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The evaluation of an osteoporosis medication management service in community pharmacy, a cohort study

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ABSTRACT

Background: Effective treatment of osteoporosis is hindered by poor adherence and lack of persistence with medical therapy. Interventions can be designed to elicit and address patients' concerns about side effects and promote self-management. **Objective(s):** The aim was to develop and evaluate the impact of a community pharmacy-based medication management intervention on patients' adherence to osteoporosis medicines using both objective and subjective measures of adherence. Secondary aims were to report the proportion of patients that had been referred to their General Practitioner (GP) for assistance with osteoporosis management, and to measure patients' experiences with the service. **Methods:** This study used a cohort design. Community pharmacy dispensing data were obtained as an objective measure of adherence. Self-reported beliefs about medicines (Beliefs about Medicines Questionnaire) and self-reported adherence (Medication Adherence Reporting Scale 5) were also collected. Data were collected and compared between baseline, 4 weeks after intervention, and endpoint (approximately a year after intervention). Analysis of correlations between measures was also conducted. GP referral percentage and perceived service quality scale (pSQS-SF6) was obtained. **Results:** Pharmacists and support staff from 26 Australian community pharmacies were recruited and trained to implement the service, and 107 patients were recruited. Of these, 71 were available for follow-up interviews by research team at 4 weeks, and 54 at the endpoint. No changes were found in pre-post analysis for the objective or self-reported measures of adherence. Patients' concerns about osteoporosis medicines were lower at 4 weeks and at the study endpoint compared to baseline. Uptake of pharmacists' referrals to patients' GPs was 48.1% by 4 weeks. Patient experience was rated highly (median pSQS-SF6 = 6.5/7). **Conclusions:** This study demonstrates the potential of community pharmacy interventions designed to optimize medication adherence by eliciting patients' thoughts and feelings about using osteoporosis medicines and addressing them using motivational interview techniques.

1. Introduction

Osteoporosis is a chronic disease resulting in weakened bones and fragility fractures.[1] It is a major health condition affecting over 200 million people worldwide.[1] Fragility fractures are associated with substantial chronic pain, disability, loss of independence and premature death.[1,2]

In Australia, over 1.2 million people are living with osteoporosis.[3] This extracts a high socioeconomic toll of $3 billion AUD each year from the health system.[3] The number and proportion of older Australians have been increasing and as osteoporosis mainly impacts older individuals, the number of people with osteoporosis in Australia is also increasing.[2] Hospitalizations, length of stay, and health expenditure have all increased for osteoporosis related problems.[2] As such, one priority area within Australia's National Strategic Action Plan for Osteoporosis (2019) is to "develop and promote access to self-management resources, education and training opportunities for allied health professionals including pharmacists that provide people with osteoporosis information and skills to enhance their ability to take an active role in their own health care, including appropriate diet, safe and effective

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exercise and adherence to pharmaceutical treatment if required".[3]

The burden of osteoporosis can be reduced by treatment which is typically long-term and may extend to be lifelong.[4,5] Whilst effective pharmacotherapy exists for osteoporosis, challenges such as lack of timely diagnosis, delayed initiation of treatment, and poor adherence to medication therapy, results in reduced efficacy and clinical benefit.[6] Specifically, poor adherence is a major concern for osteoporosis medications as bone loss continues unabated, and poor adherence can substantially contribute to fractures and hospitalization.[4,7] Alternatively, higher adherence rates to osteoporosis medications are associated with higher bone mineral density (BMD) gains, lower fracture risk, decreased mortality and less severe consequences from osteoporosis.[8–12] Alarmingly, adherence rates to osteoporosis medications has been reported from 8% to 82% internationally.[8] Australian data reports that 40 to 53% of patients are not adherent to osteoporosis medications.[5,6]

Avoiding treatment interruptions is especially important for denosumab, which is prescribed to 76% of Australians receiving osteoporosis medications.[13] Denosumab is usually administered 6 monthly. Administration of denosumab in intervals of >7 months without alternative osteoporosis medication has been associated with rapid bone loss and spontaneous rebound fractures.[14–16] Over a 4-year period, 35% of Australians using denosumab had a treatment gap, and 34% had ceased denosumab altogether. Of these, <5% had transitioned to another osteoporosis medication.[13]

Adherence to osteoporosis medications is reported to be worse than medications used to treat other chronic conditions.[17,18] This is due to both unintentional poor adherence caused by forgetfulness, medication shortages, and difficulties associated with the timing of doses for some oral medicines, and intentional poor adherence due to deliberate choices by the patient to discontinue or to reduce the frequency of dosing and therefore amount used.[17,18] Other factors have been reported to contribute to poor adherence to osteoporosis therapy such as older age, polypharmacy, concerns about side effects prior to starting treatment, side effects while on treatment, cost, low health literacy, lack of patient education, patient perceptions regarding the necessity of treatment, misconceptions about osteoporosis as an inevitable part of aging, and skepticism about personal susceptibility to fractures.[5,19] Optimization of adherence in osteoporosis has been challenging and adherence rates remain suboptimal despite long-term efforts in adherence-related research.[19,20]

Osteoporosis adherence research has tended to lack the active involvement of pharmacists, despite their recognized importance in medication management.[19,21,22] Pharmacists have the capacity to address poor adherence and potentially alleviate the time burden on other practitioners.[19,21,22] Systematic reviews have attempted to characterize components of successful adherence interventions for anti-osteoporosis medications.[19,23] Mixed impact on adherence rates have been found for interventions centered on patient education, monitoring and supervision.[19] More positive results were found where interventions were multimodal, had patient involvement, counselling and shared decision making.[19] In regard to osteoporosis therapy specifically, it has been recommended that interventions should address patients concerns about therapy and optimize lifestyle management while ensuring that patient experience is monitored.[23]

Pharmacists are trusted health care professionals and are suitably positioned to provide specific osteoporosis management services, including medication management reviews.[21,24–26] When patients perceive that their community pharmacies provide high quality service, the patients are more likely to self-report being adherent to their regular medicines.[27] One Australian program, MedsCheck, provides a remunerated medication review service offered by pharmacists.[28] MedsCheck aims to enhance consumers' understanding and knowledge of their medications, with a view to correcting poor medication adherence (among other issues). While MedsChecks could be considered a general medication check-up, specific MedsChecks for chronic conditions like diabetes and pain have been implemented.[28,29] The application and evaluation of MedsChecks with osteoporosis as a specific focus remains unexplored.

1.1. Aim

The aim of this study was to evaluate the impact of a community pharmacy-based medication management intervention on patients' adherence to osteoporosis medicines using both objective and subjective measures of adherence. Given the vital role of the General Practitioner (GP) in supporting medication adherence, the study also aimed to report the proportion of patients that had been referred to the GP for assistance with osteoporosis, as a component of the service. The study also aimed to measure patients' experiences with the service.

2. Method

A STROBE checklist has been included in the supplementary material for methodological rigor of this cohort study (Supplementary Material 1). This study was approved by the University of Sydney Human Research Ethics Committee [2021/137]. This study was funded by the Osteoporosis Consumer Awareness Grant GO3113 from the Australian Government Department of Health and Aged Care.[30] The recruitment period ran from September 2021 to December 2022. The observation period was from just prior to the intervention up to 14 months after the intervention.

2.1. Design of the osteoporosis intervention

The intervention was designed to reflect the existing MedsCheck service, adapted to meet the specific purpose of improving bone health. MedsCheck are structured and collaborative clinical pharmacy services that take place in the pharmacy to optimize the safe and quality use of medicines by patients.[28,31] These services generally involve a review of patient medicines, a face-to-face consultation between the pharmacist and patient, and the development of a medication profile and an action plan.[28,31] MedsChecks focus on education and self-management and aim to identify medication-related problems (e.g. non-adherence), improve effective use of medicines and provide education about medicines.[28,31]

The specific details of how the intervention was designed, implemented and conducted was informed by stakeholder interviews and is reported elsewhere.[32] The intervention was named the Osteoporosis MedsCheck. Pharmacists utilized the tools they regularly used to conduct MedsCheck services, and were provided with promotional material, resources and training. In essence, pharmacists were encouraged to initiate conversations regarding osteoporosis management using the techniques of motivational interviewing.[33] To facilitate these conversations, pharmacists were provided with a purpose-designed questionnaire. The questionnaire probed patients' subjective thoughts and feelings about osteoporosis therapy and collected self-report data of medication-taking behaviors. This included questions specifically related to osteoporosis therapy, including disease status, falls and fractures history and nutrients and supplements. This questionnaire was developed by the research team, which included endocrinologists, academic pharmacists, and consumer representatives.[30] This collaborative approach ensured that pharmacists had access to a questionnaire and interview guide that was clinically relevant and user-friendly for both pharmacist and patients.

During a regular MedsCheck, pharmacists may ask the patient to complete some pre-interview questions.[31] As such, in the intervention, pharmacists either provided the purpose-designed questionnaire to patients to complete before the interview or they could assist the patient to complete it during the interview. At the conclusion of the intervention, the pharmacist provided the patient with a medication profile, obtained by utilizing the Best Possible Medication History as a guide.[34] In addition, the patient was provided with an action plan, counselling regarding osteoporosis, and information brochures to support any lifestyle advice.

The intervention was intended to be conducted face-to-face within a community pharmacy's private consultation room, however, was also able to be completed or via telepharmacy during the COVID pandemic, consistent with Australian Government policy at the time.[28]

2.2. Eligibility, recruitment and consent

Australian community pharmacies were eligible to participate if they were able to provide MedsCheck services as per the Australian Government guidelines.[28] Invitations to participate for Australian community pharmacies were disseminated through the Pharmaceutical Society of Australia's (PSA) distribution outlets, social media, and convenience sampling. When community pharmacists expressed interest, participant information sheets were provided and informed consent was obtained from the owner or manager of each participating pharmacy.

Eligible pharmacy patients were identified and invited to participate by their community pharmacists (this would most likely be their regular pharmacy, however, pharmacy patients in Australia are not restricted to visit only a single pharmacy). Pharmacies were instructed to prioritize the recruitment of patients who they considered were poorly adherent to their prescribed osteoporosis medication(s). Pharmacists could identify patients via the methods usually used for MedsChecks including prescreening of dispensing records, and/or opportunistically utilizing their pharmacists (or their assistants) personal knowledge of their patients' needs and preferences. For example, eligible patients could be identified when they were collecting prescriptions for osteoporosis medicines, or during informal conversations in the pharmacy. In addition, patients were able to initiate requests to participate in the study as two promotional posters were provided to participating pharmacies for display. Pharmacies were requested to recruit up to 20 patients each.

Eligible pharmacy patient participants met the following criteria:

- Aged over 18
- Held a valid Australian Medicare card or Department of Veterans Affairs card
- Eligible to receive a MedsCheck[28,31]:
  - Had not received a MedsCheck, Diabetes MedsCheck, Home Medicines Review, or Residential Medication Management Review in the past 12 months
  - Lived at home in a community setting
  - Took 5 or more prescription medicines, OR has recently experienced a significant medical event, OR takes a medication associated with a high risk of adverse events.
- Had previously been dispensed an osteoporosis medication at the community pharmacy within the last 24 months
- English speaking
- Able to provide written informed consent

2.3. Financial incentives to participate

Participating pharmacies were offered initial payments of $600AUD from the research team to reimburse the associated costs of participation such as training, staff time, utilization of space, and utilities. After the first 10 interventions were provided, $300AUD was provided, and another $300AUD was provided after the second 10 interventions. Additionally, pharmacies which participated in the additional training and assessment with the simulated patient were paid $100AUD from the researchers. Pharmacies may have also claimed payment through the Medication Management Programs by the Pharmacy Programs Administrator ($66.53AUD per MedsCheck), but claims for these payments were not part of the research data collected. Patients were not provided any financial incentives to participate.

2.4. Training

Mandatory training was provided to staff of community pharmacies via modules developed by the research team, in consultation with PSA who are the leading providers of continuing professional development (CPD) for pharmacists in Australia.[35] Pharmacies were given the opportunity for training to be provided via online video calls or face-to-face training with academic pharmacist members of the research team. The training took approximately 40 min and included how to conduct the intervention, brief therapeutic updates on osteoporosis, medication adherence related to osteoporosis therapy, and the techniques of motivational interviewing. Pharmacy participants were provided a resource kit, including a training manual reiterating the intervention process, video recording of the training, supplementary materials on osteoporosis pathophysiology, pharmacotherapy, and the role of the pharmacist in osteoporosis management, Healthy Bones Australia consumer fact sheets ('Osteoporosis Treatment and Bone Health', 'Vitamin D and Bone Health', 'Calcium and Bone Health, and 'Exercise and Bone Health').[36] In addition to the mandatory training, optional relevant accredited CPD resources created by the research team was also offered to the pharmacy participants including a webinar on the role of the pharmacist in osteoporosis, an article on the role of the pharmacist in osteoporosis, online training on vitamin D and calcium, and a workshop regarding osteoporosis therapeutic updates and motivational interviewing for osteoporosis medication adherence.[24,35,37,38]

To test the intervention fidelity and the confidence of pharmacists to deliver the intervention after the training, 5 pharmacists were offered the opportunity to participate in a simulated patient interview with a consumer representative. Afterwards, they would complete a self-reflection and be provided with feedback by the simulated patient and research team. This simulated experience was audio recorded and graded using a marking rubric comprising of 34 items across 4 domains: service delivery, communication, actions taken and effectiveness.[39] Self-assessments using the same rubric were also recorded by the pharmacists. Pharmacists were then given feedback on their performance from the research team and simulated patient/consumer representative.

2.5. Data collection, definitions, and measures

The pharmacist performing the intervention recorded study data prior to, during, and just after the intervention. After the intervention, the pharmacies returned the relevant data to the researchers, including the patient's medication profile, osteoporosis specific questionnaire, action plan, and dispensing history. Then, at 4 weeks and at the endpoint of the study, which was between 12 and 14 months after the intervention, the patient was contacted by the research team via phone call, where a follow-up interview was conducted, and data was recorded. A summary table of data collected is available in Supplementary Material 2.

Adherence can be defined as the extent to which a patient follows a prescribed regimen of medicine.[18] According to Vrijens et al. taxonomy, there are 3 components in medication adherence: 1) initiation – occurs when the patient takes the first dose of a prescribed medication, 2) implementation - the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation to the last dose, and 3) discontinuation - when the patient stops taking the prescribed medication, for whatever reason(s).[20] Persistence is the length of time between initiation and the last dose, which immediately precedes discontinuation.[20] Measures of adherence for osteoporosis medication remain complicated, where several methodologies have been applied, particularly when using real world data and factoring in the individual medications' pharmacology.[40–43]

2.6. Objective measures of adherence

The objective measurement of adherence in this study was pharmacy dispensing records.[44] This study focused on the *implementation* stage of adherence since at recruitment, eligible patients had at least one prescribed osteoporosis medicine dispensed within the previous 2 years.

The pharmacies dispensing records of patients were used to calculate adherence. These dispensing records document when the pharmacy processes a prescription. This record therefore is typically created on the same day it is collected by the patient, but the date may be before the date of collection because the patient had pre-ordered for collection later.

Patients were classified as either adherent or non-adherent using retrospective data collected at two time points, at baseline and at endpoint. At baseline a two-year window was used. That is, adherence was estimated using the dispensing records for the period beginning on the date of the first dispensing of the osteoporosis medication within 24 months prior to the intervention, until the date of the intervention. At endpoint, adherence was estimated using a window which began on the date of the intervention and ended at the earlier of a) 14 months after the service or b) the last prescription dispensed at the pharmacy.

In this study, different criteria were used to classify adherence using dispensing records according to drug class. To be classified adherent to denosumab, a patient must have received denosumab dispensing without any intervals exceeding 211 days (maximum permissible gap). This timeframe was selected because denosumab is typically administered every 6 months, and the literature reports poor adherence and increased risk of spontaneous rebound fractures if doses are delayed.[14–16] There is conflicting evidence regarding when denosumab administration delays become clinically significant, and this is an evolving area.[45–48] Some studies suggest that bone turnover markers can remain suppressed for up to 9 months after a missed dose, while others indicate that vertebral fractures have been reported with short-term delays of as little as 4 weeks.[14,15,49]

For all other osteoporosis medications including bisphosphonates and teriparatide, a Medication Possession Ratio (MPR) of $\geq$ 0.80 was considered adherent. This MPR cut-off of $\geq$ 80% was chosen as improvements in fracture reduction and mortality benefit has been found at this ratio.[9,50] The MPR upper bound was restricted to a maximum of 1. Oversupply beyond the observation window was excluded to avoid overestimation of adherence. If patients refilled before exhausting the previous supply, the oversupply was used to cover future gaps but not gaps prior to the refill event. Approximating medication adherence using MPR from dispensing histories is considered a standard methodology.[51,52] The MPR for each observation period was measured based on the following calculation:

Medication Possession Ratio = (number of days supply in observation period) ÷ (number of days in observation period)

2.7. Subjective measures of adherence

The Beliefs About Medicines Questionnaire (BMQ) was used to measure patients' beliefs about medicines and the Medication Adherence Report Scale 5 (MARS-5) was used as a subjective measure of adherence.[53,54] With the permission of the originator, the 10-item BMQ was adapted to the therapeutic area and used to capture the patients' beliefs about their osteoporosis medications.[53] The BMQ has two subscales, BMQ-Specific Necessity (BMQ-SN) scale, which in this context measures patients' specific beliefs about the need to use osteoporosis medicines, and BMQ-Specific Concerns (BMQ-SC) scale, which measures patients' specific concerns about using osteoporosis medicines. The BMQ reports scores on a 5-point Likert type scale (1 = Strongly disagree, 2 = Disagree, 3 = Uncertain, 4 = Agree, 5 = Strongly agree). Items for each of the sub-scales are summed to create a score ranging from 5 to 25. Higher BMQ-SN scores and lower BMQ-SC scores are predictive of higher medication adherence, respectively.[55]

The 5-item Medication Adherence Report Scale 5 (MARS-5) was used to capture self-reported adherence.[54] This tool includes 4 items to detect intentional poor adherence and 1 item for unintentional poor adherence.[54] The MARS-5 reports scores on a 5-point scale (5 = Never, 4 = Rarely, 3 = Sometimes, 2 = Often, 1 = Always). Items are summed to create a score ranging from 5 to 25. Higher scores corresponds to higher self-reported adherence.[54]

These subjective measures were captured by at baseline, 4 weeks, and at the endpoint of the study. At baseline, the patient and/or pharmacist completed the data form during or just prior to the MedsCheck interview. At 4 weeks and at the study endpoint, these measures were collected by researchers using telephone interviews with the patient.

2.8. Patient experience

The study utilized the Perceived Service Quality Scale (pSQS-SF6)[56] which is the short form version of the Perceived Service Quality Scale (pSQS) to assess patients' perception of service quality for the intervention.[57,58] The pSQS-SF6 tool comprises 6 statements corresponding to 6 dimensions of service quality. Responses were recorded using a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). An overall pSQS-SF6 score is created by summing the scores and dividing by the number of items which creates a theoretical range from 1 to 7. Higher scores indicate greater perceived service quality. The pSQS-SF6 was captured at 4 weeks after the intervention by the researchers via telephone call.

2.9. Other outcomes measured

Other outcomes were collected at baseline using the purpose-designed questionnaire including falls risk, calcium and vitamin D supplementation, exercise, falls history and fracture history within the last 12 months.[59] These outcomes were then collected at 4 weeks and endpoint by the research team. In addition, at 4 weeks patients were asked if they had discussed their action plan or spoken about osteoporosis with their GP (yes/no). Qualitative results, including participant interviews and detailed analysis of the action plan recommendations, were also captured and reported elsewhere.[32]

2.10. Data analysis

Data were analyzed and reported using SPSS 29.[60] Data were aggregated into means and medians for the BMQ-SN, BMQ-SC, MARS-5, and pSQS-SF6. A Mann-Whitney test was applied to determine differences in service quality perception, pSQS-SF6, between the interventions conducted face-to-face, and telepharmacy. A McNemar Test was applied to determine changes in pre-post adherence for the overall cohort. A Friedman test was applied to determine if there were differences in MARS-5, BMQ-SN, and BMQ-SC for patients who responded at all 3 time points - baseline, 4 weeks, and endpoint. The Wilcoxon Signed Ranks test was applied as the post hoc test to determine where the differences occurred.

A point-biserial correlation coefficient was used to estimate the relationship between adherence measured by dispensing history and BMQ-SN, BMQ-SC, MARS-5, and pSQS-SF6. The relationship between BMQ-SN, BMQ-SC, MARS-5, and pSQS-SF6 were estimated using Spearman's correlation coefficient.

3. Results

3.1. Pharmacy participant details

In total, 26 Australian community pharmacies were recruited and trained. The pharmacies were located in Greater Sydney ($n = 14$), regional NSW ($n = 7$), ACT ($n = 3$), and Greater Melbourne ($n = 2$). Of these 26 pharmacies, 11 completed at least one intervention. Reasons for non-participation were pandemic related, including lockdowns, staff illness, staff turnover, and having competing priorities such as the vaccination rollout.

After completing the training package, 5 pharmacists undertook the patient simulation to test training efficacy. The total median scores [IQR] for the simulated patient experience (competency assessment) were 78.6% [73.3–92.2] for the observers and 73.1% [68.7–84.1] for self-report. These results suggested that the training was sufficient for pharmacists to be competent and confident in conducting the intervention.

3.2. Patient characteristics at baseline

During the study period, a total of 111 patients consented to participate in this study and completed the intervention. Of these, 99 were completed face-to-face and 12 were completed via telepharmacy. All 12 telepharmacy interventions were conducted by the same pharmacy. The data from 4 patients were excluded from the analysis for the following reasons: incomplete patient data collection form ($n = 2$), no longer taking any prescription osteoporosis medications ($n = 1$) and withdrawal due to death ($n = 1$). This study therefore reports the data from 107 patients. Their characteristics at baseline are found in Table 1.

Table 1
– Patient characteristics at baseline.

Characteristic	Total $n = 107$
Mean age [SD] (range)	77.7 [10.26] (50.5–96.3)
Gender	
Female	$n = 90$ (84.1%)
Male	$n = 17$ (15.9%)
Pharmacy location	
Greater Sydney	$n = 48$ (44.9%)
ACT	$n = 42$ (39.2%)
Regional NSW	$n = 16$ (14.9%)
Osteoporosis medication	
Denosumab	$n = 88$ (82.2%)
Oral bisphosphonates	n = 14 (13.1%)
IV bisphosphonates	n = 4 (3.7%)
Teriparatide	n = 1 (0.9%)
Uses Calcium supplementation	
Yes	$n = 56$ (52.3%)
No	n = 48 (44.9%)
Didn't answer	n = 3 (2.8%)
Uses Vitamin D supplementation	
Yes	$n = 84$ (78.5%)
No	$n = 21$ (19.6%)
Didn't answer	n = 2 (1.9%)
Falls risk	
2 or more falls in last 12 months	
Yes	$n = 12$ (11.2%)
No	$n = 91$ (85.0%)
Didn't answer	n = 4 (3.7%)
Difficulty with vision	
Yes	$n = 13$ (12.1%)
No	$n = 71$ (66.3%)
Didn't answer	$n = 23$ (21.5%)
Difficulty with balance	
Yes	$n = 34$ (31.8%)
No	$n = 68$ (63.6%)
Didn't answer	n = 5 (4.7%)
Difficulty walking	
Yes	$n = 35$ (32.7%)
No	$n = 67$ (62.6%)
Didn't answer	n = 5 (4.7%)

Consistent with the eligibility requirements, all patients had a history of being prescribed an osteoporosis medication in the previous 2 years. The proportion of those categorized as adherent to osteoporosis medicines was 80/107 (74.8%). Those using denosumab prior to the intervention were less likely to be categorized as adherent 62/88 (70.5%) as those not using denosumab ($n = 18/19$ 94.7%), $p < 0.038$.

3.3. Beliefs about medicines and self-reported adherence

The overall scores for patients' specific beliefs about the necessity of using osteoporosis medicines (BMQ-SN), specific concerns about osteoporosis medicines and self-reported adherence to osteoporosis medicines (MARS-5) that were documented during, or just before, their MedsCheck interviews are presented in Table 2. The theoretical range of scores for each of these tools are 5–25, so at baseline patients reported to pharmacists that overall, they were moderately convinced that osteoporosis medicines are necessary (median = 17), they had relatively low concerns about osteoporosis medicines (median = 10), and they self-reported very high levels of adherence to osteoporosis medicines (median = 25). Cronbach's Alpha, calculated on the data captured at baseline revealed that these measures had good internal consistency for each, $\alpha = 0.677$ (BMQ-SC), 0.818 (BMQ-SN), 0.813 (MARS-5). Theoretically, having higher specific beliefs that medicines are necessary (BMQ-SN) and lower specific concerns (BMQ-SC) should be associated with higher adherence at any particular time[44] and Table 3 reports associations between BMQ scores and MARS-5. At baseline, there were no significant associations between beliefs about medicines (BMQ-SC or BMQ-SN) scores and MARS-5 score. There were also no significant associations between beliefs about medicines (BMQ-SC or BMQ-SN) and the objective measure of adherence. However, the MARS-5 score was weakly correlated with the objective measure of adherence (point-biserial correlation = 0.206, $p = 0.034$).

3.4. Measures collected at 4-week follow-up

At the 4-week follow-up, 71/107 (66.3%) of patients were contactable and willing to participate in the researcher interview. Up to four contacts were made before the patient was deemed not contactable. There were various reasons for the high loss to follow-up and included not being contactable for example phone number disconnected, not answering the phone calls, not willing to participate due to being too busy, recent hospitalization, and no reason provided. Beliefs about medicines (BMQ-SN and BMQ-SC) and self-reported adherence (MARS-5) captured during that interview are reported in Table 2. At this time point, there was no association between BMQ-SN and self-reported adherence but there was a significant negative association between BMQ-SC scores and MARS-5 (Spearman's rho = −0.367 ($p = 0.002$), $n = 71$). There was no additional capture of objective measures of adherence at 4 weeks. At the 4-week follow-up, patients rated the service quality for the intervention very highly using the pSQS-SF6 ($n = 71$) median [IQR] = 6.5 [5.67–7.00]. Only one pharmacy completed the intervention using telepharmacy and that pharmacy completed 8 face-to-face and 12 telepharmacy consultations. Of these, at the 4-week follow up, 8 face-to-face were available, and 7 telepharmacy. There was no significant difference in pSQS-SF6 scores for face-to-face interventions ($n = 8$) median [IQR] = 6.33 [6.04–7.00] compared with telepharmacy (n = 7) 6.33 [6.00–6.67], ($p = 0.694$).

3.5. Study endpoint

At study endpoint, 54/107 (50.5%) of patients were contactable and willing to participate in the researcher interview. Again, the high loss to follow-up interviews was attributed to the same reasons as at 4-weeks. Three patients had switched to alternative osteoporosis medications. Three patients reported that were informed by their doctor to cease anti-

Table 2
Beliefs about medicines and self-reported adherence[1] at baseline, 4-week follow-up and at study endpoint.

	Baseline (n = 107)	4-week (n = 71)	Endpoint (n = 54)
	Median scores [Interquartile range], (significance compared with baseline)[2]		
Specific necessity beliefs	17 [14–19]	18 [14–20] (0.102)	17 [13–19] (0.255)
Specific concerns	**10 [9–12]**	**9 [7–10] (< 0.001)**	**8 [6–10.25] (0.003)**
Self-reported adherence[3]	25 [25–25]	25 [25–25] (0.724)	25 [25–25] (0.067)

[1] Specific necessity beliefs (BMQ-SN), specific concerns (BMQ-SC) and Self-reported medication adherence (MARS-5) scales theoretically range between 5 and 25.
[2] These comparisons used repeated measures for patient participants with available data across the three time periods using the Friedman test (n = 44). The results of the post-hoc Wilcoxon Signed Ranks was then reported to compare Concern beliefs at baseline with 4-weeks and endpoint (emboldened).
[3] To provide a clearer understanding of MARS-5 scores as the interquartile range report the maximum score of 25, the range of MARS-5 scores was 17–25, 18–25, and 9–25 for baseline, 4-week, and endpoint respectively.

Table 3
Correlations between self-reported adherence and patient participants' beliefs about medicines[1] and objective measure of adherence[2] at baseline, at 4-week follow-up and at study endpoint.

	Self-reported adherence[2]		
	Baseline (n = 107)	4-week (n = 71)	Endpoint (n = 54)
Specific necessity beliefs[3]	0.027 (0.780)	−0.004 (0.973)	−0.051 (0.713)
Specific concerns[3]	−0.039 (0.689)	**−0.367 (0.002)**	−0.131 (0.343)

[1] Specific necessity beliefs (BMQ-SN), specific concerns (BMQ-SC) and Self-reported medication adherence (MARS-5) scales theoretically range between 5 and 25.
[2] The objective measure of medication adherence was calculated at baseline using a 24-month dispensing history prior to the intervention and at the study endpoint, was calculated between intervention and endpoint.
[3] Spearman's correlation coefficient.

osteoporosis therapy. These verbal reports were considered when calculating objective measures of adherence at the endpoint, whereby being informed to cease by their medical practitioner was categorized as adherent.

3.6. Changes in objective measure of adherence before and after intervention

At the endpoint of the study, pharmacy dispensing histories were received for all 107 patients. During the period after intervention, patients had most recently been dispensed denosumab (n = 87/107, 81.3%), oral bisphosphonates (n = 14/107, 10.2%), zoledronic acid (n = 3/107, 2.8%), and none for teriparatide. The proportion of patients categorized as adherent at the endpoint (79/107, 73.8%), was not significantly different (p = 1.0) from the proportion categorized as adherent at baseline (80/107, 74.8%). A sub-analysis of those using denosumab versus not, reflected a similar result. At the endpoint, there was no significant difference (p = 0.148) in the proportion of those categorized as adherent, for those using denosumab (62/88, 57.9%) or not (17/19, 89%). Among those using denosumab at the endpoint, there was no significant difference (p = 1.0) in the proportion of those categorized as adherent at endpoint (62/88, 57.9%) compared with those at baseline (62/88, 57.9%). Among those not using denosumab at the endpoint, there was no significant difference in the proportion of those categorized as adherent at endpoint (17/19, 89.5%) compared with those at baseline (18/19, 94.7%).

3.7. Changes in beliefs about medicines and self-reported adherence before and after intervention

Patients' beliefs about osteoporosis medicines and their self-reported adherence to osteoporosis medicines captured by researchers at the endpoint of the study are presented in Table 2. Repeated measures tests on the data from patients who had recorded responses at each of the 3 time points (n = 44) were performed. Comparisons revealed that there was no significant change in necessity beliefs (BMQ-SN) and self-reported adherence (MARS-5) over time. However, the Friedman test reported significant differences in scores for specific concerns about osteoporosis medicines (BMQ-SC) among the 3 time points, $\chi2(2) = 14.513$, $p < 0.001$. Post-hoc Wilcoxon Signed Ranks tests found that compared with baseline, there had been significant reduction in BMQ-SC at both 4 weeks after the intervention (median = 9 vs 10, $p < 0.001$) and at the endpoint of the study (median = 8 vs 10, $p = 0.003$). No significant differences were found using the Friedman test for beliefs about the specific needs for osteoporosis medicines BMQ-SN $\chi2(2) = 3.038$, $p = 0.219$, or for self-reported adherence MARS-5 $\chi2(2) = 4.204$, $p = 0.122$.

At study endpoint, there was no statistically significant correlation between BMQ-SN or BMQ-SC scores and MARS-5 score (Table 3) or between BMQ-SN, BMQ-SC or MARS-5 and the objective measure of adherence after intervention.

3.8. Associations between patient experience and beliefs about medicines, self-reported adherence and objective measures of adherence

Correlation analyses were used to determine whether patients experience of participating in the MedsCheck interventions influenced beliefs about medicines and/or self-reported adherence captured at that time. Correlations were also used to determine whether patient experience was associated with any of these measures and objective measures of adherence at study endpoint. There was a weak-moderate negative correlation between pSQS-SF6 and specific concerns at 4 weeks (Rho = 0.263, $p = 0.027$) (Table 4). This means that at 4 weeks after the MedsCheck, patients' perceptions that the service quality provided for the MedsCheck was high and was associated with lower concerns about osteoporosis medicines. This relationship was not sustained at study endpoint. There were no other statistically significant associations between patients' experience, beliefs about medicines, self-reported adherence and objective measures of adherence at 4-weeks or at study endpoint.

Table 4
Correlations between patient experience,[1] beliefs about medicines,[2] self-reported adherence[2] and objective measures of adherence[3].

	Patient experience	
	Correlation coefficient (*p*) [*n*]	
	4-week follow-up	Endpoint
Specific necessity beliefs[4]	0.087 (0.575) [71]	0.117 (0.449) [54]
Specific concerns[4]	**−0.263 (0.027)** [71]	0.081 (0.600) [54]
Subjective measure of Adherence[4]	0.134 (0.268) [70]	−0.059 (0.704) [54]
Objective measure of adherence[5]	–	0.156 (0.195) [71]

[1] Patient experience was measured with the pSQSF-SF6 scale with a theoretical range of 1–7.
[2] Specific necessity beliefs (BMQ-SN), specific concerns (BMQ-SC) and Self-reported medication adherence (MARS-5) scales theoretically range between 5 and 25.
[3] The objective measure of medication adherence was calculated between intervention and endpoint.
[4] Spearman's correlation coefficient.
[5] Point bi-serial correlation coefficient.

3.9. Action plans documented by pharmacists

From the 107 initial interventions, 92 action plans were provided to the researchers by pharmacists. Within these action plans, 37 had documented a written referral for the patient to see their GP. Other action plans had no referral to GP documented but there were a range of other actions for the patient to consider.

At 4-week follow-up, an analysis of the self-reports of 71 patients who were available for interview revealed that 35 (49%) had visited their GP to discuss osteoporosis. Of the 27 patients that had a documented referral to their GP in their action plan, 13 (48.1%) reported that they had visited their GP to discuss osteoporosis. Of the 44 participants where there was no written referral to GP, 22 (50%) reported seeing their GP about osteoporosis.

4. Discussion

This pre-post study developed and evaluated the impact of a community pharmacy service designed to optimize osteoporosis medication management with a view to improve medication adherence. The intervention had a particular focus on eliciting and addressing patients' beliefs and concerns about osteoporosis therapy, using motivational interview techniques and the generation of an action plan given to patients to assist with their ongoing osteoporosis care and self-management. Consistent with Australian trends away from oral bisphosphonates, towards denosumab, 82% of patients were using denosumab at baseline. The pharmacists participating in the study had been instructed to consider preferentially identifying and recruiting patients who were struggling with adherence to anti-osteoporotic medicines. While patients who were recruited had moderate levels of concerns about anti-osteoporosis drugs, they also self-reported high levels of adherence to therapy and objective measures of adherence showed that the patients were not particularly non-adherent. At baseline, using dispensing records as an objective source of data, patients not using denosumab demonstrated very high levels of adherence (95%). However, just 70% of patients using denosumab were categorized as adherent over a two-year period (adherent patients were those that did not exceed the 211-day permissible gap). The level of adherence is broadly consistent with Australian data which used Pharmaceutical Benefits Scheme (PBS) claims as a source.[6] These treatment gaps and the consequent increase in fracture risk associated with such gaps indicates that there is a clear need for interventions designed to optimize denosumab therapy.[15] At the endpoint of the observation period (12-14 months), no significant change in adherence was observed, based on patients' dispensing histories compared to baseline.

A recent review of interventions designed to improve adherence to osteoporosis therapies highlighted that there was an absence of interventions that reported specifically attempting to elicit and address patients' perceptions about the need to be treated or their concerns about using osteoporosis medicines.[23] It is of interest that the present intervention was designed to elicit and address patients' concerns about osteoporosis therapy and that the study demonstrated some positive impacts on psycho-social aspects of medication adherence. At 4-weeks after the intervention there was a significant reduction in patient's specific concerns about osteoporosis medications (BMQ-SC), and which remained significant at the end of the observation period. The reduction at the end of the observation period is encouraging because the literature indicates that improvements in specific concern scores after intervention tend to regress towards baseline levels over time.[61] Such regression is attributed to factors such as worsening health with age and an increased timeframe for adverse effects.[61] In regard to medication adherence in general, lower specific concern scores have been correlated with improved adherence, particularly in reducing intentional non-adherence and persistence.[62] The impact of the reduction in patients' specific concerns at the 4-week time-point, was highlighted by a significant negative cross-sectional correlation between patients' specific concerns and self-reported adherence using the MARS-5 tool. Therefore, the reduction in patients' specific concerns about osteoporosis medicines observed in this study is particularly relevant because poor adherence is most frequently attributed to patients deliberate choices, rather than simply unintentionally forgetting.[63,64] Lack of persistence and treatment gaps are fueled by the well-known fears of experiencing side effects such as osteonecrosis of the jaw (ONJ), as expressed in qualitative reviews of patients' and health providers' perspectives.[64–66]

This study builds on the knowledge derived from a meta-analysis of the enduring impact of patient's beliefs about medicines on medication adherence, across a wide variety of settings and diseases.[44] The meta-analysis highlighted the benefits and limitations of using the MARS-5 tool for assessing medication adherence and recommended that intervention studies consider more widespread use of objective measures.[44] Consistent with previous studies, the present study observed high and a relative lack of variation of scores in the MARS-5 tool, as patients using self-reported measures tend not to admit that their medication-using behavior varies from that prescribed.[44] Nevertheless, at baseline, this study did observe a weak correlation between the MARS-5 tool and the objective measure of adherence. The MARS-5 tool adapted all questions faithfully, which meant including one question that had no relevance and no variation for denosumab: since patients in Australia are unlikely to administer the medicine themselves: "I take less of my osteoporosis medication than instructed". Nevertheless, as this intervention sought to address beliefs and concerns about osteoporosis medications, the MARS-5 and BMQ tools may be useful in stimulating conversations around medication adherence.

It has been recommended that interventions targeting osteoporosis should ensure that patient experience is monitored.[23] Interventions that elicit and try to address patients concerns about treatment have potential to be confronting. It is important therefore to note that 4 -weeks after the intervention, patients rated the experience very highly (median perceived service quality score = 6.5/7). It is of further interest that at this time point, patients who rated the service quality higher had lower

concerns about osteoporosis medicines. There was also a non-significant trend towards higher self-reported adherence at 4 weeks and a non-significant trend towards higher adherence measured objectively at study endpoint.

To capitalize on existing pharmacy infrastructure, this study adapted MedsCheck, an established service, which is delivered no more frequently than 12 months, to improve osteoporosis medication adherence. While the pharmacy was funded for the single interview, it was provided to patients by their existing pharmacy and was likely to lead to ongoing conversations centered around osteoporosis when patients returned to collect their osteoporosis and other medicines in the future. For example, pharmacists providing Diabetes MedsChecks (MedsChecks designed to improve diabetes care) believe that the service improved the patients trust in the pharmacist and resulted in improved ongoing patient-pharmacist relationships.[67] This is not surprising, since improved health provider relationship quality is associated with improved medication adherence in a range of settings.[68] A component of the MedsCheck both in general and in this study, is for the pharmacist to provide patients with an action plan. The action plan outlines self-management advice and resources and may include referral to the patient's GP if deemed necessary by the pharmacist. This study reported that 48.1% of patients who had been referred to their GP for issues related to osteoporosis such as testing for BMD, calcium, and vitamin D, reported that they had done so within one month after the MedsCheck interview.

This study has several strengths, foremost among them being its real-world setting, which enhances its ecological validity. Conducted with a range of metropolitan and regional community pharmacies, increases generalizability. This paired with the utilization of an existing pharmacist skillset and infrastructure reduces costs and providing an opportunity for scalability. The patient sample was representative of demographics of people with osteoporosis in Australia in age, gender, and osteoporosis medication. However, the sample had a higher level of baseline adherence than reported in the literature. The generalizability of this study is limited to an Australian context, as the study built upon the existing pharmacy service model, however, it may be adapted for international pharmacy medication review services. This study has limitations, including potential sampling, observer, and social-desirability biases, as pharmacists may have recruited patients who they are familiar with or have pre-existing therapeutic relationships. This study is also limited by a small patient sample size, influenced by factors such as COVID-19, patient privacy concerns due to recent data breaches, and competing priorities among pharmacies. The pandemic and associated lockdowns led to a decrease in osteoporosis treatment adherence, making it an opportune time to reaffirm the necessity of ongoing treatment.[69,70] However, pharmacy staff had a reduced capacity to provide clinical services during this period.[71] While the drop out percentage was considerable, it was comparable to other MedsCheck service studies.[29] The limited information regarding those lost to follow up may have impact results if they were individuals reporting low service quality or higher concerns. The follow up duration of 12–14 months is adequate for capturing short term changes in adherence, however, in the context of osteoporosis this timeframe doesn't allow for capture of the direct outcomes of osteoporosis such as changes in bone mineral density, falls, and fractures. There was also a reliance on recall and interpretation of the questions by elderly patients. The authors acknowledge the limitations of utilizing the dispensing records from the intervention pharmacy, however a systematic review found that this is the most common method of measuring osteoporosis medication adherence.[72] This method is limited in this context because some patients may have their osteoporosis medication filled at multiple pharmacies, reducing reported adherence levels.[73] Currently, integration of dispensing data from multiple pharmacies into a centralized database such as the My Health Record is possible for PBS subsidized prescriptions, and may generate a more complete history.[73] There are issues with PBS records as well, as they don't record dosing instructions and do not record when patients pay for their medications out of pocket.[74] Administration of denosumab may not be immediately after dispensing, and some patients may have denosumab dispensed but not administered, which is another limitation of this history collection methodology. Additional methodological considerations would be to contact those who administer the denosumab injections such as GP clinics, or to also collect dispensing data from patients' secondary pharmacies. These methods were not feasible in this study due to cost, time, and ethical considerations. Currently, there is no gold standard of measuring osteoporosis medication adherence and future research should aim to develop guidelines for specific medications.[41,51,73] The lack of improvement in objective measures of medication adherence may not be entirely unsurprising, considering improvements in medication adherence using these methods tends to decrease over time in general, and specifically in relation to osteoporosis medicines.[51,75] It is accepted that there is a limitation to the potential benefit of medication adherence intervention centered on a single interview.[76] A Cochrane review supports the benefit of multimodal, multiple time-point adherence management programs for medication adherence in general, and a literature review regarding osteoporosis, specifically.[76,77] Finally, this research was conducted as a prospective cohort study, as funding directives did not allow the incorporation of a control group, as the overarching grant objective was to raise awareness of osteoporosis.

Future research should continue to focus on interventions to address poor adherence to osteoporosis medications. Additionally, it should be stated that judicious use of osteoporosis medicines such as the risk- and cost-benefit to individual patients needs to be considered within these studies despite aiming to increase rates of adherence. Research should address all stages of adherence via longer-term studies with a control group. Longitudinal research could investigate the potential impact of the role of the patient-pharmacist relationships on medication adherence after interventions that elicit and addressing patients concerns about osteoporosis. Financial viability and current models of care must be addressed, ensuring that the service's funding—whether by patients, pharmacies, or government—is sufficient to prioritize and complete services while being economically viable. A model of care where the quality of service is remunerated rather than quantity should be considered. The feasibility and acceptability of this methodology to patients and pharmacists should also be investigated, including qualitative exploration of the ongoing effects of training on pharmacists' practice. Additionally, it is essential to investigate how pharmacists integrate training and experience into their practice, such as the application of motivational interviewing techniques.

5. Conclusions

This study designed and evaluated the impact of a community pharmacy intervention for osteoporosis medication adherence, specifically designed to elicit and address patients concerns about their osteoporosis medicines. Compared with baseline, patients reported lower concern scores about using their osteoporosis medicines, at 4-weeks and at one year after the intervention. No changes were found in perceived necessity or objective measures of adherence to osteoporosis medications. Patient experience with the intervention was rated very highly. This study demonstrates the potential of community pharmacy interventions designed to elicit patients' thoughts and feelings about using medicines and addressing them using motivational interview techniques. Large-scale, randomized-controlled studies utilizing longer observation periods appear warranted.

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CRediT authorship contribution statement

Jonathan Phuong: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sunny Manon:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Rebekah Moles:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Deborah Mason:** Writing – review & editing, Project administration. **Carol Vleeskens:** Writing – review & editing, Methodology, Data curation. **Fatima Rezae:** Writing – review & editing, Methodology. **Christopher White:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Jacqueline Center:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Stephen Carter:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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