Vertical Thinking in ADaM Programming

Penny Pang

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Introduction

ADaM data structure

- Subject-Level Analysis Dataset (ADSL)
- Basic Data Structure (BDS)
- Further ADaM Data Structures
  - Occurrence Data Structure (ODS)
  - Time to Event Data Structure (TTE)

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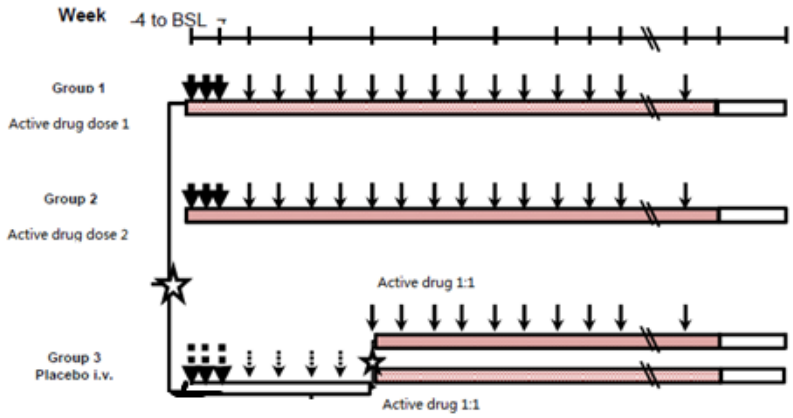
Example 1

Using adsl to derive bigN



Study Design:

1) Subject randomized into 3 group: 2 active drug and PBO
2) PBO subject re-randomized into 2 Active drug group at period 3.

Programming idea:

1) Scan TRT01AS for all subjects
2) Scan TRT03AS for PBO switchers

SUBJID	TRT01AS	TRT03AS
101	ACTDRUG1	ACTDRUG1
102	PBO	ACTDRUG1
103	PBO	ACTDRUG2
104	PBO	

Table 14.3.1-10.2 (Page 1 of 1)

Any Active Drug Dose 1 N = N1 n (%)	Any Active Drug Dose 2 N = N2 n (%)	Placebo N = N3 n (%)
101	103	102
102		103
		104

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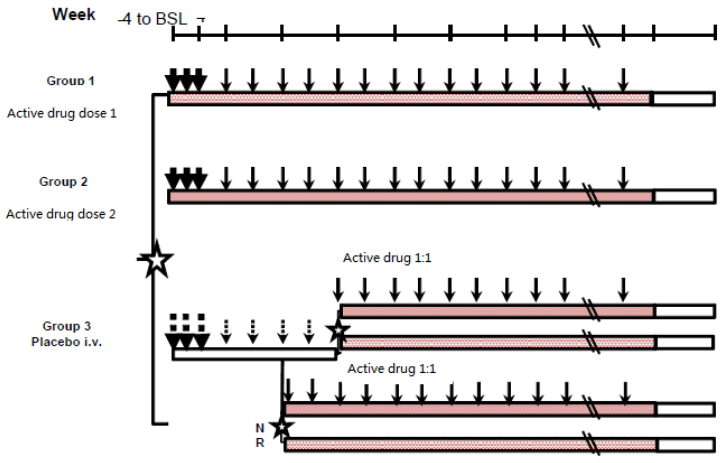
Example 1

Using adsl to derive bigN: Multi period and rescue



Study Design:

1) Subject randomized into 3 group: 2 active drug and PBO
2) Some PBO subject re-randomized into 2 Active drug group at period 3. (Rescue)
3) Other PBO subjects re-randomized into 2 Active drug group at period 3.

Programming idea:

1) Scan TRT01AS for all subjects.
2) Check whether the subject has rescue
3) Scan TRT03AS for rescue subjects.
4) Scan TRT04AS for Non-rescue subjects.

Table 14.3.1-10.2 (Page 1 of 1)

Any Active Drug Dose 1 N = N1 n (%)	Any Active Drug Dose 2 N = N2 n (%)	Placebo N = N3 n (%)
101	104	102
102		103
103		104

SUBJID	TRT01AS	TRT03AS	TRT04AS	RESCUE
101	ACTDRUG1	ACTDRUG1	ACTDRUG1	
102	PBO	ACTDRUG1	ACTDRUG1	Y
103	PBO	PBO	ACTDRUG1	N
104	PBO	PBO	ACTDRUG2	N

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Example 1

Using adsl to derive bigN: Multi studies

In the project we have several studies with similiar study design, to write a program that can calculate the big N for all the studies, we need to consider:

- Whether this study has RESCUE
- Which period does the PBO subject switch in the study
- The different wording of TRTXXA among different studies

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Example 1

Using adsl to derive bigN: Thinking vertically!!!

SUBJID	TRT01AS	TRT02AS	TRT03AS	TRT04AS	TRT05AS	RESCUE
101	ACTDRUG1	ACTDRUG1	ACTDRUG1			
102	PBO	PBO	ACTDRUG1	ACTDRUG1	ACTDRUG1	Y
103	PBO	PBO	PBO	ACTDRUG2		N
104	PBO	PBO				N

Convert adsl to SE structure

SUBJID	APERIOD	TRTAS
101	1	ACTDRUG1
101	2	ACTDRUG1
101	3	ACTDRUG1
102	1	PBO
102	2	PBO
102	3	ACTDRUG1
102	4	ACTDRUG1
102	5	ACTDRUG1
103	1	PBO
103	2	PBO
103	3	PBO
103	4	ACTDRUG2
104	1	PBO
104	2	PBO

Remove dup

SUBJID	TRTAS
101	ACTDRUG1
102	PBO
102	ACTDRUG1
103	PBO
103	ACTDRUG2
104	PBO

1) No need to consider whether this study has rescue or when to switch.
2) Can work when some of the period is missing for a subject.
3) Handle all subjects and no need to select the switchers.
4) The program can work in every study

Contribute Elements to big N

Table 14.3.1-10.2 (Page 1 of 1)

Any Active Drug Dose 1 N = N1 n (%)	Any Active Drug Dose 2 N = N2 n (%)	Placebo N = N3 n (%)
101	103	102
102		103
		104

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Example 2

Prior & Concomitant Medication: basic design

APERIOD and TRTA is generated by compare CM start date with period start date. But these variables can not be directly used in output generation.

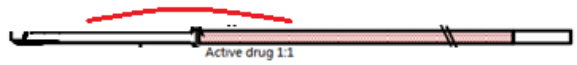
USUBJID	CMDECOD	CMSTDTC	CMENDTC	AP01SDT	AP02SDT	AP03SDT
101	CMXXX	2013-07-07	2013-08-23	2013-03-19	2013-05-14	2013-07-09

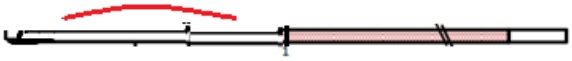
Table 14.1-8.1 (Page 1 of 8)
Concomitant medications by ATC class and preferred term

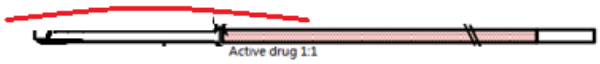
ATC class Preferred term	Any Active Drug Dose 1 N = N1 n (%)	Any Active Drug Dose 2 N = N2 n (%)	Placebo N = N3 n (%)

This CM should be contribute to both PBO column and active drug column

It will be more complicated when the study have complicated design.







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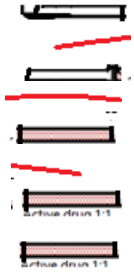
Example 2

Prior & Concomitant Medication: Thinking vertically

Split into 5 periods



SUBJID	TRSDT	TREDT	TRTAS
101	2013-03-19	2013-05-05	PBO
101	2013-05-05	2013-07-19	PBO
101	2013-07-19	2014-03-20	ACTDURG1
101	2014-03-20	2014-07-11	ACTDURG1
101	2014-07-11	2014-11-12	ACTDURG1

Compare CM start/end date with each period start end date.

SUBJID	APERIOD	CMDECOD	TRTAS
101	1	CMXXXXX	
101	2	CMXXXXX	PBO
101	3	CMXXXXX	ACTDURG1
101	4	CMXXXXX	ACTDURG1
101	5	CMXXXXX	

Table 14.1-8.1 (Page 1 of 8)
Concomitant medications by ATC class and preferred term

ATC class / Preferred term	Any Active Drug Dose 1 N = N1 n (%)	Any Active Drug Dose 2 N = N2 n (%)	Placebo N = N3 n (%)

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Example 2

Prior & Concomitant Medication: Sample code

Sample code:

```
data adcm_se1(where=(not missing(aperiod)));
merge  data_a.adcm(rename=(aperiod=_aperiod)) data_a.adsl;

array APST{5} AP01SDT AP02SDT AP03SDT AP04SDT AP05SDT;

do i=1 to 5;
   if not missing(APST{i}) then do;
      if _aperiod=i then FL="Y";
          if ASTDT=. or _aperiod<i then do;
             if missing(CMENDTC) then FL="Y";
                else if
CMENDTC>=substr(put(APST{i},IS8601DA.),1,length(CMENDTC)) then FL="Y";
          end;
    end;
    if FL= "Y" then do;
       aperiod=i;
       output;
    end;
end;
run;
```


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Example 3

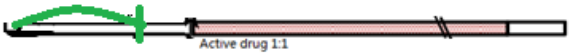
TTE dataset for AE: Basic design

Data structure: ADTTEAE

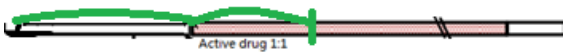
SUBJID	TRTA	PARAM	AVAL	CNSR
101	ACTDRUG1	Time to AEXXX1	498	1
102	PBO	Time to AEXXX1	8	0
102	ACTDRUG1	Time to AEXXX1	360	1
102	PBO	Time to AEXXX2	70	1
102	ACTDRUG1	Time to AEXXX2	360	1

1) Complex study design, rescue
2) We also need to generate TTE up to period 3.

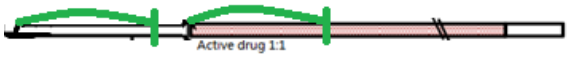
No event, Censored in PBO and active drug treatment



Event in PBO period, Censored in active drug



Event in active drug period, Censored in PBO



Event in both PBO and AIN period.

No event, discontinued in PBO period, Censored in PBO.

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Example 3

TTE dataset for AE: long table shell

		The period a subject has gone through			The period an event falls into								
SUBJID	ARM	1 and 2 (D1-W16)	3 (W16-W24)	>3 (>W24)	1 and 2 (D1-W16)	3 (W16-W24)	>3 (>W24)	CNSR (0=event, 1=no event)	TRTA	start	ADT	AVAL (time to the event)	APHASE
101	PBO	y			y			0	PBO	D1	event date	ADT - start + 1	Entire Treatment
102	PBO	y						1	PBO	D1	end of APERIOD 2	ADT - start + 1	Entire Treatment
103	PBO-PBO	y	y		y			0	PBO	D1	event date	ADT - start + 1	Entire Treatment
104	PBO-PBO	y	y			y		0	PBO	D1	event date	ADT - start + 1	Entire Treatment
105	PBO-PBO	y	y					1	PBO	D1	end of APERIOD 3	ADT - start + 1	Entire Treatment
201	PBO-XXX-XXX	y	y	y	y			0	PBO	D1	event date	ADT - start + 1	Entire Treatment
201	PBO-XXX-XXX	y	y	y	y			1	XXX	start of APERIOD 3	end of treatment	ADT - start + 1	Entire Treatment
202	PBO-XXX-XXX	y	y	y		y		1	PBO	D1	start of APERIOD 3	ADT - start	Entire Treatment
202	PBO-XXX-XXX	y	y	y		y		0	XXX	start of APERIOD 3	event date	ADT - start + 1	Entire Treatment
203	PBO-XXX-XXX	y	y	y			y	1	PBO	D1	start of APERIOD 3	ADT - start	Entire Treatment
203	PBO-XXX-XXX	y	y	y			y	0	XXX	start of APERIOD 3	event date	ADT - start + 1	Entire Treatment

Any quicker solutions?

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Example 3

TTE dataset for AE: Thinking vertically!!!

Convert ADSL to DSE type, get the duration of all periods.

SUBJID	APERIOD	TRTA	APSDT	APEDT	DUR
101	1	PBO	2012-04-25	2012-06-19	55
101	2	PBO	2012-06-19	2012-08-16	58
101	3	ACTDURG1	2012-08-16	2012-10-10	55
101	4	ACTDURG1	2012-10-10	2013-04-24	196
101	5	ACTDURG1	2013-04-24	2013-10-09	168

Remove all the period after AE happened.

SUBJID	APERIOD	TRTA	DUR
101	1	PBO	55
101	2	PBO	58
101	3	ACTDURG1	55
101	4	ACTDURG1	137

Merge the dataset with AE event by aperiod, re-generate the duration with the period with AE start date- period start date.

SUBJID	APERIOD	TRTA	APSDT	APEDT	DUR	ASTDT
101	1	PBO	2012-04-25	2012-06-19	55	
101	2	PBO	2012-06-19	2012-08-16	58	
101	3	ACTDURG1	2012-08-16	2012-10-10	55	
101	4	ACTDURG1	2012-10-10	2013-04-24	137	2013-02-24
101	5	ACTDURG1	2013-04-24	2013-10-09	168	

Add up the duration together group by TREATMENT

AEDECOD	SUBJID	TRTAG1S	totdur
AEXXXX	3007003	PBO	113
AEXXXX	3007003	XXXX1	361

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Summary

- The basic concept of thinking vertically is to convert the subject level/ occurence level dataset structure into period level BDS structure.
- This method has advantage especially when the study design is complicated.
- This method can also solve other potentials issues if needed. When you have some difficulties when thinking horizontally, then you may change your mind.

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