



**Assessment of change in medication adherence and self-assessed health status in Aboriginal and Torres Strait Islander patients with chronic disease receiving integrated pharmacist support within Aboriginal Community -Controlled Health Services (IPAC project)**

**REPORT TO THE PHARMACEUTICAL SOCIETY OF AUSTRALIA FOR THE IPAC PROJECT**

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Prepared by: Couzos S, Smith D, Buttner P, Biro E. College of Medicine and Dentistry, James Cook University, on behalf of the IPAC Project Team.

*Integrating Pharmacists within Aboriginal Community Controlled Health Services (ACCHSs) to improve Chronic Disease Management (IPAC) Project.*

Correspondence:

Associate Professor Sophia Couzos  
General Practice and Rural Medicine  
**College of Medicine and Dentistry,  
James Cook University,  
Townsville, Queensland, 4811  
Australia**

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## ABSTRACT

**Objective:** To assess the impact of integrated pharmacist interventions on self-reported medication adherence and self-assessed health status in Aboriginal and Torres Strait Islander adults with chronic disease attending Aboriginal Community Controlled Health Services (ACCHSs) enrolled in the IPAC study, compared with usual care (pre-intervention), and to develop and validate the performance of a self-reported adherence tool in this context.

**Design and participants:** The study was a non-randomised, prospective, pre and post quasi-experimental community-based, participatory, and pragmatic trial that integrated a registered pharmacist within ACCHS in Queensland, the Northern Territory or Victoria. The intervention comprised non-dispensing medicines-related services, collaborative and coordinated care, including the provision of medication management reviews. Participants were usual patients of the ACCHSs aged 18 years or older with a chronic disease. Participants consented to receive the intervention and were followed for up to 15 months. In order to enable assessment of barriers to medication adherence in the context of the IPAC study, the NACCHO Medication Adherence Response Scale (NMARS) was newly developed and validated following standard principles of psychometric testing.

**Methods:** The NMARS tool was developed within a formal conceptual framework and was then refined by an expert panel, pre-tested with Aboriginal consumers, and pilot tested involving IPAC participants. Content and construct validity of NMARS was assessed. Reliability was evaluated with Cronbach's alpha, inter-item, and item-test correlation. Dimensionality was assessed by principal component analysis (PCA). Semi-structured interviews with IPAC pharmacists were conducted to collect feedback about NMARS practicality and suitability.

For comparison of adherence pre- and post-intervention, de-identified participant data were electronically extracted from health records and pharmacist logbook. Main outcome measures included participant scores using a self-reported adherence assessment with a single-item question (SIQ), the adherence assessment according to the NMARS tool, and the self-assessed health status derived from the first question (SF1) of the Short Form (SF)-36 health related quality of life instrument. Adherence testing scores were dichotomised to "adherence" and "non-adherence", and the 6-point SF1 ordinal results were dichotomised to "very good to excellent" health status versus lesser categories. Changes in binary outcome measures were calculated and are presented with cluster-adjusted (ACCHS) 95% confidence intervals. Statistical comparisons of changes in the three outcome measures were conducted using cluster-adjusted (ACCHS) conditional fixed-effect logistic regression analyses for paired data. The effect of participant, health service, and intervention characteristics on differences of outcome measures were examined, including the influence of Home Medicines Review and other comprehensive medication management reviews, using cluster-adjusted (ACCHS and participant clusters) logistic regression analyses.

**Results:** NMARS content and construct validation procedures affirmed acceptable validity for the newly developed tool. Cronbach's alpha was 0.66 indicating the upper limit for validity and acceptable internal consistency for the purpose of the study. PCA analysis supported unidimensionality of the tool. Pharmacists reported the NMARS and SIQ tools were useful to assess participant adherence.

Participants with paired SIQ and NMARS data (n= 1,103) and paired SF1 data (n=975) were enrolled from 18 ACCHSs involving 26 integrated pharmacists with a median of 213 (IQR: 134-303) and 201 (IQR: 126-279) days between assessments, respectively. Almost all participants were Aboriginal and/or Torres Strait Islander with a mean age at baseline of 58 (SD 29.8) years. At baseline, 70.8% (781/1103) of participants were adherent according to SIQ (scores 6 or 7), 73.3% (808/1103) were adherent according to NMARS (scores 8 to 11), and 18% (175/975) had 'excellent to very good' health status according to SF1. There was a 12.8% (142/1103) and 10.3% (114/1103) net absolute increase in the number of participants adherent to medications at the end of the study compared with baseline (p<0.001), using NMARS and SIQ measures respectively, and a 23.9% (233/975) net absolute increase in the number of participants with improved self-assessed health status (p<0.001).

### Conclusion:

Integrated pharmacists embedded into usual care within ACCHSs in a range of geographical settings, significantly improved the medication adherence of Aboriginal and Torres Strait Islander adults with chronic disease, as well as their self-assessed health status. The NMARS tool was a valid and reliable research tool when used to evaluate the extent of medication adherence and reasons for medication non-adherence in the context of this study.

## INTRODUCTION

Many Aboriginal peoples and Torres Strait Islanders are unable to access medicines to the same degree as non-Indigenous Australians. Even with a nearly three times higher burden of chronic disease, Indigenous Australians were only able to access 41 cents in every dollar of Pharmaceutical Benefits Scheme (PBS) expenditure in 2013-14.<sup>1</sup> This suggests that Indigenous Australians are missing out on the medicines they need, which may partly explain their much higher hospitalization rates.<sup>2</sup> Strategies to enhance Aboriginal peoples and Torres Strait Islanders medication adherence is a national priority as it is for all Australians. It has been estimated that medication non-adherence adds a \$7 billion annual cost burden on the Australian healthcare system due to increased clinic visits, hospitalization, and productivity losses to the nation.<sup>3</sup>

Medication adherence describes the extent to which a patient can take or is able to access medicines as agreed with their prescriber. A range of factors influence adherence including patient characteristics, condition-related, therapeutic, socioeconomic, and healthcare team or system factors as outlined by the World Health Organisation (WHO).<sup>4</sup> It has been suggested that considerable barriers to adherence exist for Aboriginal peoples and Torres Strait Islanders across all these factors,<sup>5</sup> thereby requiring a whole of health system response to tackle them.

One strategy has been to integrate pharmacists within primary health care multidisciplinary teams so that patients and teams can receive better medication management support, direct care from a pharmacist, and a more coordinated experience of care. This strategy is intended to compliment and extend the services provided as usual care by community pharmacists. Increasingly, studies are reporting that the addition of pharmacists to healthcare teams enhances quality prescribing,<sup>6</sup> biomedical outcomes,<sup>7 8</sup> and reduces hospitalisation.<sup>9 10</sup> Co-location of pharmacists within general practice appears to enable greater communication, collaboration and relationship building among health professionals.<sup>11</sup> However, the impact of integrated pharmacists on health outcomes for patients with chronic disease has never been evaluated in Aboriginal health settings.

The Australian Government Department of Health, under the Pharmacy Trials Program (PTP, Tranche 2) funding as part of the Sixth Community Pharmacy Agreement (6CPA) sought to improve clinical outcomes for patients utilizing the full scope of pharmacists' practice in

delivering primary health care services. This Program supported a project to investigate the potential gains in health outcomes arising from integrated models of care within Aboriginal health settings- the *Integrating Pharmacists within Aboriginal Community Controlled Health Services (ACCHSs) to improve Chronic Disease Management (IPAC)* Project. The project explored if integrating a registered non-dispensing pharmacist as part of the primary health care (PHC) team within ACCHSs (the intervention) led to improvements in the quality of the care received by Aboriginal and Torres Strait Islander peoples with chronic diseases, when compared with prior (usual) care. Integration within ACCHSs meant that pharmacists had identified positions and core roles, shared access to clinical information systems, provided continuous clinical care to patients, received administrative and other supports from primary health care staff, and adhered to the governance, cultural, and clinical protocols within ACCHSs as part of their shared vision.

If integrated pharmacists support patients to better address all the WHO dimensions of medication adherence,<sup>12</sup> this may play a significant role in improving patient outcomes as 'drugs don't work in patients who don't take them'.<sup>13</sup> In order to evaluate the impact of this intervention, valid and reliable measures of medication adherence were needed. Self-reported measures of medication adherence have particular value because of the ease of data collection but also because they can inform on both the extent of adherence as well as reasons for non-adherence.<sup>14</sup> Health measurement scales exploring health beliefs and behavioural impediments to adherence can be used to infer and predict medication adherence and may facilitate better patient-provider partnerships to enhance therapeutic outcomes.<sup>15</sup> However, all measures of medication adherence, including direct and objective measures of utilisation, have limitations. There are more than 40 different self-reported adherence scales available, many of which explore behaviour, barriers to medication adherence, and beliefs about taking medicines.<sup>16</sup> A systematic review evaluated studies that reported medication adherence *outcomes* involving the Australian Aboriginal and Torres Strait Islander population and found that few studies explained how they measured adherence. Studies that reported methods used either an unvalidated single question about missing medicines, or pill counts with small-sized cohorts.<sup>17</sup> No study used a self-reported measurement scale specifically applicable to Aboriginal and/or Torres Strait Islander participants to infer medication adherence.

The IPAC evaluators examined existing internationally recognised self-reported measures of medication adherence but considered them unsuitable for use in the Aboriginal and Torres

Strait Islander context. Use of existing instruments would have also required their modification and revalidation for the purpose of the evaluation to ensure that what is inferred by the test is actually correct. Cronbach indicated that what is validated is not the test itself, but the proposed interpretation of the test<sup>18</sup> and “the use to which the instrument is put”.<sup>19</sup> Revalidation aims to reproduce the psychometric properties of the test shown with the original population when it is applied to a different population.<sup>20 21</sup> Many instruments use inappropriate language, are culturally insensitive, or are onerous for patients to answer and pharmacists to administer. Furthermore, they require patients to have a high reading level, and those with Likert scales can be confusing. For example, the 8-item *Morisky Medication Adherence Scale (MMAS)*<sup>22</sup> requires a reader’s age of 13-15 years, but scales aimed for those whose educational levels are unknown should not exceed reading skills of a 12-year-old (Appendix 1).<sup>23</sup> As many scales are disease-specific this also makes them unsuitable for use in generalist settings.<sup>24</sup>

Consequently, the IPAC project used a self-reported indirect method to assess the extent of medication adherence using a single-item question (SIQ): ‘*How many days in the last week have you taken this medication?*’ This question was used to estimate the proportion of days with the correct number of doses taken, which is a frequent summary statistic used for reporting medication adherence.<sup>25</sup> This single question and its variations have been used in the Kanyini study involving Aboriginal and Torres Strait Islander peoples in Australia<sup>26</sup> and internationally.<sup>27 28 29</sup> Even though self-report adherence measures have significant limitations, one study of medication non-adherence measured objectively by gaps in prescription fills was significantly associated with self-reported non-adherence that was defined as at least ‘two days missed’ when taking medicines over the past week.<sup>30</sup> In order to obtain a more comprehensive assessment of adherence-related behaviour, a specific tool exploring the reasons for non-adherence was developed and evaluated for the IPAC project and used by pharmacists together with the SIQ to inform beliefs and behaviour about taking medications and evaluate change in adherence-related behaviour.

The IPAC project hypothesized that pharmacists integrated within ACCHSs may assist Aboriginal and Torres Strait Islander patients with chronic disease to overcome barriers associated with taking medicines. In order to test this hypothesis, changes in medication adherence measures over time were explored. The influence of such change on participant self-assessed health status was assessed as measures of self-assessed health status can

predict mortality and morbidity in people with chronic disease.<sup>31 32</sup> The medication adherence tools were validated as measures of adherent-related behaviour and feedback from pharmacists was additionally sourced regarding the usefulness of these tools. This report describes the medication adherence and self-assessed health status outcomes for participants enrolled in the IPAC trial as well as development, validation, and pharmacists' perceptions of the adherence tools.

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## **METHOD**

### **Study Design**

The IPAC project was a pragmatic, community-based, participatory, non-randomised, prospective, pre and post quasi-experimental study (Trial Registration Number and Register: ACTRN12618002002268) that integrated a registered pharmacist within the ACCHS primary healthcare team for up to a 15-month period. A total of 26 registered pharmacists were recruited to participate in the project, providing 12.3 full-time equivalent pharmacist services for the duration of the study within ACCHS services (n=18). These ACCHSs were recruited for the project across three jurisdictions: Victoria, Queensland and the Northern Territory (NT), and comprised 34% (18/53) of all ACCHSs in these jurisdictions.

The IPAC project methodology has been described in detail elsewhere,<sup>33</sup> including the characteristics of participating health services.<sup>34</sup> Briefly, IPAC pharmacists delivered non-dispensing clinical medication-related services within ACCHSs through a coordinated, collaborative and integrated approach to improve the quality of care of patients (the intervention). The intervention phase of the IPAC study comprised the period from participant enrolment to the end of the study (31<sup>st</sup> October 2019).

### **Study participants**

Patients were eligible to participate in the study if they were aged 18 years and over with a diagnosis of cardiovascular disease (CVD), Type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), or other chronic conditions and at high risk of developing medication-related problems (e.g. polypharmacy). Patients attending ACCHSs for their usual care who met the study inclusion criteria were recruited as participants by health service staff and pharmacists. A non-probabilistic sampling method was adopted to reflect the pragmatic study design where all patients who had the chronic disease conditions were invited to participate without setting criteria for compliance or other restrictions.<sup>35</sup> Patients were consented into the study by pharmacists or other health service staff according to the cultural protocols of the ACCHS.<sup>36</sup> Once consented, pharmacists provided supportive clinical care as part of the primary healthcare team to meet the individual needs of the participant. All participating health service sites included participant access to a general practitioner.

### **Study sites**

ACCHSs deliver culturally appropriate comprehensive primary health care services to predominantly Indigenous Australians and were selected as IPAC services using an expression of interest process, supported by criteria to ensure geographical diversity. The majority of ACCHSs (n=13 of 18) were located in outer regional and remote locations of Australia, and in regions of relative greater disadvantage for Indigenous Australians than other locations based on the Indigenous Relative Socioeconomic Outcomes (IRSEO) index.<sup>37</sup> Participating ACCHS sites were similar to other ACCHSs in their jurisdiction according to geographic location, and proportionate patient distribution by sex and Aboriginality [data not shown].

### **Integrated pharmacist interventions**

As a pragmatic trial, pharmacists functioned within existing and usual primary health care service delivery systems and were trained to deliver ten core roles during the intervention phase. Pharmacists provided medication management reviews (to resolve identified medication -related problems and optimise prescribing quality), assessed adherence and medication appropriateness, provided medicines information and education and training, collaborated with healthcare teams, delivered preventive care, liaised with stakeholders such as community pharmacy, provided transitional care, and undertook a drug utilisation review to support quality improvement within the ACCHS. Medication management reviews comprised either a Home Medicines Review (HMR) or a non-HMR which was defined as a comprehensive medication management review comprising some or all of the elements of a HMR, but not fulfilling all relevant HMR criteria stipulated by the Medicare Benefits Schedule (MBS).

The pharmacist intervention targeted both consented patients (participants) and practices, with practice-specific activities directed to health professionals and systems within the service. All pharmacists had access to participants' electronic medical records held at the ACCHS in order to function as a member of the health care team.

### **Pharmacists**

The Pharmaceutical Society of Australia (PSA) recruited pharmacists to be integrated within ACCHSs by contracting with community pharmacy or directly with pharmacists in partnership with the National Aboriginal Community Controlled Health Organization (NACCHO). IPAC pharmacists fulfilled the following eligibility criteria: registration with the Australian Health

Practitioners Regulation Agency (AHPRA); more than 2 years' post-registration experience; and post-graduate clinical qualifications or demonstrated clinical experience. Accreditation to conduct an HMR was preferred, however it was not mandatory. These criteria enabled the selection of pharmacists with skills aligned to the expected scope of practice for this project.

### Data collection

De-identified participant data was collected from two existing clinical information systems (CIS) used by ACCHSs (Best Practice and Communicare) to manage patients' electronic health records and a bespoke online database (pharmacist logbook) that was used by integrated pharmacists to record participant responses to adherence measures and SF1 assessments. Demographic indices (such as age, sex, ethnicity, pensioner status, number of medications and doctors encounters, prior medication review) were extracted from CISs in de-identified form using an electronic tool called GRHANITE. This tool required remote installation and regular extraction from IPAC sites for the term of the project.<sup>38</sup> Participant consent was recorded in the CIS by pharmacists. GRHANITE extracted data only from consented patients and copied it to a JCU databank employing internationally recognised point-to-point encryption (P2PE) mechanisms to protect data in transit. The participant identification numbers in the GRHANITE extractions were linked with deidentified participant data recorded by pharmacists in the logbook. The pharmacist logbook was a secure password protected online database, accessible from any device connected to the internet, with dual recording and reporting functionality. The electronic interface was developed to be intuitive and user-friendly to minimise the burden of data entry and reporting by pharmacists.

The participants' primary place of residence was not collected for privacy reasons, and so the location of the health service that was attended by the participant was used instead. Participant data on clinical diagnoses, and if they were engaged in a separate initiative known as the Health Care Homes (HCH) program, was also sourced from the logbook. All IPAC services concurrently participating in the HCH program which was designed to better coordinate the health care of patients with chronic disease<sup>39</sup> were located in the NT and predominantly in remote locations. Some participants were also enrolled in an expanded Community Pharmacy in HCH Trial program which provided additional pharmacy support, but these were later excluded from the analysis.

## Outcome measures

Change in adherence-related behaviour assessed using the single item question (SIQ): *'How many days in the last week have you taken this medication?'* was asked for each medication the participant was taking. Pharmacists were trained to express the score as a proportion of the number of days the participant took the correct doses of the medication as prescribed in the preceding week. For example, if the patient took half the doses prescribed for the preceding week, this would be expressed as 50% of the days in the previous 7 days. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day.<sup>40</sup> The mean number of adherent days (score) in the preceding week ranged from 0-7 days, and was based on the mean score for all medications taken by the participant as SIQ responses were assessed for each medicine the participant was taking. This informed the proportion of days with the correct number of doses taken. If the mean number of adherent days for participants was at least 6 of 7 days, this approximated medication adherence for at least 80% of the days indicated, which is a commonly accepted cut-point defining adherence.<sup>41</sup>

An 11-item patient survey tool was developed for the IPAC project to assess the participants' reasons for non-adherence, and was designated the NACCHO Medication Adherence Response Scale (NMARS). The process of development and validation of NMARS is described below. Participant responses to the NMARS were also recorded in the logbook and coded in the participants CIS for data linkage. Pharmacists were not required to calculate adherence test scores. With NMARS, the evaluators derived the total score by summing individual participant scores from each question (item) after applying reverse coding for two items. Out of 11 questions, on an a priori basis, two questions (3 and 5, Table 1) explored a positive trait (knowing how to take medicines; feeling that medicines are good for health) that were reverse scored, whilst the remainder explored negative traits (various difficulties with taking medicine). This yielded a medication adherence score from 0-11, with higher scores representing fewer barriers and therefore better medication adherence. None of the items in the NMARS were negatively worded as such questions are known to be problematic with understanding and interpretation.<sup>42</sup> Adherence and non-adherence cut-scores for the NMARS were set to match the SIQ participant adherence response frequencies as the SIQ had been used as a measure of adherence in other studies. Single-item question scoring was dichotomized to define adherence (a score 6-7 when averaged for all medicines), or non-adherence (a score 0-5).

Self-assessed health status was determined using the first question of the Short Form (SF)-36 health-related quality of life instrument that asks: *'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'*. An extra response option – 'very poor' – was added (as in the SF-8 survey) to reduce the potential for respondents to overstate their health status.<sup>43</sup> Responses to this single-item (SF-1) question have been shown to correlate well with multi-item tools measuring the same construct,<sup>44 45</sup> and are used in the National Aboriginal and Torres Strait Islander Social Survey.<sup>46</sup> Given the SF-1 question is an acceptable method for assessing health-related quality of life, it was used in the IPAC study to minimise survey fatigue<sup>47</sup> for both participants and pharmacists, in accordance with the pragmatic study design.<sup>48 49</sup>

### Timing and process of data collection

Pharmacists underwent prior training (on and off-site) in cultural orientation and were trained to ask and elicit participant answers to the questions from the two medication adherence instruments and self-assessed health status so that data collection was standardized. The pharmacist conducted the assessment as a single instrument, and were unaware that they were using two methods to ascertain adherence. Participant responses were predominantly sourced by pharmacists, with occasional collection from other healthcare staff trained by the pharmacist where appropriate (such as Aboriginal Health Workers). Pharmacists were trained to record activity details into the logbook including participant assessment results. These assessments were completed predominantly within the first three months after participant recruitment into the study (baseline), and again prior to the end of the study.

### Covariates to change in adherence and self- assessed health status

Changes in NMARS, SIQ and SF1 responses that could be attributable to a range of baseline participant, health service, and intervention-related characteristics (defined as covariates) were examined. The participant-related covariates included: mean age at baseline; median length of time in the study (and/or length of time between adherence measures); sex; the median number of medications; and baseline SF1 response. Health service-related characteristics included the IRSEO score of the health service location. Intervention-related characteristics investigated the influence of a HMR and non-HMR type of medication management reviews, as well as MBS rebates for item 10987 and 10997 (participant follow-

up including for medication adherence that is undertaken by a practice nurse or Aboriginal and Torres Strait Islander Health Practitioner).

### Data analysis

All participants with less than 90 days of follow-up were removed from the analysis due to their short length of stay in the study (n=90). Health Care Homes (HCH) participants who were also concomitantly enrolled in another program known as the 'Community Pharmacy in Health Care Homes Trial'<sup>50</sup> were also removed from the analysis (n=47) due to the potential for confounding from the additional support given to individuals in this program. The remaining HCH participants were retained in the analysis. Participants with missing adherence and SF1 data to enable paired data analyses (baseline compared with follow-up) were excluded from the analysis.

Participant characteristics and biomedical indices data was extracted from the JCU SQL Server database using the Navicat 15 for SQL Server (PremiumSoft) database management tool or from the pharmacist logbook as Microsoft Excel files. All data was subsequently analysed using a number of statistical programs including the SPSS Statistics Premium version 24 (IBM) statistical package, Stata/MP 13.0 (StataCorp LP), and Microsoft Excel 2016 (Microsoft). Categorical variables are presented as absolute and relative frequencies. Depending on their distribution, numerical variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) as indicated accordingly. Statistical analyses were cluster-adjusted as the study design involved cluster sampling using ACCHSs as the primary sampling units.

For the outcome measures NMARS, SIQ, and SF1, the first assessment within the first 90 days was defined as baseline, whilst the last assessment prior to the end of the study was defined as the follow-up assessment. Change in SF1 assessment from baseline was defined as 'improved' or 'worsened'. The original six SF1 categories were converted to binary outcomes so that 'yes' pertained to 'excellent, very good' ratings and 'no' pertained to 'good, fair, poor, very poor' ratings. 'Improved' was defined as a change from 'no' to 'yes' and 'worsened' was defined as the reverse change when baseline and follow-up assessments were compared. Responses to the SIQ tool which originally ranged from 0 to 7, were categorised into scores 0 to 5 as "non-adherence" and 6 or 7 as "adherence" (consistent with the commonly accepted cut-point defining adherence) and improvement or worsening was similarly defined as changes between these categories when baseline and follow-up assessments were compared.

Responses to the NMARS tool which originally ranged from 0 to 11, were categorised into scores 0 to 7 as “non-adherence” and 8 to 11 as “adherence” (to match the cut-scores for the SIQ) and improvement or worsening was similarly defined as changes between these categories when baseline and follow-up assessments were compared. Changes in categorised outcome measures were calculated and are presented with cluster-adjusted (ACCHS) 95% confidence intervals. Statistical comparisons of changes in the three outcome measures were conducted using cluster-adjusted (ACCHS) conditional fixed-effect logistic regression analyses for paired data (svy: clogit command of Stata).

The most recent HbA1c value in the 12 months prior to enrolment for participants with T2DM was defined as baseline. For all other biomedical indices the mean baseline values from participants during the preceding 12-month period prior to trial enrolment was used. The effects of participant, health service, and intervention characteristics on the changes in the three outcome measures were examined using cluster-adjusted (ACCHS and participant clusters) logistic regression analyses (svy: logit command of Stata). Statistical significance was defined at the conventional 5% level. Statistical methods used to assess reliability and validity of the adherence measures used are described below.

### **Ethics approval**

Ethics approval for the project was received from four ethics committees in the three jurisdictions including St Vincent’s Hospital Melbourne (SVHM) Human Research Ethics Committee (HREC), Victoria (HREC/17/SVHM/280), James Cook University HREC (mutual recognition of SVHM HREC, approval HREC/H7348), Menzies School of Health Research (HREC/2018-3072) and the Central Australian HREC (HREC/CA-18-3085).

### **Development and validation of adherence measure NMARS**

#### **Development of the NMARS and conceptual framework**

Existing international self-reported measures of medication adherence were reviewed to identify those relevant to the Aboriginal and Torres Strait Islander context (SEAMS<sup>51</sup>, MMAS-4/8<sup>52</sup>, ASK-12,<sup>53</sup> ARMS,<sup>54</sup> RAMS,<sup>55</sup> and BMQ<sup>56</sup>); including a systematic review that explored the reasons for medication non-adherence involving Indigenous Australians.<sup>57</sup> From this review, an initial 16-item scale was derived to explore the reasons for medication non-adherence (Appendix 2). The items were categorised into distinct domains based on the Theoretical Domains Framework that summarises 33 theories of the determinants of human behaviour

(including the Health Belief Model).<sup>58</sup> This conceptual framework offered an explicit theoretical basis for NMARS items for face and content validity, covering issues known to affect the adherence-related behaviour of Aboriginal peoples and Torres Strait Islanders. This tool could then be used to guide pharmacist interventions to influence participant behaviour.

The NMARS items aimed to explore the following reasons for medication non-adherence:

- forgetting to take doses
- stopping medicines once feeling better
- sharing or swapping medicines
- beliefs about not needing to take medicines
- travelling away from home or the community
- issues with obtaining medicines whilst away from home
- having other priorities such as sociocultural obligations
- inadequate safe storage of medicines at home
- cost of medicines
- complex dosing schedules.<sup>59</sup>

The items were phrased to be consistent with behaviour change theories such as the Health Belief Model (HBM), which is a psychological framework to predict health behaviour and inform motivational interviewing.<sup>60</sup> Used with participants, NMARS items aimed to explore perceived benefits arising from medication adherence, perceived barriers such as difficulty taking medicines; and perceptions of the severity of outcomes from non-adherence. Success factors for adherence included a belief in the necessity for medication and trust that the medication would be of benefit to health; that the prescription could be paid for and filled; and that there was self-efficacy (confidence in one's ability to take medications, and the capacity for self-management including in situations like travel and responding to social obligations towards the sharing of medicines), knowledge, and cognitive ability. In this way, the items aimed to inform on adherence related behaviour and differentiate people who took their medicines as agreed (adherent) from those who didn't (non-adherent).

As patients tend to overreport adherence to avoid disapproval from their healthcare providers (social desirability bias),<sup>61</sup> questions were phrased to generate a 'yes' response as recommended by other scale developers.<sup>62</sup> For example, non-adherent patients could find it challenging to answer 'no' to the following question: 'did you remember to take your medicines?' Rather, asking a non-adherent patient: 'did you forget to take any of your

medicines yesterday'? would generate a 'yes' which may reduce underreporting of adherence.<sup>63</sup>

NMARS responses were set as categorical and dichotomous (yes/no) to best suit low English literacy and time-restricted clinical research settings such as the IPAC project. Likert scales were not developed to grade answers to questions as they are potentially problematic for populations with low literacy in English such as in ACCHS and remote settings<sup>64 65</sup> and considerably lengthen the time to administer the survey. Visual analogue scales were not used as the scale was scored by pharmacists and was not administered by participants themselves.

### Face and content validity of NMARS

The content validity of the NMARS tool was evaluated iteratively after adaptation of an existing clinical sensibility tool<sup>66</sup> from which a scale-specific content validity index (S-CVI) was derived (Appendix 3A). An item-specific content validity index (I-CVI, Appendix 3B) was derived and adapted from other sources.<sup>67 68</sup> The project team (n=9), comprising of medical researchers, pharmacists, and Aboriginal and Torres Strait Islander academics, initially completed this testing, which led to revision and reduction of the scale from 16 to 11-items by consensus after clinical sensibility testing.

Further testing of the 11-item NMARS was conducted with:

- i) a broader 15-member multidisciplinary expert panel comprising pharmacists, Aboriginal and Torres Strait Islander academics, and public health physicians;
- ii) 15 members of the North Queensland Aboriginal community (pre-testing).

Expert panel members were asked to rate each item within the NMARS with regard to relevance and clarity (Appendix 3B). An item was considered *relevant* if it explored the 'extent' of medication adherence and 'reasons for non-adherence'. The item had *clarity* if it was unambiguous, easy to use, and Aboriginal and Torres Strait Islander patients were likely to understand it. The S-CVI and I-CVI were reported as the proportion of agreement by experts for the scale as a whole and for each item in the scale. An I-CVI and S-CVI of > 79% meant the item was appropriate, 70% -79% meant it needed revision, and < 70% meant it needed elimination.<sup>69</sup> Revisions were made to the items based on results and feedback and the NMARS tool was subsequently endorsed by the JCU Evaluation Team on 1 May 2018.

## Question properties of NMARS

### *Reading level*

The reading level of the NMARS was assessed with the online *Readability Consensus Calculator* using the Flesch Reading Ease Scale and other scales.<sup>70</sup> Results were confirmed using the reading level calculator (Flesch Reading Ease Scale) in Microsoft Word. The scale was assessed for ambiguous and incomprehensible terms using the online *Question and Understanding Aid (QUAID)* tool.<sup>71</sup> The tool identified potential problems that respondents might have in comprehending the meaning of questions on questionnaires.<sup>72</sup>

### *Floor and ceiling effects*

Floor and ceiling effects were assessed by mapping adherence test response frequencies. A ceiling or floor effect for individual items was evident if more than 80% of participants achieved the best score for a single item.<sup>73</sup>

### *Pre-testing (Aboriginal and Torres Strait Islander consumer group)*

To assess if the NMARS items were easy to understand, the revised scale was pre-tested (single round) with 15 members of a North Queensland Aboriginal community. Members of the community were recruited and interviewed in several locations including: local shopping centres, hardware stores, and in five private residences. An Aboriginal academic (Chair of the Aboriginal and Torres Strait Islander Peoples Strategic Committee, College of Medicine and Dentistry, James Cook University) conducted the interviews from 23rd -27th April 2018. The NMARS was administered verbally, mostly to individuals, and the answers were recorded. Interviewees were also asked to comment on the clarity of each question. Interviewees were provided with a \$25 voucher for their time. The perspectives of the Aboriginal academic who conducted the interviews were also noted.

### *Pilot testing of adherence measures NMARS and SIQ*

Pilot study data was used to initially evaluate the adherence tests and the practicality of administration. Pharmacists entered deidentified participant responses to the two tests of adherence (NMARS and SIQ) into the logbook in real-time. This pilot used baseline data from the first 150 participants recruited into the IPAC study (8 August–12 October 2018).

### Construct validity of NMARS tool

Assessing construct validity means to assess a scale's ability to perform as expected. In order to validate the SIQ as a proxy criterion and comparator to the NMARS for construct validity testing, the correlations between SIQ responses and certain biomedical indices at baseline were evaluated. The baseline clinical indices that were explored included systolic and diastolic blood pressure (BP), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and glycated haemoglobin (HbA1c) in participants with type 2 diabetes mellitus (T2DM). The aim of this analysis was to assess if associations between biomedical indices and SIQ scores were in line with clinical expectations. Spearman rank correlation coefficients together with 95% confidence intervals are presented.

If the NMARS identified medication adherence to the same extent as the SIQ and the two tools were highly correlated, this would provide supportive evidence for convergent validity which is a type of construct validity testing for instruments assessing the same or similar constructs.<sup>74</sup> In this respect, the NMARS was tested for construct validity by assessing for:

- a) the convergence of participant responses with a comparative tool (the SIQ),
- b) associations between adherence scores and the number of medications per participant,
- c) known-group comparisons, and
- d) if self-reported adherence scores were associated with self-assessed health status (SF1).

Details for these assessments are described below.

#### *a) Convergent validity of NMARS*

To support convergent validity testing,<sup>75</sup> the degree of overall agreement (%) between the SIQ and NMARS was assessed after using the SIQ definition of adherence to set the cut-off scores for adherence from participant responses to the NMARS.

Using NMARS and SIQ responses, the prevalence of adherence at baseline was compared between participant subgroups to assess if the two tools produced similar adherence to non-adherence ratios. The subgroups comprised participants stratified by a mean systolic blood pressure (SBP) < or  $\geq$ 140 mmHg; a clinical diagnosis of chronic kidney disease and a mean baseline albumin-creatinine ratio of < or  $\geq$  30mg/g; and a baseline HbA1c of < or  $\geq$  6.5% in participants with T2DM.

### *b) Correlation between adherence and number of medications*

Further construct validity testing of both NMARS and SIQ adherence tools examined if there was a logical correlation between medication adherence scores and the number of medications prescribed for participants. Spearman's correlation coefficients and 95% confidence intervals were calculated and scatterplots depict the associations. In the pilot study (results not shown), there was better adherence as the number of medications prescribed for participants increased. A positive correlation was therefore proposed between better adherence and polypharmacy. Usually, participants taking many medications are expected to have less adherence than those taking fewer medications, although this relationship is context specific and more complex than it appears,<sup>76</sup> particularly as this effect can be modulated by devices such as dose-administration aids (DAA).<sup>77</sup>

### *c) Known-group comparisons*

Testing for known-groups validity using both NMARS and SIQ scores was undertaken by exploring tool performance in participant groups that logically should have different (or no difference in) adherence-related behaviour from each other. This was to assess whether the hypothesized association with adherence was reflected in the expected direction of the adherence scores of the groups. Based on international studies, we did not expect differences in medication adherence between those with elevated or normal BMI<sup>78 79</sup> or between male and female participants at baseline.<sup>80 81 82</sup> Participant scores for NMARS and SIQ were therefore examined with regard to i) dichotomized BMI ( $\geq 25$  kg/m<sup>2</sup> and  $< 25$  kg/m<sup>2</sup>), and ii) sex.

### *d) Correlation between adherence tools and SF1*

Construct validity was also assessed by comparing SIQ and NMARS responses at baseline and at the end of the study with another tool for self-assessed health status (the SF1) to examine if these instruments showed associations in the expected direction.<sup>83</sup> Spearman's correlation coefficients were calculated and presented with 95% confidence intervals. Analysis was based on responses that were z-transformed to compare scales with similar ranges.

## Reliability testing of NMARS tool

### *a) Internal reliability*

As a measure of the internal reliability of derived test scores, Cronbach's alpha was computed for the NMARS tool. An alpha value of 0.7-0.9 was considered acceptable for group comparisons.<sup>84</sup> The effect of NMARS item deletion on Cronbach's alpha was also explored. If the effect of item deletion was to increase the alpha value by >10%, this would potentially warrant item deletion from the scale.<sup>85</sup>

### *b) Inter-item correlation*

An inter-item correlation matrix was also examined for the NMARS by calculating respective Pearson's correlation coefficients. Correlation coefficients inform the degree to which scores on one item relate to scores on each other item in a scale.<sup>86</sup> An average inter-item correlation in the range of 0.15 to 0.50 was considered ideal,<sup>87</sup> suggesting the items are assessing a common construct. Inter-item correlations less than 0.15 suggest distinctive traits or states are being explored (noting that this may be desirable for validity). High correlations suggest items may be overly redundant or repetitive and fail to capture the degree of variance in the construct.

### *c) Item-test (item-total) correlation*

Similarly, item-test correlation (an index of item validity) by calculating respective Pearson's correlation coefficients, was undertaken between each NMARS item and the overall total scale score, using the same ideal coefficient reference range as for inter-item correlation. A higher coefficient reflects a higher degree of correlation between the item and the total scale score as an indicator of internal consistency.

## Dimensionality

Principal Component Analysis (PCA) was undertaken to ascertain if the NMARS tool was unidimensional. In PCA, if the scale is unidimensional, the items should be highly loaded with only one principal component (factor). Factor loadings for each item was based on yes-no participant responses. We adopted the standard where the eigenvalue of the first factor should account for at least 20% of the variance in the scale items, although there are widely varying standards to define 'considerable' loading onto the first factor.<sup>88</sup> Item loadings of at least 0.4 were considered acceptable and representative of a relevant contribution of the item to a factor.<sup>89</sup> Although the optimal subject-to-item ratio to undertake PCA is unable to be

specified, we accepted a ratio of at least 10:1,<sup>90</sup> which was satisfied given the size of the study.

#### Pharmacist feedback on the use of adherence tools

Pharmacist feedback on the adherence tools was sourced through semi-structured interviews conducted with IPAC pharmacists between June and August 2019. The interviews took place after pharmacists had completed at least 6 months of their placement within ACCHSs using an interview proforma developed by the qualitative evaluation team based on the project protocol. Consent was sourced at the time of pharmacist recruitment into the project. IPAC pharmacists were invited to participate via email and provided with a list of potential interview times. Interviews were undertaken by Zoom or telephone by two members of the qualitative evaluation team and digitally recorded, transcribed verbatim through the program TRINT and imported to the qualitative management software package, NVivo 12 [62] to facilitate data management and qualitative analysis. Interviews were part of a broader qualitative evaluation of the IPAC project that has been reported elsewhere.<sup>91</sup>

Not for distribution

## RESULTS

Of 1,733 patients who consented to participate in the study, the IPAC cohort included in the analysis after initial exclusions comprised 1,456 enrolled participants who remained in the study until the end (Figure 1 and 2). Initial participant exclusions were for those with insufficient data for analysis (n=138), or if study enrolment was less than 90 days (n=40). Participants were also withdrawn from the study (n=99) if evidence of consent was missing (n=38), if there was concomitant enrolment in the HCH community pharmacy support program (n=47), or for other reasons (n=14).

Paired data for medication adherence assessments was available from 75.8% (n=1,103) of participants. The remainder (n= 353) had either missing baseline or follow-up adherence assessments. For participants included in the adherence analysis, the median length of stay in the study from enrolment was 266 (IQR 210-325) days. The median time interval between adherence assessments was 213 (IQR: 134-303) days. Paired data for SF1 assessments was available from 70.0% (n=975) of participants (Figure 2). For participants included in the SF1 analysis, the median length of stay in the study from enrolment was 281 (IQR 218-336) days. The median time interval between SF1 assessments was 201 (IQR: 126-279) days.

### Participants

The characteristics of participants with paired medication adherence assessments are shown in Table 2 (n=1103). The mean age of participants was 58 (SD 29.8) years, 61.6% were female, the vast majority (93.2%) were Aboriginal and/or Torres Strait Islander, 84.4% were eligible for social support (pensioner or other concession card holders), and 88.3% had one or more chronic diseases, requiring a mean of 7.3 (SD 13.3) medications each. Most participants (73.8%) attended health services located in inner and outer regional locations, and most of the remainder (23.5%) attended remote or very remotely located health services. Very few participants (2.7%) attended health services located in urban centres.

At baseline, nearly 18% (175/975) of participants with paired medication adherence assessments who also had a SF1 result, had 'excellent to very good' self-assessed health status. At baseline, the mean number of days that participants were deemed to be adherent to medications (SIQ score) was 6.1 (SD 6.6) of the previous 7 days. Only 10.5% of participants had a HMR in the 12 months prior to their enrolment in the project.

The characteristics of participants with paired SF1 assessments is shown in Table 3 (n=975), and were very similar to those with paired medication adherence assessments.

### Change in medication adherence

The changes to participant medication adherence after follow-up are shown in Tables 4 and 5 according to NMARS and SIQ, respectively. By the end of the study, there was a significant increase in the number of participants who were adherent to medications compared with baseline, which was evident using both tests of adherence. According to the NMARS, there was a 12.8% (142/1103) net increase in the number of participants adherent to medications at the end of the study compared with baseline ( $p<0.001$ ). This was derived from the number of participants who improved their adherence (changed from not adhering (score  $<8$ ) to adhering (score of 8-11) during follow-up) and subtracting those whose adherence worsened (changed from adhering to not adhering during follow-up). There were 204 (18.5%, 95%CI 15.4%-22.1%) participants who improved, whilst 62 (5.6%, 95%CI 3.5%-9.0%) had worse adherence, leaving 142 participants with a net improvement in medication adherence. According to the SIQ, there was also a significant net 10.3% (114/1103) increase in the number of participants who were adherent to their medications at follow-up compared with baseline ( $p<0.001$ ).

Based on the measure of adherence using the NMARS, participants with poorer self-assessed health status at baseline were more likely to improve their adherence to medications than those whose self-assessed health status was superior ( $p=0.01$ ). According to the SIQ test, whether a participant rated their health as excellent or poor at baseline, made no difference to adherence outcomes at follow-up ( $p=0.56$ ). The relatively larger shifts in adherence detected by the NMARS test compared with the SIQ test in those with poorer self-assessed health status may explain these differences (Table 4).

Whilst both HMR and non-HMR recipients significantly improved their medication adherence, HMR recipients had a greater net improvement in adherence at follow-up than non-HMR recipients although this difference was not statistically significant using NMARS ( $p=0.06$ ).

This difference was significant using the SIQ adherence test, showing that HMR recipients were more likely to improve their medication adherence than non-HMR recipients at follow-up compared with baseline ( $p<0.001$ , Table 5).

According to the SIQ, participants younger than 58 years of age were significantly more likely to improve their medication adherence than those 58 years or older ( $p=0.002$ , Table 5), whereas this association was not identified using the NMARS ( $p=0.46$ , Table 4). None of the other covariates appeared to differentially influence the medication adherence of participants as measured using the NMARS or SIQ, with all participant subgroups showing improved adherence from baseline estimates.

### **Change in self-assessed health status**

Change in the SF1 measure for participants after follow-up is shown in Table 6 and Figure 3. By the end of the study, there was a significant increase in the number of participants whose self-assessed health status improved when compared with baseline ( $n=233/975$ , 23.9%,  $p<0.001$ ).

Irrespective of the type of covariate examined, self-assessed health status improved upon follow-up. Participants who were already adherent at baseline according to the SIQ ( $n=783$ ) were more likely to improve their SF1 rating at follow-up, than participants who were non-adherent at baseline ( $n=192$ ,  $p=0.007$ , Table 6). Participants who were prescribed 7 or more medications at baseline ( $\geq$  median medication,  $n=554$ ), were also more likely to improve their SF1 rating upon follow-up than those prescribed fewer medications at baseline ( $n=421$ ,  $p=0.013$ , Table 6).

### **Validation of adherence measure NMARS**

#### **Conceptual framework for the NMARS (face validity) and content validity**

An outline of the conceptual framework for NMARS is shown in Table 7. There were conceptual differences between the NMARS and other comparative self-reported medication adherence tools. However, any similarities between the items in the tools may have been a function of the limited number of ways in which to ask about a specific problem - a known problem with the development of new health measurement scales.<sup>92</sup>

Expert panel testing of the NMARS revealed an I-CVI of 80% or above for all questions on relevance (Table 8), and for 9 of the 11 questions for clarity. Two survey questions (Questions 6 and 10) needed revision to enhance clarity (I-CVI=73%, Table 9). These two questions contained wording thought to be contentious such as “scared” and taking medicines in the way “you have been told” and were reworded. Other feedback included recommendations to

reorder the questions and to broaden the question about the cost of medicines. In response to feedback, wording was made more consistent (such as use of the word 'medicines', and 'sometimes'), and clearer (such as replacing 'fewer' with 'less'). Expert panel content validity testing of the revised scale as a whole demonstrated a mean S-CVI of 77% of overall agreement between respondents (95%CI 63.6 - 89.7%, Table 10), which was considered acceptable.

## Question properties of NMARS tool

### *Reading level*

The NMARS reading level was assessed to be 'easy to read' and suitable for a 10-11-year-old reading age (Flesch Reading Ease Scale score of 81.5, where a higher score indicates easier reading on a scale of 0-100). In comparison, the 8-item Morisky Medication Adherence Scale<sup>93</sup> was assessed to be of standard/average readability, suitable for 13-15-year olds (Flesch Reading Ease Scale score of 66.6).

### *Ambiguity*

QUAID testing of each item in the NMARS demonstrated few problems with wording, syntax, or semantics. Items containing the term 'sometimes' were identified as having frequency ambiguity. Question 9 had 'quantification ambiguity' with the inclusion of words such as 'much' or 'more' as well as 'working memory overload' that "requires the respondent to hold too much information in mind at the same time". The question was modified after pilot testing to just one 'or' item eliminating the 'working memory overload' result on QUAID. This change did not affect internal consistency in the pilot study as tested with Cronbach's alpha. Fidelity to the conceptual framework was maintained given that 'running out' of medicines is consistent with 'missing out' on taking the medicine. The quantifying terms such as 'much' and 'more' were retained because they were familiar to respondents involved in the pre-test, and the scale needed a reference to frequency and quantity despite the imprecision in language.

The word 'sometimes' was not removed from the NMARS despite frequency ambiguity as its inclusion was thought to make the question less accusatory and more relatable to Aboriginal and Torres Strait Islander participants ensuring validity within the study context. 'Sometimes' running out of medicine, was interpreted to mean the same as 'any recent occurrence' of running out of medicine, with the reference time period for recall being deliberately

unspecified. Rather, the construct aimed to elicit the perception of 'running out' of medicines, not a quantitative estimate of the frequency of this event. As the experience of 'running out' of medicines changes over time (ceases altogether, or becomes apparent), it was assumed that a respondent's perception of 'running' out of medicine would also change. It was also noted that the MMAS-8 scale<sup>94</sup> also included the word 'sometimes'.

### Pre-testing of NMARS tool

Of the 15 Aboriginal community members interviewed to pre-test the NMARS, 9 were female (60%), 8 were aged 35-50 years (53%) whilst the remainder were over 50 years. Seven interviewees (47%) had some form of employment and the remainder were either retired or unemployed. The majority of the interviews were conducted one-on-one, including with one couple.

All interviewees were able to answer each question, and no interviewee asked to have the question repeated. Each question was rated as 'very clear'. Interviewees felt the questions stimulated discussion, were unthreatening and made them willing to share information. The interviewer reported: *"I was really quite surprised with their willingness to voice...to air their thought processes around their medication taking"*. The questions highlighted issues that interviewees wanted to talk about. The couple sometimes discussed the questions between each other. There was no sense that the questions encouraged dishonesty as interviewees were comfortable sharing their true feelings. The interviewer reported: *"I thought the answers were really honest, and the replies were genuine"*. The interviewer indicated that respondents believed this was the first time anyone, other than the doctor, had asked them about their medications and they felt this showed that someone cared about them.

Broadening the question about the cost of medicines as a barrier to 'get more' medicines was justified as *"the cost [of medicines for interviewees] was not an issue like it was in the past"*. This question was modified after content validity testing by the expert panel. The modified question (Q9) asked: *"do you sometimes run out of medicines because it costs too much or it is hard to get more?"*

### Pilot testing of NMARS tool

Pilot testing of the NMARS with 150 participants did not lead to any other changes to the scale. Reliability by Cronbach's alpha was 0.66 with less than 10% reduction following item

deletion, so no item was deleted. In view of the minimal change to the scale arising from QUAID testing and no change to the theoretical construct, pilot-testing data was merged with IPAC participant data as a whole as has been recommended elsewhere.<sup>95</sup>

### NMARS and SIQ response frequencies

Item-specific response frequencies to the NMARS at baseline are shown in Table 11. Items 3, 5, 6, and 10 had ceiling effects (scores clustered towards the best possible score) indicating that participants expressed little variation in knowledge about taking their medications, the necessity for medications, and behaviour about rationing or sharing medicines, so that responses were directed towards adherence.

### Construct validity of NMARS tool

#### *SIQ correlations with biomedical indices at baseline*

Of participants with T2DM, 65% (441/677) had baseline HbA1c results that were assessed for correlation with the baseline SIQ number of adherent days. Participants with a higher HbA1c at baseline tended to have poorer medication adherence according to the SIQ (Spearman's correlation coefficient = -0.20,  $p < 0.001$ , Table 12). Participants with higher baseline measures for TC, TG and LDL-C also had significantly poorer medication adherence with Spearman's correlation coefficients of -0.15 ( $p = 0.0006$ ), -0.09 ( $p = 0.026$ ), and -0.12 ( $p = 0.012$ ) respectively (Table 12,). No statistically significant correlation was found between the baseline level of HDL-C, SBP and DBP with regard to SIQ adherence score (data not shown). Overall, these results support acceptable construct validity of the SIQ as a comparator to the NMARS test.

#### *Convergent validity of the NMARS tool*

The SIQ cut-off score for adherence (score of 6-7) indicated that 781 of 1103 (70.8%) of participants were adherent to their medications at baseline. An NMARS cut-off score for adherence that matched this prevalence was a score of  $\geq 8$ , and this applied to 808 of 1103 (73.3%) participants. Based on a dichotomous distribution of scores (adherent and non-adherent), the participant response frequencies for the NMARS and SIQ assessments are shown in Table 13. There was 79.6% overall agreement between SIQ and NMARS participant responses in the classification of adherence and non-adherence (196 + 682/1103).

Both NMARS and SIQ adherence tests showed a consistent 30:70 proportionate split in non-adherence to adherence for every participant subgroup considered (Table 14). In other words,

more than two thirds of participants were designated as adherent to their medications at baseline irrespective of their clinical condition (such as whether participants were hypertensive or normotensive), and this was evident using both adherence tests.

#### *Correlation between adherence and number of medications*

A positive and significant linear correlation between higher SIQ scores and the number of medications per participant at baseline is shown in Figure 4 (Spearman's correlation coefficient = 0.24, 95% CI 0.18-0.30,  $p < 0.0001$ ). Similarly, higher NMARS scores positively correlated with a higher number of medications per participant at baseline (Spearman's correlation coefficient = 0.15, 95%CI 0.09- 0.21,  $p < 0.0001$ , Figure 5). This means that at baseline, the more medications prescribed for participants, the more likely they were to be adherent to their medications, and this was evident with both tests of adherence.

#### *Known-group comparisons*

Neither the NMARS nor the SIQ tool identified a difference in adherence category by participant sex or by BMI, which is consistent with our hypothesis (Table 15). Both adherence tests performed similarly in identifying the adherence pattern of participants according to their sex or BMI. Participants with BMI up to 24.9 kg/m<sup>2</sup> were just as adherent as participants with BMI  $\geq 25$  kg/m<sup>2</sup>. Similarly, female participants were just as adherent to their medications as males, using both the SIQ and NMARS. The largest difference noted was 4.5% between the sexes for adherence according to SIQ.

#### *Correlation between adherence tools and SF1*

Baseline and follow-up SF1 responses positively correlated with both baseline and follow-up SIQ and NMARS responses. Spearman's correlation coefficients ranged from +0.12 to +0.28 showing weak to moderate positive correlations; all associations were statistically significant ( $p \leq 0.0001$ ). NMARS responses correlated more strongly with SF1 compared to SIQ responses (Table 16). This analysis shows that both adherence tools exhibited a logical relationship between adherence and self-assessed health status, in that participants with better adherence tended to rate their health status higher.

#### *Reliability of NMARS adherence measurement*

Cronbach's alpha computed for all participant responses to the NMARS was 0.66 providing acceptable evidence for internal consistency (reliability) for the purpose of the IPAC study.

Item deletion minimally reduced Cronbach's alpha (Table 17) and any increase in Cronbach's alpha from item deletion was considerably less than 10%.

#### *Item-test correlation*

Item-test correlation showed a similar degree of correlation between the score for each item and the total scale score computed from the other items in the set, with the exception of items 3, 5, 6 and 10 (Table 17), as there was little variability in answers to these items due to the ceiling effects (Table 11).

#### *Inter-item correlation*

All items demonstrated statistically significant correlations with at least one or other items ( $p < 0.05$ , Table 18). Most items had a Pearson's correlation coefficient of at least 0.15 with another item (up to 0.43) which is consistent with the ideal range and suggests the items are largely measuring the same construct. The exceptions were items 3, 5, 6 and 10 with inter-item correlation coefficients  $< 0.15$ . Overall, the NMARS had a low to moderate item homogeneity, which means it has a broad coverage of the adherence construct without redundancy and repetition, as all inter-item correlations were  $< 0.75$ .<sup>96</sup>

Most items correlated negatively with items 3 and 5 supporting reverse scoring of these items. Item 5 correlated negatively with items 1, 7 and 8. Item 5 asks: *'do you feel that taking your medicines will be good for your health?'*. Health belief theory suggests that a perceived benefit of medicines should be linked with better adherence behaviour, so a 'yes' answer to item 5 would be expected to negatively correlate with a 'yes' answer to item 1 that asks *'did you forget to take any of your medicines yesterday?'* or item 7 that asks: *'do you sometimes stop taking your medicines because you think you are ok?'*. The same reasoning applies for item 8 that asks *'do you sometimes stop taking your medicine because you think it might make you sick?'*. Item 3 asked *'do you know when and how to take your medicines?'* which correlated negatively with items 4, 7 and 11, but there was negligible correlation with the other items. Item 10 showed correlation only with item 2.

Items 3 and 5 lacked correlation with each other. This result is best explained by the lack of variability in the traits measured by these items, including with items 6 and 10, because of ceiling effects (Table 11).

## Dimensionality

### *Principal component analysis for NMARS*

Principal component analysis showed that 30.3% of the variance in the 11 items was accounted for in the first factor, with an eigenvalue that was 2.4 times that of the next factor with a clear inflection point as shown in the scree plot (Table 19 and Figure 6). This supports scale unidimensionality (measurement of a single attribute) based on a recommendation that the first factor should account for at least 20% of the variance.<sup>97</sup>

Analysis of NMARS items indicate that most items loaded on the dominant first factor (Table 20) although none of the items loaded to at least a value of 0.4 on any factors. Items 3, 5, 6 and 10 did not load well on factor 1 or other factors, again likely reflecting the lack of variability in participant responses to these items. Item 9 also loaded on other factors suggesting that concerns about running out of medicines may also reflect other traits as well as forgetfulness and health beliefs explored by the NMARS. For all other items, the percentage of variance explained by the second and third factors was too small to conclude that they represented meaningful separate attributes in the construct of adherence.

### *Pharmacist feedback on the use of adherence tools*

Integrated pharmacists (n=24) were interviewed regarding the use of the NMARS and SIQ,<sup>98</sup> and most found the tools useful for the purpose of assessing participant adherence. In particular, pharmacists repeatedly described the NMARS as a conversation starter about taking medicines, that also acted as a prompt to discuss adherence barriers that might not have otherwise been raised. Just over half of the pharmacists reported that the NMARS questions were generally easily understood by participants but that some further explanation or clarification may have been required for some of the questions depending on the individual. Many pharmacists adapted the delivery of the questions into a conversational style, whilst reassuring the participant that there were 'no right or wrong' answers.

Some of the NMARS questions were difficult to understand for participants with very little English, particularly as some questions differed in subtle ways. For example, participants remarked on the similarity of items 3 and 4. One pharmacist reported that item 7 which asked: 'do you sometimes stop taking your medicines because you think you're okay?' was difficult for patients to understand. The main concern was that the question appeared to suggest that stopping medicine was 'the correct' answer. One pharmacist noted that whilst

item 1 referred to forgetfulness, the issue for some participants was intentional rather than unintentional nonadherence. With regard to the SIQ, a few participants had difficulty remembering the number of days that they had taken all doses of their medications over the previous 7 days.

Pharmacists felt that participants were not necessarily honest with their answers the first time they completed the NMARS. Two-thirds of the pharmacists felt that participant responses were more honest at follow-up encounters than baseline due to the enhanced rapport in the therapeutic relationship. Pharmacists also reported that participants had told them that their adherence had much improved since the initial survey encounter, with some participants admitting that they had not been entirely honest with their answers at that time.

Some pharmacists noted that little had been done in the past to address the issue of medication adherence with patients at their health service. Participants had told pharmacists that staff had previously not taken the time to explain their medications to them. Subsequently, improvements in medication adherence were attributed to enhanced participant education, changes in prescribed medications, and simplification of medication regimens as recommended by pharmacists.

Not for distribution

## DISCUSSION

Integrated pharmacist interventions led to significant increases in self-reported medication adherence and improvements in self-assessed health status of Aboriginal and Torres Strait Islander adults with chronic disease enrolled in the IPAC study. These changes were evident over a median interval between assessments of just over 6 and a half months, using both measurement tools for adherence and the SF1 measure. Participants comprised patients attending ACCHSs with at least one chronic disease, where nearly 90% also had comorbidity ( $\geq 1$  chronic medical conditions); and the average age of the cohort was 58 (SD 29.8) years.

A statistically significant net improvement in adherence and self-assessed health status was observed for all participants, irrespective of the number of medications prescribed at baseline. Self-assessed health status also improved to a significantly greater extent in participants prescribed more medications at baseline ( $\geq 7$ ), or those already adherent at baseline, than those prescribed fewer medications or less adherent at baseline. This is consistent with the positive correlation identified at baseline between the number of prescribed medications per participant and the extent of self-reported adherence to these medications.

A statistically significant net improvement in self-assessed health status was observed for all participants, irrespective of whether they were HMR or non-HMR recipients. In contrast, medication adherence improved in HMR recipients to a greater extent than non-HMR recipients, shown with both tests of adherence, although this was only significant with the SIQ test. Elsewhere it was shown that demographic and clinical characteristics of HMR and non-HMR recipients did not meaningfully differ,<sup>99</sup> although a greater proportion of non-HMR recipients attended remote and very remote health services than HMR recipients.<sup>100</sup> This suggests that the lesser improvement in adherence in non-HMR recipients may have been influenced by remoteness factors rather than the type of medication management review being conducted. It was observed that relative to the the median IRSEO score, the location of health services (level of Indigenous socioeconomic disadvantage) by IRSEO score made no difference to improvements to either participant adherence or self-assessed health status.

Change in medication adherence was assessed in this study using the SIQ and a new 11-item tool (NMARS) tested for validity and internal reliability. The NMARS was developed as a patient survey for use with Aboriginal and Torres Strait Islander peoples in culturally

appropriate comprehensive primary healthcare settings, to enable valid inferences to be drawn about medication adherence given the lack of other validated measures suitable for this context. The NMARS was used together with the SIQ to offer direct and indirect self-reported measures of adherence. The SIQ quantified self-reported measures of adherence over a 7-day recall period (direct), whilst the NMARS predominantly explored the reasons for non-adherence and/or behavioral barriers to adherence (indirect). Each item in the NMARS represented unique, but additive factors that contributed to an overall assessment of adherent behaviour acting as 'causal' indicators in a composite variable of adherence, rather than 'effect' indicators.<sup>101</sup> The conceptual framework for the NMARS outlined the relevance of each item to Aboriginal and Torres Strait Islander peoples focussing on perceived benefits of medicines, the necessity for and knowledge of medicines, self-efficacy, trust in health services, the perception of illness as a threat, the rationing and sharing of medicines, and the effect of cost and other difficulties accessing medicines.

There were four NMARS items that demonstrated participant response ceiling effects (items 3, 5, 6, 10), where the best score was achieved by more than 80% of participants. At baseline, nearly 92% of participants reported having a good understanding of when and how to take their medicines (item 3), 89% agreed on the necessity of medications for health (item 5), less than 10% were rationing their medicines (item 6), with fewer than 2% giving away or sharing medicines to the extent of running out (item 10). The latter finding contrasts with a qualitative analysis of Aboriginal health practitioner perspectives that medication sharing within Victorian Aboriginal communities was widespread and was an expression of community caring.<sup>102</sup> With the exception of these four items, all items demonstrated acceptable inter-item correlation. As the NMARS was assessing distinctive traits or states associated with medication nonadherence as causal indicators of the construct, it was not necessary for every item to correlate with each other provided they are causally related to the construct.<sup>103</sup> In the NMARS, one trait (or state) associated with non-adherent behaviour did not imply that another would also be present in the same participant. Thus, the lack of inter-item and item-total correlation in the four aforementioned items may be because these items were measuring a different trait/state from other items, or the lack of variability in participant responses to these items is a more likely explanation. The negative inter-item correlation for items 3 and 5 affirmed reverse scoring for these items. For example, a perception that medicines may cause harm (Q8) was negatively correlated with views that medicines are good

for health (Q5), which is consistent with other behaviour assessment scales used to measure change in medication adherence.<sup>104</sup>

Items 6 and 10 in the NMARS also provided empirical evidence that relatively few Aboriginal and Torres Strait Islander participants with chronic disease rationed or shared their medicines with others to the point of insufficient supply. This may be a common but underrecognised practice in any population because these questions are rarely asked of patients.<sup>105</sup> Nevertheless, up to 10% of patients attending ACCHSs may be sharing or rationing medications, and recognising this can help to address this behaviour or to mitigate it by prescribing medications that are less likely to be affected by delayed or missed doses despite imperfect adherence.<sup>106</sup>

The SIQ measured the extent of adherence with adherence defined as a participant taking all of the prescribed medication doses at least 6 of 7 (~80%) of the days indicated. Based on the SIQ, the prevalence of medication adherence for the IPAC cohort as a whole was 71% at baseline. This represents a similar level of adherence to that reported in a systematic review of studies that found two-thirds of Indigenous Australians were adherent to medications<sup>107</sup> which is also similar to that reported for other populations indicating adherence up to 79%.<sup>108</sup> This result and the positive correlation between SIQ scores and higher baseline biomedical indices supported the selection of the SIQ as a comparator to the NMARS given the absence of any other comparative gold standard method of assessing medication adherence in the context of the IPAC study. An NMARS score of 8-11 was set to distinguish adherent patients from non-adherent patients as effectively as the SIQ based on overall participant response frequencies with 79.6% agreement between the tests.

Construct validity for both the SIQ and the NMARS was evident given similar estimates of adherence (approximately two-thirds of participants) irrespective of differences in their baseline blood pressure, HbA1c, or degree of albuminuria in the presence of chronic kidney disease. It was also postulated that the tools should identify a similar prevalence of medication adherent behaviour using known-group comparisons such as participant sex or BMI, and this was shown for both tests. Sex was selected as a trait to test the construct validity of SIQ and NMARS given that most studies show no association between sex and medication adherence. Systematic reviews and overviews indicate little evidence for sex as a predictor of adherent behaviour,<sup>109 110 111 112</sup> although male gender has been reported to have both a positive and

negative effect on adherence.<sup>113</sup> Similarly, obesity and overweight was selected as a characteristic that would not be associated with adherence scores, as systematic reviews of patient-related and condition-related factors influencing medication adherence rarely include obesity as a risk factor influencing adherence one way or the other.<sup>114 115</sup>

Construct validity was also supported given that medication adherence was greater for IPAC participants who took more medications - a positive correlation that was shown at baseline for both tests of adherence. Although decreased adherence is usually expected with polypharmacy,<sup>116 117</sup> many studies have reported no relationship between the number of medicines taken and adherence,<sup>118</sup> whilst others have reported increased adherence.<sup>119</sup> This suggests the nature of the relationship between the number of prescribed medications and adherence is complex, as some patients with chronic disease co-morbidities may be more adherent than those with fewer comorbidities, and patients with some types of chronic disease may be more adherent than others.<sup>120</sup> Meanwhile, the use of dose administration aids (DAA) in patients with appropriate polypharmacy has been shown to enhance medication adherence.<sup>121 122 123</sup> Improved adherence in those with serious disease and polypharmacy may also be explained by an increased motivation to take medications and better access to supports than others.<sup>124</sup> Moreover, patients taking more medications tend to have stronger beliefs about the necessity to take medications which predicts better adherence.<sup>125 126</sup> Serious illness warranting treatment with multiple medications may also trigger an adaptive behavioural response towards better adherence.<sup>127</sup> Indeed, in a qualitative analysis for the IPAC study, all but one of the integrated pharmacists estimated that between 33% to 100% of participants were using DAA's at the start of the study.<sup>128</sup> The observed positive correlation between adherence and the number of medications in our cohort is therefore likely to be real, which validates the construct of the NMARS to identify behaviour reflective of non-adherence.

As the IPAC project progressed, DAA use by participants improved,<sup>129</sup> and the primary reason given for contact between the integrated pharmacist and community pharmacy was for DAA preparation and supply on behalf of the study participants.<sup>130</sup> Community pharmacists also reported that integrated pharmacists facilitated patients from the ACCHS receiving DAA's.<sup>131</sup> Improved DAA use as well as other supports provided by integrated pharmacists such as medication management reviews,<sup>132</sup> improvements to prescribing quality,<sup>133 134</sup> education and increased liaison with community pharmacy and other healthcare providers for the transitional care of patients,<sup>135 136</sup> are factors that are most likely to explain the significant

increase in adherence reported by this study.

As participants were supported to optimise medication adherence, improvements to clinical endpoints were expected. As reported elsewhere, IPAC participants had significant improvements to blood pressure, lipids, and glycaemic control (in participants with T2DM), as well as a reduction in the rate of eGFR decline.<sup>137</sup> Given that improved adherence to antihypertensive medication is associated with higher odds of blood pressure control,<sup>138</sup> and good adherence is associated with lower mortality for a range of conditions,<sup>139</sup> improving the medication adherence of Aboriginal peoples and Torres Strait Islanders is an important intervention to optimise the care of those with chronic disease.

A significantly greater proportion of participants rated their health as excellent or very good by the end of the study than at baseline according to the SF1. Other Australian studies involving non-Indigenous Australians have also used a five-point SF1 with patients to self-rate health status and found a better health rating after patients had received support from chronic disease self management programs, but no change in medication adherence.<sup>140</sup> A large US study involving mostly unemployed adults (mean age of 60 years) with cardiovascular disease showed that adherence to medications was associated with better self-rated health status and that non-adherence to medications was associated with socioeconomic stressors.<sup>141</sup> In this study, the positive correlation between medication adherence (tested using the self-reported ARMS-7 instrument) and self-rated health (tested using a 10-item patient reported tool) was similar to that observed in the IPAC study with a Spearman's rho of + 0.21.<sup>142</sup> The IPAC study finding that improved adherence can somewhat predict improvement in self-assessed health status further reinforces the value of efforts to overcome the barriers that Aboriginal peoples and Torres Strait Islanders face when taking medications.

The NMARS demonstrated adequate face, content, and construct validity, with readability suitable for the population for whom it was intended, using validation methods consistent with international standards.<sup>143 144</sup> Testing also affirmed adequate internal consistency (reliability), and unidimensionality meaning the scale measured a single construct that was reflective of non-adherent behaviour. The NMARS offered a composite measure of a range of participant traits (or 'states' if behaviour is transient) to inform efforts to modify nonadherent behaviour, even when the behaviour was not directly observable by pharmacists.<sup>145</sup> The NMARS tool standardised assessment of commonly held beliefs about taking medicines

opening up conversations between pharmacists and participants about adherent-related behaviour. Opening up discussion about adherence with patients is vital as educational and behavioural interventions to enhance medication adherence have been repeatedly shown in systematic reviews to be most effective.<sup>146 147</sup> Participant responses to the NMARS items assisted pharmacists to assess and tailor personalised strategies as these are more likely to improve and support good medication-taking behaviour.<sup>148</sup>

A strength of this study is the large sample of Aboriginal and Torres Strait Islander patients with existing chronic disease that were surveyed for adherence-related behaviour and perceptions of their health status, repeatedly over time. Two self-report methods of adherence were assessed, unlike most previous studies that adopted one method.<sup>149</sup> All participants were recipients of pharmacist services integrated within primary health care settings and followed-up prospectively. They were usual patients accessing ACCHSs, were general patients, a large number of ACCHSs participated in the study, and the study design was pragmatic being consistent with usual care. Furthermore, pharmacists acting as healthcare providers within the ACCHSs collected the self-reports from participants (rather than research personnel) which is consistent with usual care. Improvements in self-assessed health and medication adherence would therefore be generalisable to the broader ACCHS adult patient population with chronic disease if they received support from pharmacists integrated within these health services.

### Limitations

A limitation of this study is that adherence measures relied on self-reported adherence rather than objective measures of medication adherence such as independent community pharmacy dispensing records, pill counts, or daily medication diaries. Subjective measures such as self-reports tend to overestimate adherence due to social desirability bias which is a known limitation.<sup>150</sup> Whilst all methods of adherence assessment (including objective measures) have drawbacks,<sup>151</sup> self-reporting is known to be a reasonably accurate measure of adherence,<sup>152</sup> providing additional information about the reasons for non-adherence that objective measures cannot provide,<sup>153</sup> is more practical,<sup>154</sup> and is the most common method used in research and clinical settings.<sup>155 156</sup> In order to improve the accuracy of adherence assessment, the use of more than one measure is often recommended,<sup>157 158</sup> however, pre-existing measures of self-reported adherence validated in our context were not available for the present study. This may be a limitation or a strength, as the use of more complex self-

report tools could have been further problematic as pharmacists found some participants had difficulty understanding some NMARS questions. A seven day recall of medication taking was also problematic for participants when using the SIQ, and there is a suggestion from other studies that a 3 or 4-day recall may be just as effective in eliciting adherence from self-reports.<sup>159</sup>

Criterion-based validity assessments of NMARS could not be conducted in the absence of a relevant gold-standard criterion that had been validated to assess self-reported medication adherence in this target population. Discriminant validity testing could not be conducted in the absence of participant test results from an unrelated but comparable test construct. Further, test-retest reliability (assessing for intra and inter-observer reliability) was not undertaken due to the pragmatic study design. According to international standards, assessing test-retest reliability is not essential with patient experience measurement scales.<sup>160</sup>

Without an external and randomised control group, it is possible that participant medication adherence as measured using the SIQ and NMARS improved independently of the IPAC intervention. Whilst participants tended to overreport adherence due to social desirability bias at baseline, this settled to more honest representations of adherence towards the end of the study, as reported by pharmacists. This would have the effect of minimising or even reversing the observed change in adherence from baseline. Moreover, qualitative analysis of accounts from participants, integrated pharmacists, and community pharmacists revealed a universal belief that participant adherence to medications had been improved during the course of the study.

Other indirect influences on participant behaviour or self-assessed health status may have also independently increased participant adherence to medications, such as quality improvement in service activity as a whole. This possible influence was investigated through repeated health system assessments of participating ACCHSs. ACCHS characteristics and service activity during the course of the study did not change in ways that were independent of integrated pharmacists that may otherwise explain the increase in participant adherence to medications.<sup>161</sup>

The influence of other potentially confounding programs on participant behaviour was

removed from the analysis. This included those participants concurrently enrolled in the *Community Pharmacy in Health Care Homes* Trial program that was undertaken around the same time as the IPAC project.<sup>162</sup> The few IPAC participants concurrently enrolled in the broader HCH program were not in receipt of additional community pharmacy support beyond that available through usual care. Moreover, the IPAC pharmacist was integrated within the services operating as a HCH trial site, meaning that the HCH program could not have acted as a confounder independently of the pharmacist to influence participant behaviour.

Interviewer bias may have influenced the adherence scores reported by pharmacists when using both SIQ and NMARS which is a study limitation that applies to the use of any instrument testing self-report.<sup>163</sup> However, pharmacists were not expected to calculate a composite score from the use of the tools, although they could interpret the pattern of item responses at an individual level to tailor the supports they provided to participants.

This study provided evidence to support the interpretability of NMARS scores but did not assess for responsiveness (longitudinal validity) which is another type of construct validity testing to measure change in adherence scores over time to assess if they mirror a change in scores from another criterion.<sup>164</sup> This type of validation is not considered essential for research tools exploring patient reported outcome measures,<sup>165</sup> and was not essential to the primary objective of the IPAC study.

Consumer focus groups were not used to derive scale items for the NMARS as a recent systematic review of barriers faced by Indigenous Australians had been published.<sup>166</sup> Rather, Aboriginal informants participated in feasibility and clarity testing, shaping the wording of the NMARS questions whilst not changing the intent. One-on-one interviews with informants rather than group discussions were conducted by an academic who was a member of the Aboriginal community, even though group discussions are sometimes recommended.<sup>167</sup> In the Aboriginal context, people may feel more comfortable expressing honest views with a member of their own community than an outsider. Complex Indigenous family relational and group dynamics may be a source of strength or weakness in group discussions.<sup>168</sup>

A Cronbach's alpha value of 0.7-0.9 is usually considered acceptable for group comparisons<sup>169</sup> although an alpha below 0.7 is acceptable in certain contexts.<sup>170 171</sup> The low degree of variance for four questions in the NMARS may explain an alpha of 0.66 and low inter-item correlations

for these items in our cohort. Whilst the reliability of a measure is linked to the characteristics of the population to which it is applied,<sup>172</sup> precision could have been enhanced by the addition of more scale items, but this would have increased test length. Ordinal rating scales were avoided in favour of dichotomous response choices which reduced information about behaviour variance, but this was a trade-off to minimise respondent burden.<sup>173 174</sup>

## **CONCLUSION**

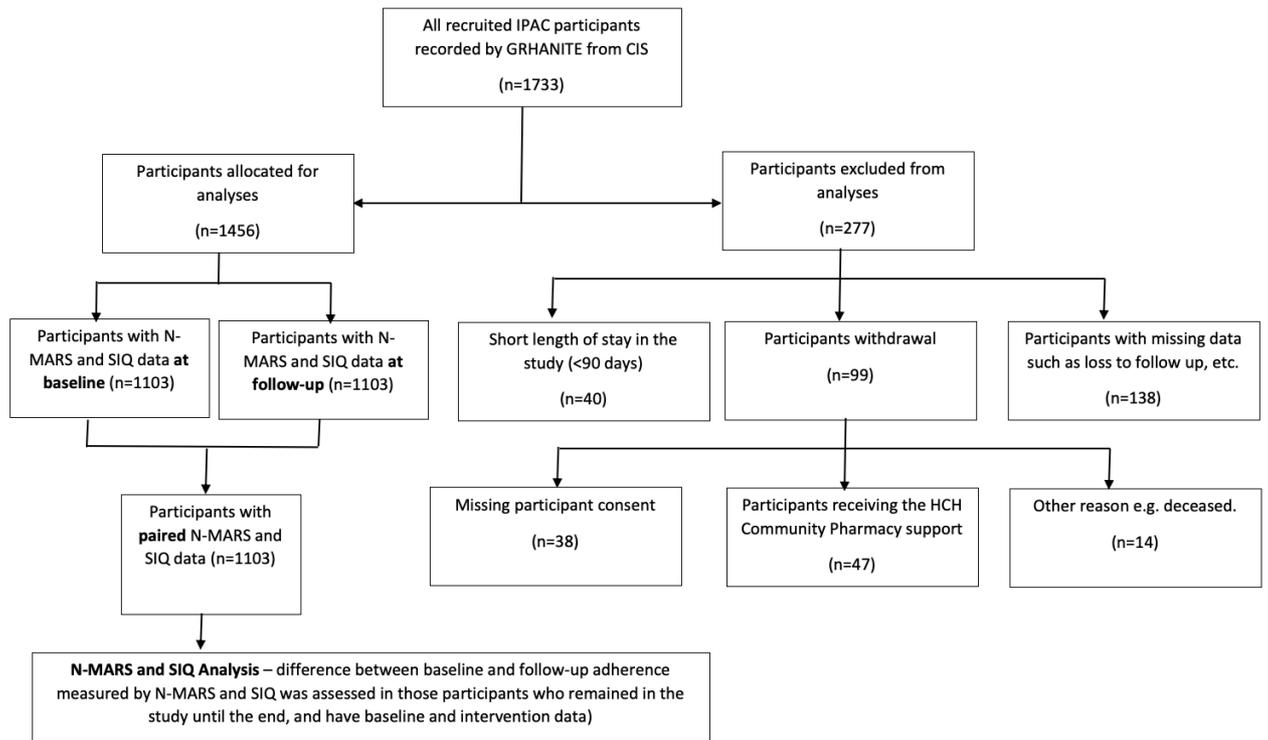
This is the first study to investigate the impact of integrated pharmacist interventions on medication adherence and self-assessed health status with regard to Aboriginal and Torres Strait Islander participants with chronic disease. The intervention comprised non-dispensing medicines-related services, collaborative and coordinated care, including the provision of medication management reviews by pharmacists integrated within Aboriginal community-controlled health services. Medication adherence was assessed using two self-reported tools shown to be valid, reliable, and suitable for the context of this study. The tools measured the extent of adherence as well as informed on common behavioural determinants of medication adherence relevant to the Aboriginal and Torres Strait islander adult population at all participant literacy levels irrespective of their medical condition. The study findings show that integrated pharmacists embedded into usual care in a range of geographical settings, significantly improved the medication adherence of Aboriginal and Torres Strait islander adults with chronic disease, as well as their self-assessed health status.

**Table 1. The NMARS used with participants in the IPAC study.**

<b>Question</b>	<b>N-MARS patient survey</b>	<b>Scoring</b>
<b>Q1</b>	Did you forget to take any of your medicines yesterday? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q2</b>	Is it hard for you to remember to take your medicines? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q3</b>	Do you know when, and how, to take your medicines? <b>Yes/No</b>	Yes= 1 (reverse scored)
		No=0
<b>Q4</b>	Is it hard for you to take your medicines in the right way, like the doctor, nurse, or AHW said? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q5</b>	Do you feel that taking your medicines will be good for your health? <b>Yes/No</b>	Yes= 1 (reverse scored)
		No=0
<b>Q6</b>	Do you sometimes take less medicine to make the medicine last longer? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q7</b>	Do you sometimes stop taking your medicines because you think you are ok? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q8</b>	Do you sometimes stop taking your medicine because you think it might make you sick? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q9</b>	Do you sometimes 'run out' of medicines because it costs too much, or it is hard to get more? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q10</b>	Do you sometimes run out of medicines because you give them away or share them with other people? <b>Yes/No</b>	Yes= 0
		No=1
<b>Q11</b>	Do you go without your medicines when you are away from home? <b>Yes/No</b>	Yes= 0
		No=1

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. Questions 3 and 5 were reverse scored.

**Figure 1. Participant flow diagram for medication adherence assessment analysis in the IPAC study cohort**



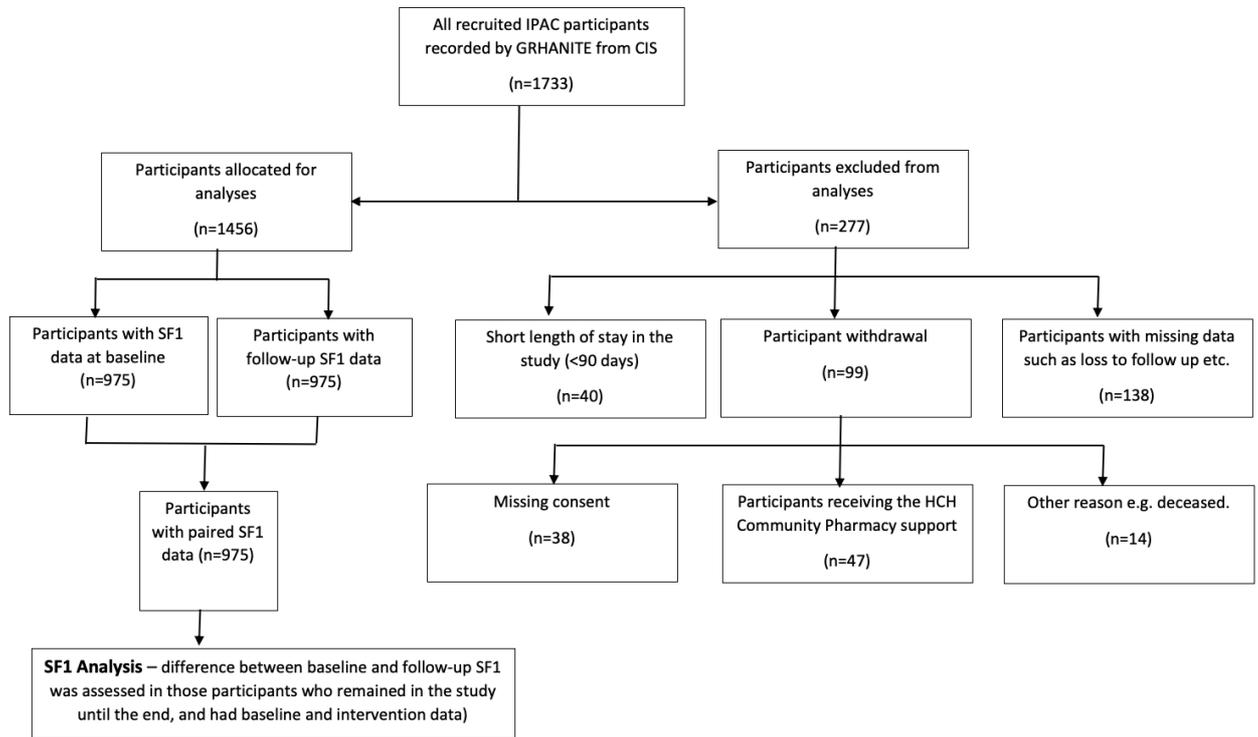
*CIS= Clinical information systems*

*GRHANITE= Data extraction tool*

*NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11.*

*SIQ= A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking, generating a score defining adherence from 6 to 7.*

**Figure 2. Participant flow diagram for self-assessed health status assessment (SF1) analysis in the IPAC study cohort.**



*CIS= Clinical information systems*

*GRHANITE= Data extraction tool*

*SF1= Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: 'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'*

Not for citation

**Table 2. Baseline characteristics of IPAC participants with paired self-reported medication adherence assessments (N-MARS and SIQ, n=1103).**

Participant characteristics	IPAC participants (n=1103)
<b>Location classification by ASGS-RA (2016)</b>	
Major city (RA1)	30/1103 (2.7%)
Inner regional (RA2)	317/1103 (28.7%)
Outer regional (RA3)	497/1103 (45.1%)
Remote (RA4)	110/1103 (10.0%)
Very remote (RA5)	149/1103 (13.5%)
<b>Mean age at baseline (SD) [years]</b>	<i>n</i> =1100
	58 (29.8)
<b>Sex (n,%)</b>	
Female	677/1100 (61.6%)
Male	423/1100 (38.4%)
<b>Ethnicity (n,%)</b>	
Aboriginal and/or Torres Strait Islander	1024/1099 (93.2%)
Non-Indigenous	75/1099 (6.8%)
<b>Pensioner/concessional (n, %)</b>	928/1100 (84.4%)
<b>CTG scripts eligible (n,%)</b>	819/1100 (74.5%)
<b>Patient engaged in Health Care Home program (n, %)<sup>a</sup></b>	114/1103 (10.3%)
<b>Number of medications<sup># b</sup></b>	<i>n</i> =1103
Mean (SD )	7.3 (13.3)
Median (IQR)	7 (5-9)
<b>Prior medication review (MBS item 900) <sup>c</sup> (n,%)</b>	116/1103 (10.5%)
<b>Doctors' encounters prior to enrolment (per 12 months) <sup>d</sup></b>	<i>n</i> =1037
Mean (SD)	7.8 (19.3)
Median (IQR)	6 (3-10)
<b>Mean number of medication 'adherent days' (SD)<sup>e</sup></b>	<i>n</i> =1103
	6.1 (6.6)
<b>Self-assessed health status score (SF1) (n,%)<sup># f</sup></b>	
Excellent	42/975 (4.3%)
Very good	133/975 (13.6%)
Good	414/975 (42.5%)
Fair	276/975 (28.3%)
Poor	89/975 (9.1%)
Very poor	21/975 (2.2%)
<b>Recorded clinical diagnoses (n,%)<sup>#</sup></b>	
T2DM	677/1103 (61.4%)
Hypertension	706/1103 (64.0%)

Dyslipidaemia	557/1103 (50.5%)
Patients with established or existing CVD <sup>g</sup>	365/1103 (33.1%)
Chronic kidney disease	439/1103 (39.8%)
Patients with a diagnosis of rheumatic heart disease (RHD) or Acute rheumatic fever (ARF)	34/1103 (3.1%)
Chronic obstructive pulmonary disease (COPD)	94/1103 (8.5%)
Depressive disorder	61/1103 (5.5%)
Patients with comorbidity (1 or more chronic diseases)	974/1103 (88.3%)
Patients with multi-morbidity (2 or more chronic diseases)	866/1103 (78.5%)

SD = cluster-adjusted standard deviation (ACCHS cluster); IQR = inter-quartile range;

CTG= Close the Gap prescriptions (for Aboriginal peoples and Torres Strait Islanders) to waive or reduce the Pharmaceutical Benefits Scheme (PBS) patient contribution (co-payment).

CVD= cardiovascular disease.

MBS= Medicare Benefits Schedule.

# Sourced from the pharmacist's logbook.

<sup>a</sup> Health Care Homes (HCH) program funded by the Australian Government designed to better coordinate the health care of patients with chronic disease

<sup>b</sup> Denominator was sourced from logbook data entered by pharmacists with regard to the medication adherence of participants.

<sup>c</sup> Prior MBS item 900 claim measured for the 12-month period prior to participant enrolment. This rebate pertains to a Home Medicines Review (HMR).

<sup>d</sup> Medicare GP consultation claim items: vocational registration: 3, 23, 36, 44. Non-vocational registration: 52, 53, 54, 57.

<sup>e</sup> A self-reported single-item question (*'How many days in the last week have you taken this medication?'*) exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking.

<sup>f</sup> Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: *'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'*

<sup>g</sup> CVD= cardiovascular disease: It refers to any of the following: coronary heart disease, cerebrovascular disease, and peripheral vascular disease.

Not for distribution

**Table 3. Baseline characteristics of IPAC participants with paired self-assessed health status assessments (SF1, n=975).**

Participant characteristics	IPAC participants (n=975)
<b>Location classification by ASGS-RA (2016)</b>	
Major city (RA1)	26/975 (2.7%)
Inner regional (RA2)	280/975 (28.7%)
Outer regional (RA3)	410/975 (42.1%)
Remote (RA4)	110/975 (11.3%)
Very remote (RA5)	149/975 (15.3%)
<b>Mean age at baseline (SD) [years]</b>	<i>n</i> = 975 57.9 (28.1)
<b>Sex (n,%)</b>	
Female	606/972 (62.4%)
Male	366/972 (37.7%)
<b>Ethnicity (n,%)</b>	
Aboriginal and/or Torres Strait Islander	899/971 (92.6%)
Non-Indigenous	72/971 (7.4%)
<b>Pensioner/concessional (n, %)</b>	813/972 (83.6%)
<b>CTG scripts eligible (n,%)</b>	696/972 (71.6%)
<b>Patient engaged in Health Care Home program (n, %)<sup>a</sup></b>	114/975 (11.7%)
<b>Number of medications<sup># b</sup></b>	<i>n</i> = 975
Mean (SD )	7.2 (12.2)
Median (IQR)	7 (5-9)
<b>Prior medication review (MBS item 900) <sup>c</sup> (n,%)</b>	96/975 (9.9%)
<b>Doctors' encounters prior to enrolment (per 12 months) <sup>d</sup></b>	<i>n</i> = 912
Mean (SD)	7.6 (17.2)
Median (IQR)	6 (3-10)
<b>Mean number of medication 'adherent days' (SD)<sup>e</sup></b>	<i>n</i> = 975 6.1 (5.9)
<b>Self-assessed health status score (SF1) (n,%)<sup># f</sup></b>	
Excellent	42/975 (4.3%)
Very good	133/975 (13.6%)
Good	414/975 (42.5%)
Fair	276/975 (28.3%)
Poor	89/975 (9.1%)
Very poor	21/975 (2.2%)
<b>Recorded clinical diagnoses (n,%)<sup>#</sup></b>	
T2DM	590/975 (60.5%)
Hypertension	624/975 (64.0%)
Dyslipidaemia	493/975 (50.6%)
Patients with established or existing CVD <sup>g</sup>	324/975 (33.2%)

Chronic kidney disease	398/975 (40.8%)
Patients with a diagnosis of rheumatic heart disease (RHD) or Acute rheumatic fever (ARF)	31/975 (3.2%)
Chronic obstructive pulmonary disease (COPD)	86/975 (8.8%)
Depressive disorder	59/975 (6.1%)
Patients with comorbidity (1 or more chronic diseases)	868/975 (89.0%)
Patients with multi-morbidity (2 or more chronic diseases)	772/975 (79.2%)

SD = cluster-adjusted standard deviation (ACCHS cluster); IQR = inter-quartile range;

CTG= Close the Gap prescriptions (for Aboriginal peoples and Torres Strait Islanders) to waive or reduce the Pharmaceutical Benefits Scheme (PBS) patient contribution (co-payment).

CVD= cardiovascular disease.

MBS= Medicare Benefits Schedule.

# Sourced from the pharmacist's logbook.

<sup>a</sup> Health Care Homes (HCH) program funded by the Australian Government designed to better coordinate the health care of patients with chronic disease

<sup>b</sup> Denominator was sourced from logbook data entered by pharmacists with regard to the medication adherence of participants.

<sup>c</sup> Prior MBS item 900 claim measured for the 12-month period prior to participant enrolment. This rebate pertains to a Home Medicines Review (HMR).

<sup>d</sup> Medicare GP consultation claim items: vocational registration: 3, 23, 36, 44. Non-vocational registration: 52, 53, 54, 57.

<sup>e</sup> A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking.

<sup>f</sup> Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: 'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'

<sup>g</sup> CVD= cardiovascular disease: It refers to any of the following: coronary heart disease, cerebrovascular disease, and peripheral vascular disease.

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**Table 4. Effect of the intervention on participant medication adherence (n=1103) according to N-MARS score stratified by selected participant, ACCHS and intervention characteristics, and adjusted for health service cluster.**

IPAC participants with paired data for N-MARS (n=1103)	Number (%) of IPAC participants who adhered to their medications according to N-MARS (score 8 to 11)				P-value
	Number of participants adhering at baseline (%)	Number of participants adhering at final observation (%)	Number of participants who changed from not adhering to adhering during follow-up (%); 95% CI	Number of participants who changed from adhering to not adhering during follow-up (%); 95% CI	
	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
	808/1103 (73.3%)	950/1103 (86.1%)	204/1103 (18.5%); 15.4 to 22.1	62/1103 (5.6%); 3.5 to 9.0	<b>&lt;0.001<sup>^</sup></b>
<b>Participant-related characteristics</b>					
Median age at baseline =58 years	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.46 <sup>^^</sup>
<Median (n=520)	337/520 (64.8%)	407/520 (78.3%)	113/520 (21.7%); 17.9 to 26.1	43/520 (8.3%); 5.1 to 13.1	
≥Median (n=583)	471/583 (80.8%)	543/583 (93.1%)	91/583 (15.6%); 11.5 to 20.8	19/583 (3.3%); 1.8 to 5.8	
Median length of stay in the study =294 days (IQR 230-359)	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.58 <sup>^^</sup>
<Median (n=551)	397/551 (72.1%)	467/551 (84.8%)	100/551 (18.2%); 14.4 to 22.7	30/551 (5.4%); 2.7 to 10.8	
≥Median (n=552)	411/552 (74.5%)	483/552 (87.5%)	104/552 (18.8%); 14.1 to 24.7	32/552 (5.8%); 3.9 to 8.6	
Sex	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.52 <sup>^^</sup>
Female (n=677)	489/677 (72.2%)	581/677 (85.8%)	132/677 (19.5%); 15.8 to 23.8	40/677 (5.9%); 3.2 to 10.8	
Male (n=423)	317/423 (74.9%)	367/423 (86.8%)	71/423 (16.8%); 13.0 to 21.5	21/423 (5.0%); 3.4 to 7.3	
Median number of medications =7	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.27 <sup>^^</sup>
<Median (n=474)	320/474 (67.5%)	371/474 (78.3%)	91/474 (19.2%); 14.9 to 24.3	40/474 (8.4%); 4.9 to 14.2	
≥Median (n=629)	488/629 (77.6%)	579/629 (92.1%)	113/629 (18.0%); 14.2 to 22.4	22/629 (3.5%); 1.8 to 6.6	
Self -assessed health status score at baseline (SF1)	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	<b>0.01<sup>^^</sup></b>
'Good, Fair, Poor, Very Poor' (n=800)	562/800 (70.3%)	677/800 (84.6%)	159/800 (19.9%); 16.5 to 23.7	44/800 (5.5%); 2.8 to 10.5	

'Excellent' or 'very good' (n=175)	149/175 (85.1%)	155/175 (88.6%)	17/175 (9.7%); 5.8 to 15.9	11/175 (6.3%); 2.9 to 13.1	
<b>ACCHS-related characteristics</b>					
Median IRSEO score =50	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
< 60 (n=548)	419/548 (76.5%)	500/548 (91.2%)	102/548 (18.6%); 14.6 to 23.5	21/548 (3.8%); 3.0 to 4.9	0.31^^
>= 60 (n=555)	389/555 (70.1%)	450/555 (81.1%)	102/555 (18.4%); 14.0 to 23.8	41/555 (7.39%); 4.1 to 12.9	
<b>Intervention-related characteristics</b>					
Participants who had a HMR compared to participants who had a non-HMR	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
Non-HMR (n=483)	347/483 (71.8%)	393/483 (81.4%)	81/483 (16.8%); 12.8 to 21.7	35/483 (7.3%); 3.7 to 13.6	0.06^^
HMR (n=411)	294/411 (71.5%)	371/411 (90.3%)	90/411 (21.9%); 17.3 to 27.3	13/411 (3.2%); 1.7 to 5.7	
Participants who received an MBS service for item 10987 or 10997 during the follow-up period	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
No (n=552)	403/552 (73.0%)	478/552 (86.6%)	105/552 (19.0%); 15.5 to 23.2	30/552 (5.4%); 2.7 to 10.5	0.17^^
Yes (n=551)	405/551 (73.5%)	472/551 (85.7%)	99/551 (18.0%); 14.6 to 21.8	32/551 (5.8%); 3.8 to 8.8	

95% CI= cluster adjusted 95% confidence intervals (ACCHS cluster). SD= cluster adjusted standard deviation (ACCHS cluster). Bold p-values imply statistically significant change at the 0.05 level.

^P-value= cluster adjusted p-value (ACCHS cluster) that were determined using the . svy linearized : clogit Stata command with adherence results as the outcome measure.

^^P-value= cluster adjusted p-value (ACCHS and participant cluster) that were determined using the . svy linearized : logit Stata command with adherence results as the outcome measure.

Health service= Aboriginal community-controlled health service (ACCHS)

HMR= Home Medicines Review. A completed HMR represents a comprehensive medication management review that fulfils the criteria for a Medicare Benefits Scheme (MBS) claim for item 900, as sourced from the integrated pharmacist's logbook.

IRSEO= Indigenous Relative Socioeconomic Outcomes index. The IRSEO reflects relative advantage or disadvantage at the Indigenous Area level, where a score of one (1) represents the most advantaged area and a score of 100 represents the most disadvantaged area.<sup>175</sup>

MBS= Medicare Benefits Schedule. MBS items 10987 and 10997 provide a rebate for a service by a practice nurse or an Aboriginal and Torres Strait Islander Health Practitioner (e.g. staff within ACCHSs) that includes a follow-up the assessment of the medication adherence of an Indigenous patient.

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11.

Non-HMR= a comprehensive medication management review that was not an HMR, as sourced from the integrated pharmacist's logbook.

SF1= Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: 'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'

**Table 5. Effect of the intervention on participant medication adherence (n=1103) according to SIQ score, stratified by selected participant, ACCHS and intervention characteristics, and adjusted for health service cluster.**

IPAC participants with paired data for Q1a (n=1103)	Number (%) of IPAC participants who adhered to their medications according to SIQ (score 6 to 7)				P-value
	Number of participants adhering at baseline (%)	Number of participants adhering at final observation (%)	Number of participants who changed from not adhering to adhering during follow-up (%); 95% CI	Number of participants who changed from adhering to not adhering during follow-up (%); 95% CI	
	N (%)	N (%)	N (%);95% CI	N (%); 95% CI	
	781/1103 (70.8%)	895/1103 (81.1%)	194/1103 (17.6%); 14.4 to 21.3	80/1103 (7.3%); 5.6 to 9.3	<0.001 <sup>^</sup>
<b>Participant- related characteristics</b>					
Median age at baseline =58 years	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.002 <sup>^^</sup>
<Median (n=520)	312/520 (60.0%)	383/520 (73.7%)	114/520 (21.9%); 18.1 to 26.3	43/520 (8.3%); 6.5 to 10.5	
≥Median (n=583)	469/583 (80.5%)	512/583 (87.8%)	80/583 (13.7%); 9.6 to 19.3	37/583 (6.4%); 4.3 to 9.3	
Median length of stay in the study =294 days (IQR 230-359)	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.97 <sup>^^</sup>
<Median (n=551)	377/551 (68.4%)	438/551 (79.5%)	101/551 (18.3%); 14.4 to 23.0	40/551 (7.3%); 4.9 to 10.5	
≥Median (n=552)	404/552 (73.2%)	457/552 (82.8%)	93/552 (16.9%); 12.2 to 22.7	40/552 (7.3%); 5.3 to 9.9	
Sex	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.27 <sup>^^</sup>
Female (n=677)	467/677 (69.0%)	546/677 (80.7%)	125/677 (18.5%); 14.5 to 23.3	46/677 (6.8%); 4.6 to 9.9	
Male (n=423)	311/423 (73.5%)	346/423 (81.8%)	69/423 (16.3%); 13.4 to 19.7	34/423 (8.0%); 5.8 to 11.1	
Median number of medications =7	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	>0.99 <sup>^^</sup>
<Median (n=474)	287/474 (60.6%)	336/474 (70.9%)	97/474 (20.5%); 16.8 to 24.8	48/474 (10.1%); 8.4 to 12.2	
≥Median (n=629)	494/629 (78.5%)	559/629 (88.9%)	97/629 (15.4%); 12.0 to 19.5	32/629 (5.1%); 2.9 to 8.7	
Self -assessed health status score at baseline (SF1)	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.56 <sup>^^</sup>

'Good, Fair, Poor, Very Poor' (n=800)	548/800 (68.5%)	635/800 (79.4%)	145/800 (18.1%); 14.3 to 22.8	58/800 (7.3%); 5.0 to 10.3	
'Excellent' or 'very good' (n=175)	132/175 (75.4%)	148/175 (84.6%)	29/175 (16.6%); 11.6 to 23.2	13/175 (7.4%); 5.0 to 11.0	
<b>ACCHS-related characteristics</b>					
Median IRSEO score =50	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.13^^
< 60 (n=548)	413/548 (75.4%)	467/548 (85.2%)	90/548 (16.4%); 12.0 to 22.1	36/548 (6.6%); 5.0 to 8.6	
>= 60 (n=555)	368/555 (66.3%)	428/555 (77.1%)	104/555 (18.7%); 14.2 to 24.3	44/555 (7.9%); 5.5 to 11.3	
<b>Intervention-related characteristics</b>					
Participants who had a HMR compared to participants who had a non-HMR	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	<0.001^^
Non-HMR (n=483)	337/483 (69.8%)	370/483 (76.6%)	74/483 (15.3%); 10.3 to 22.3	41/483 (8.5%); 6.5 to 11.5	
HMR (n=411)	294/411 (71.5%)	357/411 (86.9%)	83/411 (20.2%); 16.2 to 24.9	20/411 (4.9%); 2.9 to 8.1	
Participants who received an MBS service for item 10987 or 10997 during the follow-up period	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.15^^
No (n=552)	396/552 (71.7%)	459/552 (83.2%)	104/552 (18.8%); 15.4 to 23.2	41/552 (7.4%); 5.6 to 9.7	
Yes (n=551)	385/551 (69.9%)	436/551 (79.1%)	90/551 (16.3%); 12.9 to 20.4	39/551 (7.1%); 5.0 to 10.0	

95% CI= cluster adjusted 95% confidence intervals (ACCHS cluster). SD= cluster adjusted standard deviation (ACCHS cluster). Bold p-values imply statistically significant change at the 0.05 level.

^P-value= cluster adjusted p-value (ACCHS cluster) that were determined using the . svy linearized : clogit Stata command with adherence results as the outcome measure.

^^P-value= cluster adjusted p-value (ACCHS and participant cluster) that were determined using the . svy linearized : logit Stata command with adherence results as the outcome measure.

Health service= Aboriginal community-controlled health service (ACCHS)

HMR= Home Medicines Review. A completed HMR represents a comprehensive medication management review that fulfils the criteria for a Medicare Benefits Scheme (MBS) claim for item 900, as sourced from the integrated pharmacist's logbook.

IRSEO= Indigenous Relative Socioeconomic Outcomes index. The IRSEO reflects relative advantage or disadvantage at the Indigenous Area level, where a score of one (1) represents the most advantaged area and a score of 100 represents the most disadvantaged area.<sup>176</sup>

MBS= Medicare Benefits Schedule. MBS items 10987 and 10997 provide a rebate for a service by a practice nurse or an Aboriginal and Torres Strait Islander Health Practitioner (e.g. staff within ACCHSs) that includes a follow-up the assessment of the medication adherence of an Indigenous patient.

Non-HMR= a comprehensive medication management review that was not an HMR, as sourced from the integrated pharmacist's logbook.

SF1= Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: 'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'

SIQ= A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking. A score of 6-7 was defined as adherence.

**Table 6. Effect of the intervention on self-assessed health status (n=975) according to SF1 assessment, stratified by selected participant, ACCHS and intervention characteristics, and adjusted for health service cluster.**

IPAC participants with paired data for SF1 (n=975)	SF1 score				P-value
	Number of participants with SF 1 “very good” or “excellent” at initial assessment (%)	Number of participants with SF 1 “very good” or “excellent” at final assessment (%)	Number of participants with improved SF1 assessment* (%); 95% CI	Number of participants with worsened SF1 assessment* (%); 95% CI	
	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
	175/975 (18.0%)	303/975 (31.1%)	406/975 (41.6%); 34.6 to 49.1	173/975 (17.7%); 14.2 to 22.0	<b>&lt;0.001<sup>^</sup></b>
<b>Participant -related characteristics</b>					
Median age at baseline =59 years	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.21 <sup>^^</sup>
<Median (n=466)	71/466 (15.2%)	122/466 (26.2%)	187/466 (40.1%); 32.4 to 48.4	86/466 (18.5%); 14.1 to 23.8	
≥Median (n=509)	104/509 (20.4%)	181/509 (35.6%)	219/509 (43.0%); 35.8 to 50.6	87/509 (17.1%); 13.4 to 21.6	
Median length of stay in the study =281 days (IQR 218-336)	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.08 <sup>^^</sup>
<Median (n=486)	86/486 (17.7%)	137/486 (28.2%)	188/486 (38.7%); 29.1 to 49.2	92/486 (18.9%); 14.9 to 23.8	
≥Median (n=489)	89/489 (18.2%)	166/489 (34.0%)	218/489 (44.6%); 38.7 to 50.6	81/489 (16.6%); 12.7 to 21.3	
Sex	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	0.47 <sup>^^</sup>
Female (n=606)	105/606 (17.3%)	180/606 (29.7%)	246/606 (40.6%); 33.9 to 47.6	110/606 (18.2%); 14.9 to 22.0	
Male (n=366)	70/366 (19.1%)	122/366 (33.3%)	159/366 (43.4%); 33.8 to 53.6	63/366 (17.2%); 12.8 to 22.8	
Adherent ( <i>baseline</i> )	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	<b>0.007<sup>^^</sup></b>
No: <i>SIQ score 0-5</i> (n=192)	27/192 (14.1%)	30/192 (15.6%)	62/192 (32.3%); 23.5 to 42.6	44/192 (22.9%); 16.7 to 30.5	
Yes: <i>SIQ score 6-7</i> (n=783)	148/783 (18.9%)	273/783 (34.9%)	344/783 (43.9%); 37.1 to 51.0	129/783 (16.5%); 13.1 to 20.5	
Median number of medications =7	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	<b>0.013<sup>^^</sup></b>
<Median (n=421)	83/421 (19.7%)	126/421 (29.9%)	163/421 (38.7%); 31.6 to 46.3	75/421 (17.8%); 13.4 to 23.3	

≥Median (n=554)	92/554 (16.6%)	177/554 (31.95%)	243/554 (43.9%); 36.5 to 51.5	98/554 (17.7%); 13.8 to 22.4	
<b>ACCHS- related characteristics</b>					
Median IRSEO score =61	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
< 60 (n=485)	105/485 (21.7%)	146/485 (30.1%)	197/485 (40.6%); 35.4 to 46.0	104/485 (21.4%); 16.8 to 27.0	0.61^^
≥ 60 (n=490)	70/490 (14.3%)	157/490 (32.0%)	209/490 (42.7%); 30.1 to 56.2	69/490 (14.1%); 11.7 to 16.8	
<b>Intervention-related characteristics</b>					
Participant who had a HMR compared to participant who had a non-HMR	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
Non-HMR (n=458)	65/458 (14.2%)	117/458 (25.6%)	176/458 (38.4%); 29.4 to 48.3	67/458 (14.6%); 11.6 to 18.21	0.34^^
HMR (n=352)	70/352 (19.9%)	126/352 (35.8%)	161/352 (45.7%); 33.7 to 58.3	71/352 (20.2%); 12.7 to 30.6	
Patients who received an MBS service for item 10987 or 10997 during the follow-up period	N (%)	N (%)	N (%); 95% CI	N (%); 95% CI	
No (n=496)	77/496 (15.5%)	150/496 (30.2%)	208/496 (41.9%); 33.2 to 51.2	83/496 (16.7%); 13.1 to 21.2	0.89^^
Yes (n=479)	98/479 (20.5%)	153/479 (31.9%)	198/479 (41.3%); 33.7 to 49.4	90/479 (18.8%); 13.4 to 25.6	

95% CI= cluster adjusted 95% confidence intervals (ACCHS cluster). SD= cluster adjusted standard deviation (ACCHS cluster). Bold p-values imply statistically significant change at the 0.05 level.

^P-value= Cluster adjusted p-value (ACCHS cluster) determined using the svy linearized : clogit Stata command with differences of SF1 as the outcome measure.

^^P-value= Cluster adjusted p-values (ACCHS and participant cluster) determined using the svy linearized : logit Stata command with differences of SF1 as the outcome measure.

\* Change in SF1 assessment from baseline was defined as 'improved' or 'worsened'. The six SF1 ordinal and categorical outcomes were converted to binary outcomes so that 'yes' pertained to 'excellent, very good' ratings and 'no' pertained to 'good, fair, poor, very poor' ratings. Improved was defined as a change from 'no' to 'yes' and worsened was defined as change from 'yes' to 'no'.

Health service= Aboriginal community-controlled health service (ACCHS)

HMR= Home Medicines Review. A completed HMR represents a comprehensive medication management review that fulfils the criteria for a Medicare Benefits Scheme (MBS) claim for item 900, as sourced from the integrated pharmacist's logbook.

IRSEO= Indigenous Relative Socioeconomic Outcomes index. The IRSEO reflects relative advantage or disadvantage at the Indigenous Area level, where a score of one (1) represents the most advantaged area and a score of 100 represents the most disadvantaged area.<sup>177</sup>

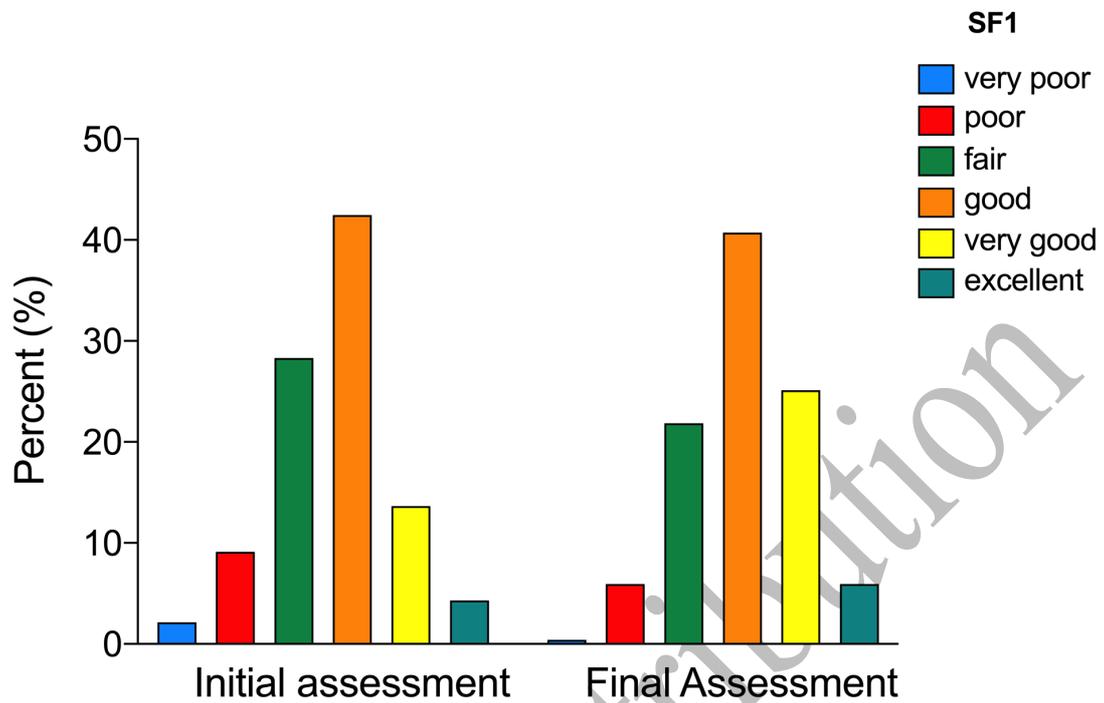
MBS= Medicare Benefits Schedule. MBS items 10987 and 10997 provide a rebate for a service by a practice nurse or an Aboriginal and Torres Strait Islander Health Practitioner (e.g. staff within ACCHSs) that includes a follow-up the assessment of the medication adherence of an Indigenous patient.

Non-HMR= a comprehensive medication management review that was not an HMR, as sourced from the integrated pharmacist's logbook.

SF1= Derived from the first question of the Short Form (SF)-36 health related quality of life instrument that asks: 'In general, would you say your health is excellent, very good, good, fair, poor, or very poor?'

SIQ= A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking. A score of 6-7 was defined as adherence.

Figure 3. Graphical representation of change in participant responses to SF1 testing (single-item self-assessed health status) at baseline (initial assessment) compared with the end of study (final assessment), by percentage of participants.



Not for distribution

**Table 7. Conceptual framework for the NMARS with comparisons to other self-report tools assessing medication adherence.**

Item #	NMARS questions	Comparative tool*	Comment	Domain (TDF)**
Q1	<b>Did you forget to take any of your medicines yesterday?</b>	<p>The MMAS-8 asks <i>“did you take all your medicine yesterday?”</i> MMAS-4 asks <i>“do you ever forget to take your medicine?”</i> MMAS-8 asks: <i>Do you sometimes forget to take your pills?</i></p> <p>The ASK-12 scale includes: <i>“I just forget to take my medicines some of the time”.</i></p> <p>The ARMS asks: <i>“How often do you forget to take your medicine?”</i></p> <p>RAMS asks: <i>“I sometimes forget to take my medicines”; “Some people forget to take their medicines. How often does this happen to you?”</i></p>	<p>Forgetfulness is a significant predictor of non-adherence,<sup>178</sup> with most self-assessment scales including similar such questions.<sup>179</sup> Q1 is phrased to be more appropriate to Aboriginal and Torres Strait Islander patients as it asks the patient to <i>recall forgetfulness</i> when taking medicines. The recall time is short, pertaining only to the previous day. Replies are categorical (yes/no) rather than requiring the patient to estimate the frequency. The scale asks about missing ‘any medicine’ rather than taking “all medicines” to be less confrontational. It does not ask if medicines are forgotten ‘sometimes’ or ‘ever’ as forgetfulness can be very unpredictable, and responses may not be sensitive to change after intervention.</p>	Memory, attention and decision processes
Q2	<b>Is it hard for you to remember to take your medicines?</b>	<p>The SEAMS asks: <i>“How confident are you that you can take your medicines correctly when you are not sure how to take the medicine?”.</i></p>	<p>This question explores the patient’s <i>confidence in their ability (self-efficacy)</i> to remember to take their medications, which is consistent with behaviour change theories such as the Health Belief Model. Patients expressing difficulty remembering to take medicines (cognitive decline and/or inadequate health literacy) are less likely to take their medications.<sup>180 181</sup> The degree of self-efficacy is a potent positive predictor of behaviour change and disease self-management, but it may not be predictive of distal health outcomes with regard to medication adherence related behaviour.<sup>182</sup></p>	Beliefs about capabilities; Memory, attention and decision processes
Q3	<b>Do you know when, and how, to take your medicines?</b>	<p>The BMQ includes: <i>“My medicines are a mystery to me”.</i></p>	<p>This question explores the patient’s knowledge about their medicines and a belief about self-capability or <i>confidence in an ability (self-efficacy)</i> to take medications, which is consistent with behaviour change theories such as the Health Belief Model. Lack of comprehension of disease and treatment is a known patient-related dimension negatively affecting adherence.<sup>183</sup> Enhanced knowledge of self-care and proper use of medications can enhance adherence.<sup>184 185</sup> The BMQ question pertains to ‘concerns about medicines’ which negatively correlate with adherence. A lack of knowledge of medicines is a known barrier to adherence for many Aboriginal peoples, mainly mediated by a lack of trust and limited communication with mainstream health services.<sup>186</sup> Aboriginal health workers have reported that Aboriginal patients who don’t know how to take their medicines, what to do if a dose is missed, or what happens if they stop taking the medicine will cease taking their medications. Communication difficulties may be layered upon feelings of shame about asking questions.<sup>187</sup></p>	Knowledge; Beliefs about capabilities

Q4	<p><b>Is it hard for you to take your medicines in the right way? (like the Dr/nurse/AHW said)</b></p>	<p>The SEAMS scale asks: <i>“How confident are you that you will be able to take all or most of your medicines as directed?; How confident are you that you can take your medicines correctly when no-one reminds you to take the medicine?”</i></p>	<p>This question explores perceived difficulties with taking medications, that may be influenced by the environmental context and resources, social influences, emotion, knowledge of medicines, and may also be influenced by the degree of <i>confidence in the ability</i>, to take medications. See Q3 and Q2.</p>	<p>Environmental context and resources; Social influences; Knowledge; Emotion; Beliefs about capabilities</p>
Q5	<p><b>Do you feel that taking your medicines will be good for your health?</b></p>	<p>The BMQ* includes: <i>“My life would be impossible without medicines.”; Without my medicines I would be very ill; My health in the future is dependent on my medicines; My medicines protect me from becoming worse; My health at present depends on medicines”.</i></p>	<p>This question explores the patient’s <i>perceived benefits</i> that may arise from taking medications, which is consistent with behaviour change theories such as the Health Belief Model. Like the BMQ subscale items, it explores the <i>perceived necessity</i> of the medication for maintaining health.<sup>188</sup> Negative beliefs about the efficacy of treatment negatively affects adherence.<sup>189</sup> In patients with hypertension, stronger beliefs of the necessity of medications contribute substantially to positive medication adherence.<sup>190</sup> Patients who believe their medicine to be necessary are more adherent with their medications, and this has been shown for a range of diseases.<sup>191 192</sup></p> <p>For some Aboriginal peoples, <u>a belief that western medicines are inferior to traditional medicines</u>, combined with fear that contact with mainstream health services will bring more illness is a barrier to adherence. One focus group respondent explained: <i>“As soon as you touch hospital you get sickness. Medicine they give us, it kills us”</i>. Other cultural beliefs about the cause of illness may also influence perceptions about the necessity for medications: <i>“Blackfella way causes sickness, if you get sick for nothing.”</i> Some community members perceive that young people still die at a young age even <i>without</i> smoking, drinking or eating unhealthy food. This may be perceived as the outcome of sorcery as punishment, or from other causes like jealousy and spite. If illness arises from sorcery, western medicine is considered ineffective. If a smoker, <i>“smoking sickness”</i> is considered inevitable rather than avoidable.<sup>193</sup></p>	<p>Beliefs about consequences; Knowledge</p>
Q6	<p><b>Do you sometimes take less medicine to make the medicine last longer?</b></p>	<p>ARMS asks: <i>“How often do you change the dose of your medicines to suit your needs (like when you take more or less pill than you’re supposed to)?”</i></p> <p>RAMS asks: <i>“I sometimes alter the dose of my medication to suit my own needs”; “Some people miss out on a dose of their medicine or adjust it to suit their own needs. How often do you do this?”.</i></p>	<p>This question explores behaviour that limits or alters the use of medicines and if it is related to rationing the use of medicines (make it “last longer”). The <i>Reported Adherence Measurement Scale</i> (RAMS) asks patients to report if they alter the dose of medications and the frequency of that behaviour, but does not explore reasons.<sup>194</sup> Rationing may or may not be related to health beliefs about <i>severity</i> of the illness (see Q7) and/or <i>perceptions of benefit</i>. Sharing or swapping medicines has been reported as barrier to medication adherence in the Aboriginal and Torres Strait Islander population.<sup>195</sup> Rationing may be a response to difficulties in the social context that affect access to medicines such as cost or other barriers (see Q9). It is possible that interventions to</p>	<p>Intentions; Beliefs about consequences; Environmental context and resources; Social influences</p>

			address the need to ration medicines can reduce this behaviour. Few studies have explored this phenomenon.	
Q7	<p><b>Do you sometimes stop taking your medicines because you think you are ok?</b></p>	<p>MMAS-4 asks: <i>“When you feel better do you sometimes stop taking your medicine?”</i></p> <p>The BMQ asks: <i>“My health in the future is dependent on my medicines”; “without my medicines I would be very ill”; “my life would be impossible without my medicines”; “my medicines protect me from becoming worse”.</i></p>	<p>This question explores <i>perceptions about the severity</i> of the health problem, consistent with the Health Belief Model, as well as beliefs about <i>the necessity</i> of taking medications. It is proposed that the greater the perceived threat of disease severity, the better the adherence to treatment. Conversely, if the patient thinks the health issue is not severe, they are less likely to continue to take medicine. The <i>perception of severity</i> is related to a belief about the potential for the health condition (or issue) to cause physical harm and interfere with social functioning.</p> <p>A relationship between this belief and medication adherence has been shown in meta-analysis. The degree of patient awareness of the severity of their health issue was positively predictive of their adherence to medications. In other words, the greater the perceived disease severity threat, the better the adherence.<sup>196</sup></p> <p>For some Aboriginal peoples, disease is not a concern if one is still able to function as explained by a quote from a male Aboriginal health worker: <i>“As long as you can do what you want to do, then you don’t worry about health”</i>. The perception that people are ‘ok’ and don’t need medications is especially linked with asymptomatic diseases like diabetes.<sup>197</sup></p> <p>The BMQ asks patients to rate how important their medicine is for their health, eliciting responses that reflect beliefs about <i>the necessity</i> of the medicines that have been shown to correlate positively with adherence, and are quite different questions to the MMAS. Question 7 is different from the MMAS, because it explores <i>perception</i> about illness (think you are ok) rather than clinical improvement (you feel better). It is expressed in a way that is more appropriate to the Aboriginal health context.</p>	<p>Beliefs about consequences; Intentions</p>
Q8	<p><b>Do you sometimes stop taking your medicine because you think it might make you sick?</b></p>	<p>MMAS-4 asks: <i>“Sometimes if you feel worse when you take the medicine, do you stop taking it?”</i></p> <p>The SEAMS scale asks: <i>“How confident are you that you can take your medicines correctly when you are feeling sick (like having a cold or the flu)?”</i></p> <p>ASK-12 includes: <i>“Have you skipped or stopped taking a medicine because it made you feel bad?”</i></p> <p>ARMS asks: <i>“How often do you miss taking your medicine when you feel sick?”</i></p> <p>The BMQ asks: <i>“I sometimes worry about the long-term effects of taking medicines,”; “Having to take this medicine worries me”.</i></p>	<p>This question explores perceptions of trust in health services, perceptions that medicines may be harmful, perceptions of vulnerability to adverse effects, and knowledge of the necessity for medicines (see Q7). Patients who perceive medicines as a threat exceeding the threat of disease, are less likely to be adherent.<sup>198</sup> Patients who think that the treatment <i>might</i> make them ill have less adherence.<sup>199</sup> This item should differentiate perceptions about disease threat versus medicines threat, rather than behavioural responses to adverse effects. For example, if adverse effects are actually causing harm, the patient should stop taking the medicine.<sup>200</sup> Patients who feel worse after taking a medicine, should seek advice to review the appropriateness of drug choices.</p> <p>This question is similar to the intent of the BMQ that explores perceptions the patient may have of medicines as a threat, expressed as a <i>concern</i> that medicines may generate adverse effects. However, the BMQ uses likert scale responses to these</p>	<p>Beliefs about consequences; Intentions</p>

			<p>items.</p> <p>For some Aboriginal peoples, a lack of trust in health services leads them to stop taking medicine because of belief the body cannot cope with it, fear the clinic may poison them, and fear of the medicine.<sup>201</sup></p> <p>The SEAMS scale explores the degree of <i>confidence in the ability</i> to take medications correctly in spite of illness. Other 11-item questions already explore the theme of <i>self-efficacy</i>.</p> <p>Q8 explores if the patient <u>thinks</u> the medicine might make them sick (perception of the drug as a threat/concern) rather than if it actually makes them sick. The MMAS explores ‘feeling worse’ when taking the medicine, which may be an actual adverse drug effect, although there is some ambiguity with interpretation. ASK-12 and ARMS surveys ask similar questions to the MMAS.</p>	
Q9	<p><b>Do you sometimes 'run out' of medicines because it costs too much, or it is hard to get more?</b></p>	<p>ASK-12 includes: <i>“Have you skipped, stopped, not refilled, or taken less medicine because of the cost?”; “I run out of my medicine because I don't get refills on time.”</i></p> <p>ARMS asks: <i>“How often do you put off refilling your medicines because they cost too much money?; How often do you forget to get prescriptions filled?; How often do you plan ahead and refill your medicines before they run out?”</i></p>	<p>This question explores <i>perceived barriers</i> to taking medications, which is consistent with the Health Belief Model. Cost is a well-known barrier to medication adherence.<sup>202</sup></p> <p>However, in view of the alleviation of some of the cost-barriers for the Aboriginal and Torres Strait Islander population through improved health policy (PBS co-payment measures, and access to medicines through S100 of the National Health Act (1953)), other access barriers may pose a bigger threat to adherence than cost alone. This question was expanded to include other factors that make it ‘hard’ for patients to have a suitable supply of medications.<sup>203</sup></p> <p>Factors that influence how ‘hard’ it is to source medicines include: a patient’s psychological profile (being too distracted or busy; poor coping skills, cynicism, poor insight, lack of self-worth, anxiety and depression, and other factors affecting motivation), concomitant social issues such as alcohol or substance abuse; and transport difficulties. These factors have all been shown to negatively affect adherence.<sup>204</sup></p>	<p>Environmental context and resources; Social influences; Emotion; Behavioural regulation</p>
Q10	<p><b>Do you sometimes run out of medicines because you give them away or share them with other people?</b></p>	<p>ARMS asks: <i>“How often do you run out of medicine?”</i></p> <p>ARMS asks: <i>How often do you take someone else's medicine?</i> [This Q was removed from the final set].</p>	<p>This question explores ‘running out of medicine’ as an outcome of sharing. It does not explore behaviour to ration the use of medicines, making it conceptually different to Q6. The sharing of medicines has been reported in studies about Aboriginal peoples and Torres Strait Islanders.<sup>205</sup> Aboriginal health workers in NSW reported that the practice of sharing medications by Aboriginal patients was common.<sup>206</sup></p> <p>Behaviour that involves sharing of medicines may be influenced by culture (kinship obligations), arise from inadequate <i>perceptions of the severity</i> of the illness (see Q7) and/or <i>perceptions about benefit</i>, or lack of knowledge about when and how to take the medicine (Q3). Few studies have explored the impact that sharing medicines has on medication adherence given that the person sharing has less available to take, and the recipient has less incentive to seek medicines.</p>	<p>Environmental context and resources; Social influences; Emotion; Intentions; Behavioural regulation; Knowledge; Beliefs about consequences</p>

Q11	<p><b>Do you go without your medicines when you are away from home?</b></p>	<p>ASK- 12 scale includes: <i>“Have you not had medicine with you when it was time to take it?”</i>.</p> <p>The MMAS-8 asks: <i>When you travel or leave home, do you sometimes forget to bring along your medicine?</i></p>	<p>Being away from community has been identified as a barrier to medication adherence for Aboriginal peoples and Torres Strait Islanders.<sup>207</sup> To be away from home without medicines may be intentional (‘shame’ associated with carrying medicines, being seen to be ‘sick’, storage issues, etc) or unintentional (forgetfulness). Aboriginal and Torres Strait Islander peoples may be away from home when visiting other communities on sorry business, to fulfil kinship responsibilities, or other reasons. Whether the outcome is intentional or unintentional, going without medicines means being non-adherent to medicines.</p> <p>The MMAS only explores forgetfulness making it unsuitable for use in the Aboriginal context as patients may not ‘bring along’ their medicine when away from home for social reasons (as outlined) and not merely forgetfulness. Moreover, forgetfulness is already explored in Q1 of the 11-item scale. In addition, Q11 does not use the term ‘travel’. In the Aboriginal context, the issue is about being ‘away from community or home’ (a connection ‘with country’) which is an Aboriginal definition of well-being,<sup>208</sup> rather than ‘travel’, or ‘leaving’ home, with the latter suggesting permanent departure. Q11 does not use the word ‘sometimes’.</p> <p>The ASK-12 scale does not specifically explore being away from home.</p>	<p>Memory, attention and decision processes; Environmental context and resources; Social influences; Intentions; Behavioural regulation</p>
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NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11.

\*The *Morisky Medication Adherence Scale* (MMAS4/8) is a 4-item or 8-item scale exploring self-reported medication adherence. Most validation studies pertain to use in patients with hypertension.<sup>209</sup>

\*\*Theoretical Domains Framework (v2).

The *Beliefs about Medicine Questionnaire* (BMQ) is a 5-point likert scale that explores medication beliefs and has been validated for use in patients with a range of chronic diseases. It explores patient beliefs about the necessity of their medications and their concerns about the potential adverse effects of taking it, with higher necessity scores correlating with better adherence.<sup>210 211 212</sup>

The *Self-efficacy for Appropriate Medication Use* (SEAMS) scale was validated for use with low-literacy patients with coronary heart disease and other co-morbidities as a measure of self-efficacy with taking medications.<sup>213</sup> However, it has not been shown to have construct validity with regard to predicting biomedical health outcomes such as blood pressure changes or changes in blood glucose levels in patients with diabetes.<sup>214</sup>

The *Adherence Starts with Knowledge* (ASK-12) survey informs on patient reported barriers to medication adherence and adherence-related behaviour. Validation studies pertain to patients with chronic disease with 56% being African American.<sup>215</sup>

The *Adherence to Refills and Medications Scale* (ARMS) is a 12-item scale designed to assess medication adherence in patients with low literacy levels with chronic disease in primary health care settings.<sup>216</sup> The ARMS was modified from the Morisky tool and the Hill-Bone Instrument (specific for hypertension).

The *Reported Adherence Measurement Scale* (RAMS) is a 4-item scale that ascertains the level of agreement with “sometimes forgetting to take or sometimes altering the dose of medication” and frequency according to a 5-point likert scale.<sup>217</sup>

**Table 8. Item-specific content validity index (I-CVI) for 11-item NMARS scale: relevancy.**

Item	Relevant (rating 3 or 4)	Not relevant (rating 1 or 2)	I-CVI	Interpretation
1	14	1	0.93	Appropriate
2	14	1	0.93	Appropriate
3	12	3	0.80	Appropriate
4	12	3	0.80	Appropriate
5	12	3	0.80	Appropriate
6	13	2	0.87	Appropriate
7	15	0	1.00	Appropriate
8	15	0	1.00	Appropriate
9	14	1	0.93	Appropriate
10	13	2	0.87	Appropriate
11	14	1	0.93	Appropriate

Results are based on assessment of 15- member multidisciplinary expert panel.  
Ratings are results of responses to Appendix 3B questions.

**Table 9. Item-specific content validity index (I-CVI) for 11-item NMARS scale: clarity.**

Item	Clarity (rating 3 or 4)	No clarity (rating 1 or 2)	I-CVI	Interpretation
1	13	2	0.87	Appropriate
2	15	0	1.00	Appropriate
3	14	1	0.93	Appropriate
4	12	3	0.80	Appropriate
5	13	2	0.87	Appropriate
6	11	4	0.73*	Need revision
7	15	0	1.00	Appropriate
8	14	1	0.93	Appropriate
9	13	2	0.87	Appropriate
10	11	4	0.73*	Need revision
11	15	0	1.00	Appropriate

\* The wordings of questions 6 and 10 were revised.

Results are based on assessment of 15- member multidisciplinary expert panel.  
Ratings are results of responses to Appendix 3B questions.

**Table 10. Scale-specific content validity testing (S-CVI) for 11-item scale: percentage agreement among expert panel members.**

Question	Number of experts	Rating 4 or 5*	% Agreement
1 To what extent are the questions directed at important issues pertaining to the assessment of medication adherence as reported by Aboriginal and Torres Strait Islander patients?	15	14	93.3
2 Are there important issues pertaining to the assessment of medication adherence that should be included in the questionnaire which have been omitted?	15	8	60.0
3 To what extent are the questions simple and easily understood?	15	13	86.7
4 To what extent are questions likely to elicit information about medication adherence in Aboriginal and Torres Strait Islander patients?	15	12	80.0
5 How many questions are inappropriate or not needed?	15	9	66.7
6 How likely is the questionnaire to assess medication adherence in Aboriginal and Torres Strait Islander patients?	15	11	73.3
Mean % agreement and 95% confidence interval			76.7 (95% CI 63.6 to 89.8)

S-CVI: scale-specific content validity index

\*Rating of 4-5 refers to the option choices shown below.

Option choice	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Rating
Answer	Small Extent	Crucial Gaps	Small Extent	Small Extent	Very Many	Very Unlikely	1
Answer	Limited Extent	Important Gaps	Limited Extent	Limited Extent	Many	Unlikely	2
Answer	Fair Extent	Minor Gaps	Fair Extent	Fair Extent	Some	Likely	3
Answer	Moderate Extent	Minimal Gaps	Moderate Extent	Moderate Extent	A few	Quite Likely	4
Answer	Large Extent	Insignificant Gaps	Large Extent	Large Extent	Hardly Any	Very Likely	5

**Table 11. Item-specific response frequencies to each question in the 11-item NMARS scale at baseline (n=1103 participants)**

Item	Questions	Yes (n, %)
Q1	Did you forget to take any of your medicines yesterday?	363 (32.9%)
Q2	Is it hard for you to remember to take your medicines?	425 (38.5%)
Q3	Do you know when, and how, to take your medicines?	1013 (91.8%)
Q4	Is it hard for you to take your medicines in the right way? <i>(like the Dr/nurse/AHW said)</i>	319 (28.9%)
Q5	Do you feel that taking your medicines will be good for your health?	986 (89.4%)
Q6	Do you sometimes take less medicine to make the medicine last longer?	107 (9.7%)
Q7	Do you sometimes stop taking your medicines because you think you are ok?	239 (21.7%)
Q8	Do you sometimes stop taking your medicine because you think it might make you sick?	222 (20.1%)
Q9	Do you sometimes 'run out' of medicines because it costs too much, or it is hard to get more?	357 (32.4%)
Q10	Do you sometimes run out of medicines because you give them away or share them with other people?	19 (1.7%)
Q11	Do you go without your medicines when you are away from home?	306 (27.7%)

Not for distribution

**Table 12. Spearmans correlation coefficients between SIQ result and participant biomedical indices at baseline.**

Biomedical indices	N, %	Correlation coefficient	p-value	95%CI*
HbA1c	441/677 (65.1%)	-0.20	<0.0001	-0.29 to -0.11
Total cholesterol	558/1103 (50.6%)	-0.14	0.0006	-0.23 to -0.06
Triglycerides	606/1103 (54.9%)	-0.09	0.026	-0.17 to -0.01
Low density lipoprotein cholesterol	470/1103 (42.6%)	-0.12	0.012	-0.20 to -0.03

\*95%CI = 95% confidence interval

Not for distribution

**Table 13. Response frequencies to SIQ and NMARS adherence assessments from IPAC participants (n=1103)**

NMARS score**	Single-item question (SIQ) score*		Total
	Non-Adherent (0-5)	Adherent (6-7)	
<b>Non-Adherent (0-7)</b>	196	99	<b>295</b>
<b>Adherent (8-11)</b>	126	682	<b>808</b>
<b>Total</b>	<b>322</b>	<b>781</b>	<b>1103</b>

79.6% overall agreement between the two tools.

\*SIQ= A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking. A score of 6-7 was defined as adherence and dichotomized to a mean adherence (score  $\geq 6$ ), or non-adherence (0-5).

\*\* NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. NMARS scoring used a cut-off score that produced a similar proportion of adherent respondents to the single-item question.

Not for distribution

**Table 14. Medication adherence scores according to participant subgroups as measured by NMARS and SIQ adherence tools**

Indicator at baseline	Adherence at baseline		Adherence at baseline	
	SIQ score (n, %)		NMARS total score (n, %)	
	No (0-5)	Yes (6-7)	No (0-7)	Yes (8-11)
Normal BP (<140 mmHg; systolic), <i>n</i> =601	173/601 (28.8%)	428/601 (71.2%)	157/601 (26.1%)	444/601 (73.9%)
High BP (≥140 mmHg; systolic), <i>n</i> =234	70/234 (29.9%)	164/234 (70.1%)	63/234 (26.9%)	171/234 (73.1%)
CKD A1 (<30 mg/g ACR) <i>n</i> =278	85/278 (30.6%)	193/278 (69.4%)	76/278 (27.3%)	202/278 (72.7%)
CKD A2 and A3 (30-300 and >300 mg/g ACR) <i>n</i> =121	38/121 (31.4%)	83/121 (68.6%)	35/121 (28.9%)	86/121 (71.1%)
HbA1c <6.4% <i>n</i> =4	0/4 (0%)	4/4 (100%)	1/4 (25%)	3/4 (75%)
HbA1c 6.5% or higher <i>n</i> =437	129/437 (29.5%)	308/437 (70.5%)	131/437 (30.0%)	306/437 (70.0%)

BP= blood pressure

CKD= chronic kidney disease

CKD (A1, A2, A3) = albuminuria categories in chronic kidney disease

HbA1c= haemoglobin A1c

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. NMARS scoring used a cut-off score that produced a similar proportion of adherent respondents to the single-item question.

SIQ= A self-reported single-item question ("How many days in the last week have you taken this medication?") exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking. A score of 6-7 was defined as adherence and dichotomized to a mean adherence (score ≥6), or non-adherence (0-5).

Figure 4. Scatterplot for the assessment of association between SIQ score and the number of medications prescribed per participant (Spearman's correlation coefficient = 0.24, 95%CI 0.19- 0.30,  $p < 0.0001$ ,  $n = 1103$ ).

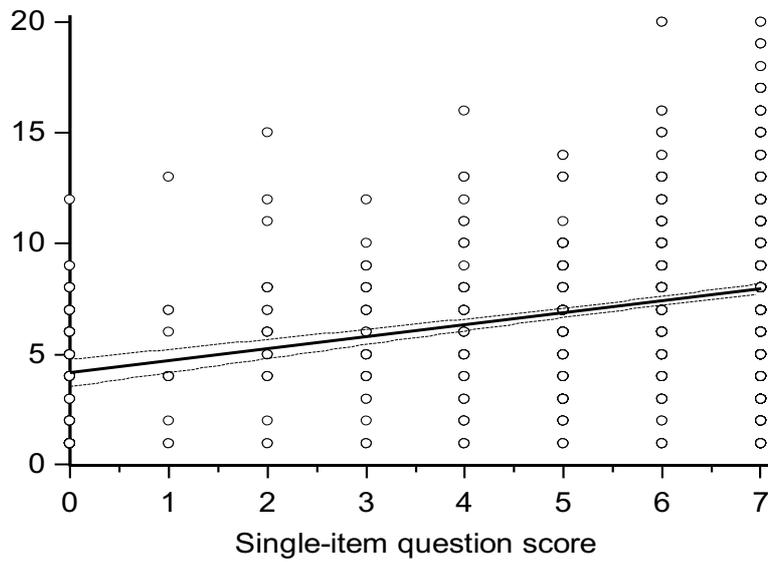
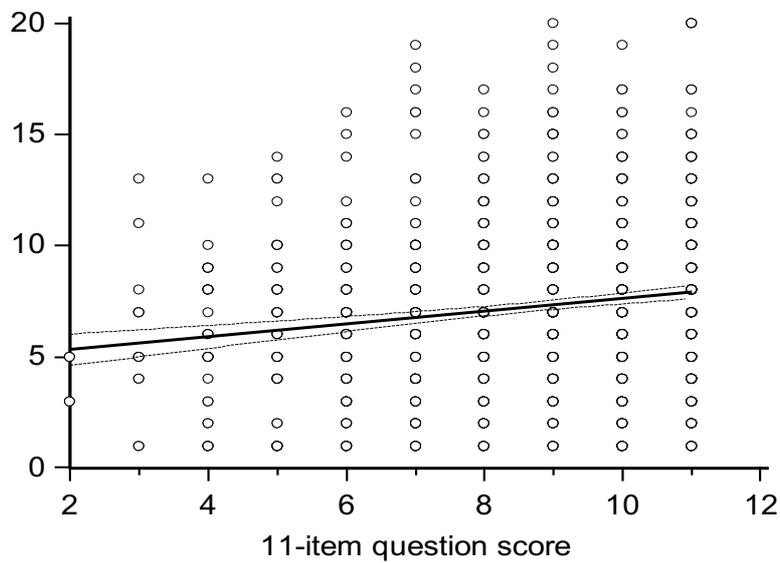


Figure 5. Scatterplot for the assessment of association between NMARS score and the number of medications prescribed per participant (Spearman's correlation coefficient = 0.15, 95%CI 0.09- 0.21,  $p < 0.0001$ ,  $n = 1103$ ).



**Table 15. Known groups comparison: medication adherence scores by BMI and sex as measured by NMARS and SIQ tests**

Indicator at baseline	Adherence at baseline		Adherence at baseline	
	SIQ score (n, %)		NMARS total score (n, %)	
	No (0-5)	Yes (6-7)	No (0-7)	Yes (8-11)
Female	210/677 (31.02%)	467/677 (68.98%)	188/677 (27.77%)	489/677 (72.23%)
Male	112/423 (26.48%)	311/423 (73.52%)	106/423 (25.06%)	317/423 (74.94%)
BMI to 24.9	46/154 (29.87%)	108/154 (70.13%)	38/154 (24.68%)	116/154 (75.32%)
BMI ≥25	170/659 (25.8%)	489/659 (74.2%)	168/659 (25.49%)	491/659 (74.51%)

BMI= Body Mass Index (kg/m<sup>2</sup>)

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. NMARS scoring used a cut-score that produced a similar proportion of adherent respondents to the single-item question.

SIQ= A self-reported single-item question ('How many days in the last week have you taken this medication?') exploring the extent of non-adherence, assessed as a mean score for all medications. An 'adherent day' was defined as not missing any doses of prescribed medicines on that day. Pharmacists recorded the number of adherent days for each medication the patient was taking. A score of 6-7 was defined as adherence and dichotomized to a mean adherence (score >=6), or non-adherence (0-5).

Not for distribution

**Table 16. Spearman’s correlation coefficient between baseline and end of study SF1 and SIQ and NMARS responses (paired data, n=975).**

Adherence measure	Correlation with SF1	p-value	95%CI*
<b>Baseline</b>			
SIQ	0.12	0.0001	0.06 to 0.19
NMARS	0.20	<0.0001	0.14 to 0.26
<b>End of study</b>			
SIQ	0.15	<0.0001	0.09 to 0.21
NMARS	0.28	<0.0001	0.22 to 0.33

Correlations were based on z-scores transformed responses.

\*95%CI = 95% confidence interval

Not for distribution

**Table 17. Item to test (total) correlation using participant responses to the NMARS to assess reliability with Cronbach's alpha, and effect on Cronbach's alpha of item deletion.**

Item	N	Sign	Item-test correlation	covariance	Cronbach's alpha	Change in Cronbach's alpha if item is deleted
Q1	1103	+	0.59	0.02	0.62	-0.04
Q2	1103	+	0.61	0.02	0.62	-0.05
Q3	1103	-	0.23	0.03	0.67	0.01
Q4	1103	+	0.60	0.02	0.62	-0.05
Q5	1103	-	0.27	0.03	0.67	0.01
Q6	1103	+	0.37	0.03	0.66	-0.01
Q7	1103	+	0.60	0.02	0.62	-0.05
Q8	1103	+	0.52	0.02	0.63	-0.03
Q9	1103	+	0.48	0.02	0.65	-0.01
Q10	1103	+	0.11	0.03	0.67	0.01
Q11	1103	+	0.60	0.02	0.62	-0.05
Test scale				0.02	<b>0.66</b>	

Item-test correlation shown as Pearson's correlation coefficients

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. NMARS scoring used a cut-score that produced a similar proportion of adherent respondents to the single-item question.

-Sign pertains to reverse scoring of the item.

N=number of participant observations

Not for distribution

**Table 18. Inter-item correlation matrix for the NMARS (unadjusted alpha, n=1103)**

Variables	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Q1	<b>1.00</b>										
Q2	<b>0.33</b>	<b>1.00</b>									
Q3	-0.05	<b>-0.06</b>	<b>1.00</b>								
Q4	<b>0.28</b>	<b>0.43</b>	<b>-0.12</b>	<b>1.00</b>							
Q5	<b>-0.09</b>	-0.05	0.03	<b>-0.10</b>	<b>1.00</b>						
Q6	<b>0.07</b>	<b>0.09</b>	0.00	<b>0.10</b>	-0.02	<b>1.00</b>					
Q7	<b>0.28</b>	<b>0.21</b>	<b>-0.06</b>	<b>0.25</b>	<b>-0.18</b>	<b>0.15</b>	<b>1.00</b>				
Q8	<b>0.20</b>	<b>0.14</b>	-0.01	<b>0.22</b>	<b>-0.13</b>	<b>0.20</b>	<b>0.34</b>	<b>1.00</b>			
Q9	<b>0.15</b>	<b>0.20</b>	-0.01	<b>0.11</b>	0.02	<b>0.22</b>	<b>0.18</b>	<b>0.16</b>	<b>1.00</b>		
Q10	0.01	<b>0.07</b>	-0.01	0.05	-0.02	-0.02	0.00	0.00	0.03	<b>1.00</b>	
Q11	<b>0.27</b>	<b>0.28</b>	<b>-0.10</b>	<b>0.23</b>	-0.04	<b>0.21</b>	<b>0.33</b>	<b>0.22</b>	<b>0.21</b>	0.04	<b>1.00</b>

Inter-item correlation matrix represented by Pearson's correlation coefficients.

NMARS= NACCHO Medication Adherence Response Scale (11-item) for the assessment of the reasons for medication non-adherence, generating a score defining adherence from 8 to 11. NMARS scoring used a cut-score that produced a similar proportion of adherent respondents to the single-item question.

Unadjusted refers to directionless alpha computation. Values in bold refer to ideal alpha value  $\geq 0.15$  and are different from 0 with a significance level  $p < 0.05$ . Items 3 and 10 show no inter-item correlation with any items.

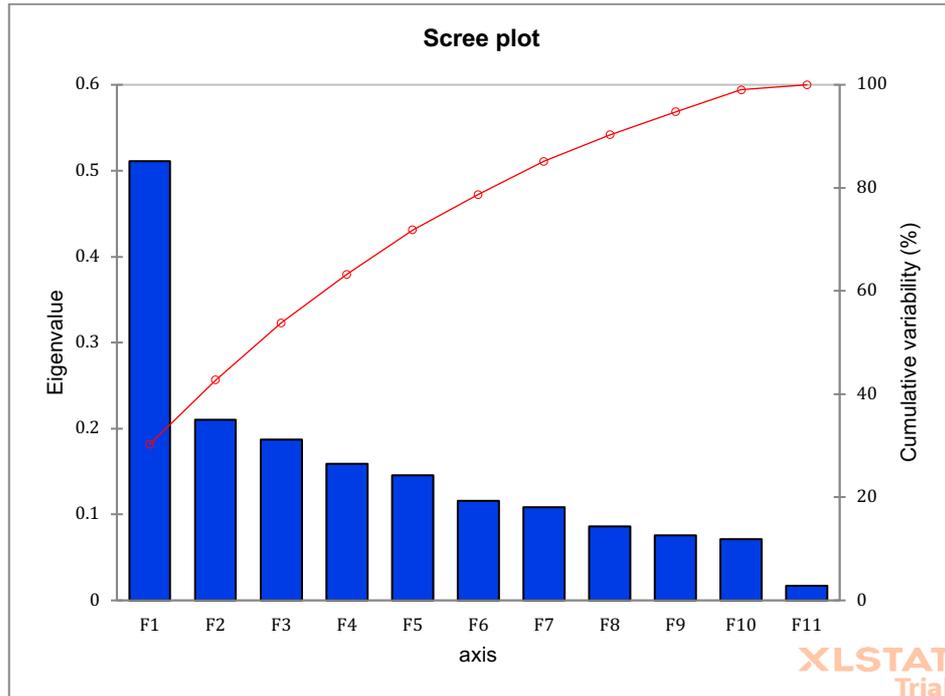
Not for distribution

**Table 19. Principal component analysis for the NMARS: eigenvalues**

	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Eigenvalue	0.51	0.21	0.19	0.16	0.15	0.12	0.11	0.09	0.08	0.07	0.02
Variability (%)	30.28	12.47	11.07	9.40	8.63	6.88	6.43	5.12	4.48	4.25	0.99
Cumulative %	30.28	42.75	53.82	63.22	71.85	78.73	85.16	90.28	94.76	99.01	100.000

\*Cronbachs alpha for NMARS tool = 0.66

**Figure 6. Scree plot indicating the Eigenvalues after principal component analysis of the NMARS in the IPAC study**



**Table 20. Principal components analysis factor loadings of each item in the NMARS (n=1103)**

	F1	F2	F3	F4	F5
Q1	0.301	-0.080	-0.066	-0.333	-0.064
Q2	0.340	-0.177	0.209	0.036	0.049
Q3	-0.034	0.018	0.005	-0.017	-0.023
Q4	0.291	-0.181	0.030	0.176	-0.087
Q5	-0.048	0.018	0.080	-0.018	0.056
Q6	0.080	0.088	-0.009	0.041	0.006
Q7	0.238	0.079	-0.188	0.040	-0.046
Q8	0.187	0.092	-0.175	0.104	-0.148
Q9	0.208	0.327	0.236	-0.020	-0.084
Q10	0.007	-0.003	0.006	0.004	0.004
Q11	0.274	0.101	-0.099	0.026	0.311

F=factor. No factor had an item loading  $\geq 0.4$ . Only the first five factors are shown. Shaded rows highlight lower loadings onto factor 1 and pertain to items 3, 5, 6 and 10 which were noted to have ceiling effects.

## APPENDIX 1

The *MMAS* was specifically unsuitable for the IPAC Project for a range of other reasons as outlined in Table A-1.

**Table A-1. Reasons why the Morisky Medication Adherence Scale was not used in the IPAC study.**

1. A decision to cancel an application for the license to use the Morisky Medication Adherence Scale (MMAS) was endorsed by the Project Partners in April 2018. The MMAS is arguably the most widely used self-report measure of medication adherence internationally. This decision arose following an unexplained 35% increase in the cost of the license, lack of adequate funds in the project budget to accommodate the increase, concern about the appropriateness of the tool in the Aboriginal context, and concern about the probity and ethics of the process to grant the license from the US developers. A recent article in the *Science* magazine outlined international concerns about the developers "demands for money".<sup>218</sup>
2. The licence to use the MMAS included the requirement for specific training that could only be delivered in the USA with timing that conflicted with IPAC project timelines.
3. The MMAS licence also required the use of the software provided by the developers to capture scores, which raised data security issues.
4. The MMAS would have required revalidation to infer meaningful information about medication adherence for Aboriginal and Torres Strait Islander patients. The inferences drawn from using the MMAS are validated for a specific purpose (predominantly for elderly patients with hypertension in the US health care system context). These conditions need to be matched in order to validate the inferences about medication adherence that arise from the use of the tool.<sup>219</sup>
5. The language and readability of the MMAS scale is too complex for use in the Australian setting. This was confirmed with readability testing.
6. The scale should ideally help the pharmacist to tailor strategies to suit the individual patient's issues, as such strategies are more likely to support good medication-taking behaviour.<sup>220</sup> The scale used needed to offer a consistent and standardized approach for pharmacists to explore medication adherence with IPAC patients. The MMAS had a limited scope with regard to behavioural factors and beliefs that may impact on adherence regarding Aboriginal peoples.
7. The scale needed to be able to draw valid inferences about medication adherence for patients with any chronic disease, whilst the MMAS was principally validated for hypertensives, which made it unsuitable given the broad patient inclusion criteria for the IPAC trial.
8. Given that the revalidation process is similar to the process used to undertake the development and validation of a new scale, and the range of other issues outlined above, a process to develop a new scale was agreed.

## APPENDIX 2

### A: Original 16-item scale to assess medication adherence for the IPAC project

	Yes	No
1. Is it hard <b>to remember</b> to take all your medicines properly?	0	1
2. Did you <b>forget to take</b> any of your medicine's yesterday?	0	1
3. Are you <b>unsure</b> how or when to take your medicines?	0	1
4. When you are away from home, do you sometimes <b>forget to bring</b> your medicines with you?	0	1
5. Do you sometimes <b>run out</b> of medicine/s and then stop taking them for a while?	0	1
6. Do you sometimes <b>give away</b> your medicines or <b>share</b> them with other people?	0	1
7. Do you sometimes <b>lose</b> your medicines?	0	1
8. Do you sometimes try to make the packet/box last longer by <b>taking fewer medicines</b> ?	0	1
9. When you have no money, do you sometimes <b>stop buying</b> your medicine/s?	0	1
10. Do you <b>stop your medicine/s</b> when you <b>feel sick</b> (such as a cold)?	0	1
11. Do you think the medicine/s <b>makes you feel sick</b> ?	0	1
12. Do you sometimes <b>stop taking your medicines</b> because you think you are ok, or <b>don't need</b> them?	0	1
13. Do you think <b>you can take</b> your medicines in the way the Dr said?	1	0
14. Are you able to <b>get a new prescription</b> before you run out of your medicines?	1	0
15. Do you feel that taking the medicine/s will <b>benefit you</b> ?	1	0
16. Can you remember to take your medicine when there is <b>no-one around</b> to remind you?	1	0

## APPENDIX 3

### A: Scale-specific content validity testing tool

Question		Selection <i>Please select below from the list</i>
1	To what extent are the questions directed at important issues pertaining to the assessment of the 'extent and the reasons' for medication non-adherence as reported by Aboriginal and Torres Strait Islander patients?	Not Selected Small Extent Limited Extent Fair Extent Moderate Extent Large Extent
2	Are there important issues pertaining to the assessment of the 'extent and reasons' for medication non-adherence that should be included in the questionnaire which have been omitted?	Not Selected Crucial Gaps Important Gaps Minor Gaps Minimal Gaps Insignificant Gaps
3	To what extent are the questions simple and easily understood?	Not Selected Small Extent Limited Extent Fair Extent Moderate Extent Large Extent
4	To what extent are questions likely to elicit information about the 'extent and the reasons' for medication non-adherence in Aboriginal and Torres Strait Islander patients?	Not Selected Small Extent Limited Extent Fair Extent Moderate Extent Large Extent
5	How many questions are inappropriate or not needed?	Not Selected Very Many Many Some A few Hardly Any
6	How likely is the questionnaire to assess the 'extent and reasons' for medication non-adherence in Aboriginal and Torres Strait Islander patients?	Not Selected Very Unlikely Unlikely Likely Quite Likely Very Likely

*\*This clinical sensibility testing tool has been adapted from: Appendix to Burns KEA, Duffett M, Kho M, et al.; ACCADEMY Group. A guide for the design and conduct of self-administered surveys of clinicians. CMAJ 2008;179(3):245-52.*

**B: Item-specific content validity testing tool**

Questions	Relevancy testing	Clarity testing	Suggested modification to the question to enhance clarity and relevance
	Please select below	Please select below	
Q1	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q2	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q3	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q4	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q5	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q6	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q7	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q8	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q9	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
Q10	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	

Q11	NOT SELECTED not relevant item need some revision relevant but need minor revision very relevant	NOT SELECTED not clear item need some revision clear but need minor revision very clear	
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