Use of pharmacy records to measure treatment adherence: a critical review of the literature

Utilização de registros de dispensação de medicamentos na mensuração da adesão: revisão crítica da literatura

Uso de registros de farmacia para medir la adherencia al tratamiento: una revisión crítica de la literatura

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Abstract

The current frame of reference on adherence to pharmacotherapy includes a set of behaviors experienced by the user, with observation of the detailed and continuous history of the use of each dose of the medication. Indicators based on pharmacy records have been used to measure adherence. The current review aimed to identify and describe indicators based on pharmacy records and to discuss their adequacy and limitations for measuring adherence. An exploratory literature review was conducted in three databases using the terms "adherence", "pharmacy records/administrative data", and "measure" to compose the descriptors for the selection of 81 articles and the elaboration of a chart with the denomination, sources, methods for calculation, description, and interpretation of the operational and referential meaning of 14 indicators. Given the most recent taxonomy for adherence proposed in the literature, we concluded that the indicators can be useful for identifying patients with medication-seeking behavior-related problems and analysis of persistence. The distance between supply-related events and difficulties in treatment follow-up can influence an analysis based exclusively on the use of these indicators.

Medication Adherence; Indicators of Health Services; Pharmaceutical Services

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Adherence to drug therapy can be included in the scope of the overall concept of adherence adopted by the World Health Organization (WHO) [1] (p. 3), which defines it as *"the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider"*.

The theoretical framework of the WHO is broad, since it considers multiple determinants of adherence, from those farthest from the patient/user (includes the health system and services) to the closest, such as issues related to the medication. In order to justify measuring adherence, some criteria need to be met, such as a prescription based on a proven therapeutic need, correct dose indication, dosing regimen, treatment time, and availability of an adequate amount of the medication [2].

The literature presents and classifies the methods for measuring adherence as direct and indirect. Measures based on direct criteria are considered the most reliable, since they are based on objective verification of intake (directly observed therapy) or on plasma titration of the drug [2,3].

Meanwhile, indirect measures – resulting from interaction between the user and instruments for measuring adherence (e.g., interviews and self-completed questionnaires) – are susceptible to recall bias or exercise of the patient/user's will [2,4]. In order to create conditions of objectivity, the information resulting from the interview or questionnaire is backed by scales, which transform the data into measurable items [4,5]. The scales include elements on medication-seeking behavior, medication-taking behavior, beliefs, and barriers to adherence and their determinants. Not all scales measure adherence under the same clinical conditions or in the same contexts [4].

Other indirect measures like physical or electronic counts of available medications for use attempt to generate data on frequency of intake. Although more objective than interviews or self-report, it is not possible to guarantee that the counted medications are actually taken.

The current taxonomy on adherence to medication includes a set of behaviors by the user [6] and emphasizes the need to seek answers in the "dosing history", translated as the detailed and continuous trajectory in use of the medication, at each dose [7]. In this sense, adherence could be defined as a stage in the multifactor regressions between the drug's prescription and the therapeutic effect [8,9]. In the final analysis, measuring adherence is intended to predict a clinical outcome: the medication's effectiveness [10].

In studies on adherence, secondary databases can be useful by offering the possibility for quick access to a set of individualized information from a large number of users. However, the clinical context is sometimes indispensable to compare and determine the information's validity [11]. Considering the limited availability of clinical and prescription records, many studies are limited to national or local information systems with records on the supply and dispensing of medications [12,13,14,15]. These records have been used to construct indicators for the analysis of adherence and its determinants [12,16,17,18,19,20,21,22].

The current study thus aimed to identify and characterize indicators based on pharmacy records and discuss their adequacy and limitations for measuring adherence, based on a literature review. The decision was made to address methodological aspects related to the measurement of adherence, with a focus on analyzing the applicability of these indicators and theoretical, conceptual, and practical assumptions that justify and provide the basis for this measurement.

Methodological approach

We conducted an exploratory literature review in PubMed, SciELO, and Scopus, using the terms "adherence", "pharmacy records/administrative data" and "measure" to compose the descriptors and boolean equations [OR, AND], allowing the selection of articles published in English, Spanish, and Portuguese, with no limitation on year of publication. Next, the following exclusion criteria were applied in two stages (reading the abstracts and full texts), as shown in the flowchart (Figure 1): (i) duplicate articles, (ii) full text unavailable, or (iii) articles that did not address adherence and/or did not use administrative data or pharmacy records.

Information from the literature supported the elaboration of a descriptive chart of the indicators, including sources and application, method of calculation, description, and interpretation of the indicator's operational meaning and frame of reference.

Figure 1

Flowchart for article selection process.
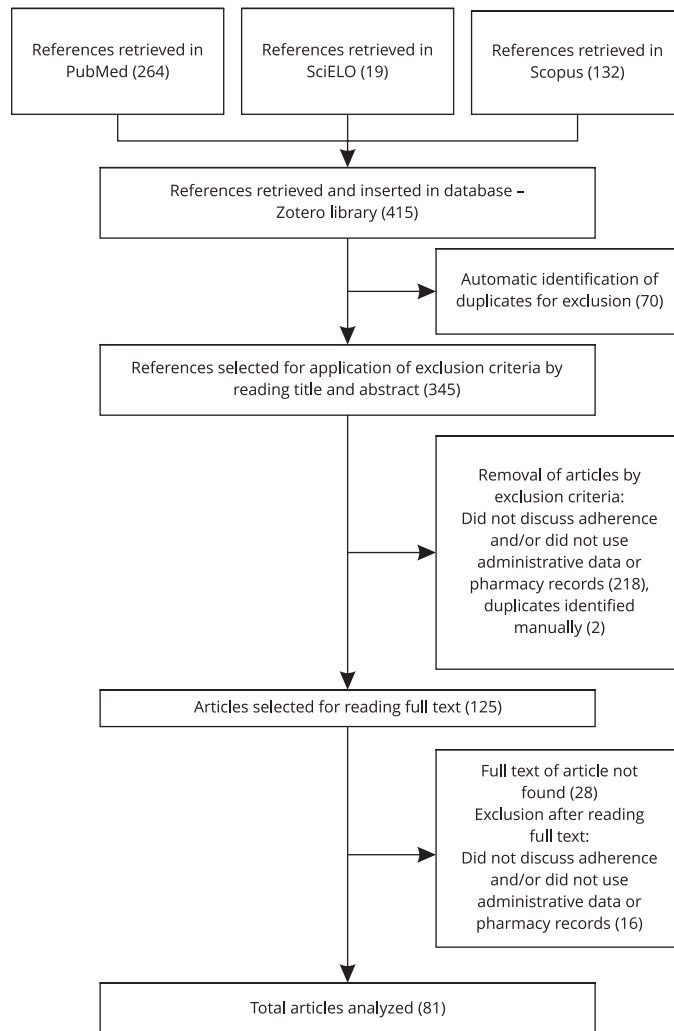
The chart revealed the implications for use of the indicators and precautions in interpretation of the results, assuming that it is not possible to study adherence without being certain that the patient received the medication in the prescribed quantity and at the right time [2,23]. We attempted to define aspects related to treatment coverage and possession versus gaps in the medication as ways of exploring the possible proximal or distal relations between availability of the medication, use, and adherence.

Finally, we drew on the theoretical and conceptual framework of adherence drawing on "dosing histories", based on which a new taxonomy was developed, which strengthens the concept of adherence as therapeutic result [2,4,6,7,24]. Three reasons were weighed on the adequacy and limits of the indicators which provide the basis for measuring adherence in practical terms: (i) evaluation of a drug intervention's therapeutic effects; (ii) determination of the influence of adherence on specific clinical conditions; and (iii) identification of patients that need orientation or support to use their medications better [4]. These reasons and the above-mentioned theoretical concepts provided the basis for analyzing the indicators and orienting the discussion.

Results

Indicators based on the dispensing process have been developed over the years in research and health service settings, based on practical criteria – given the greater availability of administrative or supply records than prescription data or consumption per se [8,25,26,27,28].

These indicators (i) focus on the dynamics of individual supply (dispensing of the medication), (ii) translate critical information on the amounts supplied (number of units/doses), and (iii) allow verifying the supply timeline. The method calculates the periods, generally in days, in which one assumes the patient's possession of the medication following its dispensing or the possible gaps resulting from irregular receipt of the drug.

Fourteen studies, among the 81 retrieved, addressed the relationship between pharmacy records and adherence, but did not present descriptive measures (indicators) of this relationship [18,29,30,31,32,33, 34,35,36,37,38,39,40,41]. Some 40 studies pointed to measures (indicators) based on supply records to measure adherence [42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79, 80,81,82,83,84,85] and were mostly published before Vrijens et al. [6] proposed a new taxonomy. The literature refers to the principal indicators used to measure adherence in various types of chronic diseases as medication possession ratio (MPR) and proportion of days covered (PDC). The studies diverge as to their usefulness in the strict evaluation of adherence [40,42]. However, there is use of these indicators to measure treatment adherence in mental disorders [43,44], depression [45], schizophrenia [46,47,48,49,50], diabetes [50,51,52,53,54,55], hypertension [51,56,57,58,59,60,61,62], coronary diseases [63,64,65,66,67], osteoporosis [68,69], rheumatoid arthritis [70,71], lupus [70], chronic obstructive pulmonary disease [72,73,74], asthma [75,76,77,78], HIV/AIDS [79,80,81] and hepatitis [82], post-transplant [83], Parkinson's disease [84], and multiple sclerosis [85].

Table 1 lists the indicators described in the selected studies. Eleven indicators provided the basis for treatment coverage (period with possession of the medication) and three for gaps during the period. Some studies used similar names for the same measure [26,27,28,55,73,83], so that calculation of the indicator was considered the basis for its definition and distinction.

In general, the parameters for analysis of the amount (or doses) of the medication and the periodicity of expected dispensing were the medical prescription or therapeutic protocol [86,87]. Based on the prescription, the ideal therapeutic behavior projected over time generated an estimate of the medications to be consumed during the period. Based on this ideal scenario, one verifies the translation of the idea of "coverage" or "percentage of coverage" [8,28].

The concept of coverage has been operationalized by calculating the days' supply, which represents the amount (in days of treatment) that the total medication covers, in one or more episodes of dispensing, over the period (in days) theoretically covered by the amount dispensed. Often, any observed gap is expressed as the difference between the total observation period and the number of days' supply in possession.

In addition to the possession or lack of the medication, the development of the indicators was based on the adoption of two other aspects, in distinct combinations, that gave each measure's specificity: (a) whether the indicator's result is treated as a dichotomous or continuous variable and (b) whether the verification occurs in one or multiple dispensing intervals [8].

While not sharing the same calculation method, the indicators represented different expressions of the same measurement logic [78]. In the numerator, this logic could be stated as "days' supply of medication obtained" or "number of days in which the patient was in possession of the medication as prescribed", as expressions of the treatment supplied/obtained. In the denominator, "observation period" (in days) or "period between the first and latest dispensing" (in days) emerged as expressions of the ideal coverage time. Since they contained the same unit in the numerator and in the denominator, the results were adimensional.

Continuous single-interval of medication availability (CSA) and continuous multiple-interval of medication availability (CMA), as well as continuous single-interval of medication gap (CSG) and continuous multiple-interval of medication gap (CMG), are examples of measures that sought to reflect the balance between the analysis of single or multiple episodes of dispensing. The expression of the result for a single dispensing (in the case of CSA, CSG) appeared useful for indicating the fraction of coverage in acute diseases. However, for the analysis of adherence in the continuous treatment of chronic diseases, the proposal has been to use the mean of the measurements of single intervals

Table 1

Indicators based on pharmacy supply records.

Measure/Sources, and Application	Calculation	Observations
Measures based on actual supply (possession)		
CSA [8,26,47,49]	Number of days with supply of the medication according to prescription */single observation period (in days).	Measures the time interval in which the patient had the medication available from a single dispensing. The interval of observations begins with the dispensing. Aims to express the coverage of a given period and is generally expressed as a fraction. In periods with more than one dispensing, the mean should be used. Values greater than 1 mean "oversupply".
CMA [8,26,49,78]	Total number of days with supply of medications according to prescription/observation period (in days).	Measures the sum of time intervals in which the patient had a given medication available in a series of dispensing intervals. Aims to express coverage in multiple serial periods and is generally expressed as a fraction. Values greater than 1 mean "oversupply".
	Total number of dispensing episodes (of the amount of medication) for an observation period/expected number of dispensing episodes in the observation period.	Measures the proportion of observed dispensing episodes in the expected number, in a period set by the researcher.
MPR [26,27,28,42,45,48,49, 50,52,54,62,70,71,74,78,79,80, 82,85,104,105,106,107,108]	Number of days in which the patient has the medication available according to prescription/ observation period (in days).	Measures the single interval or multiple (total) time intervals in which the patient has the medication available, like CSA and CMA, respectively. Usually expressed as a fraction. For cases of polypharmacy, it is suggested to consider the mean of the values for the numerator before dividing by the denominator. Values greater than 1 mean "oversupply", but some studies suggest that MPR should be truncated at 1. The indicator is sometimes expressed as a ratio whose antecedent is the fractional result of the calculation and the consequent is always 1.
PDC [26,27,28,42,48,49,57, 58,59,60,63,68,72,78,80,105, 106,107]	[Number of days on which the patient has the medication available according to prescription/ observation period (in days)] x 100.	Single interval or multiple (total) time intervals in which the patient has the medication available, as in CSA, CMA, and MPR. May infer all the medicines as the object the "treatment", rather than only one medicine. It is thus assumed that the patient needs to have possession of all the medicines in treatment, simultaneously. Usually expressed as a percentage, without allowing values greater than 100%, which would indicate "oversupply".
PPDC [76]	Days' supply during the observation period/total days of treatment (expected) according to prescription.	Considers the planned treatment period for each case (in days) in the denominator.
MPRm [28,49]	Number of days on which the patient has the medication available according to prescription/period between first and last dispensing (in days), plus the period covered by the last dispensing minus 1 (day of last dispensing).	Allows calculating coverage, even assuming a possible information gap. The measure includes the last part of the observation period, whatever it is, when it is unknown. Seeks to avoid arbitrary definition of the end of the observation period by taking the dispensing dates as the basis. By presenting coverage periods for the last dispensing in the numerator and denominator, it seeks to compensate for lack of knowledge on the final period of use. (Removes one day to be sensitive, ruling out a "duplicate" day in the analysis).

(continues)

Table 1 (continued)

Measure/Sources, and Application	Calculation	Observations
Measures based on actual supply (possession)		
Truncated MPR [48]	[Number of days on which patient has the medication available according to prescription / observation period (in days)]. Final result is ≤ 1.	MPR value is "truncated" when > 1. Seeks to rule out the "assumed" excess in the measure. This happens because the numerator considers the days' supply, including the last episode of dispensing, about which there may not be feedback. By truncating, the indicator solves a problem, but information is lost on the medication received in amounts greater than theoretically used for the observed period.
RCR [26,28]	{[Sum of the amount during the observation period)/amount to take per day according to prescription]/ period between first and last dispensing (in days)} x 100.	Measures percentage of coverage. This fraction's numerator specifies the calculation of the number of days on which the patient has medication available (days' supply), like numerous others already discussed (CSA, CMA, MPR). Attempts to avoid arbitrary definition of the end of the observation period by taking the dispensing dates as the basis (as in MPRm). However, it does not discount the duplicate day (MPRm) or compensate for excess coverage (like MPRm and truncated MPR).
CR [26,28,49,62]	Days' supply in all the dispensing episodes except for last/period between first and last dispensing (in days)] x 100.	Measures percentage of coverage (including excess) in a known and defined dispensing interval. Seeks to correct for lack of knowledge of the final coverage period, eliminating from calculation of the days' supply from the numerator, the amount supplied in the last dispensing, unlike MPRm, which corrects by addition of these days in both terms of the fraction.
DBR [26,28,49,62]	{1 - [(Period between first and last dispensing - days' supply)/period between first and last dispensing]} x 100.	Also measures percentage of coverage using a device for adjustment. Proposes adjusted behavior of the measure (1 - gap) in relation to 100% (idealized behavior. "(1 - gap) x 100" attempts to adjust a centesimal scale. to the real meaning of the total.
MRA [26,28]	Days' supply/observation period (in days)] x 100.	Expresses coverage (like CMA), but as a percentage. Values >100 mean "oversupply".
Measures based on supply not made (gap)		
CSG [8]	(Total observation period - days' supply)/single observation period (in days).	For a single dispensing, it is the time interval in which the patient did not have the medication available (dispensing gap). In periods with more than one dispensing, one can use the mean (mean gap in a given interval). Since the observation period is set arbitrarily, it is not based on the real history of use. If the observation period is the period between the first and the last, the measure has fewer limitations. There are limitations in the cases of "oversupply". In cases with excess, the measure can only be used for multiple cases (patient population) in which the negative values (referring to excess, in calculating the gap) can be redefined as 0, as presented in the literature.

(continues)

Table 1 (continued)

Measure/Sources, and Application	Calculation	Observations
Measures based on supply not made (gap)		
CMG [8,26,27,28,42,49,53,64, 81,103,106]	(Total observation period - days' supply)/observation period (in days).	In series of dispensing intervals, the sum of the time intervals in which the patient did not have the medication available (total gap).
		Periods of "oversupply" involve negative values in the indicator, usually redefined as 0.
		It is a simplified measure that does not have the power to estimate the number of days on which the patient was without the medication ("real" gap). Not based on the dosing history. It is like a 'mean'.
CMOS [26,28,49]	(Total observation period - days' supply)/observation period (in days).	Similar to the previous measures (CSG, CMG), but allows negative values.
		If the indicator's result is positive, it represents the number of days on which the patient does not have the medication (gap); if negative, it represents "oversupply".

CMA: continuous multiple-interval of medication availability; CMG: continuous multiple-interval of medication gap; CMOS: continuous multiple-interval measure of over-supply; CR: compliance rate; CSA: continuous single-interval of medication availability; CSG: continuous single-interval of medication gap; DBR: days between fills adherence rate;   MPR: medication possession ratio; MPRm: medication possession ratio modified; MRA: medication refill adherence; PDC: proportion of days covered; PPDC: proportion of prescribed days covered; RCR: refill compliance rate.

* The supply records contain information on the amount dispensed. To transform the amounts of medications dispensed and/or supplied into number of days, it is necessary to consider the treatment regimen on the prescription (dose, interval, and treatment period), as well as the registered pharmaco-technical unit.

as the expression of continuous availability. However, this would involve a loss of information on coverage gaps in sequential periods, disguising coverage gaps in the past with medication surpluses in the future [8,26].

Another relevant aspect relates to the definition of the observation interval in the denominator. The studies treated the terms "interval" and "days evaluated" as synonymous. In Table 1, the denominator in the indicators CMA, CMG, MPR, PDC, medication refill adherence (MRA), and continuous multiple-interval measure of over-supply (CMOS) is described as the "observation period" and denotes an arbitrarily defined period, dates for the start and finish of the data collection, in which the target variables are examined. Meanwhile, the definition of the denominator as the "period between the first and last dispensing", as in the indicators refill compliance rate (RCR), compliance rate (CR), and days between fills adherence rate (DBR) appears to have avoided the arbitrary definition of the observation interval. In these indicators, the limit of the observation period was defined as the date of a dispensing episode.

Finally, in the numerator and/or denominator, the indicator may or may not include the amount furnished in the last dispensing in the days' supply. Inclusion in the numerator would mean the possibility of higher results than unity (or greater than 100%). Values greater than one or one hundred percent may or may not mean oversupply.

As shown in Table 1, the proposal for some indicators resulted from the attempt to refine the underlying logic, based on the empirical data, to deal with difficulties in comparing the expected and the observed values. This is especially true of the indicators that inserted a critique or adjustment to refine the results obtained. These adjustment strategies (or mathematical devices) occurred in the numerator of RCR, CR, and DBR, in the denominator of medication possession ratio modified (MPRm), or in the expression of the final result (truncated MPR).

Discussion

The analysis of the specific variations between the methods for each indicator's calculation allowed understanding the operational limitations involved in the extraction and standardization of the data and the identification of necessary precautions when interpreting the results.

The search strategy allowed identifying studies that incorporated indicators based on supply records as measures of adherence, for the construction of Table 1. Other studies retrieved in the search defined adherent patients based on administrative supply records, but either did not describe in detail the indicator employed, or used complementary methods to validate the measure of adherence [18,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102]. The latter feature the methodological care in using more than one strategy to obtain information on adherence, although not detailing specific measures for its assessment (the focus of this review).

The supply records in the studies on use of medications generate simple, low-cost, non-invasive measures that dispense for the use of questionnaires/interviews [11,86,87]. In computerized systems, information is concentrated in databases or software programs [87], facilitating data access and organization. When the medication is supplied by a single agency or entity with a computerized system, the patient's history can be viewed rapidly [81,87].

The inference between the dynamics of pharmacy supply of medications expressed in indicators based on supply records and adherence is conditioned on three assumptions. The first is that the database on dispensing includes all the sources for obtaining the prescribed medications. The second is that lack of supply of medications in the amounts and on the proper dates implies the impossibility of use as prescribed [86]. It is not possible to study adherence without the certainty that the patient received the medication in the adequate amount [2,23]. The third is that if the medications were dispensed in the expected period, they were consumed as prescribed [3,81,86]. Another quite radical assumption is necessary – that everything supplied was taken at the prescribed amounts, at the prescribed hours, and for the prescribed time – that is, when estimating adherence based exclusively on supply data, one assumes perfect adherence to all the other unmeasured aspects.

In addition, the use of indicators based on supply records as measures of adherence requires careful consideration of the reasons behind the measure in clinical practice [4].

The first issue focuses on the discussion of which relations are possible between the medication's supply and its therapeutic effects. The literature claims the indicators' pertinence as the measure of adherence based on empirical demonstrations of their predictive validity for clinical outcome and their correlation with alternative methods for measuring adherence [29,39,40,43,44,56,70,103,104,105,106,107,108,109]. However, despite their usefulness as predictors of target clinical outcomes, the assertion does not imply the validity of their use as measures of adherence. The point here is not to question such indicators based on the inherent limitations of the sources employed and the method for calculation, but to discuss what can be reasonably inferred from the results.

Adherence has traditionally been estimated either as a dichotomous indicator or as a percentage, in which the patient's medication-taking behavior is recorded by the health professional, measured on a scale from 0 to 100 [108,110]. To transform the interval measures in dichotomous, cutoffs points are set for the respective disease according to the literature, which requires caution. The variable's dichotomization prevents distinguishing between types of non-adherence: consistent or sporadic; patients at different stages in the medication-taking process, etc.

Vrijens et al. [6] debated the phenomenon of adherence after conducting a review on the topic and producing a consensus with 80 experts from 13 European countries, based on the study of the drug-dosing histories. The authors proposed to define adherence as a process consisting of three components: initiation, implementation, and discontinuation. The components correspond respectively to use of the first prescribed dose, the dynamic of maintaining the treatment regimen (length, frequency, and hours of dose administrations), and the definitive interruption of use, for various reasons. Permeating these phases is an attribute known as persistence, described as the period of time between initiation and the last dose [6,42,108,111].

Persistence is a measure associated with the time of uninterrupted maintenance of the treatment regime and can be measured through the episodes of the patients' return to pick up their medications,

over time. It is an important outcome for evaluating treatment adherence and has been displayed visually as Kaplan-Meier curves, like survival [6,7,66], or inferred as a measure resulting from the use of the PDC indicator [42,69,100,112]. However, although persistence is related to adherence – and is sometimes confused with it in the literature [65,99,112] –, persistence is not synonymous with adherence, nor is it an unequivocal predictor of it according to dosing history. Treatment persistence is possible without adherence to the prescribed recommendations. Therefore, the most satisfactory measure of adherence is that which includes persistence and all the stages defined in the new paradigm of adherence [7].

Quantification of implementation requires comparison of two time series: the prescribed treatment regimen, which can be compared to the expected parameter, and the patient's treatment history, corresponding to the observed parameter [6]. The result of measuring implementation can be expressed by a single summary measure (normally a percentage of adherence at the end of a defined period) – which is the most common in practice – or by a longitudinal sequence of measurements [110]. Supporting the former is the practicality of classifying discrete outcomes (adherent *versus* non- adherent) on a predetermined scale of relative distances between the expected and the observed. However, the same result, or percentage of implementation, can mean completely different medication-taking behaviors, that is, treatment regimen histories, or differentiated adherence, with direct implications for the medication's effectiveness [7]. At the limit, differences exist in effectiveness, even among patients that follow their treatment regimen correctly (and which are thus adherent to it), expressing the so-called "unreliable link" between use of the medication and the therapeutic effect [7].

Thus, the first aspects to be considered in the sequence of explanatory events that lead to the body's response to the treatment regimen are not those related to possession of medication or continuity or volume of the supply, but those involving ingestion of the dose, followed by pharmacokinetic aspects, which directly explain the therapeutic effects, based on the drug's absorption and metabolism [7,113,114]. In this sense, establishing a correlation, even if indirect, between the indicator based on records and supply and the therapeutic effect means ignoring a series of intermediate elements in the dosing history that were not investigated.

To understand the factors that influence adherence under specific clinical conditions, it is necessary to characterize not only the time sequence of events involving the treatment regimen, but their determinants. Since adherence involves a series of phases and attributes — initiation, implementation, discontinuation, persistence [6] – the factors associated with some of these attributes are not necessarily associated with all of them [24]. It is necessary to investigate specific factors related to the different components of adherence. The indicators reviewed here do not allow investigating how the treatment was initiated or discontinued, or the characteristics of its implementation. Meanwhile, persistence allows the incorporation of time limits on the implementation of adherence and can thus be measured by the indicators. However, there are limitations on the measure of persistence that are inherent to the use of secondary databases [11,44,47,51,64,69,115]. In a systematic review, Kardas et al. [24] found 771 different variables for expressing factors associated with adherence to prolonged therapies. Most were related to implementation, while 47 were related to persistence.

This discussion should conclude by highlighting the usefulness of indicators based on supply records. Osterberg & Blaschke [2] contended that supply data on medications can be an estimate of the extent to which the patient persists with the treatment. However, as discussed, one should not assume that possession of the medication or persistence in retrieving it, per se, mean adherence. At any rate, lack of the medication certainly constitutes a factor for non-adherence. Therefore, the relevance of these indicators is clear in the identification (screening) of patients that need orientation or support to improve their use of medications for chronic diseases [10], especially when associated with other methods [116].

In Brazil, most studies involving the use of indicators based on supply records focus on antiretroviral therapy [12,18,117], available in the System for Logistic Control of Medications (Siclom), which combines prescription with supply (but without addressing all the stages of dispensing). Recording in this database is mandatory for nearly all of the pharmacies accredited for antiretroviral dispensing. Some studies that used Siclom combined pharmacy records with different sources of information (self-report, patient diary, pharmacy records, and laboratory data) to measure the percentage of non-adherent patients, focusing on supply gaps. Cardoso & Galera [17] and Fonseca et al. [20] also considered

the time interval recorded between dispensing episodes for analysis of the use of medications and treatment dropout, respectively. A more recent study, on biological therapy in rheumatic diseases, specified the use of the PDC indicator to identify patients without adherence to treatment [21]. Other studies from Brazil and elsewhere have focused on persistence as the outcome measure for use of indicators based on pharmacy records, which suggests evolution in adherence concepts as the result of dosing history [56,95,100,112].

Final remarks

This review presented a map of indicators reported in the literature, used to analyze adherence to pharmacotherapy. The strategy to build a descriptive picture of indicators based on pharmacy supply records allowed identifying the precautions and limitations in studies on the use of medications that can contribute to the design and comparability of future studies in the field.

As discussed, the indicators, stemming from different evaluations of the supply dynamics in medications, based on pharmacy records, resulted from the refinement of a single logic: that the time of exposure to treatment was calculated from the amount of medications supplied for an assumed time period. This improvement and the resulting variations reflect the operational difficulties in obtaining and use of the measures.

By expressing the fraction (adimensional) equivalent to a time segment of the treatment, the indicators' results refer more adequately to the "persistence" component, in the taxonomy adopted for adherence. They are thus adequate as outcome measures in analyses of factors associated with this component of adherence. These indicators are also clearly useful for identifying patients with problems related to medication-seeking behavior, indicating lack of adherence.

It is true that traditionally, studies on the use of medications employ supply data to estimate consumption. However, the gap between supply-related events and difficulties in treatment follow-up that impact consumption disallow relating the results of the indicators with clinical aspects, essential in the discussion of adherence.

Contributors

E. C. Lima-Dellamora and C. G. S. Osorio-de-Castro contributed to the study coordination, conception, design, and planning, literature review, analysis and interpretation of results, writing and approval of the final version. L. G. S. L. Madruga collaborated to the literature review, analysis and interpretation of results, writing and approval of the final version. T. B. Azeredo participated in the study conception, design, and planning, literature review, analysis and interpretation of results, writing and approval of the final version.

References

1. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003.
2. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005; 353:487-97.
3. Polejack L, Seidl EMF. Monitoramento e avaliação da adesão ao tratamento antirretroviral para HIV/aids: desafios e possibilidades. Ciênc Saúde Coletiva 2010; 15 Suppl 1:S1201-8.
4. Nguyen TM, La Caze A, Cottrell N. What are validated self-report adherence scales really measuring? A systematic review. Br J Clin Pharmacol 2014; 77:427-45.
5. Pasquali L. Psicometria: teoria dos testes na psicologia e na educação. 2ª Ed. Petrópolis: Editora Vozes; 2004.

6. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol 2012; 73:691-705.

7. Blaschke TF, Osterberg L, Vrijens B, Urquhart J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. Annu Rev Pharmacol Toxicol 2012; 52:275-301.

8. Steiner JF, Prochazka AV. The assessment of refill compliance using pharmacy records: methods, validity, and applications. J Clin Epimiol 1997; 50:105-16.

9. Steiner JF. Rethinking adherence. Ann Intern Med 2012; 57:580-5.

10. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002; 40:794-811.

11. Harper S. Using secondary data sources for pharmacoepidemiology and outcomes research. Pharmacotherapy 2009; 29:138-53.

12. Gomes RRFM, Machado CJ, Acurcio FA, Guimarães MDC. Utilização dos registros de dispensação da farmácia como indicador da não-adesão à terapia anti-retroviral em indivíduos infectados pelo HIV. Cad Saúde Pública 2009; 25:495-506.

13. Soares C, Silva GA. Uso de registros de assistência farmacêutica do Sistema de Informações Ambulatorial para avaliação longitudinal de utilização e adesão a medicamentos. Cad Saúde Colet (Rio J.) 2013; 21:245-52.

14. Freitas FP, Pinto IC. Percepção da equipe de saúde da família sobre a utilização do Sistema de Informação da Atenção Básica – SIAB. Rev Latinoam Enferm 2005; 13:547-54.

15. Lima-Dellamora EC, Matos GC. Perspectivas e importância da investigação sobre uso de medicamentos no cenário brasileiro. Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde 2013; 4:4-5.

16. Blatt CR, Citadin CB, Souza FG, Mello RS, Galato D. Avaliação da adesão aos anti-retrovirais em um município no Sul do Brasil. Rev Soc Bras Med Trop 2009; 42:131-6.

17. Cardoso L, Galera SAF. Doentes mentais e seu perfil de adesão ao tratamento psicofarmacológico. Rev Esc Enferm USP 2009; 43:161-7.

18. Rocha GM, Machado CJ, Acurcio FA, Guimarães MDC. Monitoring adherence to antirretroviral treatment in Brazil: an urgent challenge. Cad Saúde Pública 2011; 27 Suppl 1:S67-78.

19. Romeu GA, Tavares MM, Carmo CP, Magalhães KN, Nobre ACL, Matos VC. Avaliação da adesão a terapia antirretroviral de pacientes portadores de HIV. Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde 2012; 3:37-41.

20. Fonseca LC, Martins FJ, Alves RCPV, Pereira RMC, Ferreira AS, Raposo NRB. Evaluation of inadequate anti-retroviral treatment in patients with HIV/AIDS. Rev Soc Bras Med Trop 2012; 45:151-5.

21. Dabés CGS, Almeida AM, Acurcio FA. Não adesão à terapia biológica em pacientes com doenças reumáticas no Sistema Único de Saúde em Minas Gerais, Brasil. Cad Saúde Pública 2015; 31:2599-609.

22. Acurcio FA, Machado MAA, Moura CS, Ferre F, Guerra Júnior AA, Andrade EIG, et al. Medication persistence of DMARDs and anti-TNF agents in a cohort of patients with rheumatoid arthritis in Brazil. Arthritis Care Res 2016; 68:1489-96.

23. Osorio-de-Castro CG, Suárez-Mutis MC, Miranda ES, Luz TCB. Dispensing and determinants of non-adherence to treatment for non complicated malaria caused by *Plasmodium vivax* and *Plasmodium falciparum* in high-risk municipalities in the Brazilian Amazon. Malar J 2015; 14:471.

24. Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. Front Pharmacol 2013; 4:91.

25. Capellà D. Descriptive tools and analysis. In: Dukes MNG, editor. Drug utilization studies: methods and uses. Copenhagen: WHO Regional Publications, WHO Regional Office for Europe; 1993. p. 55-78. (European Series, 45).

26. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. Ann Pharmacother 2006; 40:1280-8.

27. Sattler ELP, Lee JS, Perri M. Medication (re)fill adherence measures derived from pharmacy claims data in older Americans: a review of the literature. Drugs Aging 2013; 30:383-99.

28. Raebel MA, Schmittdiel J, Konieczny JL, Karter AJ, Steiner JF. Standardizing terminology and definitions of medication adherence and persistence in research employing electronic databases. Med Care 2013; 8 Suppl 3:S11-21.

29. Grenard JL, Munjas BA, Adams JL, Suttorp M, Maglione M, McGlynn EA, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med 2011; 10:1175-82.

30. Robinson RL, Long SR, Chang S, Able S, Baser O, Obenchain RL, et al. Higher costs and therapeutic factors associated with adherence to NCQA HEDIS antidepressant medication management measures: analysis of administrative claims. J Manag Care Pharm 2006; 12:43-54.

31. Ross-Degnan D, Pierre-Jacques M, Zhang F, Tadeg H, Gitau L, Ntaganira J, et al. Measuring adherence to antiretroviral treatment in resource-poor settings: the clinical validity of key indicators. BMC Health Serv Res 2010; 10:42.

32. Rougemont M, Stoll BE, Elia N, Ngang P. Antiretroviral treatment adherence and its determinants in Sub-Saharan Africa: a prospective study at Yaounde Central Hospital, Cameroon. AIDS Res Ther 2009; 6:21.

33. Rubio-Valera M, March Pujol M, Fernández A, Peñarrubia-María MT, Travé P, López del Hoyo Y, et al. Evaluation of a pharmacist intervention on patients initiating pharmacological treatment for depression: a randomized controlled superiority trial. Eur Neuropsychopharmacol 2013; 9:1057-66.

34. Townsend ML, Jackson GL, Smith R, Wilson KH. Association between pharmacy medication refill-based adherence rates and cd4 count and viral-load responses: a retrospective analysis in treatment-experienced adults with HIV. Clin Ther 2007; 4:711-6.

35. Choo PW, Rand CS, Inui TS, Lee ML, Cain E, Cordeiro-Breault M, et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. Med Care 1999; 9:846-57.

36. Ginde AA, Von Harz BC, Turnbow D, Lewis LM. The effect of ED prescription dispensing on patient compliance. Am J Emerg Med 2003; 4:313-5.

37. Buscher A, Hartman C, Kallen M, Giordano T. Validity of self-report measures in assessing antiretroviral adherence of newly diagnosed, HAART-Naïve, HIV patients. HIV Clin Trials 2011; 5:244-54.

38. Glanz K, Beck AD, Bundy L, Primo S, Lynn MJ, Cleveland J, et al. Impact of a health communication intervention to improve glaucoma treatment adherence. Results of the interactive study to increase glaucoma adherence to treatment trial. Arch Ophthalmol 2012; 10:1252-8.

39. Hall KS, White KO, Reame N, Westhoff C. Studying the use of oral contraception: a review of measurement approaches. J Womens Health (Larchmt) 2010, 12:2203-10.

40. Lam WY, Fresco P. Medication adherence measures: an overview. Biomed Res Int 2015; 2015:217047.

41. Gutierrez EB, Sartori AMC, Schmidt AL, Piloto BM, França BB, Oliveira AS, et al. Measuring adherence to antiretroviral treatment: the role of pharmacy records of drug withdrawals. AIDS Behav 2012; 6:1482-90.

42. Peterson AM, Nau DP, Cramer JA, Benner J, Gwadry-Sridhar F, Nichol M. A checklist for medication compliance and persistence studies using retrospective databases. Value Health 2007; 10:3-12.

43. Sajatovic M, Velligan DI, Weiden PJ, Valenstein MA, Ogedegbe G. Measurement of psychiatric treatment adherence. J Psychosom Res 2010; 6:591-9.

44. Brodtkorb E, Samsonsen C, Sund JK, Bråthen G, Helde G, Reimers A. Treatment non-adherence in pseudo-refractory epilepsy. Epilepsy Res 2016; 122:1-6.

45. Ettinger AB, Good MB, Manjunath R, Edward Faught R, Bancroft T. The relationship of depression to antiepileptic drug adherence and quality of life in epilepsy. Epilepsy Behav 2014; 36:138-43.

46. Campagna EJ, Muser E, Parks J, Morrato EH. Methodological considerations in estimating adherence and persistence for a long-acting injectable medication. J Manag Care Spec Pharm 2014; 7:756-66.

47. Frey S, Stargardt T. Performance of compliance and persistence measures in predicting clinical and economic outcomes using administrative data from German sickness funds. Pharmacotherapy 2012; 10:880-9.

48. Martin BC, Wiley-Exley EK, Richards S, Domino ME, Carey TS, Sleath BL. Contrasting measures of adherence with simple drug use, medication switching, and therapeutic duplication. Ann Pharmacother 2009; 43:36-44.

49. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. Prospective validation of eight different adherence measures for use with administrative claims data among patients with schizophrenia. Value Health 2009; 12:989-95.

50. Gosmanova J, Dixon LB, McCarthy JF, Soliman S, Ignacio RV, Valenstein M. Does adherence to medications for type 2 diabetes differ between individuals with vs without schizophrenia? Schizophr Bull 2010; 36:428-35.

51. Christensen AJ, Howren MB, Hillis SL, Kaboli P, Carter BL, Cvengros JA, et al. Patient and physician beliefs about control over health: association of symmetrical beliefs with medication regimen adherence. J Gen Intern Med 2010; 25:397-402.

52. McAdam-Marx C, Bellows BK, Unni S, Wygant G, Mukherjee J, Ye X, et al. Impact of adherence and weight loss on glycemic control in patients with type 2 diabetes: cohort analyses of integrated medical record, pharmacy claims, and patient-reported data. J Manag Care Spec Pharm 2014, 20:691-700.

53 Ratanawongsa N, Karter AJ, Quan J, Parker MM, Handley M, Sarkar U, et al. Reach and validity of an objective medication adherence measure among safety net health plan members with diabetes: a cross-sectional study. J Manag Care Spec Pharm 2015; 21:688-98.

54. Vink NM, Klungel OH, Stolk RP, Denig P. Comparison of various measures for assessing medication refill adherence using prescription data. Pharmacoepidemiol Drug Saf 2009; 18:159-65.

55. Kocarnik BM, Liu C-F, Wong ES, Perkins M, Maciejewski ML, Yano EM, et al. Does the presence of a pharmacist in primary care clinics improve diabetes medication adherence? BMC Health Serv Res 2012; 12:391.

56. Caetano PA, Lam JMC, Morgan SG. Toward a standard definition and measurement of persistence with drug therapy: examples from research on statin and antihypertensive utilization. Clin Ther 2006; 28:1411-24.

57. Leslie RS, Tirado B, Patel BV, Rein PJ. Evaluation of an integrated adherence program aimed to increase Medicare Part D star rating measures. J Manag Care Spec Pharm 2014; 12:1193-203.

58. Lester CA, Mott DA, Chui MA. The influence of a community pharmacy automatic prescription refill program on Medicare Part D adherence metrics. J Manag Care Spec Pharm. 2016, 22:801-7.

59. Raebel MA, Ellis JL, Carroll NM, Bayliss EA, McGinnis B, Schroeder EB, et al. Characteristics of patients with primary non-adherence to medications for hypertension, diabetes, and lipid disorders. J Gen Intern Med 2012; 27: 57-64.

60. Gosmanova EO, Lu JL, Streja E, Cushman WC, Kalantar-Zadeh K, Kovesdy CP. Association of medical treatment nonadherence with all-cause mortality in newly treated hypertensive US veterans. Hypertension 2014; 64:951-7.

61. Meddings J, Kerr EA, Heisler M, Hofer TP. Physician assessments of medication adherence and decisions to intensify medications for patients with uncontrolled blood pressure: Still no better than a coin toss. BMC Health Serv Res 2012; 12:270.

62. Moita B, Robalo J, Duarte A, Santana R. The use of administrative data sources for measurement of angiotensin receptor blockers therapeutic adherence. Rev Port Saúde Pública 2016; 34:20-9.

63. Chan DC, Shrank WH, Cutler D, Jan S, Fischer MA, Liu J, et al. Patient, physician, and payment predictors of statin adherence. Med Care 2010; 48:196-202.

64. Gazmararian JA, Kripalani S, Miller MJ, Echt KV, Ren J, Rask K. Factors associated with medication refill adherence in cardiovascular-related diseases: a focus on health literacy. J Gen Intern Med 2006; 12:1215-21.

65. Lachaine J, Rinfret S, Merikle EP, Tarride J-E. Persistence and adherence to cholesterol lowering agents: evidence from Regie de l'Assurance Maladie du Quebec data. Am Heart J 2006; 152:164-9.

66. Padwal R, Kezouh A, Levine M, Etminan M. Long-term persistence with orlistat and sibutramine in a population-based cohort. Int J Obes 2007; 31:1567-70.

67. Lee JK, Grace KA, Foster TG, Crawley MJ, Erowele GI, Sun HJ, et al. How should we measure medication adherence in clinical trials and practice? Ther Clin Risk Manag 2007; 3:685-90.

68. Patrick AR, Brookhart MA, Losina E, Schousboe JT, Cadarette SM, Mogun H, et al. The complex relation between bisphosphonate adherence and fracture reduction. J Clin Endocrinol Metab 2010; 95:3251-9.

69. Burden AM, Paterson JM, Gruneir A, Cadarette SM. Adherence to osteoporosis pharmacotherapy is underestimated using days supply values in electronic pharmacy claims data. Pharmacoepidemiol Drug Saf 2015; 24:67-74.

70. de Achaval SD, Suarez-Almazor ME. Treatment adherence to disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus. Int J Clin Rheumtol 2010; 5:313-26.

71. Richards JS, Cannon GW, Hayden CL, Amdur RL, Lazaro D, Mikuls TR, et al. Adherence with bisphosphonate therapy in US veterans with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2012; 12:1864-70.

72. Simoni-Wastila L, Wei Y-J, Qian J, Zuckerman IH, Stuart B, Shaffer T, et al. Association of chronic obstructive pulmonary disease maintenance medication adherence with all-cause hospitalization and spending in a Medicare population. Am J Geriatr Pharmacother 2012; 10:201-10.

73. Huetsch JC, Uman JE, Udris EM, Au DH. Predictors of adherence to inhaled medications among veterans with COPD. J Gen Intern Med 2012; 11:1506-12.

74. Ismaila A, Corriveau D, Vaillancourt J, Parsons D, Dalal A, Su Z, et al. Impact of adherence to treatment with tiotropium and fluticasone propionate/salmeterol in chronic obstructive pulmonary diseases patients. Curr Med Res Opin 2014; 30:1427-36.

75. Bender BG, Cvietusa PJ, Goodrich GK, Lowe R, Nuanes HA, Rand C, et al. Pragmatic trial of health care technologies to improve adherence to pediatric asthma treatment: a randomized clinical trial. JAMA Pediatr 2015; 169:317-23.

76. Blais L, Kettani F-Z, Beauchesne M-F, Lemiere C, Perreault S, Forget A. New measure of adherence adjusted for prescription patterns: the case of adults with asthma treated with inhaled corticosteroid monotherapy. Ann Pharmacother 2011; 45:335-41.

77. Menckeberg TT, Bouvy ML, Bracke M, Kaptein AA, Leufkens HG, Raaijmakers JAM, et al. Beliefs about medicines predict refill adherence to inhaled corticosteroids. J Psychosom Res 2008; 64:47-54.

78. Vollmer WM, Xu M, Feldstein A, Smith D, Waterbury A, Rand C. Comparison of pharmacy-based measures of medication adherence. BMC Health Serv Res 2012; 12:155.

79. Amico KR, Marcus JL, McMahan V, Liu A, Koester KA, Goicochea P, et al. Study product adherence measurement in the iPrEx placebo-controlled trial: concordance with drug detection. J Acquir Immune Defic Syndr 2014; 66:530-7.

80. Puttkammer N, Zeliadt S, Balan JG, Baseman J, Destine R, Domercant JW, et al. Development of an electronic medical record based alert for risk of HIV treatment failure in a low-resource setting. PLoS One 2014; 11:e112261.

81. Inciardi JF, Leeds AL. Assessing the utility of a community pharmacy refill record as a measure of adherence and viral load response in patients infected with human immunodeficiency virus. Pharmacotherapy 2005; 25:790-6.

82. Allard N, Dev A, Dwyer J, Srivatsa G, Thompson A, Cowie B. Factors associated with poor adherence to antiviral treatment for hepatitis B. J Viral Hepat 2017; 24:53-8.

83. Chisholm MA, Lance CE, Williamson GM, Mulloy LL. Development and validation of the immunosuppressant therapy adherence instrument (ITAS). Patient Educ Couns 2005; 59:13-20.

84. Wei Y-J, Palumbo FB, Simoni-Wastila L, Shulman LM, Stuart B, Beardsley R, et al. Antiparkinson drug adherence and its association with health care utilization and economic outcomes in a Medicare Part D population. Value Health 2014; 17:196-204.

85. Kozma CM, Dickson M, Phillips AL, Meletiche DM. Medication possession ratio: implications of using fixed and variable observation periods in assessing adherence with disease-modifying drugs in patients with multiple sclerosis. Patient Prefer Adherence 2013; 7:509-16.

86. Berg K Brodtkorb M, Arnsten JH. Practical and conceptual challenges in meaasutring antiretriviral adherence. J Acquir Immune Defic Syndr 2006; 43 Suppl 1:S79-87.

87. Obreli-Neto PR, Baldon AO, Guidoni CM, Bergamini D, Hernandes KC, Luz RT, et al. Métodos de avaliação de adesão à farmacoterapia. Rev Bras Farm 2012; 93:403-10.

88. Avgil Tsadok M, Jackevicius CA, Rahme E, Humphries KH, Behlouli H, Pilote L. Sex differences in stroke risk among older patients with recently diagnosed atrial fibrillation. JAMA 2012; 307:1952-8.

89. Bell CM, Brener SS, Gunraj N, Huo C, Bierman AS, Scales DC, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. JAMA 2011; 306:840-7.

90. Bollinger ME, Mudd KE, Boldt A, Hsu VD, Tsoukleris MG, Butz AM. Prescription fill patterns in underserved children with asthma receiving subspecialty care. Ann Allergy Asthma Immunol 2013; 111:185-9.

91. Cote I, Gregoire J-P, Moisan J, Chabot I, Lacroix G. A pharmacy-based health promotion programme in hypertension: cost-benefit analysis. Pharmacoeconomics 2003; 21:415-28.

92. Esposito D, Wahl P, Daniel G, Stoto MA, Erder MH, Croghan TW. Results of a retrospective claims database analysis of differences in antidepressant treatment persistence associated with escitalopram and other selective serotonin reuptake inhibitors in the United States. Clin Ther 2009; 31:644-56.

93. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. JAMA 2002; 288:462-7.

94. Lauffenburger JC, Gagne JJ, Song Z, Brill G, Choudhry NK. Potentially disruptive life events: What are the immediate impacts on chronic disease management? A case-crossover analysis. BMJ Open 2016; 6:e010958.

95. Kaur AD, McQueen A, Jan S. Opioid drug utilization and cost outcomes associated with the use of buprenorphine-naloxone in patients with a history of prescription opioid use. J Manag Care Pharm 2008; 14:186-94.

96. Alsabbagh MW, Lix LM, Eurich D, Wilson TW, Blackburn DF. Multiple-domain versus single-domain measurements of socioeconomic status (SES) for predicting nonadherence to statin medications: an observational population-based cohort study. Med Care 2016; 54: 195-204.

97. Fairley CK, Permana A, Read TRH. Long-term utility of measuring adherence by self-report compared with pharmacy record in a routine clinic setting. HIV Med 2005; 6:366-9.

98. Fischer MA, Stedman MR, Lii J, Vogeli C, Shrank WH, Brookhart MA, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. J Gen Intern Med 2010; 25:284-90.

99. Haupt D, Krigsman K, Nilsson JLG. Medication persistence among patients with asthma/COPD drugs. Pharm World Sci 2008; 30: 509-14.

100. Hromadkova L, Heerdink ER, Philbert D, Bouvy ML. Association between concomitant psychiatric drug use, and patients' beliefs about and persistence with chronic cardiovascular medication. Int J Clin Pract 2015; 69:328-35.

101. Marhefka SL, Tepper VJ, Farley JJ, Sleasman JW, Mellins CA. Brief report: assessing adherence to pediatric antiretroviral regimens using the 24-hour recall interview. J Pediatr Psychol 2006; 31:989-94.

102. Jentzsch NS, Camargos PAM, Colosimo EA, Bousquet J. Monitoring adherence to beclomethasone in asthmatic children and adolescents through four different methods. Allergy 2009; 64:1458-62.

103. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. Am J Geriatr Pharmacother 2011; 9:11-23.

104. Palacio AM, Uribe C, Hazel-Fernandez L, Li H, Tamariz LJ, Garay SD, et al. Can phone-based motivational interviewing improve medication adherence to antiplatelet medications after a coronary stent among racial minorities? A randomized trial. J Gen Intern Med 2015; 30:469-75.

105. Lehmann A, Aslani P, Ahmed R, Celio J, Gauchet A, Bedouch P, et al. Assessing medication adherence: options to consider. Int J Clin Pharm 2014; 36:55-69.

106. Giardini A, Martin MT, Cahir C, Lehane E, Menditto E, Strano M, et al. Toward appropriate criteria in medication adherence assessment in older persons: position paper. Aging Clin Exp Res 2016; 28:371-81.

107. Sorensen TD, Pestka DL, Brummel AR, Rehrauer DJ, Ekstrand MJ. Seeing the forest through the trees: improving adherence alone will not optimize medication use. J Manag Care Spec Pharm 2016; 22:598-604.

108. Andrade SE, Kahler KH, Feride F, Chan A. Methods for evaluation of medication adherence and persistence using automated databases. Pharmacoepidemiol Drug Saf 2006; 15:565-74.

109. Blum MA, Koo D, Doshi JA. Measurement and rates of persistence with and adherence to biologics for rheumatoid arthritis: a systematic review. Clin Ther 2011; 33:901-13.

110. McCaffrey DJ. Padrões de utilização dos medicamentos. In: Yang Y, West-Strum D, organizadores. Comprendendo a farmacoepidemiologia. Porto Alegre: Editora McGraw-Hill; 2011. p. 132-52.

111. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, et al. Medication compliance and persistence: terminology and definitions. Value Health 2008; 11:44-7.

112. Hershman DL, Kushi LH, Hillyer GC, Coromilas E, Buono D, Lamerato L, et al. Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL). Breast Cancer Res Treat 2016; 157:133-43.

113. Meibohm B, Derendorf H. Basic concepts of pharmacokinetic/pharmacodynamic (PK/PD) modelling. Int J Clin Pharmacol Ther 1997; 35:401-13.

114. Derendorf H, Meibohm B. Modeling of pharmacokinetic/pharmacodynamic (PK/PD) relationships: concepts and perspectives. Pharm Res 1999; 16:176-85.

115. Akincigil A, Bowblis JR, Levin C, Walkup JT, Jan S, Crystal S. Adherence to antidepressant treatment among privately insured patients diagnosed with depression. Med Care 2007; 45:363-9.

116. Rickles NM, Svarstad BL. Relationships between multiple self-reported nonadherence measures and pharmacy records. Res Social Adm Pharm 2007; 3:363-77.

117. Ernesto AS, Lemos RM, Huehara MI, Morcillo AM, Santos Vilela MM, Silva MT. Usefulness of pharmacy dispensing records in the evaluation of adherence to antiretroviral therapy in Brazilian children and adolescents. Braz J Infect Dis 2012; 16:315-20.

Resumo

O marco atual sobre a adesão à farmacoterapia compreende um conjunto de comportamentos experimentados pelo usuário em que se observa a trajetória detalhada e contínua do uso de cada dose do medicamento. Indicadores provenientes de registros de dispensação de medicamentos têm sido utilizados para a mensuração da adesão. A presente revisão visou a identificar e a caracterizar indicadores provenientes de registros de dispensação e a discutir sua adequação e limitações para mensuração da adesão. Foi realizada uma busca bibliográfica exploratória em três bases de dados a partir dos termos "adesão", "registros de farmácia/ dados administrativos" e "medida" na composição dos descritores para a seleção de 81 artigos e elaboração de um quadro com a denominação, fontes, método de cálculo, descrição e interpretação do significado operacional e referencial de 14 indicadores. Tendo em vista a mais recente taxonomia da adesão proposta na literatura, concluiu-se que os indicadores encontrados podem ser úteis na identificação de pacientes com problemas relacionados ao comportamento de busca de medicamentos e na análise da persistência. A distância entre os eventos relacionados ao fornecimento e as dificuldades no seguimento da terapêutica podem influenciar a análise baseada exclusivamente no uso desses indicadores.

Adesão à Medicação; Indicadores de Serviços; Assistência Farmacêutica

Resumen

El marco de referencia actual sobre la adherencia a la farmacoterapia incluye un conjunto de comportamientos experimentados por el usuario, con observación de la historia detallada y continua del uso de cada dosis de la medicación. Se han utilizado indicadores basados en registros de farmacia para medir la adherencia. La revisión actual tuvo como objetivo identificar y describir indicadores basados en registros de farmacia y discutir su adecuación y limitaciones para medir la adherencia. Se realizó una revisión exploratoria de la literatura en tres bases de datos utilizando los términos "adherencia", "registros de farmacia/ datos administrativos" y "medida" para componer los descriptores para la selección de 81 artículos y la elaboración de un cuadro con la denominación, métodos de cálculo, descripción e interpretación del significado operacional y referencial de 14 indicadores. Dada la taxonomía más reciente para la adherencia propuesta en la literatura, concluimos que los indicadores pueden ser útiles para identificar pacientes con problemas relacionados con el comportamiento de búsqueda de medicamentos y el análisis de la persistencia. La distancia entre los eventos relacionados con la oferta y las dificultades en el seguimiento del tratamiento puede influir en un análisis basado exclusivamente en el uso de estos indicadores.

Cumplimiento de la Medicación; Indicadores de Servicios; Servicios Farmacéuticos