DATA MANAGEMENT • BIOSTATISTICS • PROGRAMMING • MEDICAL WRITING • PHARMACOVIGILANCE

Global Solutions from the World's Largest Data-Focused CRO

Determining medication adherence using administrative pharmacy claims data

www.quanticate.com

Agenda

- Adherence definition
- Different sources of adherence information
- Measures of adherence
- Example
- Conclusions

Medication compliance/adherence

- *Refers to the act of conforming to the recommendations made by the provider with respect to timing, dosage, and frequency of medication taking.*
- *May be defined as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen."*
- *Is measured over a period of time and reported as a percentage*

(Cramer at all, 2008)

Why do we care?

Quanticate
The Clinical Data Experts

adherence

↓

health outcomes

„Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment" (WHO, 2003)

Source of adherence info

- Patient diaries
- Tablet count
- Electronic monitoring by medication containers
- **Administrative pharmacy claims data**

Pharmacy claims – limitations

Patient ID	Drug	Fill date	Days supplied
1	A	01/01/2018	30
1	A	01/01/2018	0
1	A	02/01/2018	15
1	B	01/01/2018	5
1	B	10/01/2018	8
2	A	17/02/2018	30
2	A	17/03/2018	30

- Patient received a drug, but no guarentee that the drug has been used
- Patient does need to follow dosing instruction
- Intepretation of overlaps, multiple prescription fills at single day, messy days supplied

Adherence measures

- Medication Possesion Ratio (MPR)

$$\text{MPR} = \min\left(\frac{\text{Number of Days } \mathbf{Supplied} \text{ within the time interval}}{\text{Number of Days in time interval}}, 1\right)$$

- Proportion of Days Covered (PDC)

$$\text{PDC} = \frac{\text{Number of Days } \mathbf{Covered} \text{ within the time interval}}{\text{Number of Days in time interval}}$$

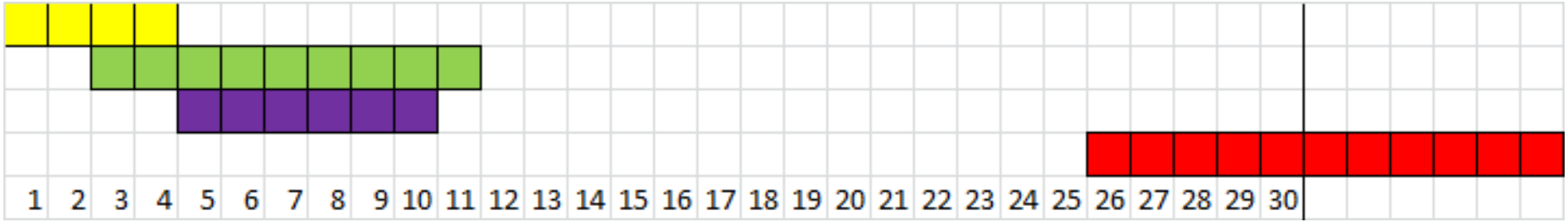
Adherence measures - MPR

- Denominator:
  - Fixed period of time
  - Time between the first fill and the end of the last fill
- Numerator:
  - Sum of Days Supplied during the specified period
    - truncation of days supplied that falls after the specified interval
- Ratio>1→ truncation

Adherence measures - PDC

- Denominator:
  - Fixed period of time
- Numerator:
  - Number of Days Covered during the specified period
  - Early refills – stockpiling?
    - Full stockpiling → patient finishes the supply for the preceding fill before starting the new supply
    - Allow only e.g. 14 days stockpiling
    - Do not allow any stockpiling

Example: MPR

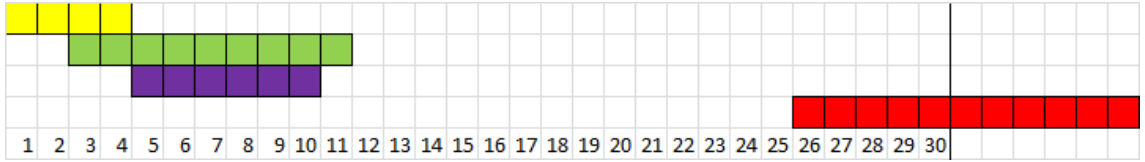


$$MPR_1 = min\left(\frac{4+9+6+11}{30}, 1\right) = min\left(\frac{30}{30}, 1\right) = \frac{30}{30} = 100\%$$

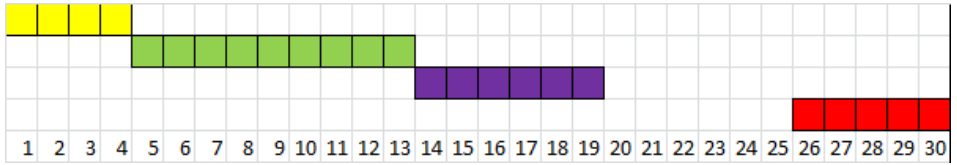
$$MPR_2 = min\left(\frac{4+9+6+5}{30}, 1\right) = min\left(\frac{24}{30}, 1\right) = \frac{24}{30} = 80\%$$

Example: PDC

Claim records

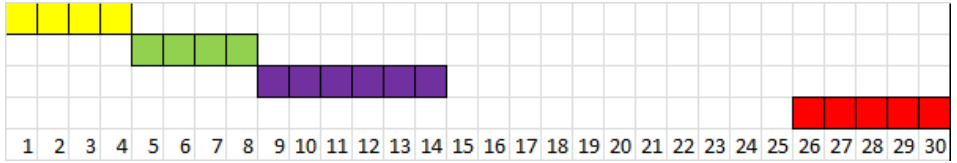


Full stockpiling



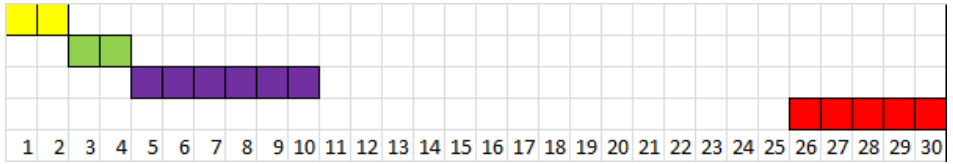
$$PDC_1 = \frac{24}{30} = 80\%$$

4 days stockpiling



$$PDC_2 = \frac{19}{30} \approx 63\%$$

No stockpiling



$$PDC_3 = \frac{15}{30} = 50\%$$

MPR vs PDC

- MPR:
  - Easy to calculate
  - Assumes that all drugs are used within the time period
  - Overestimate adherence to a drug class (i.e. if multiple products can be used simultanously)
  - Cannot be used to asses adherence to a combination therapy (e.g. 2 drugs to be taken simultanously)
- PDC:
  - Difficult to calculate
  - Different assumptions can be used
  - More conservative estimate of adherence
  - Can be used to asses adherence to a drug class and a combination therapy

Using SAS methods to compute PDC

Quanticate
The Clinical Data Experts

- Alternative methods can be used to calculate PDC including using SAS code
- These include, but are not limited to
  - Using arrays with data in a wide format
  - Using the lag function with data in a long format
- Both methods will be explained on the following slides

Using SAS methods to compute PDC (cont)

Quanticate
The Clinical Data Experts

SUBJID	FILL_DT	DAYS_SUPP	START_DATE
409	01/01/2018	28	01/01/2018
409	26/01/2018	28	01/01/2018
409	15/02/2018	28	01/01/2018
863	15/04/2018	28	15/04/2018
863	16/05/2018	28	15/04/2018
863	02/06/2018	28	15/04/2018
863	29/06/2018	28	15/04/2018

Background

- Using the same data layout as previously
- SUBJID – Subject identifier
- FILL_DT – Fill date, date prescription collected
- DAYS_SUPP – Number of days supplied at fill date
- START_DATE – The first fill date

Using SAS methods to compute PDC (cont)

Quanticate
The Clinical Data Experts

Method 1

```
data pdc;
   set <input data>;
   by subjid fill_dt;
   *Calculate day duration from start date to fill date;
   rxday = fill_dt - start_date + 1;
   *Creating dummy days covered variables (day_x) and filling with 0 before processing;
   retain day_1 - day_365;
   array pst {365} day_1-day_365;
   if first.subjid then do i = 1 to 365;
      pst(i)=0;
   end;
   *Initiate do loop with i=1;
   i=1;
   *Do loop calculating treatment days covered up to end of duration;
   do while (rxday + i - 1 <= 365);
      if rxday + i - 1 <= 365 then do;
         if i=1  then ds = ds + min(14,pst(rxday));
         if ds>0 then  pst(rxday + i - 1)=ds;
         if ds<=0 then pst(rxday + i - 1)=0;
      end;
      *Decrease days supplied by 1 for next loop;
      ds=ds-1;
      *Increase i by 1 for next loop;
      i=i+1;
   end;
   *Take last subject row for final output;
   if last.subjid;
run;
```

Using SAS methods to compute PDC (cont)

Quanticate
The Clinical Data Experts

Method 1 (cont)

```
data pdc2;
   set pdc;
   by subjid;
   *Set up array for days covered to find total days covered;
   array pst {365} day_1-day_365;
   *Dummy in pdc_numerator to initiate at 0;
   pdc_numerator=0;
   *Loop across days covered to sum up all days where treatment allocation is >0;
   do i=1 to 365;
      if pst(i)>0 then do;
         pdc_numerator = pdc_numerator + 1;
      end;
   end;
   *Set PDC denominator to duration used previously;
   pdc_denominator = 365;
   *Calculate PDC using Number of days covered within
       time interval/Number of days in time interval;
   pdc = pdc_numerator / pdc_denominator;
run;
```

Using SAS methods to compute PDC (cont)

Quanticate
The Clinical Data Experts

Method 2

```
data pdc;
    set <input data>;
    by subjid fill_dt;
    retain stockpile;
    last_date = lag(fill_dt);
    last_ds = lag(days_supp);
    *start by setting everything to zero;
    if first.subjid then do;
       current_supply = 0;
       last_date = .;
       last_ds = 0;
       stockpile = 0;
    end;
```

Using SAS methods to compute PDC (cont)

Quanticate
The Clinical Data Experts

Method 2 (cont)

```
        else do;
            *add the last supply to the stockpile;
            stockpile = stockpile + last_ds;
            *if the stockpile is less than the gap between collections, empty the stockpile into the current supply;
            if last_date + stockpile <= fill_dt then do;
                current_supply = stockpile;
                stockpile = 0;
            end;
            else do;
                *if the stockpile is greater than day between collections,
                only move the needed days of medication into the current supply;
                *at this stage, cap the stockpile at the limit;
                current_supply = fill_dt - last_date;
                stockpile = min(stockpile-current_supply,14);
            end;
        end;
        *if we have reached the last record, add all the stockpile
         and collected medication to the current supply;
        if last.subjid then do;
            *in addition, if we now have more days medication than the fixed duration allows, cap the current supply;
            if fill_dt-start_date + days_supp + stockpile >= 365 then
                 current_supply = current_supply + (start_date + 365 - fill_dt);
            else current_supply = current_supply + days_supp + stockpile;
        end;
    run;
```

Using SAS methods to compute PDC (cont)

Method 2 (cont)

```
*sum the current supplies add divide for the PDC;
proc sql;
    create table pdc2 as
        select subjid,
               365 as denom,
               sum(current_supply) as numer,
               calculated numer / calculated denom as pdc
        from pdc
        group by subjid;
quit;
```

Adherence = dychotomus measure?

Quanticate
The Clinical Data Experts

- Specific threshold to be selected

  MPR (or PDC) ≥ x% → adherent

- How to select x?

„This level should be based on results of studies showing detrimental health outcomes when compliance drops below a certain level.”

(Leslie, 2008)

Adherence measures importance

Quanticate
The Clinical Data Experts

- Unmeasured low adherence can lead to unnecessary therapy intensification
- Drug adherence need to be taken into account when analyzing treatment effectiveness
  - Poor adherence in clinical trials may results in miscalculation of treatment efficacy and dose-response relationships.

Conclusion

- Assumptions used in adherence measures calculations should be clearly defined and described in details in study documentation
- Algorithm should take into account drug specificity

Questions?

Quanticate
The Clinical Data Experts

Author:
Ewa Śleszyńska-Dopiera
ewa.sleszynska@quanticate.com

Thanks to:
Jessica Whittaker-Dixon
jessica.whittaker-dixon@quanticate.com
Charles Wright
charles.wright@quanticate.com

Thank you for listening.