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Designing co-medication matrices using a Burt table principle

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ABSTRACT

Monitoring how and to whom drugs are prescribed in daily practice is considered imperative to learn whether and how pharmacotherapy and cost-effectiveness in daily life situations can be optimized. One of the issues involved is the use of particular drugs in the line of therapy and in what combinations those drugs are prescribed. One of our methods to get a quick overview of co-medication use is based on a Burt table principle. With this table, a quick and overall insight is given in how many patients use which drug combination. A further enhancement is to change actual numbers into percentages. The effect is that the Burt symmetry disappears but that it is more general applicable. In my presentation and paper I will show the necessary steps to create such a table. I will also show how to subsequently apply a heat map such that the more frequent combinations of drugs are immediately clear.

INTRODUCTION

The PHARMO medical record linkage system is a population-based patient-centric data tracking system that includes high quality and complete information of patient demographics, drug dispensings, hospital morbidity, clinical laboratory, pathology and GP information of approximately 3 million community-dwelling inhabitants of 48 geo-demographic areas in the Netherlands. In our out-hospital pharmacy database we represent currently 16% of the Dutch population. The PHARMO registers are linked on a patient level and contain unprecedented accurate and complete information required for many health outcome and epidemiology studies. Amongst are clients are global pharmaceutical companies. Many of our studies are focused on diabetes, asthma/COPD and oncology. The objectives of these studies often include questions regarding the kind and number of medications that are used concomitantly. To get a quick insight into the co-medication patterns of a particular group of patients we have developed the Comedburt macro which creates a cross table of all possible combinations of drugs and indicates how often they are used concomitantly. This macro is a SAS macro that has been created in SAS® 9.2 (enterprise guide 4.3).

PREPARING YOUR DATA

The input dataset should contain a column for the patient number and a column for the drug description. You have to make sure that you select drugs of which you know that they are used at the same time by the specified patient. At our company we use an episode macro which calculates from when to when a certain drug is used based on our out-hospital pharmacy database and applicable rules and guideline as agreed upon with our customers. We select a certain reference point in time and if the drug is used at that time point according to our calculated episode we will include the particular drug for the particular patient. For a clinical study you could make a selection of all drugs that are ongoing at start or end of the study.

USING THE COMEDBURT MACRO

If your dataset is well prepared the usage of the comedburt macro is fairly easy. There are 4 input variables:

- Inds= for specifying the input dataset
- MyMedName= for specifying the variable name of the medication
- Pid= for specifying the variable name of the patient number
- MinimalOccurrence= for specifying how often a medication should occur to appear in the table

```
%CoMedBurt(inds=,MyMedName=,pid=,MinimalOccurrence=);
```

The macro will then execute and produce a table in which the percentage of patients reporting a medication in the first column is also using a medication in one of the columns. We could have shown the actual numbers of patients as well but the drawback then was that the numbers are mirrored diagonally. So you then see twice the same information. While in the set-up we now use we present the total number of patients using a drug in the corresponding first column and we present then the percentage of these patients using any of the drugs presented in the headers.

The example below is a simplified example where we have divided R03 medication often used by astma en COPD patients into 4 categories. R03A: SYMPATHICOMIMETICS FOR INHALATION; R03B: OTHER ASTHMA/COPD DRUGS FOR INHALATION; R03C: SYMPATHICOMIMETICS FOR SYSTEMIC USE en R03D: OTHER ASTHMA/COPD DRUGS FOR SYSTEMIC USE.

ATC 4 level	R03A	R03B	R03D	R03C
R03A (N=220144)		36.6%	4.4%	0.1%
R03B (N=124143)	64.9%		4.5%	0.1%
R03D (N=12120)	79.3%	46.0%		0.4%
R03C (N=376)	59.6%	39.6%	13.6%	

R03A: SYMPATHICOMIMETICA VOOR INHALATIE; R03B: OVERIGE MIDDELEN BIJ ASTMA/COPD VOOR INHALATIE; R03C: SYMPATHICOMIMETICA VOOR SYSTEMISCH GEBRUIK en R03D: OVERIGE MIDDELEN BIJ ASTMA/COPD VOOR SYSTEMISCH GEBRUIK.

As can be seen from the example above, the order of the medications in the first column and in the headers is based on the frequency of occurrence. Of the 220144 patients in our database using a R03A drug 36.6% also uses a R03B drug. On the other hand, of the 124143 patients using a R03B drug, 64.9% uses a R03A drug.

MACRO STEPS AND CALCULATIONS

STEP 1: DEFINE THE NUMBER PATIENTS USING EACH DRUG, ORDER AND RECODE

The databases used in health outcome and epidemiology studies are large. Therefore, a good tactic for quick processing of databases is to recode text variables to numbers. At the same time we can order our drugs by how often they occur.

First we count the number of distinct patients using each drug and only drugs which occur more than the number of occurrences we defined are selected.

```
PROC SQL;
    CREATE TABLE products AS
           SELECT DISTINCT &MyMedName, COUNT(DISTINCT &pid) AS NProd
           FROM &inds
           GROUP BY &MyMedName HAVING nprod > &MinimalOccurrence;
QUIT;
```

Thereafter, we order our drugs descendingly by the number of patients, give it a corresponding order number, create a label including the number of patients and make a macro variable containing the total number of drugs. The order number will be added to the original dataset so that it can be used for further processing by this number.

```
PROC SORT DATA=products;
    BY descending Nprod;
RUN;

DATA products;
    SET products;
    BY descending nprod;
    ProdNo=_N_;          /* Order number for presentation */
                         /* Label for presentation */
    _MyProduct=STRIP(LEFT(&MyMedName))||" (N="||STRIP(PUT(nprod,Best8.))||")";
    CALL SYMPUT('totprod',STRIP(PUT(_N_,4.))); /* Total number of drugs */
RUN;

    /* Add order number to original dataset */
PROC SQL;
    CREATE TABLE _Tmp1 AS
           SELECT a.*, b.prodno, b.nprod FROM &inds AS a
           INNER JOIN products as b on a.&MyMedName=b.&MyMedName
           ORDER BY a.&pid;
QUIT;
```

STEP 2: CREATE A DATASET WITH ONE ROW PER PATIENT

For correctly using the CORRESP procedure in SAS we need to have the used drugs in columns next to each other rather than below each other. Therefore we need to make a dataset with one row per patient and 1 column per drug. First it will be ensured that there is one row per patient and drug and an additional variable is added in which it is indicated that the patient uses the drug. Thereafter the dataset will be transposed and in case a drug is not used by a patient the corresponding values is filled with a zero. This has to be done because the CORRESP procedure does not work correctly when the value is missing.

```
/* Make one unique record per patient and product */
PROC SQL;
    CREATE TABLE _Tmp3 AS
           SELECT DISTINCT &pid , prodno, prodno as MyRes FROM _Tmp1
           ORDER BY &pid;
QUIT;

/* Transpose all drugs next to each other */
PROC TRANSPOSE DATA=_Tmp3 PREFIX=P OUT=_tmp4;
    BY &pid;
    VAR Myres;
    ID prodno;
RUN;

/* Add zero's in case a drug is not used by the corresponding patient */
DATA _tmp4 (DROP=i);
    SET _Tmp4;
    ARRAY prod{&totprod} p1-p&totprod ;
    DO i = 1 TO &totprod;
           IF prod{i} = . THEN prod{i}=0;
    END;
RUN;
```

An array is used to add the zero's, which ensures that all variables for each patient are filled with a zero in case it is missing. The macro variable totprod which is created in the previous step is now used to indicate the number of different drugs and correspondingly the number of different variables that are in the dataset.

STEP 3: CORRESP PROCEDURE AND TRANSFORMATION OF THE OUTPUT

The CORRESP procedure produces a Burt table which will be shown in the output. It results in output with number of patients for all possible combinations of drugs and usage profiles (yes or no). Using the outf option the output will be stored in a results dataset with observed and expected values. We will only use the observed values. Because we filled the contents of the p variables with their respective product numbers we can trace the results easily back.

```
/* First the proc corresp is performed resulting in the output table _Brt1*/
proc corresp data=_Tmp4 mca outf=_Brt1;
     tables p1-p&totprod;
run;
```

STEP 4: CALCULATE RELATIVE NUMBERS AND PRESENT

Based on the datasets created above the relative percentages can be calculated and after another transpose the data can be presented.

```
    PROC SQL;
       /* Calculate relative percentages  */
           CREATE TABLE _Brt5 AS
                  SELECT input(row,Best8.) as prodnox,
                         input(column,best8.) as prodnoy,
                         count as npat,
                         ROUND((count/b.nprod)*100,.1) AS ppat,
```

```
                    b._MyProduct AS prodnamex,
                    c.&MyMedName AS ProdNameY
                FROM (SELECT * FROM _Brt1
                    WHERE row<>"0" and column<>"0" and _type_="OBSERVED") AS a
                  INNER JOIN products as b on input(a.row,best8.)=b.prodno
                  INNER JOIN products AS c on input(a.column,best8.)=c.prodno;
        QUIT;

/* Make character variable for presenting */
DATA _Brt5;
        SET _Brt5;
        xppat=PUT(ppat,5.1);
RUN;
/* Sort */
PROC SORT DATA=_;
        BY prodnox prodnamex;
RUN;

/* transpose */
PROC TRANSPOSE DATA=_Brt5 OUT=_Brt6 (DROP=_NAME_) prefix=p;
        BY prodnox prodnamex;
        var xppat;
        ID prodnoy;
        idlabel prodnamey;
RUN;

/* present */
TITLE '% patients with combinations of drugs';
PROC REPORT DATA=_Brt6 NOWINDOWS;
        COLUMNS prodnamex p1-p&totprod;
RUN;
```

CONCLUSION

The above macro is a quick and easy way to get insight into the different drugs used by the patients in a cohort or a clinical study. Small additions like columns with indications of patients who have had more than 2 concomitant medications or patients who do not have had any concomitant medications can be made giving insight in that kind of information as well.

CONTACT INFORMATION (HEADER 1)

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