

END-TO-END WORKFLOW FOR CDISC ESTIMAND FRAMEWORK IN CLINICAL TRIALS

Translating Complex Intercurrent Event Definitions into Submission-Ready ADaMs & TLGs

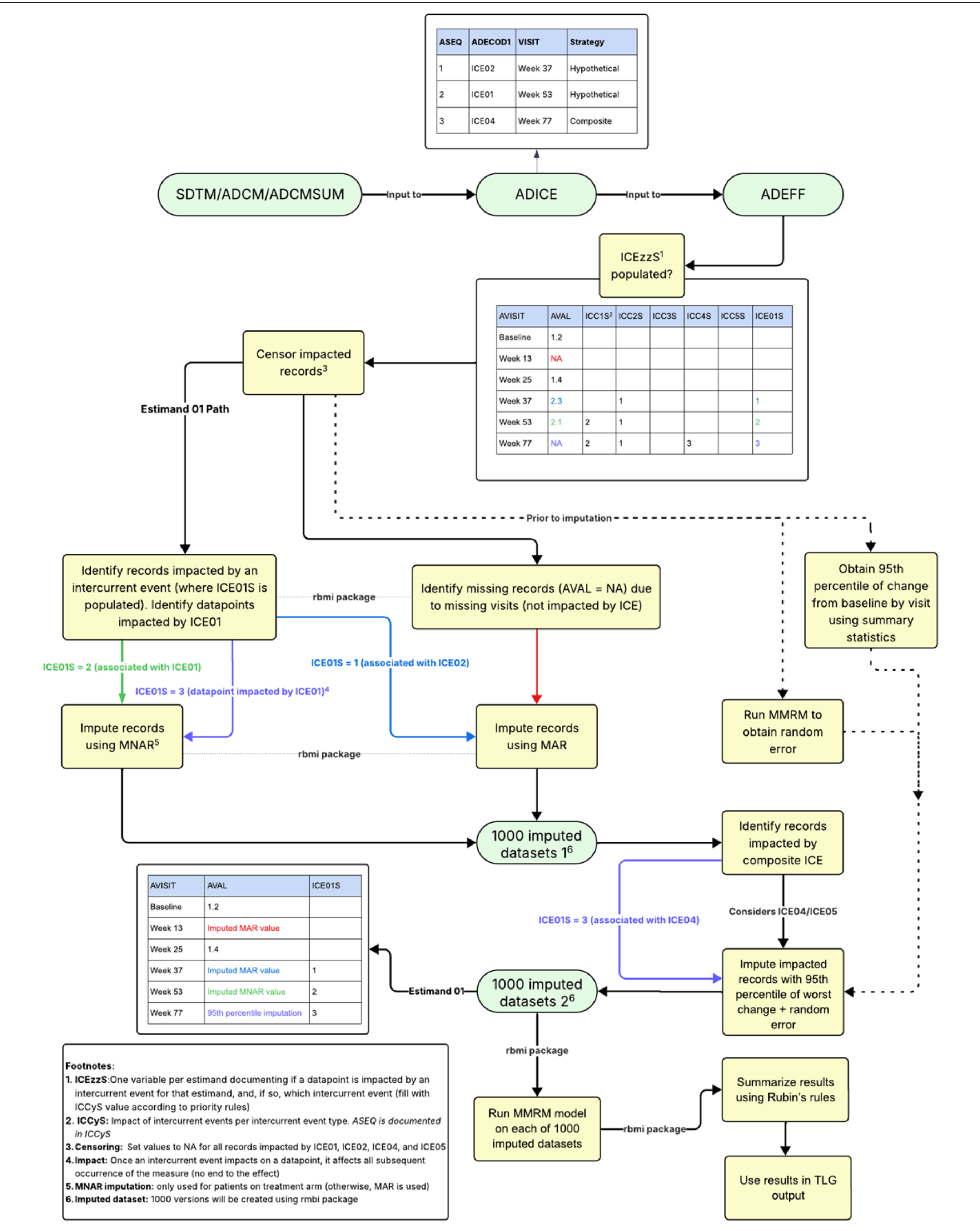
THE CHALLENGE

In late phase Nephrology, analysis of endpoints like **UPCR/eGFR** are highly sensitive to Intercurrent Events (ICEs). The initiation of prohibited corticosteroids can create a treatment effect that confounds the study objectives. Our team established an end-to-end **process** to translate ICH E9(R1) estimand framework into traceable datasets, ensuring that complex datasets are submission-ready for regulatory.

- Defining a standard ADICE OCCDS and intermediate ADaM (ADCMSUM).
- Establishing traceability from CRF to the final MMRM analysis
- Applying intercurrent event prioritization to drive imputation logic
- Managing simultaneous MNAR/MAR handling for various end points

DATA FLOW FROM ADICE TO TLG OUTPUT FOR PRIMARY ESTIMAND

Figure 2. Simplified schematic illustrating how the ICH E9(R1) estimand framework is operationalized through ADICE and downstream imputation to derive final analysis values. The diagram depicts one subject’s efficacy records across six scheduled visits and demonstrates how intercurrent event prioritization governs imputation strategy and inclusion in the final MMRM analysis.

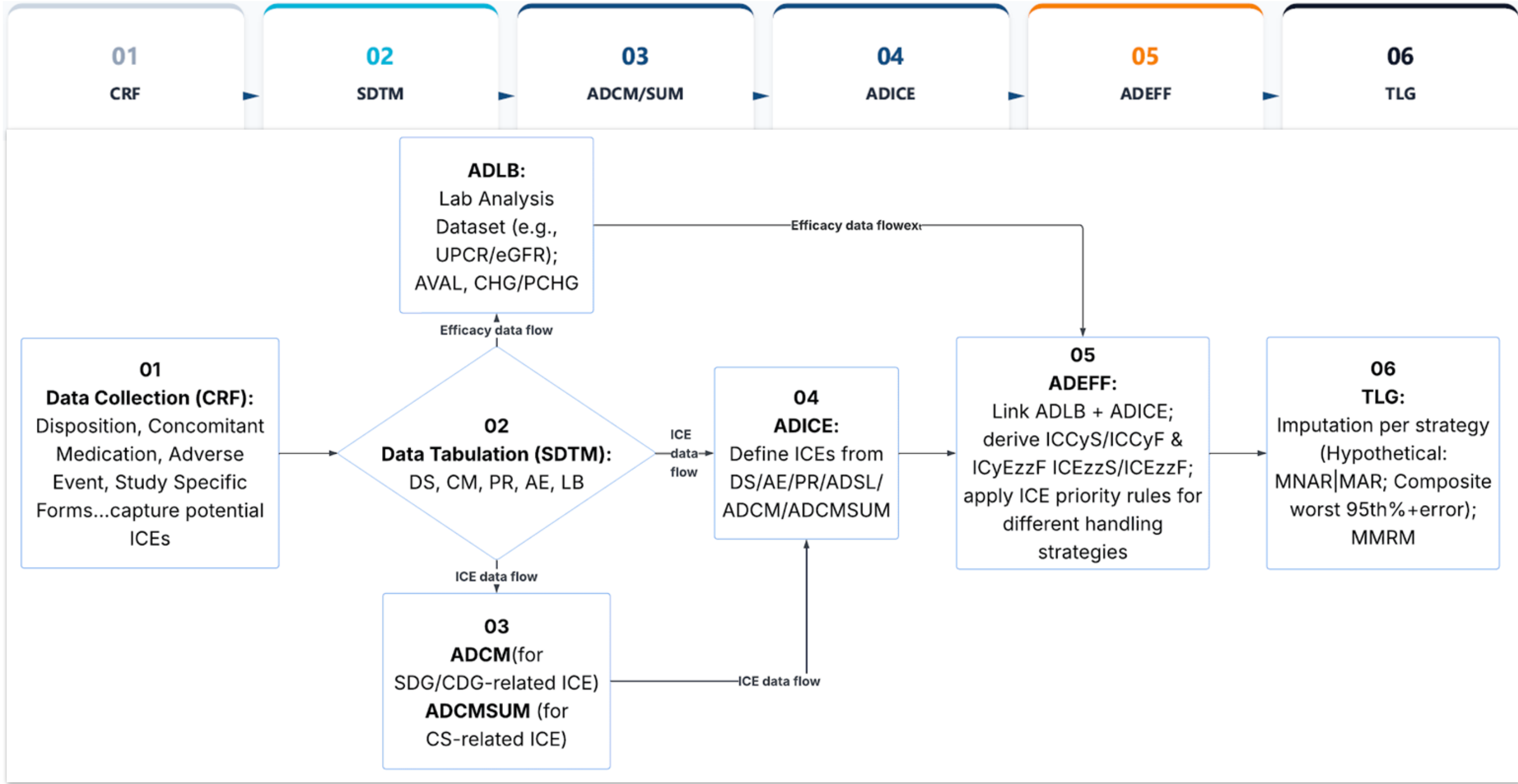


CONCLUSION & LESSONS LEARNED

Complex estimand strategies and intercurrent event handling can be operationalized within standard ADaM structures using a traceable, end-to-end approach. The proposed ADICE-driven framework improves consistency, reduces downstream rework, and supports generation of submission-ready TLGs for nephrology trials.

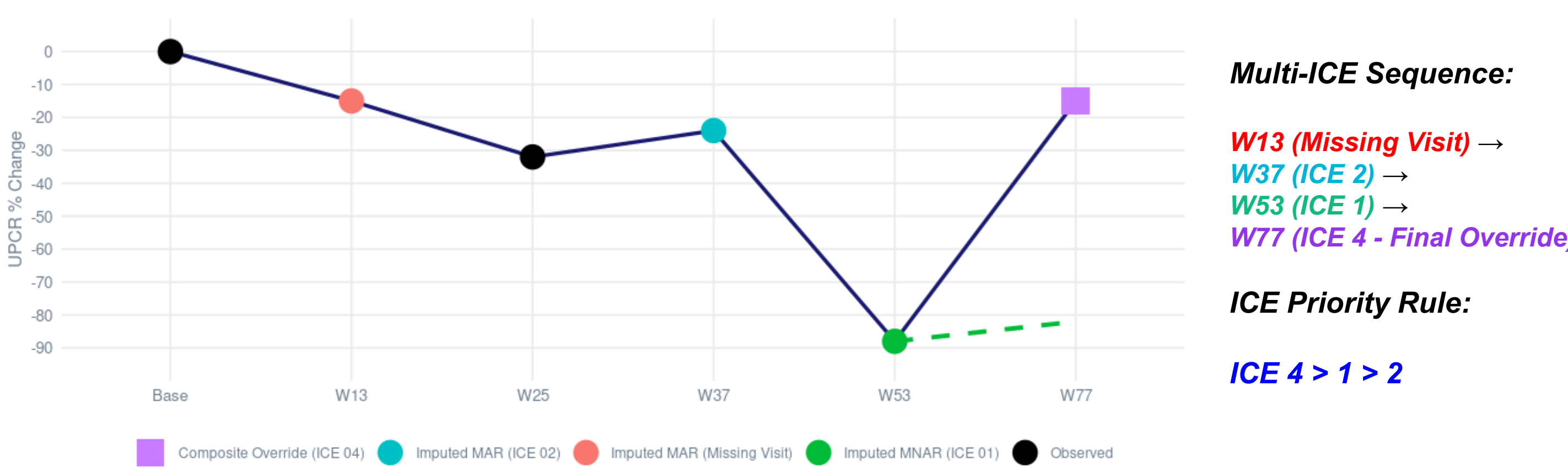
END-TO-END DATA FLOW

Figure 1. Integrating clinical logic from CRF design through to the final TLG output



ESTIMAND-DRIVEN EFFICACY TRAJECTORY

Figure 3. This subject-level trajectory illustrates how the prioritization of intercurrent events dictates the imputation strategy and resulting analysis values across scheduled visits. Note that these trajectories may vary based on the specific estimand and the nature of the analysis (e.g., supplementary vs. primary analyses).



SUBMISSION-READY OUTPUTS

Table 1. ICE Summary Table

	Placebo Arm (N=nnn)	Treatment Arm (N=nnn)
Total number of patients with at least one intercurrent event	nn (xx.x%)	nn (xx.x%)
ICE 01	nn (xx.x%)	nn (xx.x%)
ICE 02	nn (xx.x%)	nn (xx.x%)
ICE 03	nn (xx.x%)	nn (xx.x%)
ICE 04	nn (xx.x%)	nn (xx.x%)
ICE 05	nn (xx.x%)	nn (xx.x%)
ICE 06	nn (xx.x%)	nn (xx.x%)

Table 2. Efficacy Endpoint Summary Table (MMRM Analysis)

Visit Statistics	Placebo Arm (N=nnn)	Treatment Arm (N=nnn)
Week xx		
n	nnn	nnn
Adjusted Mean (SE)	XXX.XX (XX.XXX)	XXX.XX (XX.XXX)
95% CI	(XXX.XX, XXX.XX)	(XXX.XX, XXX.XX)
Difference in Adjusted Mean (SE)		XXX.XX (XX.XXX)
95% CI		(XXX.XX, XXX.XX)
Percent Reduction (%)		XX.X%
P-value (MMRM)		X.XXXX
.....		
Week xx		
n	nnn	nnn
Adjusted Mean (SE)	XXX.XX (XX.XXX)	XXX.XX (XX.XXX)
95% CI	(XXX.XX, XXX.XX)	(XXX.XX, XXX.XX)
Difference in Adjusted Mean (SE)		XXX.XX (XX.XXX)
95% CI		(XXX.XX, XXX.XX)
Percent Reduction (%)		XX.X%
P-value (MMRM)		X.XXXX