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Development and validation of the 15-STARS - A novel self-report pharmacy-based questionnaire to screen for medication non-adherence

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ABSTRACT

Background: Published scales measuring medication adherence are myriad. There is a need for a tool that guides towards downstream adherence interventions.
Objective: To develop and validate a self-report questionnaire able to detect modifiable determinants of medication non-adherence.
Methods: Workshops, surveys and meetings were used to identify items. Validation was performed in French and German (Switzerland) between March and April 2022. Face validation, content validation, construct validation, internal consistency and test-retest reliability were assessed. The questionnaire was finalized in August 2022.
Results: The first draft in English included 13 items divided into four areas. Following translation, validation was performed with 144 patients (63 German-, 81 French-speaking) who were recruited in 35 community pharmacies. Acceptability was good (<5% missing data). Psychometric properties were acceptable with good content validity and moderate construct validity. Internal consistency was acceptable for the French version (Cronbach's alpha = 0.71 [item 1–5] - 0.61 [item 6–9]) and less acceptable for the German version (Cronbach's alpha = 0.43 [item 1–5] - 0.45 [item 6–9]). Test-retest was given for all items (r = 0.52 to 1.0) except item 10 in French (r = 0.25). The final instrument is a 15-item questionnaire called the 15-STARS (Screening Tool for AdheRence to medicineS) that assesses practical difficulties with medicine use, reasons for non-adherence, doses missed, and need for further help.
Conclusions: Our findings support the validity and clinical utility of the 15-STARS questionnaire. Reliability was inconclusive due to incoherent internal consistency, but explainable by the single-item nature of the scale. This new tool will enable the detection of patients who experience difficulties that negatively influence medication adherence. Pharmacists will be able to propose specific and tailored adherence interventions to the patients. Next steps will focus on evaluating its usefulness for developing targeted interventions that optimize medication adherence in routine care and research settings.

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1. Introduction

Medication adherence i.e., alignment of the patient's behaviour with the provider's recommendation(s),[1] has been reconceptualized in 2012.[1] A European consensus-based taxonomy has defined three phases of adherence: initiation (i.e., taking the first dose), implementation (i.e., taking the medicines as prescribed over time) and discontinuation (i.e., omitting the planned next doses).[1] Patient non-adherence is a multifaceted and global problem[2] and is associated with an increased mortality,[3] morbidity[4] and costs.[5,6] Healthcare providers need a tool that helps identify patients with poor adherence. Whilst there is evidence in the literature on the application of scales to measure adherence,[7,8] the availability of so many instruments makes it difficult for healthcare providers to choose the best one for their practice.

Current instruments tend to focus on two distinct concepts. The first attempts to quantify medicine use directly relative to a given time period.[9] Examples include "*Did you miss a tablet yesterday?*[10]" or "*How many days over the past month did you not take the prescribed doses?*[11]". Assessing the frequency of a behavior is challenging because the length of the recall period must be sufficiently long to detect the behavior in question, whilst recognizing that people can have problems recalling past events.[12] Additionally, response scales such as Likert scales can be interpreted subjectively (e.g., "often"), and the number of options (e.g., 5 or 7) may encourage a more neutral response towards the middle option.[13]

In the second concept, the items elicit responses regarding medicine use behavior, barriers to, and determinants of, adequate medicine use behavior, or beliefs about medicines that may influence medicine use behavior.[14] Research has focused on the most influential patient factors for non-adherence.[15] Overall, the scales that have been developed to date are variable in terms of the underlying concepts, target population, disease and number of items,[16] meaning that a critical appraisal is necessary prior to use.[7] In addition, their psychometric properties may not have been sufficiently evaluated.[14,17]

Whilst there are many methods to measure medication adherence, questionnaires remain the most simple, inexpensive, non-invasive, and well accepted way to obtain answers from individuals.[7] Furthermore, self-report questionnaires are time-efficient, easy to distribute and to use.[8] They can be administered routinely in daily practice at the point of care. Most importantly, self-reporting represents the only method that can both measure medicine use behavior and determine the reasons for non-adherence.[14,18]

Thus, there is a need for a user-friendly tool not only to identify adherence problems[7] in everyday practice but to allow for meaningful downstream adherence support with interventions. Adherence-enhancing interventions need to address two distinct challenges namely being targeted to the problem and tailored to the patient. Thus, patient modifiable determinants[19] should be central to the assessment process.

Therefore, we aimed to develop a self-report tool to assess medication non-adherence that fulfils the following requirements: (i) short completion time; (ii) useable by ambulatory patients; (iii) pertains to the adherence phase of implementation; (iv) identifies patient-specific modifiable reasons for non-adherence; and (v) includes a quantitative estimate of adherence.

2. Methods

2.1. Research design, data collection and analysis for the development of the instrument

An iterative process similar to participatory action research[20] was used to develop the instrument. Data were collected during and after annual conferences of the Pharmaceutical Care Network Europe (PCNE; www.pcne.org) that were held in person in February 2020 in the Netherlands, and 2021 online during the COVID-19 pandemic. Participants were pharmacists from different countries, mainly from Europe (Additional Material, table 1). Qualifications ranged from PhD candidate to Professor in the field of clinical pharmacy and pharmacy practice. The common language was English; however, no participant was a native English speaker. A cross-sectional design was used to validate the instrument with pharmacists and patients.

Online surveys were created with the platform REDCap® to generate consensus after the workshops. The survey link was sent by e-mail to members of one or more of the three main societies promoting adherence research that are, PCNE; the European Society of Clinical Pharmacy (ESCP) and the International Society for Medication Adherence (ESPACOMP). Yes/no answers options were mandatory and optional free text fields were available after each question. Online Zoom meetings, lasting 1 h, were held with the participants to finalize the discussions after the workshops, to discuss the results of the surveys, to decide upon the next steps, and to approve the final version. Participants of the 2020 workshop were invited to attend the 2021 and 2022 meetings. No audio or video recording was used to collect the data. In addition to voting, moderators of the workshops and meetings made field notes.

Data were extracted from REDCap® and analyzed. Agreement was calculated as proportion of panelists who agreed (i.e., rating "yes") on the descriptor of the individual items, with values between 0 and 1. Agreement was defined as moderate (50–75%), consensus (75–95%), or strong (>95%).[21] Items with agreement <0.50 were excluded and not presented in the next session. Values >0.79 indicate appropriateness of the item; values between 0.79 and 0.70 indicate the necessity of item revision; values <0.70 entailed an item elimination.[22] For phrasing and answer options, values <0.79 implied a reevaluation of the wording but no elimination. A thematic analysis with inductive approach according to Thomas and Harden[23] was performed with the comments generated by participants (pharmacists and patients). Analysis of the qualitative data was done to guide the adaptions of the tool (i.e., the items, introductory sentences, answer options, layout). Thus, actual themes, illustration of themes with comments etc. in line with the standard approach of thematic analysis are not presented, but new and relevant comments are reported together with the adaptions that followed.

2.2. Development of the instrument in three steps

We used the methodological guidelines for the development of patient-reported outcomes (PRO) instruments.[24–26] We developed our instrument in three steps (Fig. 1).

Step one: To select relevant items from 22 published self-reporting adherence questionnaires and to create new items where appropriate (Additional material, table 2, box). We used the adherence issues proposed by Athavale et al.[27] and the ABC adherence taxonomy[1] to categorise the questionnaires. The 21 participants of the 2020 workshop formed 5 groups and selected the most pertinent items, out of the 189 items available, or created new items. After a final group discussion, a total of 36 items remained of which 19 items were already included in published questionnaires (Additional material, table 2). An online survey with these 36 items was sent to 87 medication adherence researchers. Between 29th April and 10th May 2020, 48 panelists participated (55.2% response rate) of whom 22 (45.8%) had attended the 2020 workshop. The panelists were on average 45.7 ± 12.4 years old (range: 25–70 years), 52.1% were women, and 41.7% were working in academia. Panelists were asked to estimate if each item was "Essential to include" or "Not essential to include". A total of 28 items obtained at least consensus. The item "Problems in drug taking" was the only one to obtain strong agreement (I-CVI = 0.98; see below for definition) (Additional material, table 3).

Step two: This involved reducing items, grouping them, (re)phrasing and/or selecting answer options. This was conducted by 13 participants of the 2021 workshop. From the 28 initial items, 17 remained after eliminating items with identical or similar concepts (Additional material, table 4). For the item grouping, the remaining 17 items were

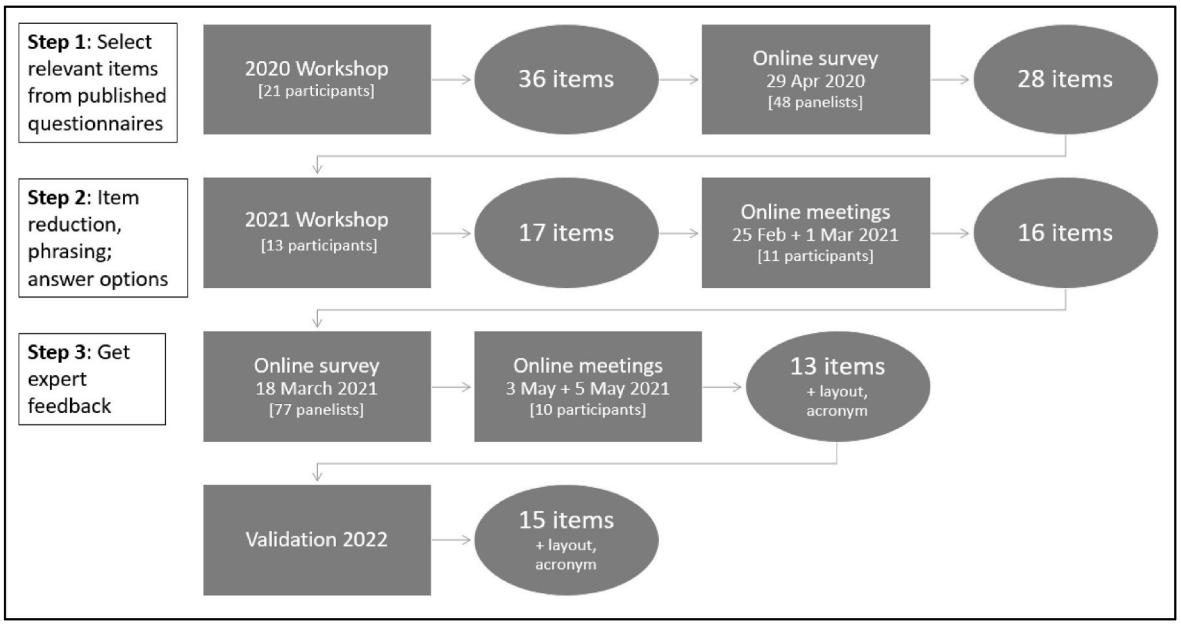

Fig. 1. Steps of the development of the 15-STARS with corresponding workshops, surveys and meetings (rectangle), number of participants (brackets) and output with number of items (oval). See text for details.

categorized into "Sensitive items" in other words, the patient may reveal a personal trait that needs a certain degree of trust, or "Not sensitive items" i.e., practical issues. During grouping, two items were merged due to similar concepts. A total of 16 items remained consisting of seven sensitive and nine not sensitive items **(**Additional material, table 4**)**. It was decided to start the questionnaire with items that were not sensitive. These were phrased as statements with yes/no answer options. During two online meetings on 25th February 2021 and 1st March 2021 with 11 participants of the 2020 workshop, the sensitive items were transformed into questions, the phrasing of the items was adapted to obtain a universal meaning, and the answer options were finalized **(**Additional material, table 4**)**. For the item inquiring about doses missed, consensus was reached on the recall period of 14 days, and on a 5-point Likert scale as answer option with subjective frequencies (from very rarely to very often). The designation "medicines" was preferred to "drugs" because of the connotation of illicit substance use with the latter. A native English speaker (LS) reviewed the items to ensure they were appropriately phrased in English.

Step three: The objective was to get expert feedback on the new tool. We invited all individuals who had participated to PCNE conferences in 2019, 2020 and 2021 and were involved in adherence research. An online survey with 16 items and instruction for completion was disseminated to 77 experts between 18th March 2021 and 8th April 2021. Participants of the 2021 workshop were asked to abstain from answering the survey. The expert panelists had to answer, "Is the item essential?", "Is the phrasing adequate?" and "Is the answer option adequate?" with a yes/no mandatory option. Free text fields were optional. Answers from 54 panelists (70.1% participation rate) were obtained, with 35 (45.5%) complete datasets for analysis. The panelists were on average 43.5 ± 11.3 years old (range: 25–71 years), 74.3% were women, and 42.9% were working in academia. The item "Believe your medicine does more harm than good" was rated as not essential (I-CVI = 0.63) and, therefore, eliminated. Seven items needed rephrasing and two items had inappropriate answer options (I-CVI <0.70) **(**Additional material, table 5**)**. The 303 comments noted by the panelists were analyzed by three investigators (MA, IA, CE). A total of 116 comments (28.3% of all comments) were new suggestions and were implemented (e.g., "Change the term addicted to dependent" or "Avoid negative formulation in sentence"). Two online meetings took place with a total of ten participants of the 2021 workshop over two sessions on 3rd and 5th May 2021 to discuss the new suggestions. Phrasing was revised in line with the panelists' comments. The answer option "I don't know" was added for two items, and the additional answer option "I do not remember" was added for the two items that request a response relative to a specific time period. The introductory sentence before the sensitive items was reworded to causal sentences with the main clause being "I do not take my medicines as prescribed …" and the subordinate clause beginning with "… because …". The reasons were reworded based on simplicity and ease of understanding. Final consensus was obtained for 13 items divided into 4 blocks including not sensitive items (5), sensitive items/reasons for non-adherence (4), beliefs and feeling well (2), and missed doses (2). The acronym 13-STARS (Screening Tool for AdheRence to medicineS) was adopted.

2.3. Translation of the instrument

The instrument developed in English was translated into German and French with a preferred translation method procedure adapted from the ISPOR Task Force for Translation and Cultural Adaptation[28] and endorsed by the PCNE on 19th February 2021. In brief, the key steps include: (i) forward translation by a native speaker into the target language; (ii) independent backward translation by an English native speaker, (iii) back translation review with reconciliation of the translated text, (iv) cultural adaption with a professional linguist, (v) cognitive debriefing with 5–8 pharmacists using an evaluation sheet with a 6-point Likert scale as per Breuer.[29] The cognitive debriefing with patients was generated during the validation procedure.

2.4. Clinical utility

Criteria for clinical utility of questionnaires have been proposed by Harris and Warren.[30] These are important considerations that provide insights into how useful a tool is in the clinical setting.[31] The criteria include applicability (i.e., appropriateness for the purpose under consideration), practicability (i.e., information provided is clinically useful, outcomes are important for the patient, time needed for completion is acceptable, questionnaire is easy to understand, score and interpret), and comprehensiveness (i.e., completeness of the underlying

dimensions of concepts). In line with others,[32] we developed five utility questions for pharmacists whether (1) they need a short adherence questionnaire in their daily practice, (2) the instrument is useful to detect non-adherence in patients with ≥3 medicines for ≥3 months, (3) the instrument is easy to use by their patients, (4) the instrument is acceptable to their patients, (5) they are able to develop interventions following the results of the instrument. Answer options were yes/no. Optional free text fields were available after each question. We calculated the proportion of pharmacists who agreed (i.e., rating "yes") with the utility descriptors.

We developed seven utility questions for patients whether (1) the fond size is easy to read; (2) completion time is 5–10 min; (3) instructions are easy to understand; (4) questions are easy to understand; (5) questions are precise; (6) it is helpful that my pharmacist offers such a questionnaire; (7) I would appreciate if my pharmacist would help me with my medications. Answers were obtained with a 4-point Likert scale from 1 (no, do not agree at all) to 4 (yes, fully agree). Optional free text fields were available after each question**.** We calculated the mean of the marks given by patients regarding the utility descriptors. A value > 3 on the Likert scale indicated positive agreement levels and confirmed utility.

2.5. Validation of the instrument

For the validation, we followed the COSMIN guidelines.[31] Sensitivity to change was not assessed because no intervention addressing adherence was conducted during the validation process and therefore, no change in the underlying construct could be expected. Convergent validity was not assessed because of the nature of our instrument. To the best of our knowledge, there is no equivalent screening tool measuring medication non-adherence that is based on modifiable patient's determinants. Thus, there is no other instrument that measures the same (or similar) constructs. Full validation was performed with German and French instruments in Switzerland between February and May 2022. Twenty-two community pharmacies were recruited from within the network of the investigator (SC) in the German-speaking canton of Berne (G: 10), and the French-speaking cantons of Vaud and Valais (F: 12). In total, 16 pharmacies (G: 8, F: 8; 73% participation rate) and 35 pharmacists (G: 18, F: 17) participated.

Patients entering the participating community pharmacies were eligible if they were 18 years of age or older, taking three medicines or more for three months or more. Pregnant women and those who were cognitively unable to meet the study requirements at the pharmacist's discretion were excluded. Patients who agreed to participate completed the documents in the pharmacy.

2.5.1. Sample size

The sample size was defined according to the COSMIN checklist[31] that recommends a minimum of 6 experts for qualitative analysis, 30 experts for quantitative analysis for content validation, and a minimum of 100 subjects for reliability testing.[31] For cross-cultural validity, the rule of thumb for sample size is a minimum of 5 times the number of items and this corresponds to a minimum of 65 subjects for a 13-item questionnaire. To account for attrition, the target was set at 120 patient questionnaires per language. Each pharmacy was expected to recruit 10 to 30 patients per week over four weeks.

2.5.2. Validity

Validity was estimated by face, content and construct validation. **Face validation** was assessed based on clarity of the instrument, based upon <5% missing data for each item. Marks of the survey questions were averaged. Values <3.0 required an adaption. Proportion of agreement to a descriptor (i.e., rating "yes") was calculated. Values <0.75 indicated the item should be revised. **Content validation** was assessed using the pharmacists' answers to the clarity and the relevance of each item. The item content validity index (I-CVI) was calculated in line with Zamanzadeh et al.[22] as proportion of respondents who agree (i.e., rating "yes") on clarity and relevance of the items. An "X" placed between the answering options "yes" and "no" was considered as a "no". The I-CVI values lay between 0 and 1, with values <0.79 indicating the necessity of item revision.[33] An average value I-CVI/AVE >0.80 indicated the content validity of the entire scale.[33] **Construct validation** used two index questions derived from Wilson et al.[9] as a proxy measure of adherence. These have been tested for understanding in older patients.[34] The questions refer to the last 30 days and ask: (1) "Have you ever not taken at least one of your medicine(s)?" (2) "If yes: on how many days did you miss at least one dose of any of your medicines? Please write in the number of days: (0–30)". A score between 0% and 100% is obtained after transformation as follows[9]: [(30-X)/30] * 100 where X is the number of days from index question 2. Marking "no" in index question 1 without indicating a number in index question 2 qualifies as 100%. The scores of the two index questions were compared with the results of two items of the instrument that is, item 12 ("Over the past 2 weeks, how often have you missed taking any of your medicines?") and item 13 ("Over the past 6 months, have you ever decided to interrupt/stop taking any of you medicines?"). The answer options were averaged after transformation as follows: never 100%; very rarely 80%; rarely 60%; sometimes 40%; often 20%; very often 0%; I do not remember 50% (for item 12), and yes 100%; no 0%; I do not remember 50% (for item 13). Spearman's correlation was calculated using the two scores.

2.5.3. Reliability

Reliability was estimated by internal consistency and test-retest reliability. **Internal consistency** was determined with the items 1 to 9 of the instrument using Cronbach's alpha and Varimax rotation. Values for Cronbach's alpha range between 0 and 1, with values closer to 0 indicating that the items were poorly related to one another. Values of 0.70–0.95 indicated a positive rating for internal consistency.[35] Varimax rotation was applied to determine the dimensions of the scale i.e., whether the items form one overall scale or more than one. The number of factors was determined by eigenvalues >1. **Test-retest reliability** was tested at a 2-week interval. Patients were asked to fill out the instrument at home two weeks after their visit to the pharmacy, and either to bring the completed instrument back to the pharmacy or to send it to the pharmacy by post. Spearman's correlation was calculated with the two time points.

2.6. Generating the final questionnaire from the validation results

The results and comments generated during the validation procedure in two languages were discussed during two online meetings on 18th August 2022 and 22nd February 2023 with seven researchers. The final version was shared with 13 researchers from seven countries who had participated to all meetings since 2020. A final English version was generated.

2.7. Statistical analysis

Microsoft's Excel Version 16.73 (Microsoft Corporation, Redmond, USA) spreadsheet program was used for data analysis. The validation results are presented with mean and standard deviation or median and interquartile range for continuous variables (assumption of normality assessed using the Shapiro-Wilk test), and number and associated percentages for categorical variables, where appropriate. We applied Spearman's correlation coefficients to analyze relationships between continuous variables. A correlation coefficient <0.40 was interpreted as poor, 0.40 to 0.59 as fair, 0.60 to 0.74 as good, and >0.75 as excellent.[36] We applied a Bonferroni correction for multiple testing. A p-value <0.001 was considered statistically significant.

2.8. Ethical approval

The study was approved by the Ethic committee of the canton of Vaud in Switzerland (Req-2021-00303). Patients received verbal and written information about the study and gave written informed consent prior to participation.

3. Results

The instrument developed contains 13 items divided into 4 blocks with instruction and transition sentences. It fits into one A4-page and contains 12 yes/no answer options and one 6 point-Likert scale to quantify the doses missed during the past two weeks.

3.1. Pharmacists' and patients' characteristics

The 35 participating pharmacists were on average 39.9 ± 12.2 years old (range: 25–65 years) and had an average of 14 years in practice (range: 0.5–40 years), 69% were women. Of the 240 patients who were approached, 144 (G: 63; F: 81) accepted the invitation to participate and completed the documents (60% response rate). Mean age was 66.7 years (range: 20–95 years) for French-speaking patients and 70.3 years (range: 29–93 years) for German-speaking patients. Gender repartition was not balanced (men: G: 52%; F: 40%). The mean number of medicines taken was 5.5 (range: 3–12) for French-speaking patients and 6 (range: 3–16) for German-speaking patients.

3.2. Content and clinical utility

Pharmacists estimated the instrument to be useful to detect medication non-adherence (G: 94%; F: 80%), easy to use with their patients (G: 75%, F: 88%) and acceptable by their patients (G: 87%; F: 93%). The majority reported being confident to develop interventions based upon the results assessed with the instrument (G: 81%; F: 88%). Responses related to clinical utility statements were positive as indicated by >75% of pharmacists who agreed with the descriptors, with 33% German-speaking and 77% French-speaking pharmacists who reported the need for a short questionnaire to manage non-adherence.

French- and German-speaking patients agreed that 5–10 min was needed for completion. The font size (3.8 ± 0.7), time needed for completion (3.6 ± 0.6), clarity of questions (3.7 ± 0.5) and instructions (3.7 ± 0.6) were judged appropriate.

3.2.1. Validity

The rate of missing data per item was 2.2% (G) and 1.3% (F). Most missing data concerned the items asking the reasons for not taking the medicines (block of items 6–9). When interviewed, patients indicated that, since they were taking all their medicines as recommended, they could not tick any reason why they did not take their medicines, and left the boxes unmarked. The language was deemed acceptable for both German and French, but the specific sentences regarding the block of items 6–9 were modified.

Content validity was confirmed with average I-CVI values for clarity and relevance between 0.89 (relevance in G) and 0.95 (relevance in F). Four items were slightly below the acceptance level with values between 0.71 and 0.79. In the French version, item 9 ("because of the costs") was considered as not relevant (I-CVI = 0.79) and item 12 ("Over the past 2 weeks, how often have you missed taking any of your medicines?") as not clear (I-CVI = 0.71). In the German version, item 2 ("I can easily prepare all my medicines for use") was considered as not clear (I-CVI = 0.78) and item 5 ("I manage to get refills for all my medicines before I run out of them") as not relevant (I-CVI = 0.72).

The analysis of the pharmacists' comments suggested using numbers instead of words in the answer options to indicate a frequency (item 12); adding forgetfulness to the reasons (item 6–9); adding an open question regarding how pharmacists help patients with their treatment; and including the question to ask if patients need help from their pharmacist. All recommendations were followed, and items were changed accordingly.

Construct validity was confirmed by statistically significant, moderate correlation between the answers from 140 German- and French-speaking patients (r = 0.363; p <0.001). One German patient did not know how often he had forgotten to take his medicines over the past 2 weeks (item 12), and 6 patients (G: 4; F: 2) did not remember if they had stopped taking at least one medicine over the past 6 months (item 13). A total of 47 patients (G: 20; F: 27) indicated that they missed doses on a mean of 3.5 ± 4.4 days (index question 2; range: 1–30 days). Scores for doses taken were 86.0 ± 23% (range: 0–100%) with items 12 and 13, and 96.3 ± 10% (range: 0–100%) with the index questions. The data were skewed with 56.4% and 65.7% of the patients reaching a maximum value of 100% with the 13-STARS and the index questions, respectively (data not shown).

3.2.2. Reliability

Internal consistency was inconclusive overall with an acceptable Cronbach's alpha coefficient for the French version (item 1–5: 0.71; item 6–9: 0.61), and not acceptable for the German version (item 1–5: 0.43; item 6–9: 0.45). Item 9 ("because of the costs") was answered with "yes" by 98.4% of the German-speaking respondents and was eliminated from the Varimax calculation. Results from the Varimax rotation indicated that four items of the French version and five items of the German version explained 64.4% and 69.0% of the total variance, respectively (Table 1). Only item 3 ("I understand the instructions for all the medicines I use") had identical factor loading for both versions.

Test-retest-reliability was assessed with 128 patients. In total, 92% (n = 75) of the French-speaking and 89% (n = 53) of the German-speaking patients returned a second questionnaire. Mean time between the two questionnaires was 15.4 ± 5.1 days (range: 4–32 days) for the French-speaking patients, and 14.9 ± 2.9 days (range: 7–23 days) for the German-speaking patients. Spearman's correlations for individual items ranged from 0.52 to 1.0 and was observed with all items in both languages (Table 2) except for item 10 ("Do you believe you benefit from your medicines?") in French-speaking patients (r = 0.25).

3.3. Generating the final questionnaire from the validation results

The summary of the validation process in two languages (Table 3) and the comments provided by the participating pharmacists were discussed on 18th August 2022. Because of the screening nature of the questionnaire, no remedial actions were undertaken following the inconclusive psychometric properties of the tool in German and French language. After reaching consensus, structural adaptions were made regarding the organization of the blocks and items, and consisted of: (i) moving item 10 ("Believe that medication helps") to block 2 despite a

Table 1
Varimax rotation with factor loading of the 13-STARS questionnaire in French and German.

Item	Factor loading (component) - FRENCH	Factor loading (component) - GERMAN
1	0.627 (2)	0.737 (1)
2	0.872 (2)	0.817 (1)
3	0.892 (2)	0.646 (2)
4	0.580 (4)	0.644 (1)
5	0.745 (3)	−0.840 (5)
6	0.716 (1)	0.867 (3)
7	0.739 (1)	0.855 (3)
8	0.587 (1)	0.851 (2)
9	0.819 (4)	NO
10	−0.723 (3)	−0.667 (2)
11	0.573 (3)	0.845 (4)
12	−0.502 (3)	0.553 (5)
13	0.741 (1)	0.556 (4)

Table 2
Test-retest correlation of the 13-STARS from 75 French- and 53 German-speaking patients.

Item number	Formulated item	Spearman's correlation	
		French [n = 75]	German [n = 53]
1	I am able to recognise all the medicines I use (by their shapes, their colours, their sizes etc.).	0.87	0.90
2	I can easily prepare all my medicines for use.	0.92	1.00
3	I understand the instructions for all the medicines I use.	0.77	1.00
4	I have problems with the use of at least one of my medicines (e.g. swallowing pills, using the inhaler device, counting drops, injection).	0.57	0.62
5	I manage to get refills for all my medicines before I run out of them.	0.70	1.00
	I do not take my medicines as prescribed …		
6	… because I am concerned about possible side effects of some of my medicines.	0.93	0.57
7	… because I am concerned that I am taking too many medicines.	0.64	0.57
8	… because I am concerned about becoming dependent on some of my medicines.	0.53	0.86
9	… because of the costs of my medicines.	0.57	0.57
10	Do you believe you benefit from your medicines?	0.25	0.65
11	Do you interrupt taking some of your medicines if you are feeling well?	0.79	0.81
12	Over the past 2 weeks, how often have you missed taking any of your medicines?	0.72	0.52
13	Over the past 6 months, have you ever interrupted taking any of your medicines on your own?	0.91	0.81

Table 3
Summary of the results generated during the validation of the 13-STARS with the French and German versions with corresponding statistical method.

	French	German
Face validation		
% missing data	1.3	2.2
items with comments	no comments	items 6-9
Content validation		
min. value I-CVI "clear"	$I\text{-}CVI_{12} = 0.71$	$I\text{-}CVI_{5} = 0.72$
min. value I-CVI "relevant"	$I\text{-}CVI_{9} = 0.79$	$I\text{-}CVI_{2} = 0.78$
Construct validation		
Spearman's correlation	r = 0.69	r = 0.52
Internal consistency		
Cronbach's alpha	a = 0.72 (items 1–5) a = 0.61 (items 6–9)	a = 0.43 (items 1–5) a = 0.45 (items 6–9)
Test-retest reliability		
Spearman's correlation	r = 0.53–0.92 r = 0.25 for item 10	r = 0.52-1.0

negative factor loading because it is undeniably a reason, and one beliefs item is needed for completeness; (ii) adding skip instructions in the transition sentences of item 6–9 for people who are not concerned with reasons for not using their medicines; (iii) using numerical ranges for the answer option of item 12 ("doses missed in the past 2 weeks") instead of vague quantifiers; (iv) completing item 13 ("stop taking medicine in the past 6 months") by "without the doctor's agreement" to make the question clearer; (v) adding a further item "if patients would like help from the pharmacy" to cover potentially missing individual determinants; (vi) rephrasing items in block 1 to have opposite directions with two negative and three positive items; (vii) add "sensory impairment" as new reason for not taking medication.

In addition, English editing was performed by a native speaker (LS). Adaptions were: (viii) replace "interrupt" by "stop"; (ix) write uniformly "use" instead of "take" to cover all medicines and not only the oral dosage forms. The next draft of the instrument was shared with participants on 22nd February 2023. It was accepted pending minor modifications of the instructions and the layout. The final instrument contains 15 items divided in 4 blocks that are, practical difficulties (5 items), reasons for not taking medicines (6 items), number of doses missed (3 items) and whether patients wish to receive further help from the pharmacist (1 item). It is named the 15-STARS (Fig. 2).

3.4. Scoring of the 15-STARS

The qualitative items 1 to 12, 14 and 15 are coded with 1 (answer "yes") or 0 (answer "no") with reverse coding of items 1, 3 and 5. The sum ranges from 0 to 14, with a higher score indicating determinants linked to non-adherence. For the quantitative item 13, the scoring is the values of the frequency.

4. Discussion

We developed and validated a novel self-report questionnaire that screens for medication non-adherence and focuses on modifiable patient barriers. Pharmacists who are researchers in the field of medication adherence were involved at each stage in the process considering that the instrument is intended to be used in their practice. This represents an evidence-based method to develop new scales.[37,38] The final 15-STARS instrument fulfills all pre-specified requirements i.e., short to complete; useable by ambulatory patients in the implementation stage of treatment; identifying patient-specific modifiable reasons for non-adherence and with a quantitative estimation of medicine use. The instrument contains 15 items and assesses practical difficulties (5 items), reasons for non-adherence (6 items), doses missed (3 items) and need for help (1 item). Acceptability was good with a very low rate of missing responses. Validity and reliability were achieved with acceptable psychometric properties.

4.1. Validation procedure

Some psychometric values were below acceptable thresholds, such as the correlation for construct validation or Cronbach's coefficient alpha for internal consistency. In addition to statistical considerations, the moderate to low statistical results might be explained by the fact that our tool covers various aspects of one construct. Thus, we selected various single-items to detect different facets of non-adherent behavior. Compared to multi-item scales of one construct, this yields less precise measurements.[39] This is clear from the inconsistent factor loadings of the German and French versions of the 13-STARS. Similarly, Cronbach's alpha is not appropriate for single-item scales.[39] Nevertheless, we presented multiple pieces of evidence for the validity and reliability of our instrument, including results from pharmacists in two different languages for content validation, very low item missing data for face validation, and thematic saturation of comments from online surveys. Furthermore, our sample sizes were large enough for quantitative analyses. Thus, we claim that the moderate validity and reliability estimates of our instrument are due to its focus (i.e., a screening tool for various barriers), and how the items were developed (i.e., from literature through workshops and surveys), and not the result of a lack of sensitivity.[39] Our tool is acceptable in German, French and English.

4.2. Scope of use of the 15-STARS, targeted patients

Our validation findings confirm the suitability of the 15-STARS instrument to be used in community pharmacy practice settings. It allows the pharmacy teams to better understand the patient's rationale for their

Please select whether you agree (yes) or disagree (no) with the following statements. Please put an «X» in the corresponding box.

		yes	no
1.	I recognise all the medicines I use (by their shapes, their colours, their sizes etc.)	☐	☐
2.	I have difficulties getting my medicines ready before I use them (e.g., popping them out of a packaging, halving tablets, counting drops)	☐	☐
3.	I understand the instructions for using for all the medicines I use	☐	☐
4.	I have problems with the use of at least one of my medicines (e.g., swallowing pills, using the inhaler device, injection)	☐	☐
5.	I get all my medicines before I run out of them	☐	☐

Dealing with medicines in everyday life may sometimes be challenging and many people do not always use their medicines. If you always use all your medicines as recommended, please go to question 12.
If it is the case that you do not always use your medicines as recommended, please tell us why.

		yes	no
6.	Because I am concerned about possible **side effects** of some of my medicines	☐	☐
7.	Because I am concerned that I am taking **too many medicines**	☐	☐
8.	Because I am concerned about becoming **dependent** on some of my medicines	☐	☐
9.	Because I believe I have **no benefits** from some of my medicines	☐	☐
10.	Because I **forget** to take some of my medicines	☐	☐
11.	Because of the **price** of some of my medicines	☐	☐

People may sometimes not use their medicines as recommended. These last questions address this topic.

		yes	no
12.	Do you stop taking some of your medicines if you are feeling well?	☐	☐

13. Over the past 2 weeks, how often have you missed taking any of your medicines?

0 times	1-2 times	3-4 times	5 or more times	everyday	I do not know
☐	☐	☐	☐	☐	☐

14. Over the past 6 months, have you ever stopped taking any of your medicines without informing your doctor?

yes	no	I do not know
☐	☐	☐

Please tell us if we can be of any help.

		yes	no
15.	**Would you like some help from the pharmacist?**	☐	☐

Thank you for your time!

Fig. 2. The finalized questionnaire named 15-STARS with 15 items within 4 blocks that assess practical difficulties (5 items), reasons for non-adherence (6 items), doses missed (3 items) and need for further help (1 item).

medicine use behavior. Apart from forgetfulness, non-adherent behavior can be intentional with patients making a rational decision how to take or not to take their medicines.[40] As patient's actions regarding medicine use are based on knowledge, experience and beliefs about the disease and its treatment,[41] it is not surprising that non adherence is widely prevalent. Thus, our instrument tackles the source of these behaviors. Based on these findings, adherence-enhancing interventions can be tailored to the patient's needs. However, identifying patients who are non-adherent is still a challenge in daily practice.[42] It is possible that healthcare professionals provide help to those who are already adherent instead of those who are not.[43] Thus, a self-report short questionnaire with a screening focus may offer a novel opportunity as it does not have a single cut-off point to distinguish between adherent and non-adherent individuals.[44,45] One main reason to remove these thresholds was that they are mostly arbitrary. The most used cut-off point corresponds to patients with 80% of their medicines taken.[46] However, a large

controversy exists about the use of this threshold.[47] Predominantly, the sensitivity and specificity of the cut-off points have rarely been assessed against clinical outcomes.[48] Finally, dichotomizing medicine use behavior can hide the different ways in which people are non-adherent (i.e., skipping doses or skipping days) within the phases of the adherence process.[1] The 15-STARS may identify aspects of medicine use during the implementation phase and the persistence, excluding initiation of a new treatment.[1] Thus, we have targeted patients with chronic illness and long-term use of medicines. This suggests that our instrument can be used over a longer time or at specific time points e.g., after key health events that shape long-term medication adherence with varying sequences of regressive, progressive, and stable times of medicine use.[49]

4.3. Selected items and structure of the 15-STARS

We have selected items that are not illness or disease-specific. Thus, we have generated a comprehensive and inclusive set of items that covers a wide range of modifiable problems with any medicine. The order of the blocks of items follows common principles of survey design such as asking first easy, straightforward questions, or adding transitional phrases and instructions when switching topics.[50] The 15-STARS starts with 5 items on practical barriers that are not deemed sensitive. Physical barriers are often explored in adherence instruments, such as visual problems in reading labels,[51] dexterity issues in opening the container[51] and difficulty swallowing medicines.[18] However, we were not interested in the single physical barriers but in their consequences on patients' practical behavior. Thus, we focused on recognition, preparation, use, understanding the instruction for using, and obtaining refills of medicines.

The instrument then continues with six reasons for non-adherence including beliefs and costs. During the development, specifically during the 2021 workshop, those items were intensely debated and finally classified as sensitive because of their relationship to personal issues. Nevertheless, they are crucial reasons for non-adherent behavior e.g., fear of side effects or of becoming dependent.[52] As J.W. von Goethe stated, "*Belief is not the beginning but the end of all knowledge*", which highlights the importance of understanding beliefs. To encourage patients to complete these sensitive items, they are introduced by an acknowledgement that many people do not always use their medicines as recommended. Furthermore, the block is placed after not sensitive items, in other words, it is anchored to unproblematic content. By doing so, we expect a carry-over effect from the initial items[53] that positively influences the respondent's willingness to complete the questionnaire. For these reasons, two different types of interventions can be offered. Firstly, a cognitive type with attempts to improve patients' knowledge and understanding of the benefits of medicines. Secondly, a practical intervention linked to the simplification of the dosing schedule, such as taking all medicines at the same time of the day or the use of dosette boxes, or switching to long-acting medicines or fixed-dose combination products to diminish the pill burden[54] and thus improve adherence.

Independent of the health insurance coverage, the cost of the medicines can be a major barrier to adherence and may result in patients not getting timely refills of medicines, rationing in order to extend the supply[55] or delaying prescriptions. Among seven countries with different subsidy systems, the rates of non-adherence due to medication cost ranged from 3% in the Netherlands to 20% in the United States of America.[56] As cost-related non-adherence has been linked to more outpatients' visits, and increased hospitalization and emergency department visits,[57] we considered it fundamental to include a corresponding item in our tool. Finally, forgetting to take medicines was added as independent item because it is a well-known major reason of unintentional non-adherence, with up to 39% of older adults receiving polypharmacy in Portugal mentioning this as reason for poor adherence.[58]

The third block with 3 items focuses on the discontinuation of medicines. This behavior is often related to unexpected healthcare issues such as side effects or withdrawal symptoms. The item "stopping to take the medicines if one is feeling well" is placed apart because the decision to continue using a medicine while "feeling good" is counterintuitive. As an example, some people are unaware that "feeling good" is the sign of the medicine's efficacy and that continuing the treatment is required to maintain illness management and control. Similarly, patients may attribute side effects to a particular medicine, but this may not be the responsible agent. Thus, there is a need to explore what patients have experienced, and reframe the story, where necessary.

We defined one quantitative item with a precise reference period of "past 2 weeks". In the literature, the time frame ranges from 1 day to 12 months[14] with a mode of 7 days.[59] A short recall period such as the past week is said to minimize recall errors.[51] However, the time frame with least bias is unknown.[59] In our view, 2 weeks is short enough that patients will be able to recall and includes a weekend. This was viewed as crucial because forgetfulness is most likely to occur when the daily rhythm is broken, which occurs predominantly on Saturday and/or Sunday.[60]

4.4. Answer options of the 15-STARS

We selected a categorical yes/no forced-choice response format for 14 out of 15 items to reduce response burden as it is less resource-intensive than an opened-ended format. Thus, the completion time is shortened, which is also likely to positively impact upon the acceptance and successful completion of the questionnaire. Furthermore, yes/no is less subjective than for example a Likert-scale or other multi-category approaches. It also increases the accuracy of the tool. We are aware that patients may mark only the "yes" answers without checking any "no" answers. However, if sporadically present, non-response to an item can be interpreted as "not yes" and facilitate the interpretation.[61] By adding skip instructions in the transitional sentence for people always using their medicines as recommended, patients who do so can easily follow this skip option. This may result in more honest responses and lead to a higher rate of useable answers with less imputation of missing data.

Responding to the question "How often did you …" is challenging especially when the behavior is irregular or when the frequency varies with time. Likert-scales using vague quantifiers as response options (e.g., never - rarely - sometimes - always) are subjective and therefore are inadequate to measure actual frequencies. Conversely, numerical ranges are easier to answer because respondents are allowed to estimate when they do not remember the exact number.

Taking all the above-mentioned elements into consideration, we have selected a 5-point Likert-scale with 4 numerical ranges and 1 vague quantifier "everyday". By doing so, we have insured that the response categories were exhaustive and mutually exclusive. Finally, we have added the option "I don't know" (DK) for the two items with a recall period (item 13, 14). The literature is inconsistent as to whether omitting or providing a DK option affects the quality of survey data.[50] However, including a DK response category lessens the likelihood of respondents either omitting the answer of doing so with a socially desirable response. In our study, indicating DK does not assume a lack of opinion or unwillingness to provide an opinion, but enables a more personalized approach to answering the item. With only 3% of all participants using the DK option, and only 0.6–2.2% of overall missing values, we feel confident that the DK option is appropriate and is marked by participants who could not remember. Thus, it is likely that our DK option reduces the number of forced or omitted answers and thus, delivers valid responses.[62]

4.5. Last item of the 15-STARS

Item 15 asks if participants would like some help from the pharmacist and is thus an outlier. However, some patients might still have treatment-related questions that were not covered. This last item gives

them the opportunity - and even encourages them - to ask any question about a medicine or a health and care concern and can be used especially by people with low health literacy.[63] Finally, this last item may also further supports the screening purpose of the tool.

Strengths of this study include firstly the clear order of the blocks of items and the yes/no forced answer options for 14 out of the 15 items. This reduces response burden and shortens completion time. These factors are major facilitators for patients and healthcare providers in today's daily practice. Thus, our instrument is likely to be well accepted by patients and healthcare providers. Secondly, we have targeted the dual conceptualization of reasons for, and extent of, non-adherence.[64] By doing so, we give patients the opportunity to express their knowledge with different cognitive representation of medicine use. Thus, we claim that the 15-STARS detects indirectly most barriers associated with medicine use. Thirdly, the validation process is in line with current guidelines but with a multicenter approach in 2 countries and 3 languages and was supervised by a core group of international researchers. By doing so, we were able to generate a final version of the instrument that took all the validation results and comments into consideration. Fourthly, test-retest evaluation indicates that the 15-STARS may be useful in the evaluation of adherence interventions whereas positive answers to clinical utility related statements support the suitability for using the tool in healthcare practice and research settings.

Limitations of this study include firstly the selection of the topics that was influenced by the literature. As an example, misunderstanding was not integrated although it can also lead to non-adherence, especially when an individual does not see the need for the medicine or does not understand that it takes time to see results, especially with long-life treatments or in primary prevention. However, the concept is difficult to condense into one item and is part of beliefs. In addition, the last item asking for help from a healthcare provider will address this gap. Secondly, this study has currently been validated only in two languages. It is possible that the context and culture in other countries may require future iterations to ensure reliability. Thirdly, in an increasingly diverse society, it is likely that patients in Ireland for example, may not have English as their first language. These patients are likely the ones who are most in need of individualized and tailored advice and guidance and they may not be captured unless further translations are available.

5. Conclusions

This study provides insights on the validity, reliability and clinical utility of the 15-STARS. Reliability was inconclusive due to incoherent internal consistency of the German version, but explainable by the single-item nature of the scale. Thus, the scene is set for further integration of the tool into pharmaceutical care services and research. There are numerous ways in which the 15-STARS can be incorporated into future research. The feasibility for pharmacists to use it as part of routine practice, its acceptability among patients, whether this tool can be integrated into pharmacist-led pharmaceutical care services, are just a few of the valuable research opportunities. As a next step, an international multi-centric study will test the use of the 15-STARS in detecting and ameliorating non-adherence through tailored pharmacist-led interventions. Additionally, the translation and cultural adaption into several languages is needed. Lastly, the effectiveness of the 15-STARS both in tailored intervention trials and daily (community pharmacy) practice remains to be shown. The originators of the instrument invite researchers to ask for the current version of the scale, which will be provided free of charge.[65]

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CRediT authorship contribute statement

Arnet Isabelle: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Visualization, Supervision, Project administration. Sahm Laura J: Investigation, Writing - Review & Editing, Gregório João: Investigation, Writing - Review & Editing, Tuula Anita: Investigation, Writing - Review & Editing, Krüger Manfred: Investigation, Writing - Review & Editing, Wurmbach Viktoria S: Investigation, Writing - Review & Editing, Hoti Kreshnik: Investigation, Writing - Review & Editing, Schulz Martin: Writing - Review & Editing, Eickhoff Christiane: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing - Review & Editing, Visualization, Supervision. All the authors read and approved the final manuscript.

Declaration of competing interest

None.

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Additional material

Table 1
Repartition of the participants in the different workshops (WS) and online surveys in 2020 and 2021 with corresponding countries of origin.

	WS Feb 2020 (in the Netherlands)	Online survey 2020	WS Feb 2021 (Online)	Online survey 2021
Number of participants	38 pharmacists	48 panelists	13 pharmacists	35 panelists
Number of countries	14	13	8	15
Number and name of European countries	12: Belgium	11: Belgium	8: Austria	13: Belgium
	Denmark	Denmark	Denmark	Croatia
	Germany	Germany	Estonia	Denmark
	Ireland	Ireland	Germany	Estonia
	Luxembourg	Netherlands	Norway	France
	Netherlands	Norway	Portugal	Germany
	Norway	Portugal	Spain	Netherlands
	Poland	Serbia	Switzerland	Norway

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Table 1 (*continued*)

	WS Feb 2020 (in the Netherlands)	Online survey 2020	WS Feb 2021 (Online)	Online survey 2021
	Portugal Serbia Slovenia Switzerland	Slovenia Switzerland United Kingdom		Poland Portugal Serbia Slovenia Switzerland
Number and name of non-European countries	2: Australia Jordan	2: Australia Canada		2: Australia Canada

Table 2
List of 36 items generated by the participants of the 2020 PCNE workshop, selected from published questionnaires or newly created, according to a pre-defined adherence category. The origin of the item is indicated with - for a new creation, or with the abbreviation of the scale and the number (in bracket) of the corresponding 22 published articles (box below the table).

Category	Subcategory	Item description	Origin
Practicability	Packaging	1. Problems in opening the outer packaging	–
		2. Problems in opening the immediate packaging	–
		3. Distinguish the packages	–
	Drug taking	4. Problems in reading/understanding the instruction for use	–
		5. Problems in preparing the medication for use	–
		6. Problems in drug taking (e.g. swallowing pills, using the inhaler device, counting drops)	–
	Costs	7. Patient cannot afford this medication	MARS (20)
	Availability	8. Get refill on time	ASK-12 (13)
Beliefs and behaviours	Necessity	9. Patient feels he needs this medication	–
		10. Patient is convinced about the importance of this medication	AE (14)
		11. Patient is convinced he would be very ill without this medication	BMQ (9)
		12. Patient believes this medication will improve his health	–
	Overall concerns	13. Patient has any concerns regarding this medication	–
		14. Patient worries about having to take this medication	BMQ (9)
		15. Patient worries about having to take too many medications	MARS (20)
	Concerns about side effects and consequences	16. Fear of side effects	MARS (20)
		17. Worry about side effects	MEDS (2)
		18. Concerns about long-term effects of this medication	MARS (20)
		19. Worry about getting addicted to this medication	MEDS (2)
		20. Patient is convinced that this medication will do more harm than good	AE (14)
		21. Patient is convinced that this medication will hurt him	–
	Concerns about costs	22. Worry about costs for this medication	MEDS (2)
		23. Financially burdened by the expenses for this medication	AE (14)
	Behaviour, attitude	24. Patient stops this medication to see whether it is still needed	MARS (20)
		25. Patient only uses this medication if he feels sick	MARS-9 (8)
		26. Patient uses this medication only if he has to, if other things don't work	MARS-9 (8)
Quantification	Frequency	27. How many doses did you miss?	ACTG (4)
		28. How often did you miss to take your medication?	–
	Recall period	29. Yesterday	MASRI (21)
		30. One week	–
		31. Four weeks	–
	Time point	32. When was the last time you missed a dose of this medication?	ACTG (4)
Forgetfulness	–	33. Remember to take this medication	–
		34. Forget to take this medication	–
Non-persistence	–	35. Do you still have this medication?	–
		36. Did you stop taking this medication?	–

no	Citation	Name of the scale or author
1	Alhomoud F, Millar I, Johnson J, Hudson S. A medication adherence risk assessment tool (RAT) compared with medication adherence report scale (MARS). Int J Clin Pharm. 2011; 33:285–467 (Poster presented at the 39th ESCP European symposium on clinical pharmacy & 13th SFPC congress, 21–23 October 2010, Lyon, France)	RAT Medication Adherence Risk Assessment Tool
2	Athavale AS, Bentley JP, Banahan BF 3rd, McCaffrey DJ 3rd, Pace PF, Vorhies DW. Development of the medication adherence estimation and differentiation scale (MEDS). Curr Med Res Opin. 2019; 35(4):577-85.	MEDS Medication Adherence estimation and differentiation scale
3	Byerly MJ, Nakonezny PA, Rush AJ. The Brief Adherence Rating Scale (BARS) validated against electronic monitoring in assessing the antipsychotic medication adherence of outpatients with schizophrenia and schizoaffective disorder. Schizophr Res. 2008; 100(1–3):60-9.	BARS Brief Adherence Rating Scale
4	Chesney MA, Ickovics JR, Chambers DB et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). AIDS Care. 2000; 12(3):255-66.	ACTG Adherence Questionnaire
5	Chisholm MA, Lance CE, Williamson GM, Mulloy LL. Development and validation of the immunosuppressant therapy adherence instrument (ITAS). Patient Educ Couns. 2005; 59(1):13–20.	ITAS Immunosuppressant Therapy Adherence Scale
6	DiMatteo MR, Sherbourne CD, Hays RD et al. Physicians' characteristics influence patients' adherence to medical treatment: results from the Medical Outcomes Study. Health Psychol. 1003; 12(2):93–102.	General Adherence Scale
7	Ediger JP, Walker JR, Graff L et al. Predictors of medication adherence in inflammatory bowel disease. Am J Gastroenterol. 2007; 102(7):1417-26.	Obstacles to Medication Use Scale
8	Horne R, Weinman J. Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. Psychol Health 2002; 17:1,17–32.	MARS-9 Medication Adherence Report Scale

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Table 2 (*continued*)

9	Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health. 1999; 14:1–24.	BMQ Beliefs about Medicines Questionnaire
10	Kim MT, Hill MN, Bone LR, Levine DM. Development and testing of the Hill-Bone compliance to high blood pressure therapy scale. Prog Cardiovasc Nurs. 2000; 15(3):90–96.	Hill-Bone HBP therapy revised scale
11	Maggiolo F, Ripamonti D, Arici C et al. Simpler regimens may enhance adherence to antiretrovirals in HIV-infected patients. HIV Clin Trials. 2002; 3(5):371-8.	mod. ACTG Adherence Questionnaire
12	Marsicano Ede O, Fernandes Nda S, Colugnati F et al. Transcultural adaptation and initial validation of Brazilian-Portuguese version of the Basel assessment of adherence to immunosuppressive medications scale (BAASIS) in kidney transplants. BMC Nephrol. 2013; 14:108.	BAAS Basel Assessment of Adherence Scale
13	Matza LS, Park J, Coyne KS, Skinner EP, Malley KG, Wolever RQ. Derivation and validation of the ASK-12 adherence barrier survey. Ann Pharmacother. 2009; 43(10):1621-30.	ASK-12
14	McHorney CA. The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. Curr Med Res Opin. 2009; 25(1):215-38.	AE Adherence estimator
15	Menckeberg TT, Horne R. Beliefs about medicines predict refill adherence to inhaled corticosteroids. J Psychosom Res 2008; 64:47–54.	MARS-5 Medication Adherence Report Scale
16	Morisky D. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986; 24:67–74.	MMAS-4
17	Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008; 10(5):348-54.	MMAS-8
18	Shea S, Misra D, Ehrlich MH, Field L, Francis CK. Correlates of nonadherence to hypertension treatment in an inner-city minority population. Am J Public Health. 1992; 82(12):1607-12.	Shea scale
19	Svarstad BL, Chewning BA, Sleath BL, Claesson C. The Brief Medication Questionnaire: a tool for screening patient adherence and barriers to adherence. Patient Educ Couns. 1999; 37(2):113-24.	Brief medication questionnaire
20	Unni EJ, Farris KB. Development of a new scale to measure self-reported medication nonadherence. Res Social Adm Pharm. 2015; 11(3):e133-e143.	MARS Medication Adherence Reason Scale
21	Walsh JC, Mandalia S, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS. 2002; 16(2):269-77.	MASRI Medication Adherence Self-Report Inventory
22	Zeller A, Schroeder K, Peters TJ. An adherence self-report questionnaire facilitated the differentiation between nonadherence and nonresponse to antihypertensive treatment. J Clin Epidemiol. 2008; 61(3):282-88.	ASQR Adherence self-report questionnaire

Table 3
List of 28 items reaching at least 50% consensus generated during the 2020 online survey, including the percentage of agreement to "essential to include" and the adherence category (P=Practicability; BB=Beliefs and behaviors; Q = Quantification; F=Forgetfulness; NP=Non-persistence).

Consensus	Item description	Percentage of agreement (N = 48)	Adherence category				
			P	BB	Q	F	NP
Strong (>95%)	Problems in drug taking (e.g. swallowing pills, using the inhaler device, counting drops)	97.9% (n = 47)	x				
Consensus (75%–95%)	Patient only uses this medication if he feels sick	89.6% (n = 43)		x			
	Problems in reading/understanding the instruction for use	87.5% (n = 42)	x				
	Did you stop taking this medication?	87.5% (n = 42)					x
	Problems in opening the immediate packaging	83.3% (n = 40)	x				
	Distinguish the packages	83.3% (n = 40)	x				
	Patient has any concerns regarding this medication	83.3% (n = 40)		x			
	Forget to take this medication	83.3% (n = 40)				x	
	Problems in preparing the medication for use	81.3% (n = 39)	x				
	Get refill on time	79.2% (n = 38)	x				
	Patient stops this medication to see whether it is still needed	79.2% (n = 38)		x			
	one week	79.2% (n = 38)			x		
	Worry about side effects	77.1% (n = 37)		x			
	How often did you miss to take your medication?	77.1% (n = 37)			x		
Moderate (50–75%)	Patient worries about taking too many medications	72.9% (n = 35)		x			
	Patient beliefs this medication will improve his health	70.8% (n = 34)		x			
	Patient cannot afford medication	66.7% (n = 32)	x				
	Concerns about long-term effects of this medication	66.7% (n = 32)		x			
	When was the last time you missed a dose of this medication?	66.7% (n = 32)			x		
	Patient feels he needs this medication	62.5% (n = 30)		x			
	Patient is convinced that this medication will do more harm than good	62.5% (n = 30)		x			
	Remember to take this medication	62.50% (n = 30)				x	
	Do you still have this medication?	60.42% (n = 29)					x
	Patient worries about having to take this medication	58.33% (n = 28)		x			
	Patient is convinced about the importance of this medication	58.33% (n = 28)		x			
	Worry about costs for this medication	52.08% (n = 25)		x			
	Worry about getting addicted to this medication	50.00% (n = 24)		x			
	Financially burdened by the expenses for this medication	50.00% (n = 24)		x			
Disagreement (<50%)	Fear of side-effects	47.9% (n = 23)		x			
	Problems in opening the outer packaging	45.8% (n = 22)	x				
	Patient uses this medication only if he has to, if other things don't work	39.6% (n = 19)		x			
	four weeks	39.6% (n = 19)			x		
	How many doses did you miss yesterday?	35.4% (n = 17)			x		
	Patient is convinced he would be very ill without medication	27.1% (n = 13)		x			
	Patient is convinced that this medication will hurt him	27.1% (n = 13)		x			
	yesterday	25.0% (n = 12)			x		

Table 4
List of 16 items after item reduction generated during 2021 PCNE workshop and categorized as "not sensitive" (NS) or "sensitive" (S), with corresponding phrasing and answer options that were generated during two online meetings on 25th February 2021 and 1st March 2021.

Item number	NS	S	Item description	Phrasing	Answer option
1	x		Distinguish the packages	I am able to differentiate the packages of all the medicines I use.	Yes/No
2	x		Problems with getting medicine out of the packaging/preparing the medication for use	I can easily get medicine out of the packaging or prepare all the medicines I use.	
3	x		Problems in accessing/reading/understanding the instruction for use	I can obtain, read and understand the instructions for all the medicines I use.	
4	x		Problems in drug taking (e.g., swallowing pills, using the inhaler device, counting drops, injection)	I have problems to take some of my medicines (e.g swallowing pills, using the inhaler device, counting drops, injection).	
5	x		Get refill on time	I usually refill my medicines on time.	
6	x		Worry about immediate side effects	I am worried about possible side effects of my medicines.	
7	x		Patient worries about taking too many medications	I am concerned because I take too many medicines.	
8	x		Concerns about long-term effects of this medication	I am afraid of long-term effects of my medicines.	
9	x		Worry about getting addicted to this medication	I am worried to get addicted to some of my medicines.	
10		x	Needs this medication	In general, I feel like I need my medication. (strongly agree-strongly disagree)	Likert Scale
11		x	Patient only uses this medication if he suffers	I only use my medication if/when I'm not feeling well/have/expect symptoms.	Not clearly decided
12		x	Patient is convinced that this medication will do more harm than good	In general, I believe my medication does more harm than good. (Agree-disagree)	Likert Scale
13		x	Costs	The cost of medicine is a problem for me. (never-sometimes-often-always)	Likert Scale
14		x	Forget to take this medication	In the past 14 days did you forget to take your medication?	Yes/No
15		x	How often did you miss to take your medication	People often miss to take their medication for several reasons (work schedules, holidays etc.) In the past 14 days how often did you miss yours? (Never-sometimes-often-always)	Likert Scale
16		x	Did you stop taking this medication?	Did you stop taking any of the medication on your own?	Yes/No

Table 5
Results of the item content validity index (I-CVI) for essentiality, phrasing and answer options of 16 items generated during the online survey 2021 (see table 4 for exact phrasing). Values > 0.79 indicate appropriateness; between 0.79 and 0.70 indicate a need for revisions; <0.70 (marked in bold) suggest elimination (N = 54 panelists).

		I-CVI		
		Essentiality	Phrasing	Answer option
1	differentiate the packages of the medicines	0.89	0.91	**0.69**
2	get my medicine out of the packaging or prepare the medicine	0.97	0.89	0.86
3	obtain, read and understand the instructions	0.89	**0.54**	0.86
4	problems to take my medicine	1.00	0.80	0.83
5	refill my medicine on time	0.86	**0.60**	0.80
6	worried about possible side effects	1.00	0.94	0.80
7	concerned because I take too many medicines	0.86	0.94	0.86
8	afraid of long-term effects	0.71	0.83	0.86
9	worried to get addicted	0.71	0.89	0.86
10	believe you need your medicine	0.89	0.74	0.83
11	use your medicine only if you are not feeling well	0.91	**0.69**	0.86
12	believe your medicine does more harm than good	**0.63**	0.80	0.91
13	costs	0.86	**0.66**	0.89
14	did you miss to take your medicine	0.94	**0.57**	0.83
15	how often did you miss to take your medicine	0.80	0.86	0.71
16	stop taking your medicine on your own	0.89	**0.66**	0.91

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2023.11.005.

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