PharmaSUG 2015 – Paper DS09

ADaM Example for a Complex Efficacy Analysis Dataset

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ABSTRACT

This paper walks through a complex analysis need and an ADaM solution. The analysis need involved summarizing both pain data and pain medications data across multiple time points. Our methodology was to first understand our analysis need, and then determine whether we could use ADaM structures to get us there, while always following the ADaM fundamental principles. The design work was a joint effort of the study lead statistician, CRO study statistician, and an ADaM consultant. Our solution made use of interim ADaM BDS datasets to collect and consolidate the data from each SDTM domain before combining into the ADaM dataset actually used for analysis. These interim datasets provided traceability between the SDTM datasets and the ADaM dataset used for analysis, and were also instrumental for data review and listing generation.

INTRODUCTION

The analyses required consolidation of collected pain data and pain medication (opioid) data by time point, as shown in this table mock-up:

Table XX.XX.XX

Proportion of Subjects with Adequate Pain and Opioid Data by Time Point

Population: [POP]

	Treatment (N=x)			[Control] (N=x)			Total (N=x)		
Time-Point	Adequate Pain Data[a]	Adequate Opioid Data[b]	Adequate Pain and Opioid Data[c]	Adequate Pain Data[a]	Adequate Opioid Data[b]	Adequate Pain and Opioid Data[c]	Adequate Pain Data[a]	Adequate Opioid Data[b]	Adequate Pain and Opioid Data[c]
Run-In	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Week 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Week 6	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Week 12	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Run-In,Week 6 and 12	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Run-In, Week 3, 6 and 12	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

[a]Adequate pain data = non-missing pain score data for 4 of 7 days within a time point

[b]Adequate Opioid data = non-missing Opioid data for 4 of 7 days within a time point

[c]Adequate pain and Opioid data = non-missing pain score and Opioid data for 4 of 7 days within a time point; data need not be from consecutive days, and dates for Opioid data and pain score data do not need to be the same.

Figure 1: Layout of Primary Efficacy Analysis Results

As described in the table footnotes, to be considered evaluable for the baseline (“Run-In”) week, a subject had to have a minimum number of days of collected data. Pain data was easier to summarize than pain medication data, because medications needed summarization also by type of medication.

In order to transition from SDTM data, structured as one row per subject per test or medication per day, into something that could be plugged into analysis procedures to generate the numbers on this table, we expected we would need some sort of an interim step. We initially focused on following the fundamental principles of ADaM: ensuring the analysis data datasets would facilitate clear and unambiguous communication, provide traceability, and be readily useable by commonly available software tools. After a structure for each dataset was determined, we evaluated to determine if we could make any of them compliant with an ADaM structure, such as BDS.

PAIN DATA

Pain data were collected at screening, week 3, week 6 and every six weeks thereafter. During each reporting week, data was collected for 7 consecutive days and tabulated in the SDTM QS domain. For this analysis, we were interested in two of the daily questions from the pain questionnaire: the worst pain in the past 24 hours (BPI #3), and the average pain in the past 24 hours (BPI #5):

STUDYID	USUBJID	QSTESTCD	QSTEST	QSORRES	VISIT	QSDTC	QSDY	QSTPTNUM
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	2	SCREENING	2012-09-06	-7	1
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	6	SCREENING	2012-09-07	-6	2
STUDYA	S1	PAINAV24	BPI #3 Worst Pain in Last 24 Hrs	2	SCREENING	2012-09-08	-5	3
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	6	SCREENING	2012-09-09	-4	4
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	3	SCREENING	2012-09-10	-3	5
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	6	SCREENING	2012-09-11	-2	6
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	2	SCREENING	2012-09-12	-1	7

Figure 2: Layout of Pain Data for BPI #3 Question

STUDYID	USUBJID	QSTESTCD	QSTEST	QSORRES	VISIT	QSDTC	QSDY	QSTPTNUM
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	2	SCREENING	2012-09-06	-7	1
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	2	SCREENING	2012-09-06	-6	2
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	2	SCREENING	2012-09-08	-5	3
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	3	SCREENING	2012-09-09	-4	4
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	3	SCREENING	2012-09-10	-3	5
STUDYA	S1	PAINAV24	BPI #5 Avg Pain in Last 24 Hrs	2	SCREENING	2012-09-11	-2	6
STUDYA	S1	PAINWO24	BPI #3 Worst Pain in Last 24 Hrs	2	SCREENING	2012-09-12	-1	7

Figure 3: Layout of Pain Data for BPI #5 Question

Note that VISIT is used to capture the week, and QSTPTNUM is the day of the week.

ADPAIN INTERIM DATASET VARIABLES

As we walk through dataset specifications for selected variables of this interim BDS dataset, note that we needed only two daily tests from the SDTM QS domain: QSTESTCDs of “PAINWO24” (worst pain in the past 24 hours) and “PAINAV24” (average pain in the past 24 hours).

We transposed the data for these two tests, so that each of these results for the 7 days in the week became a supportive column (BPIDAY1-BPIDAY7), using QSTPTNUM as the one-digit day. This suite of seven variables gave us traceability back to SDTM, plus supported statistical review and listing generation. Group ID, visit, and date variables were also included to provide traceability.

Because we are using two different scores from SDTM, after the transpose we had 2 rows for each weekly visit. We defined parameter codes of BPI3AVG for the worst daily pain, and BPI5AVG for the average daily pain.

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
STUDYID	ALL	Study Identifier	QS.STUDYID
USUBJID	ALL	Unique Subject Identifier	QS.USUBJID
ASTDT	PBPI3AVG PBPI5AVG	Analysis Start Date	For every visit, QS.QSDTC where QS.QSTPT is the earliest under the same visit.
AENDT	PBPI3AVG PBPI5AVG	Analysis End Date	For every visit, QS.QSDTC where QS.QSTPT is the latest under the same visit.
AVISIT	ALL	Analysis Visit	QS.VISIT where the record is derived from, except where VISIT = 'SCREENING" then set to "RUN-IN"
AVISITN	ALL	Analysis Visit (N)	QS.VISITNUM where the record is derived from
PARAM	PBPI3AVG PBPI5AVG	Parameter	BPI #3 Worst Pain Last 24 h - Averaged BPI #5 Avg Pain Last 24 h - Averaged
PARAMCD	PBPI3AVG PBPI5AVG	Parameter Code	PBPI3AVG PBPI5AVG
QSGRPID	ALL	Group ID	QS.QSGRPID
BPIDAY1	PBPI3AVG PBPI5AVG	BPI Score Day 1	Set QS.QSSTRESN where QS.QSTPTNUM = 1 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY2	PBPI3AVG PBPI5AVG	BPI Score Day 2	Set QS.QSSTRESN where QS.QSTPTNUM = 2 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY3	PBPI3AVG PBPI5AVG	BPI Score Day 3	Set QS.QSSTRESN where QS.QSTPTNUM = 3 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY4	PBPI3AVG PBPI5AVG	BPI Score Day 4	Set QS.QSSTRESN where QS.QSTPTNUM = 4 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY5	PBPI3AVG PBPI5AVG	BPI Score Day 5	Set QS.QSSTRESN where QS.QSTPTNUM = 5 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY6	PBPI3AVG PBPI5AVG	BPI Score Day 6	Set QS.QSSTRESN where QS.QSTPTNUM = 6 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"
BPIDAY7	PBPI3AVG PBPI5AVG	BPI Score Day 7	Set QS.QSSTRESN where QS.QSTPTNUM = 7 within each AVISIT For PBPI3AVG use QSTESTCD = "PAINWO24" For PBPI5AVG use QSTESTCD = "PAINAV24"

Figure 4: ADPAIN Interim Dataset Variables - Set 1

For this daily data, we derived a weekly AVAL by averaging the BPIDAY1-BPIDAY7 columns that were transposed. We also derived an additional variable, PNRECS to count the number of days that a pain evaluation was recorded. PNRECS is not specified in the ADaMIG, but is included in the dataset to help with traceability, data review, and listing generation.

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
AVAL	PBPI3AVG PBPI5AVG	Analysis Value	Set to the average of (BPIDAY1-BPIDAY7)
PNRECS	PBPI3AVG PBPI5AVG	Total Days Pain Recorded	Count the number of days (BPIDAY 1 through 7). Do not include missing records/values in the count.

Figure 5: ADPAIN Interim Dataset Variables - Set 2

In addition to the daily data above, we also brought in weekly collected data, copying the test result directly to AVAL:

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
AVAL	PAINBPI3	Analysis Value	QS.QSSTRESN where QS.QSTESTCD=PAINWO7D
AVAL	PAINBPI5	Analysis Value	QS.QSSTRESN where QS.QSTESTCD=PAINAV7D

Figure 6: ADPAIN Interim Dataset Variables - Set 3

With AVAL defined for each parameter, we were able to derive additional standard variables specified in the ADaM BDS structure:

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
BASE	ALL	Baseline Value	Set to AVAL where VISIT = 'RUN-IN"
CHG	ALL	Change from Baseline	AVAL - BASE *should be missing for AVISIT = RUN-IN and any visit prior (not applicable currently)*
PCHG	ALL	Percent Change from Baseline	100*(AVAL - BASE) / BASE *should be missing for AVISIT = RUN-IN and any visit prior (not applicable currently)* *Set to missing if BASE = 0.*

Figure 7: ADPAIN Interim Dataset Variables - Set 4

This ADPAIN interim dataset follows the BDS structure (one record per subject, parameter, and timepoint). Although it includes a handful of variables that aren't technically BDS, including BPIDAY1-BPIDAY7 which were derived by transposing the SDTM QS data, these are useful for traceability. ADPAIN also follows the ADaM fundamental principles, in that it provides clear and unambiguous communication, provides traceability of the data's lineage, is readily useable with common tools, is associated with metadata, and is ready for use for listings.

ADPAIN INTERIM DATASET USES

The ADPAIN dataset starts to summarize the collected pain data. It serves multiple purposes. Not only does it provide traceability from the SDTM questionnaire data to the actual analysis dataset used to create the table, it also helps with statistical review and generation of listings.

USUBJID	AVISIT	PARAMCD	D1	D2	D3	D4	D5	D6	D7	PNRECS	BASE	AVAL	CHG	PCHG	CRIT4	CRIT4FL
S1	RUN-IN	PBPI3AVG	5	6	5	5	5	5	6	7		5.3	.	.	Adequate Pain Assessment	Y
S1	WEEK 3	PBPI3AVG	.	6	6	6	5	6	6	6	5.3	5.8	0.5	10.4	Adequate Pain Assessment	Y
S1	WEEK 6	PBPI3AVG	2	2	2	2	2	2	3	7	5.3	2.1	-3.1	-59.5	Adequate Pain Assessment	Y
S1	WEEK 12	PBPI3AVG	3	6	3	3	3	3	.	6	5.3	3.5	-1.8	-33.8	Adequate Pain Assessment	Y
S1	RUN-IN	PBPI5AVG	2	2	2	3	3	2	2	7	2.3	2.3	.	.	Adequate Pain Assessment	Y
S1	WEEK 3	PBPI5AVG	.	2	3	2	2	3	3	6	2.3	2.5	0.2	9.4	Adequate Pain Assessment	Y
S1	WEEK 6	PBPI5AVG	1	1	1	1	1	1	1	7	2.3	1.0	-1.3	-56.3	Adequate Pain Assessment	Y
S1	WEEK 12	PBPI5AVG	2	3	2	2	2	2	.	6	2.3	2.2	-0.1	-5.2	Adequate Pain Assessment	Y

Figure 8: ADPAIN Listing

PAIN MEDICATIONS (OPIOIDS) DATA

Pain medication data was collected at Run-In (baseline), Week 3, Week 6 and every six weeks thereafter. During each reporting week, data was collected for 7 consecutive days. In addition to the medication name, total daily dose, dose units, dose route (oral, topical, etc.), dosage form (tablet, patch, solution etc.), and opioid formulation (Immediate Release, Sustained Release) were also collected. This data was stored in SDTM CM and SUPPCM. For any reporting period to be eligible for analyses, the subject had to have reported the opioid for at least 4 of the 7 days.

Here is an example of some pain data from SDTM CM:

STUDYID	USUBJID	CMDECOD	CMDOSE	CMDOSU	CMDOSFRM	CMDOSTOT	CMROUTE	VISIT	CMSTDTC	CMSTDY	CMSTTPT
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/6/2012	-7	DAY 1
STUDYA	S1	OP-XYZ	5	mg	TABLET	5	ORAL	SCREENING	9/6/2012	-7	DAY 1
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/7/2012	-6	DAY 2
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/7/2012	-6	DAY 2
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/8/2012	-5	DAY 3
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/8/2012	-5	DAY 3
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/9/2012	-4	DAY 4
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/9/2012	-4	DAY 4
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/10/2012	-3	DAY 5
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/10/2012	-3	DAY 5
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/11/2012	-2	DAY 6
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/11/2012	-2	DAY 6
STUDYA	S1	OP-XYZ	10	mg	TABLET	20	ORAL	SCREENING	9/12/2012	-1	DAY 7
STUDYA	S1	OP-XYZ	5	mg	TABLET	0	ORAL	SCREENING	9/12/2012	-1	DAY 7

Figure 9: Layout of Pain Medication (Opioid) Data

Note that VISIT is used to capture the week, and CMSTTPT is the day of the week.

ADOPIO INTERIM DATASET VARIABLES

The pain medication data was complex in structure and the analyses more complicated than the pain data described above. We'll now walk through dataset specifications for selected variables of the interim BDS dataset used for this pain medication data.

Similar to the interim pain dataset described above, for each reporting period we first transposed the daily total dose the subject took of each of the opioids. In this way, the results for the 7 days in the reporting week became a supportive column (ADOSDAY1-ADOSDAY7), using CMSTTPT as the day identifier. This suite of seven variables helped give us traceability back to SDTM, plus supported statistical review and listing generation. Group ID, visit, and date variables also provide traceability. These records are indicated in the figure below by DTYPE=TRANSPOSE.

Each PARAM was established for these records by combining the opioid name with the route it was taken by, example 'Oxycodone (oral)', 'Fentanyl (oral)', 'Fentanyl (patch)'. In the figure below, these are indicated with generic name MEDPARAM. The intent of this step was to retain all details (route, dose unit, formulation etc.) of the opioids taken and recorded on the CRF.

For each time point the next step was to summarize the total dose of the opioid/s taken by each PARAM. Following ADaM BDS, these new summary records within each parameter were indicated with a DTYPE=SUMMARY. This summarization facilitated collapsing records where a subject could take the same medication in 2 different dose strengths (Oxycodone-oral 5mg and 10 mg).

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
STUDYID	ALL	Study Identifier	CM.STUDYID or PM.STUDYID
USUBJID	ALL	Unique Subject Identifier	CM.USUBJID or PM.USUBJID
DTYPE	MEDPARAM	Derivation Type	There are two DTYPES within each medication parameter a) DTYPE = TRANSPOSE: These are the records that present the transpose of the total daily dose (CMDOSTOT) by PARAM b) DTYPE = SUMMARY These are the records created to summarize the doses of each PARAM
AVISIT	MEDPARAM	Analysis Visit	Where DTYPE = TRANSPOSE: CM.VISIT(s) from the transposed records Where DTYPE = SUMMARY set equal to the AVISIT summarized Note for all, SCREENING in the SDTM data should be changed to "RUN-IN". Do not summarize visits where CM.VISIT is missing or contains the word "DAY".
AVISITN	ALL	Analysis Visit (N)	Assign according to AVISIT. (1 = SCREENING, 60 = WEEK 6, 120 = WEEK 12, etc.)
ASTDT	MEDPARAM - Where DTYPE = TRANSPOSE	Analysis Start Date	For each MEDPARAM (DTYPE = TRANSPOSE) take the first CM.CMSTDTC where CM.CMDOSTOT **>=** 0
AENDT	MEDPARAM - Where DTYPE = TRANSPOSE	Analysis End Date	For each MEDPARAM (DTYPE = TRANSPOSE) take the last CM.CMENDTC where CM.CMDOSTOT **>=** 0
ADOSDAY2	MEDPARAM	Dose on Day 2	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 12 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY2 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)
ADOSDAY3	MEDPARAM	Dose on Day 3	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 3 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY3 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)
ADOSDAY4	MEDPARAM	Dose on Day 4	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 4 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY4 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)
ADOSDAY5	MEDPARAM	Dose on Day 5	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 5 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY5 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)
ADOSDAY6	MEDPARAM	Dose on Day 6	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 6 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY6 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)\
ADOSDAY7	MEDPARAM	Dose on Day 7	1. Where DTYPE = TRANSPOSE set to: CM.CMDOSTOT where CM.CMSTTPT = DAY 7 2. Where DTYPE = SUMMARY set to: sum of ADOSDAY7 from records within AVISIT from #1 above (DTYPE = TRANSPOSE)

Figure 10: ADOPIO Interim Dataset Variables – Set 1

Similar to the ADPAIN datasets, for each reporting period for all records with DTYPE=TRANSPOSE we derived AVAL which summed all the doses in columns ADOSDAY1-ADOSDAY7.

In addition, the average over ADOSDAY1-ADOSDAY7 was taken for DTYPE=SUMMARY.

We also derived variable OPNRECS to check that the subject had valid observations recorded for at least 4 of the 7 days. This check was done over all days and all opioids (PARAMs) taken during that reporting week. For example if the subject took Oxycodone on Mon-Tues and Fentanyl on Thurs-Fri, this subject was considered as having valid data for that time point. This was therefore summarized in a row by itself with PARAM='All meds this visit'.

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
AVAL	MEDPARAM	Analysis Value	Where DTYPE is TRANSPOSE, AVAL = sum(ADOSDAY1 through ADOSDAY7) Where DTYPE is SUMMARY then AVAL = mean(ADOSDAY1 through ADOSDAY)
OPNRECS	ALLMD	Days Opioid Medication Reported	For each day (ADOSDAY1 through ADOSDAY7) among all MEDPARAMS within the VISIT where DTYPE = TRANSPOSE summarize the number of days where there are no missing values in all records. For example, if patient has two TRANSPOSE within a parameter, and is missing Day 1 for the first CMSPID within the paramter and Day 5 for the second CMSPID within the parameter, then this patient would only have 5 days of non-missing, complete medication reported. However, if a patient has one DTYPE =TRANSPOSE where the entire row is missing then set OPNRECS equal to 0.

Figure 11: ADOPIO Interim Dataset Variables – Set 2

With AVAL defined, we were able to derive additional standard variables specified in the ADaM BDS structure.

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
BASE	DEFAULT	Baseline Value	Set to AVAL for all values where ABLFL = Y. *(Note this should only be populated for DTYPE= SUMMARY) or where PARAMCD = MEDPARAM-MEU or ALLMDMEU* *Do NOT Set to missing for RUN-IN visits.*
CHG	DEFAULT	Change from Baseline	AVAL - BASE should be missing for RUN-IN visits

Figure 12: ADOPIO Interim Dataset Variables – Set 1

ADOPIOID INTERIM DATASET USES

The ADOPIO dataset serves multiple purposes. Not only does it provide traceability from the SDTM questionnaire data to the actual analysis dataset used to create the table, it also helps with statistical review and generation of listings.

SUBJID	DTYPE	AVISIT	PARAM	ADOS DAY1	ADOS DAY2	ADOS DAY3	ADOS DAY4	ADOS DAY5	ADOS DAY6	ADOS DAY7	OPNRECS	AVAL
S1	TRANSPOSE	RUN-IN	Oxycodone (oral)	20	20	20	20	20	20	20		140
S1	TRANSPOSE	RUN-IN	Oxycodone (oral)	5	0	0	0	0	0	0		5
S1	SUMMARY	RUN-IN	Oxycodone (oral)	25	20	20	20	20	20	20		20.7
S1	TRANSPOSE	RUN-IN	Fentanyl (oral)	10	10	10	10	10	10	10		70
S1	TRANSPOSE	RUN-IN	Fentanyl (oral)	5	5	5	5	5	5	5		35
S1	SUMMARY	RUN-IN	Fentanyl (oral)	15	15	15	15	15	15	15		15
S1			All meds this visit	.	.	.	.	.	.	.	7	.

Figure 13: ADOPIO Listing

FINAL ANALYSIS DATASET

Although ADPAIN and ADOPIO described above were useful for statistical review and listings, they were not analysis-ready for the actual summary table shown in Figure 1. Instead, a one record per subject data set called ADEFF was developed to derive the variables needed for the efficacy statistical analyses. The criteria flags derived in the above two data sets ADPAIN and ADOPIO served as a basis for deriving other complex flags/variables in ADEFF. For the variables derived in ADEFF, multiple criteria flags from multiple time points in both ADPAIN and ADOPIO had to be checked.

We have presented some of the ADEFF variable descriptions below:

Variable Name	Parameter Identifier	Variable Label	Source / Derivation
ADR612FL		Adequate Run-in Week 6 Week12 Flag	Set to Y if a patient meets ALL the following criteria: a) ADOPIO: CRIT1FL eq Y for PARAMCD = ALLMD where AVISIT = RUN-IN b) ADPAIN: CRIT4FL eq Y for PARAMCD = PBPI3AVG where AVISIT = RUN-IN c) ADOPIO: CRIT1FL eq Y for PARAMCD = ALLMD where AVISIT = WEEK 6 d) ADPAIN: CRIT4FL eq Y for PARAMCD = PBPI3AVG where AVISIT = WEEK 6 e) ADOPIO: CRIT1FL eq Y for PARAMCD = ALLMD where AVISIT = WEEK 12 f) ADPAIN: CRIT4FL eq Y for PARAMCD = PBPI3AVG where AVISIT = WEEK 12
INOP6FL		Inadequate Opioid or Pain Data W6 Flag	Set to Y if either of these conditions are met a) ADOPIO: CRIT1FL ne Y for PARAMCD =ALLMD where AVISIT = WEEK 6 or b) ADPAIN: CRIT4FL ne Y for PARAMCD =PBPI3AVG where AVISIT = WEEK 6
INOP12FL		Inadequate Opioid or Pain Data W12 Flag	Set to Y if either of these conditions are met a) ADOPIO: CRIT1FL ne Y for PARAMCD =ALLMD where AVISIT = WEEK 12 or b) ADPAIN: CRIT4FL ne Y for PARAMCD =PBPI3AVG where AVISIT = WEEK 12

Figure 14: ADEFF Final Dataset Variables – Set 1

In ADPAIN and ADOPIO the various summarizations and criteria flags were derived for each time point. Data relevant for the efficacy analyses was primarily from Run-In, Week 3, Week 6, and Week 12. Having all these

relevant variables derived in intermediate data sets ADPAIN and ADOPIO made the ADEFF derivation of complex variables based on various time points a relatively straightforward task.

It's worth noting that ADEFF is not a BDS or other ADaM-defined structure. We considered using BDS, but it seemed to make the data less clear and traceable. We chose to go with this solution, with BDS predecessor datasets, to better follow the ADaM fundamental principles.

CONCLUSION

When we started trying to put this together, we did NOT worry about how to make the data BDS-compliant. Instead, we focused on making the data useable and following the ADaM fundamental principles. We soon realized that the interim datasets were very BDS-like, so we made a few modifications to put them into that structure.

Another goal we had was to structure the data such that any new summarization rule could be easily accommodated. For example in ADOPIO we later needed to add a summary of the opioids in terms of its morphine equivalent units (MEU). This was easily accommodated by addition of a PARAM='All meds this visit MEU'. For each time point this row had by each day the total doses in MEU over all opioids taken.

In the end, our solution provided much-needed traceability and clarity for review, flexibility for additional analysis needs, and a final dataset that was analysis-ready … exactly what the ADaM fundamental principles require.

RECOMMENDED READING

- All CDISC standards documents are available for free download at www.cdisc.org. We made extensive use of ADaM v2.1 and ADaMIG v1.0.

CONTACT INFORMATION

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