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Exploit the Window of Opportunity: Exploring the Use of Analysis Windowing Variables

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ABSTRACT

For analysis purposes, dataset records are often assigned to an analysis timepoint window rather than simply using the visits or timepoints from the collected data. The rules for analysis timepoint windows are usually defined in the Statistical Analysis Plan (SAP) and can involve complicated derivations to determine which record(s) best fulfils the analysis window requirements. For traceability, there are ADaM standard variables available to help explain how records are assigned to the analysis windows. This paper will explore these ADaM variables and provide examples on how they may be applied.

INTRODUCTION

Data for analysis is often recorded using study visits or timepoints. While study visits are usually structured to occur within certain study day ranges, issues can arise that cause a subject visit to occur outside the day range. Also, a subject may have more than one record that occurred during the visit time range. In order to standardize each subject's records, analysis timepoint windows may be used.

These analysis windows are usually defined in the Statistical Analysis Plan (SAP). The ADaM variables AVISIT/AVISITN or ATPT/ATPTN are used to document each record's assigned analysis window. Additional ADaM variables are available to document how these assignments are made and to increase traceability. Using these variables in the analysis dataset, along with the SDTM variables VISIT/VISITNUM or –TPT/--TPTNUM, help fulfil the fundamental ADaM principle of clear communication of how ADaM datasets were created.

ANALYSIS WINDOWING VARIABLES

If the analysis timepoint is determined based on special windows specified in the protocol or statistical analysis plan, then analysis windowing variables (Table 1) can be used to help explain how a timepoint is assigned to a record. The analysis windowing variables are a set of CDISC ADaM pre-defined variables that can be used whether the windowing is based on days or hours.

Variable Name	Variable Label	Type	Description
AWRANGE	Analysis Window Valid Relative Range	Char	The range of values that are valid for a given analysis timepoint.
AWTARGET	Analysis Window Target	Num	The target or most desired analysis relative day (ADY) value or analysis relative time (ARELTM) value for a given value of analysis timepoint.
AWTDIFF	Analysis Window Diff from Target	Num	Absolute difference between ADY or ARELTM and AWTARGET.
AWLO	Analysis Window Beginning Timepoint	Num	The value of the beginning timepoint (inclusive).
AWHI	Analysis Window Ending Timepoint	Num	The value of the ending timepoint (inclusive).
AWU	Analysis Window Unit	Char	Unit used for AWTARGET, AWTDIFF, AWLO and AWHI.

Table 1: CDISC ADaM Analysis Windowing Variables

If AWLO, AWHI, and AWU are used in conjunction with AWRANGE, then AWLO must be equal to the lower bound of the range. AWHI must be equal to the upper bound of the range. AWU must be equal to the units specified in the range.

It is important to note that when the analysis windowing is based on days, AWTDIFF needs to be adjusted for the fact that there is no Study Day 0 when the analysis relative day (ADY) and the analysis window target (AWTARGET) have different signs. In addition, since AWTDIFF is the absolute difference it may be necessary to use this along with ADY or analysis relative time (ARELTM) if it is important to know if the analysis timepoint occurred before or after the target timepoint when trying to select a specific record for analysis. (CDISC Analysis Data Model Team, 2021)

EXAMPLE USE CASES

Now that we have an understanding of analysis windowing variables, we turn to illustrating use cases.

WINDOWING BASED ON STUDY DAY

In this first example, we look at assigning analysis visits based on the analysis windows typically (Table 2) specified in the Statistical Analysis Plan (SAP) for the protocol specified visits (Table 3).

Analysis Visit	Range	Low	High
Screening	<= -30 DAYS		-30
Run-in	-29 to -4 DAYS	-29	-4
Week 0	-3 to 3 DAYS	-3	3
Week x	x*7 +/- 3 DAYS	x*7 - 3	x*7 + 3

Table 2: Analysis Visit Windows

Visit schedule
Screening
Run-in
Week 0
Week 2
Week 4
Week 8
Week 12

Table 3: Protocol Specified Visits

Using the sample windowing information found in Table 2, we can assign analysis visits to the following sample data (Table 4).

Row	VISIT	TRTSDT	VSDTC	ADT	ADY	AVAL
1	Screening	03MAR2023	2023-02-01	01FEB2023	-30	120
2	Screening	03MAR2023	2023-02-15	15FEB2023	-16	116
3	Week 0	03MAR2023	2023-03-01	01MAR2023	-2	114
4	***Week 2***	***03MAR2023***	***2023-03-15***	***15MAR2023***	***13***	***118***
5	***Week 2 Unscheduled***	***03MAR2023***	***2023-03-19***	***19MAR2023***	***17***	***126***
6	Week 4	03MAR2023	2023-03-25	25MAR2023	23	130
7	Week 4 Unscheduled	03MAR2023	2023-03-27	27MAR2023	25	122
8	Week 12	03MAR2023	2023-05-24	24MAY2023	83	134

Row	AWRANGE	AWTARGET	AWTDIF	AWLO	AWHI	AWU	AVISIT	ANL01FL
1	<= -30 DAYS	-30	0		-30	DAYS	Screening	Y
2	-29 to -4 DAYS	-14	2	-29	-4	DAYS	Run-in	Y
3	-3 to 3 DAYS	1	2	-3	3	DAYS	Week 0	Y
4	***11 to 17 DAYS***	***14***	***1***	***11***	***17***	***DAYS***	***Week 2***	***Y***
5	***11 to 17 DAYS***	***14***	***3***	***11***	***17***	***DAYS***	***Week 2***	
6								

Row	AWRANGE	AWTARGET	AWTDIF	AWLO	AWHI	AWU	AVISIT	ANL01FL
7	25 to 31 DAYS	28	3	25	31	DAYS	Week 4	Y
8	81 to 87 DAYS	84	1	81	87	DAYS	Week 12	Y

Table 4: Sample Data to Illustrate Windowing Based on Analysis Relative Day

Notice that for each record the analysis relative day (ADY) is compared to the different analysis windowing ranges until a match is found. If a match is found, then the corresponding analysis windowing variables (AWRANGE, AWTARGET, AWTDIFF, AWO, AWHI, and AWU) are populated accordingly as well as the analysis visit (AVISIT) variable. For example, the windowing for the Screening analysis visit is any record that has analysis day that on or prior to study day -30. Since there is no lower bound for the screening analysis visit, then AWLO is left null, but the rest of the variables are populated.

For row 3, the study day is a -2 while the analysis target day is 1. Since there is no Day 0 and these have opposite signs, when calculating the absolute difference (AWTDIFF) we have to make sure we account for no Day 0. Therefore, instead of doing a simple subtraction of ADY - AWTARGET and taking the absolute values (e.g., absolute of -2 - 1 = absolute of -3 = 3), we need to skip non-existent Day 0 (e.g., (absolute of -2 - 1) - 1 = (absolute of -2 - 1) - 1 = (absolute of -3) - 1 = 3 - 1 = 2). It is important to ensure that AWTDIFF is properly calculated since this variable is used to determine how close the record is to the target time (AWTARGET). AWTARGET can help to determine which record is used for analysis if more than one record falls within the same AVISIT, as seen on rows 4 and 5, and the analysis level flag (ANLzzFL) is used to flag the preferred record. In this example, the determining factor for selecting the correct record for analysis was the record closest to target, which is determined by AWTDIF. Note that the selection criteria will be study dependent.

In some cases, a record may be too far out of the desired analysis window and therefore the corresponding analysis window variables as well as the analysis visit variable are left null since the record cannot be assigned to a specific analysis visit as demonstrated on row 6 in Table 4.

WINDOWING BASED ON RELATIVE TIME

While the most common use of the analysis windowing variables is to aid in the assignment of AVISIT, it can be used to help assign other analysis timepoint (ATPT) as illustrated in this next example.

For this example, the record needs to be within +/- 30 minutes of the protocol indicated post dose hour (e.g., 4-hours post dose, 8-hours post dose) for each visit.

Using the sample data in Table 5 we can assign ATPT based on the derivation that is normally found in the SAP. As mentioned, previously, we are using +/- 30 minutes for this example.

Row	--TPT	EXSTDTC	EXSTDTM	ADTM	ATM	ARELTM	ARELTMU
1	4H POST	2023-03-08T09:45	08MAR2023:09:45	08MAR2023:13:50	13:50	4.0833	HOURS
2	8H POST	2023-03-08T09:45	08MAR2023:09:45	08MAR2023:17:30	17:30	7.75	HOURS
3	4H POST	2023-03-15T10:12	15MAR2023:10:12	15MAR2023:14:40	14:40	4.46667	HOURS
4	8H POST	2023-03-15T10:12	15MAR2023:10:12	15MAR2023:19:00	19:00	8.8	HOURS

Row	AWRANGE	AWTARGET	AWTDIFF	AWLO	AWHI	AWU	ATPT
1	3.5 - 4.5 HOURS	4	0.0833	3.5	4.5	HOURS	4 hr Postdose
2	7.5 - 8.5 HOURS	8	0.25	7.5	8.5	HOURS	8 hr Postdose
3	3.5 - 4.5 HOURS	4	0.46667	3.5	4.5	HOURS	4 hr Postdose
4							

Table 5: Sample Data to Illustrate Windowing Based on Analysis Relative Time Expressed as Float

The exposure start date (EXSTDTC) is the anchor date for ARELTM. Currently, there is no standard ADaM variable for the anchor date for ARELTM. EXSTDTC is converted to a numeric date format in EXSTDTM. ARELTM is the difference between the time portion of EXSTDTM and ATM expressed as a float (e.g., decimal format). AWTDIFF is the absolute difference between ARELTM and AWTARGET.

The ARELTM for each record is checked to see if it is within +/- 30 minutes 4-hours post dose or 8-hours post dose until a match is found. If a match is found, then the corresponding analysis windowing variables (AWRANGE, AWTARGET, AWTDIFF, AWO, AWHI, and AWU) are populated accordingly as well as the analysis timepoint (ATPT) variable. Because row 4 does not fall within +/- 30 minutes of the 4-hour or 8-hour post dose windows, the analysis window variables and ATPT are left null.

In this example, the values are displayed in decimal format. In other words, 30 minutes is 0.5 of an hour so the AWLO for 4-hours post dose is represented as 3.5 and AWHI is represented as 4.5. The target time is represented as an integer. Therefore, the difference between the exposure datetime and the ARELTM is also represented as a decimal (e.g., 5 minutes is 5 / 60 = 0.0833).

Table 6 illustrates an alternative way to display the analysis window variables as well as ARELTM. Instead of displaying the values as floats, the values can be displayed in a time format.

Row	--TPT	EXSTDTC	EXSTDT	ADTM	ATM	ARELTM	ARELTMU
1	4H POST	2023-03-08T09:45	08MAR2023:09:45	08MAR2023:13:50	13:50	4:05	HOURS
2	8H POST	2023-03-08T09:45	08MAR2023:09:45	08MAR2023:17:30	17:30	7:45	HOURS
3	4H POST	2023-03-15T10:12	15MAR2023:10:12	15MAR2023:14:40	14:40	4:28	HOURS
4	8H POST	2023-03-15T10:12	15MAR2023:10:12	15MAR2023:19:00	19:00	8:48	HOURS

Row	AWRANGE	AWTARGET	AWTDIFF	AWLO	AWHI	AWU	ATPT
1	3:30 – 4:30 HOURS	4:00	0:05	3:30	4:30	HOURS	4 hr Postdose
2	7:30 – 8:30 HOURS	8:00	0:15	7:30	8:30	HOURS	8 hr Postdose
3	3:30 – 4:30 HOURS	4:00	0:28	3:30	4:30	HOURS	4 hr Postdose
4							

Table 6: Sample Data to Illustrate Windowing Based on Analysis Relative Time Expressed as Time

CONCLUSION

To assist review, ADaM datasets and metadata must clearly communicate how the ADaM datasets were created. Using the analysis visit windowing variables is a standard method to document how analysis windows are assigned.

REFERENCES

CDISC Analysis Data Model Team. (2021, November). Analysis Data Model Implementation Guide v1.3. CDISC. Retrieved from https://www.cdisc.org/standards/foundational/adam

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