



Treatment Allocation in ADaM

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Also allocation of...

- APHASE, APHASSEN
- APERIODC, APERIOD
- ASPERC, ASPER



**ADTRTEV****Planned or Actual Treatment for Events**

- Enriched elements as one record per dataset per subject per phase per period (per sub-period)

ADTRTVIS**Planned or Actual Treatment for Findings**

- Enriched visit structure as one record (per dataset) per subject per visit

ADSL**Subject Level Analysis**

- One record per subject

What have we optimised?



Period Definitions



ADaM IG v1.1

- 3.2 ADSL Variables:

"A set of timing variables can be included in ADSL only if the definitions for all of the variables in the set are fixed across the study (i.e., the definitions of the start and end of each timing element for given subject do not change based on endpoint or data type)."

"If any of the definitions of the variables in the set do vary, for example, when analysis period start and stop date definitions differ for safety and efficacy analyses, then none of the variables in the set can be included in ADSL."

Treatment emergent period (Example)

- GCP ICH E9:
 - *"An event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state."*
- Diabetes trials:
 - AEs: First drug date to last drug date + 7 days
 - Hypoglycemia: First drug date to last drug date + 1 day

Treatment emergent period - Implementation

- Build ADTRTEV from:
 - SDTM.DM
 - SDTM.SE
 - SDTM.EX
 - Trial Design Datasets
 - Metadata

```
/*Execute*/
```

```
/*ADSL*/
```

```
%addlag(lag=0, applyto=ADSL)
```

```
/*ADHYPO*/
```

```
%addlag(lag=1, applyto=ADHYPO);
```

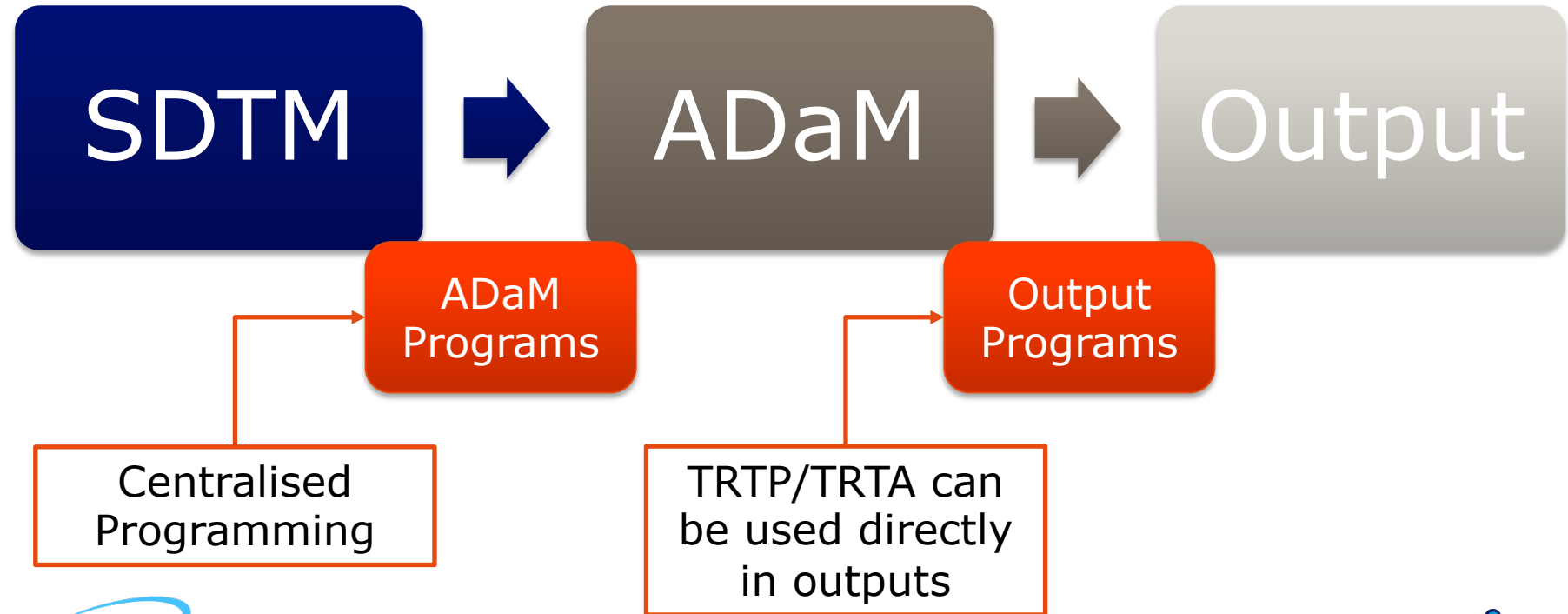
```
/*ADAE*/
```

```
%addlag(lag=7, applyto=ADAE);
```

SUBJID	APHASE	APERIODC	TRTP	TRTA	ASTDT	AENDT	APPLYTO
101001	SCREENING				03JUN2016	16JUN2016	ADSL
101001	RUN-IN				17JUN2016	11AUG2016	ADSL
101001	TREATMENT	Period 01	Drug X	Drug X	12AUG2016	10FEB17	ADSL
101001	FOLLOW-UP				11FEB2017	.	ADSL
101001	SCREENING				*****	16JUN2016	ADHYPO
101001	RUN-IN				17JUN2016	11JUN2016	ADHYPO
101001	TREATMENT	Period 01	Drug X	Drug X	12AUG2016	11FEB2017	ADHYPO
101001	FOLLOW-UP				12FEB2017	*****	ADHYPO
101001	SCREENING				*****	16JUN2016	ADAE
101001	RUN-IN				17JUN2016	11AUG2016	ADAE
101001	TREATMENT	Period 01	Drug X	Drug X	12AUG2016	17FEB2017	ADAE
101001	FOLLOW-UP				18FEB17	*****	ADAE

Treatment emergent period - ADAE

```
proc sql;
  create table adae_phuse as
  select a.*, b.TRTP, b.TRTA
        , b.APHASE, b.APERIODC
        , case
            when b.ASTDT le a.ASTDT and a.ASTDT le b.AENDT
              and b.APHASE = "TREATMENT" then "Y"
            else ""
          end as TRTEMFL
  from adae_nn as a
  left join ADaM.ADTRTEV(where=(applyto = "ADAE")) as b
    on a.USUBJID = b.USUBJID
   and (b.ASTDT <= a.ASTDT <= b.AENDT
   or   (b.ASTDT <= a.ASTDT and APHASE = "FOLLOW-UP"));
quit;
```



On-treatment period (Example)

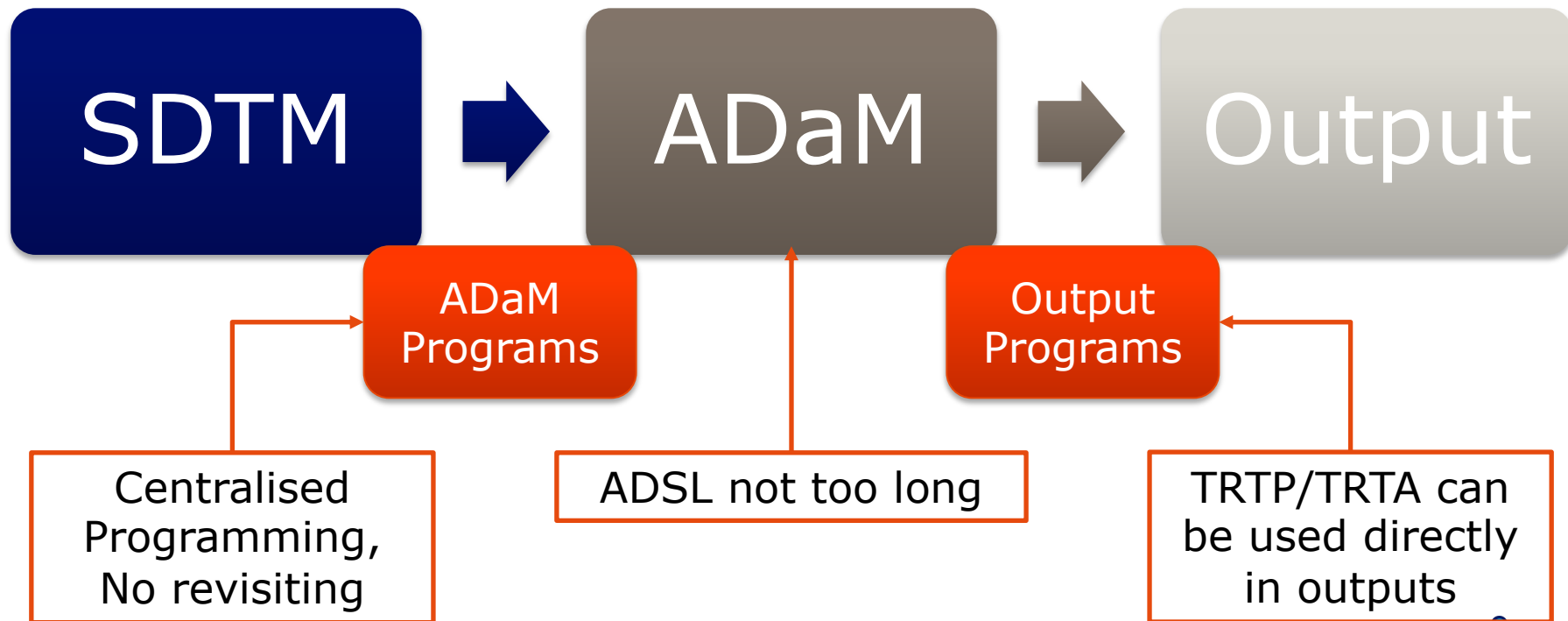
- On-treatment Timepoint:
Any dose of trial product administered within the prior 2 weeks (14 days).
- On-treatment period:
First drug date to last drug date + 14 days excluding off-treatment time intervals triggered by at least two consecutive missed doses.

SUBJID	APHASE	APERIOD	ASPERC	TRTP	TRTA	ASTDT	AENDT	APPLYTO
101001	SCREENING					30NOV2018	03DEC2018	ADAE
101001	RUN-IN					03DEC2018	13DEC2018	ADAE
101001	TREATMENT	Period 01	ON-DRUG	Drug X	Drug X	14DEC2018	03JAN2019	ADAE
101001	TREATMENT	Period 01	OFF-DRUG	Drug X		04JAN2019	24JAN2019	ADAE
101001	TREATMENT	Period 01	ON-DRUG	Drug X	Drug X	25JAN2019	07FEB2019	ADAE
101001	TREATMENT	Period 01	OFF-DRUG	Drug X		08FEB2019	14FEB2019	ADAE
101001	TREATMENT	Period 01	ON-DRUG	Drug X	Drug X	15FEB2019	28FEB2019	ADAE
101001	TREATMENT	Period 01	OFF-DRUG	Drug X		01MAR2019	21MAR2019	ADAE
101001	TREATMENT	Period 01	ON-DRUG	Drug X	Drug X	22MAR2019	28MAR2019	ADAE
101001	FOLLOW-UP					29MAR2019	*****	ADAE

On-treatment period - ADAE

```
proc sql;
  create table adae_phuse as
  select a.*, b.TRTP, b.TRTA
        , b.APHASE, b.APERIODC, b.ASPERC
        , case
            when b.ASTDT le a.ASTDT and a.ASTDT le b.AENDT
              and b.ASPERC = "ON-DRUG" then "Y"
            else ""
          end as ONTRTFL
  from adae_nn as a
  left join ADaM.ADTRTEV(where=(applyto = "ADAE")) as b
    on a.USUBJID = b.USUBJID
   and (b.ASTDT <= a.ASTDT <= b.AENDT)
quit;
```



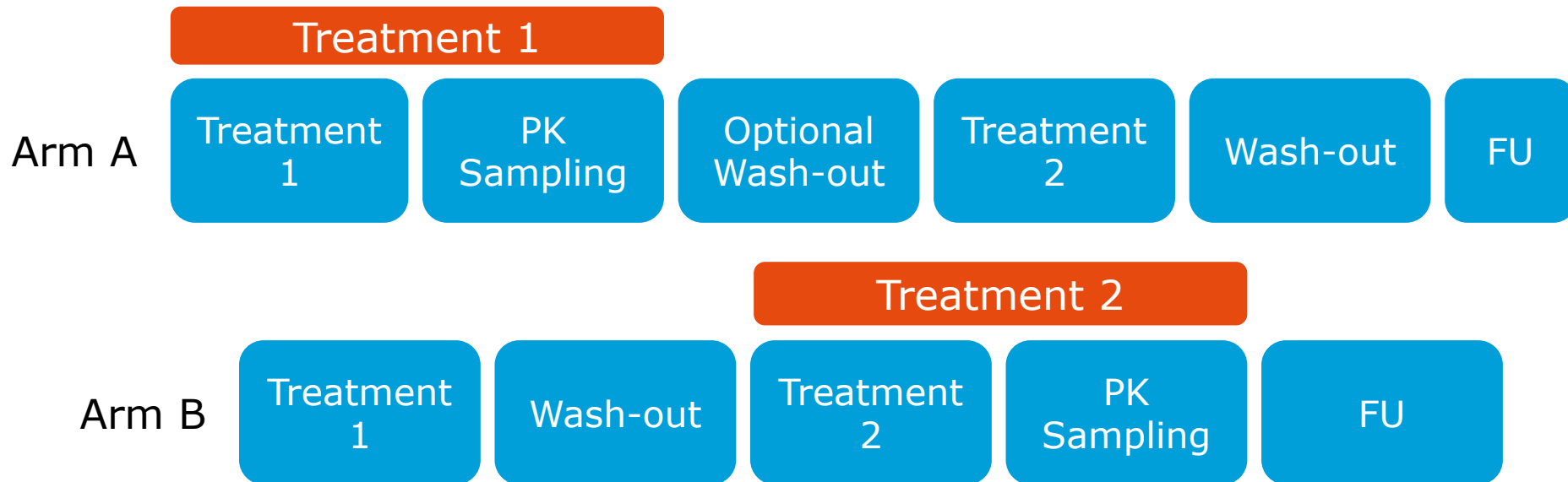


Trial Designs



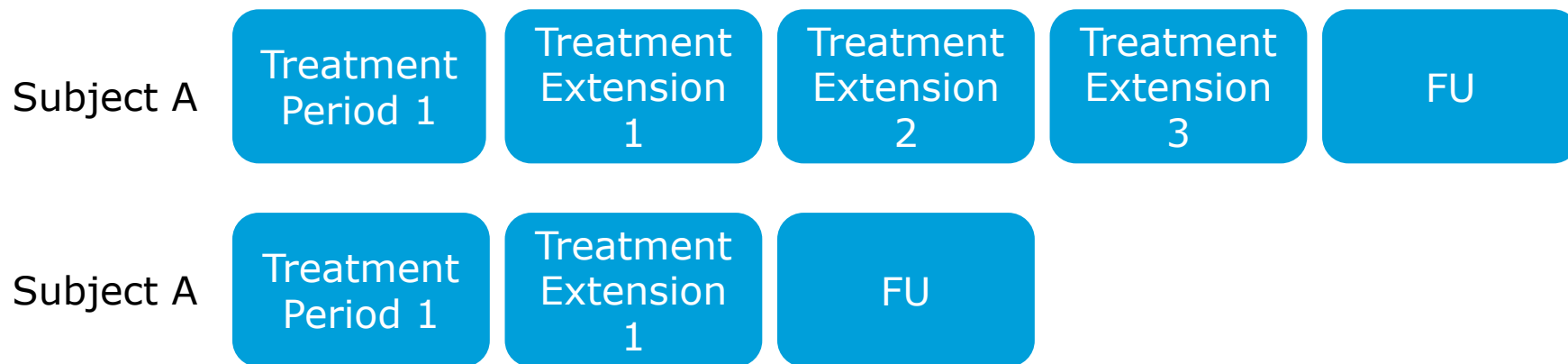
Example 1

- Cross-over with different periods depending on the randomised arm:



Example 2

- Extension period only if criteria is met



In short

ADTRTEV and ADTRTVIS:

- Supports complex trial designs and analysis periods
- 'Slims' ADSL
- Centralises programming efforts
- Simplifies code in subsequent programs