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Measuring Medication Adherence in Online Pharmacy Settings: Novel Applications of the Proportion of Days Covered

Sarah L. Bennett[1], Thomas J. Clarke[2]*

[1]Department of Pharmacy Practice, School of Pharmacy, University of Nottingham, Nottingham, United Kingdom.
[2]Department of Clinical Pharmacy, School of Pharmacy, University College London, London, United Kingdom.

***E-mail** ✉ t.j.clarke79@outlook.com

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ABSTRACT

The proportion of days covered (PDC) is a widely used indicator of medication adherence, estimating the share of time during which an individual has access to their prescribed therapy within a specified observation period. This study sought to modify the traditional PDC calculation to better reflect realistic prescription refill behaviours when using data obtained from online pharmacy providers. Medication adherence was estimated using three PDC-based algorithms applied to real-world dispensing data from an online pharmacy: the standard method (PDC1) and two alternative approaches (PDC2 and PDC3). These methods differ in their denominator definitions and represent progressively more nuanced assumptions. PDC1 defines the denominator as the total duration between the initial dispensation and a pre-specified end date. PDC2 limits the denominator to the period extending to the end of the last recorded medication supply. PDC3 further refines this approach by excluding pre-defined extended gaps between refills that may plausibly reflect appropriate treatment discontinuation rather than nonadherence. The distributions of the three PDC measures were compared across four different follow-up periods. The analysis included individuals receiving angiotensin-converting enzyme (ACE) inhibitors (n = 65,905), statins (n = 100,362), and/or thyroid hormone therapies (n = 30,637). Among users of ACE inhibitors, the proportion achieving a PDC of at least 0.8 ranged from 50% to 74% using PDC1, 81% to 91% using PDC2, and 86% to 100% using PDC3, with estimates varying by medication class and duration of follow-up. Comparable patterns were observed among individuals prescribed statins and thyroid hormones. The proposed PDC adaptations provide researchers and healthcare professionals with practical tools to evaluate medication adherence and pharmacy service performance using real-world data, particularly in contexts where individuals may obtain medications from multiple suppliers. In such settings, dispensing records from a single provider may contain temporary yet clinically appropriate interruptions in medication supply. Improved identification of adherence-related issues offers opportunities to enhance patient experience, support sustained medication use, improve health outcomes, and reduce medication waste. Further research involving patients and prescribers is needed to assess and validate the assumptions underlying these algorithms.

Keywords: Medication adherence, Real-world data, Proportion of days covered, Routinely collected data, Measurement

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Introduction

The World Health Organization (WHO) defines adherence as "the extent to which a person's behaviour—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider" [1]. Inadequate adherence to prescribed treatments can negatively influence health outcomes, act as a major obstacle to effective care, and contribute to increased healthcare expenditure [2, 3]. Estimates suggest that unused medications account for approximately £300 million in waste annually in England [4], and that improving adherence could substantially reduce this financial burden [5]. Addressing the persistent

challenge of medication nonadherence therefore depends on accurate measurement and a clear understanding of adherence behaviours.

In recent years, the conceptualisation of medication adherence has evolved. Adherence is now recognised as a process comprising several measurable components: initiation refers to the point at which the first dose of a prescribed medication is taken, which may or may not coincide with the prescription date; implementation describes how closely a person's medication-taking behaviour aligns with the prescribed regimen from initiation until the final dose; discontinuation marks the moment when the last dose is taken and no further doses are consumed; and persistence reflects the time elapsed between the first and last doses taken, spanning implementation to discontinuation [6]. This framework, known as the ABC taxonomy, supports a more nuanced understanding of medicine-taking behaviour and offers a basis for refining adherence measures by clearly identifying which component of adherence—such as implementation or persistence—is being assessed.

Evaluating medication adherence in real-world contexts can help identify unmet needs and inform targeted interventions to support optimal medicine use. While adherence measurement and intervention strategies have been extensively examined in traditional settings such as primary care and community pharmacies [7, 8], considerably less attention has been given to newer care models, including online pharmacy services. The global online pharmacy market is projected to grow from approximately $42.3 billion in 2018 to $107.5 billion by 2025 [9]. Consequently, electronic pharmacy dispensing records represent a valuable source of data for applying proxy measures of adherence and monitoring medication use longitudinally [10]. However, leveraging these data requires careful reconsideration and potential modification of adherence measures originally developed for more integrated or controlled healthcare environments, as well as flexibility in how adherence is conceptualised [6].

Although numerous approaches exist for measuring medication adherence—including self-report instruments, electronic monitoring technologies, and pharmacy database algorithms—no single method is considered the definitive standard [11, 12]. Among database-derived measures, two metrics are most commonly employed: the medication possession ratio (MPR) and the proportion of days covered (PDC) [13-15]. While neither method can verify whether medications were actually consumed as prescribed, both provide an indication of whether patients had access to their medications during the observation period.

The PDC has been endorsed by the Pharmacy Quality Alliance (PQA) as the preferred indicator for assessing adherence to long-term pharmacotherapies [16, 17]. This measure estimates the proportion of days within a period of interest (POI) during which medication is available to the individual and is typically calculated as the number of days covered by medication divided by the total number of days in the POI, multiplied by 100 [15]. Commonly used thresholds define adequate adherence as a PDC of at least 80% for most medications and 90% for antiretroviral therapies [1, 18].

Despite its widespread use, the PDC has several limitations. Although it appears straightforward, both the numerator and denominator may be defined in multiple ways depending on healthcare system structures and payer requirements. Notable contrasts exist between highly integrated electronic health systems, such as those in Sweden and Denmark—which include linked prescription and dispensing records—and more fragmented systems like the United Kingdom (UK) National Health Service (NHS) [19]. The NHS adopted electronic prescribing relatively late, and access to prescription services is influenced by provider availability, patient choice, and medication classification [19], leading to incomplete datasets. Over time, individuals may receive prescriptions from multiple clinicians and obtain medications from different pharmacies operating within unconnected networks. The growth of online pharmacies has further expanded patient choice, increasing the likelihood that medications are sourced from multiple suppliers. Despite these realities, there remains limited guidance on how PDC calculations should be adapted for quality assessment in such fragmented, real-world settings.

Although previous studies have highlighted shortcomings of the PDC [11, 15], relatively few have developed or empirically tested strategies to address these issues [20]. A key limitation of the PDC is its inability to distinguish between different causes of extended gaps in medication supply [20]. Under standard PDC assumptions, large gaps between refills are interpreted as poor implementation or intentional treatment interruptions. However, such gaps may also result from appropriate discontinuation, changes in prescribing, or patients obtaining medication from alternative pharmacies. While it is not always possible to ascertain the underlying reason for a gap—and clinically, any interruption should prompt patient follow-up—there is a clear need for methods that allow for multiple plausible explanations.

This issue has been examined by García-Sempere *et al*. who analysed osteoporosis treatment using linked prescribing and dispensing data from a large healthcare system in Spain [20]. However, linked datasets of this

nature are not routinely available in many healthcare contexts. Consequently, there remains a need for an approach that can be applied across multiple therapeutic areas, relies solely on dispensing data, and accounts for patients obtaining medications across different providers.

The objective of the present study was to enhance adherence measurement using the PDC by developing and accessing two alternative methods for defining the denominator under varying assumptions, using data from a single pharmacy provider. The proposed algorithms are illustrated with hypothetical examples and subsequently applied and evaluated using real-world dispensing data.

Materials and Methods

This study did not require approval from an institutional review board (IRB) because it was based on secondary analysis of fully anonymised data supplied by a commercial organisation. All records were stored electronically and are available for access subject to a data confidentiality agreement.

Conceptual basis for PDC calculation

The proportion of days covered (PDC) is estimated over a predefined period of interest (POI). The POI may be anchored to individual-level clinical events, such as the initiation of pharmacotherapy, or defined using fixed calendar boundaries, for example beginning on 1 January 2020. In most applications, the POI extends for a fixed duration, commonly one year. In all PDC formulations, the numerator represents the total number of days within the POI for which medication supplied by the pharmacy was available to the individual. This is calculated by aggregating the dispensed medication over the POI and converting it into days of coverage, where daily coverage is derived by dividing the quantity dispensed by the prescribed daily dose.

Definition of the denominator

The denominator represents the total number of days within the POI during which the medication is assumed to be required. As dispensing pharmacies lack direct information on clinical need or prescribing intent for each day, estimation of this denominator necessarily involves assumptions. For each individual, the denominator may be influenced by one or more of the following factors:

Variable 1

The date on which the individual first obtained the medication from the pharmacy during the POI.

Variable 2

The date on which the individual permanently ceased obtaining the medication from the pharmacy during the POI. This cessation may result from a range of circumstances, including prescriber-directed discontinuation, an intentional switch to a different pharmacy provider, relocation beyond the pharmacy's service area, death, or other non-adherence-related reasons. In these situations, cessation is assumed to be legitimate rather than indicative of poor adherence.

Variable 3

The presence and duration of interim gaps in medication supply from the pharmacy within the POI. Such gaps may arise for several reasons, which can be grouped into three categories:

1. a. A clinically appropriate temporary suspension of treatment.
2. b. Short-term acquisition of the medication from an alternative pharmacy.
3. c. Incomplete implementation of the prescribed regimen, consistent with the definition of nonadherence in the ABC taxonomy [6].

The first two categories are considered valid interruptions that do not necessarily reflect nonadherent behaviour. When adherence is assessed using data from a single pharmacy provider, the timing of treatment initiation (variable 1) and permanent cessation of dispensing from that provider (variable 2) can typically be identified. However, the specific reasons underlying cessation cannot usually be determined. Although dispensing records allow detection of temporary gaps in medication supply (variable 3), they do not permit reliable differentiation between clinically justified interruptions, use of competing pharmacies, or true nonadherence. Consequently, PDC estimates derived solely from dispensing data may misrepresent actual medication-taking behaviour. Despite these

limitations, alternative PDC estimates can be generated by applying different assumptions regarding permanent discontinuation and temporary gaps in supply. When interpreted carefully, these distinct PDC measures may provide complementary perspectives on adherence behaviour and on the performance of pharmacy supply processes. Moreover, different formulations of the PDC may be appropriate for different analytical purposes or real-world contexts.

PDC1

The conventional PDC denominator—referred to here as PDC1—is defined as the total number of days from an individual's first recorded medication supply within the period of interest (POI) to the final day of that POI. This formulation assumes continuous medication need throughout the entire observation window, including that the individual remains alive and clinically indicated for treatment from initiation until the end of follow-up. It further assumes that no legitimate events occur during the POI that would justify stopping therapy, such as changes in prescribing or appropriate discontinuation. Under this approach, if an individual ceases to refill prescriptions before the POI ends (variable 2), this information is not incorporated into the denominator.

PDC1 interprets extended intervals between refills—or complete cessation of refills at the observed pharmacy—as evidence of inadequate implementation of the prescribed regimen (variable 3, explanation c). It does not account for the possibility of clinically appropriate treatment interruptions (variable 3, explanation a), nor does it allow for the individual temporarily sourcing medication from another provider (variable 3, explanation b).

Proposed extensions to the PDC framework

Two alternative PDC formulations, PDC2 and PDC3, were developed to relax some of the assumptions underlying PDC1. These adaptations are intended to address uncertainty regarding individuals' treatment status during periods when dispensing activity is not observed.

PDC2

The first extension, PDC2, modifies the denominator by redefining the time during which medication is assumed to be required. Specifically, the denominator spans from the date of the individual's first recorded supply to the date on which their final recorded supply would be expected to be exhausted within the POI. Unlike PDC1, this approach does not assume that individuals remain alive or in need of treatment beyond the coverage period of their last refill at the observed pharmacy.

For individuals who continue refilling prescriptions until the end of the POI, the PDC2 denominator is identical to that used in PDC1. However, for those who stop refilling earlier, the denominator is shortened, resulting in higher PDC values relative to PDC1. Despite this adjustment, PDC2 retains the assumption that prolonged gaps between refills at the same pharmacy reflect suboptimal implementation of treatment (variable 3, explanation c).

PDC3

The second extension, PDC3, builds upon PDC2 by further adjusting the denominator to account for extended interruptions in dispensing. In this formulation, the denominator is calculated as the number of days from the first supply date to the exhaustion date of the final supply within the POI, minus the total duration of any gaps between refills that are classified as "large."

PDC3 differs fundamentally from the other two approaches in its interpretation of these large gaps. Rather than assuming they represent poor adherence, PDC3 treats substantial gaps as potentially reflecting either medically appropriate pauses in therapy (variable 3, explanation a) or continued adherence supported by medication obtained from alternative providers (variable 3, explanation b). In contrast, all three PDC variants—PDC1, PDC2, and PDC3—continue to interpret short gaps between refills as indicative of suboptimal implementation rather than pharmacy switching.

Defining "large" gaps between refills

Within the context of variable 3, a "large" gap is intended to represent a meaningful interruption in dispensing from the observed provider, as opposed to a minor delay in refilling. The threshold used to define a large gap is context-dependent and may vary according to the pharmacokinetic and pharmacodynamic characteristics of the medication, as well as the clinical severity of the condition being treated.

As a general illustration, a gap may be classified as large if the number of uncovered days between two refills exceeds the number of days covered by the subsequent prescription. For instance, if the next supply provides 28 days of medication, a gap of 28 days or longer would be considered large, corresponding to a multiplier of 1. For medications where temporary interruptions are unlikely to result in harm, a more permissive threshold could be applied, such as 1.5 times the number of days covered by the next prescription. Conversely, for treatments addressing life-threatening conditions—where prolonged interruption may lead to serious harm or death—a much shorter gap may be sufficient to suggest legitimate non-use, and a smaller multiplier (e.g. 0.5) may be more appropriate.

When no gaps meet the criteria for being classified as large, PDC3 yields the same result as PDC2. Similarly, when individuals do not discontinue treatment before the end of the POI, PDC2 and PDC1 are equivalent.

Figure 1 illustrates the three PDC approaches, highlighting the assumptions underlying each method and the research questions they are designed to address.

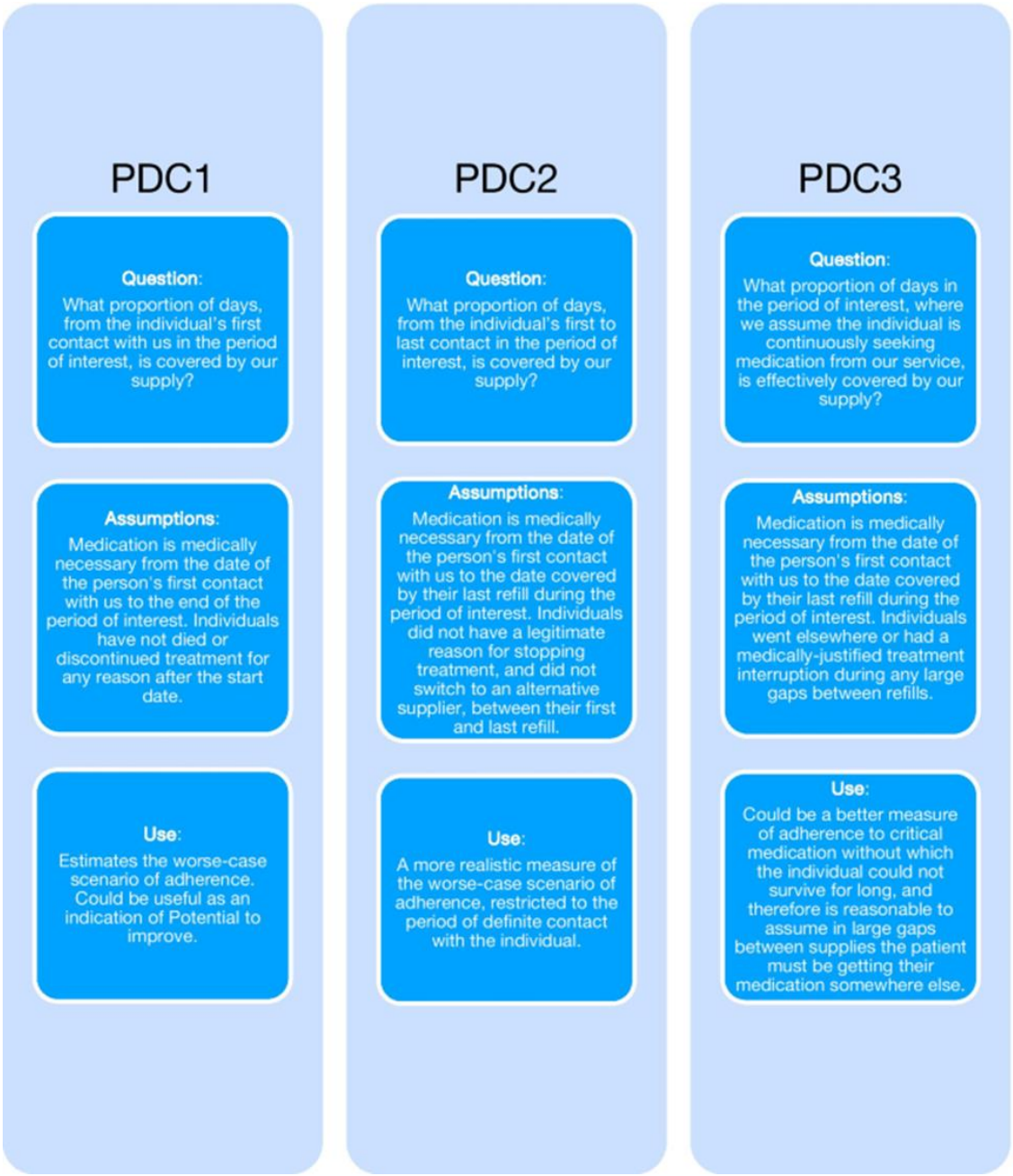


Figure 1. Comparison of underlying assumptions and research questions across the three proposed PDC approaches

Illustration of the three PDC methods

Figure 2 demonstrates the distinctions between the three PDC calculations using a hypothetical example involving two individuals who exhibit different patterns of online repeat prescription use between 1 January and 30 April of a given year. PDC estimates are calculated for two periods of interest (POIs): the full four-month observation window and a shorter 60-day interval. For the 60-day analysis, the POI is redefined to end either 60 days after the individual's first recorded supply or on 30 April, whichever occurs first. The figure also illustrates how varying the multiplier used to define legitimate gaps affects PDC3 estimates.

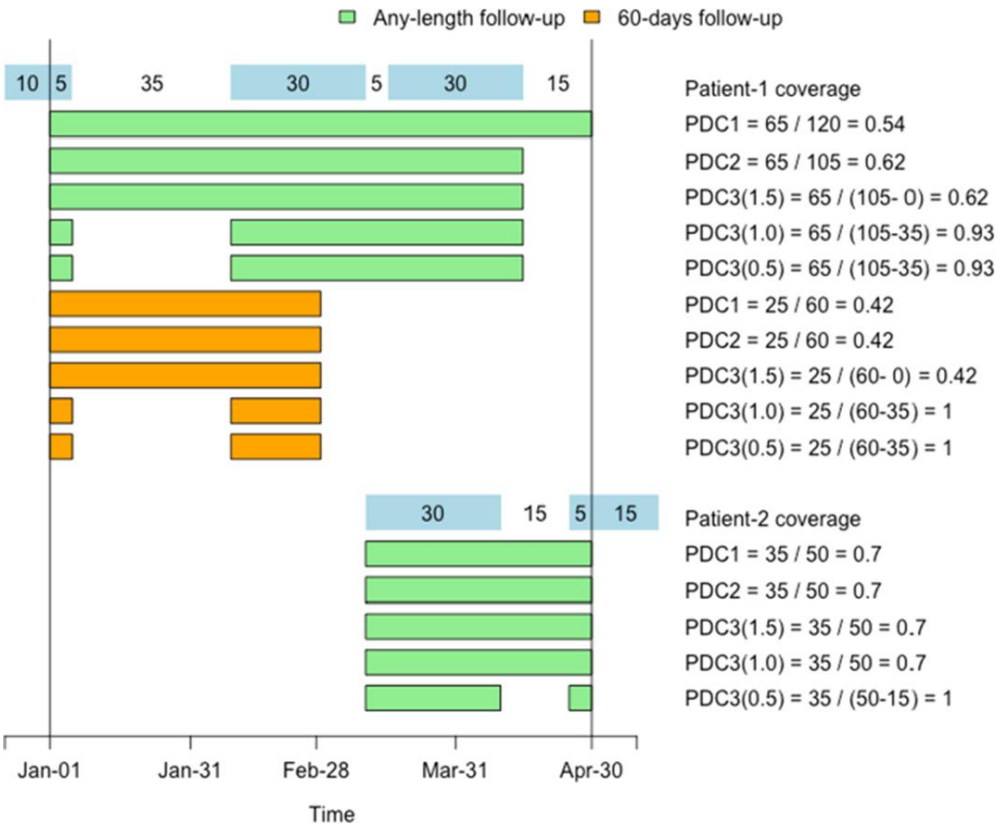


Figure 2. Visual depiction of two prescription supply patterns and corresponding PDC estimates under varying follow-up durations. The period of interest (POI) spans from 1 January to 30 April.

The example shown focuses on Patient 1, whose initial medication supply occurs on the first day of the observation window, reflecting ongoing treatment at study entry. When the full four-month POI is considered, the denominator for PDC1 extends to the final day of follow-up (day 120), yielding a PDC1 value of 65/120 = 0.54. Under PDC2, the denominator instead ends on the date when the final recorded supply is exhausted (day 105), producing a higher estimate of 65/105 = 0.62.

For PDC3, different assumptions regarding the definition of a "large" gap are applied, as indicated by the multipliers shown in parentheses. Using a multiplier of 1.5, the initial gap is not classified as large because its duration is shorter than 1.5 times the number of days supplied by the subsequent prescription ($35 < 1.5 \times 30$). As a result, this gap remains included in the denominator and the resulting PDC3 (1.5) is identical to PDC2. In contrast, when multipliers of 1.0 or 0.5 are applied, the same gap exceeds the defined threshold ($35 > 1 \times 30$ and $35 > 0.5 \times 30$, respectively). In these cases, the gap is excluded from the denominator, leading to a PDC of $65/(105 - 35) = 0.93$ for both PDC3 (1.0) and PDC3 (0.5).

When the POI is restricted to 60 days, observation of this individual ends on 1 March, during which 25 days of medication coverage are recorded. Under this shortened follow-up, PDC1, PDC2, and PDC3 (1.5) yield identical values, all lower than those observed for the full four-month period, as the 35-day gap represents a substantial portion of the truncated POI. However, under PDC3 with multipliers of 1.0 and 0.5, the gap is removed from the denominator, resulting in a PDC of 1.

In this illustrative example—and more generally—the PDC estimates follow the ordering: PDC1 ≤ PDC2 ≤ PDC3 (1.5) ≤ PDC3 (1.0) ≤ PDC3 (0.5).

Accordingly, the choice of which PDC metric to report depends on the specific research objective, the duration of follow-up, and the assumptions deemed acceptable regarding the legitimacy of extended gaps between medication dispatches.

Application to real-world data

The three PDC variants were subsequently applied to dispensing data obtained from Pharmacy2U, a United Kingdom (UK)–based online pharmacy. Pharmacy2U analysts extracted a subset of records for analysis based on the following inclusion criteria:

1. Prescriptions with a recorded dispatch date occurring between 1 January 2018 and 31 December 2019 (the POI).
2. Prescriptions containing medications from one of three therapeutic classes selected for real-world evaluation: angiotensin-converting enzyme (ACE) inhibitors, statins, or thyroid hormones. These drug classes were chosen because they are intended for continuous, long-term use rather than intermittent or as-needed dosing.
3. Prescriptions with consistent dosage instructions of "one per day" or an equivalent regimen maintained throughout the study period.
4. Prescriptions issued under the National Health Service (NHS).

All records were fully anonymised prior to transfer to the research team, and no information capable of identifying individual patients was shared. The use of customer data for this purpose is permitted under Pharmacy2U's Privacy Policy, which allows data use to support the legitimate interests associated with operating and improving its pharmacy services [21].

Within each therapeutic group, PDC estimates were calculated using four different follow-up durations following the first dispatch date within the POI: 3 months, 6 months, 12 months, and follow-up extending to the end of the POI (referred to as "any-month" follow-up). To be eligible for calculation of an X-month PDC, individuals were required to have received their first dispatch at least X months prior to the end of the POI. For example, individuals whose first dispatch occurred five months before the end of follow-up were eligible for 3-month and any-month PDC calculations, but not for 6- or 12-month analyses. For PDC3, large gaps were defined using three alternative multipliers applied to the duration of the subsequent prescription: 0.5 (liberal), 1.0 (moderate), and 1.5 (conservative).

Results and Discussion

The final Pharmacy2U dataset comprised 65,905 individuals with ACE inhibitor prescriptions, 100,362 individuals prescribed statins, and 30,637 individuals receiving thyroid hormone therapy within the study period. Among those taking ACE inhibitors, statins, and thyroid hormones, approximately 40%, 40%, and 83% were female, respectively, while 56%, 69%, and 37% were aged 60 years or older **(Table 1)**.

Table 1. Sample characteristics

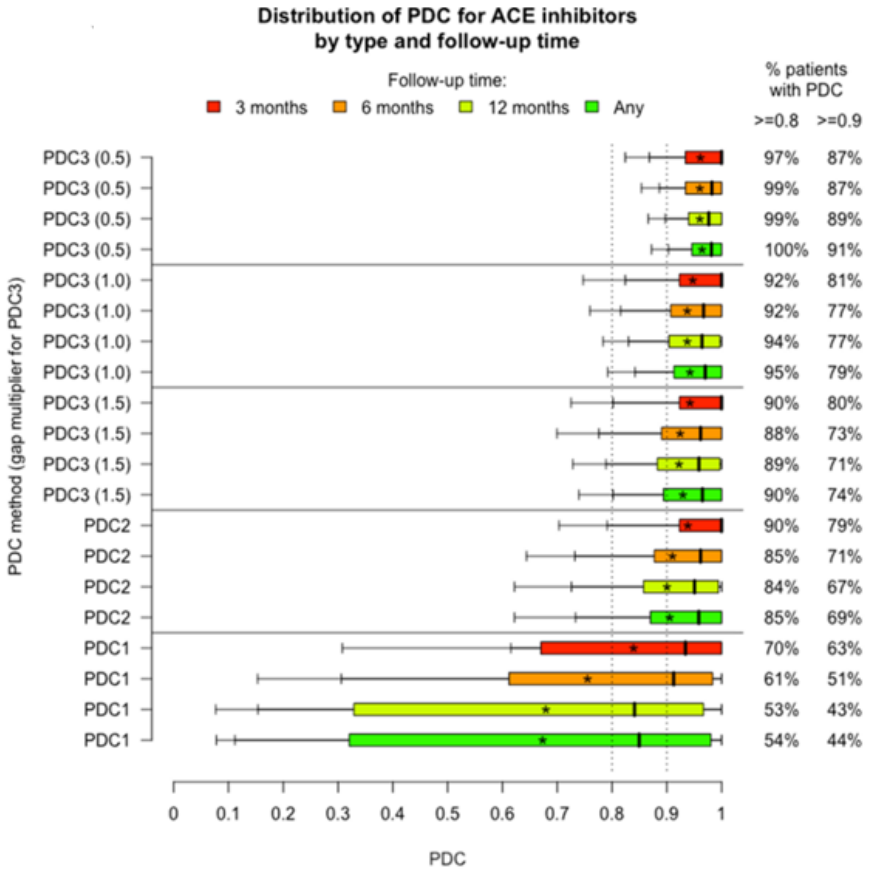
Characteristic	Statins	ACE inhibitors	Thyroid hormones
Sex			
Male	60,772 (60.6%)	39,676 (60.2%)	5,183 (16.9%)
Female	39,590 (39.4%)	26,229 (39.8%)	25,454 (83.1%)
Age group (years)			
< 18	39 (0.0%)	75 (0.1%)	216 (0.7%)
18–29	307 (0.3%)	477 (0.7%)	1,464 (4.8%)
30–39	1,683 (1.7%)	2,202 (3.3%)	3,939 (12.9%)
40–49	8,102 (8.1%)	8,396 (12.8%)	6,086 (19.9%)
50–59	21,407 (21.4%)	17,916 (27.2%)	7,492 (24.5%)
60–69	31,995 (31.9%)	18,069 (27.5%)	5,571 (18.2%)
70–79	24,153 (24.1%)	11,643 (17.7%)	3,411 (11.1%)
≥ 80	12,509 (12.5%)	7,017 (10.7%)	2,415 (7.9%)
Prescription ordering channel			

Telephone	7,449 (7.4%)	4,195 (6.4%)	1,450 (4.7%)
App	18,453 (18.4%)	13,810 (21.0%)	6,317 (20.6%)
IVR	10,626 (10.6%)	6,451 (9.8%)	3,202 (10.5%)
Web	36,530 (36.4%)	24,318 (36.9%)	11,746 (38.3%)
Direct to surgery	27,309 (27.2%)	17,134 (26.0%)	7,922 (25.9%)
Geographic region			
East Midlands	7,815 (7.8%)	5,374 (8.2%)	2,874 (9.4%)
East Anglia	12,527 (12.5%)	8,292 (12.6%)	5,181 (16.9%)
London	11,665 (11.6%)	6,512 (9.9%)	3,012 (9.8%)
North West	11,085 (11.1%)	7,222 (11.0%)	2,353 (7.7%)
North East	4,260 (4.3%)	2,835 (4.3%)	1,301 (4.3%)
Northern Ireland	1 (0.0%)	1 (0.0%)	0 (0.0%)
Scotland	8 (0.0%)	7 (0.0%)	2 (0.0%)
South West	12,989 (13.0%)	9,192 (14.0%)	4,451 (14.6%)
South East	22,265 (22.2%)	15,021 (22.8%)	6,298 (20.6%)
Wales	56 (0.1%)	39 (0.1%)	13 (0.0%)
Yorkshire and the Humber	8,606 (8.6%)	5,424 (8.2%)	2,850 (9.3%)
West Midlands	8,908 (8.9%)	5,870 (8.9%)	2,256 (7.4%)
Registration method			
App	7,374 (7.3%)	5,522 (8.4%)	2,529 (8.3%)
Partnerships	971 (1.0%)	528 (0.8%)	122 (0.4%)
Online	63,310 (63.1%)	43,808 (66.5%)	21,127 (69.0%)
Telephone	8,137 (8.1%)	4,451 (6.8%)	1,652 (4%)
RegForm	20,575 (20.5%)	11,599 (17.6%)	5,207 (17.0%)
CCG restricted[a]			
Yes	29,562 (29.5%)	19,352 (29.4%)	9,496 (31.0%)
No	70,805 (70.5%)	46,556 (70.6%)	21,141 (69.0%)

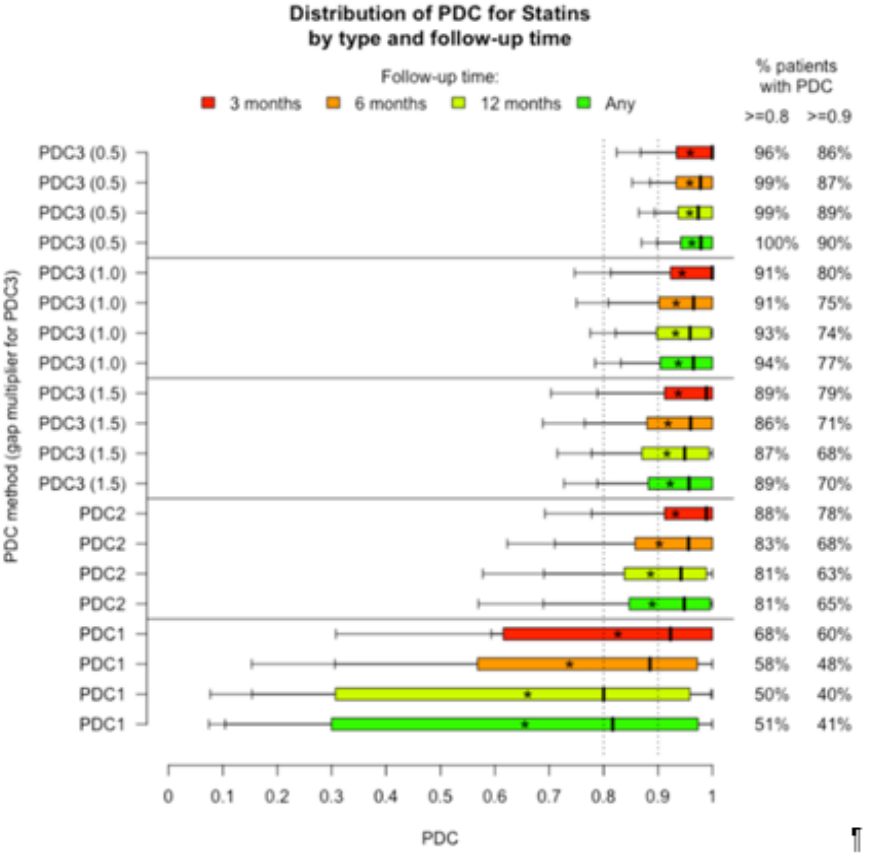
CCG Clinical Commissioning Group, IVR Interactive voice response

[a]CCG restriction refers to situations in which certain medications must be requested directly through General Practitioner (GP) surgeries rather than being obtained via the pharmacy.

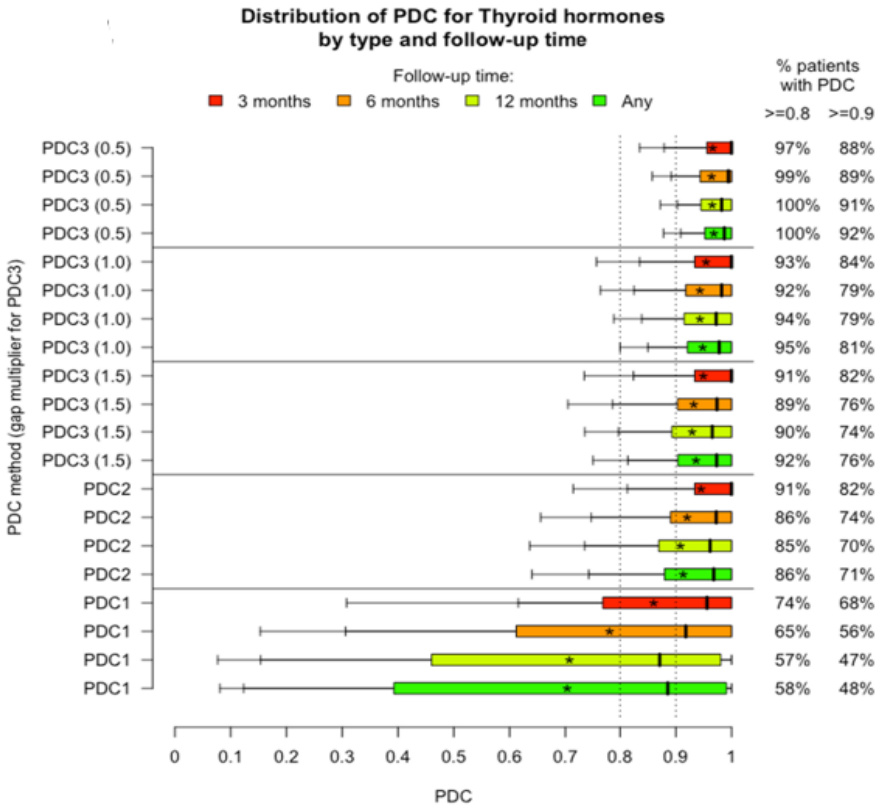
Figure 3 presents boxplots illustrating the distributions of the three PDC measures across four periods of interest, as well as across three alternative definitions of long gaps applied in the calculation of PDC3. Across all three medication classes, a much larger proportion of individuals exhibit low adherence when assessed using PDC1 compared with PDC2 or PDC3. For follow-up of any duration within the study period, individuals prescribed ACE inhibitors had a median PDC of 0.85 using PDC1, whereas the corresponding median increased to 0.96 with PDC2 and to between 0.97 and 0.98 with PDC3 (median values are indicated by the thick black vertical lines in the boxplots in **Figure 3**). A comparable pattern was observed for statins, with median values of 0.82 for PDC1, 0.95 for PDC2, and 0.96–0.98 for PDC3. For thyroid hormones, the respective medians were 0.89, 0.97, and 0.97–0.99.


Distribution of PDC for ACE inhibitors
by type and follow-up time
Follow-up time:
3 months
6 months
12 months
Any
% patients with PDC
>=0.8
>=0.9
PDC3 (0.5) 97% 87%
PDC3 (0.5) 99% 87%
PDC3 (0.5) 99% 89%
PDC3 (0.5) 100% 91%
PDC3 (1.0) 92% 81%
PDC3 (1.0) 92% 77%
PDC3 (1.0) 94% 77%
PDC3 (1.0) 95% 79%
PDC3 (1.5) 90% 80%
PDC3 (1.5) 88% 73%
PDC3 (1.5) 89% 71%
PDC3 (1.5) 90% 74%
PDC2 90% 79%
PDC2 85% 71%
PDC2 84% 67%
PDC2 85% 69%
PDC1 70% 63%
PDC1 61% 51%
PDC1 53% 43%
PDC1 54% 44%
PDC method (gap multiplier for PDC3)
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
PDC

a)


Distribution of PDC for Statins
by type and follow-up time
Follow-up time:
3 months
6 months
12 months
Any
% patients with PDC
>=0.8
>=0.9
PDC3 (0.5) 96% 86%
PDC3 (0.5) 99% 87%
PDC3 (0.5) 99% 89%
PDC3 (0.5) 100% 90%
PDC3 (1.0) 91% 80%
PDC3 (1.0) 91% 75%
PDC3 (1.0) 93% 74%
PDC3 (1.0) 94% 77%
PDC3 (1.5) 89% 79%
PDC3 (1.5) 86% 71%
PDC3 (1.5) 87% 68%
PDC3 (1.5) 89% 70%
PDC2 88% 78%
PDC2 83% 68%
PDC2 81% 63%
PDC2 81% 65%
PDC1 68% 60%
PDC1 58% 48%
PDC1 50% 40%
PDC1 51% 41%
PDC method (gap multiplier for PDC3)
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
PDC

b)



c)

Figure 3. Presents the application of three alternative PDC calculations to real-world pharmacy data for patients prescribed (a) ACE inhibitors, (b) statins, and (c) thyroid hormones. Each boxplot corresponds to a specific PDC method combined with a particular follow-up duration, which is indicated by colour and explained in the legend. The interquartile range (25th–75th percentiles) is shown by the box, the median by a black line, and the mean by an asterisk. Whiskers extend to the 5th, 10th, 90th, and 95th percentiles. For PDC3, periods classified as long gaps—defined as 0.5, 1, or 1.5 times the average prescription duration—are excluded from the denominator under the assumption that medication supply was obtained elsewhere during those intervals.

This section focuses on contrasts between the three PDC approaches at commonly used adherence thresholds, as this is a standard way to summarise adherence at the population level. Findings are described primarily for ACE inhibitors, with notable differences for statins and thyroid hormones highlighted where applicable.

Differences across PDC approaches

The estimated proportion of ACE inhibitor users achieving a PDC of at least 0.8 varied markedly depending on the assumptions embedded in each method. Across follow-up periods, PDC1 produced estimates between 53% and 70%, whereas PDC2 yielded substantially higher values (84–90%). Estimates increased further under PDC3, ranging from 88% to 100%. Comparable patterns were observed for statins and thyroid hormones. These differences demonstrate that assuming medication use ends after the final observed refill (PDC2 versus PDC1) substantially increases estimated adherence. Treating predefined long gaps as legitimate rather than as nonadherence (PDC3) further inflates adherence estimates and, in some scenarios, results in near-complete adherence at the group level.

Applying a more stringent adherence threshold of PDC $\geq$ 0.9 showed the same overall pattern but with lower percentages. For ACE inhibitors, estimates ranged from 43–63% using PDC1, increased to 67–79% with PDC2, and rose to 71–91% under PDC3. Similar ranges were observed for the other two medication classes.

Impact of gap definitions in PDC3

Adherence estimates derived from PDC3 were sensitive to how long gaps between refills were defined. For ACE inhibitors, the proportion of individuals with PDC3 ≥ 0.8 was 88–90% when conservative gap thresholds were applied, increased to 92–95% under moderate thresholds, and reached 97–100% under liberal assumptions. Statins and thyroid hormones showed comparable sensitivity to gap definitions.

Effect of follow-up duration

Increasing the length of follow-up generally resulted in lower proportions of individuals classified as adherent using PDC1 and PDC2, although this pattern was not entirely consistent. For PDC1, the proportion with values ≥0.8 declined from 70% at 3 months to 54% at any-month follow-up. For PDC2, corresponding values were 90%, 85%, 84%, and 85%.

In contrast, longer observation periods were associated with equal or higher adherence estimates under PDC3, particularly when liberal or moderate gap exclusions were used. For PDC3 (0.5), the proportion with values ≥0.8 increased from 97% at 3 months to 100% at any-month follow-up. For PDC3 (1.0), values ranged from 92% to 95%. No clear trend was evident under conservative assumptions, where estimates remained close to 90%. Similar trends were observed across all medication groups.

Differences between medication classes

Overall adherence patterns were consistent across ACE inhibitors, statins, and thyroid hormones regardless of the PDC definition applied. However, thyroid hormone users consistently exhibited higher adherence levels than users of ACE inhibitors or statins, with larger proportions meeting both the 0.8 and 0.9 thresholds **(Figure 4)**. These differences may be partly explained by demographic variation, particularly a younger age distribution and a higher proportion of female patients among those prescribed thyroid hormones.

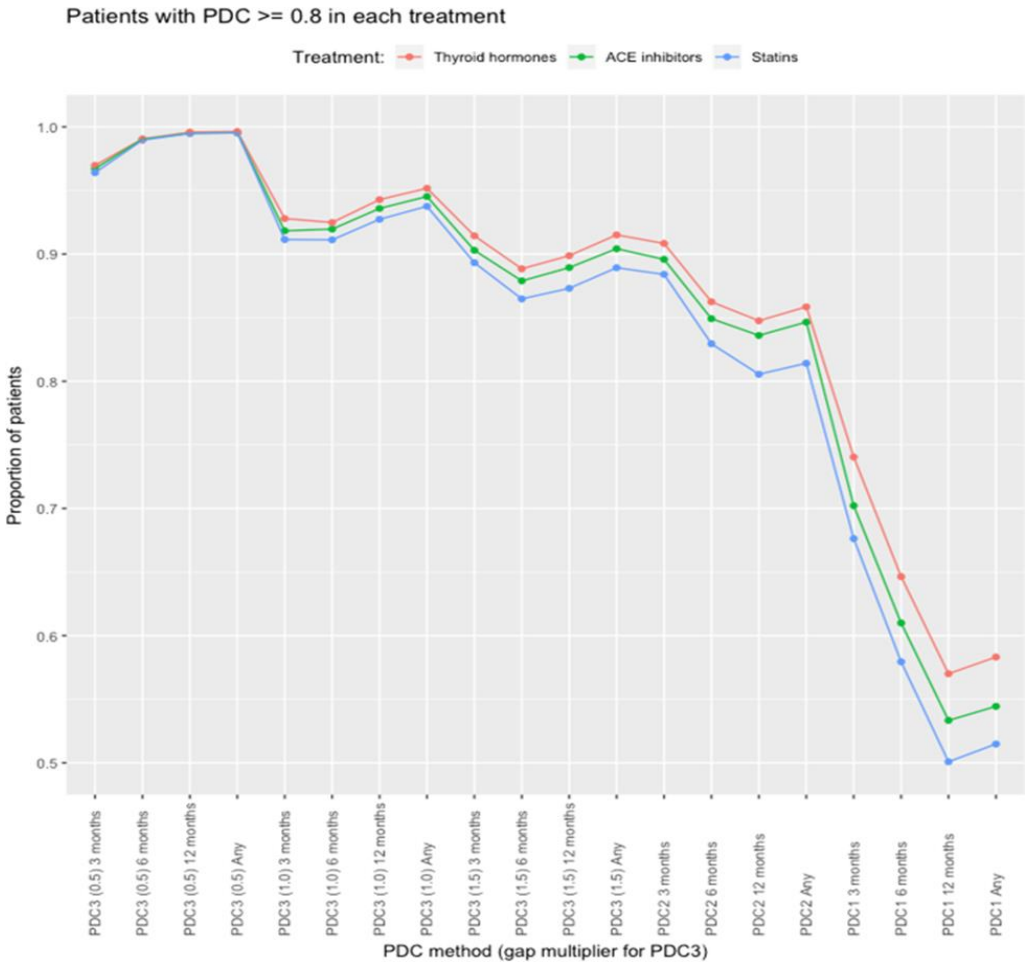


Figure 4. Compares the percentage of patients achieving a PDC of at least 0.8 across the three medication groups: thyroid hormones, ACE inhibitors, and statins.

Differences by patient characteristics

Across all PDC definitions, subgroup trends are consistent, as indicated by largely parallel lines. However, when PDC definitions assume greater medication coverage, observed differences between subgroups tend to narrow. The most pronounced variation is seen across age categories and ordering platforms. Comparable patterns were observed for the other medication classes.

This study set out to develop and test modified versions of the PDC metric suitable for situations in which only dispensing and order data from a single pharmacy are available. Each proposed PDC variant addresses a distinct analytical question and reflects different assumptions about whether patients continue to require medication and whether they may obtain supplies from alternative providers. Collectively, these approaches are intended to support real-world applications in which organisations—such as payors or online pharmacies—seek to use PDC as an indicator of adherence, service quality, and opportunities to improve patient care.

Applying the different algorithms to online pharmacy data resulted in systematically different adherence estimates. As anticipated, PDC1 produced the lowest estimates, followed by PDC2, with PDC3 yielding the highest values. The magnitude of these differences depends on the underlying adherence behaviour of the population: in highly adherent groups, estimates converge across algorithms, whereas in populations with more inconsistent medication use, divergence between PDC1, PDC2, and PDC3 becomes more pronounced.

There is limited published work examining alternative PDC formulations designed to better reflect adherence in real-world contexts [20]. This study contributes to that gap by proposing and evaluating PDC variants that are particularly relevant in settings where a single provider's data may be incomplete. This includes online pharmacies that do not have access to linked prescribing records. Such methodological flexibility is increasingly important given the expansion of online pharmacy services and growing patient autonomy in selecting medication suppliers. Reliable assessment tools are therefore essential for evaluating service quality and, eventually, for comparing performance across providers.

A practical illustration of the value of these alternative PDC approaches can be found in NHS England's electronic prescription service. Patients who opt into this system designate a "nominated pharmacy" to receive their prescriptions electronically, but they may change this nomination at any time without notifying the original pharmacy [19]. Additionally, patients may request paper prescriptions regardless of electronic enrolment status [19]. These choices can generate apparent gaps in a pharmacy's dispensing records that are unrelated to nonadherence, underscoring the need for adherence measures that can accommodate such data discontinuities.

PDC is already widely recognised as a quality metric, particularly in the United States. Beyond endorsement by the Pharmacy Quality Alliance [17], PDC measures are mandated by the Centers for Medicare & Medicaid Services (CMS) for several therapeutic categories, including renin–angiotensin system antagonists, statins, and diabetes medications [22]. Employing alternative PDC formulations offers an opportunity to better characterise medication use behaviours in online pharmacy populations and to identify areas where additional patient support—such as reminders or outreach—may be warranted.

Pharmacies can leverage outputs from multiple PDC calculations in several ways. Any observed gap in medication supply—regardless of which PDC definition is used—represents a potential opportunity to engage with the patient. While simple reminders may be effective when nonadherence is driven by forgetfulness or practical barriers, they are less likely to succeed when concerns about side effects or doubts about treatment necessity predominate [23]. Systematic assessment of adherence barriers, for example via online surveys, could enable pharmacies to deliver more tailored interventions. Evidence from a randomised controlled trial indicates that pharmacist-led telephone interventions can improve adherence, reduce medication-related problems, and shift patients' beliefs toward recognising the necessity of treatment over concerns about adverse effects [24]. Similar strategies could be adapted for digital delivery in online pharmacy settings.

Beyond patient-level insights, PDC measures may also serve as indicators of supplier performance. From a service delivery perspective, PDC1 and PDC2 likely reflect how well a provider meets overall customer demand, whereas PDC3 may better capture performance in supplying patients who remain actively engaged with that provider.

At present, the proposed algorithms calculate PDC for a single medication or medication class at a time. For patients prescribed multiple drugs for the same condition, it may be useful to develop combined adherence measures. A straightforward approach would involve averaging individual PDC values (either equally or with weighting). However, alternative definitions—such as the proportion of days with all medications available or at least one medication available—may provide more meaningful insights. Further methodological development and validation would be required to assess these options.

When used as indirect indicators of adherence, all PDC measures must be interpreted cautiously. PDC1 and PDC2 effectively assume that an absence of recorded supply equates to nonuse, representing a conservative (lower-bound) estimate of adherence. In contrast, PDC3 assumes that extended gaps may reflect either medically appropriate interruptions or continued supply from other providers. None of these assumptions can be verified using dispensing data alone. Consequently, PDC1 or PDC2 may be viewed as lower bounds, with PDC3 representing a plausible upper bound. Given that PDC3 depends on a user-defined gap threshold, sensitivity analyses are strongly recommended when reporting results.

The availability of multiple PDC formulations may also help align adherence measurement with the ABC taxonomy [6]. Traditional PDC1 treats large gaps as evidence of nonadherence but does not distinguish between discontinuation and poor implementation. Because PDC2 and PDC3 exclude time beyond the last observed refill, they are less likely to conflate these behaviours and may therefore be more appropriate when implementation is the focus. In contexts where it is reasonable to assume that large gaps reflect use of alternative suppliers, PDC3 may provide a more accurate representation of implementation.

Several limitations should be acknowledged. The study lacked an independent data source—such as patient interviews, self-reported adherence measures, or clinical indicators—that could validate the different PDC estimates. Results also demonstrated that adherence estimates are sensitive to how large gaps are defined, highlighting the need for context-specific assumptions. Future studies incorporating qualitative methods could clarify the reasons underlying extended gaps. Longitudinal studies comparing PDC estimates with other adherence measures over defined treatment periods would further enhance understanding of how initiation, implementation, and persistence relate to PDC metrics.

Conclusion

The development of alternative PDC algorithms enables researchers and service providers to select adherence measures that best align with their research objectives and underlying assumptions. The approaches described here allow organisations with dispensing data to monitor patient medication use over time and to assess the impact of adherence-focused interventions. Greater use of such methods in real-world data analysis may improve understanding of adherence behaviours and help identify meaningful opportunities for intervention. Ultimately, improving adherence has the potential to enhance patient outcomes while also reducing medication waste and healthcare expenditure.

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