Adherence to oral pharmacological treatment in cancer patients: Systematic review

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Abstract

The objective was to identify the best-validated scale for assessing oral pharmacological adherence in oncology patients.

A bibliographic search was performed in MEDLINE via Ovid, EMBASE, CENTRAL and LILACS. We included all studies in which a validation of adherence scales to oral pharmacological treatment was performed in oncology patients older than 18 years without gender distinction. We excluded studies that included newly diagnosed patients. No statistical analysis was performed due to the nature of the study. A total of 4609 studies were found. After screening, six studies were selected for qualitative analysis. In the analysis of the six included studies, a total of 855 patients older than 18 years with oncological diagnoses were found. Two of the studies, Bagcivan *et al*. and Amorim *et al*., used scales that show acceptable validity and reliability to adequately measure adherence to pharmacological treatment in each of the patients. In this way, the quality of patient care and success in pharmacological treatments can be guaranteed. According to the results obtained in the evaluation of biases and analysis of psychometric properties, the best-validated scales are as follows: Adherence Determinants Questionnaire (ADQ) (Brazilian version) and the Oral Chemotherapy Adherence Scale (OCAS). These are valid, reliable and useful scales that can be adapted to any cultural context.

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Introduction

Cancer is the second leading cause of death worldwide. In 2015, 8.8 million deaths were attributed to cancer, and annual cases of cancer are expected to increase from 14 million in 2012 to 22 million over the next two decades.[1] In Colombia, 138,000 Colombians are diagnosed with cancer per year, with an annual death rate of 33,100 people. A total of 16,300 of these deaths are men who typically have stomach, lung, prostate, or colorectal cancer or leukemia. The remaining 16,800 deaths are women who primarily suffer from cervical, stomach, breast, lung or colorectal cancer. The largest number of cases occur in the central region of the country, *i.e*., Eje cafetero, Antioquia, Valle del Cauca, Los Santanderes, Bogotá and Meta.[2] In the city of Cali, the relative frequencies of the ten leading causes of cancer mortality from 2011 - 2015 in both sexes were stomach cancer (11.5%), lung cancer (11.0%), colorectal cancer (9.2%), breast cancer (8.3%), prostate cancer (7.9%), liver cancer (5.4%), lymphoma-myeloma (4.9%), pancreatic cancer (4.3%), leukemia (4.0%) or cervical cancer (3.8%).[3] To improve patient quality of life, modern technological advances have led to the development of powerful drugs that increase life expectancy by curing or preventing the progression of many diseases. However, the positive impact of these advances is diminished when patients do not follow medical recommendations.[4] Therefore, it is important to evaluate adherence to treatment using an appropriate scale. In Colombia, however, oral therapeutic adherence in cancer is not usually measured, although scientific evidence suggests that lack of therapeutic adherence is a major problem among patients who are prescribed oral treatment for cancer. However, physicians do not use a validated scale for measurement. Given that cancer is a public health problem in Colombia, it is important to conduct an epidemiological study to identify the best-validated scale to evaluate oral therapy adherence in oncology patients. This study will contribute to the formulation of new knowledge and ideas that enrich the intervention processes in these patients.

Methods of research

A systematic review was performed according to the recommendations of the Cochrane Collaboration and the MOOSE guidelines for reporting. The protocol was described in PROSPERO: CRD42018094882. All observational studies that supported a validation of oral pharmacological adherence scales in cancer patients were included. The inclusion criteria were as follows: all studies that performed validation of scales for evaluation of oral pharmacological adherence in patients with oncological diagnosis older than 18 years without gender distinction. Studies with newly diagnosed patients were excluded. The primary outcome was the evaluation of the oral pharmacological adherence among patients with cancer by means of an accepted international scale.

Sources and search strategy

The search was performed in MEDLINE via Ovid, EMBASE, The Central Register of Controlled Trials (CENTRAL) and LILACS from its inception until nowadays. Gray literature (unpublished) was also searched in the form of conference abstracts and reference lists of the selected articles. When the complete information was not available, the authors were contacted to expand knowledge of published or unpublished articles. Additionally, Google Scholar, thesis databases and the Open Grey database were reviewed. The results of these searches were cross-checked to eliminate duplicates. There was no language restriction.

Study selection

Two researchers independently and blindly identified and selected the titles and abstracts that were obtained during the search strategy. Later, the studies were evaluated, and their inclusion in the study was determined based on the inclusion and exclusion criteria and the research question under the PICO model.

Collection process

To extract information of interest, a template was designed in Microsoft Excel that included the following data: source (authors and title), method (type of study, duration, and calculation of the sample size), sociodemographic characteristics of the participants, instrument (psychometric properties and utility), and results. The researchers confirmed and verified the data at least twice. In the case of articles where information was missing, the authors were contacted to complete the data.

Risk of bias

The risk of bias was evaluated following the adaptation of the STROBE guidelines for each of the articles. This was performed independently by two evaluators.

Statistical analysis

No statistical analysis was performed given the nature of the study and the research question.

Results

Selection of studies

With the search strategy described above, we found a total of 4609 studies with 1215 duplicates. After the title and abstract review, six studies met the study criteria for full-text analysis (Figure 1).

Characteristics of included studies

Six studies on the validation of instruments for oral pharmacological adherence in cancer patients were included.[5-10] The instruments included are described in Tables 1-4.

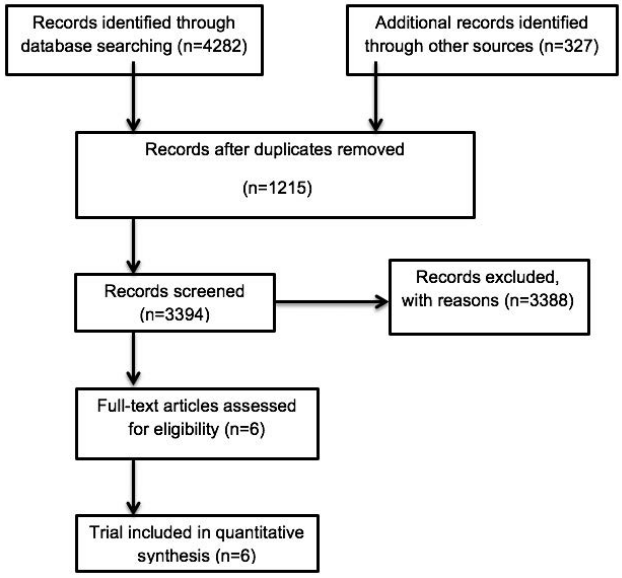

Figure 1. PRISMA flow diagram of study selection process.

Table 1. Characteristics of included studies.

Study (author)	Year	Sample size calculation	Scale
Bagcivan *et al.*	2015	The formula Item number Patient number (24 items X 10 patients = 240)	Built
Baudot *et al.*	2016	As recommended by the EORTC questionnaire: -pre-test = 15 patients; -Validation = 67 patients	Built
Daoupharset *al.*	2013	Does not report SS calculation. 46 patients in the study	Built
Jacobsen*et al.*	2008	Does not report SS calculation. 33 patients in the study	Built
Urzúa *et al.*	2012	Does not report SS calculation. Pre-test= 40 patients Validation = 120 patients	Built
Amorim *et al.*	2015	Calculated by means of the recommendation of a number of 5 to 10 participants per variable, the ADQ scale is formed by 38 items; multiplying 38 by 5, you get the number 190. Pre-test = 30 patients Validation = 198 patients	Adapted

SS, Sample size; ADQ, Adherence Determinants Questionnaire.

Table 2. Characteristics of included scales.

Study (author, year)	Number of items in total	Domains of the scales	Validity	Reliability	Time to complete
Bagcivan *et al.*, 2015	19 items	Factors (expected behaviors related to the treatment period; barriers; expected behaviors during drug use)	Face, content, criterion concurent, construct	Cronbach's alpha 0.738	Not specified
Baudot *et al.*, 2016	6 items	6 questions about adherence	Face, content, discriminant criterion	Pearson correlation coefficient <0.09	4-20 minutes
Daouphars *et al.*, 2013	10 items	10 questions about adherence	Not specified	Cronbach's alpha 0.55	10 minutes
Jacobsen *et al.*, 2008	50 items	Adherence and patient concerns	Construct	Cronbach's alpha 0.70	Not specified
Urzúa *et al.*, 2012	20 items	Expectations and personal tools to face the disease, beliefs about the treatment and perceived effects of the treatment	Construct	Cronbach's alpha 0.96	15-20 minutes
Amorim *et al.*, 2015	38 items	38 items	Content, criterion, construct	Cronbach's alpha 0.829	Not specified

Table 3. Summary the psychometric properties of the scales.

Scale (author, year)	Internal consistency	Face validity	Content validity	Criterion validity	Construct validity
Bagcivan *et al.*, 2015	+	+	+	+*	+
Baudot *et al.*, 2016	-	+	+	-	+
Daouphars *et al.*, 2013	-	-	-	-	-
Jacobsen *et al.*, 2008	+	-	-	-	+
Urzúa A, *et al.*, 2012	+	-	+	-	+
Amorim *et al.*, 2015	+	+	+	+*	+

The asterisk indicates the criterion validity *with standard gold tools*. (+) Positive, (-) Negative.

Table 4. Utility analysis.

Author	Year	Filling time	Need for training	Characteristics of the scale format	Ease to rate the scale
Bagcivan *et al.*	2015	Minimum time and good execution	No	Instrument with short text of 3 factors (expected behaviors related to the treatment period, barriers and expected behaviors during the use of drugs) conformed with 19 items	Simple
Baudot *et al.*	2016	4-20 minutes Minimum time and good execution	No	6 questions	Simple: It is a numerical visual scale from 1 to 4, with the facility qualified in 1 and the difficulty classified in 4
Daouphars *et al.*	2013	10 minutes Minimum time and good execution	No	10 questions about adherence	1 to 10 points
Jacobsen R, *et al*	2008	Not specified	Not specified	Adherence 4 items, Concerns of patients (BQ-II) 27 items, Pain 19 items	Likert type of 5 points
Urzúa *et al.*	2012	*Pre-test:* 20 minutes and it was assisted. *Validation:* 15-20 minutes	No	Expectations and personal tools to face the disease (ten items), beliefs about the treatment (six items) and perceived effects of the treatment (four items). Instrument with short text of 20 items.	Simple: Likert type 1-4
Amorim *et al.*	2015	Not specified	No	38 ítems	Simple: Likert type 1-5

BQ-II, The Barriers Questionnaire II.

Risk of bias evaluation

According to the STROBE statement, it was evident that the study by Daouphars *et al*. presented a *high* risk in most of its items, making it difficult to control for recall bias in adherence measurement by means of counting pills and microelectronic monitoring systems. The study by Baudot *et al*. had a selection bias because it was voluntary; thus, there is a risk that it was not representative of the target population. In addition, there were patients who did not speak or understand French. The study by Jacobsen *et al*. had two main biases as follows: first, patients were able to overestimate the degree of adherence in an attempt to *please the doctor* or to avoid negative judgments or sanctions; and second, the adherence was measured through self-reporting, which relied on potentially inaccurate patient memory. On the other hand, the study by Urzúa *et al*. had a *medium* risk for most items, and only the articles by Bagcivan *et al*. and Amorim *et al*. had a *low* risk.

Description of validated scales

The characteristics of the oral pharmacological adherence evaluation instruments used are presented in Table 2. The number of items that make up each instrument and its domains, the applicability and the psychometric properties of each instrument are described. It was found that the instruments contained between 6 and 50 items, which includes domains that evaluate the expected behaviors related to the treatment period, patient concerns, barriers and the expected behavior during the use of drugs.

Discussion

At present, a questionnaire that aims to measure some aspect of health, such as adherence to pharmacological treatment in this case, must provide researchers with quality information from each of the responses generated by patients. This systematic review analyzed the evaluation of the content, construction and psychometric properties of the scales used to evaluate pharmacological adherence in oncological patients. The results of this study showed that scales and modified scales are available to evaluate adherence, since questionnaires should be easy to apply and interpret, which is why it is considered an art that requires careful planning.[11] Scales should have properties of reliability and validity that are standardized and subsequently produce appropriate information.[5] Reliability is usually analyzed using Cronbach's alpha. There are different reports on acceptable alpha values, ranging from 0.70 to 0.95[12] (Table 2).

The validity of the content consists of guaranteeing the representativeness and relevance of the questions (scenarios in this case) and items (responses proposed for each scenario) that make up the questionnaire in relation to the measured concept. Essentially, it measures what should be measured. The study by Bagcivan *et al*. used the model created by Lawshe (1975) to determine a quantitative index for content validity, which consists of organizing a Content Evaluation Panel composed of specialists in the task to be evaluated (which can be competences, knowledge, abilities, functions or another type of distinctive element of the capacity of a subject that is going to be evaluated) who have a copy of the test or the set of items to be analyzed and on which they should express their opinion using the following three categories: essential, useful but not essential, not necessary. When consensus of the specialists is established for the *essential* category, Lawshe proposes the *Content Validity Ratio (CVR*), defined by the following expression: $CVR = n_e\text{-}N/2 \div N/2$. The content validity of an instrument that is determined by agreement between judges and an objective indicator of validity of the instrument is not issued.[13] Baudot *et al*. and Amorim *et al*. only consulted with experts, and each one made observations about all the questions and items of the questionnaire regarding the language, the response modalities. The experts gave suggestions for deleting or adding questions or elements. Daouphars *et al*., Jacobsen *et al*. and Urzúa *et al*. do not mention evaluation of content validity. The criterion validity analysis is important, since it adequately reflects the results obtained using a *gold standard.*[14] Only two studies included in this research (Bagcivan *et al*. and Amorim *et al*.) performed this analysis by comparing the scale to be validated with the gold standard. Construct validity is defined as the degree to which a test or measure evaluates what it was designed to measure,[15] which, in this case, is oral pharmacological adherence in oncological patients. In all of the studies, this measure was analyzed by means of factorial analysis; three studies (Bagcivan *et al*., Urzúa *et al*., and Amorim *et al*.) analyzed the sample size first by means of Kaiser-Meyer-Olkin and Bartlett's test to see if it was appropriate to perform the factorial analysis.

Like any procedure, the evaluation of methodological quality is prone to bias. Therefore, researchers should use tools that are capable of objectively evaluating methodological quality. According to our results, the sample sizes of the studies by Baudot *et al*., Daouphars *et al*., and Jacobsen *et al*. were small, making them more at risk for type II errors.

At present, the Professional Society for Health Economics and Outcomes Research notes that the clinical results of a pharmacological treatment are affected not only by how the medication is administered but also by how long it is taken. For this reason, the term *persistence* has been used in recent years to define the time during which the patient continues with the treatment, that is, the amount of time that elapses from the beginning to the interruption.[16]

These investigations showed important factors that influence the adherence to pharmacological treatment, such as forgetting, medication side effects, motivation, and physical limitations, among others. The results resemble the current situation and the medical literature, where strategies have been implemented that help the clinician to assess adherence.

Strengths and limitations of the study

The study was limited by the high heterogeneity between the studies analyzed. The included studies varied according to patient inclusion criteria, the scale with which the adherence to pharmacological treatment was measured, the methodology used, the duration of tracking, geographical location, and other factors.

Clinical application

According to the results obtained in the present systematic review, there are two scales that are statistically and analytically appropriate, and after adjusting the scales to other cultural contexts, they can be validated in Colombia with respect to pharmacological adherence in adult oncological patients.

Conclusions

According to the results obtained in the evaluation of biases and analysis of psychometric properties, the best-validated scales are the Adherence Determinants Questionnaire (ADQ) (Brazilian version) and the Oral Chemotherapy Adherence Scale (OCAS). These scales are valid, reliable and useful and can be adapted to any cultural context.

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