



From CDISC ARS to Drill-Down Reporting: A Proof-of-Concept

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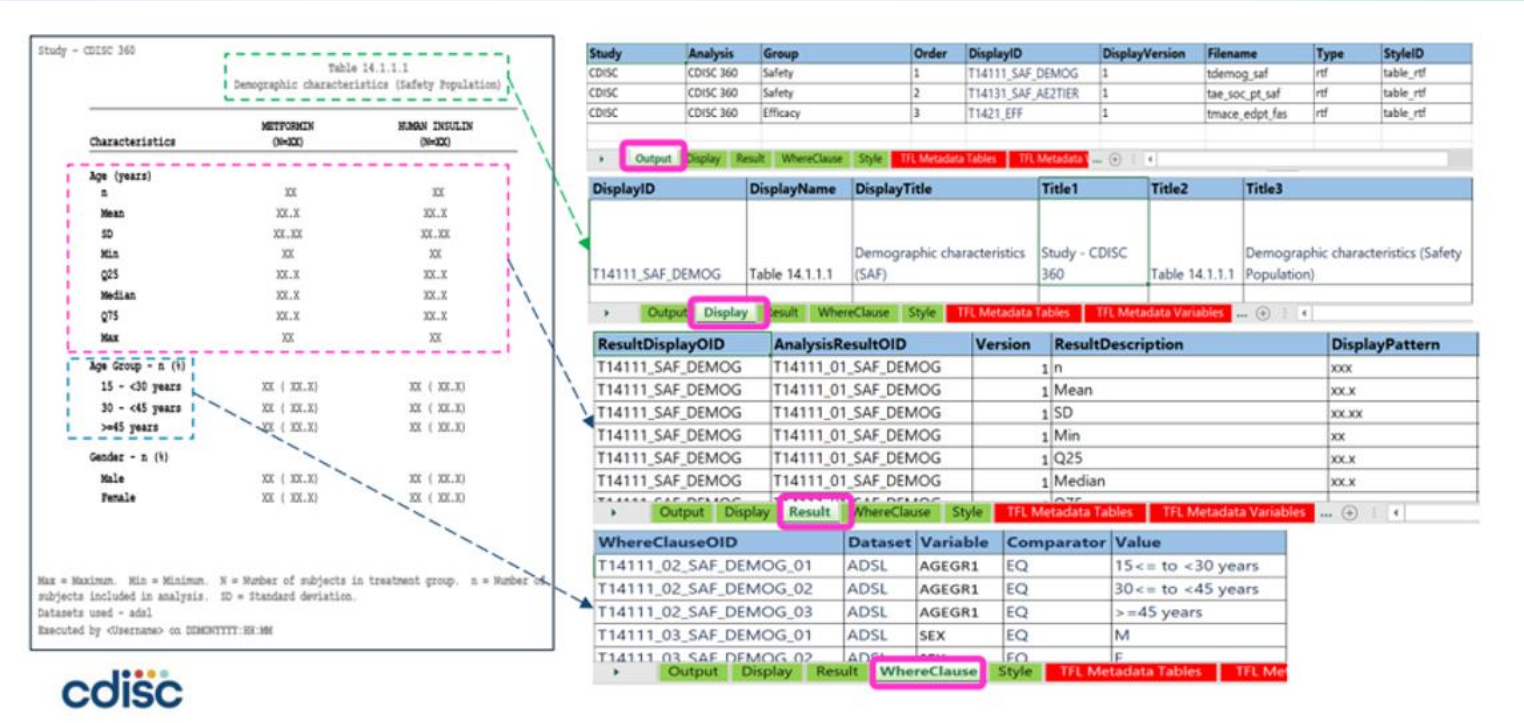
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Introduction to CDISC Analysis Results Standards

Large trials produce numerous analysis results, but these are often not machine-readable and lack standardization, hindering automation, reproducibility, and reusability. CDISC's Analysis Results Standard (ARS) addresses these issues by promoting automation, reproducibility, reusability, and traceability of analysis results data. ARS metadata is a core component of the ARS.

Figure 1. Example of CDISC ARS Metadata Structure



*The screenshot above is taken from the CDISC portal.

Project Overview

Objective: Develop a proof of concept for adopting CDISC ARS for TLFs generated in R.

Approach: Enhance internally developed R-based analysis workflows using the R package {metalite} to generate ARS-compliant metadata and analysis results, for small sample of tables following internal reporting standards.

Key Deliverables

- Baseline Characteristics & Specific AE tables based on internal reporting standards
- ARS metadata — Develop ARS metadata for Baseline Characteristics and Specific AE tables in machine-readable formats based on Linked Data Modeling Language (LinkML)
- Drill Down App — Develop a prototype application that leverages ARS metadata and corresponding ADaM datasets to dynamically render reports and support drill-down exploration.
- ARD (Analysis Results Dataset) — Machine-readable, standardized dataset of all computed analysis results exported as JSON for traceability and interoperability.

Introduction to {metalite} ecosystem

- {metalite}
Core R package that defines a reusable metadata structure for ADaM-based clinical analysis and reporting.
- {metalite.sl}
Extension package for subject-level summaries such as baseline characteristics in clinical trials.
- {metalite.ae}
Extension package for standard adverse event analysis, including AE summaries, specific AE analyses, and AE listings.

Key idea:

Define analysis metadata once with {metalite}, then reuse it to produce consistent, reproducible clinical tables, listings, and figures.

Overview of Creating Tables Using {metalite}

A `list` (object which contains elements of different types) including the metadata information for deliverables is generated from **{metalite}** package (metalite.R)

Figure 2. Example of Metadata Objects

```
meta
#> ADaM metadata:
#>   .$data_population   Population data with 254 subjects
#>   .$data_observation  Observation data with 1191 records
#>   .$plan              Analysis plan with 4 plans
#>
#>
#> Analysis population type:
#>   name      id group var      subset      label
#> 1 'apat' 'USUBJID' 'TRTA' SAFFL == 'Y' 'All Participants as Treated'
#>   group_order
#> 1 Xanomeline High Dose, Placebo
#>
#>
#> Analysis observation type:
#>   name      id group      var      subset      label      ae_var
#> 1 'wk12' 'USUBJID' 'TRTA' AEREL, AESER SAFFL == 'Y' 'Weeks 0 to 12' 'AEDECOD'
#>
#>
#> Analysis parameter type:
#>   name      label      subset
#> 1 'any'      'any adverse events'
#> 2 'rel'      'drug-related adverse events' AEREL %in% c('POSSIBLE', 'PROBABLE')
#> 3 'ser'      'serious adverse events'      AESER == 'Y'
#>
#>
#> Analysis function:
#>   name      label
#> 1 'ae_summary' 'Table: adverse event summary'
#> 2 'ae_specific' 'Table: specific adverse event'
```

- Defines populations such as APaT (All Participants as Treated) and ITT (Intent-to-Treat)
- Builds study and table level metadata via {metalite} pipeline and saves to meta.rds

```
meta$plan
#>   mock      analysis population observation      parameter mockup
#> 1   1   ae_summary      apat      wk12 any;rel;ser  TRUE
#> 2   2 ae_specific      apat      wk12      any  TRUE
#> 3   2 ae_specific      apat      wk12      rel  TRUE
#> 4   2 ae_specific      apat      wk12      ser  TRUE
#>
#>   output_report
#> 1 ./tlf/mock-ae_summary.rtf
#> 2 ./tlf/mock-ae_specific.rtf
#> 3 ./tlf/mock-ae_specific.rtf
#> 4 ./tlf/mock-ae_specific.rtf
```

Overview of Creating Tables Using {metalite}

- *{metalite}* and its extensive packages, i.e., *{metalite.ae}*, *{metalite.sl}*, provide an end-to-end process to create WMA standard tables in RTF format from the prepared ADaM datasets.

Figure 3. Baseline Characteristics Table with Corresponding Function Call

```

outdata <- meta |>
  prepare_sl_summary(
    population = "apat",
    analysis = "base_char",
    parameter = "age;gender;race"
  ) |>
  format_base_char(display_col = c("n", "prop", "total"),
    digits_prop = 2)
save(outdata, file = "base0char1.rda")

outdata |>
  metalite.sl::rtf_sl_summary(
    source = "Source: [CDISCpilot: adam-adsl]",
    path_outdata = file.path("base0char1.rtf"),
    path_outtable = tempfile(".Rdata")
  )

```

	Placebo	Low Dose	High Dose	Total
	n (%)	n (%)	n (%)	n (%)
Participants in population	86	84	84	254
Age				
<65	14 (16.28)	8 (9.52)	11 (13.10)	33 (12.99)
>80	30 (34.88)	29 (34.52)	18 (21.43)	77 (30.31)
65-80	42 (48.84)	47 (55.95)	55 (65.48)	144 (56.69)
Mean	75.2	75.7	74.4	75.1
SD	8.6	8.3	7.9	8.2
SE	0.9	0.9	0.9	0.5
Median	76.0	77.5	76.0	77.0
Q1 to Q3	69.25 to 81.75	71 to 82	70.75 to 80	70 to 81
Range	52 to 89	51 to 88	56 to 88	51 to 89
Sex				
F	53 (61.63)	50 (59.52)	40 (47.62)	143 (56.30)
M	33 (38.37)	34 (40.48)	44 (52.38)	111 (43.70)
Race				
AMERICAN INDIAN OR ALASKA NATIVE	0 (0.00)	0 (0.00)	1 (1.19)	1 (0.39)
BLACK OR AFRICAN AMERICAN	8 (9.30)	6 (7.14)	9 (10.71)	23 (9.06)
WHITE	78 (90.70)	78 (92.86)	74 (88.10)	230 (90.55)
SD=Standard deviation; SE=Standard error; Q1=First quartile, Q3=Third quartile.				
Source: [CDISCpilot: adam-adsl]				

Key Feature

- `{metalite}` has the ability to create the RTF tables with the subset criteria through `metalite::collect_n_subject()`

Figure 4. Example Raw Results and Metadata Derived from function call in Figure 3

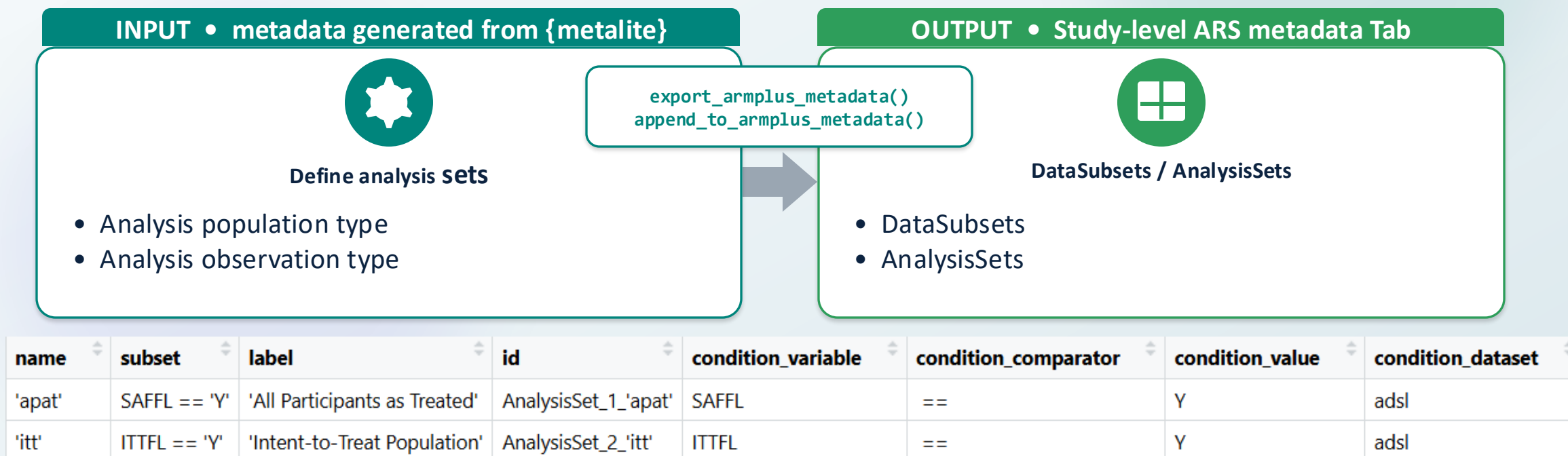
name<chr>	Placebo<chr>	Low Dose<chr>	High Dose<chr>
Number of Subjects	86	84	84
Race	NA	NA	NA
Subjects with Data	86	84	84
AMERICAN INDIAN OR ALASKA NATIVE	0 (0.0%)	0 (0.0%)	1 (1.2%)
BLACK OR AFRICAN AMERICAN	8 (9.3%)	6 (7.1%)	9 (10.7%)
WHITE	78 (90.7%)	78 (92.9%)	74 (88.1%)

name	Placebo	Low Dose	High Dose
Number of Subjects	TRUE & TRTA == 'Placebo' & SAFFL == 'Y'	TRUE & TRTA == 'Low Dose' & SAFFL == 'Y'	TRUE & TRTA == 'High Dose' & SAFFL == 'Y'
Subjects with Data	(! is.na(RACE)) & TRTA == 'Placebo' & SAFFL == 'Y'	(! is.na(RACE)) & TRTA == 'Low Dose' & SAFFL == 'Y'	(! is.na(RACE)) & TRTA == 'High Dose' & SAFFL == 'Y'
NA	is.na(RACE) & TRTA == 'Placebo' & SAFFL == 'Y'	is.na(RACE) & TRTA == 'Low Dose' & SAFFL == 'Y'	is.na(RACE) & TRTA == 'High Dose' & SAFFL == 'Y'
AMERICAN INDIAN OR ALASKA NATIVE	RACE == 'AMERICAN INDIAN OR ALASKA NATIVE' & TRTA ...	RACE == 'AMERICAN INDIAN OR ALASKA NATIVE' & TRTA ...	RACE == 'AMERICAN INDIAN OR ALASKA NATIVE' & TRTA ...

Process to Create DataSubsets/AnalysisSets tab

- Extracts meta\$population subset conditions → AnalysisSets tab
- Extracts meta\$observation subset conditions → DataSubsets tab
- Both map to standard ARS fields: id, name, label, condition_dataset, condition_variable and condition_value

Figure 5.1 Raw *meta* objects to standard ARS metadata

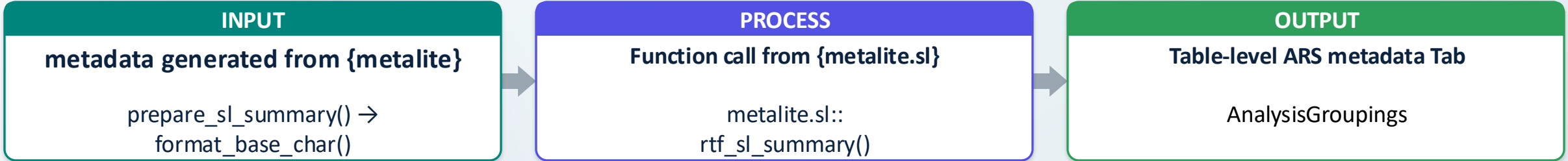


Process to Create AnalysisGroupings

Figure 5.2. Raw *meta* objects to standard ARS metadata

```
outdata <- meta |>
  prepare_sl_summary(
    population = "apat",
    analysis = "base_char",
    parameter = "age;gender;race"
  ) |>
  format_base_char(display_col = c("n", "prop", "total"),
    digits_prop = 2)
save(outdata, file = "base0char1.rda")

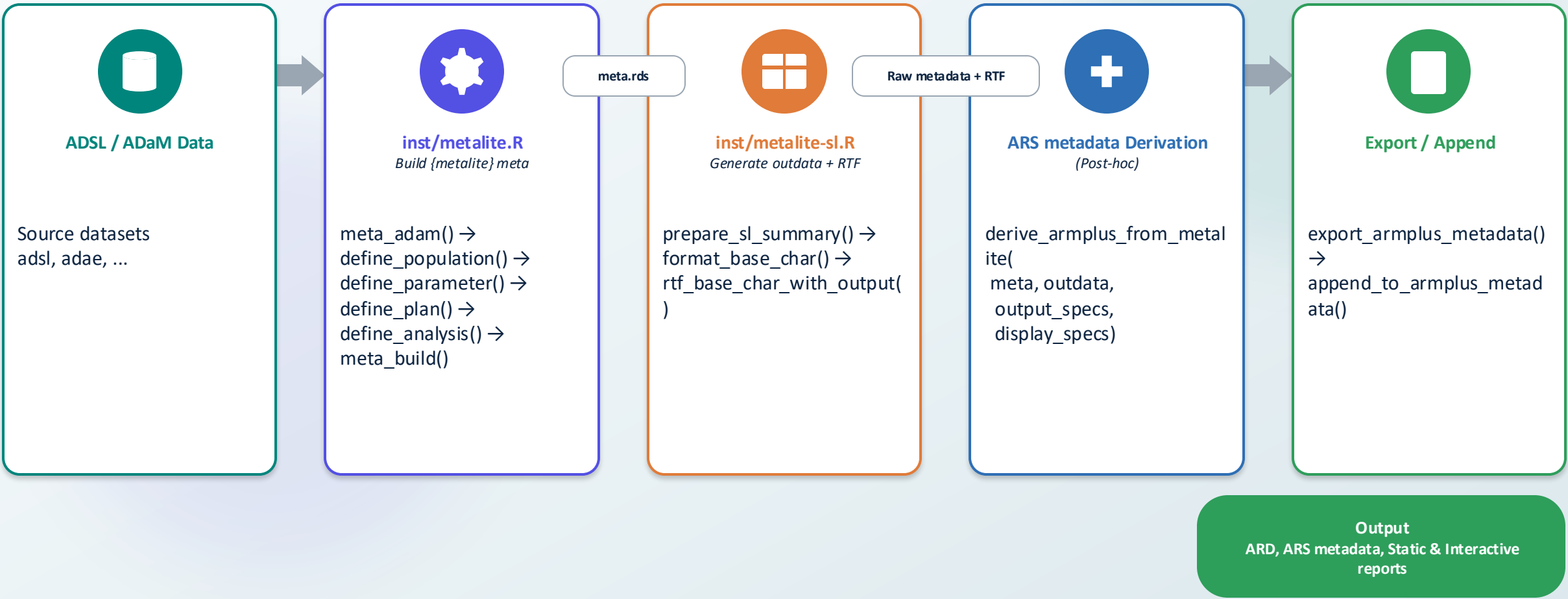
outdata |>
  metalite.sl::rtf_sl_summary(
    source = "Source: [CDISCpilot: adam-ads1]",
    path_outdata = file.path("base0char1.rtf"),
    path_outtable = tempfile(".Rdata")
  )
```



id	name	label	groupingDat	groupingVar	dataDriven	group_id	group_label	group_level	group_order	group_condi	group_condi	group_condi	group_condition_value
AnlsGrouping_01_Tr	Trt	Treatment	ADSL	TRT01A	FALSE	AnlsGrouping_01_Tr	Placebo	1	1	ADSL	TRT01A	EQ	Placebo
AnlsGrouping_01_Tr	Trt	Treatment	ADSL	TRT01A	FALSE	AnlsGrouping_01_Tr	Xanomeline Low Dose	1	2	ADSL	TRT01A	EQ	Xanomeline Low Dose
AnlsGrouping_01_Tr	Trt	Treatment	ADSL	TRT01A	FALSE	AnlsGrouping_01_Tr	Xanomeline High Dose	1	3	ADSL	TRT01A	EQ	Xanomeline High Dose
AnlsGrouping_02_AgeGp	AgeGp	Age Group	ADSL	AGEGR1	FALSE	AnlsGrouping_02_AgeGp	< 65	1	1	ADSL	AGEGR1	EQ	< 65
AnlsGrouping_02_AgeGp	AgeGp	Age Group	ADSL	AGEGR1	FALSE	AnlsGrouping_02_AgeGp	>= 65	1	2	ADSL	AGEGR1	EQ	>= 65
AnlsGrouping_03_Sex	Sex	Gender	ADSL	SEX	FALSE	AnlsGrouping_03_Sex	Female	1	1	ADSL	SEX	EQ	F
AnlsGrouping_03_Sex	Sex	Gender	ADSL	SEX	FALSE	AnlsGrouping_03_Sex	Male	1	2	ADSL	SEX	EQ	M
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	American Indian or Alaska	1	1	ADSL	RACE	EQ	AMERICAN INDIAN OR ALASKA NATIVE
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Asian	1	2	ADSL	RACE	EQ	ASIAN
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Black or African American	1	3	ADSL	RACE	EQ	BLACK OR AFRICAN AMERICAN
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	White	1	4	ADSL	RACE	EQ	WHITE
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Multiple	1	5	ADSL	RACE	EQ	MULTIPLE
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Not Reported	1	6	ADSL	RACE	EQ	NOT REPORTED
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Unknown	1	7	ADSL	RACE	EQ	UNKNOWN
AnlsGrouping_04_Race	Race	Primary Race	ADSL	RACE	FALSE	AnlsGrouping_04_Race	Other	1	8	ADSL	RACE	EQ	OTHER

Current State

Figure 6. Metadata During Table Development



Demo

The screenshot displays the RStudio interface with the following components:

- Source Editor (Left):** Contains R code for defining metadata and parameters. The code includes comments about Metalite metadata, loading the `metalite` library, reading data from `adsl.sas7bdat`, and defining parameters for age, gender, and race.
- Console (Right):** Shows the execution of the code, including the `runApp` command and the message "Loading mkdrilldown".
- Environment (Bottom Left):** Displays the current environment with variables like `adsl`, `meta`, and `plan`.
- Files (Bottom Right):** Shows the file structure of the project, including `startup.R`, `metalite.R`, `develop_ae_specific.Rmd`, `develop_baseline_char.Rmd`, and `app.R`.

```

1 # Base Metalite Metadata
2 # This file contains population and subject-level definitions that are
3 # shared across all deliverables (demographics, AE tables, etc.)
4 # Domain-specific metadata (e.g., AE-specific) should reference these populations
5
6 library(metalite)
7
8 adsl <- haven::read_sas(file.path(path$adam, "adsl.sas7bdat"))
9
10 adsl$TRT01A <- factor(adsl$ARM,
11   levels = c("Placebo", "Xanomeline Low Dose", "Xanomeline High Dose")
12 )
13
14 # Define base metadata with shared population definitions
15 meta <- meta_adam(
16   population = adsl,
17   observation = adsl
18 )
19
20 define_plan(plan = rbind(
21   plan(analysis = "base_char", population = "apat",
22     observation = "apat", parameter = "age;gender;race"),
23   plan(analysis = "base_char", population = "itt",
24     observation = "itt", parameter = "age;gender;race")
25 ))
26
27 define_observation(
28   name = "apat",
29   group = "TRT01A",
30   subset = quote(SAFFL == "Y"),
31   label = "All Participants as Treated"
32 )
33
34 define_observation(
35   name = "itt",
36   group = "TRT01A",
37   subset = quote(RANDFL == "Y"),
38   label = "Intent-to-Treat Population"
39 )
40
41 define_population(
42   name = "itt",
43   group = "TRT01A",
44   subset = quote(RANDFL == "Y"),
45   var = c("USUBJID", "TRT01A", "SAFFL", "AGEGR1", "SEX", "RACE"),
46   label = "Intent-to-Treat Population"
47 )
48
49 define_parameter(
50   name = "age",
51   var = "AGE",
52   label = "Age (years)",
53   vargroup = "AGEGR1"
54 )
55
56 define_parameter(
57   name = "gender",
58   var = "SEX",
59   label = "Gender"
60 )
61
62 define_parameter(
63   name = "race",
64   var = "RACE",
65   label = "Race"
66 )
67
68 define_analysis(
69   name = "base_char",
70   title = "Participant Baseline Characteristics by Treatment Group",
71   label = "baseline characteristic table"
72 )
73
74 meta_build()
75 > runApp('inst/shiny/app')
76 i Loading mkdrilldown
77
78 Listening on http://127.0.0.1:6461
79
80 >

```

Conclusion

What We Achieved:

- Fully functional, end-to-end ARS-compliant reporting workflow built entirely in R for standard AE & Baseline Table
- Seamless integration of {metalite}, {r2rtf}, and ARS metadata into a single reproducible pipeline
- Machine-readable metadata exports (JSON & RDS) aligned with CDISC ARS specifications
- Analysis Results Dataset (ARD) providing standardized, traceable statistical outputs
- Metadata-driven Shiny application enabling interactive drill-down exploration without code changes

Value Delivered:

- Full traceability from final outputs back to source ADaMs
- Single Source of Truth for Study, Analysis, and Table-Level Metadata

Next Steps

- Establish ARS metadata template for reuse across therapeutic areas
- Enable metadata-driven automation for reporting, validation, traceability, and drill-down applications for TA - study specific analysis
- Scale up to cover additional table types (e.g., efficacy endpoints, lab summaries, time-to-event analyses)

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Leadership	Amy Gillespie, Susan Kramlik, Keaven Anderson & Jason Clark



Q&A



Thank you