Assessing Medication Adherence Using Stata

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Abstract. In this article I introduce the `medadhere` package, which computes medication adherence rates for two commonly-used measures in research and practice -- the medication possession ratio (MPR) and proportion of days covered (PDC). `medadhere` computes adherence rates for a single medication or multiple medications, and its options provide great flexibility to support the specific needs of the user.

Keywords: medication adherence, medication compliance, medication possession ratio, proportion of days covered, pharmacy claims

1 Introduction

While most patients leave the doctor's office with a medication prescription, many fail to take their medication as prescribed. According to the World Health Organization, medication adherence (also referred to as *compliance*) rates in developed countries average only about 50 percent (Sabaté 2003), and even patients in closely monitored clinical trials have been reported to maintain adherence rates of only 43 to 78 percent (Osterberg and Blaschke 2005). Given its association with increased morbidity, mortality, health services use and cost (Psaty et al. 1990; Rasmussen et al. 2007; Kulkarni et al. 2008; Linden and Adler-Milstein 2008; Sokol et al. 2005; Dragomir et al. 2010; Roebuck et al. 2011), medication non-adherence is a major concern to practitioners, payors, and policy-makers, alike. Accordingly, measuring adherence is an essential component of any strategy to improve clinical outcomes using pharmacotherapy.

Over the past two decades, administrative pharmacy claims have increasingly been used as a data source for measuring medication adherence, under the assumption that filling (and refilling) a prescription is consistent with taking the medication as directed. Adherence measures derived from administrative data are appealing because they are convenient, objective, non-invasive, and cost-effective for use in large populations (Steiner and Prochazka 1997; Osterberg and Blaschke 2005; Hess et al. 2006). Two of the most widely-used adherence measures reported in the literature are the medication possession ratio (MPR) and proportion of days covered (PDC) (see below for descriptions) (Andrade et al. 2006; Cramer et al. 2008; McMahon et al. 2011; Sattler et al. 2013; Lam and Fresco 2015). The Centers for Medicare & Medicaid Services (CMS) currently reports PDC rates for diabetes, hypertension, and cholesterol drugs as part of the annual star rating system that measures the quality of care received by beneficiaries enrolled in Medicare Advantage Plans (managed care) and Prescription Drug Plans (CMS 2018).

In this article, I introduce the new `medadhere` package for Stata that computes medication adherence rates using MPR and PDC. `medadhere` can compute rates for a single medication and for multiple medications (for each individual drug separately), and its options provide great flexibility to support the specific needs of the user.

2 Methods

The computation of any pharmacy claims-based adherence measure requires patient-level records captured over a particular time interval. Patient-level information includes the dates on which the prescriptions were filled and the number of days supply for the medication (e.g. 60 pills to be consumed twice per day for 30 days). These variables are used to calculate the amount of drug patients have on hand over the course of a given study period. The two most common methods investigators use to set the study period are a fixed date range (e.g. January 1, 2017 to December 31, 2017), or a variable study period, in which each patient's follow-up period is allowed to vary within a set time interval (e.g. 180 days from each patient's first prescription fill). As described in the following sections MPR and PDC use these date elements somewhat differently for computing adherence rates.

2.1 Medication Possession Ratio (MPR)

The MPR is generally defined as a ratio of the total days of available supply (of a medication) to the number of days in a specified study period (Steiner and Prochazka 1998). As an example, Table 1 presents pharmacy data for a patient who filled her prescription 7 times between December 30, 2012 and June 27, 2013. To illustrate the computation of MPR for a fixed study period, let us assume the study seeks to compute her MPR between January 1, 2013 and June 29, 2013 (180 days, inclusive).

Table 1. Example pharmacy fill data for a single patient

	User-provided		Derived	
Fill No.	Fill-date	Days-supply	Fill-end-date	Supply
1	30Dec2012	30	28Jan2013	28
2	23Jan2013	30	21Feb2013	30
3	27Feb2013	30	28Mar2013	30
4	03Apr2013	30	02May2013	30
5	30Apr2013	30	29May2013	30
6	29May2013	30	27Jun2013	30
7	27Jun2013	30	26Jul2013	3

As shown, only 28 days of supply (out of 30) are counted from the first fill because 2 days of supply are from before the study start date (January 1, 2013). Similarly, only 3 days of supply are counted in the 7th fill because the remaining days of supply are beyond the study end date (June 29, 2013). Thus, the MPR is computed as the sum of supply (181) divided by the number

of days in the study period (180), which in this case equals 1.01. However, one will note that there is more medication on hand than days in the study period (181 vs. 180) because both the 2nd and 5th refills were obtained earlier than when the supply of the previous refill was exhausted. This issue highlights a limitation of the MPR: it can overestimate adherence if patients regularly refill their prescriptions early, or if they switch medications before consuming all the prior supply. Some investigators handle this problem by capping the adherence rate at 1.00 (Hess et al. 2006).

2.2 Proportion of Days Covered (PDC)

The PDC is generally defined as the number of days on which the patient has the medication available divided by the number of days in a specified study period (Brenner et al. 2002). In contrast to MPR that sums the total supply of medication available, PDC sums the number of days in which the medication is available. More specifically, each day is categorized as either 1 or 0, representing whether the patient had medication available on that day or not.

Table 2 illustrates how the daily supply is quantified for the PDC calculation when there are either overlapping days of supply or no supply available. The first seven observations highlight the overlapping days of medication supply from January 23rd to January 29th for the patient data presented in Table 1. Here the supply equals 1, even though the patient actually had more medication on hand for those days due to refilling the prescription early. The next six observations (February 22nd to February 26th) highlight days in which no supply was available, and therefore is coded as 0. On February 27th, the patient refilled her prescription, and therefore a value of 1 is assigned to that day's supply.

Table 2. Quantifying daily supply for the PDC calculation using the patient data in Table 1.

Date	Study day	Supply
23Jan2013	23	1
24Jan2013	24	1
25Jan2013	25	1
26Jan2013	26	1
27Jan2013	27	1
28Jan2013	28	1
29Jan2013	29	1
……	..	..
22Feb2013	52	0
22Feb2013	53	0
23Feb2013	54	0
24Feb2013	55	0
25Feb2013	56	0
26Feb2013	57	0
27Feb2013	58	1

In using the same study period as in the MPR example above (January 1, 2013 through June 29, 2013), the sum of the number of days in which the medication is available is 170. As such, the PDC is 0.94 (170/180), which is more conservative than the 1.01 derived using MPR.

A modification to the PDC can be implemented that involves shifting refill dates forward to the day after the supply of medication is exhausted. This procedure essentially credits the patient for having additional supply on hand (due to early refilling). Table 3 illustrates how the original fill-dates and fill-end-dates (from Table 1) are modified to separate overlapping days of supply. For example, whereas the second medication fill originally occurred on January 23rd (5 days before the existing supply was exhausted), the modified refill date has been shifted forward to the day after that refill was exhausted (January 29th). Due to this shift, the supply for this 2nd refill is now exhausted on February 27th, rather than on the original date (February 21st). All other subsequent overlapping refill periods are shifted forward, accordingly. It should be noted that shifting is only correct when all data is known and does not credit dispensed medication before the study period or when not available.

Using this modification while retaining the same study period as in the previous examples (January 1, 2013 through June 29, 2013), the sum of the number of days in which the medication is available is 176. Thus, the PDC is now 0.98 (176/180), which lies somewhere between the values derived for MPR and the basic PDC (1.01 and 0.94, respectively).

Table 3. Modifying the original fill dates (from Table 1) to credit the patient for additional supply

	Original dates		Modified dates	
Fill No.	Fill-date	Fill-end-date	Fill-date	Fill-end-date
1	30Dec2012	28Jan2013	30Dec2012	28Jan2013
2	23Jan2013	21Feb2013	29Jan2013	27Feb2013
3	27Feb2013	28Mar2013	28Feb2013	29Mar2013
4	03Apr2013	02May2013	03Apr2013	02May2013
5	30Apr2013	29May2013	03May2013	01Jun2013
6	29May2013	27Jun2013	02Jun2013	01Jul2013
7	27Jun2013	26Jul2013	02Jul2013	31Jul2013

3 The `medadhere` package

This section describes the syntax of the `medadhere` package which computes the Medication Possession Ratio (MPR) and the Proportion of Days Covered (PDC).

3.1 Syntax

`medadhere` *fill_date days_supply* `[`*if*`][`*in*`], [id(`*string*`) drug(`*string*`) start(`*string*`) end(`*string*`) length(`#`) credit]`

In the syntax, *fill_date* is the date when the prescription was filled and *days_supply* is the number of days that the medication was intended to last (e.g. 60 tablets taken twice per day for 30 days; [days_supply] is 30).

3.2 Options

`id`(*string*) the patient identifier if the data contain multiple patients. When `id`() is not specified, the command assumes that there is a single patient in the data.

`drug`(*string*) the variable specifying the drug if the data contain multiple medications per patient. When `drug`() is not specified, the command assumes that there is only one medication per patient in the data.

`start`(*string*) specifies the desired start date of a study period as a *literal date*, such as `start`(01jan2013) or `start`(01/01/2013); (see [D] **datetime translation**). When `start`() is not specified, the command uses the first *fill_date*.

`end`(*string*) specifies the desired end date of a study period as a *literal date*, such as `end`(31dec2018) or `end`(31/12/2018); (see [D] **datetime translation**). When `end`() is not specified, the command uses the last refill's end-date (*fill_date* + *days_supply*) - 1.

`length`(#) specifies a study duration as an alternative to specifying `end`(). Either `length`() or `end`() can be specified, but not both.

`credit` specifies that overlapping refill periods should be spaced out by shifting the next *fill_date* forward to the day after the previous refill has been exhausted. This essentially gives the individual "credit" for having more supply of medication on hand. The `credit` option affects only the PDC.

3.3 Data generated by `medadhere`

`medadhere` replaces the data in memory with variables relevant to adherence rates computed for MPR and PDC. Table 4 describes these variables, and indicates under which circumstances they are generated.

Table 4. Variables that replace the data in memory when medadhere is executed

Variable	Description	When generated
id	Patient identifier	When id() option specified
drug	Medication identifier	When drug() option specified
study_start_dt	Start of study period	Always
study_end_dt	End of study period	Always
study_days	Number of days in study period	Always
supplyMPR	Total supply on hand (MPR)	Always
supplyPDC	Total supply on hand (PDC)	Always
mpr	Computed MPR	Always
pdc	Computed PDC	Always

The study_start_dt and study_end_dt variables are drawn directly from the start() and end() options when they are specified. If start() is not specified, then the first *fill_date* in the data is calculated as the study_start_dt. Likewise, if end() is not specified, then the last (*fill_date* + *days_supply*) – 1 is calculated as the study_end_dt, that is, unless length() is specified, in which case the study_end_dt is calculated as (study_start_dt + length) – 1. study_days is calculated as (study_end_dt – study_start_dt) + 1. Both mpr and pdc variables are computed as their respective supply ÷ study_days.

4 Examples

The medadheredata file contains pharmacy data for 8 patients spanning the period of January 7, 2012 to December 31, 2013. While all patients refilled prescriptions for at least two different medications, five of the patients refilled prescriptions for three different drugs. The scope of these data allows us to illustrate all the salient features of the medadhere package.

There are four possible scenarios in which the medadhere package can be implemented: 1) a single patient on a single medication, 2) a single patient on multiple medications, 3) multiple patients on a single medication, and 4) multiple patients on multiple medications. The examples below are described accordingly.

4.1 A single patient on a single medication

In this example, we assume there is only a single patient in the dataset. First, we load the medadheredata file and keep only the observations for the first patient and drug 1 (note: this can also be performed using the [if] [in] syntax, but for exposition, we use keep instead):

```
. use medadheredata.dta, clear
. keep if id==1 & drug==1
```

If the data are for a single patient and single medication, we do not specify either `id()` or `drug()`. Here we specify the start and end dates of the study period to span all days in 2013. We then use the command `list` to present the results in the Results window (alternatively, the user can review the data in the data editor):

```
. medadhere fill_date days_supply, start(01jan2013) end(31dec2013)
. list, clean noobs abbreviate(14)

    study_start_dt   study_end_dt   study_days   supplyMPR   supplyPDC       mpr        pdc
         01jan2013      31dec2013          365         354         329   .969863   .9013699
```

On this single patient, the results indicate that PDC is more conservative than MPR (0.90 vs 0.97). As a reminder, a value of 1.0 indicates perfect adherence.

4.2 A single patient on multiple medications

In this example, we again assume there is only a single patient in the dataset, but refilling prescriptions for multiple medications.

First, we load the `medadheredata` file and keep only the observations for the first patient (and all his/her drugs):

```
. use medadheredata.dta, clear
. keep if id==1
```

If the data are for a single patient on multiple drugs, we do specify `drug()` but not `id()`. Here we specify the start date and `length` of the study period to span 365 days in 2013 (as an alternative to specifying `end()`).

```
. medadhere fill_date days_supply, drug(drug) start(01jan2013) length(365)
. list, clean noobs abbreviate(14)

    drug   study_start_dt   study_end_dt   study_days   supplyMPR   supplyPDC       mpr        pdc
       1        01jan2013      31dec2013          365         354         329   .969863   .9013699
       2        01jan2013      31dec2013          365         358         331   .9808219   .9068493
```

4.3 Multiple patients on a single medication

In this example, we have multiple patients in the dataset, but assume they are all taking a single medication. We reload the `medadheredata` file and keep only the observations where drug = 1:

```
. use medadheredata.dta, clear
. keep if drug==1
```

If the data are for multiple individuals and a single drug, we specify `id()` but not `drug()`. Here we implement `medadhere` and do not specify the start date, which means that the command will use the earliest *fill_date* as the start date. We set the end date of the study period at 30June2013 (thereby allowing each patient to have a different study duration).

```
. medadhere fill_date days_supply, id(id) end(30jun2013)
. list, clean noobs abbreviate(14)
```

id	study_start_dt	study_end_dt	study_days	supplyMPR	supplyPDC	mpr	pdc
1	07dec2012	30jun2013	206	214	196	1.038835	.9514563
2	11apr2012	30jun2013	446	400	390	.896861	.8744395
3	07jan2012	30jun2013	541	524	501	.9685767	.9260628
4	27dec2012	30jun2013	186	188	174	1.010753	.9354839
5	22may2013	30jun2013	40	30	30	.75	.75
6	03apr2012	30jun2013	454	394	386	.8678414	.8502203
7	17jan2012	30jun2013	531	210	182	.3954802	.3427495
8	20feb2013	30jun2013	131	106	98	.8091603	.7480916

As shown, each patient's `study_start_dt` corresponds to their first *fill_date* resulting in different study periods for each patient.

4.4 Multiple patients on multiple medications

In this example, we use all the data – for all patients and all drugs.

```
. use medadheredata.dta, clear
```

If the data are for multiple patients and multiple medications, we specify both `id()` and `drug()`. Here we implement `medadhere` and do not specify either the start date or the end date, but instead specify the observation period as being 180 days. We also specify the `credit` option.

```
. medadhere fill_date days_supply, id(id) drug(drug) length(180) credit
. list, clean noobs abbreviate(14)
```

id	drug	study_start_dt	study_end_dt	study_days	supplyMPR	supplyPDC	mpr	pdc
1	1	07dec2012	04jun2013	180	187	180	1.038889	1
1	2	07feb2012	04aug2012	180	176	172	.9777778	.9555556
2	1	11apr2012	07oct2012	180	160	160	.8888889	.8888889
2	2	28sep2012	26mar2013	180	176	174	.9777778	.9666666
2	3	10feb2012	07aug2012	180	127	127	.7055556	.7055556
3	1	07jan2012	04jul2012	180	176	175	.9777778	.9722222
3	2	07jan2012	04jul2012	180	176	175	.9777778	.9722222
3	3	07jan2012	04jul2012	180	176	175	.9777778	.9722222
4	1	27dec2012	24jun2013	180	182	179	1.011111	.9944444
4	2	15jan2012	12jul2012	180	178	178	.9888889	.9888889
5	1	22may2013	17nov2013	180	109	109	.6055555	.6055555
5	2	25mar2013	20sep2013	180	77	77	.4277778	.4277778
5	3	19jan2012	16jul2012	180	120	120	.6666667	.6666667
6	1	03apr2012	29sep2012	180	162	162	.9	.9
6	2	12oct2012	09apr2013	180	165	165	.9166667	.9166667
6	3	01may2012	27oct2012	180	161	161	.8944445	.8944445
7	1	17jan2012	14jul2012	180	118	105	.6555555	.5833333
7	2	01feb2012	29jul2012	180	91	88	.5055556	.4888889
7	3	11jan2012	08jul2012	180	144	144	.8	.8
8	1	20feb2013	18aug2013	180	156	155	.8666667	.8611111
8	2	02feb2012	30jul2012	180	170	170	.9444444	.9444444

As shown, each patient's `study_start_dt` corresponds to their first *fill_date* and their `study_end_dt` is 180 days beyond that date, resulting in 180-day study periods that are unique for each patient and each drug.

4.5 Dichotomizing MPR and PDC as a measure of adherence

While both MPR and PDC are fractional measures of adherence ranging from 0 to 1 (except in cases where MPR over-counts the supply on hand, resulting in a value greater than 1.0), it is very common to find them dichotomized at a cut-point of 0.80 in which patients above the cut-point are considered adherent and those below the cut-point are considered non-adherent (Cramer et al 2008; Sikka 2005; CMS 2018).

In this example we use the PDC output from the previous implementation of `medadhere` (example 4.4) and generate a new variable called `pdc80`. We then tabulate this variable by drug type.

```
. generate pdc80 = cond(pdc >= .80,1,0)
. tabulate pdc80 drug, column

           |                drug
     pdc80 |         1          2          3 |     Total
-----------+---------------------------------+----------
         0 |         2          2          2 |         6
           |     25.00      25.00      40.00 |     28.57
-----------+---------------------------------+----------
         1 |         6          6          3 |        15
           |     75.00      75.00      60.00 |     71.43
-----------+---------------------------------+----------
     Total |         8          8          5 |        21
           |    100.00     100.00     100.00 |    100.00
```

From the table we see that adherence in this sample of patients was 75%, 75%, and 60% for drugs 1, 2 and 3, respectively.

5 Discussion

Measuring medication adherence is an essential component of any strategy to improve patient outcomes and increase the quality of care. As big data has become more readily available (via administrative claims, electronic health records, and patient generated data through various applications and portals), capable software programs are needed to process these measures efficiently.

In this article I introduced the `medadhere` package for Stata, which measures medication adherence using two common measures in practice -- the Medication Possession Ratio and Proportion of Days Covered. As demonstrated in the examples, the `medadhere` package provides users with great flexibility to tailor the measures to meet their specific needs. More complex specifications can be also implemented in conjunction with the [if] [in] syntax. While guidance on the use and reporting of these measures is beyond the scope of this article (see Peterson et al. (2007) for a comprehensive discussion), the `medadhere` package (and Stata more generally) can easily support these approaches as well.

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7 References

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