Medication Adherence:
Focus on Secondary Database Analysis

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ISPOR Student Forum Presentation
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Objective

- Highlight important issues in measuring and assessing adherence when using secondary databases.
Outline

- Definitions
- Assumptions
- Medication Possession Ratio (MPR)
- Proportion of Days Covered (PDC)
- Persistence
Definitions

- **Medication Compliance (Synonym: Adherence)**
  - “…extent to which a patient acts in accordance with the prescribed interval and dose of and dosing regime…”

- **Medication Persistence**
  - “…is the accumulation of time from initiation to discontinuation of therapy…”

Source: Value in Health 2003;6: 566-73
Assumptions

- Secondary databases provide limited information regarding adherence
  - Data assessed is only as accurate as the data that was input
  - Assume that the patient was in “possession” of the medication—no guarantees that medications were taken
  - Patterns of no drug therapy may not indicate non-adherence
    - Doctor may have discontinued or verbally informed patient to change daily regimen (e.g., BID to QD or cut pills in half)
    - Patient may have been given samples
- Although there are a number of “unknowns,” secondary databases provide an acceptable estimate of adherence with large patient populations
Medication Possession Ratio

MPR

- Number of days of medication supplied within the refill interval / number of days in refill interval
- To calculate ratio, need at least 2 fill dates (e.g., index date and at least 1 refill)

\[
\frac{\text{total Rx days of supply}}{\text{last Rx date} - \text{first Rx date} + \text{last Rx days of supply}}
\]

OR

\[
\frac{\text{total Rx days of supply} - \text{last days supply}}{\text{last Rx date} - \text{first Rx date}}
\]
**MPR**

- **Numerator**
  - **Days supply**
    - Distribution of data
    - Data coding errors
      - Examine quantity vs. days supply
        - QD medications: quantity = days supply
      - Outliers

\[
\text{total Rx days of supply} = \frac{\text{last Rx date} - \text{first Rx date} + \text{last Rx days of supply}}{}
\]
**MPR**

- **Denominator**
- **Refill interval**
  - last refill as the end point
    - E.g., depression
- **Fixed interval**
  - Special cases (e.g. seasonal use)
    - ADHD, Allergies, Asthma

\[
\text{total Rx days of supply} = \frac{\text{last Rx date} - \text{first Rx date} + \text{last Rx days of supply}}{\text{Fixed interval (365 days)}}
\]
Continuous
- Increases power
- Relevance of MPR increasing from 10% to 30%?

Dichotomous
- Cut-off value is typically arbitrary
  - 80% conventional
  - Disease specific (e.g., HIV/AIDS)

MPR >1.0 (100%)
- Truncation
  - What % of data is >1.0 >1.2?
- Overadherence
  - Common with VA databases

SENSITIVITY ANALYSES are a must!!
For several chronic disease states, it is important that patients take more than one medication concomitantly. 

- E.g., diabetes, hypertension, HIV/AIDS

**Dual therapy MPR**

\[
\text{Dual therapy MPR} = \frac{\text{total Rx days of supply}/2}{\text{last Rx date} - \text{first Rx date} + \text{last Rx days of supply}}
\]

**Triple therapy MPR**

\[
\text{Triple therapy MPR} = \frac{\text{total Rx days of supply}/3}{\text{last Rx date} - \text{first Rx date} + \text{last Rx days of supply}}
\]

**Fixed-dose combination therapies**
Proportion of Days Covered

**PDC**

\[
\text{PDC} = \frac{\text{total days all drug(s) available}}{\text{days in follow-up period}}
\]

- Provides more conservative estimate of medication adherence (compared to MPR) when multiple medications are intended to be used concomitantly.
- PDC avoids double-counting days of medication coverage because a day is only counted if all medications are available on that day.
- PDC values range from 0 to 1.
PDC vs. MPR

Patient with HIV/AIDS on a 5-drug regimen. Is this patient adherent?

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MPR \( \frac{1260}{5} = 252 \)

MPR \( \frac{360}{360} = 1 \)

PDC \( \frac{0}{360} = 0 \)
# PDC vs. MPR

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**MPR**
- 1440/5
- 360

**PDC**
- 180
- 360
# PDC vs. MPR

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### MPR

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<th>72</th>
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### PDC

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 Persistence

- Number of days until discontinuation
- Percentage of individuals remaining on therapy (persistent) until a specified time interval

All patients below have 50% adherence, but... Which patient is persistent????
Persistence

- What can persistence patterns reveal about medication taking behaviors?
  - A and E could represent seasonality
  - B could represent problem resolution
  - C could represent a financial issue or patient taking half of the dose
  - D could represent episodic need or toleration of side effects
Persistence

- Time from the initial prescription fill until the patient has a *gap* in therapy
  - Continuous measure

- Proportion of patients persistent for a specified number of days without a *gap* in therapy

- Gap periods
  - Usually days (e.g., 30, 60, 90, 1.5x last days supply)
  - Depends on
    - clinical relevance
    - prescription plan day supply limits (e.g., mail order, community pharmacy, Medicaid)

- SENSITIVITY ANALYSES are a must!!
### Which Patient is Persistent?

Patients persisted, on average, 126 days w/o a 60-day gap.

Patients persisted, on average, 96 days w/o a 30-day gap.

<table>
<thead>
<tr>
<th>Patient</th>
<th>MPR</th>
<th>Months--30 days/month</th>
<th>Days persistent w/(X-day) gap</th>
<th>Persist (X days) w/o 30-day gap (y/n)</th>
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<tbody>
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<td>50%</td>
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3/5 (60%) patients were persistent for 90 days w/o a 30-day gap.

1/5 (20%) patients were persistent for 180 days w/o a 30-day gap.
Summary

- Adherence is a complex concept
- Important to understand
  - Characteristics of data and patients
  - Disease state and clinical relevance
  - Importance of various measures to payors
- Must be transparent with methods and provide valid reasons based on above information
- Sensitivity analyses are imperative!
Questions

- Thank you for the opportunity to share!
References


