2026 Korea CDISC Day

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Applying the Estimand Framework in ADaM : From Concepts to Implementation

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29 October 2026



Agenda

1. Estimand and Intercurrent Events
2. ADaM Implementation
3. Worked Examples
4. Reference

Speaker



Sujin Park

Sujin Park has 16 years of experience in clinical trial statistics, specializing in statistical analysis, CDISC standards, and ADaM implementation. She also has extensive experience in statistical team leadership, training, and standardization of statistical processes.

Estimand and Intercurrent Events

Estimand

A precise description of the treatment effect reflecting the clinical question posed by the trial objective

Attributes of an estimand

- Treatment
- Population
- Variable
- Summary
- ICE & Strategy

Intercurrent Events

Events occurring after treatment initiation that affect the interpretation or existence of the measurements tied to the clinical question.

Handling strategies

Treatment policy

ICE occurrence is considered regardless of the TRT effect; Use the observed value regardless of the ICE.

Hypothetical

Envisage a scenario in which the ICE would not occur.

Composite variable

The ICE is considered in itself to be informative, so it is incorporated into the definition of the variable.

While on treatment

Response before the ICE occurs is of interest.

Principal stratum

Target population is the stratum in which the ICE would occur.

ADaM Implementation

ADaM: New ADSL Variable

Analysis set flags

Variable	Label	Type	Codelist	Core	CDISC Notes
PSyFL	Principal Stratum y Set Flag	Char	YN	Cond	Flags subjects in principal stratum y (y = stratum index). **Used when an estimand handles ICEs with a principal stratum strategy**; several strata are possible, and each estimand may use a different one. Required when this strategy is used.

ADaM: New Analysis Dataset – ADICE

ADICE Dataset

Attribute	Value	Attribute	Value
Dataset	ADICE	Class – Subclass	**Occurrence Data Structure** – Intercurrent Events
Description	Intercurrent Events Analysis Dataset	Structure	One record per subject per intercurrent event

Structure Variables List

Variable	Label	Notes
ACATy	Analysis Category {y}	**Categorisation of ICEs**. For example: ACAT1 = "Treatment Discontinuation“ / "Start of administration of Rescue Therapy"
ESTzzSTP	Estimand zz* planned handling strategy	**Planned strategy** for handling the ICEs related to estimand zz, per CT ICESTRG (such as “TREATMENT POLICY”, “HYPOTHETICAL”, “COMPOSITE”, “WHILE ON TREATMENT” and “PRINCIPAL STRATUM”).
ESTzzSTA	Estimand zz* actual handling strategy	**Actual strategy** for handling the ICEs related to estimand zz, per CT ICESTRG. **Consider the priority rules.**

ADaM: New Analysis Dataset Variables

IC[Cy][Ezz][S]: Impact of ICE class y for estimand zz (Seq.). Links ICEs to datapoints through the ICE identifier (typically ASEQ).

ICCyS	Identifies ICEs **impacting the interpretation or use** of the datapoint; y indexes a value of one ADECODy / ACATy variable from ADICE.
ICEzzS	Identifies the one ICE impacting use of the datapoint for estimand zz, based on strategy; **assumes priority rules**.
ICCyEzzS	For complex cases: refines ICCy per estimand, e.g. a different ADECODy / ACATy per estimand.

USUBJID	PARAMCD	AVISIT	[…]	AVAL	[…]	IC[Cy][Ezz][*]

Extra suffixes: [D] Domain · [V] Variable · **[F] Flag** · [N] Numeric flag

“Impact"?

- meaning that the **interpretation and** consequently the possible **usage of a datapoint** in an analysis is **influenced** by the presence of an intercurrent event.
- leaving implementers some **flexibility to further specify the impact concept** according to their needs, **with a reminder to document** in Define-XML/ADRG the exact definition they have adopted
- the exact notion of impact depends on sponsor needs/decision and will **typically involve** some form of **actual impact**

“Actual impact" mean?

Determined based on strategies associated with the estimand and intercurrent event if the datapoint can be **used in the analyses or should be replaced/removed**.

For Example:

- **Treatment policy**: Datapoint is used as is, even if affected by the ICE → **No actual impact**
- **Hypothetical**: Affected datapoint is replaced / removed from the analysis → **Actual impact**

Worked Examples - 1

Example 1

ICE strategies for Estimand 01		Estimand 02
ICE1	Starting other pharmacological treatments	Treatment policy → Composite
ICE2	Treatment discontinuation due to geopolitical logistical restrictions	Hypothetical → Hypothetical
ICE3	Treatment discontinuation due to AE / lack of efficacy	Treatment policy → Treatment policy

Priority Rule per subject ICE2 > ICE1 > ICE3

ICE2: Hypothetical for Estimand 01,02

ADICE

USUBJID	ASEQ	ATERM	ACAT1	VISIT	VISITNUM	ASTDT	AENDT	SRCDOM	SRCSEQ	EST01STP	EST01STA	EST02STP	EST02STA
ABC002	1	LOGISTICAL PROBLEM	Treatment discontinuation due to geopolitical logistical restrictions	WEEK 2	3	2022-03-30		DS	3	HYPOTHETICAL	HYPOTHETICAL	HYPOTHETICAL	HYPOTHETICAL
ABC002	2	FLUOXETINE	Starting other pharmacological treatments	UNSCHEDULED WEEK 2.1	3.1	2022-04-03		CM	1	TREATMENT POLICY		COMPOSITE	

ICE1: Treatment policy for Estimand 01

ICE1: Composite for Estimand 02

ADEFF

USUBJID	PARAMCD	AVAL	VISIT	ADT	ICC1S	ICC2S	ICC3S	ICC1E01F	ICC2E01F	ICC3E01F	ICC1E02F	ICC2E02F	ICC3E02F	ICE01S	ICE02S
ABC002	HAMD118	31	WEEK 0	2022-03-16											
ABC002	HAMD118	31	WEEK 1	2022-03-23											
ABC002	HAMD118	30	WEEK 2	2022-03-30		1			Y			Y		1	1
ABC002	HAMD118	16	WEEK 2.1	2022-04-03	2	1			Y		Y	Y		1	1
ABC002	HAMD118	30	WEEK 3	2022-04-06	2	1			Y		Y	Y		1	1
ABC002	HAMD118	32	WEEK 4	2022-04-13	2	1			Y		Y	Y		1	1
ABC002	HAMD118	30	WEEK 5	2022-04-20	2	1			Y		Y	Y		1	1
ABC002	HAMD118	34	WEEK 6	2022-04-27	2	1			Y		Y	Y		1	1
ABC002	HAMD118	29	WEEK 7	2022-05-04	2	1			Y		Y	Y		1	1
ABC002	HAMD118	28	WEEK 8	2022-05-11	2	1			Y		Y	Y		1	1

ICE2: Hypothetical for Estimand 01

ICE1: Treatment policy for Estimand 01

ADICE

USUBJID	ASEQ	ATERM	ACAT1	VISIT	VISITNUM	ASTDT	AENDT	SRCDOM	SRCSEQ	EST01STP	EST01STA	EST02STP	EST02STA
ABC002	1	LOGISTICAL PROBLEM	Treatment discontinuation due to geopolitical logistical restrictions	WEEK 2	3	2022-03-30		DS	3	HYPOTHETICAL	HYPOTHETICAL	HYPOTHETICAL	HYPOTHETICAL
ABC002	2	FLUOXETINE	Starting other pharmacological treatments	UNSCHEDULED WEEK 2.1	3.1	2022-04-03		CM	1	TREATMENT POLICY		COMPOSITE	

ADEFF

USUBJID	PARAMCD	AVAL	VISIT	ADT	ICC1S	ICC2S	ICC3S	ICC1E01F	ICC2E01F	ICC3E01F	ICC1E02F	ICC2E02F	ICC3E02F	ICE01S	ICE02S
ABC002	HAMD118	31	WEEK 0	2022-03-16											
ABC002	HAMD118	31	WEEK 1	2022-03-23											
ABC002	HAMD118	30	WEEK 2	2022-03-30		1			Y			Y		1	1
ABC002	HAMD118	16	WEEK 2.1	2022-04-03	2	1			Y		Y	Y		1	1
ABC002	HAMD118	30	WEEK 3	2022-04-06	2	1			Y		Y	Y		1	1
ABC002	HAMD118	32	WEEK 4	2022-04-13	2	1			Y		Y	Y		1	1
ABC002	HAMD118	30	WEEK 5	2022-04-20	2	1			Y		Y	Y		1	1
ABC002	HAMD118	34	WEEK 6	2022-04-27	2	1			Y					1	1
ABC002	HAMD118	29	WEEK 7	2022-05-04	2	1			Y		Y	Y		1	1
ABC002	HAMD118	28	WEEK 8	2022-05-11	2	1			Y		Y	Y		1	1

Priority Rule : ICE2>ICE1>ICE3

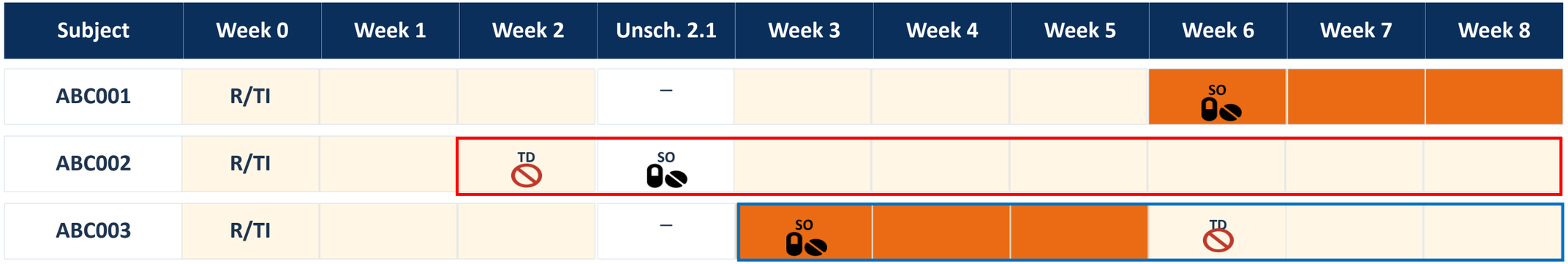
Worked Examples - 2

Example 2

ICE strategies for Estimand 01

ICE1	Start other medications for MDD	Hypothetical
ICE2	Treatment discontinuation	Treatment policy

Priority rule per subject Treatment policy > Hypothetical



ADICE

USUBJID	ASEQ	ATERM	ADECOD1	ACAT1	ASTDT	AENDT	EST01STP	EST01STA	SRCDOM	SRCSEQ
ABC001	1	DULOXETINE	Starting other pharmacological treatments	Starting other pharmacological treatments	20APR2022		Hypothetical	Hypothetical	CM	1
ABC002	1	ADVERSE EVENT	Treatment discontinuation due to adverse events	Treatment discontinuation	30MAR2022		Treatment Policy	Treatment Policy	DS	3
ABC002	2	FLUOXETINE	Starting other pharmacological treatments	Starting other pharmacological treatments	03APR2022		Hypothetical		CM	1
ABC003	1	LORAZEPAM	Starting other pharmacological treatments	Starting other pharmacological treatments	06APR2022	20APR2022	Hypothetical	Hypothetical	CM	1
ABC003	2	LACK OF EFFICACY	Treatment discontinuation due to lack of efficacy	Treatment discontinuation	27APR2022		Treatment Policy	Treatment Policy	DS	3

ADICE

USUBJID	ASEQ	ATERM	ADECOD1	ACAT1	ASTDT	AENDT	EST01STP	EST01STA	SRCDOM	SRCSEQ
ABC001	1	DULOXETINE	Starting other pharmacological treatments	Starting other pharmacological treatments	20APR2022		Hypothetical	Hypothetical	CM	1
ABC002	1	ADVERSE EVENT	Treatment discontinuation due to adverse events	Treatment discont			Treatment Policy	Treatment Policy	DS	3
ABC002	2	FLUOXETINE	Starting other pharmacological treatments	Starting other pharmacological treatments	03APR2022		Hypothetical		CM	1
ABC003	1	LORAZEPAM	Starting other pharmacological treatments	Starting other pharmacological treatments	06APR2022	20APR2022	Hypothetical	Hypothetical	CM	1
ABC003	2	LACK OF EFFICACY	Treatment discontinuation due to lack of efficacy	Treatment discontinuation	27APR2022		Treatment Policy	Treatment Policy	DS	3

ICE1: Hypothetical for Estimand 01

ICE2: Treatment policy for Estimand 01

ADEFF

USUBJID	PARAMCD	ADT	AVISIT	AVAL	BASE	CHG	ICC1S	ICC2S	ICE01S
ABC003	HDRS	16MAR2022	BASELINE	26	26				
ABC003	HDRS	23MAR2022	WEEK 1	21	26	-5			
ABC003	HDRS	30MAR2022	WEEK 2	19	26	-7			
ABC003	HDRS	06APR2022	WEEK 3	16	26	-10	1		1
ABC003	HDRS	13APR2022	WEEK 4	19	26	-7	1		1
ABC003	HDRS	20APR2022	WEEK 5	15	26	-11	1		1
ABC003	HDRS	27APR2022	WEEK 6	21	26	-5	1	2	
ABC003	HDRS	04MAY2022	WEEK 7	18	26	-8	1	2	
ABC003	HDRS	25MAY2022	WEEK 8	16	26	-10	1	2	

Priority Rule : Treatment policy > Hypothetical

Worked Examples - 3

Example 3

ICE strategies for Estimand 01

ICE1	Start of protocol-prohibited corticosteroids or immunosuppressive treatment	Hypothetical (MAR)
ICE2	Start of other protocol-prohibited therapy	Hypothetical (MAR)
ICE3	Treatment discontinuation	Treatment policy
ICE4	Death	Hypothetical (MNAR,J2R)
ICE5	Receipt of Kidney Replacement Therapy (KRT)	Hypothetical (MNAR,J2R)

Priority rule per subject ICE4 / ICE5 > ICE1 > ICE2 > ICE3

ADICE

USUBJID	ADECOD1	ASTDT	EST01STP	AVISIT	ASEQ
10001	ICE2	2024-09-03	Hypothetical (MAR)	Week 37	1
10001	ICE1	2024-10-03	Hypothetical (MAR)	Week 53	2
10001	ICE5	2025-01-15	Hypothetical (MNAR)	Week 77	3

It does not provide variables such as selections or actions flags in the guideline. That part is left to the implementers.

ADEFF

USUBJID	PARAMCD	ADT	AVISIT	AVAL	ICC1S	ICC2S	ICC3S	ICC4S	ICC5S	ICC1E01F	ICC2E01F	ICC3E01F	ICC4E01F	ICC5E01F	ICE01S	METHOD01
10001	TEST01	2023-12-19	Baseline	1.2												
10001	TEST01		Week 13													MI-MAR
10001	TEST01	2024-06-11	Week 25	1.4												
10001	TEST01	2024-09-03	Week 37	2.3		1					Y				1	MI-MAR
10001	TEST01	2024-10-03	Week 53	2.1	2	1				Y	Y				2	MI-MAR
10001	TEST01	2025-01-15	Week 77		2	1			3	Y	Y		Y		3	J2R

Priority Rule : ICE4 / ICE5 > ICE1 > ICE2 > ICE3

Worked Examples - 4

Example 4

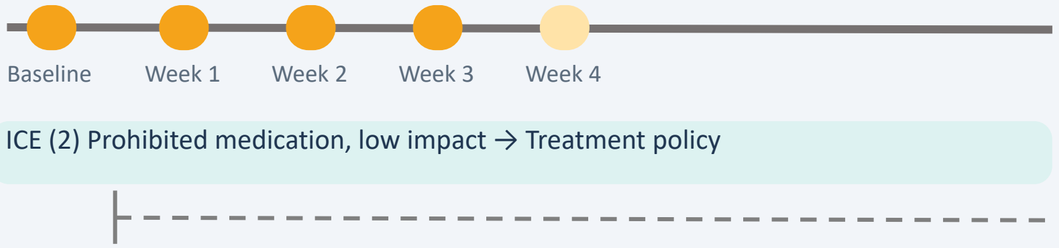
ICE strategies for Estimand 01

ICE1	Treatment non-compliance	Hypothetical (MAR)
ICE2	Prohibited medication, low expected impact	Treatment policy
ICE3	Prohibited medication, high expected impact	Hypothetical (MAR)
ICE4	Discontinuation, probably caused by treatment	Hypothetical (MNAR,J2R)
ICE5	Discontinuation, unlikely caused by treatment	Treatment policy

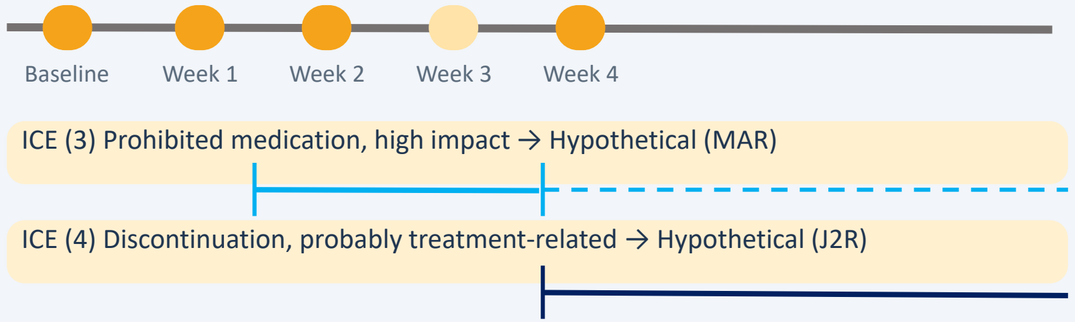
Priority rule per subject Hypothetical (J2R) > Hypothetical (MAR) > Treatment policy

Priority Rule : Hypothetical (J2R) > Hypothetical (MAR) > Treatment policy

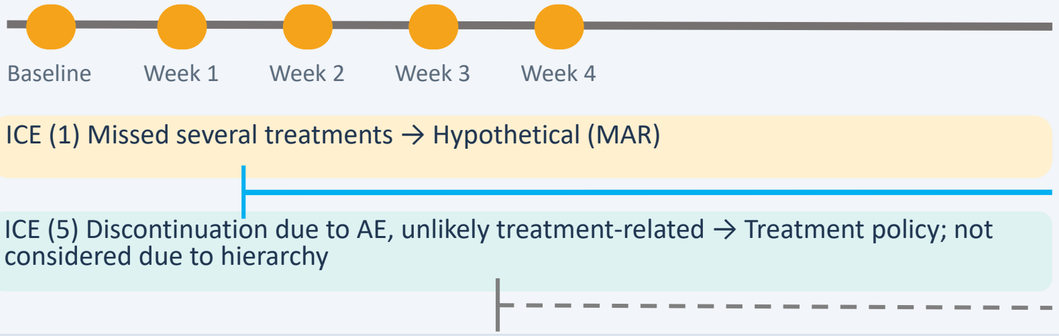
Subject ABC001



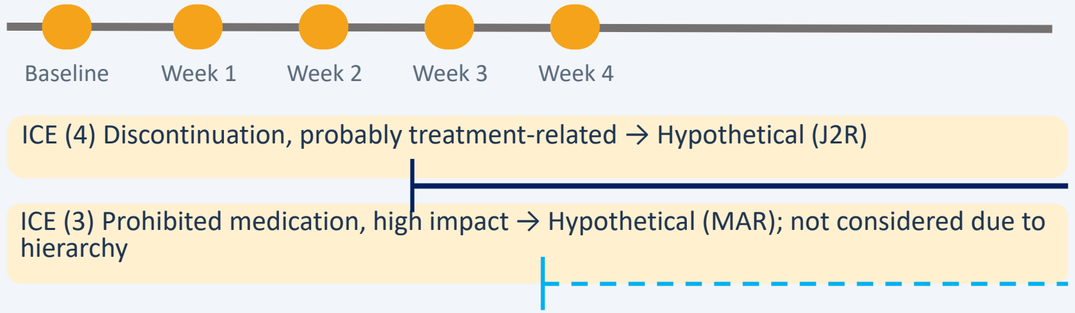
Subject ABC002



Subject ABC003



Subject ABC004



Reference

Reference

1. ICH E9(R1) Addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Updated 20 November, 2019

2. PHUSE deliverables- 2025- Implementation of Estimands (ICH E9 (R1)) using Data Standards

3. PHUSE Whitepaper: Implementation of ICH E9(R1) Estimands Framework Using Data Standards, 2025

4. End-to-End Workflow for CDISC Estimand Framework in Clinical Trials, Paper PP20.

5. 2024 CIDSC EUROPE Interchange: Estimands implementation using data standards

6. Estimands: How to Make ADaM Implementation Your Friend, Paper DS13.

7. ICH E9(R1) Estimands Framework 데이터표준구현, 박규리

Thank You

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