



Designing co-medication matrices using a Burt table principle

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- PHARMO Medical Record Linkage System
 - Records of different databases linked
 - Out-patient pharmacy (16% of Dutch population)
 - In-patient pharmacy
 - GP database
 - Hospitalisations
 - Clinical Laboratory
 - Dutch cancer registration South
 - Pathology

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- Research department
- Epidemiology research
- Patient Characteristics
- Drug utilisation
- Healthcare resource utilisation
- Outcomes research
- Post-Authorisation Safety Study (PASS)
- Marketing and sales information products
- Reporting back to health professionals
 - Pharmacists
 - GPs
 - ...

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- Main therapeutic area's
 - Diabetes
 - Respiratory diseases
 - Oncology
 - Cardiovascular diseases
 - Mother and Child health
 - Geriatrics

Epidemiology and Health outcomes

- Often results that are not expected based on the scientific studies and registrations
- Get insight in off-label use
- Get insight in line of therapy

Co-medication macro

- Get quick insight in
 - medications that are used concomitantly
 - numbers and percentages of patients using the drugs concomitantly or that do not use any concomitant drugs
 - frequency order in which medications are used
- Burt Table principle
 - A Burt table is a partitioned symmetric matrix containing all pairs of crosstabulations among a set of categorical variables.

Example

	<i>SALBUTAMOL</i>	<i>SALMETEROL/ FLUTICASON</i>	<i>TIOTROPIUM</i>	<i>FLUTICASON</i>	<i>SALMETEROL</i>	<i>TERBUTALINE</i>	<i>SALBUTAMOL/ IPRATROPIUM</i>
SALBUTAMOL (N=86972)	86972	16436 (18.9%)	8643 (9.9%)	14733 (16.9%)	1345 (1.5%)	209 (0.2%)	608 (0.7%)
SALMETEROL/FLUTICASON (N=48636)	16436 (33.8%)	48636	11362 (23.4%)	1195 (2.5%)	440 (0.9%)	255 (0.5%)	594 (1.2%)
TIOTROPIUM (N=36391)	8643 (23.8%)	11362 (31.2%)	36391	1466 (4.0%)	1129 (3.1%)	378 (1.0%)	616 (1.7%)
FLUTICASON (N=28908)	14733 (51.0%)	1195 (4.1%)	1466 (5.1%)	28908	1013 (3.5%)	148 (0.5%)	173 (0.6%)
SALMETEROL (N=5244)	1345 (25.6%)	440 (8.4%)	1129 (21.5%)	1013 (19.3%)	5244	31 (0.6%)	63 (1.2%)
TERBUTALINE (N=4020)	209 (5.2%)	255 (6.3%)	378 (9.4%)	148 (3.7%)	31 (0.8%)	4020	19 (0.5%)
SALBUTAMOL/IPRATROPIUM (N=1938)	608 (31.4%)	594 (30.7%)	616 (31.8%)	173 (8.9%)	63 (3.3%)	19 (1.0%)	1938

Input dataset

- Only need one dataset with 2 columns
 - Patient number
 - Medication
- Make sure that the dataset represents the status of the patient at a particular moment
 - Definition 1: all medications used within a pre-specified period are considered concomitant
 - Definition 2: all medications used at a particular date (for example start study) are considered concomitant

Macro input

%*MakeCMTable*

```
(inds=,          /* specify input dataset */  
MyMedName=, /* specify drug var */  
pid=,          /* specify patient var */  
MinimalOccurence=,  
ShowTop=,  
MinimalPct=,  
AddNoComed=Y,  
Show=);          /* PCT / NUM / NUMPCT */
```

Macro Step 1: Prepare data

```
PROC SQL;  
  CREATE TABLE products AS  
    SELECT DISTINCT &MyMedName,  
      COUNT(DISTINCT &pid) AS NProd FROM &inds2  
    GROUP BY &MyMedName  
    HAVING nprod > &MinimalOccurence;
```

```
RUN;
```

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

```
RUN;
```

```
DATA products;  
  SET products;  
  BY descending nprod;  
  ProdNo=_N_;  
  _MyProduct=STRIP(LEFT(&MyMedName)) ||  
    " (N=" || STRIP(PUT(nprod,Best8.)) ||  
  CALL SYMPUT('totprod',STRIP(PUT(_N_,4.)));
```

```
RUN;
```

Count number of patients per drug.

Only select drugs if they comply with the minimal occurrence rule.

Sort to get the highest used drugs first.

Number each drug according to this sorting

Make label for presentation including

Make a macro variable for total number of drugs

Macro Step 1: prepare data

```
PROC SQL;  
  CREATE TABLE _Tmp1 AS  
    SELECT a.*, b.prodno, b.name  
    FROM &inds2 AS a  
      INNER JOIN products as b  
        ON a.&MyMedName=b.&MyMedName;  
QUIT;
```

Join back to
original dataset

Make sure there
is only 1 row per
patient and drug

```
PROC SQL;  
  CREATE TABLE _Tmp3 AS  
    SELECT DISTINCT &pid , prodno, prodno as MyRes  
    FROM _Tmp1  
    ORDER BY &pid;  
QUIT;
```

Analysis will be performed on
product number to reduce
processing time

Product number is also
saved as result to easily
identify output of proc
corresp

Macro step 2: Transpose data

```
PROC TRANSPOSE DATA= Tmp3 PREFIX=P OUT= tmp4;
```

Pat.	P1	P2	P3	P4	P5	P6	P7	P8
1	1	0	3	0	5	0	0	8
2	0	2	3	0	0	0	7	0
3	0	0	0	4	0	6	0	0
4	1	0	0	4	0	0	0	0
5	0	2	3	0	0	6	0	0
6	0	0	0	4	0	6	7	0

R

D

```
DO i = 1 TO &totprod;
  IF prod{i} = . THEN prod{i}=0;
END;
```

```
RUN;
```

low per
n per

y fields

Macro step 3: Analyse

```
PROC CORRESP DATA=_Tmp4 MCA OUTF=_brt1 NOPRINT;
  TABLES p1-p&totprod;
RUN;
```

Tables to identify
variables to cross
tabulate

MCA=Multiple
Components
Analysis

Noprint, but
output to _brt1
dataset

Burt Table

		Obs	TYPE	Row	Column	Count	Percent	0	5	6	7
0	71	9	OBSERVED	0	0	67650	0.8709	67650			1330
1								856			
0	39	10	OBSERVED	0	5	3899	0.0502	105			
2	32							487			
0	43	11	OBSERVED	0	0	67738	0.8721				
3	27	12	OBSERVED	0	6	3811		3515	41		1322
0	57	13	OBSERVED	0	0	70219	0.904	35262	1129	36013	378
4	14	14	OBSERVED	0	7	1330	0.0171	25382	4231	125741	3872
0	67	15	OBSERVED	1	0	0	0	27895	1013	28760	148
5	38	16	OBSERVED	1	1	86972	1.1197	53277	0	149288	3989
0	67	17	OBSERVED	1	0	70536	0.9081	0	5244	5213	31
6	38	18	OBSERVED	1	2	16436	0.2116	49288	5213	154501	0
0	70	19	OBSERVED	1	0	78329	1.0084	3989	31	0	4020
7	13	20	OBSERVED	1	3	8643	0.1113	51402	5181	152582	4001
								1875	63	1919	19
										0	1938

All possible
combinations of all
values in all columns
are counted

Macro step 4: Process output

```
PROC SQL;
  CREATE TABLE _Br5 AS
    SELECT INPUT(row,Best8.) as prodno,
           INPUT(column,best8.) as prodnoy, COUNT as npat,
           ROUND((npat/b.nprod)*100,.1) AS ppat,
           b._MyProduct AS prodnameX, c.&MyMedName AS ProdNameY
  FROM (SELECT * FROM _Br1
        WHERE row<>"0" and column<>"0"
        _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;
```

Calculate Pct as
counted / total number
of distinct subjects in
row

Remove data if 0
and keep only
OBSERVED

Join columns and rows
with corresponding
labels and total numbers

Macro step 5: Present output

```
PROC TRANSPOSE DATA=_Br15 OUT=_Br16 (DROP=_NAME_) prefix=p;  
  BY prodnox prodnamex;  
  VAR xppat;  
  ID prodnoy;  
  IDLABEL prodnamey;  
RUN;
```

Row values and labels
including number of
subjects

Column values (ID) and
labels (IDLABEL)

```
PROC REPORT DATA=_Br16 NOWINDOWS;  
  COLUMNS prodnamex p1-p&totprod;  
RUN;
```

&totprod is an important
macro variable used
throughout the macro

Example

	SALBUTAMOL	SALMETEROL/ FLUTICASON	TIOTROPIUM	FLUTICASON	SALMETEROL	TERBUTALINE	SALBUTAMOL/ IPRATROPIUM
SALBUTAMOL (N=86972)		18.9	9.9	16.9	1.5	0.2	0.7
SALMETEROL/FLUTICASON (N=48636)	33.8		23.4	2.5	0.9	0.5	1.2
TIOTROPIUM (N=36391)	23.8	31.2		4	3.1	1	1.7
FLUTICASON (N=28908)	51	4.1	5.1		3.5	0.5	0.6
SALMETEROL (N=5244)	25.6	8.4	21.5	19.3		0.6	1.2
TERBUTALINE (N=4020)	5.2	6.3	9.4	3.7	0.8		0.5
SALBUTAMOL/IPRATROPIUM (N=1938)	31.4	30.7	31.8	8.9	3.3	1	

Additional steps

- AddNoComed=Y
 - Add rows to input dataset for subjects who have only 1 drug reported. Drug name will be “NO COMED”
- MinimalPct=
 - Already counted number of distinct patients per drug
 - Count total number of distinct patients
 - Calculate % of subjects having the product
 - In case % smaller than &minimalPct then delete the product

Additional steps

- ShowTop=
 - After ordering of the products dataset, only select the products with an ordering number equal or smaller than &ShowTop
- Show = NUM / PCT / NUMPCT
 - Before transposing the data to the final presentation make a character variable and fill with the required data. This variable will be used in the transpose procedure.

Macro advantages

- Short processing time
 - Due to usage of product numbers instead of character variables.
 - Processes a dataset of over a million records within 15 seconds
- Quick insight in data
 - Number of patients with each combination
 - Pct of patients with each combination
 - Ordered according to usage frequency
- Straightforward and robust
 - Removes doubles
 - Not dependent on variable lengths
 - Additional code does not interfere with primary process

Last Example: Oral antidiabetica market

% Patients on each combination	NO COMED	A10BA02	A10BB12	A10AB05	A10AE04	A10BB03	A10AD05	A10BB09	A10AE05	A10AC01
A10BA02 (N=97161)	45.1		16.4	7.3	8.4	10.9	6.1	7.3	4.3	2.7
A10BB12 (N=20010)	13.6	79.6		2.6	7.8	1.5	1.8	0.6	3.1	2.2
A10AB05 (N=18417)	13.2	38.7	2.8		40.5	1.3	5.0	1.2	29.9	9.7
A10AE04 (N=15134)	5.3	54	10.3	49.2		5.4	1.9	4.8	0.9	0.9
A10BB03 (N=14391)	20.9	73.5	2.1	1.7	5.7		1.4	0.6	3.1	3.2
A10AD05 (N=10485)	34.9	56.2	3.4	8.8	2.7	1.9		1.8	2.3	1.5
A10BB09 (N=9192)	15.9	77.1	1.3	2.5	8.0	1.0	2.0		3.6	4.4
A10AE05 (N=8015)	2.8	52.1	7.8	68.7	1.8	5.5	3.0	4.1		1.4
A10AC01 (N=4399)	5.4	58.5	10.0	40.5	3.2	10.5	3.5	9.2	2.5	

Questions



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