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Development and Validation of a Drug-Specific Questionnaire to Assess Adherence to Osteoporosis Treatment: A Psychometric Study

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Abstract

This study developed and validated drug-specific questionnaires to assess treatment adherence in osteoporosis patients, stratified by administration route (oral, daily injectable, and 6-month injectable). An initial item bank was generated from systematic literature searches and refined through expert panels and patient feedback. Content validity was evaluated using Content Validity Ratio (CVR) and Content Validity Index (CVI) from 16 experts and 10 patients. Face validity was assessed via impact scores, and construct validity was examined through exploratory and confirmatory factor analyses. Sample sizes were 113 for oral drugs, and 50 each for daily and 6-month injectable drugs.

From 101 initial items, the final questionnaires comprised 14 items for oral drugs, 10 for daily injectables, and 8 for 6-month injectables. Exploratory factor analysis revealed three factors for the oral questionnaire and two for each injectable type. Confirmatory factor analysis demonstrated good model fit ($CFI > 0.9$, $TLI > 0.9$, $RMSEA < 0.1$, $SRMR < 0.1$). Reliability was confirmed by Cronbach's alpha (0.85, 0.80, and 0.86, respectively) and Cohen's Kappa, indicating strong internal consistency and test-retest reliability.

These valid and reliable questionnaires enable periodic monitoring of adherence, facilitating timely interventions to optimize osteoporosis management and improve patient outcomes.

Keywords: Osteoporosis, Validation study, Psychometrics, Treatment adherence, Patient Compliance

Introduction

Osteoporosis is a metabolic disorder affecting the skeletal system, distinguished by the progressive reduction in bone density. Every year, osteoporosis leads to 10 million fractures globally (1). Fractures resulting from osteoporosis contain considerable morbidity and mortality; furthermore, the initial fracture substantially increases the likelihood of subsequent fractures (2). In a comprehensive population-based survey conducted in Iran, the age-standardized prevalence rates of osteoporosis were found to be 24.6% among males and 62.7% among females aged 60 years and older (3).

The management of chronic conditions typically requires prolonged administration of pharmacological interventions. To achieve optimal treatment outcomes, particularly the avoidance of osteoporosis fractures, the medications recommended for osteoporosis patients are generally utilized for several years (4). Medications can reduce the risk of vertebral, hip and non-vertebral fractures by 30 to 70% (5). Osteoporosis management involves various pharmacological agents classified by their method of administration (oral or injectable) and frequency of use (daily, weekly, or biannual). Key treatments include bisphosphonates, Selective Estrogen Receptor Modulators (SERMs), parathyroid hormone analogues, calcitonin, and Hormone Replacement Therapy (HRT)(6). Oral bisphosphonates are the most widely used osteoporosis drugs, reducing vertebral fractures by 40-50% and non-vertebral fractures by 20-40%(7).

The efficacy of any therapeutic protocol relies on the patient's adherence to treatment. Adherence to a pharmacological regimen is commonly described as the degree to which patients consume medications as instructed by their healthcare providers (8). Non-adherence to anti-osteoporosis treatment is associated with increased fracture risk and higher healthcare costs (9), and it is a major contributor to frequent fractures, hospitalization, treatment inefficiency, and prolonged disease duration (10). Poor adherence can result in losing approximately 50% of the potential clinical benefits of osteoporosis drugs (11). Specifically, non-adherence and non-persistence in osteoporosis treatment elevate fracture risk by 28% and 32%, respectively (12). Non-adherence to osteoporosis treatment is estimated to double the cost per quality-adjusted life-year (11). Evidence shows that between 50% and 75% of patients prescribed anti-osteoporotic drugs discontinue them within one year (13, 14). Furthermore, approximately 20% to 30% of patients on daily or weekly medications may discontinue treatment within 6 to 12 months of initiation (15). Accurate measurement of treatment adherence is crucial for improving patient health outcomes and reducing healthcare costs. To address the challenge of measuring adherence to osteoporosis medication, a reliable and practical tool is needed. Our study aimed to develop a specific tool that accurately assesses adherence and distinguishes between compliance and persistence in osteoporosis treatments.

Material and Methods

This psychometric study was conducted from January 2022 to January 2023. Osteoporosis patients on medication who were referred to three medical centers in Tehran (Rheumatism Center of Iran, Baharlu Hospital, and Shariati Hospital) were recruited through convenience sampling.

This study consisted of two stages. The initial stage focused on constructing of the questionnaire, while the subsequent stage aimed at assessing its validity and reliability. Face and content validity were assessed based on feedback from both patients and experts, while construct validity was evaluated by analyzing patients' responses. To evaluate the validity of the developed questionnaire, face-to-face interviews were conducted with patients diagnosed with osteoporosis. The inclusion criteria for patients were as follows: diagnosis of osteoporosis confirmed by a bone mineral density (BMD) test conducted by a physician, have been diagnosed with osteoporosis for at least one year, having 50 years old age and above, and be capable of answering the questions. All osteoporosis patients provided informed consent before the interviews (patient details are presented in Supplementary File 1). Likewise, the study objectives were thoroughly explained to expert reviewers and scoring panel members, and informed consent was obtained from all participants prior to their involvement.

To gather information from experts for evaluating the validity of the questionnaire, a list of esteemed professors in the fields of endocrinology, rheumatology, pharmacology, orthopedics, and epidemiology was compiled from the faculty directories of the nation's medical universities. The experts included professors from several medical universities and the Endocrinology and Metabolism Research Institute at Tehran University of Medical Sciences. Sixteen Professors including 4 rheumatologists, 1 orthopedists, 6 endocrinologists, 2 epidemiologists, 2 medical education specialist and 1 pharmacologist were contacted via email and invited to review various aspects of the questionnaire, specifically regarding its comprehensiveness and validity and reliability indicators.

First Step: Construction of the questionnaire

First, the relevant concepts and dimensions of adherence to osteoporosis treatment were clarified; according to Waltz et al.'s tool design process (16). Compliance was defined as *“Voluntary cooperation of the patient in taking medication or treatment as prescribed, including timing, dosage and frequency”* (17). Persistence is defined as *“the duration of being under treatment (from the beginning to the end of the treatment) and shows the long-term persistence of the patient after the start of the treatment”* (18). Adherence is defined as *“a general term that includes both aspects of compliance and persistence”* (19).

Secondly, a systematic review was conducted using PubMed, Embase, Scopus, and ISI databases to identify questionnaires assessing adherence to osteoporosis therapy. The search strategy and data extraction process details were described elsewhere (20). The collected questionnaires were utilized to create an item bank.

Third, expert panel sessions were held to finalize the items, ensuring they covered various of osteoporosis treatment adherence. Additionally, osteoporosis treatment guidelines were referenced to guarantee thorough item extraction.

Second Step: validation

In this stage, face validity, content validity, construct validity as well as reliability tests were assessed. Face validity assesses the extent to which questionnaires seem to measure what they purport to measure, relying on subjective judgment. By assessing content validity, we ensured that the questionnaires were comprehensive, accurate, and relevant. Through construct validity, we verified that questionnaires accurately measure the theoretical constructs it is designed to assess. A reliability assessment was conducted to ensure that measurement instruments are dependable, consistent, and valid.

Face validity

Face validity was evaluated through quantitative and qualitative approaches. In the qualitative phase, osteoporosis patients were interviewed regarding their experiences with questionnaires about oral, daily injectable, and six-month injectable medications, emphasizing the clarity, relevance, and difficulty of the questions. Patients assessed the importance of each item using a five-point Likert scale, where 5 represented 'absolutely significant' and 1 indicated 'not significant at all'. For quantitative analysis, an impact score was calculated. Each item on the scale is rated with a five-point Likert system: 5 - Extremely important, 4 – Important, 3 - Moderately important, 2 - Slightly important, 1 - Not at all important. Items with scores above 1.5 were considered suitable for further evaluation, whereas those below were revised. The threshold of 1.5 was derived from an average score of 3 and a frequency of 50%. The impact factor was calculated by multiplying the percentage of ratings of 4 and 5 by their importance.

Content validity

Content validity was assessed using both qualitative and quantitative methods. Experts offered written feedback on the questionnaire, concentrating on aspects such as grammar, word choice, relevance, and the order of questions. They assigned a rating for the comprehensiveness of the questionnaire based on a 4-point Likert scale (4: completely comprehensive, 3: comprehensive, 2: somewhat comprehensive, 1: not comprehensive). For the quantitative part, the Content Validity Ratio (CVR) and Content Validity Index (CVI) were applied; CVR values exceeding 0.45 were considered acceptable, prompting modifications or removal for lower-scoring items. Items that had a CVI score below 0.70 were deemed unacceptable and removed(21).

Construct validity

We examined the construct validity using both exploratory and confirmatory factor analysis methods as follows:

- Exploratory factor analysis

Bartlett's test was used to confirm that the correlation matrix for factor analysis was significantly different from zero. A factor was considered reliable if the minimum correlation and factor loading of its two variables exceeded 0.7. A factor loading above 0.7 indicates a strong relationship between each variable and its underlying factor(22).

Based on various sources recommending 5 to 10 participants per question (23-25), the required sample sizes were 113 for oral drugs (with initial 14 items) and 50 each for daily injectable (with initial 10 items) and 6-month injectable drugs (with initial 8 items). The Kaiser-Meyer-Olkin (KMO) test assessed sample size adequacy, with values over 0.7 indicating sufficiency

for exploratory factor analysis. It suggests that the relationships among variables in the dataset are sufficiently strong to justify using factor analysis(26, 27). Considering the correlation between underlying factors, principal axis factoring and direct oblimin methods(28) were applied for factor extraction and rotation. Factors having an eigenvalue of one or more and based on scree plot deemed significant. The process of choosing factors in a scree plot is visual; the cutoff for selecting factors occurs at the point of inflection, where there is a sharp decline or elbow in the slope of the graph(29). Statistical analysis was conducted using SPSS software version 25.

- Confirmatory factor analysis

Confirmatory factor analysis was performed using the maximum likelihood method. The model's fit was evaluated based on the criteria of Standardized Root Mean Square Residual (SRMR) and Root Mean Square Error of Approximation (RMSEA) values being below 0.1, and Comparative Fit Index (CFI) and Tucker–Lewis Index (TLI) values exceeding 0.9 (30). The analysis used STATA software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Reliability test

The internal reliability of the questionnaire was evaluated using Cronbach's alpha, based on responses from 110 patients for the oral drugs questionnaire, 50 patients for the daily injectable drug questionnaire, and 50 patients for the six-month injectable drugs questionnaire, with a minimum acceptable threshold set at 0.7. External reliability was evaluated through the test-retest method, where 20 patients completed the questionnaires twice, two weeks apart. Cohen's kappa was then calculated to measure the level of agreement between the two completions for each participant.

Scoring method to determine cut points

A subjective approach was used to assign weights to questions and establish a cut-off point for the questionnaire. An extensive 2.5-hour meeting with eight specialists—three endocrinologists, a rheumatologist, a nursing Ph.D., and three epidemiologists—was held to finalize this cut-off point. Key factors considered included the importance of treatment adherence for osteoporosis medications, the significance of outcomes, and adherence scope. The adherence range was determined by the judges' perspectives and by calculating maximum and minimum scores. The evaluators agreed that treatment adherence and persistence were equally important. However, in the case of the oral medication questionnaire, the timing of medication intake was deemed more significant than the method of administration. Experts agreed to weight questions in the oral questionnaire based on their importance. Questions about medication timing received a weight of 2, while those about intake methods received a weight of 1. Each of the three questions in the treatment persistence section was also given a weight of 2. A coefficient of 2 was applied to the persistence section questions to ensure balance between the treatment adherence and persistence sections.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Tehran University of Medical Sciences with the ethics code: IR.TUMS.EMRI.REC.1400.037. The study followed the international and

national standards for research ethics. All methods were performed in accordance with the relevant guidelines and regulations.

Results

The initial draft of the questionnaire included 14 questions for oral drugs, 10 for daily injectable drugs, and 8 for injectable drugs within 6 months (20) (Figure 1).

Regarding face validity; four questions were revised in terms of wording and structure based on feedback from patients and experts. The quantitative face validity assessment indicated that two questions in the oral medication questionnaire, one in the daily injectable medication questionnaire, and one in the 6-month injectable medication questionnaire, had impact scores below 1.5. However, these questions were corrected rather than eliminated.

In terms of the content validity, of the 16 consulted experts, including epidemiologists, endocrinologists, orthopedists, rheumatologists, nurses, and pharmacologist, 8 (50%) found the questionnaire entirely comprehensive, 6 (37.5%) considered it comprehensive, and 2 (12.5%) viewed it as somewhat comprehensive, resulting in 14 experts (87.5%) deeming it adequately comprehensive. Three questions with a CVR value below 0.45 were removed from all questionnaires. However, after extensive discussions, the research team kept the question “Do you intend to continue your treatment?” due to its importance in predicting future treatment persistence and patient inclination. Table 1 shows the results of the content validity ratio and content validity index for all questionnaire items.

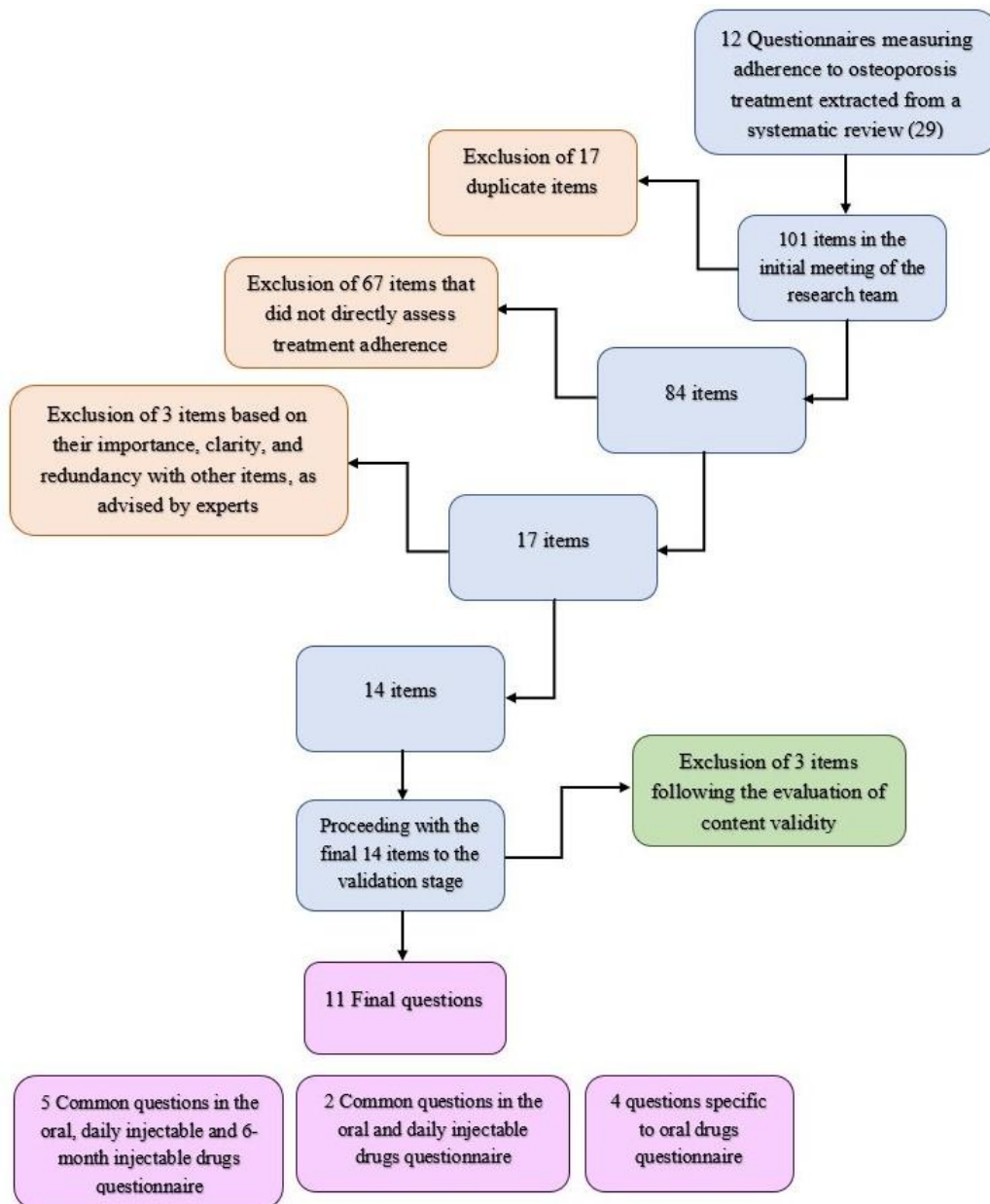


Figure 1. Process flowchart of the questionnaire's development

Table 1. CVI, CVR and Impact Score for questionnaire items

Question	Items	CVI		Conclusion	CVR		Conclusion	Impact score	Conclusion
		Patients	Experts		Patients	Experts			
Oral drugs	1. Do you take the medicine on time?	1	1	Accept	1	1	Accept	4.4	Accept
	2. Which drink do you usually take your medicine with?	1	1	Accept	0.8	0.8	Accept	3.2	Accept
	3. With how much drink do you usually take it?	0.9	0.9	Accept	1	0.8	Accept	2.2	Accept
	4. How long after taking your medication do you stay upright?	0.9	0.9	Accept	0.8	1	Accept	3.2	Accept
	5. How long after taking your medicine do you eat breakfast or medicine (food)?	0.9	0.9	Accept	0.8	1	Accept	2.7	Accept
	6. Did you take your osteoporosis medication the last time you were supposed to take it?	0.9	0.9	Accept	0.8	0.6	Accept	4.1	Accept
	7. How often do you forget to take your medicine?	1	0.8	Accept	0.8	0.6	Accept	4.1	Accept
	8. Do you take your medicine when you travel or leave home for a long time?	0.9	0.8	Accept	0.8	0.3	Accept	2.1	Accept
	9. Are you careless about when to take your medication?	1	0.6	Reject	0.4	0.06	Reject	1.4	Reject
	10. How much trouble do you have remembering to take all your medications?	1	0.8	Accept	0.4	0.3	Reject	1.8	Accept
	11. Have you forgotten your medication in the last three months?	0.9	1	Accept	0.8	0.6	Accept	3.8	Accept
	12. How many times did you forget to take your medicine in the last month (previous 30 days)?	0.8	0.9	Accept	1	0.4	Accept	4.2	Accept
	13. How easy is it for you to take the medicine as prescribed by the doctor (pharmacist)?	0.6	0.6	Reject	0.6	0.3	Reject	1.3	Reject
	14. Do you plan to continue your treatment?	0.8	0.7	Accept	0.6	0.06	Accept	3.2	Accept
Dialy injectable drugs	1. Do you take the medicine daily?	1	1	Accept	1	1	Accept	4.4	Accept
	2. Did you take your osteoporosis medication the last time you were supposed to take it?	0.9	0.9	Accept	0.8	0.6	Accept	4.8	Accept
	3. How often do you forget to inject your medications?	0.9	0.9	Accept	0.6	0.4	Accept	3.8	Accept
	4. Do you take your medicine when you travel or leave home for a long time?	0.8	0.8	Accept	0.8	0.7	Accept	3.8	Accept
	5. Are you careless at times about taking your medicine?	0.9	0.7	Accept	0.4	0.06	Reject	2.4	Accept
	6. How much trouble do you have remembering to take all your medications?	1	0.7	Accept	0.6	0.06	Reject	1.4	Reject
	7. Have you forgotten to inject your medicines in the last three months?	0.8	1	Accept	0.8	0.8	Accept	3.5	Accept

6-month injectable drugs	8. How many times did you forget to inject your medicine in the last month (previous 30 days)?	0.9	0.9	Accept	0.8	0.8	Accept	3.5	Accept
	9. How easy is it for you to take the medicine as prescribed by the doctor (pharmacist)?	0.9	0.8	Accept	0.6	0.06	Reject	3	Accept
	10. Do you plan to continue your treatment?	0.6	0.8	Accept	0.8	0.4	Accept	3.5	Accept
	1. Do you inject the drug every 6 months?	1	1	Accept	1	1	Accept	3.8	Accept
	2. Did you take your osteoporosis medication the last time you were supposed to take it?	0.9	0.9	Accept	1	0.6	Accept	4	Accept
	3. Are you careless at times about taking your medicine?	1	0.8	Accept	0.4	0.2	Reject	1.3	Reject
	4. How much trouble do you have remembering to take all your medications?	1	0.8	Accept	0.6	0.2	Reject	2.6	Accept
	5. Have you forgotten to inject your medicines in the last 2 years?	0.9	1	Accept	1	1	Accept	4.1	Accept
	6. How many times did you inject your medicine in the last 1 year?	0.9	1	Accept	1	1	Accept	3.9	Accept
	7. How easy is it for you to take the medicine as prescribed by the doctor (pharmacist)?	0.7	0.8	Accept	1	0.2	Reject	1.4	Reject
	8. Do you plan to continue your treatment?	0.7	0.6	Accept	1	0.2	Accept	2.4	Accept

Exploratory Factor analysis

The KMO test results for all three questionnaires exceeded 0.7, indicating a sufficient sample size for factor analysis (0.788 for oral drugs questionnaire, 0.709 for daily injectable drugs questionnaire, 0.737 for 6-month injectable drugs questionnaire). Bartlett's test also confirmed significant correlations among variables, supporting the analysis ($P < 0.001$ for all three questionnaires). All identified factors had eigenvalues greater than one. The scree plot further validated that the eigenvalues for all factors exceeded one. Factor analysis revealed three factors for the oral medication questionnaire, explaining 68.6% of its variance. Two factors were identified for the daily injectable medication questionnaire, explaining 67.4% of its variance. Additionally, two factors were identified for the 6-month injectable medication questionnaire, explaining 87.5% of its variance (Table 2). Most of the factor loading was above 0.7, which is generally considered substantial and showed that the item has a strong correlation strongly correlates with the underlying construct. This indicated that the items were a good representative of the construct being measured (Table 3).

Table 2. Eigenvalues and percentage of the total explained variance resulting from the extracted factors

Questionnaire	Factors	Eigenvalues		
		Total	Percentage of variance	Cumulative percentage
Oral drugs	Adherence to the timing of drug consumption	4.67	42.5	42.5
	Adherence to the method of drug consumption	1.58	14.39	56.89
	Persistence	1.29	11.72	68.61
Daily injectable drugs	Adherence	3.27	46.84	46.84
	Persistence	1.44	20.59	67.43
6-month injectable drugs	Adherence	3.33	66.77	66.77
	Persistence	1.03	20.74	87.52

Table 3. Factors, items and factor loadings after rotation

Questionnaire	Factors	Items	Factor load
Oral drugs	Compliance to the medication schedule	Do you take the medicine on time?	0.893
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.528
		How often do you forget to take your medicine?	0.635
		Do you take your medicine when you travel or leave home for a long time?	0.695
	Compliance to how to take medicine	Which drink do you usually take your medicine with?	0.593
		With how much drink do you usually take it?	0.522
		How long after taking your medication do you stay in the upright position?	0.936
		How long after taking your medicine do you eat breakfast or medicine (food)?	0.752
	Persistence	Have you forgotten to take your medication in the last three months?	0.910
		How many times did you forget to take your medicine in the last month (previous 30 days)?	0.977
		Do you plan to continue your treatment?	0.601
Daily injectable drugs	Compliance	Do you take the medicine on time?	0.856
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.507
		How often do you forget to inject your medications?	0.898
		Do you take your medicine when you travel or leave home for a long time?	0.838
	Persistence	Have you forgotten to take your medication in the last three months?	0.910
		How many times did you forget to take your medicine in the last month (previous 30 days)?	0.792
		Do you plan to continue your treatment?	0.797
6-month injectable drugs	Compliance	Do you inject the drug every 6 months?	0.914
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.869
	Persistence	Have you forgotten to inject your medicines in the last 2 years?	0.901
		How many times did you inject your medicine in the last 1 year?	0.736
		Do you plan to continue your treatment?	0.961

Confirmatory factor analysis

The confirmatory factor analysis for all three questionnaires showed appropriate model fit (Figure 2), with CFI and TLI values exceeding 0.9, and RMSEA and SRMR values below 0.1.

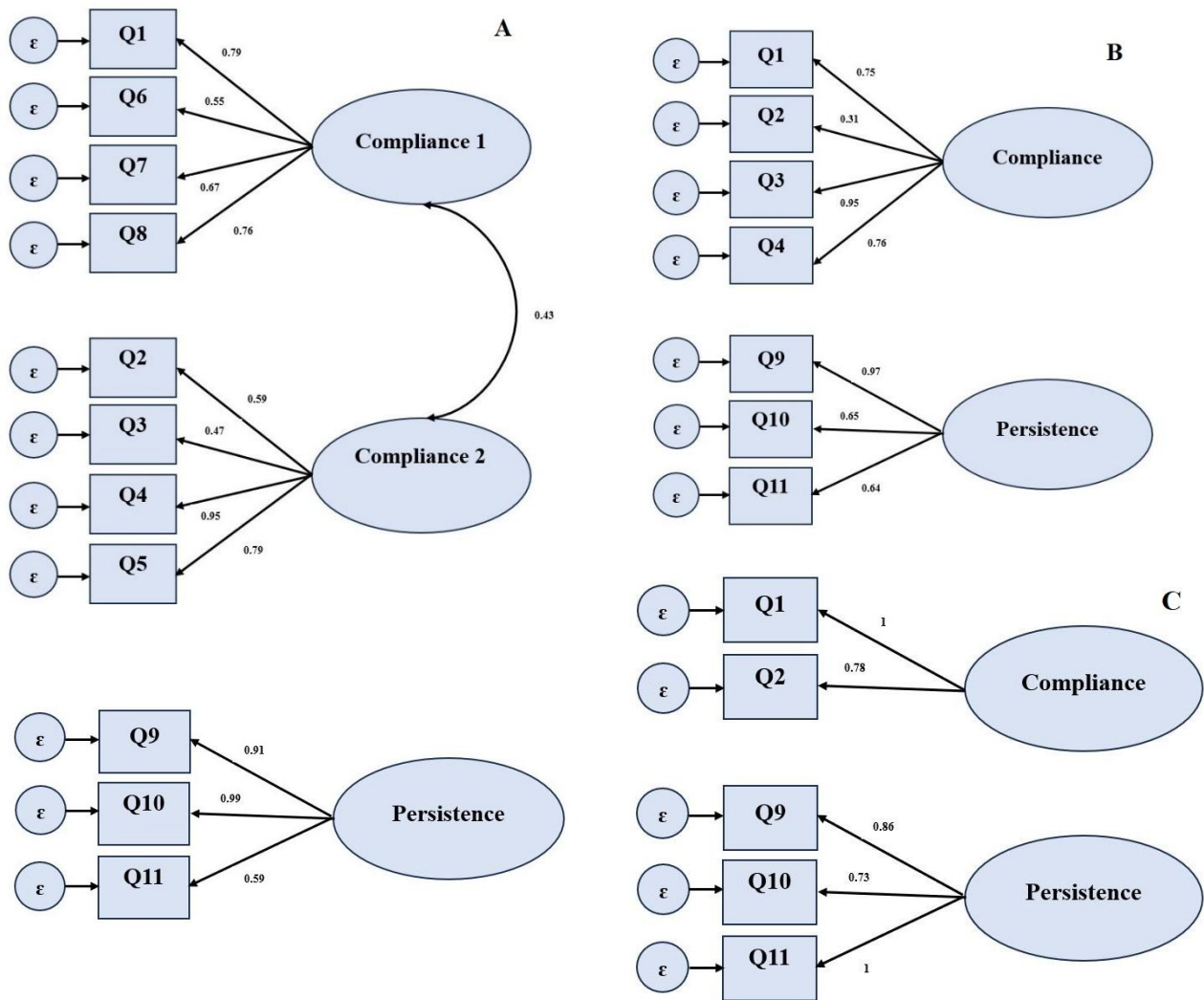


Figure 2. Models resulting from confirmatory factor analysis

A: The model was designed for the oral questionnaire's two factors of medication adherence -compliance 1 (adherence to medication-taking timing) and compliance 2 (adherence to medication-taking methods) – and medication persistence. B: The model injectables was designed for the factor of medication compliance and persistence in the daily injectable drugs questionnaire. C: The model 6-month injectables designed for the factor of medication compliance and persistence in the 6-month injectable drugs questionnaire. The numbers on the arrows represent the path coefficients between the latent variables (compliance and persistence) and the observed variables (questions).

Reliability test results

The ronbach's alpha coefficient for the oral drug questionnaire was determined to be 0.85. The domains of compliance in drug administration schedule, compliance in medication intake methods, and persistence exhibited Cronbach's alpha coefficients of 0.77, 0.79, and 0.86, respectively.

The Cronbach's alpha coefficient was computed as 0.80 for the daily injectable drugs questionnaire. The corresponding values for the domains of compliance and persistence were 0.79 and 0.79, respectively.

The questionnaire for 6-month injectable medication had a Cronbach's alpha coefficient of 0.86. In this context, the compliance and persistence domains exhibited coefficients of 0.87 and 0.87, respectively.

The external reliability assessment of the questionnaires indicated satisfactory reliability across all three questionnaires. The Kappa index ranged from 0.507 to 0.91, with all coefficients demonstrating statistical significance. The highest Kappa coefficient was associated with carrying medications while travelling and away from home, while the lowest Kappa coefficient belonged to the question about fasting for half an hour after taking the medication (Table 4).

Table 4. External reliability of osteoporosis treatment adherence questionnaires

Questionnaire	Domains	Items	Kappa (SE)	P value
Oral drugs	Compliance in Drug administration schedule	Do you take the medicine on time?	0.907(0.09)	<0.001
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.832(0.16)	<0.001
		How often do you forget to take your medicine?	0.901(0.09)	<0.001
		Do you take your medicine with you when you travel or leave home for a long time?	0.911(0.08)	<0.001
	Compliance in how to take the medicine	Which drink do you usually take your medicine with?	0.776(0.21)	<0.001
		With how much drink do you usually take it?	0.776(0.21)	<0.001
		How long after taking your medication do you stay in the upright position?	0.776(0.21)	<0.001
		How long after taking your medicine do you eat breakfast or medicine (food)?	0.507(0.23)	0.006
	Persistence	Have you forgotten to take your medication in the last three months?	0.775(0.15)	<0.001
		How many times did you forget to take your medicine in the last month (previous 30 days)?	0.893(0.10)	<0.001
		Do you plan to continue your treatment?	0.832(0.16)	<0.001
Daily injectable drugs	Compliance	Do you take the medicine on time?	0.650(0.18)	<0.001
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.776(0.21)	<0.001
		How often do you forget to inject your medications?	0.804(0.13)	<0.001
		Do you take your medicine when you travel or leave home for a long time?	0.741(0.16)	<0.001
	Persistence	Have you forgotten to take your medication in the last three months?	0.889(0.10)	<0.001
		How many times did you forget to take your medicine in the last month (previous 30 days)?	0.696(0.19)	0.004
		Do you plan to continue your treatment?	0.614(0.24)	0.001
6-month injectable drugs	Compliance	Do you inject the drug every 6 months?	0.773(0.21)	<0.001
		Did you take your osteoporosis medication the last time you were supposed to take it?	0.643(0.32)	0.002
	Persistence	Have you forgotten to inject your medicines in the last 2 years?	0.643(0.32)	0.002
		How many times did you inject your medicine in the last 1 year?	0.828(0.16)	<0.001
		Do you plan to continue your treatment?	0.773(0.21)	<0.001

Scoring

In general, the cut-off points for adherence based on judges' agreement were as follows: Perfect scores demonstrate excellent adherence, scores 80% and above indicate good adherence, 79%-50% suggests average adherence, and below 50% indicates poor adherence. Applying these cutpoints, the scores were defined as the following:

- In the oral medication questionnaire, a total score of 24 signified excellent adherence, with a range of scores defining good (19-23), moderate (13-18), and poor adherence (12 or less).
- For the daily injectable medication questionnaire, a total score of 8 represented excellent adherence, with good (6-7), moderate (4-5), and poor (3 or below) scores.
- Lastly, the 6-month injectable medication questionnaire had a total score of 4, where a score of 4 indicated excellent adherence, 3 signifies good adherence, 2 reflected moderate adherence, and 1 or less suggested poor adherence.

Discussion

In this study, we developed three distinct questionnaires to measure adherence to the treatment of oral drugs, daily injectable drugs, and 6-month injectable drugs for osteoporosis. Each questionnaire addresses two critical aspects of treatment adherence: compliance and persistence. The results demonstrated that all three questionnaires exhibit good validity and reliability.

Self

Our questionnaires cover all facets of osteoporosis drug use, aligning with the latest treatment guidelines. A key characteristic of our questionnaires is their comprehensive assessment of treatment adherence across various types of medications, including both oral and injectable drugs. In contrast, other questionnaires have focused solely on oral medications(31, 32).

In these questionnaires, we aimed to include only those questions that precisely measure adherence to treatment, based on established definitions of adherence. The World Health Organization (WHO) defines adherence as "the degree to which a person's behavior, including medication-taking, aligns with the recommendations provided by a healthcare professional"(33). For instance, the widely recognised Morisky Green questionnaire includes questions regarding the factors that may prevent an individual from taking their medications. For example, does an individual discontinue their medications when they feel better or when they feel worse?(34). The internal consistency of this scale was moderate (Cronbach's alpha = 0.62)(35). Medication Adherence Rating Scale (MARS) includes questions designed to assess patients' beliefs about medications with Cronbach's alpha of 0.67(36). However, our questionnaire does not include these items. As a result, we removed questions about the individual's knowledge, attitudes toward osteoporosis, and reasons for non-adherence. Given the significance of treatment adherence and persistence in the management of osteoporosis, our designed questionnaire addresses both aspects. For drug therapy to be effective, osteoporotic patients need to follow their doctor's prescriptions and maintain consistent medication use. Additionally, all three designed questionnaires achieved a Cronbach's alpha of at least 0.8. In the osteoporosis compliance questionnaire, the compliance was considered 100% if the patients had no missed dose within the last month(37). Our questionnaire uses a categorical scoring system and specifies the degree of treatment adherence, making it easier to understand adherence levels.

In 2022, Aghajanlou et al. measured the treatment adherence of osteoporosis patients in Zanjan using Morisky questionnaire (38). In Iran, the psychometric properties of Morisky questionnaire have been investigated in patients with diabetes. The findings of this study showed that the Persian version of Morisky questionnaire has good reliability for measuring medication adherence, but it does not have acceptable validity (39). Morisky's questionnaire is a tool to measure adherence to the treatment of patients with hypertension. It was designed by Donald Morisky and colleagues in 1986 (40). In 2012, Reynolds et al modified the Morisky Questionnaire to measure adherence to osteoporosis treatment for bisphosphonate drugs and the questionnaire was renamed Osteoporosis-Specific Morisky Medication Adherence Scale (OS-MMAS) (32). This questionnaire does not consider the clinician's order about how to take oral medications, which is one of the aspects of treatment compliance. The oral medication questionnaire we developed has four questions regarding the proper use of bisphosphonates. Adhering to these recommendations will help ensure that the drug's effectiveness is not compromised. These questions include the volume of liquid consumed with the medication, the beverage used, whether the individual remains upright after taking the drug, and whether they avoid eating for at least half an hour after the medication. In addition, the OS-MMAS questionnaire is designed specifically for bisphosphonate drugs and menopausal women. In designing our questionnaire, we considered all osteoporosis medications and, during the validation process, we included individuals with osteoporosis of all ages and sexes.

Strength and limitation

This study represents a groundbreaking effort in Iran to develop and psychometrically evaluate a specialized instrument for osteoporosis, encompassing both compliance and persistence in treatment. Furthermore, the questionnaires were differentiated by the type of medication (oral or injectable). Moreover, the scoring process for these questionnaires is notably straightforward and efficient for evaluators.

A significant constraint of this study was the challenge of reaching patients who utilize daily injectable medications. These drugs are exclusively prescribed to osteoporosis patients who are at an elevated risk of fractures or have a history of fractures and hospitalizations. Additionally, this medication is recommended for patients with specific comorbidities such as dysphagia, gastrointestinal disorders, and drug malabsorption. Furthermore, the prohibitively high costs of daily injectable drugs deter most physicians from prescribing them. These factors resulted in a limited sample size for psychometric analysis due to the scarcity of patients using daily injectable drugs. Another limitation was the extraction of two items in the adherence domain of the 6-month injectable drugs questionnaire. However, since the factor loadings of these two items exceeded 0.7 in the exploratory factor analysis, this domain was retained in the 6-month injectable drugs questionnaire.

Conclusion

Self-report questionnaires are considered the most practical method for assessing patient adherence to osteoporosis treatment. For this study, three specific self-report questionnaires were developed to align with different osteoporosis medications (oral, daily injection, and 6-month injection). The findings on validity and reliability showed that all three questionnaires

are valid and reliable. Due to their simplicity and limited number of questions, these questionnaires provide a practical and effective approach to assessing adherence to osteoporosis treatment.

Declarations

Consent for publication

Not applicable

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

EH: Conceptualization, Formal analysis, Methodology, Visualization, writing – original draft. MS: Project administration, Conceptualization, Supervision, Writing – review & editing. NF: Methodology, Formal analysis, Conceptualization, Writing – review & editing. MM: Data management, systematic search, Visualization, Writing – review & editing. KK: Data acquisition, Formal analysis, Conceptualization, Writing – review & editing. AG: Data acquisition, Conceptualization Writing – review & editing. SG: Conceptualization, writing – review & editing. HA: Conceptualization, Methodology, Writing – review & editing. SS: Conceptualization, Methodology, Writing – review & editing. HK: Conceptualization, Methodology, Writing – review & editing. NP: Conceptualization, Methodology, writing – review & editing. AF: Conceptualization, Methodology, Writing – review & editing. AO: Project administration, Conceptualization, Methodology, Supervision, Writing – review & editing. All authors have made substantive contributions and attest to approving the final manuscript.

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