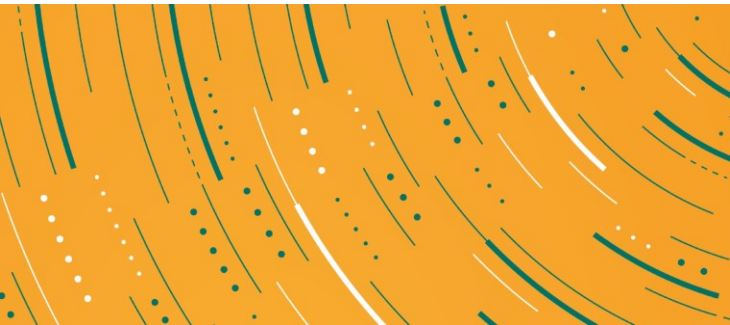# DATA.
PEOPLE.
EXCELLENCE.

ESTIMANDS AND INTERCURRENT EVENTS IN ADAMS

CDISC User Group Meeting

Munich, 2024-03-14

DATA. PEOPLE.
EXCELLENCE.

AGENDA / CONTENT

AGENDA / CONTENT

INTRODUCTION TO ESTIMANDS
Summary based on ICH E9(R1) Training Material - Motivation

Understanding treatment effects

The **key** point is that **multiple, different treatment effects** can be considered.

- The framework outlined in this addendum gives a basis for describing different treatment effects and some points to consider for the design and analysis of trials to give estimates of treatment effects that are reliable for decision making.

19

Source: ICH E9(R1) Training Material Module 2.1. Introduction

Concerns with current practice ⚠️

Currently:

- Targets of estimation that are not clearly stated and cannot necessarily be inferred from information in the study protocol and statistical analysis plan.

- Choices are made for data handling and statistical analysis that are not consistent with the treatment effect of interest

Endpoint	Population
Statistical analysis	Missing data
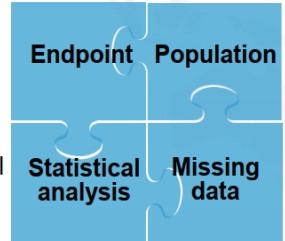
- **Practice should be reversed:**
  - o The **target of estimation** should be clear from the **study protocol**;
  - o The **statistical analysis** should be **aligned to the agreed target of estimation**.

30

INTRODUCTION TO ESTIMANDS
Summary based on ICH E9(R1) Training Material - Definition

Estimand attributes

The attributes below are used to construct the estimand, defining the treatment effect of clinical interest
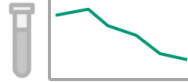
Treatment **Population** **Variable**

Intercurrent events may be incorporated into the treatment, population and/or variable attributes

Other intercurrent events (not included in other attributes)

Population-level summary
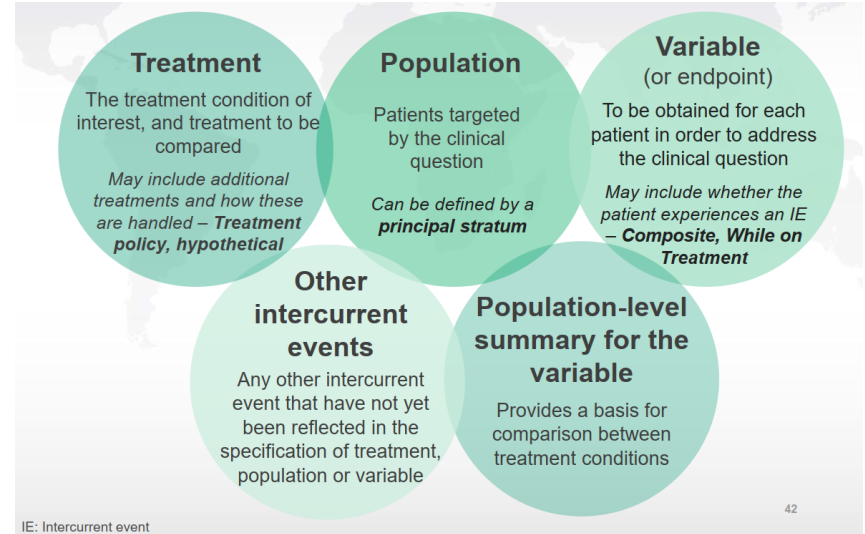
% ratio Σ

41

Treatment

The treatment condition of interest, and treatment to be compared

May include additional treatments and how these are handled – Treatment policy, hypothetical

Population

Patients targeted by the clinical question

Can be defined by a principal stratum

Variable (or endpoint)

To be obtained for each patient in order to address the clinical question

May include whether the patient experiences an IE – Composite, While on Treatment

Other intercurrent events

Any other intercurrent event that have not yet been reflected in the specification of treatment, population or variable

Population-level summary for the variable

Provides a basis for comparison between treatment conditions

IE: Intercurrent event

42

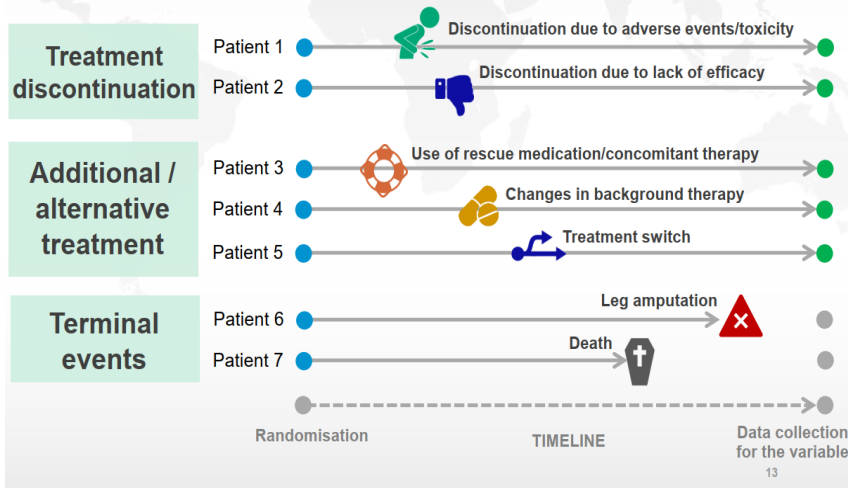Source: ICH E9(R1) Training Material Module 2.3. Estimands

AGENDA / CONTENT

INTERCURRENT EVENTS (ICES) AND BASIC STRATEGIES
Summary based on ICH E9(R1) Training Material

Intercurrent events - examples

Treatment discontinuation	Patient 1	Discontinuation due to adverse events/toxicity
	Patient 2	Discontinuation due to lack of efficacy
Additional / alternative treatment	Patient 3	Use of rescue medication/concomitant therapy
	Patient 4	Changes in background therapy
	Patient 5	Treatment switch
Terminal events	Patient 6	Leg amputation
	Patient 7	Death

Randomisation — TIMELINE — Data collection for the variable

13

Source: ICH E9(R1) Training Material Module 2.3. Estimands

Strategies to address intercurrent events

A "**strategy**" reflects the choice made on **how to address intercurrent events**, in order to describe the **treatment effect** that is targeted.

- The addendum introduces **five strategies** that can be used alone or in combination to **address different intercurrent events.**

- o Treatment policy
- o Hypothetical
- o Composite
- o While on treatment
- o Principal stratum

28

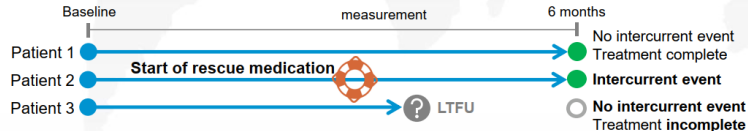Source: ICH E9(R1) Training Material Module 2.1. Introduction

INTERCURRENT EVENTS (ICES) AND BASIC STRATEGIES
Summary based on ICH E9(R1) Training Material

1. Treatment policy strategy - example

- **Estimand:** Difference in means between treatment conditions in the change from baseline to month 6 in the targeted patient population, regardless of whether rescue medication was used.
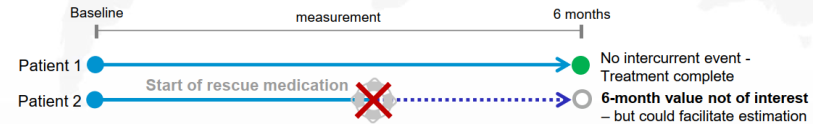
- **If rescue medication (intercurrent event) is used…**

Baseline | measurement | 6 months

Patient 1 — **Start of rescue medication** → ● No intercurrent event / Treatment complete
Patient 2 → ● **Intercurrent event**
Patient 3 → ? LTFU → ○ **No intercurrent event** / Treatment **incomplete**

- **Applying the treatment policy strategy**

Patient 1 — Start of rescue medication → ● No intercurrent event / Treatment complete
Patient 2 → ● **6-month value still considered** / **Intercurrent event disregarded**
Patient 3 → ? LTFU → ○ **No intercurrent event - Patient** included but data are missing

Legend:
● 6-month value has been collected
○ 6-month value has not been collected, data are missing
? LTFU - Patient lost to follow-up
Intercurrent event - in grey when disregarded
— Part of patient time course considered
···· Part of patient time course not observed and needs to be imputed/predicted

2. Hypothetical strategies - example

- The **estimand** assesses the difference in means between treatment conditions in the change from baseline to month 6 in the targeted patient population, in an alternative, hypothetical setting where rescue medication was not available to patients.

- **Applying a hypothetical strategy**

Baseline | measurement | 6 months

Patient 1 → ● No intercurrent event - Treatment complete
Patient 2 — Start of rescue medication ✕ ···· → ○ **6-month value not of interest** – but could facilitate estimation

Legend:
● 6-month value has been collected and outcome is positive
○ No need to collect 6-month value
— Part of patient time course considered
···· Part of patient time course not observed, may need to be imputed/predicted
✕ Intercurrent event hypothetically not present. Time of intercurrent event marks the end of data collection unless it facilitates estimation.

26

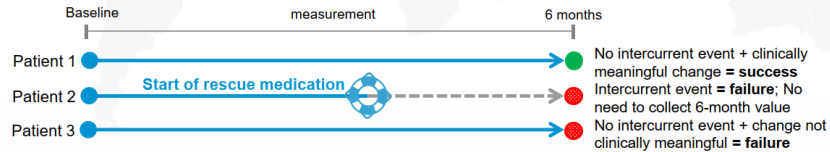Source: ICH E9(R1) Training Material Module 2.3. Estimands

INTERCURRENT EVENTS (ICES) AND BASIC STRATEGIES
Summary based on ICH E9(R1) Training Material

3. Composite strategies - example

- The **estimand** assesses the treatment effect based on a clinically meaningful change in the designated measurement in patients who do not take rescue medication.

- **Applying a composite strategy (on a categorical scale)**

Baseline — measurement — 6 months

Patient 1 — No intercurrent event + clinically meaningful change **= success**

Patient 2 — **Start of rescue medication** — Intercurrent event **= failure**; No need to collect 6-month value

Patient 3 — No intercurrent event + change not clinically meaningful **= failure**

- This is **not the only way** to address intercurrent events using the composite strategy; other ways include trimmed means or quantiles (see next slide).
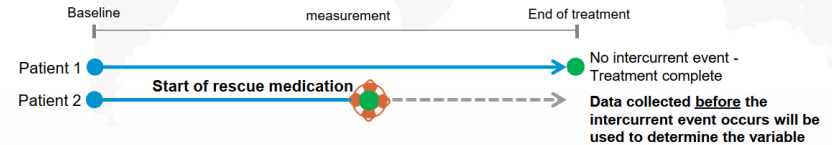
Legend:
- 6-month value has been collected and outcome is positive
- Outcome is negative regardless of having been collected
- Part of patient time course considered
- Part of patient time course not considered
- Intercurrent event as part of the composite variable. Time of intercurrent event marks the end of data collection.

28

4. While on treatment strategies - example

- The **estimand** assesses the treatment effect on the variable measurement. The variable chosen here addresses the outcomes while being on treatment, i.e., before start of rescue medication.

- **Applying a while on treatment strategy**

Baseline — measurement — End of treatment

Patient 1 — No intercurrent event - Treatment complete

Patient 2 — **Start of rescue medication** — **Data collected before the intercurrent event occurs will be used to determine the variable**

⚠ Difficulties arise in deriving an estimate that is reliable for inference when follow-up times are different between groups.

Legend:
- End point value has been collected
- Part of patient time course considered
- Part of patient time course not considered
- Time of intercurrent event marks end of data collection (merged with green dot).

32

Source: ICH E9(R1) Training Material Module 2.3. Estimands

INTERCURRENT EVENTS (ICES) AND BASIC STRATEGIES
Summary based on ICH E9(R1) Training Material

5. Principal stratum strategies - example

- A given patient can receive either treatment or placebo.

- When receiving treatment some patients will require rescue medication, others not. The same applies for patients on placebo.

- The **estimand** can assess, for example, the treatment effect in the stratum of patients which <u>would not use rescue medication</u> regardless to which treatment arm they would be assigned → corresponding to stratum S11 (see below).

Patients fall into exactly one of these four strata:

- S_{00}: stratum of patients who require rescue medication independently of treatment or placebo;

- S_{01}: stratum of patients who require rescue medication on placebo and do not require it on treatment;

- S_{10}: stratum of patients who require rescue medication on treatment and do not require it on placebo;

- S_{11}: stratum of patients who do not require rescue medication independently of treatment or placebo. This is the only stratum where the intercurrent event of use of rescue medication does not occur.

A population can be defined by membership of one or more of these strata.

		Treatment	
		Rescue medication	No rescue medication
Placebo	Rescue medication	S_{00}	S_{01}
	No rescue medication	S_{10}	S_{11}

35

Source: ICH E9(R1) Training Material Module 2.3. Estimands

AGENDA / CONTENT

01 Introduction to Estimands

02 Intercurrent Events (ICEs) and basic strategies

03 Example: ICEs in ADaM (ADICE)

04 Example: Strategies after ICEs in other ADaMs

05 Discussion

EXAMPLE 1: ICES IN ADAM (ADICE)
Overview over Estimands in SAP – Primary Estimand

Treatment	Active versus Placebo
Population	Subjects with certain disease as described in protocol
Variable	Combined Symptom and Medication Score (sum of daily symptom score and daily medication score) averaged over certain period for each subject.
ICEs	The following intercurrent events (ICEs) were identified: (1) Treatment non-compliance (2) Absence from primary location (3) Use of prohibited medication that may have an impact on symptoms (4) Infections that may have an impact on symptoms
Population level summary	Difference in mean score between active and placebo group

EXAMPLE 1: ICES IN ADAM (ADICE)

Overview over ICEs and their strategies in SAP – Primary Estimand

ICE	Strategy
	Primary Estimand
Treatment non-compliance	Treatment policy
Absence from primary location	Adapted while on treatement strategy: Ignore all values during absence, but use again values after absence.
Use of prohibited medication that may have an impact on symptoms	Composite variable strategy: Increase medication score
Infections that may have an impact on symptoms	Treatment policy

EXAMPLE 1: ICES IN ADAM (ADICE)

Overview over Estimands and ICEs and their strategies in SAP – Supplementary Estimands

ICE	Strategy	Strategy	Strategy	...
	Primary Estimand	Supplementary Estimand 1	Supplementary Estimand 2	
Treatment non-compliance Absence from primary location	Treatment policy	Treatment policy	Treatment policy	
	Adapted while on treatement strategy	Adapted while on treatement strategy	Adapted while on treatement strategy	
Use of prohibited medication that may have an impact on symptoms	Composite variable strategy	Hypothetical Strategy *	Composite variable strategy	
Infections that may have an impact on symptoms	Treatment policy	Treatment policy	Adapted while on treatement strategy	

* Hypothetical strategy:

Estimate treatment effect assuming subjects had no prohibited medication taken, i.e. set values to missing and impute them based on subjects without infections.

EXAMPLE 1: ICES IN ADAM (ADICE)

Overview over Estimands and ICEs and their strategies in SAP – Key Secondary Estimands

	Primary Estimand	Key Secondary Estimand 1	Key Secondary Estimand 2	…
Treatment	Active versus Placebo.			
Population	Subjects with certain disease as described in protocol			
Variable	Combined Symptom and Medication Score (sum of daily symptom score and daily medication score) averaged over certain period for each subject.	Symptom score averaged over certain period for each subject.	Combined Symptom and Medication Score (sum of daily symptom score and daily medication score) averaged over another period for each subject.	
ICEs	The following intercurrent events (ICEs) were identified: (1) Treatment non-compliance (2) Absence from primary location (3) Use of prohibited medication that may have an impact on symptoms (4) Infections that may have an impact on symptoms			
Population level summary	Difference in mean score between active and placebo group			

EXAMPLE 1: ICES IN ADAM (ADICE)

Overview over ICEs and their strategies in SAP – Order of implementation

In case several ICEs occur in one subject, the following strategy will be applied:

- If an ICE occurs that should be handled with a **while-on-treatment** or **adapted while-on-treatment strategy**, this will be implemented first, i.e., all days affected will be ignored for any further analysis.

- If an ICE occurs that should be handled with a **hypothetical strategy**, the values will be set to missing and imputed, i.e., the days will be kept in the analysis, but the values will be set to missing. This will only be done for days that are not affected by an ICE that was handled with a while-on-treatment or adapted while-on-treatment strategy.

- If an ICE occurs that should be handled with a **composite variable strategy**, the corresponding values will be adapted, only if they were not set to missing previously due to other ICEs.

- If an ICE occurs that should be handled with a **treatment policy strategy**, no further adaptions will be done, except the ones triggered by other ICEs.

EXAMPLE 1: ICES IN ADAM (ADICE)

Set up of ADICE (Structure OTHER)

SubjID	ICECATID	ICECAT	ICETERM	ICESTDTC	ICEENDTC	PRIMEST	SUPPEST1	SUPPEST2	KSDSSPG	KSCSMSEG
002	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
002	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
003	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Treatment policy	Treatment policy	Adapted while-on-treatment strategy	Treatment policy	Treatment policy
006	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
007	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
003	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Treatment policy	Treatment policy	Adapted while-on-treatment strategy	Treatment policy	Treatment policy
004	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
004	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
007	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
012	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
016	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
001	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
006	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
007	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy
007	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
002	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
003	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
004	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
005	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
006	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
007	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
006	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Treatment policy
010	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
001	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Treatment policy
003	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy	Adapted while-on-treatment strategy
004	(3)	Prohibited medication	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Composite variable strategy	Hypothetical strategy	Composite variable strategy	Treatment policy	Composite variable strategy
004	(3)	Prohibited medication	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Composite variable strategy	Hypothetical strategy	Composite variable strategy	Treatment policy	Composite variable strategy
010	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
012	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
017	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
020	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
020	(4)	Infection	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
020	(1)	Treatment non-compliance	Dummy text	YYYY-MM-DD		Treatment policy	Treatment policy	Treatment policy	Treatment policy	Treatment policy
023	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
023	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy
023	(2)	Absence	Dummy text	YYYY-MM-DD	YYYY-MM-DD	Not applicable	Not applicable	Not applicable	Not applicable	Adapted while-on-treatment strategy

Primary Estimand

Supplementary Estimands

Key Secondary Estimands

AGENDA / CONTENT

EXAMPLE: STRATEGIES AFTER ICES IN OTHER ADAMS
ADCSMSDL: Composite Variable Strategy and Hypothetical Strategy

SUBJID	PARAMCD	PARAM	QSDTC	ADT	AVAL	DTYPE
004	CDSSTOT	CSMS: Daily Symptom Score (dSS)	YYYY-MM-DDTHH:MM	11JUN2023	1.166666667	
004	CDMSTOT	CSMS: Daily Medication Score (dMS)	YYYY-MM-DDTHH:MM	11JUN2023	0	
004	CDMSTOT	CSMS: Daily Medication Score (dMS)	YYYY-MM-DDTHH:MM	11JUN2023	1	COMPOSITE VARIABLE STRATEGY
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023	1.166666667	
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023	2.166666667	COMPOSITE VARIABLE STRATEGY
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023		HYPOTHETICAL STRATEGY

EXAMPLE: STRATEGIES AFTER ICES IN OTHER ADAMS
ADCSMSDL: Analysis Flags

SUBJID	PARAMCD	PARAM	QSDTC	ADT	AVAL	DTYPE
004	CDSSTOT	CSMS: Daily Symptom Score (dSS)	YYYY-MM-DDTHH:MM	11JUN2023	1.166666667	
004	CDMSTOT	CSMS: Daily Medication Score (dMS)	YYYY-MM-DDTHH:MM	11JUN2023	0	
004	CDMSTOT	CSMS: Daily Medication Score (dMS)	YYYY-MM-DDTHH:MM	11JUN2023	1	COMPOSITE VARIABLE STRATEGY
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023	1.166666667	
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023	2.166666667	COMPOSITE VARIABLE STRATEGY
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	YYYY-MM-DDTHH:MM	11JUN2023		HYPOTHETICAL STRATEGY

Primary Estimand **Supplementary Estimands**

SUBJID	PARAMCD	AVAL	DTYPE	ANL01FL	ANL02FL	ANL04FL	ANL05FL	ANL07FL	ANL08FL	ANL10FL	ANL11FL	ANL12FL
004	CDSSTOT	1.1666667						Y	Y			
004	CDMSTOT	0										
004	CDMSTOT	1	COMPOSITE VARIABLE STRATEGY		Y		Y					
004	CSMSTOT	1.1666667										
004	CSMSTOT	2.1666667	COMPOSITE VARIABLE STRATEGY	Y		Y					Y	Y
004	CSMSTOT		HYPOTHETICAL STRATEGY							Y		

Key Secondary Estimands

EXAMPLE: STRATEGIES AFTER ICES IN OTHER ADAMS

ADCSMSDL: Selection of records for each analysis and multiple imputation

SUBJID	PARAMCD	PARAM	ADT	AVAL	DTYPE	ANL01FL
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	01JUN2023			Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	02JUN2023	1.5		Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	03JUN2023	2		Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	04JUN2023	6	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	05JUN2023	5	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	06JUN2023	2	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	07JUN2023	1.6666666667	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	08JUN2023	4	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	09JUN2023	2.1666666667	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	10JUN2023		COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	11JUN2023	2.1666666667	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	12JUN2023	2.3333333333	COMPOSITE VARIABLE STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	13JUN2023	2	COMPOSITE VARIABLE STRATEGY	Y

Missing values will be imputed via Multiple Imputation

Resulting dataset: ADCSMSDM1 stored, but considered as "Analysis Dataset", not ADaM

EXAMPLE: STRATEGIES AFTER ICES IN OTHER ADAMS

ADCSMSDL: Selection of records for each analysis and multiple imputation

SUBJID	PARAMCD	PARAM	ADT	AVAL	DTYPE	ANL10FL
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	01JUN2023			Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	02JUN2023	1.5		Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	03JUN2023	2		Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	04JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	05JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	06JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	07JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	08JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	09JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	10JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)	11JUN2023		HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)			HYPOTHETICAL STRATEGY	Y
004	CSMSTOT	CSMS: Daily Combined Symptom Medication Score (CSMS)			HYPOTHETICAL STRATEGY	Y

Missing values will be imputed via Multiple Imputation

Resulting dataset: ADCSMSDM2 stored, but considered as "Analysis Dataset", not ADaM

AGENDA / CONTENT

01 Introduction to Estimands

02 Intercurrent Events (ICEs) and basic strategies

03 Example: ICEs in ADaM (ADICE)

04 Example: Strategies after ICEs in other ADaMs

05 Discussion

DISCUSSION

- Any thoughts?
- Suggestions?
- Further ideas?

THANK YOU VERY MUCH!

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