Validating a Medication Adherence Index in a Large Urban Population

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Introduction

Medication adherence remains a poorly quantified yet highly valuable predictor of disease progression in long-term diseases.[1] Without a gold standard and practical adherence measure, opportunities for early intervention in deteriorating patients are missed.[2]

Proportion Days Covered (PDC) offers a method of estimating adherence by harnessing pharmacy refill data.[3] Although a practical measure, PDC is not validated.[4]

Objectives

We aim to validate the PDC index (and the most reliable formulation of PDC) in 2 assessments:

1. Association between PDC index and subjective adherence by a clinician.
2. Association between PDC index and objective measure of long-term disease progression (e.g. systolic blood pressure)

N_0: There is no association of PDC index with subjective or objective measure of adherence.

Methods

Longitudinal, person-level data from **Northeast London GP EHRs** spanning the last 25 years. Including demographic covariates and pharmacy refill data (dispensed orders and prescribed statements).

Multiple PDC formulations were calculated using the base equation below:

$$PDC = \frac{\#\ of\ days\ supplied^{*}}{\#\ of\ days\ in\ POI^{**}}$$

1 Multi-level adjusted logistic regression

Cohort: Those with a clinician-recorded adherence code and prescription of Long-Term Condition medication*** (LTCm) within Period of Interest (POI).

POI: date of clinician-recorded adherence code +/- 12 months, 6 months and 3 months.

$$adherence\ code \sim PDC + covariates^{****}$$

2 Adjusted linear regression

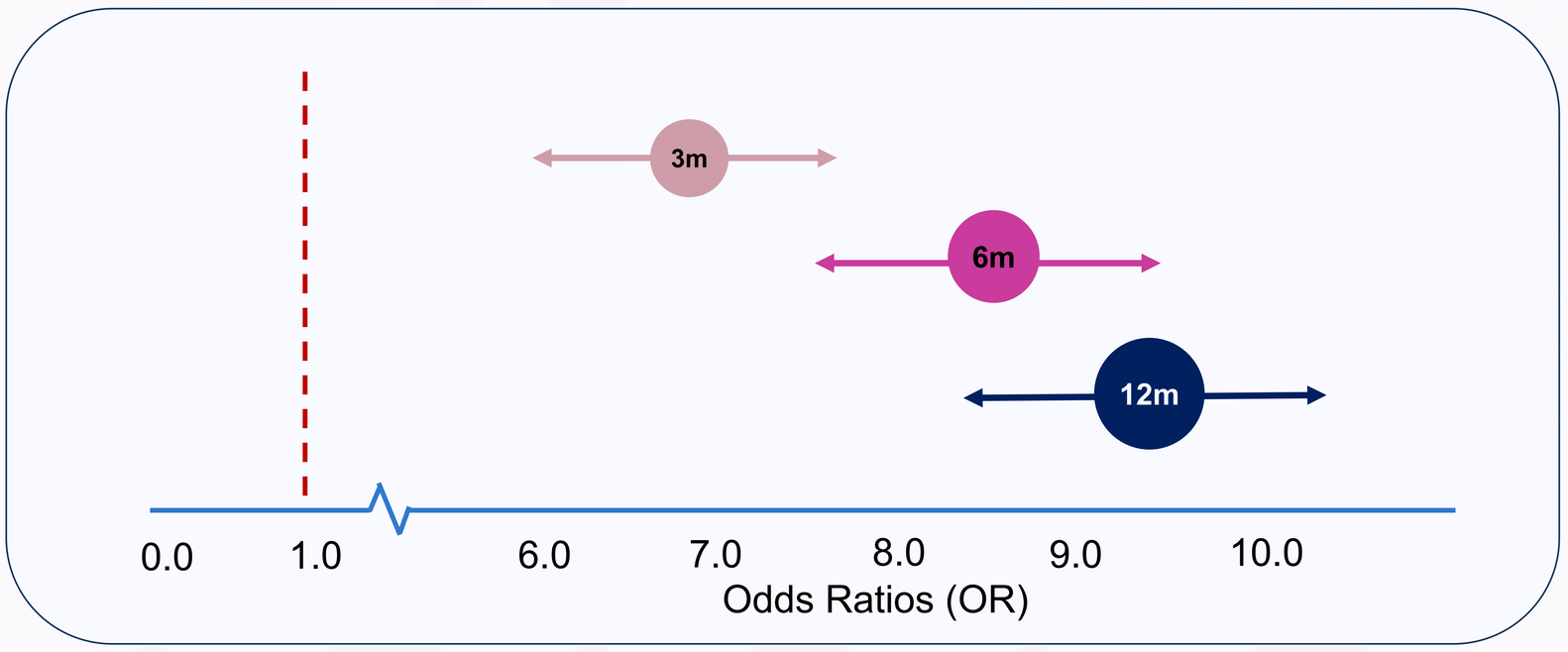
Cohort: Those on LTCm. Excluded if: on LTCm < 1yr or < 2 biological measurements at the start and end of LTCm course.

POI: Days LTCm prescribed on statement (used as PDC denominator).

$$change\ in\ biomarker \sim PDC + covariates$$

Results

1. All PDC formulations showed significant associations with clinician-recorded adherence codes, with the largest effect size in the 12 months prior to a coded status (n=300,843; OR: 9.31, CI:8.61 to 10.07).



2. PDC was significantly associated with reductions in relevant biomarkers in the 3 LTCm cohorts

Lipid-lowering n=86,051	Normal range < 3.0 mmol/L	↑ PDC = ↓ LDL by 0.21 mmol/L	95% CI: -0.24 to -0.18
n=424,289 Anti-hypertensives	Normal range < 120/80 mmHg	↑ PDC = ↓ SBP by 2.39 mmHg	95% CI: -2.56 to -2.21
Anti-diabetic n=149,984	Normal range < 42 mmol/mol	↑ PDC = ↓ HbA1c by 3.38 mmol/mol	95% CI: -3.70 to -3.06

Conclusion

- **Findings:** PDC was significantly associated with clinician-recorded adherence and improvements in key biomarkers, supporting its use as a pragmatic measure of long-term adherence in clinical practice and research.
- **Strengths:** Large longitudinal dataset and inclusion of both subjective and objective adherence measures for validation against PDC.
- **Limitations:** Possible residual confounding from lifestyle and/or dietary factors affecting BP, cholesterol, and HbA1c.

References and additional information

1. Robin DiMatteo, M. PhD*; Giordani, Patrick J. MA*; Lepper, Heidi S. PhD†; Croghan, Thomas W. MD‡. Patient Adherence and Medical Treatment Outcomes: A Meta-Analysis. Medical Care 40(9):p 794-811, September 2002.3. Dalli, L.L. *et al.* (2022)
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3. Prieto-Merino D, Mulick A, Armstrong C, Hoult H, Fawcett S, Eliasson L, Clifford S. Estimating proportion of days covered (PDC) using real-world online medicine suppliers' datasets. J Pharm Policy Pract. 2021 Dec 29;14(1):113. doi: 10.1186/s40545-021-00385-w. PMID: 34965882; PMCID: PMC8715592.
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*Unique days covered vs overlapping days were investigated.
**POI end was evaluated as both the end of the period (regardless of statement end) and the end of the statement.
*** LTCm's were drugs within BNF classes for anti-hypertensives (beta-blockers, ACEi, ARBs, CCBs), anti-diabetics (sulphonylureas, biguanides, other antidiabetic drugs) and lipid-lowering drugs.
**** clustered by person to account for within participant correlations.