Paper 108

Concomitant Medications: What a Programmer Needs to Know
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ABSTRACT:

When tabulating concomitant medications it is often necessary to categorize data by preferred term. How this categorization occurs is a commonly misunderstood process. There are several different ways to summarize concomitant medication data: Preferred term, ATC Text, Indication by Preferred term, and various other combinations. Regardless of how the data is to be tabulated, it is essential to understand how your data is recorded and classified before starting to program statistical tables and data listings.

INTRODUCTION:

Concomitant medications can be recorded in many different ways ranging from trade (brand) name to nonproprietary names. Due to the variability in how medications are recorded, a standard naming convention is required in order to tabulate this data effectively. A common method of standardization is to categorize medications by their *Preferred Term.* In order to do this, medications must be coded using the World Health Organization Drug Dictionary (WHODRUG). It is important to understand how to programmatically assign the preferred term using the drug dictionary in order to verify that coded medications are recorded consistently both within and across studies. In addition to categorizing concomitant medications by preferred term, an ATC code (Anatomical-Therapeutic-Chemical classification) is used for the coding of therapeutic uses of drugs. This paper will describe the WHODRUG dictionary, it's contents, and how to programmatically assign the preferred term, followed by a brief description of the ATC classification system.

THE WHODRUG DICTIONARY:

The WHODRUG dictionary was started in 1968 in response to a growing need to conduct drug utilization studies on an international level. The dictionary contains information on both single and multiple ingredient medications. Drugs are classified according to the type of drug name being entered, (i.e. proprietary/trade name, nonproprietary name, chemical name, etc.). At present, 52 countries submit medication data to the WHO Collaborating Center which is responsible for the maintenance and distribution of the drug dictionary. Updates to the dictionary are offered four times per year.

DICTIONARY CONTENTS:

```
 # VARIABLE  TYPE  LEN  POS   LABEL
---------------------------------------------------
 1  MEMOID    Num    8    0
 2  DRUGNAME  Char  45    8    Drug Name
 3  DRUGRECN  Char   6   53    Drug Record Number
 4  SEQNUM1   Char   2   59    Sequence Number 1
 5  SEQNUM2   Char   3   61    Sequence Number 2
 6  CHECKDIG  Char   1   64    Check Digit
 7  DESIGNAT  Char   1   65    Designation
 8  SOURCEYE  Char   2   66    Source Year
 9  SOURCE    Char   4   68    Source Code
10  COMPANYC  Char   5   72    Company Code
11  INGRDNUM  Char   2   77    Number of Ingredients
12  SLTESTER  Char   1   79    Salt / Ester code
13  YEAR      Char   2   80    Year
14  QUARTER   Char   1   82    Quarter
```

The highlighted variables are of primary interest for purposes of programmatically selecting the Preferred Term.

- **DRUG NAME:**
  Drugs can be recorded using both proprietary and nonproprietary names. This variation in naming has resulted in the need for a standard convention when tabulating medication data.

- **DRUG RECORD NUMBER:**
  Drugs are assigned a record number in consecutive order as they are entered into the database according to their active ingredient(s).

- **SEQUENCE NUMBER 1:**
  Used to differentiate between salts / esters of a given substance.

- **SEQUENCE NUMBER 2:**
  Used to differentiate between trade names with the same ingredient(s).

SAMPLE DICTIONARY DATA:

DRUGNAME	DRUGRECN	SEQNUM1	SEQNUM2
METHYLDOPA	000001	01	001
ALDOMET	000001	01	002
PRESINOL	000001	01	003
DOPAMET	000001	01	004
HYPERPAXA	000001	01	005
SEMBRINA	000001	01	006
HYPERPAX	000001	01	007
ALDOMIN	000001	01	008
MEDOPA	000001	01	009
MEDOPAL	000001	01	010

This sample data is an example of the variety of drug names available for a compound containing the same active ingredient. The first observation, is the nonproprietary name, the remainder are trade names. The issue however, is not the variety of trade names available but the variability in how concomitant medication data is manually recorded on the case report forms. Information being entered into a database must appear exactly as it was written on the case report form. Thus any issues with spelling, spacing, hyphenation etc. would cause the medication to be counted separately if tabulating data by the reported drug name. Thus the preferred term is used in order to tabulate this data. To select the preferred term of a drug, the highest-level drug name must be selected. To do this, sort the drug dictionary by drug record number where sequence number 1 = 01 and sequence number 2 = 001, keeping only unique drug record numbers. This will provide the first specific name for a particular compound and will serve as the preferred term.

```
PROC SORT DATA=IN.WHODRUG OUT=WHO_DRG
NODUPKEY;
  BY DRUGRECN;
  WHERE (SEQNUM1='01' AND SEQNUM2='001');
RUN;
```

DRUGNAME	DRUGRECN	SEQNUM1	SEQNUM2
METHYLDOPA	000001	01	001
ORCIPRENALINE	000002	01	001
AMINOSALICYLIC ACID	000003	01	001
DIPHENHYDRAMINE	000004	01	001

The preferred term has now been identified for medications

listed in the WHODRUG dictionary and can now be merged with the concomitant medication data set.

When merging the drug dictionary data with the concomitant medication (conmed) data do not overwrite any information contained within conmed. To do this, rename drugname to preferm within the drug dictionary data. The data sets are then merged by drugrecn keeping data only if it is present in conmed.

FOR EXAMPLE:

```
PROC SORT DATA=IN.WHODRUG;
  OUT=WHO_DRG(KEEP=DRUGNAME DRUGRECN
     RENAME=(DRUGNAME=PREFTERM)) NODUPKEY;
  BY DRUGRECN;
  WHERE (SEQNUM1='01' AND SEQNUM2='001');
RUN;

DATA CONMED CHECK;
  MERGE CONMED(IN=INCONMED)
WHO_DRG(IN=INWHO);
  BY DRUGRECN;
  IF INCONMED AND NOT INWHO THEN OUTPUT
CHECK;
  IF INCONMED THEN OUTPUT CONMED;
RUN;
```

DRUGNAM	PREFTERM	DRUGRECN
BENADRYL	DIPHENHYDRAMINE	000004
ACTIFED	ACTIFED	000056
(SPIRONOLACTONE)ALDACTONE	SPIRONOLACTONE	000062
ALDACTONE	SPIRONOLACTONE	000062
DEXAMETHASONE	DEXAMETHASONE	000160
DEXAMTHASONE	DEXAMETHASONE	000160
ACTRAPID INSULIN	INSULIN	000305
VIT K	PHYTOMENADIONE	000324
VIT K1	PHYTOMENADIONE	000324
VIT K1 (PAYTOMENADIONE)	PHYTOMENADIONE	000324
VIT. K	PHYTOMENADIONE	000324

The variable DRUGNAM is from the conmed data set and appears as it was recorded on the case report form. The highlighted observations illustrate the importance of categorizing drug names by preferred term to better analyze and interpret the data.

In summary, the main purpose of assigning the preferred term is to standardize the recorded drug name into a format that can be tabulated and analyzed effectively. Utilizing the SAS® system, the programmer is quickly able to select the preferred term and merge this data with the concomitant medication data set thus standardizing the drug names prior to creating statistical tables and data listings.

ANATOMIC-THERAPEUTIC-CHEMICAL CLASSIFICATION (ATC):

In addition to categorizing medication data by preferred term, drugs are classified according to their Anatomic-Therapeutic-Chemical (ATC) classification in order to present and compare how they are being utilized. The ATC classification system divides drugs into 5 different groups depending on their site of action and therapeutic and chemical characteristics. It is important to note that one drug can code to several ATC codes depending upon its therapeutic application. The various ATC categories are as follows:

LEVEL 1: ANATOMICAL MAIN GROUP (14 main groups)
LEVEL 2: THERAPEUTIC MAIN GROUP
LEVEL 3: THERAPEUTIC SUBGROUP
LEVEL 4: CHEMICAL/THERAPEUTIC SUBGROUP
LEVEL 5: CHEMICAL SUBSTANCE SUBGROUP

The following example shows the ATC categorization for the Therapeutic Main Group: *Stomatological Preparations* (to level 4):

```
              ATC
LEVEL CODE   ATC TEXT
----------------------------------------------
1     A      ALIMENTARY TRACT AND METABOLISM
2     A01    STOMATOLOGICAL PREPARATIONS
3     A01A   STOMATOLOGICAL PREPARATIONS
4     A01AA  CARIES PROPHYLACTIC AGENTS
4     A01AB  ANTIINFECTIVES FOR LOCAL ORAL TRT
4     A01AC  CORTICOSTEROIDS FOR LOCAL ORAL TRT
4     A01AD  OTHER AGENTS FOR LOCAL ORAL TRT
```

In this example, all codes fall under the Anatomical Main Group: *Alimentary Tract and Metabolism*.

It is important to note when creating statistical tables and data listings for concomitant medications in which preferred terms and ATC codes are being used, there may be situations in which a drug would be counted once by preferred term but have multiple ATC codes. For example, *Tylenol* has the preferred term of *Paracetamol* but if used for different therapeutic indications, it would appear under multiple ATC classifications.

CONCLUSION

It is important to note the primary reason for categorizing concomitant medication data according to ATC or Preferred Term is to allow for useful interpretation of the statistical tables. Understanding the basics behind concomitant medication coding will allow you to program and QC more accurately and efficiently

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