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Estimating Patient Adherence to Medication with Electronic Health Records Data and Pharmacy Claims Combined

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ABSTRACT

Estimating patient adherence to medication is critical to comparative effectiveness, patient centered outcomes research, and epidemiological studies. Organizations may have varying availability of medication data. Some may have one or a subset of three possible data sources: physician prescriptions from Electronic Health Records (EHR), fill data from pharmacies or claims data from insurers. Using data from a comprehensive EHR system (EpicCare) in an ambulatory care practice for 11 years with over 1 million patients, we evaluated the prevailing adherence metrics (e.g. medication possession ratio, proportion days covered). However, these metrics cannot be estimated when a patient does not fill a medication order at all (primary non-adherent) or only fills it once (early stop). With just a little more effort, we can incorporate additional clinical information from the EHRs to obtain refined estimates of adherence. In this paper we will propose a few composite metrics that may be of specific interest to researchers and clinicians.

INTRODUCTION

Poor patient adherence to medication is one of the most common causes of increased morbidity and mortality. Lack of adherence has been estimated to cost the U.S. health care system between $100 billion and $289 billion annually in direct costs[1,2]. Many studies are carried out to examine the current situation of medication adherence, its predictors, its relationship to patient outcomes and ways to improve it. Therefore, finding accurate and standardized measurements of medication adherence is of great importance.

CONCEPTS

Medication adherence is defined as a patient's conformance with his or her provider's recommendation with respect to timing, dosage, and frequency of medication taking during the prescribed length of time[3].The Medication and Compliance Special Interest Group of International Society for Pharmacoeconomics and Outcomes Research (ISPOR) group recommends medication possession ratio (MPR) and proportion of days covered (PDC) as the preferred measurements.

MPR is a ratio between number of days of medication supply and number of days in the refill interval. It is conventionally calculated as the total number of days of medication supply divided by the sum of the number of days from first dispensing up to the date of last dispensation plus the number of days' supply obtained at the last dispensation.

PDC is defined as the total numbers of days with possession of medication in a period of time, usually also the refill interval. PDC avoids double counting when refills overlap with each other or oversupply of medications exist, but ignores the situations in which patients may refill their prescriptions before finishing the drug in hand and stockpile them for future use.

LIMITATIONS

Standardized ways of calculating MPR and PDC described above have been validated and used with data from administrative pharmacy claims previously. However, there are a few limitations that we need to keep in mind: first, MPR and PDC can only be calculated for patients with at least two dispenses. Furthermore, we can only evaluate if a patient is taking medications consistently but can't tell whether they adhere to their providers' instructions or not, due to the lack of prescription information. We can have a better understanding of these limitations by looking at Figure 1 and Figure 2.

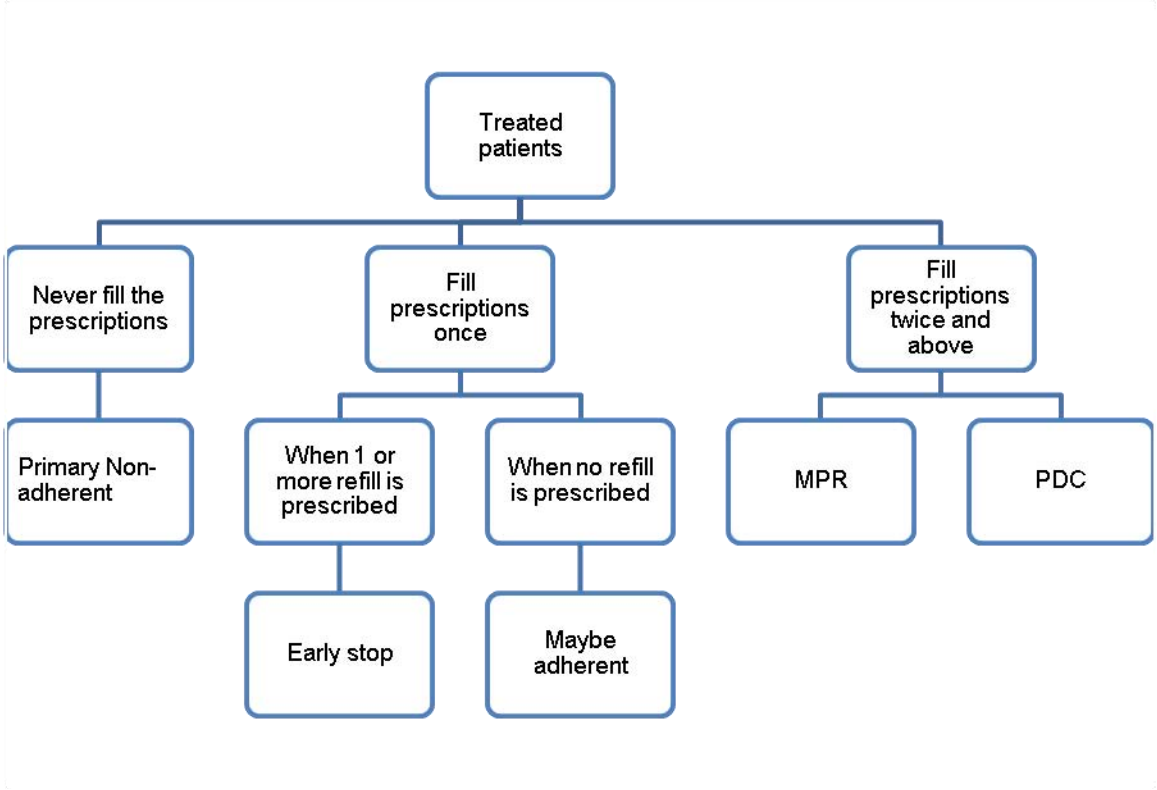

Figure 1. Overview of Possible Situations for a Patient with Medication Prescriptions

Figure 1 provides an overview of possible situations for a patient with at least one medication prescription. It shows that we would have the following bias when not including physician prescriptions into calculation of medication adherence (MPR and PDC):

1) Patients never fill a prescription will be missed
2) Patients who fill prescription only once will be missed

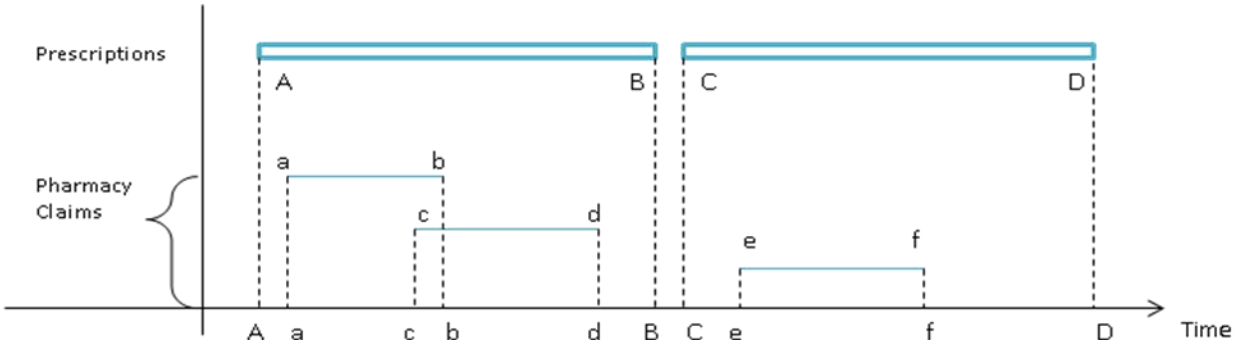

Figure 2. Example of Medication Prescription and Fill Pattern for One Patient with 2 Prescriptions and 3 Claims. The patient in Figure 2 has two prescriptions of the same medication (represented by 2 rectangles at the top with start and stop dates marked by capital letters A-D. Stop dates were generated by adding days covered by the prescriptions to the start dates. Calculation of days covered by the prescription is described in section of DATA PREPARATION) and 3 corresponding pharmacy claims (represented by 3 lines below the prescriptions with beginning and end points marked by lower case letters a-f). Distance between the letters on time axis indicates periods between the time points of the patient's prescriptions and claims.

From Figure 2, we can see some further bias if prescription information is not incorporated.

1) Beginning follow-up at the time of the first claim may overlook periods during which a patient delays starting medications compared to the time prescribed by their physicians (period Aa in Figure 2)
2) Censoring follow-up at the time of the last refill may overlook periods during which physicians continue to prescribe but the patient cease to adhere (period fD in Figure 2).

In recent years, several studies have attempted to integrate prescription data into adherence measures, which have focused upon primary non-adherence [3-6]. Singer, et al showed that adding written-prescription data to measures of adherence identified nearly twice as many non-adherent patients and markedly improved prediction of changes in low-density lipoprotein cholesterol with data from Israel, where providers and insurers were combined through 4 nationwide healthcare plans[7].

In the U.S. where nationwide integrated healthcare system is not common, no similar studies have been conducted yet. Thus in this paper, we provide one way of modifying MPR and PDC, inspired by Singer and team, by combining physician prescriptions from electronic health records data and pharmacy claims in hope of laying the foundation for future studies.

EQUATIONS AND MODIFICATIONS

There are variations in how people calculate MPR and PDC in different occasions. Here we illustrate commonly accepted equations in literature. Date points from Figure 2 are used to further clarify how the equations work.

The original MPR_o and PDC_o are based on pharmacy claims only and are prone to the biases described in the previous section.

$$\text{Original } MPR_o = \frac{\text{Total Rx Days of Supply}}{\text{Last Rx Date} + \text{Last Rx Days Supply} - \text{First Rx Date}} = \frac{ab+cd+ef}{af} \quad (1)$$

$$\text{Original } PDC_o = \frac{\text{Total Days Drug Available}}{\text{Last Rx Date} + \text{Last Rx Days Supply} - \text{First Rx Date}} = \frac{ab+bd+ef}{af} \quad (2)$$

Modified MPR_m and PDC_m could be calculated when prescription information is available as denominators. In Figure 2, the actual period during which this patient should be taking medication, as instructed by physicians, is 'AD' instead of 'af'. Thus, modified equations are:

$$\text{Modified } MPR_m = \frac{\text{Total Rx Days of Supply}}{\text{Last Prescription Date} + \text{Last Prescription Days Covered} - \text{First Prescription Date}} = \frac{ab+cd+ef}{AD} \quad (3)$$

$$\text{Modified } PDC_m = \frac{\text{Total Days Drug Available}}{\text{Last Prescription Date} + \text{Last Prescription Days Covered} - \text{First Prescription Date}} = \frac{ab+bd+ef}{AD} \quad (4)$$

From the above equations, it's easy to tell that the modified version will create different values compared to corresponding original equations (MPR_o vs.MPR_m and PDC_o vs.PDC_m) when AD and af are not the same. Adding physician prescriptions to the algorithm completes the picture and creates more accurate estimates.

When a patient never fills a prescription (primary non-adherence), the numerators in equation (3) and (4) will be 0 thus this patient has MPR_m and PDC_m equal to 0. In case a patient only has 1 pharmacy fill, the numerators for MPR_m and PDC_m will be the number of days of supply for this only fill and denominators will still be the prescribed length of time. Thus anyone with a medication prescription will have a medication adherence estimate that ranges from 0 to 1.

DATA PREPARATION

Physician prescription and pharmacy claims data are complicated both in terms of the structure and in the actual drug treatment patterns. Data preparation thus is a critical step in calculating adherence. After standardization and preparation, the following variables should be available as described below.

Prescriptions from EHR (file name 'prescriptions')		**Pharmacy Claims** (file name 'claims')	
Variables	**Description**	**Variables**	**Description**
Patient_Key	Unique patient identifier	Patient_Key	Unique patient identifier
Date_start	Date when the prescription was written	Date_fill	Date the medication was dispensed
Days_prescription	Calculated number of days covered by the prescription, details explained below.	Days_supply	Number of days of supply by the dispensing

Medication_key	Unique drug identifier	Medication_key	Unique drug identifier
Generic_name	Generic name of the drug	Generic_name	Generic name of the drug
Date_end	Date when prescription ends, indicated by the provider due to renewal of an older prescription or change in therapy plan.		
Dose	Number of pills to take each time, instructed by providers in the significance field		
Frequency	Daily frequency of drug intake		
Quantity	Total quantity in pill counts prescribed on each fill		
n_refill	Total number of refills prescribed		

Days_prescription indicates the number of days actually covered by the prescription, which is calculated using the formulas below.

First, calculate days_prescription_provider, a variable that indicates the number of days between date_start and date_end of the prescription. Days_prescription_provider=date_end-date_start+1

Second, create variable days_prescription_cover, which is the number of days the prescription can cover based on the initial instruction. Days_prescription_cover $=(\frac{quantity}{dose*frequency})*(1+n\_refills)$

Third, days_prescription (calculated number of actual days covered by the prescription) is the minimum of days_prescription_provider and days_prescription_cover.

SAS® CODE PRESENTATION

After getting data sets ready, we can start the detailed calculation process. The SAS code presented below only shows simplified key steps.

STEP1

Calculate numerators and denominators for equations of MPR_m and PDC_m. The following variables will be created: ttldsup (total days of supply by pharmacy fills for each medication); duration_generic_name (number of days covered by prescriptions for each medication at generic name level); duration_all(number of days covered by any prescriptions for each patient).

```
PROC SQL;
  CREATE TABLE work.step1 AS
   SELECT DISTINCT
     d0.patient_key,
     d2.generic_name,
     d1.ttldsup,
     (d2.index_end_dt-d2.index_dt)+1 AS duration_generic_name,
     (d3.last_order_dt-d3.first_order_dt)+1 AS duration_all

    FROM work.patient_roster AS d0

      LEFT JOIN (SELECT DISTINCT
                  patient_key,
                  generic_name,
                  SUM(days_supply) AS ttldsup
            FROM work.claims GROUP BY patient_key, generic_name) AS d1 ON
      (d0.patient_key=d1.patient_key)

      LEFT JOIN (SELECT DISTINCT
                   Patient_key,
                  Generic_name,
                  MIN(date_start) FORMAT=MMDDYY10. AS index_dt,
                  MAX(date_start+days_prescription-1) FORMAT=MMDDYY10. AS index_end_dt
```

```
                  FROM work.prescriptions
                  GROUP BY patient_key, generic_name) AS d2 ON
(d0.patient_key=d2.patient_key AND d1.generic_name=d2.generic_name)

      LEFT JOIN (SELECT DISTINCT
                   Patient_key,
                   MIN(date_start) FORMAT=MMDDYY10. AS first_order_dt,
                   MAX(date_start+days_prescription-1) FORMAT=MMDDYY10. AS
last_order_dt
             FROM work.prescriptions
             GROUP BY patient_key) AS d3 ON (d0.patient_key=d3.patient_key)

ORDER BY d0.patient_key;
QUIT;
```

STEP2

Calculate MPR for each medication for each patient. Truncate MPR at 1. If a patient has current treatments that may not start or end at the same time, adjustments need to be made. One approach is to calculate average MPR weighted by 'duration_generic_name' as the composite MPR for each patient, which is applied in the APPLICATION AND COMPARISON section.

```
/*Calculate MPR for each medication separately for each patient*/
DATA work.mpr;
    SET work.step1;
/*If the patient never filled any prescription, then MPR is zero*/
    IF ttldsup=. THEN mpr=0;
/*If there is at least 1 pharmacy claim, use formula (3) for MPR_m*/
      ELSE mpr=ROUND(MIN(ttldsup/duration_generic_name, 1.00), 0.01);
RUN;
```

STEP 3

The first new variable in PDC calculation is an end date for each pharmacy fill (date_fill_end) defined as adding days of supply to date of fill minus 1 day.
Second, make the fill and end dates for all records into non-overlapped date ranges using the LAG function in SAS.

```
PROC SORT DATA=work.claims OUT=work.pdc_step1;
      BY patient_key DESCENDING date_fill;
RUN;

DATA work.pdc_step2;
    SET work.pdc_step1;

  /*Compare the end date for each fill with the next refill date. If fill ends after
next refill then adjust date_fill_end to be 1 day before the next date_fill*/

    Lag_date_fill=LAG(date_fill);
    BY patient_key;
    IF first.patient_key THEN lag_date_fill=.;

    IF date_fill_end>=lag_date_fill THEN date_fill_end_adj=lag_date_fill-1;
        ELSE date_fill_end_adj=date_fill_end;

 /*Calculate adjusted days of supply for each fill*/
   Days_supply_adj=date_fill_end_adj-date_fill+1;
RUN;
```

Third, combine data sets and calculate PDC.

```
PROC SQL;
    CREATE TABLE work.pdc AS
      SELECT
```

```
        d1.patient_key,
        CASE
             WHEN NOT MISSING(d2.patient_key) THEN d2.sum_daysup_adj
             ELSE 0
       END AS sum_daysup_adj,
       ROUND((CALCULATED sum_daysup_adj/d1.duration_all), 0.01) AS pdc

FROM (SELECT DISTINCT patient_key, duration_all FROM work.step1) AS d1
         LEFT JOIN (SELECT DISTINCT
                      Patient_key,
                      SUM(days_supply_adj) AS sum_daysup_adj
                    FROM work.pdc_step2
              GROUP BY patient_key) AS d2 ON (d1.patient_key=d2.patient_key)
ORDER BY d1.patient_key;
QUIT;
```

APPLICATION AND COMPARISON

To evaluate how much we can improve by incorporating EHR prescriptions, we constructed a retrospective cohort of active patients 2008-2010 followed through electronic health records, pharmacy claims and billing claims. Data were de-identified according to The Health Insurance Portability and Accountability Act (HIPAA) Privacy and Security Rules. Patients who were pregnant, had cancer or other terminal diseases were excluded. Because diabetes is one of the most prevalent chronic conditions, we decided to extract patient records for those who had prescriptions of oral anti-diabetic medications for illustration. The above algorithm can be utilized to calculate modified MPR and PDC for other medications treating chronic diseases as well.

	Proportion Missing	MIN	MEAN	MEDIAN	Proportion Non-adherent
MPR_o	18%	0.08	0.83	0.91	26%
PDC_o	18%	0.08	0.71	0.75	52%
MPR_m	0	0	0.64	0.77	53%
PDC_m	0	0	0.54	0.66	76%

Table 1. Comparison between Original and Modified MPR and PDC Using Example Data

We calculated MPR and PDC both in the conventional way using pharmacy claims only and modified way using pharmacy claims combined with physician prescriptions from EHR. Results of the comparisons are shown in table 1. Based on the results, by incorporating physician prescriptions, we managed to calculate medication adherence for 18% more patients and identify 100% and 46% more non-adherent patients when using MPR and PDC (medication adherence lower than 0.8 is considered non-adherent. Proportion of identified non-adherent patients increased from 26% to 53% for MPR and 52% to 76% for PDC.). In addition, we are able to calculate primary non-adherence with MPR_m and PDC_m (15%), which is not possible with MPR_o and PDC_o. MPR and PDC each has pros and cons, decision of which one to use needs to be made case by case.

CONCLUSIONS

Combining physician prescriptions data from EHRs and administrative pharmacy claims in the calculation of medication adherence metrics will give us more complete and accurate estimates.

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