, 0=Not reported	Mixed-effects logistic regression
Number of physical health conditions	continuous number	Mixed-effects linear regression
Diabetes	1=Reported, 0=Not reported	Mixed-effects logistic regression
Asthma	1=Reported, 0=Not reported	Mixed-effects logistic regression
Hypertension	1=Reported, 0=Not reported	Mixed-effects logistic regression
Hypercholesterolaemia	1=Reported, 0=Not reported	Mixed-effects logistic regression
Arthritis	1=Reported, 0=Not reported	Mixed-effects logistic regression
Cardiovascular disease	1=Reported, 0=Not reported	Mixed-effects logistic regression
Gastro-oesophageal reflux disease, GORD	1=Reported, 0=Not reported	Mixed-effects logistic regression
Cancer	1=Reported, 0=Not reported	Mixed-effects logistic regression
Chronic obstructive pulmonary disease, COPD	1=Reported, 0=Not reported	Mixed-effects logistic regression
Osteoporosis	1=Reported, 0=Not reported	Mixed-effects logistic regression
Other health conditions	1=Reported, 0=Not reported	Mixed-effects logistic regression
General health	1=Excellent, 2=Very good, 3=Good, 4=Fair, 5=Poor	Mixed-effects linear regression
Self-reported hospital admissions during previous 6 months	1=Yes, 0=No	Mixed-effects logistic regression
Mental healthcare plan	1=Yes, 0=No/not sure	Mixed-effects logistic regression

4. Proposed outcome analysis

4.1 Primary outcome

Difference in psychotropic medication adherence rates between the IG and CG at 6-month follow-up, as objectively assessed through PBS data and pharmacy dispensing data. Self-reported assessment of adherence to all prescribed medications, as subjectively assessed using the Reported Adherence to Medication (RAM) Scale. These will be considered co-primary outcomes measuring medication adherence using different data samples. Details of the data used, definition of the variables and proposed analyses are outlined below.

4.1.1 Objective assessment of medication adherence

Data and participants: The full analysis sample for this primary outcome is the combination of the linked MBS/PBS data and pharmacy dispensing history data.

Definition: The primary outcome will be the difference in consumer participants' medication adherence rates for psychotropic medication over the 6-months trial period between the intervention group (IG) and comparator group (CG). Medication adherence rate will be a binary variable indicating whether consumer participants are adherent to psychotropic medications over 6 months. Consumer participants will be deemed as non-adherent if the average medication possession ratio (MPR) is under 80% or if an over 30 days delay is identified for a prescription refill.

Psychotropic medications will be included in the calculation if the participant has been dispensed the medication at least twice in both the pre-intervention (6 months before initial intervention/comparator service) and the post-intervention (6 months after initial intervention/comparator service) period. Pharmacy dispensing records will be used to calculate the days of supply for the eligible PBS prescriptions. Whenever pharmacy dispensing records are not available or directions for use are unclear, other available clinical data such as documented medication reviews conducted during the RCT or health summaries will be used. If no clear dosing records are available from any of the aforementioned sources, the daily dose will be determined by standard dosing from the Australian Medicines Handbook (Australian Medicines Handbook, 2022) in consideration of the indication (if known), strength, and quantity supplied. The MPR of each medication will be calculated, which refers to the proportion of days that a consumer is in possession of their medication within a defined period. In circumstances of over-supply (days of medication possession are greater than the observed period), the MPR value will be capped at one. An average of average MPR score will then be calculated based on the therapeutic class of psychotropic medication (Choudhry et al., 2018). Medication persistence for each eligible medication will be assessed using PBS data; non-persistence refers to a >30 days delay in medication refills (Sattler et al., 2013).

Primary analysis: A mixed-effects logistic regression model will be applied to compare the medication's adherence rate over the 6 months after initial intervention/comparator service between IG and CG. RCT group will be entered as fixed effect and pharmacy entered as a random intercept to account for possible non-independence of observations from participants who attend the same pharmacy. The baseline value of the outcome variable will be included as a covariable in the model. The effect estimate will be reported as an odds ratio with 95% confidence interval.

Sensitivity analysis: To assess the robustness of the results, sensitivity analysis will be performed for this primary outcome, using the linked PBS data sample.

4.1.2 Subjective assessment of medication adherence

Data and participants: The full analysis sample for this primary outcome will be the survey completion data sample.

Definition: Subjective medication adherence is measured using the Reported Adherence to Medication Scale (RAM).

Primary analysis: The difference in the RAM scores between IG and CG at 6-month follow-up will be compared using a mixed-effects linear model with baseline RAM scores adjusted. The RCT group will be entered as a fixed effect and the pharmacy will be entered as a random intercept to account for possible non-independence of observations from participants who attend the same pharmacy. The effect estimate will be reported as the mean difference in RAM scores and 95% confidence interval.

4.2 Secondary outcomes

Secondary outcomes will be the differences in the following variables between IG and CG at the 6-month follow-up point or during the six months after the initial intervention/comparator service. Different samples will be used to analyse the secondary outcomes based on the data required for each specific analysis.

Overall, for binary and ordinal outcomes, mixed-effects logistic/ordered logistic regression models will be applied to compare these outcomes between the intervention and comparator groups. For continuous outcomes, mixed-effects linear regression models will be applied; and for count data, mixed-effects Poisson regression models will be used. In all mixed-effects models, the treatment arm will be entered as a fixed effect and the pharmacy will be entered as a random intercept to account for possible non-independence of observations from participants who attend the same pharmacy. Baseline values of the outcome variable will be included as a covariate in these models when possible. Between-group comparisons will be reported as mean difference, odds ratio or incidence rate ratio with 95% confidence intervals.

4.2.1 Secondary outcomes using the linked MBS/PBS data and pharmacy dispensing history data

Data and participants: The full analysis sample for secondary outcomes regarding medication adherence for other chronic diseases and healthcare utilisations will be the combination of linked MBS/PBS data and pharmacy dispensing history data.

Table 4.1 Variables and proposed analyses using linked MBS/PBS data and pharmacy dispensing history data

Variables	Coding	Statistical analysis	Effect estimate
Medication adherence for medications for other chronic conditions	1=Adherent, 0=Non-adherent	Mixed-effects logistic regression	Odds ratio and 95% CI
General practitioner visits during the six months after the initial intervention/comparator service interview	-	Mixed-effects linear regression (consider other models, such as negative binomial model if model assumption is not met)	Mean difference and 95% CI

4.2.2 Secondary outcomes using the linked hospital data

Data and participants: The full analysis sample for secondary outcomes relating to healthcare service utilisation will be the linked hospital data sample.

Table 4.2 Variables and proposed analyses using linked hospital data

Variables	Coding	Statistical analysis	Effect estimate
All-cause hospital admissions during the six months after the initial intervention/comparator service	-	Mixed-effects logistic regression and mixed-effects negative binomial models	Mean difference and 95% CI
Mental health-related hospital admissions during the six months after the initial intervention/comparator service	-	Mixed-effects linear logistic regression and mixed-effects negative binomial models	Mean difference and 95% CI
All-cause emergency department admissions during the six months after the initial intervention/comparator service	-	Mixed-effects linear logistic regression and mixed-effects negative binomial models	Mean difference and 95% CI
Mental health-related emergency department admissions during the six months after the initial intervention/comparator service	-	Mixed-effects linear logistic regression and mixed-effects negative binomial models	Mean difference and 95% CI

4.2.3 Secondary outcomes using the survey completion data

Data and participants: The full analysis sample for these secondary outcomes will be the survey completion data sample.

Table 4.3 Variables and proposed analyses using survey completion data

Variables	Coding	Statistical analysis	Effect estimate
Quality of life measured by Assessment of Quality of Life (AQoL-6D) at 6-month follow-up	20-99	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 1 - Independent living	4-22	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 2 – Relationship	3-13	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 3 – Mental health	4-20	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 4 – Coping	3-15	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 5 – Pain	3-13	Mixed-effects linear regression	Mean difference and 95% CI
AQoL dimension 6 – Senses	3-16	Mixed-effects linear regression	Mean difference and 95% CI
Psychological wellbeing measured by Kessler-6 (K6) scale at 6-month follow-up	6-30	Mixed-effects linear regression	Mean difference and 95% CI
High risk of non-specific psychologic distress	1=Low (K6 6-9); 2=Moderate (K6 10-14); 3=High (K6 15-18); 4=Very high (K6 19-30)	Mixed-effects ordered logistic regression	Proportional odds ratio and 95% CI
Treatment burden measured by Multimorbidity Treatment Burden (MTBQ 13-item) Questionnaire at 6-month follow-up	0=No burden (score 0), 1=Low burden (score<10), 2=Medium burden (score 10-22), 3=High burden (score>=22)	Mixed-effects ordered logistic regression	Proportional dds ratio and 95% CI
Attitude to therapy measured by Drug Attitude Inventory 10 (DAI-10) at 6-month follow-up	1=Adherent, 0=Non-adherent/unsure	Mixed-effects logistic regression	Odds ratio and 95% CI
Illness beliefs measured by Brief Illness Perception Questionnaire (BIPQ) at 6-month follow-up	0-80	Mixed-effects linear regression	Mean difference and 95% CI
Physical activity measured by physical activity 'Vital Sign' questionnaire (PAVS) at 6-month follow-up	1= Met recommendation, 0=Not met recommendation	Mixed-effects logistic regression	Odds ratio and 95% CI
Alcohol, smoking, substance and non-prescribed drug use assessed by the Alcohol, Smoking and Substance			

Variables	Coding	Statistical analysis	Effect estimate
Involvement Screening Test (ASSIST) at 6-month follow-up			
Use of alcohol	0=Low risk, 1=Moderate/high risk	Mixed-effects logistic regression	Odds ratio and 95% CI
Use of tobacco products	0=Low risk, 1=Moderate/high risk	Mixed-effects logistic regression	Odds ratio and 95% CI
Sleep issues measured by Insomnia Severity Index (ISI) at 6-month follow-up	0=Non-clinical insomnia, 1=Sub-threshold, 2=Clinical insomnia (moderate severity), 3=Clinical insomnia (severe)	Mixed-effects ordered logistic regression	Proportional odds ratio and 95% CI
Risk assessment for cardiovascular disease in previous 6 months	1=Yes, 0=No/Unsure	Mixed-effects logistic regression	Odds ratio and 95% CI
Glycated haemoglobin (HbA1c) measured in previous 6 months	1=Yes, 0=No/Unsure	Mixed-effects logistic regression	Odds ratio and 95% CI

4.3 Other outcomes

Data and participants: Respective service implementation outcome data will be collected in IG and CG. The full analysis sample for these outcomes will be the service completion data sample.

Descriptive analyses will be used for measures of intervention/comparator service delivery such as time taken, mean (median) number of current medications, issues and goals identified, goals achieved and relevant pharmacists' actions or recommendations.

Table 4.4 Variables and proposed analyses using service completion data

Variables	Coding	Statistical analysis
Time taken for pharmacist-led initial interviews, minutes	-	Descriptive by group
Number and categories of the issues identified during the pharmacist-led interviews	1=Medication, 2=Physical wellbeing, 3=Mental wellbeing, 4=Lifestyle and nutrition, 5=Other	Descriptive by group
Medication-related issues identified	1=Drug selection, 2=Over or underdose, 3=Compliance, 4=Undertreated, 5=Monitoring, 6=Education or information, 7=Not classifiable, 8=Toxicity or adverse drug reaction (ADR)	Descriptive for IG participants
Number and categories of the recommendations documented during the pharmacist-led interviews	1=A change in therapy, 2= A referral required, 3=Provision of information, 4=Lifestyle recommendations, 5=Monitoring, 6=Medicines reconciliation	Descriptive by group
Severity rating of medication issues	0=Nil, 1=Low, 2=Mild, 3=Moderate, 4=High	Descriptive for IG participants
Number and categories of goals set during the pharmacist-led interviews	1=Medication, 2=Physical wellbeing, 3=Mental wellbeing, 4=Lifestyle and nutrition, 5=Other	Descriptive for IG participants
Goals achieved by the Goal Attainment Scaling (GAS)	1=Achieved-much better, 2=Achieved-a little better, 3=Achieved-as expected, 4=Not achieved-part achieved, 5=Not achieved-same as baseline, 6=Not achieved-worse	Descriptive for IG participants

5. Appendix: Proposed figures and results tables

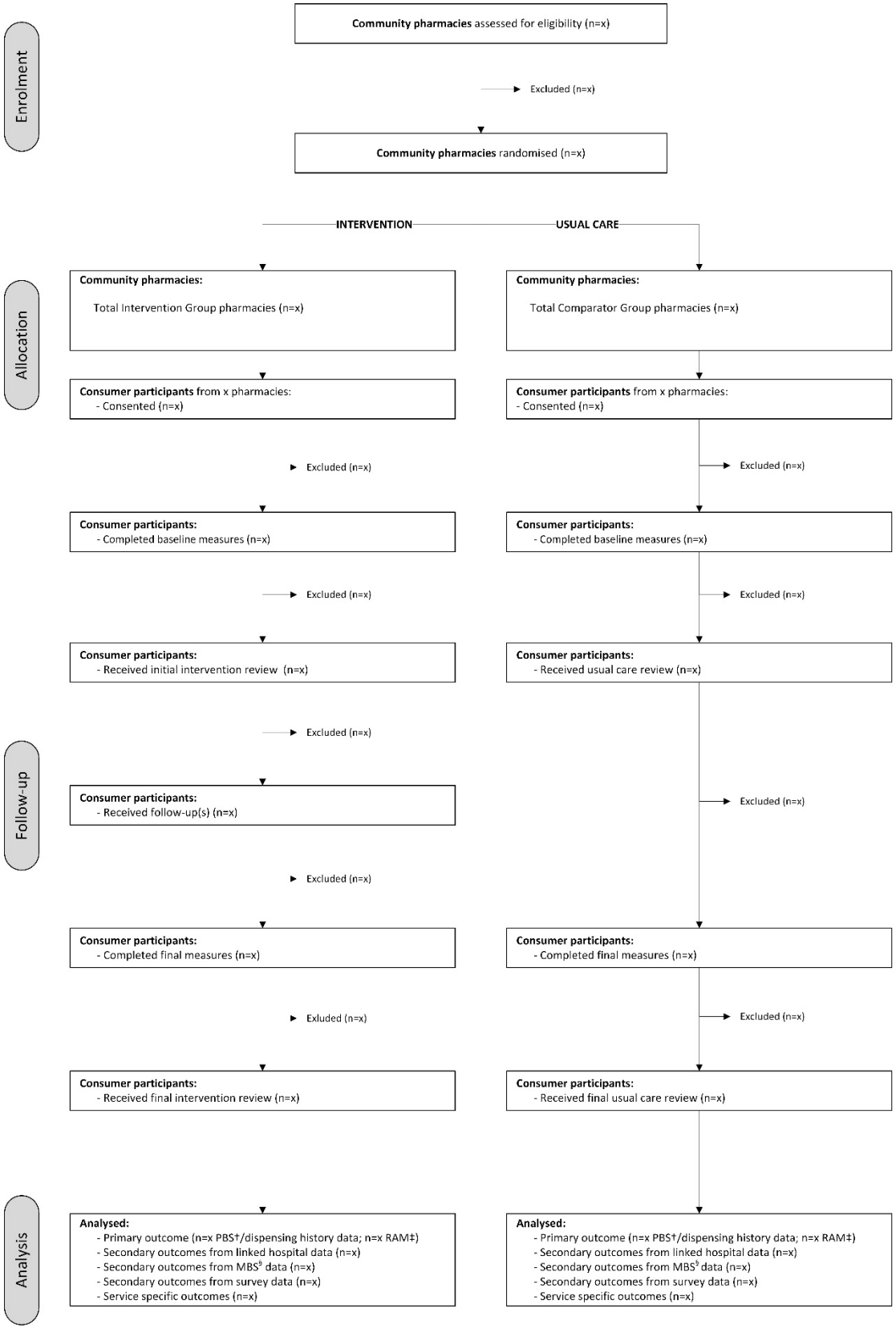

Figure 5.1: Consort flow diagram

Table 5.1 Baseline characteristics of pharmacies in the intervention and comparator groups

Pharmacy characteristics	**Intervention (*PharMIbridge*) n (%)**	**Comparator (MedsCheck) n (%)**	***p*-value**
Number of pharmacies			
Participants per pharmacy, median (range)			
Location			
Metropolitan (MMM 1)			
Non-metropolitan (MMM 2-7)			
RCT region			
Australian Capital Territory			
Hunter New England			
Northern Sydney			
Regional Victoria			
FTE pharmacists present on weekdays, median (range)			

Table 5.2 Baseline characteristics of consumer participants in the intervention and comparator groups

Consumer participant characteristics	Intervention (*PharMIbridge*), n (%)	Comparator (MedsCheck), n (%)	*p*-value
Number of participants			
Age (years), Mean (SD)			
Gender			
Male			
Female			
Born in Australia			
Indigenous identity			
English primarily spoken at home			
Education level			
Year 12 or under			
Certificate or diploma			
Undergraduate/graduate degree			
Employment status			
Employed (FT, PT, casual)			
Unemployed (including disability support pension or other)			
Number of mental illnesses			
One			
Two or more			
Mental illnesses			
Moderate/severe depression			
Moderate/severe anxiety disorder			
Bipolar disorder			
Schizophrenia/schizoaffective disorder			
Substance use disorder			
Post-traumatic stress disorder			
Personality disorder			
Other mental illness			
Physical health conditions, median (range)			
Diabetes			
Asthma			
Hypertension			
Hypercholesterolaemia			
Arthritis			
Cardiovascular disease			
Gastro-oesophageal reflux disease			
Cancer			
Chronic obstructive pulmonary disease			
Osteoporosis			
Other health condition			
Number of physical health conditions			
One			
Two or more			

Consumer participant characteristics	**Intervention (*PharMIbridge*), n (%)**	**Comparator (MedsCheck), n (%)**	***p*-value**
Self-report hospital admission during previous 6-months			
Mental health care plan			

Table 5.3 Primary outcomes

	N	Intervention (*PharMIbridge*)		N	Comparator (MedsCheck)		Between group difference at follow-up	P-value
		Baseline	Follow-up		Baseline	Follow-up	Mean difference/Odds ratio (95% CI)	
Subjective adherence measure using linked PBS data and pharmacy dispensing history data								
Adherence to psychotropic medications, n (%)								
Objective adherence measure using survey completion data								
Reported adherence to medications (RAM), mean (SD)								

Table 5.4 Secondary outcomes using survey data

Variables	**N**	**Intervention (*PharMIbridge*)**		**N**	**Comparator (MedsCheck)**		**Between group difference at follow-up**	**P-value**
		Baseline	Follow-up		Baseline	Follow-up	Mean difference/Odds ratio (95% CI)	
Quality of life, mean (SD)								
Independent living								
Relationship								
Mental health								
Coping								
Pain								
Senses								
Illness beliefs, mean (SD)								
Risk of non-specific psychological distress, mean (SD)								
High risk of non-specific psychological distress, n (%)								
Treatment burden, n (%)								
No burden								
Low burden								
Medium burden								
High burden								
Attitudes to therapy, n (%)								
Sleep issue, n (%)								
Non-clinical insomnia								
Sub-threshold								
Moderate clinical insomnia								
Severe clinical insomnia								
Physical activity recommendations met, n (%)								

Variables	**N**	**Intervention (*PharMIbridge*)**		**N**	**Comparator (MedsCheck)**		**Between group difference at follow-up**	**P-value**
		Baseline	Follow-up		Baseline	Follow-up	Mean difference/Odds ratio (95% CI)	
Alcohol use, n(%)								
Tabacco use, n(%)								
Risk assessment for Cardiovascular disease in previous 6 months								
Glycated hamoglobin (HbA1c) measured in previous 6 months								

Table 5.5 Secondary outcomes using linked MBS/PBS data and pharmacy dispensing history data

	N	Intervention (*PharMIbridge*)		N	Comparator (MedsCheck)		Between group difference at follow-up	P-value
		Baseline	Follow-up		Baseline	Follow-up	Mean difference/Odds ratio (95% CI)	
GP visits, mean (SD)								
Adherence to medications for other chronic conditions, n (%)								

*GP, general practitioner

Table 5.6 Secondary outcomes using linked hospital data, mean (SD)

	N	Intervention (*PharMIbridge*)		N	Comparator (MedsCheck)		Between group difference at follow-up	P-value
		Baseline	Follow-up		Baseline	Follow-up	Mean difference (95% CI)	
All-cause hospital admissions								
Mental health-related hospital admissions								
All-cause ED admissions								
Mental health-related ED admissions								

*ED, emergency department

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