
Compliance Report for Patient-Reported Outcomes

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Outline

- Background
- Reasons for missing data
- ADaM and programming design to support analysis
- Sample Report to display compliance and completion rates by Time Point
- Summary

Background

- Patient-Reported Outcomes (PRO) are becoming an important component in the evaluation of prescription drugs in registration, reimbursement and labeling claims.
- In addition to the classical outcomes, such as tumor control and survival, cancer trials should also evaluate the effect of a treatment on a patient's quality of life.

Background

- One of the major concerns about PRO analysis is missing data.
- Missing data leads to decrease in precision and power caused by the reduction in data, and the potential for bias in analysis
- Compliance report is used to monitor the missing data by time point to determine the time point used in analysis

Reasons for Missing Data

- Sites will collect missing mode on patient visits
- Sites may not have the information (ex: treatment discontinuation etc.)
- PRO data is provided by external vendor and has not yet transferred or reconciled
- The data may not be synced up at the time of database lock or cutoff time

Reasons for Missing Data

Examples of pre-specified reasons for missing data

- Not completed due to site staff error
- Subject in hospital or hospice
- Subject was physically unable to complete
- Translation not available in subjects language
- Subject refused for other reasons

Reasons for Missing Data

Examples of treatment discontinuation reasons to use if missing reason is not provided by vendor on a given time point

- Adverse event
- Clinical progression
- Physician decision
- Withdraw by subject

Reasons for Missing Data

Derived missing reason if the reason cannot be obtained from vendor or the treatment disposition status.

Reasons for Missing Data

Subject died

- At the time of death, the information was not entered in disposition status yet

Reasons for Missing Data

With Visit, No Record

- The visit is already in SV domain but vendor data has not been transferred yet

Reasons for Missing Data

Visit not scheduled

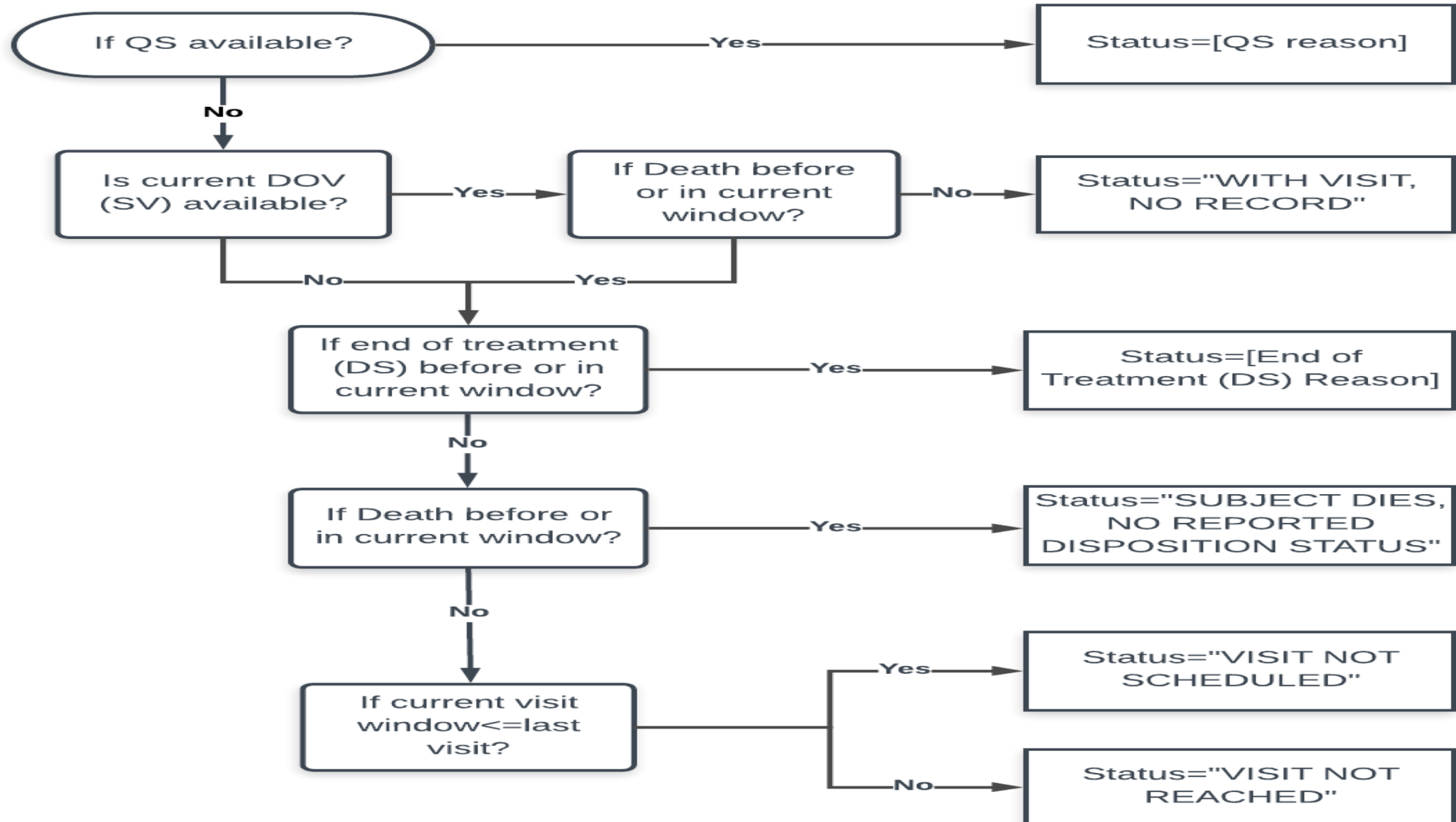
- In the defined windows, there is no scheduled visit nor PRO data

Reasons for Missing Data

Visit not reached

- In the defined windows, the subject has not reached the visit yet

Reasons for Missing Data



ADaM and Programming Design

ADaM Structure

- BDS – Basic Data Structure
- BDS variables – PARAMCD, PARAM, PARAMTYP, PARCATy, ADT, ADY, AVISIT, AVISITN, AWTARGET, AWRANGE, AWLO, AWHI, AWU, AVAL, AVALC, AVALCAT1, ANL01FL, SRCXXX...

ADaM and Programming Design

Window based variables and use of SAS format

```
proc format;  
  invalue avisitn  
    low-1  =1  
    2-10   =2  
    11-20  =3  
    21-30  =4  
    31-high=999;  
  
  value avisit  
    low-1="BASELINE"  
    2-10="WEEK 3"  
    11-20="WEEK 6"  
    21-30="WEEK 9"  
    31-high="OutofFlow";  
  
run;
```

Analysis visits AVISIT variable are often required. To ensure the analysis window derivation are flexible and consistent across the study, we recommend using format for the derivation.

avisit=put(ady, avisit.) or

avisitn=input(ady, avisitn),

similar logic can be applied to AVAL and AVALC;

ADaM and Programming Design

Variable Name	Variable Label	Type	Define Derivation
PARAM	Parameter	Char	QS.QSTEST For derived records, please refer to analysis plan for detail logics.
PARAMCD	Parameter Code	Char	QS.QSTESTCD For derived records, please refer to analysis plan for detail logics.
PARCAT1	Parameter Category 1	Char	QS.QSCAT
PARAMTYP	Parameter Type	Char	DERIVED' for derived compliance records
AVISIT	Analysis Visit	Char	Avisit represents the analysis visit for the record. Using ADY, low-1="BASELINE" 2-10="WEEK 3" 11-20="WEEK 6" 21-30="WEEK 9" 31-high="OutofFlow";
ADY	Analysis Relative Day	Num	Example derivation: ADT-ADSL.TRTSDT + 1 if ADT >= TRTSDT, else ADT-ADSL.TRTSDT if ADT < TRTSDT
AVALC	Analysis Value (C)	Char	QS.QSSTRESC For PARAMTYP ='DERIVED' compliance records, please refer to analysis plan for detail logics.
AVAL	Analysis Value	Num	Numeric representation of AVALC
AVALCAT1	Analysis Category 1	Char	Example Derivation: if AVAL = 1 then AVALCAT1 = 'Missing by design' if AVAL = 2 then AVALCAT1 = 'Expected to complete Questionnaires'

ADaM and Programming Design

SRCXXX variables such as SRCDOM, SRCVAR and SRCSEQ can be utilized in the analysis dataset for traceability

Variable Name	Variable Label	Type	Define Derivation
SRCDOM	Source Domain	Char	Example Derivation: For PARAMTYP ='DERIVED', if QS missing reason is used then SRCDOM='QS'; if DS end of treatment reason is used then SRCDOM='DS';
SRCVAR	Source Variable	Char	Example Derivation: For PARAMTYP ='DERIVED', if QS missing reason is used then SRCVAR='QSSTRESC'; if DS end of treatment reason is used then SRCVAR='DSDECOD';
SRCSEQ	Source Sequence Number	Num	Example Derivation: For PARAMTYP ='DERIVED', if QS missing reason is used then SRCSEQ=QSSEQ; if DS end of treatment reason is used then SRCSEQ=DSSEQ;

ADaM and Programming Design

With Visit, No Record

USUBJID	PARAMCD	PARAMTYP	AVISIT	AVALC	AVALCAT1	SRCDOM	SRCVAR
2222	QUECOMP	DERIVED	WEEK 36	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC
2222	QUECOMP	DERIVED	WEEK 45	WITH VISIT, NO RECORD	Expected to Complete Questionnaires		
2222	QUECOMP	DERIVED	WEEK 54	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 66	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 78	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 90	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 102	VISIT NOT REACHED	Missing by Design		

ADaM and Programming Design

Visit not scheduled

USUBJID	PARAMCD	PARAMTYP	AVISIT	AVALC	AVALCAT1	SRCDOM	SRCVAR
3333	QUECOMP	DERIVED	BASELINE	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC
3333	QUECOMP	DERIVED	WEEK 3	VISIT NOT SCHEDULED	Missing by Design		
3333	QUECOMP	DERIVED	WEEK 6	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC

ADaM and Programming Design

Visit not reached

USUBJID	PARAMCD	PARAMTYP	AVISIT	AVALC	AVALCAT1	SRCDOM	SRCVAR
2222	QUECOMP	DERIVED	WEEK 36	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC
2222	QUECOMP	DERIVED	WEEK 45	WITH VISIT, NO RECORD	Expected to Complete Questionnaires		
2222	QUECOMP	DERIVED	WEEK 54	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 66	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 78	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 90	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 102	VISIT NOT REACHED	Missing by Design		

ADaM and Programming Design

Usage of AVALCAT1:

- **Missing by Design:** reasons include but not limited to subject discontinued treatment, subject did not reach or schedule the visits, or subject has died.
- **Expected to complete Questionnaires:** reasons when subject is unable to fill out the form for another reason or vendor data has not been transferred or obtained. This category also includes subjects who completed the questionnaires.

ADaM and Programming Design

Missing by Design

USUBJID	PARAMCD	PARAMTYP	AVISIT	AVALC	AVALCAT1	SRCDOM	SRCVAR
2222	QUECOMP	DERIVED	WEEK 36	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC
2222	QUECOMP	DERIVED	WEEK 45	WITH VISIT, NO RECORD	Expected to Complete Questionnaires		
2222	QUECOMP	DERIVED	WEEK 54	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 66	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 78	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 90	VISIT NOT REACHED	Missing by Design		
2222	QUECOMP	DERIVED	WEEK 102	VISIT NOT REACHED	Missing by Design		

ADaM and Programming Design

Expected to Complete Questionnaires

USUBJID	PARAMCD	PARAMTYP	AVISIT	AVALC	AVALCAT1	SRCDOM	SRCVAR
3333	QUECOMP	DERIVED	BASELINE	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC
3333	QUECOMP	DERIVED	WEEK 3	VISIT NOT SCHEDULED	Missing by Design		
3333	QUECOMP	DERIVED	WEEK 6	COMPLETED	Expected to Complete Questionnaires	QS	QSSTRESC

Sample Report

Compliance Rate vs. Completion Rate

$$\begin{aligned} &\textit{Completion Rate} \\ = &\frac{\textit{Number of Subjects who Complete at least one Item}}{\textit{Number of Subjects in the population}} \end{aligned}$$

$$\begin{aligned} &\textit{Compliance Rate} \\ = &\frac{\textit{Number of Subjects who Complete at least one Item}}{\textit{Number of Eligible Subjects who are Expected to Complete}} \end{aligned}$$

Sample Report

Treatment Visit	Category	Treatment A		Treatment B	
		N = 50		N = 42	
		n	(%)	n	(%)
Week 6	Missing by design	8	(16.0)	29	(69.1)
	Discontinued due to adverse event	2	(4.0)	16	(38.1)
	Discontinued due to clinical progression	2	(4.0)	11	(26.2)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to withdraw by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	2	(4.0)	1	(2.4)
	Visit not scheduled	2	(4.0)	1	(2.4)
	Visit not reached	0	(0.0)	0	(0.0)
	Subject died, no reported disposition status	0	(0.0)	0	(0.0)
	Expected to complete questionnaires	42	(84.0)	13	(30.9)
	Not completed	2	(4.0)	2	(4.8)
	Subject in hospital or hospice	1	(2.0)	0	(0.0)
	Subject refused for other reasons	1	(2.0)	2	(4.8)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	With visit no record	0	(0.0)	0	(0.0)
	Completed	40	(80.0)	11	(26.2)
	Compliance (completed per protocol)*	40	(95.2)	11	(84.6)

* Compliance is the proportion of subjects who completed the PRO questionnaire among these who are expected to complete at each time point, excluding these missing by design.

Sample Report

The PRO compliance tables are counts by treatment visit with the reasons mentioned above.

Two categories are displayed, missing by design and expected to complete questionnaires.

Based on the table, we can calculate the compliance and completion rate by visit to assess the effect and reliability of PRO analysis.

Summary



To provide a meaningful PRO analysis:

1. Understand the reasons of missing data.
2. Lay out examples of some missing reasons
3. Utilize CDISC ADaM Basic Data structure and variables for compliance report to monitor the missing data.

Other Considerations

Whether to include questionnaire response and compliance in the same analysis dataset, or separate into different analysis datasets, should be decided by the company standard or study team. It is important to discuss and decide the logic based on the study PRO analysis design and data collection to ensure report accuracy and reduce bias. All questionnaire missing reasons and analysis window rules should be documented in the define document.



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