Patient Preference and Adherence

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REVIEW

Suitability of Measures of Pharmacy-Based Medication Adherence for Routine Clinical Use Among Patients with Chronic Diseases: A Systematic Review

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Purpose: To identify the suitability of pharmacy-based measures for determining medication adherence in routine clinical use.

Methods: Data were obtained through PubMed and Scopus databases up to December 2023 without publication year restrictions. This review included English studies on assessing medication adherence for hypertension, hyperlipidemia, asthma, chronic obstructive pulmonary disease, and diabetes, using pharmacy databases and providing full-text access. We investigated evidence quality utilizing the Newcastle–Ottawa Scale for non-randomized studies (cohort, case-control, and cross-sectional) and the Risk of Bias Assessment Tool for Non-randomized Studies-2 and JADAD scales for quasi-experiments and randomized control trials, respectively. We determined validity characteristics (completeness, accuracy, reliability, objectivity, continuous adherence history, non-intrusiveness, sensitivity, and specificity) and applicability (cost-effectiveness, ease of use, and interpretability) to evaluate the suitability of pharmacy-based medication adherence measures in clinical settings.

Results: This review retrieved 1513 studies, of which 74 met the inclusion criteria. All of the studies, which were published from 2000 to 2023 and mostly utilized a retrospective cohort design (n = 53), included 17.6 million patients. Of the 74 studies, 50 were conducted in the United States. Diabetes mellitus (n = 40) was the most prevalent disease, whereas the medication possession ratio (n = 46) and prescription days covered (n = 31) were the most prevalent pharmacy-based matrix. According to the results, 73 articles demonstrated validity characteristics, whereas 1 article lacked these characteristics. All 74 (100%) articles had applicability characteristics.

Conclusion: This systematic review demonstrates that pharmacy-based measures possess valid characteristics, including comprehensive, accurate, objective, reliable, and continuously updated adherence history records. These measures are designed to minimize disruption while offering high sensitivity and specificity. Furthermore, they are characterized by their practicality, being cost-effective, easy to implement, and easy to interpret. These findings suggest that pharmacy-based measures are potentially suitable to assess medication adherence for routine clinical use.

Keywords: medication possession ratio, proportion of days covered, pharmacy fill, medication adherence, chronic disease, suitability, validity, applicability, routine clinical use

Introduction

Chronic diseases have been the leading cause of death globally.[1] Data from the World Health Organization reveal that annually, chronic diseases cause deaths in 41 million individuals, equivalent to 74% of total deaths globally.[1] Low-middle-income countries (LMIC) reported the highest mortality rate of 77% caused by chronic noncommunicable diseases.[2] Hypertension, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and asthma are chronic noncommunicable diseases with high prevalence globally.[3–8] Poor adherence to prescribed medication is a widespread health problem in chronic disease management, with evidence from multiple studies across different countries consistently indicating suboptimal adherence rates.[9–12] The effect is particularly severe, causing therapeutic failure, reduced

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quality of life, comorbidity development, and increased mortality.[13–18] Healthcare professionals, particularly pharmacists, need to address this issue during clinical practice.[19]

Pharmacists are one of the health professionals with a crucial role in managing patients with medication adherence.[19,20] Furthermore, community pharmacists have the expertise to determine and address medication-related problems and have substantial clinical knowledge of medications.[19] Several studies have been conducted on the role of pharmacists in improving medication adherence.[19,21,22] For example, particular research revealed that pharmacist-provided interventions were successful in improving medication adherence with implications for enhanced patient clinical outcomes.[23] The results of measuring medication adherence serve as the basis for developing appropriate interventions. However, in reality, obtaining accurate measurement data and practicing medication adherence measurement in clinical practice remains challenging to implement.[24] Pharmacists have various requirements, including requiring visualization of medication adherence measurement results that are easy to interpret and can be seen by patients themselves, measurement data that can be sent easily through online media, and fast tools in detecting the medication adherence level.[25]

Currently, several tools are used to measure patient medication adherence; one of the most prevalently used tools is self-report.[26–28] Based on a scoping review conducted by Khoiry et al (2023), the Morisky Medication Adherence Scale-8 (MMAS-8) is the most popularly used self-report instrument, especially in LMIC.[27] Self-reporting provides many benefits, including ease of use, inexpensive, and the ability to observe behaviors and barriers related to medication adherence,[26,27,29] but it has significant drawbacks, such as recall bias, inability to accurately evaluate medication timing or patterns, adherence overestimation, and low sensitivity.[28,29] These shortcomings are significant issues as they affect the accuracy of evaluating medication adherence. Additionally, ideally, medication adherence measurement tools should be accurate.[30] Using pharmacy-based medication adherence evaluation is potentially an appropriate way to address these shortcomings. This method provides many advantages, including avoiding recall bias through real-world data, the ability to assess medication adherence through retrospective data, minimal ethical concerns, low cost, wide population applicability, and shorter measurement duration.[30–32]

A previous literature review revealed that measuring medication adherence with pharmacy-based data are suitable for measuring medication adherence. However, this review does not serve as a formal evidence-based guideline but rather only guides future research and clinical practice for healthcare professionals.[33] Studies that evaluate the suitability of adopting pharmacy-based medication adherence measures for routine clinical use are warranted to address the limitations of self-report instruments and the potential of pharmacy-based measures to meet the requirements of pharmacists in clinical use. The present systematic review aimed to evaluate the suitability of pharmacy-based measures for routine clinical use.

Material and Methods

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[34] while reporting a comprehensive systematic review of the selected research.

Information Sources and Search Strategy

The electronic databases, namely PubMed and Scopus, were searched until December 2023. The entire search strategy utilized a combination of medical subject heading terms, as stated in Table S1. Additionally, no publication year restrictions were considered to determine research suitable for evaluating medication adherence with pharmacy-based measures for routine clinical use. The selected research was published in English and measured medication adherence in five major diseases, including hypertension, hyperlipidemia, asthma, COPD, and DM, using pharmacy-based measures, as well as full-text availability.

This study excluded research that lacked abstracts, conferences, and proceedings. Additionally, articles that could not be accessed in full text after requesting access from the author were also excluded. Participants with multi-comorbidities and medication adherence measurements performed utilizing an insurance database were excluded. This was because measuring medication adherence with a pharmacy database was expected to be more accurate than with an insurance claims database.[35] Further, research focused on persistently measuring medication adherence was excluded. We defined the suitability of pharmacy-based medication adherence measures in routine clinical use by observing validity and applicability characteristics.[36,37] The characteristics that define a valid measure of medication adherence consist of multiple factors, including completeness and accuracy, thereby providing a reliable and objective assessment, having a continuous record of adherence history, being non-

intrusive to prevent affecting patient behavior, and demonstrating high sensitivity and specificity or exhibiting a statistically significant correlation.[36,37] The characteristics that improve applicability include being inexpensive, easy to use, and easy to interpret.[36,37]

Selection Process

In the first phase, WJ independent reviewers evaluated the eligibility of the research based on the title and abstract with a web-based tool called Rayyan.ai.new.[38] In the second phase of the screening process, WJ retrieved and reviewed the full text of the potentially eligible articles. Any doubt in the screening process was resolved through consensus with the QAK. Disagreements were resolved by consensus with a third reviewer, RA. Furthermore, WJ extracted data from the selected articles, and any doubts from the extraction process were resolved through consensus with SDA.

Data Collection Process

A data extraction sheet was established to extract research characteristics and information associated with the suitability of pharmacy-based measures, namely disease type, validity, and applicability. The sheet was subsequently pilot-tested utilizing five randomly selected analyses, with WJ, the reviewer, independently conducting a comprehensive data extraction. Additionally, the QAK reviewer assesses the data extraction process and addresses any uncertainties that arise.

Quality Assessment

WJ conducts the quality evaluation process independently. The QAK reviewer assesses the quality assessment. The quality assessment of both the cohort and case-control research designs was conducted with the Newcastle–Ottawa scale (NOS). This comprised four questions focused on group selection quality, one on group comparability, and three on case-control and cohort investigation exposure or outcome. The research was awarded a maximum of one star for each numbered question in the Selection and Outcomes categories. A maximum of two stars were awarded for comparability. The scoring results were interpreted as follows. Good quality: 3 or 4 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain. Fair quality: 2 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain. Poor quality: 0 or 1 star in the selection domain, 0 stars in the comparability domain, and 0 or 1 star in the outcome/exposure domain.[39] However, the modified NOS was utilized to evaluate the cross-sectional research design.[40] The NOS was adapted from the Newcastle–Ottawa Quality Assessment Scale for cohort investigations to provide a quality assessment of cross-sectional research. Furthermore, the star scoring in the selection, comparability, and outcome domains was a maximum total of 5 stars, 2 stars, and 3 stars, respectively. The assessment interpretation given is very good research: 9–10 stars, good research: 7–8 stars, satisfactory research: 5–6 stars, and unsatisfactory research: 0–4 stars.[3]

The modified JADAD Scale was used in research with a randomized control trials (RCTs) design.[41] This scale was calculated utilizing six items, with one point allocated for an agreed answer or zero points for a disagreed answer for each question. The possible score range is 0–5, with 3–5 and 0–2 scores indicating good and poor qualities, respectively.[41] The quality assessment tool we utilize for quasi-experimental research is the revised Risk of Bias Assessment Tool for Non-randomized Studies-2 (RoBANS-2).[42] This tool consists of eight domains, namely, target group comparability, target group selection, confounding, intervention/exposure measurement, assessor bias, outcome assessment, incomplete outcome data, and non-selective outcome reporting. The risk of bias assessments were low, high, and unclear.[42]

Results

Study Selection

Figure 1 illustrates that 1,513 articles were obtained from database sources, consisting of PubMed (n = 779) and Scopus (n = 734). Duplication checks were conducted utilizing the Rayyan.ai.new tool,[38] resulting in the realization of 301 duplicates. Subsequently, 1,212 articles were subjected to title and abstract screening using Rayyan.ai.new tool.[38] Furthermore, 913 articles were excluded because they did not meet the inclusion criteria with the following information, review articles, commentaries, conference proceedings, and book chapters (n = 127), using insurance databases (n = 126), treatment adherence was evaluated in patients without DM, hypertension, COPD, hyperlipidemia, and asthma (n = 546), pharmacy-based measures were not used (n = 18), and

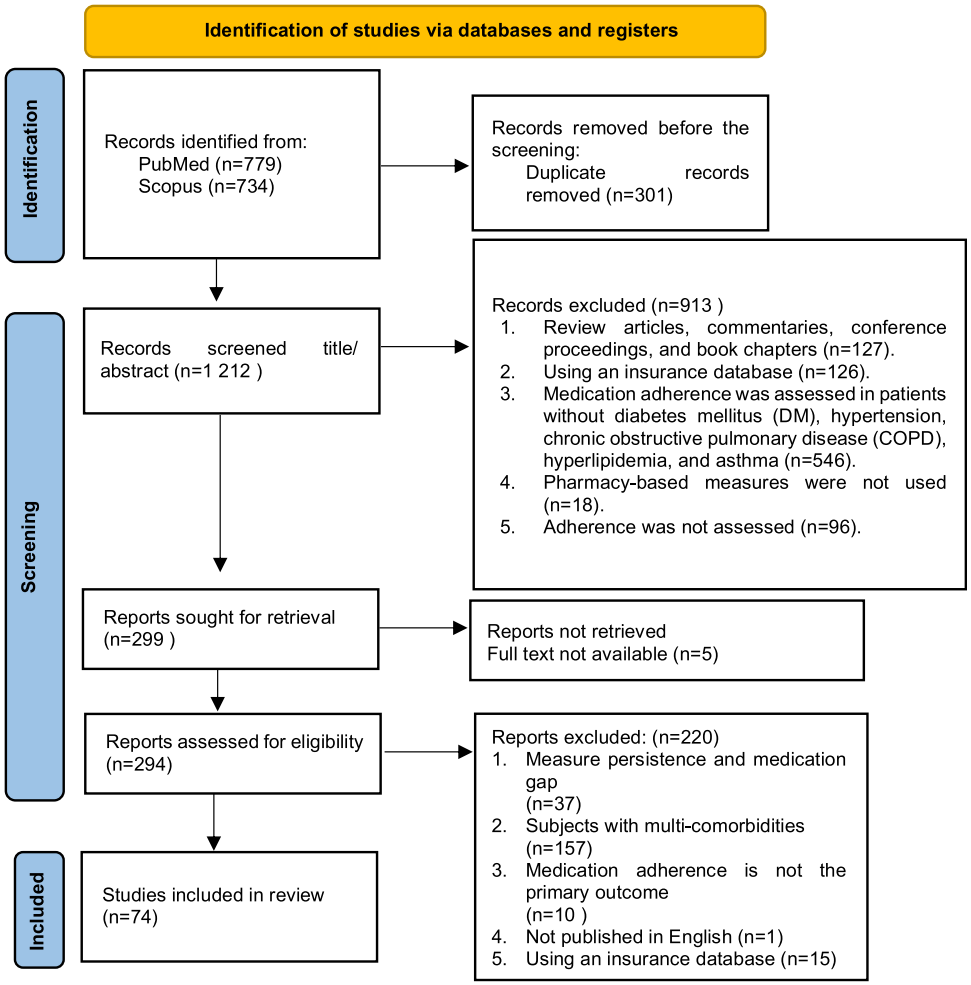

Figure 1 PRISMA Flow Diagram. Adapted from Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021; 372 :n71. Creative Commons.

adherence was not assessed (n = 96). This resulted in the realization of 299 articles, which proceeded to the full-text screening. In this phase, five articles were excluded from this study because of unavailable full texts. A contact was attempted, but no feedback was received. However, of the 294 articles screened at the full-text level, 220 were excluded from not meeting the inclusion criteria. The reasons for exclusion were as follows: persistence and medication gap measurement (n = 37), subjects with multi-comorbidities (n = 157), medication adherence as not the primary outcome (n = 10), not published in English (n = 1), and using an insurance database (n = 15). This research included the remaining 74 that met the inclusion criteria. The PRISMA flow diagram in Figure 1 illustrates the determined and excluded research at each stage of the review.

Characteristics of the Included Studies

Table S2 presents the general characteristics of the 74 articles[43–115] that met the inclusion criteria. Most of the analyses (n = 53) were retrospective cohort investigations, such as RCTs (n = 10), cross-sectional (n = 5), quasi-experimental (n = 4), pragmatic clinical trials (n = 1), and nested case-control (n = 1). A total of 74 articles were published from 2000 to 2023, encompassing 50 studies conducted across the United States. Among these, 13 studies were conducted in unspecified states, whereas 7 were located in Texas, 4 in New York, and 5 in Colorado and Oregon. Additionally, three studies were conducted in Washington; two studies were conducted in each of the states of Puerto Rico, Maryland, and California; one study was conducted in each of the following states: Alabama, Utah, Minnesota, Pennsylvania, and South Carolina, as well as in the Virgin Islands and Wisconsin; some studies were conducted in more than one state (Table S2). Furthermore, research was performed in several other countries, including 7 in Canada, 3 each in Malaysia, the Netherlands, and the United Kingdom, 2 each in Australia and

New Zealand, and 1 each in Colombia, France, Hong Kong, India, Indiana, Indonesia, Portugal, Sierra Leone, Singapore, South Africa, Brazil, and Sweden (Table S2). Approximately 17.6 million patients were included in these studies.[43–116] All the research reviewed utilized real-world data from pharmacy claims databases. The reviews on disease types frequently evaluated using the pharmacy-based measure of medication adherence included DM in 40 articles, followed by hypertension (n = 27), asthma (n = 17), hyperlipidemia (n = 16), and COPD (n = 2). However, some research focused on measuring medication adherence for more than one disease (Table S2).

The pharmacy-based measure of medication adherence was conducted with several matrix types. The most prevalently used matrix was the medication possession ratio (MPR), adopted by 46 research studies, and the prescription days covered (PDC), which were applied in 31 investigations. Additionally, some research compared MPR with PDC, adjusted MPR (aMPR), refill compliance rate, compliance ratio, modified MPR (MPRm), continuous multiple interval measurement of oversupply, and continuous single-interval measure of medication acquisition, including other measure types such as Recomp, primary adherence, number of days covered, and prescription possession ratio. Additionally, aMPR and MPRm are modifications of the MPR matrix, personally designed to suit this investigation[45,62] (Table 1).

Table 1 Distribution of Pharmacy-Based Matrix to Measure Medication Adherence

No	Matrix	Definition	Number of Research	References
1	Medication possession ratio (MPR)	The MPR was defined as the sum total of the prescription supply dispensed between the first and last pharmacy fill (with the last fill excluded), divided by the number of days between the prescriptions.	46	[45–47, 49, 51, 53, 59–62, 64, 69, 71–75, 79–82, 84–88, 91, 94, 96–109, 111–114]
2	Proportion of days covered (PDC)	PDC referred to the number of days covered, divided by the total in time period x 100.	31	[43–45, 47, 48, 50, 52–56, 58, 62, 63, 65–68, 70, 71, 76, 77, 84, 87, 92, 93, 110, 115–117]
3	Modified medication possession ratio (MPRm)	MPRm was the number of supply days, divided (Last claim date – index date) + last refill supply x 100	1	[45]
4	Refill compliance rate (RCR)	The RCR was defined as the number of supply days divided by the last claim date x 100	1	[45]
5	Compliance ratio (CR)	The CR referred to the number of days supply in index period – last refill supply, divided by the Last claim date – index date	1	[45]
6	Continuous multiple-interval measurement of oversupply (CMOS)	The CMOS was the Total days of medication gaps, divided by Total days to next fill or end of observation period	1	[45]
7	Continuous single interval measure of medication acquisition (CSA)	The CSA referred to the days supply obtained at the beginning of the interval, divided by days in the interval	1	[45]
8	Adjusted MPR (aMPR)	In order to calculate the aMPR, the MPR of each patient must be known. This was multiplied by an adjustment factor. Furthermore, the factor of each drug product type is the ratio of the average number of days between refills of 1 drug product divided by the average days supply recorded for the same drug product.	1	[62]

(*Continued*)

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Table 1 (Continued).

No	Matrix	Definition	Number of Research	References
9	ReComp	The ReComp (Refill Compliance) calculation is a measure used to determine medication adherence over a period. This was determined by the Total number of days medication available, divided by the total number of days in the measurement period.	1	[95]
10	Primary adherence	Primary adherence rate was expressed as the number of pharmacy claims records divided by the total number of pre- scription records	1	[57]
11	Number of days covered	The number of days covered was defined as the number of days in the follow-up period during which the index medication was determined to be handy based on the pharmacy claim fill date plus days supply	1	[83]
12	Prescription possession ratio (PPR)	PPR was defined by dividing the number of days prescribed during the calendar year by the number of days in the interval. This is equivalent to the proportion of days in the year when the drug was prescribed	1	[89]

Study Outcomes

Suitability

The suitability of the pharmacy-based measures was assessed based on the characteristics associated with validity and applicability. Our systematic review revealed that two articles describe pharmacy-based measures as a comprehensive method,[44,51] and 16 studies emphasize its accuracy,[44,53,55,69,71,72,80,84,85,87,90,94,95,102,103,114], (Table S2). The next validity characteristic is ensuring a reliable and objective assessment, where three studies report reliable MPR and PDC matrix measures,[85,109] whereas 30 studies highlight its objectivity,[46,47,51,54,60,61,64,66,69,72,74,75,77,79–81,85,87,88,90,94,95,97,98,105,106,108,114,115] (Table S2). Furthermore, 73 studies demonstrated that pharmacy-based measures can maintain a continuous adherence history,[43–45,47–50,52,53,55–59,61–63,66–68,70,71,73,75,76,78,80,82–84,86,88,89,91–93,95,96,98–104,106,109–111,113,115,117] (Table S2). Additionally, two studies noted that PDC and MPR were unobtrusive enough to prevent influencing patient behavior,[72] and seven studies supported high-sensitivity pharmacy-based measures,[48,73,76,93,96,97,99] (Table S2). Moreover, this systematic review uncovered further evidence supporting the validity of pharmacy-based adherence measures (Table S2). Specifically, one study indicated that medication adherence estimations are more accurate when the PDC is combined with the primary adherence matrix[78] (Table S2). Seven studies refer to this method as a validated approach for measuring medication adherence[45,70,79,85,104,110,117] whereas one study describes it as a standardized approach for adherence assessment[70] (Table S2). Another study established standard thresholds that correlated with enhanced health outcomes[43] (Table S2). Further support includes one study conducting a comparative analysis[49] and one study indicating that this adherence measurement method is unaffected by recall bias,[100] (Table S2). However, one study in this review revealed that pharmacy-based measures were not valid in certain contexts, specifically when evaluating medication adherence in patients with asthma.[65] This study utilized a PDC matrix and inhaler monitoring or sensor technology. Inhaler sensor technology provided a more objective and reliable measurement by directly capturing accurate data on medication use and adherence patterns. This technology enabled adherence to prescribed doses to be independently assessed, providing a more precise adherence measurement than pharmacy-based methods alone.[65]

In terms of applicability, our systematic review determined 3 studies indicating that it is inexpensive,[59,61,106] 39 studies demonstrating that this method is easy to interpret,[43–45,47,48,52–56,58,59,61–63,66,67,70,71,73,75–77,82–84,86,88,93,95,97–99,101,102,104,105,113,114] and 7 studies exhibiting that it is easy to use,[45,51,52,59,72,84,91] (Table S2). Additionally, we uncovered further evidence that supports the applicability of the pharmacy-based medication adherence measurement

method: 47 studies emphasized its suitability for large populations,[46–49,56,57,60–68,70,71,75,77,78,80,81,83,85,86,89,90,92–95,97–99,101,102,104,105,108,110–112,117] 1 study revealed that longer study intervals improve refill adherence measurement accuracy,[90] 5 studies denoted that it can track medication adherence during prescription switches and overlapping fills,[55,77,96,105,113] and 4 studies showed that it can measure adherence in both mono- and dual-therapy settings,[44,77,105,113] (Table S2). Furthermore, 1 study revealed early nonadherence detection[57] 5 affirmed its use of real-world data,[50,87,89,100,109] 3 noted its utility in tracking long-term medication adherence,[69,111,113] 1 confirmed feasibility to implement in clinical use, and 2 validated its effectiveness for patients with chronic diseases,[49,55] (Table S2) Additionally, 1 study revealed that it minimizes the Hawthorne effect[72] another emphasized the completeness of data from pharmacy dispensing records compared to health center prescriptions,[104] 1 study indicated that refill behavior aligns with actual medication use,[98] and 1 supported its effectiveness in chronic condition adherence measurement.[49] (Table S2). Integrating pharmacy claims databases across multiple pharmacies further improved the reliability of adherence measurements[44] (Table S2). One study indicated that pharmacy-based measures are effectively applied to evaluate medication adherence among patients with asthma and COPD, considering that the inhaler is used consistently as a control medication rather than only as needed.[106]

Quality Assessment and Publication Bias

The results revealed in the cohort investigation were within the range of 6–9 and interpreted as good quality (Table S3). The assessment of the nested case-control investigations generated a score of 9, interpreted as good quality (Table S4). The results in the cross-sectional research ranged from 7 to 10 and were categorized as good and very good (Table S5). The quality assessment result for the quasi-experimental investigation demonstrated a low risk of bias (Table S6). Results from RCTs differed in quality, ranging from poor to good (Table S7).

Discussion

Our systematic review revealed that 73 studies provided evidence of validity characteristics for pharmacy-based measures in evaluating medication adherence.[9–61,63–69,71,73–89,91–111,113–116,118–125] However, one study revealed that this method lacks validity when compared with inhaler monitoring or sensor technology. Moreover, all 74 studies emphasized that pharmacy-based methods demonstrate characteristics relevant to their applicability.[43–115]

The first aspect of determining the suitability of pharmacy-based measures for routine clinical use focuses on validity characteristics, as the methods used to measure medication adherence must be valid.[36,37,126] Moreover, validity is the ability of an instrument or tool to accurately measure the construct or outcome (medication adherence).[118] The validity characteristics of measuring medication adherence include several aspects, such as being complete and accurate, providing a reliable and objective assessment, having a continuous record of adherence history, being unobtrusive to not affect patient behavior, as well as possessing excellent sensitivity and specificity or having a statistical association.[36,37] Under the research reviewed, this method produces complete and accurate data.[44,51,53,55,71,72,74,80,84,85,87,90,94,95,102,103,114] A complete database for pharmacy-based medication adherence measurement is crucial because incomplete data cause overestimation or underestimation of the calculations, resulting in inaccurate results.[119] However, the present systematic review used all real-world data sources from primary healthcare providers, pharmacies, and national databases. This prevents recall bias, obtaining more accurate results than methods depending on subjective judgment.[30–32] Furthermore, reliability is the ability of an instrument to produce the same results whenever the measurements are repeated, thereby depicting consistency.[118] Several studies have revealed that pharmacy-based measures are reliable and consistent.[55,85,109] Moreover, reliable medication adherence measurement was utilized to ensure effective medication and optimized health outcomes, including serving as a basis for identifying appropriate interventions for patients with low adherence results.[120,127] Therefore, the data collected from measuring medication compliance must be reliable or trustworthy.

The next aspect of the validity characteristics focused on the measurement objectivity. An objective adherence measurement was conducted without being affected by subjective opinions or interpretations, both from patients and observers. Several studies have confirmed that pharmacy-based measures are an objective method.[46,47,51,60,61,66,69,72,74,75,77,79–81,85,87,88,90,94,95,97,98,105,106,108,114,115,121] (Table S2). They aimed to prevent bias in medication adherence measurement. Additionally, some studies categorized this method as belonging to the category of objective adherence measurement.[122–124] The next validity characteristic we observed was a continuous record of adherence history. This is important. Yousif et al,

(2020) demonstrated that having records or information from past care events, such as prescriptions, enabled continuous assessment.[24] Additionally, the pharmacy-based measures relied on prescription fill records as the main data in measuring medication adherence. This method uses database sources that enable a continuous record of the adherence history. Further, this was confirmed by the observation period of each investigation, which ranged from 3 to >60 months (Table S2). The database utilized to measure medication adherence provided prescription fill history records, which served as the main data on an ongoing basis, during the observation period.[43–64,66–115], (Table S2). Fénélon–Dimanche et al (2021) indicated that an ongoing adherence history is crucial to monitoring a patient's medication adherence.[25]

Another important result was that the pharmacy-based measure was unobtrusive as well as prevented the Hawthorne effect[72] to not influencing patient behavior.[46] The Hawthorne effect is a psychological phenomenon related to a change in behavior caused by the realization of being observed or watched, resulting in biased results.[125] Preventing the Hawthorne effect improves the accuracy of estimates, causing valid medication adherence measurement data.[72] Furthermore, the pharmacy-based measure is sensitive in identifying changes in medication adherence and comparable.[48,49,73,76,96,97,99] Good sensitivity is crucial, partly because the results of measuring medication adherence tend to identify the success of intervention efforts.[22] Several strengths increased the validity of this pharmacy-based measure in addition to these aspects of validity. These include standardized pharmacy-based measure thresholds related to better health outcomes and not affected by recall bias,[43] valid methods,[45,70,79,85,104,110,117] refill behaviors that correlate with actual medication consumption, and established procedures for evaluating medication adherence.[97,116] Additionally, the estimation of medication adherence is more realistic and accurate when PDC is integrated with the primary adherence measurement.[78] Therefore, pharmacy-based measures are validated for measuring medication adherence.[43–64,66–115]

The second aspect associated with determining the suitability of pharmacy-based measures in clinical use is the applicability characteristics, which are relatively inexpensive, easy to use, and easy to interpret.[36,37] Several studies have revealed that pharmacy-based measures are relatively inexpensive based on a systematic review.[59,61,106] This is crucial because relatively expensive methods may be challenging to implement in clinical practice.[102] Additionally, pharmacy-based measures are easy to interpret, with the most prevalent cut-off being ≥80% medication adherent and <80% nonadherent.[43–45,47,48,52–56,58,59,61,63,66,67,70,71,73,75–77,82–84,86,88,93,97–99,101,102,104,105,113,114,128,129] Yousif et al (2020) revealed that an issue encountered in measuring medication adherence is a lack of objective and simply interpretable information. The use of easily interpretable medication claim data are an important facilitator in measuring medication adherence.[24] The straightforward interpretation addresses the difficulties faced in clinical applications. Pharmacy-based matrix is not only easy to interpret but also simple to utilize.[45,51,52,59,84,91,130] This simplicity is crucial for time efficiency and integration with clinical practice, which affects the assessment of medication adherence. Some clinicians reported not having enough time to comprehensively assess adherence regarding time constraints.[24] The easy usage and calculation of the pharmacy-based measure is an advantage that may resolve this issue.

Several other factors, such as the ability to measure medication adherence in single and multiple medications, supported the characteristics of the applicability of pharmacy-based measures in routine clinical use.[44,77,105,113] This method utilizes real-world data[50,87,89,100,109] and one of its matrices can be utilized for the early identification of nonadherence.[57] Additionally, the use of an integrated claims database across pharmacies increases the reliability of medication adherence measurement.[44] Additionally, this method accounts for overlapping days and medication switching,[55,77,96,105,113] including measuring adherence in large populations.[43,45,47–50,52,54,56,57,59–68,70,71,75,77–79,81,84,85,89,92–98,101,103–105,108,110–112,115,117,131] Furthermore, the accuracy of measurement increases with longer prescription fill data[90] and is used to evaluate adherence to long-term medication.[69,111,113] The richness of the data prevents bias,[106] and information obtained from pharmacies is more comprehensive than drug registration data prescribed at health centers.[104] Meanwhile, the utilization of an integrated claims database across all pharmacies improves the reliability of medication adherence measurement.[74] This method is effective for measuring adherence in patients with chronic diseases[49,55] and is feasible for clinical use.[52] The filling of prescriptions is often consistent with taking medication.[87] Pharmacy-based measures are applicable potential solutions for overcoming the issues encountered in the practice of medication measurement based on the systematic review conducted.

Another key result of this systematic review is that it improves the understanding of the applicability of pharmacy-based measures. Our results indicate that this method effectively evaluates adherence in patients with asthma, considering that the inhaler is consistently utilized as a control medication rather than only as required.[106] This information confirms

that pharmacy-based measures are applicable for measuring medication adherence in patients with asthma or COPD who depend on inhalers as part of their routine control medication.

Moreover, we gathered information on the limitations of pharmacy-based measures to understand the potential constraints in employing this method. Our results indicate that 12 studies revealed the potential for overestimation and underestimation in this approach.[43,47,57,65,67,68,78,82,91,96,100,110] However, this was countered by 16 studies revealing that pharmacy-based adherence measurement is an accurate method.[44,53,55,69,71,72,80,84,85,87,90,94,95,102,103,114] Furthermore, 28 studies demonstrated that this approach cannot directly observe patients' actual drug consumption.[44,46,52,56,63,65,71–74,77,80,83,87,88,92,94,95,99,103–106,109,111,112,114,115] However, 30 other studies emphasized that pharmacy-based adherence measurement is objective.[46,47,51,54,60,61,64,66,69,72,74,75,77,79–81,85,87,88,90,94,95,97,98,105,106,108,114,115] Thus, this method still yields objective measurement results although it cannot directly measure actual drug consumption. Excluding single fills highlighted that this approach does not account for prescriptions filled only once (single fills).[43,83] However, this limitation may not significantly affect its use for evaluating medication adherence in patients with chronic illness, as these patients typically require long-term medication, causing multiple refills throughout their treatment.[132] Additionally, two studies in this research indicated that pharmacy-based measures are effective for assessing adherence among patients with chronic illness.[49,55] Additionally, we revealed that pharmacy-based measures could not capture medication switching.[43] However, we revealed that some previously reviewed studies revealed that pharmacy-based measures could capture medication switching adherence.[55,77,96,105,113] Our research determined some limitations in pharmacy-based measures, but a greater number of studies emphasized significant strengths of this method that address these drawbacks. Consequently, pharmacy-based measures are both relevant and suitable as a tool for assessing medication adherence in routine clinical use because of these benefits.

Strength and Limitations

This study is the first to determine the suitability of pharmacy-based measures for clinical use. Additionally, the review focused on five chronic diseases with high prevalence globally, namely hypertension, hyperlipidemia, asthma, COPD, and DM. The year and type of study design were not restricted, causing a comprehensive collection and review of information. Additionally, we provided information on the drawbacks of pharmacy-based measures that may influence their use in routine clinical settings. However, our review revealed that a greater number of studies highlighted the method's significant strengths that answer these limitations. Additionally, this study has limitations; only two databases were searched, indicating that some investigations may have been missed.

Conclusion

This systematic review demonstrates that pharmacy-based measures possess valid characteristics, including comprehensive, accurate, objective, reliable, and continuously updated adherence history records. These measures are designed to minimize disruption while offering high sensitivity and specificity. Furthermore, they are characterized by their practicality, being cost-effective, easy to implement, and easy to interpret. These findings suggest that pharmacy-based measures are potentially suitable to assess medication adherence for routine clinical use.

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Disclosure

The authors declare no conflicts of interest in this work.

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