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ADICE: A Proposed ADaM Dataset Structure for Intercurrent Events in the Estimand Framework

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ABSTRACT

The ICH E9(R1) addendum introduced the estimand framework, making the precise definition and handling of intercurrent events (ICEs) a central requirement in clinical trial design and analysis. Despite this, no standardized ADaM dataset structure exists to capture, classify, and trace ICEs in a consistent, submission-ready way. This paper proposes ADICE, an ADaM-compliant Occurrence Data Structure dataset designed to fill this gap.

ADICE consolidates all trial-level ICE records into a single subject-level dataset with full traceability to source SDTM domains. It supports multiple estimand strategies — composite, hypothetical, treatment policy, and while-on-treatment — through explicit strategy variables and ICE type flags, enabling downstream efficacy analysis datasets to derive estimand-aligned analysis flags from a single authoritative source.

This paper describes the ADICE dataset structure, key variables, data flow, CDISC standards alignment, and integration with efficacy endpoints. Dummy data examples illustrate single and multiple ICE scenarios, including cases where different estimand strategies apply to the same subject under a defined priority hierarchy.

INTRODUCTION

The ICH E9(R1) addendum formalized the estimand framework, placing intercurrent events (ICEs) at the center of clinical trial design and analysis. Current ADaM data standards, however, lack a dedicated dataset structure for capturing, classifying, and tracing ICEs in a consistent, submission-ready manner. This paper proposes ADICE, an ADaM-compliant occurrence dataset designed to address this gap. The sections that follow provide background on the estimand framework, describe the ADICE dataset structure and its CDISC alignment, and demonstrate its integration with efficacy endpoints through illustrative examples.

THE ESTIMAND FRAMEWORK

An estimand defines the treatment effect of interest through five attributes: the population, the variable (endpoint), the handling of ICEs, the population-level summary, and the statistical method. ICH E9(R1) defines five ICE handling strategies (ICH, 2019):

- Treatment policy strategy: the ICE and all subsequent data are included as observed.
- Hypothetical strategy: the scenario in which the ICE would not have occurred is considered; post-ICE data are set to missing and imputed per the SAP.
- Composite variable strategy: the ICE is incorporated into the endpoint definition, typically as treatment failure or non-response.
- While-on-treatment strategy: only data collected while the subject remains on treatment are used; post-ICE observations are excluded.
- Principal stratum strategy: inference is restricted to the subpopulation defined by ICE occurrence or non-occurrence.

A trial may pre-specify a primary estimand and one or more supplementary estimands, each potentially assigning a different strategy to the same ICE category (Akacha et al., 2017). This creates complex programming requirements when the same post-randomization event must be handled differently depending on which estimand is being evaluated. The principal stratum strategy, while defined in E9(R1),

is less commonly implemented in practice and is not illustrated in the examples that follow; the ADICE structure supports it through the same EST0xSTP/STA variable convention.

INTERCURRENT EVENTS IN CLINICAL TRIALS

Common ICE categories across therapeutic areas include: initiation of prohibited or rescue medications after randomization; dose escalation of permitted background therapies beyond baseline levels; early discontinuation from study treatment; and death. Each category requires a clear definition, a designated source domain, and a pre-specified handling strategy. The determination of whether a subject experienced an ICE — and exactly when — must be reproducible and consistent across all analysis datasets in a submission.

THE PROGRAMMING GAP

Current CDISC ADaM guidelines — the ADaM Implementation Guide (ADaMIG v1.3) and Occurrence Data Structure guidance (OCCDS v1.1) — do not define a dedicated dataset for ICE documentation (CDISC, 2021; CDISC, 2016). As a result, ICE derivation logic is typically embedded within each efficacy analysis dataset. This approach creates several problems: derivation logic may differ subtly across datasets; updates to ICE definitions must be propagated to every affected program; and reviewers have no single reference point to verify ICE classifications. ADICE is proposed to resolve these issues.

The sections that follow cover the ADICE dataset structure and key variables, CDISC standards alignment, data flow and traceability, integration with efficacy endpoints, and illustrative examples spanning single ICE, multiple ICE, and mixed-strategy scenarios.

ADICE DATASET STRUCTURE

DATASET OVERVIEW

ADICE is an ADaM Occurrence Data Structure (OCCDS) dataset. Its granularity is one record per subject per intercurrent event. The natural dataset keys are STUDYID, USUBJID, ASTDT (ICE start date), ATERM (ICE term), and ADECOD1 (standardized ICE decoded term). The dataset is analogous in structure to ADAE or ADCM, but is dedicated exclusively to capturing, classifying, and dating ICEs.

Because ICEs may originate from multiple SDTM source domains — a subject may simultaneously have a relevant medication change (CM domain) and a treatment discontinuation (DS domain) — ADICE unifies these into a single structured output. Each record carries SRCDOM and SRCSEQ to maintain full one-step traceability back to SDTM.

KEY VARIABLES

Table 1 summarizes the core variable groups in ADICE. ASEQ provides a unique record identifier within subject (integer starting at 1) and is used as the traceability key (ICEzzSEQ) in downstream efficacy datasets. The number of ICE flag variables (ICE01FL, ICE02FL, ...) and estimand strategy pairs (EST01STP/STA, EST02STP/STA, ...) scales with the number of ICE categories and estimands defined in the SAP.

ASEQ	Analysis sequence number	Unique record identifier within subject; integer starting at 1

Variable(s)	Label / Purpose	Derivation Notes
STUDYID, USUBJID	Subject identifiers	Required per ADaMIG; copied from DM
ACAT1	ICE category description	Full SAP-defined category label; one per ICE type
ADECOD1	Standardized ICE decoded term	Derived from sponsor classification; may concatenate subcategories
ATERM	Reported ICE term	From source decoded term

		(e.g., CMDECOD, DSDECOD)
ASTDT	Analysis start date (ICE date)	From source domain start date
ASTDY	Analysis start day (ICE day)	Derived as ASTDT - RFSTDTC + 1; integer day relative to study start
ICE01FL, ICE02FL, ...	ICE type flags	Y/null (NY_Y codelist); one flag per ICE category
EST01STP, EST01STA	Estimand 01 strategy (planned/actual)	Planned (STP): strategy pre-specified in the SAP. Actual (STA): strategy as implemented. Values e.g. COMPOSITE, HYPOTHETICAL, TREATMENT POLICY. Differ when protocol amendments or health authority requests change the strategy post-specification.
EST02STP, EST02STA	Estimand 02 strategy (planned/actual)	Same convention as EST01STP/STA for a second estimand. Additional pairs added for each supplementary estimand defined in the SAP.
SRCDOM, SRCSEQ	Source domain and sequence number	Enable direct traceability to the originating SDTM record

Table 1. Core ADICE variables.

ICE CATEGORY DESIGN

Each trial's SAP defines the ICE categories relevant to its estimand(s). ADICE accommodates any number of categories through ACAT1 and corresponding flag variables. Category definitions, source domains queried, and classification logic are fully specified in the SAP and documented in the ADICE variable-level metadata. All qualifying ICE events are retained — not just the first per subject — so that downstream programs can apply priority-ordered handling correctly.

ACAT1 carries a full human-readable description of the ICE category and is the primary grouping variable used in ICE summary tables, listings, and regulatory outputs. Each record in ADICE belongs to exactly one ICE category. ADECOD1 provides a more granular standardized term within a category (e.g., the specific medication name or disposition reason).

Because ACAT1 is displayed directly in summary outputs and regulatory tables, its wording may evolve across protocol amendments or in response to health authority feedback — for example, a category description may be revised to align with updated SAP language. ACAT1 should therefore not be used as a hard-coded filter in analysis programs. Instead, ICE0xFL flag variables serve as the stable, version-independent programmatic identifiers for each ICE category.

ESTIMAND STRATEGY VARIABLES

EST01STP and EST01STA encode the planned and actual ICE handling strategy for the primary estimand. Additional pairs (EST02STP/STA, etc.) are added for supplementary estimands. This makes the strategy assignment explicit at the record level, supporting both programming and regulatory review without cross-referencing the SAP.

The planned (STP) and actual (STA) distinction follows ICH E9(R1) guidance on separating pre-specified from as-implemented analyses. They may differ when, for example:

- A protocol amendment changes the handling strategy for an ICE category mid-study.
- A health authority requests a different strategy during review.

When no such changes occur, both variables are populated identically and serve as a consistency check between the SAP and the analysis.

CDISC STANDARDS ALIGNMENT

ADICE is designed to conform with CDISC ADaM standards, specifically ADaMIG v1.3 and OCCDS v1.1 (CDISC, 2021; CDISC, 2016). Key compliance points are:

- Dataset structure: one record per subject per intercurrent event, consistent with the OCCDS pattern for occurrence-type data.
- Required variables: STUDYID and USUBJID are included as required by ADaMIG.
- Timing variables: ASTDT follows ADaMIG Section 3.1.2 timing variable conventions.
- Analysis term variables: ATERM follows the ADaMIG convention for reported terms; ADECOD1 follows the dictionary-derived term convention (analogous to AEDECOD in ADAE); ACAT1 follows the analysis category convention used across OCCDS datasets.
- Controlled terminology: ICE flag variables use the NY_Y codelist; other flag variables follow applicable CDISC controlled terminology.
- Traceability variables: SRCDOM and SRCSEQ are included as permissible traceability variables per ADaMIG guidance for occurrence datasets.
- Estimand variables: EST01STP/STA naming aligns with emerging CDISC working group recommendations for operationalizing E9(R1) in ADaM (CDISC ADaM Team, 2023). Note: this reference reflects a working-group document; practitioners should check the current CDISC ADaM publication page for the latest status.

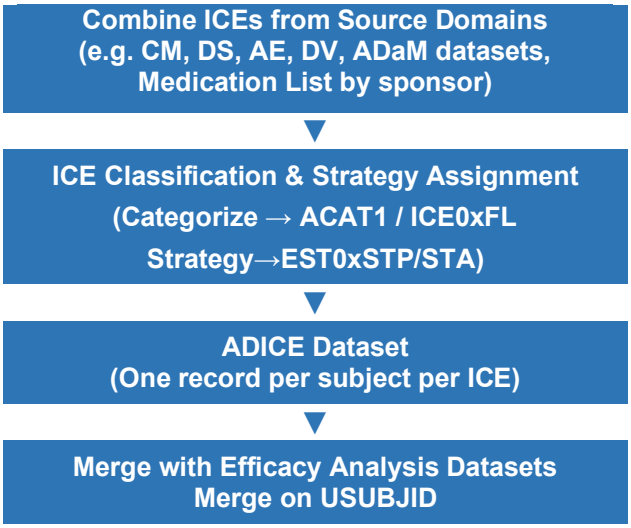
The ADICE structure is designed to be forward-compatible as CDISC guidance on estimand operationalization evolves: estimand strategy variable pairs and ICE flag variables scale to any number of estimands and categories without structural changes to the dataset.

DATA FLOW AND TRACEABILITY

INPUT SOURCES AND PROCESSING STEPS

ADICE is built from SDTM source domains, ADaM datasets, and sponsor reference files. Typical inputs include one or more event domains (CM, DS, AE, DV), DM/ADSL for subject-level dates and analysis set flags.

The general processing steps for constructing ADICE are:



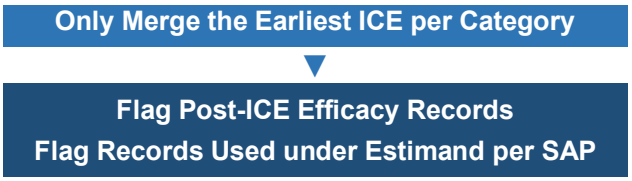


Figure 1. ADICE data flow.

Source SDTM domains and sponsor reference files feed into the ICE classification step, producing the ADICE dataset. Downstream efficacy analysis datasets merge with ADICE to generate estimand-specific analysis flags, enabling all estimand-aligned analyses from a single, consistent ICE source.

SOURCE DOMAIN TRACEABILITY

SRCDOM and SRCSEQ in every ADICE record identify the originating SDTM domain and sequence number. This allows a reviewer to navigate from any ICE flag in a downstream efficacy dataset to the SDTM source record in a single step — without re-querying the source domain. Medication-based ICEs typically carry SRCDOM="CM"; discontinuation-based ICEs carry SRCDOM="DS".

Table 2 shows dummy ADICE records for two subjects illustrating source domain traceability. Subject DEMO-001 has two ICE records from different source domains; Subject DEMO-002 has one. SRCDOM and SRCSEQ enable direct navigation to the originating SDTM record.

USUBJID	ASTDT	ASTDY	ACAT1	ICE01FL	ICE02FL	SRCDOM	SRCSEQ
DEMO-001	15MAR2024	74	Initiated rescue medication	Y		CM	12
DEMO-001	01APR2024	91	Discontinued treatment		Y	DS	3
DEMO-002	10MAY2024	120	Initiated rescue medication	Y		CM	8

Table 2. Dummy ADICE records illustrating source domain traceability.

OUTPUT AND DOWNSTREAM USE

The final ADICE dataset serves as a single lookup source for all downstream efficacy analysis datasets in the submission. Rather than each efficacy program re-deriving ICE status from raw SDTM domains, it simply merges with ADICE on USUBJID to obtain the earliest ICE date per category for each subject. Analysis flags are then set relative to each observation's assessment date, producing consistent, auditable ICE determinations across all endpoints.

This centralization has several practical benefits: ICE definition changes need to be made only once in ADICE; QC requires only a single dataset comparison rather than endpoint-by-endpoint checks; and regulatory reviewers have a single, navigable source to verify all ICE classifications across the submission package.

INTEGRATING ADICE WITH EFFICACY ENDPOINTS

ICE PRIORITY AND ORDERING

When a subject experiences multiple ICEs of different categories assigned different estimand strategies, the handling logic cannot simply use the earliest event date. Each ICE must be applied in the correct sequence, with the appropriate strategy governing the window between consecutive events. ADICE supports this by retaining a separate record for every ICE with its individual date, category, and strategy assignment.

The SAP must define a priority hierarchy among ICE categories to resolve conflicts when multiple ICEs occur for the same subject. For example: death may override all other ICEs regardless of timing; a prohibited medication use may take precedence over a prior treatment discontinuation from a specific analysis date onward. Because ADICE retains all ICE records with their dates and strategies, downstream programs can implement any SAP-defined priority rule without re-querying SDTM. This is a key design advantage over inline ICE derivation, which typically captures only the earliest or most severe event and cannot easily reconstruct the timeline of multiple ICEs for the same subject.

MERGING STRATEGY

Efficacy analysis datasets (e.g., for clinical response, functional scores) merge with ADICE on USUBJID to obtain the earliest ICE date per category per subject. In addition to ICE dates, the estimand strategy assigned to each ICE category is also carried from ADICE, ensuring that each analysis record knows not only whether an ICE occurred but also how it should be handled under each estimand.

Rationale for merging only the first ICE per category: The SAP assigns one strategy per ICE category, not per occurrence. The first event establishes the governing ASTDT for all downstream ICEzzRFL flagging and imputation. Merging later occurrences would inflate the efficacy dataset via many-to-many joins and create ambiguity in date comparisons. All occurrences remain in ADICE for traceability.

For each observation record, the assessment date (ADT) is compared against each ICE category date. Where ADT falls after an ICE date, the corresponding ICE occurrence flag is set to Y in the efficacy dataset — for example, ICE01RFL="Y" indicates the subject experienced ICE category 1 prior to that assessment. The numeric suffix is intentionally consistent: the x in ICE0xRFL in the efficacy dataset matches the x in ICE0xFL in ADICE, so ICE01FL corresponds to ICE01RFL, ICE02FL to ICE02RFL, and so on. This naming alignment makes the linkage between the two datasets explicit and reduces the risk of mismatched derivations. The efficacy dataset also carries ICEzzSEQ, populated with the ASEQ value from the merged ADICE record, providing direct traceability back to the originating ICE record. ESTzzSTP columns are not carried into the efficacy dataset — strategy information is accessed via the ICEzzSEQ join key back to ADICE.

When a subject experiences multiple ICEs of different categories before an assessment, the SAP-defined priority hierarchy determines which ICE governs the analysis for each estimand. The strategy of the governing ICE is resolved during derivation — priority rules determine which category's strategy applies from each ICE date onward. The ICE occurrence flags (ICEzzRFL) mark all post-ICE observations independently of priority, while the estimand-specific analysis flags (ESTzzRFL) reflect the final determination after priority resolution. Together, the ICE flags, sequence keys (ICEzzSEQ), and estimand flags allow full reconstruction of the derivation logic without duplicating strategy information from ADICE into the efficacy dataset.

ESTIMAND-SPECIFIC ANALYSIS FLAGS

Once ICE occurrence and strategies are determined relative to each assessment, estimand-specific record-level flags are generated in the efficacy dataset. EST0xRFL (estimand-specific record-level flag) variables are used to flag the records included under each estimand — for example, EST01RFL flags records used in the primary estimand analysis. The specific imputation rules and flag logic for each EST0xRFL variable are defined in the SAP and vary by study.

ILLUSTRATIVE EXAMPLES

The following examples use dummy data to illustrate ADICE record structure and downstream efficacy flag generation. Only ICE-related, estimand-related, and timing variables are shown. All subject identifiers (DEMO-001 through DEMO-004) and dates are fictional.

EXAMPLE 1: SINGLE ICE, COMPOSITE STRATEGY

DEMO-001 initiates prohibited rescue medication on Day 74 (ICE category 1, composite strategy). DEMO-002 completes the study without any ICE. Table 3 shows their ADICE records.

USUBJID	ASTDT	ASTDY	ACAT1	ICE01FL	EST01STP
DEMO-001	15MAR2024	74	Initiated rescue medication	Y	COMPOSITE

Table 3. ADICE records — single ICE scenario.

In the downstream efficacy dataset for a binary endpoint (clinical response) at Week 12 (Day 84, post-ICE for DEMO-001), Table 4 shows the resulting records under the primary estimand. DEMO-001's assessment falls after the ICE date (Day 74), so ICE01RFL is set to Y, indicating a post-ICE category 1 observation. Under the composite strategy of the primary estimand, an imputed non-responder record (AVALC="N", DTYPE="WC") is created and flagged with EST01RFL="Y". The original observed record remains in the dataset but is not flagged under EST01RFL. For DEMO-002, no ICE occurred, so the single original observed record is flagged directly as EST01RFL="Y".

USUBJID	AVISIT	ADY	AVALC	DTYPE	ICE01RFL	ICE01SEQ	EST01RFL
DEMO-001	Week 12	84	Y		Y	1	
DEMO-001	Week 12	84	N	WC	Y	1	Y
DEMO-002	Week 12	84	N				Y

Table 4. Efficacy dataset — binary endpoint, single ICE.

Note: In practice, ANL01FL (or similar) can be added to the efficacy dataset to select one record per subject per visit when multiple observed records exist at the same AVISIT (e.g., windowing or repeated assessments). ICE01SEQ traces back to ADICE.ASEQ, providing a direct link from the efficacy record to the originating ICE record in ADICE for full traceability.

EXAMPLE 2: MULTIPLE ICES PER SUBJECT, SAME STRATEGY

DEMO-003 experiences two ICEs: dose increase of a background medication (ICE category 1, ICE01FL) on Day 45, and early treatment discontinuation (ICE category 2, ICE02FL) on Day 62. Both are handled under the composite strategy of the primary estimand. Table 5 shows both ADICE records.

USUBJID	ASTDY	ACAT1	ICE01FL	ICE02FL	EST01STP
DEMO-003	45	Dose increase of background therapy	Y		COMPOSITE
DEMO-003	62	Discontinued treatment		Y	COMPOSITE

Table 5. ADICE records — multiple ICEs, same strategy.

Table 6 shows the continuous endpoint handling at three time points. Week 4 (Day 28) is pre-all-ICEs: the single original observed record is flagged EST01RFL="Y". Week 8 (Day 56) is post-ICE category 1 — dose increase (Day 45) but pre-ICE category 2 — treatment discontinuation (Day 62): ICE01RFL="Y"; under the composite strategy a BLOCF record is created (AVAL=BASE, EST01RFL="Y") and the original observed record is retained without EST01RFL. Week 12 (Day 84) is post both ICEs: both ICE01RFL="Y" and ICE02RFL="Y". Since both categories carry the same composite strategy, BLOCF imputation applies uniformly and a BLOCF record is generated for the primary estimand (EST01RFL="Y").

USUBJID	AVISIT	ADY	AVAL	BASE	DTYPE	ICE01RFL	ICE02RFL	ICE01SEQ	EST01RFL
DEMO-003	Week 4	28	32	40					Y

DEMO-003	Week 8	56	29	40		Y		1	
DEMO-003	Week 8	56	40	40	BLOCF	Y		1	Y
DEMO-003	Week 12	84	25	40		Y	Y	1	
DEMO-003	Week 12	84	40	40	BLOCF	Y	Y	1	Y

Table 6. Efficacy dataset — continuous endpoint, multiple ICEs.

ICE01SEQ and ICE02SEQ in the efficacy dataset trace back to ADICE.ASEQ — enabling direct lookup of each ICE's source record, date, and category in ADICE.

EXAMPLE 3: SAME ICE, DIFFERENT STRATEGIES ACROSS ESTIMANDS

DEMO-004 discontinues treatment early on Day 40 (ICE category 1, ICE01FL). The primary estimand assigns a composite strategy to this ICE; the supplementary estimand assigns a treatment policy strategy. Table 7 shows the single ADICE record with both estimand strategy variables populated.

USUBJID	ASTDY	ACAT1	ICE01FL	EST01STP	EST02STP
DEMO-004	40	Discontinued treatment	Y	COMPOSITE	TREATMENT POLICY

Table 7. ADICE record — one ICE, two estimand strategies.

Table 8 shows a binary endpoint at Week 8 (Day 56, post-ICE). ICE01RFL="Y" on all records for DEMO-004. For the primary estimand (composite strategy), an imputed non-responder record is created (AVALC="N", DTYPE="WC", EST01RFL="Y"); the original observed record carries ICE01RFL="Y" but is not flagged EST01RFL. For the supplementary estimand (treatment policy strategy), the original observed record is used directly (EST02RFL="Y"); no imputed record is needed per treatment policy strategy.

USUBJID	AVISIT	AVALC	DTYPE	ICE01RFL	ICE01SEQ	EST01RFL	EST02RFL	
DEMO-004	Week 8	Y		Y	1		Y	
DEMO-004	Week 8	N	WC	Y	1	Y		

Table 8. Efficacy dataset — binary endpoint, two estimands with different strategies.

ICE01SEQ on both efficacy records links back to ADICE.ASEQ=1 — a single join key to retrieve the ICE date, category, and all strategy assignments.

EXAMPLE 4: MULTIPLE ICES WITH PRIORITY HIERARCHY

When different ICE categories carry different strategies, the SAP-defined priority hierarchy determines which strategy governs each assessment window. Consider three ICE categories: (1) prohibited medication use — hypothetical strategy; (2) treatment discontinuation — treatment policy strategy; (3) death — composite strategy.

The priority rules applied in this example are: death (composite) always overrides all other ICEs; among the remaining ICEs, whichever occurs first governs from that point onward — if prohibited medication use occurs first, hypothetical strategy applies from that date for all subsequent assessments regardless of any later discontinuation; if treatment discontinuation occurs first, treatment policy applies until a prohibited medication use occurs, after which hypothetical strategy takes over. These priority rules are illustrative; the exact hierarchy must be pre-specified in the SAP.

Three subjects illustrate different scenarios. DEMO-002 initiates prohibited medication first (Day 25), takes a second prohibited medication (Day 57), then discontinues treatment (Day 59) — hypothetical governs throughout. DEMO-003 discontinues treatment first (Day 30), then uses a prohibited medication (Day 62) — treatment policy applies between the two ICEs, hypothetical supersedes after Day 62. DEMO-004 discontinues treatment (Day 30) then dies (Day 70) — treatment policy applies until death, composite overrides from Day 70. Table 9 shows the ADICE records.

USUBJID	ASTDY	ACAT1	ICE01FL	ICE02FL	ICE03FL	EST01STP
DEMO-002	25	Prohibited medication	Y			HYPOTHETICAL
DEMO-002	57	Prohibited medication	Y			HYPOTHETICAL
DEMO-002	59	Discontinued treatment		Y		TREATMENT POLICY
DEMO-003	30	Discontinued treatment		Y		TREATMENT POLICY
DEMO-003	62	Prohibited medication	Y			HYPOTHETICAL
DEMO-004	30	Discontinued treatment		Y		TREATMENT POLICY
DEMO-004	70	Death			Y	COMPOSITE

Table 9. ADICE records illustrating ICE priority hierarchy.

Table 10 shows the continuous endpoint for all three subjects at scheduled assessments. For each post-ICE assessment under hypothetical strategy, the original observed record is retained alongside a NULL imputed record — the original carries ICE0xRFL="Y" but no EST01RFL; the NULL record carries AVAL=missing and EST01RFL="Y". Downstream imputation models select on EST01RFL="Y" records, so only the NULL records feed into the imputation, not the original observed values. For death, a PHANTOM record is first created to represent the unobservable scheduled assessment (AVAL=missing, no EST01RFL); a COMPOSITE record is then derived from the PHANTOM record with AVAL imputed per SAP and flagged EST01RFL="Y" for inclusion in the primary estimand analysis.

USUBJID	AVISIT	ADY	AVAL	BASE	DTYPE	ICE01RFL	ICE02RFL	ICE03RFL	ICE01SEQ	EST01RFL
DEMO-002	Week 4	28	30	38		Y			1	
DEMO-002	Week 4	28	.	38	NULL	Y			1	Y
DEMO-002	Week 8	56	28	38		Y			1	
DEMO-002	Week 8	56	.	38	NULL	Y			1	Y
DEMO-002	Week 12	84	32	38		Y	Y		1	
DEMO-002	Week 12	84	.	38	NULL	Y	Y		1	Y
DEMO-003	Week 4	28	32	40						Y
DEMO-003	Week 8	56	29	40			Y			Y

DEMO-003	Week 12	84	26	40		Y	Y		2	
DEMO-003	Week 12	84	.	40	NULL	Y	Y		2	Y
DEMO-004	Week 4	28	35	42						Y
DEMO-004	Week 8	56	31	42			Y			Y
DEMO-004	Week 12	84	.	42	PHANTOM		Y	Y		
DEMO-004	Week 12	84	42	42	BLOCF		Y	Y		Y

Table 10. Efficacy dataset — layered ICE priority, continuous endpoint.

ICEzzSEQ values in the efficacy dataset trace back to ADICE.ASEQ — e.g., DEMO-002's ICE01SEQ=1 points to the first prohibited medication (Day 25), while the second occurrence (Day 57, ASEQ=2) is retained in ADICE but not merged as a separate key.

CONCLUSION

The estimand framework has fundamentally changed how clinical trials are designed, analyzed, and reported. Intercurrent events are a formally defined component of the treatment effect question, and their consistent, auditable documentation is a regulatory expectation. ADICE provides a practical ADaM occurrence dataset purpose-built to meet this need.

By consolidating ICE identification, classification, dating, and traceability into a single dataset, ADICE eliminates redundant derivations across efficacy endpoints, creates a single source of truth for regulators and reviewers, and simplifies the propagation of ICE-related updates. The integration pattern with downstream efficacy datasets is generalizable across therapeutic areas, endpoint types, and estimand strategies, and scales naturally with the number of ICE categories and estimands in the SAP.

The dummy data examples in this paper demonstrate that ADICE supports not only simple single-ICE scenarios but also complex cases where multiple ICEs occur for the same subject under different estimand strategies with a defined priority hierarchy — a scenario that conventional inline derivation approaches handle poorly. As CDISC formalizes guidance on estimand operationalization in ADaM, the ADICE framework offers an implementable model that can inform that development and improve consistency across industry submissions. Practical implementation will require sponsor-specific metadata definitions, validation tooling aligned to the dataset structure, and coordination with existing submission conventions. These represent areas for further development as CDISC guidance on estimand operationalization matures.

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