EPH92

A Targeted Literature Review on Medication Adherence: A Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) Study

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BACKGROUND

Adherence to medications is critical to ensuring optimal therapeutic benefit. Measuring adherence using secondary data can be challenging especially for biologics and other medicines that may have variable dosing regimens in which the medication dosage may vary through the course of treatment.

OBJECTIVE

To investigate how adherence and persistence are measured using secondary source via a scoping literature review.

METHODS

Full text articles were identified using the following keywords: compliance, adherence, administrative claims, real-world, and observational. There was no date restriction in this search.

Articles identified:
- PubMed (n=757)
- Embase (n=423)
- Web of Science (n=755)

→ Articles removed before review:
- Duplicates (n=433)

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Articles screened (n=1,505) → Articles excluded (n=840):
- Meeting abstract only (n=18)
- Cost/Economic analyses (n=36)
- Duplicates (n=136)
- Not healthcare related (n=23)
- Non-human subjects (n=4)
- Did not discuss adherence (n=488)
- Physiology/pharmacology (n=23)
- Randomized control trials (n=5)
- Reviews/Commentary (n=9)
- Study design/protocol (n=36)
- Technology management (n=2)
- Vaccine adherence (n=13)
- Not secondary data (n=8)
- Predictive models (n=3)

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Articles reviewed (n=665) → Articles excluded (n=67):
- Meeting abstract only (n=4)
- Cost/Economic analyses (n=9)
- Did not discuss adherence (n=50)
- Reviews/Commentary (n=3)
- Not secondary data (n=1)

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Articles in analysis (n=598)

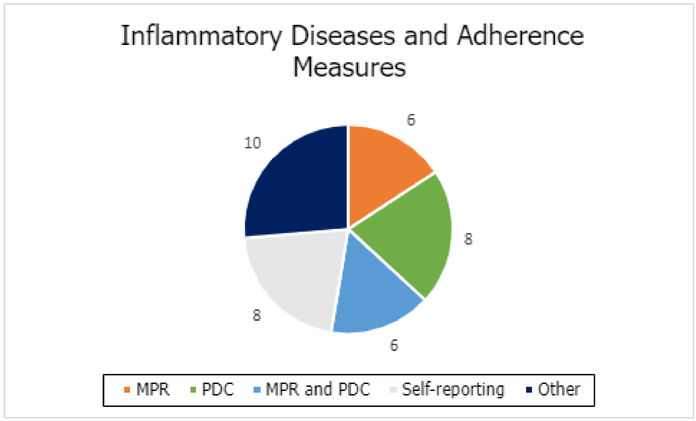
RESULTS

Adherence was measured with the Medication Possession Ratio (MPR) in 41.0% of the studies and with the Proportion of Days Covered (PDC) in 49.7% of the studies. The calculations for MPR and PDC can be found below. Furthermore, a cutoff of 80% was typically applied to the MPR and the PDC for categorizing patients as adherent vs. non-adherent.

$$MPR = \frac{sum\ of\ days\ supply\ in\ time\ period}{number\ of\ days\ in\ time\ period} \qquad PDC = \frac{number\ of\ days\ covered\ in\ time\ period}{number\ of\ days\ in\ time\ period}$$

A breakdown of the other methods used to measure adherence and persistence can be seen in the table to the right. In addition, a subset of articles focused specifically on defining switching and reinitiation without discussing the MPR and PDC.

As we were particularly interested in looking at products with variable dosing, we identified studies specifically focused on inflammatory diseases being treated with monoclonal antibodies (e.g., adalimumab, infliximab, secukinumab, and ustekinumab). These 38 articles included 16 on rheumatoid arthritis, 9 on Crohn's disease and ulcerative colitis, and 13 on psoriasis. A breakdown of the measures used to define adherence for these diseases can be seen in the pie chart below.



Variable dosing definitions differed based on the medication being studied and clinical indication:
- The days supply for the medication and the recommended frequency of administration, e.g., every 30 days (n=10).
- The number of administrations of a procedure or injection that took place in a specified period relative to the expected number of administrations based upon the labeled treatment schedule (n=5).

The dosing schedule and days supply remained generally consistent throughout the articles for the specified medications and injections, however, the allowable treatment gap between refills varied:
- Allowable gap of 60 days between the end of the days supply of the medication and being considered as discontinued (n=11).
- Allowable gap of 90 days (n=7).

Methods to Measure Adherence and Persistence (N=598 Articles)		N (%)
Adherence/Compliance		517 (86.5)
MPR	212 (41.0)	
PDC	257 (49.7)	
Time from initiation to discontinuation	7 (1.4)	
Self-reported	30 (5.8)	
Morisky Medication Adherence Scale	8 (26.7)	
Other[1]	11 (36.7)	
Not specified	14 (46.7)	
Pharmacy refill after index supply	31 (6.0)	
Number of infusions/medical products used	16 (3.1)	
Other[2]	12 (1.9)	
Persistence		226 (37.8)
Time to discontinuation	79 (35.0)	
Treatment gap	75 (33.2)	
PDC	20 (8.9)	
Remaining on index treatment after a defined period	53 (23.5)	
Switch	23 (10.2)	
MPR/Other	9 (4.0)	
Discontinuation		36 (6.0)
Treatment gap between 0-30 days	1 (2.8)	
Treatment gap between 31-60 days	9 (25.0)	
Treatment gap between 61-90 days	11 (30.6)	
Treatment gap of 90+ days	8 (22.2)	
No refill after index supply	7 (19.4)	
Switching		6 (1.0)
Reinitiation		5 (0.8)

Other[1]: Morisky Green Levine Scale, Kemp's seven-point scale, Medication Adherence Questionnaire, Italian 5-item Compliance Questionnaire for Rheumatology, Original Adherence Scale, Time Reference Scale, 4-Point Likert-Type Scale, Medication Adherence Report Scale for Asthma, Antiretroviral Medications Self-Report Questionnaire

Other[2]: HEDIS treatment adherence criteria; guidelines-based algorithm using disease-specific pain medication classes grouped as first-line, later-line, or not recommended; gap in supply; serum concentration/dose ratio at admission of <75% of the patient's own control value; asthma medication ratio; group-based trajectory models; total minutes in the 30 days prior to a study visit minus the number of uncovered minutes in the same interval, divided by the total minutes in the interval ×100; Number of inpatient days or inpatient admissions

CONCLUSIONS/NEXT STEPS

Although it was clear that MPR and PDC were most commonly used, we found a variety of methods to measure adherence and persistence that will provide a useful starting point for us to further investigate the topic. We will apply these algorithms to large data sources available to our group to explore adherence and persistence for various originator biologics and biosimilar products.

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