

Concomitant Medication Duration Calculation Using SAS® DS2 Procedure

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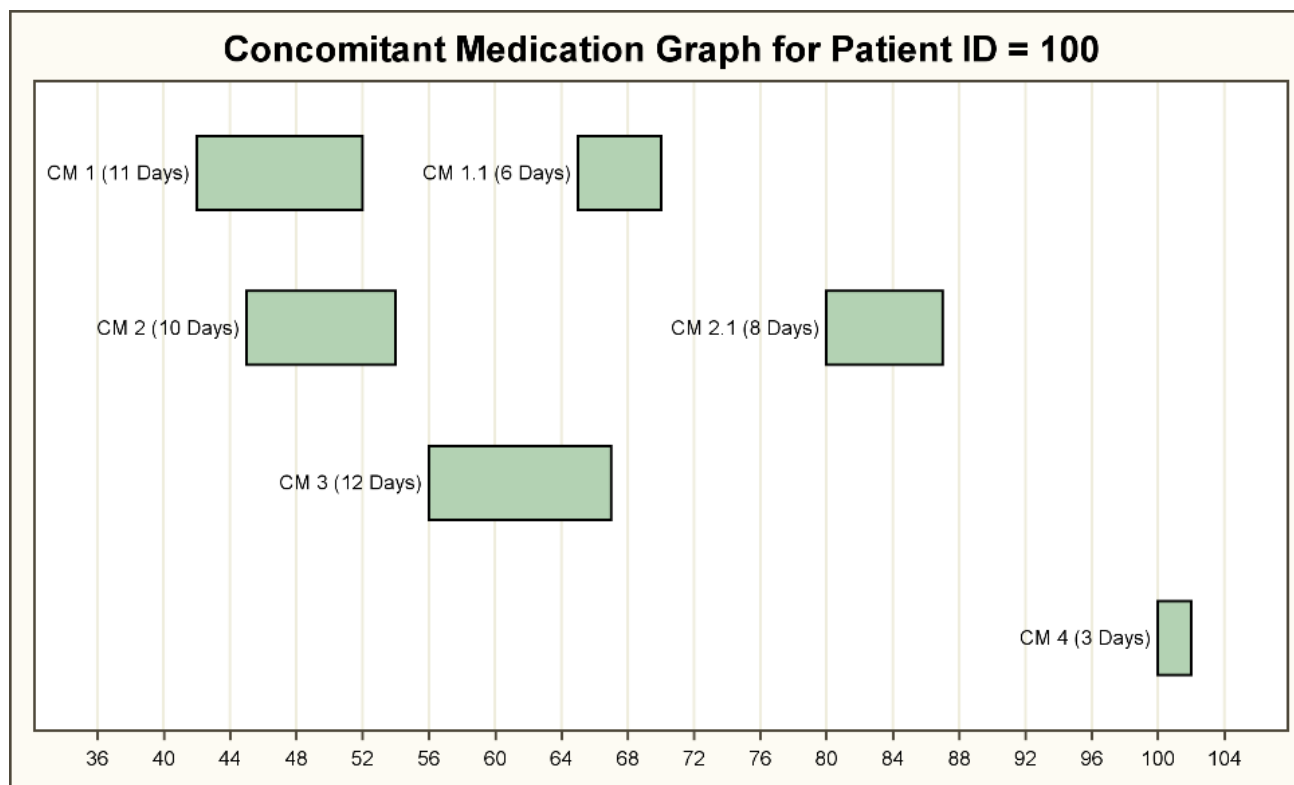
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Background

- During a clinical trial, a subject may take multiple concomitant medications (CM thereafter).
- The duration of CM has been requested by Health Technology Authority to calculate the costs and resource burden.
- Typical scenarios include sequential treatment, on and off treatment and overlapping among these treatments. This causes lots of complexity when performing the overall duration calculation.



Simulated CM Dataset and Example



	usubjid	trt	trtn	cmstdt	cmendt	refdt	cmstdy	cmendy	cmseq
1	1	Treatment	1	16MAR2001	30MAR2001	27DEC2000	80	94	1
2	1	Treatment	1	21APR2001	28APR2001	27DEC2000	116	123	1.1
3	1	Treatment	1	28MAR2001	30MAR2001	27DEC2000	92	94	2
4	1	Treatment	1	08APR2001	11APR2001	27DEC2000	103	106	2.1
5	1	Treatment	1	17APR2001	18APR2001	27DEC2000	112	113	3
6	1	Treatment	1	13MAY2001	27MAY2001	27DEC2000	138	152	4
7	2	Control	2	15FEB2001	02MAR2001	27DEC2000	51	66	1
8	2	Control	2	12MAR2001	24MAR2001	27DEC2000	76	88	1.1
9	2	Control	2	27FEB2001	01MAR2001	27DEC2000	63	65	2
10	2	Control	2	31MAR2001	07APR2001	27DEC2000	95	102	2.1
11	2	Control	2	05MAR2001	08MAR2001	27DEC2000	69	72	3
12	2	Control	2	17MAR2001	28MAR2001	27DEC2000	81	92	4
13	1	Treatment	1	06JAN2001	23JAN2001	29DEC2000	9	26	1
14	1	Treatment	1	29JAN2001	04FEB2001	29DEC2000	32	38	1.1
15	1	Treatment	1	22JAN2001	31JAN2001	29DEC2000	25	34	2
16	3	Treatment	3	06FEB2001	20FEB2001	29DEC2000	40	54	2.1
17	3	Treatment	3	31JAN2001	12FEB2001	29DEC2000	34	46	3
18	3	Treatment	3	18MAR2001	25MAR2001	29DEC2000	80	87	4

- ❑ Duration for CM 1 = 11 (day 42 to day 52) + 6 (day 65 to day 70) = 17 days
- ❑ Duration for CM 2 = 10 (day 45 to day 54) + 8 (day 80 to day 87) = 18 days
- ❑ Duration for CM 3 = 12 days (day 56 to day 67)
- ❑ Duration for CM 4 = 3 days (day 100 to day 102)
- ❑ Total duration = 17 + 18 + 12 + 3 – 8 – 3 = 39 days

SAS DS2 Procedure

Benefits:

- Re-usability and portability
- Multithreading capability
- Numerical precision
- Efficiency



Components:

- DS2 array
 - Temporary array
 - Variable array
- Multithreading
- DS2 package

DS2 Array

- DS2 array is implemented to check whether the CM Day is in any of the 6 concomitant medication sessions (the on/off medication is counted as 2 sessions).
- If yes, then duration is accumulated.

```
proc ds2;
  data cm_cal (overwrite=yes);
    retain i dur;

    vararray double cmstart[6] cmstdy1 - cmstdy6;
    vararray double cmstop[6] cmendy1 - cmendy6;

    declare double minstart maxstop cmdy i dur init;

    method run();

      set {select * from cm_horizon} ;

      minstart=min(of cmstdy:);
      maxstop=max(of cmendy:);

      dur=0;
      do cmdy=minstart to maxstop;
        i=1;
        init=0;
        do while (init=0 and i<=6);
          if (cmstart[i]<=cmdy<=cmstop[i]) then init=1;
          i+1;
        end;
        if init=1 then dur+1;
      end;

    end;
  enddata;
run;
quit;
```

Multithreading

- Multithreading has an impact on task turnaround time by determining the maximum number of threads for efficiency.
- The optimal number of threads is dependent on the number of CPU(s) factoring in the number of cores and logical processors available.
- If a thread is enclosed within a DS2 procedure, then data is dispersed across multiple processes for increased efficiency.

```
proc ds2;
  thread newcal/overwrite=yes;
    retain i dur;

    vararray double cmstart[6] cmstdy1 - cmstdy6;
    vararray double cmstop[6] cmendy1 - cmendy6;

    declare double minstart maxstop cmdy i dur init;

    method run();

      set cm_horizon;

      minstart=min(of cmstdy:);
      maxstop=max(of cmendy:);

      dur=0;
      do cmdy=minstart to maxstop;
        i=1;
        init=0;
        do while(init=0 and i<=6);
          if(cmstart[i]<=cmdy<=cmstop[i]) then init=1;
            i+1;
          end;
          if init=1 then dur+1;
        end;
      end;
    endthread;
run;
proc ds2;
  data cm_cal_method2 (overwrite=yes);
    declare thread newcal cm_horizon;
    method run();
      set from cm_horizon threads=10;
    end;
  enddata;
run;
quit;
```

DS2 Package

- The goal of DS2 package is to convert the dataset to vertical format and then remove the duplicate days.
- Based on the length of CM duration, the whole simulated dataset contains 5735 records.

Declare the package

Call the package

```
proc ds2;
    package cmv /overwrite=yes;
    method output(char(100) tablename,
                  char(100) indata);

        declare package sqlstmt stmt('create table ' || tablename || ' as
        select usubjid, count(distinct cmdy) as dur
        from ' || indata ||
        'group by usubjid');

        stmt.execute();

    end;
endpackage;
run;
quit;

proc ds2;
    data _null_;
    method init();
        declare package cmv f();
        f.output('cm_v1', 'cm_vertical');
        f.output('cm_v2', 'cm_vertical where cmseq=1 or cmseq=1.1');
        f.output('cm_v3', 'cm_vertical where cmseq=2 or cmseq=2.1');
        f.output('cm_v4', 'cm_vertical where cmseq=3');
        f.output('cm_v5', 'cm_vertical where cmseq=4');

    end;
enddata;
run;
quit;
```

Results

- The above three methods generate a subject level dataset which is used to produce a descriptive statistics table that feeds into the resource burden calculation.
- The results from each method are the same.

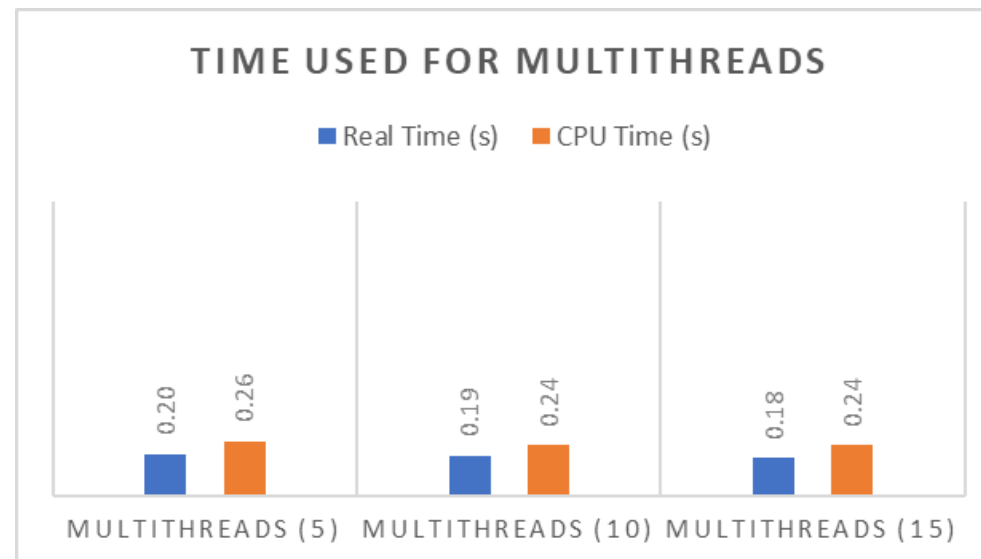
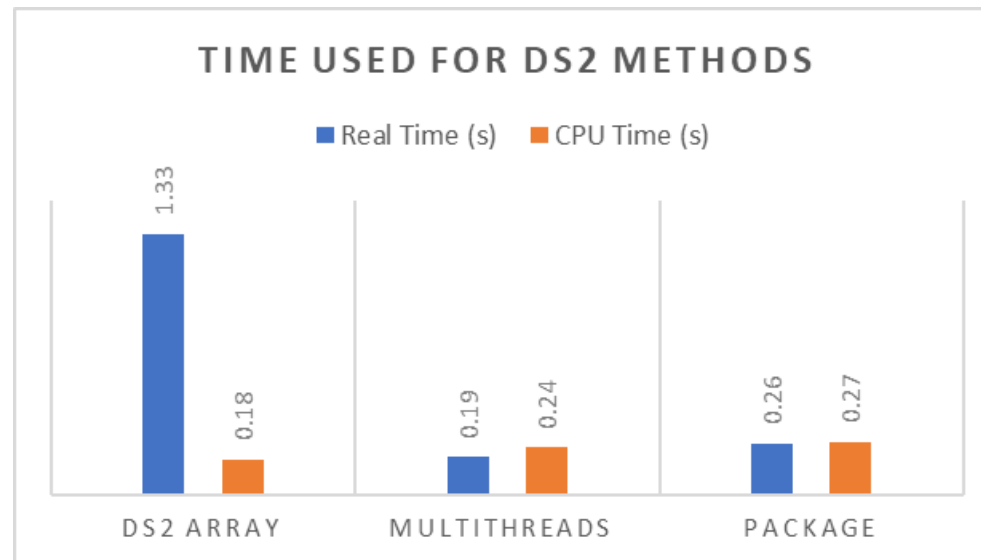
Descriptive Analysis for Concomitant Medication Duration

	N	Mean (95% CI)	s.d.
CM 1	100	17.8 (16.5, 19.1)	6.4
CM 2	100	19.4 (18.1, 20.8)	6.9
CM 3	100	8.3 (7.4, 9.1)	4.3
CM 4	100	11.8 (10.7, 13.0)	5.8
Total	100	47.1 (44.9, 49.2)	10.7

Comparison of Time Efficiency

The machine used to conduct the testing has 4 cores and 8 processors. It runs PC-SAS 9.4 TS Level 1M6 on Windows 10 Pro-64bit.

- CPU: Intel® Core™ i5-10310U @1.70GHz
- Base Speed: 2.21GHz
- Cores: 4
- Logical Processors: 8



Conclusion and Future Research



- The results obtained from three methods are identical, but they show different advantages:
 - DS2 arrays are easy to understand and can be easily executed in one step
 - Multithreading method exhibits the best time efficiency
 - DS2 packages can accommodate multiple populations in one procedure
- Future research can expand the DS2 procedure to calculate the duration of Adverse Event which encapsulates three scenarios covered.
- The DS2 procedure can also call the data from other databases such as DB2 and MySQL. In addition, it can work on the cloud based analytic platform, SAS Viya, to accelerate the processing time.

Reference

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Shostak, J. (2005). SAS® Programming in the Pharmaceutical Industry. Cary, NC: SAS Institute Inc.

Thank you

Your comments and questions are valued and encouraged. Please contact:

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