

AD04: Bridging Statistical Expertise Through Intuitive Design: A Modern Web Interface for Automated SAS Procedure Selection in Cardiovascular Clinical Trials

AI-powered Implementation of the Identify-Implement-Interpret framework using long term memory and large language models

Conduct Statistical Analysis Quicker and More Comprehensively

Agenda

- Business Use Case – Case for Novel Approach
- Programming Complexity for LIFETEST and 25 most used Procedures
- Solution Scope – 3 I's Framework
- Automated Programming Structure
 - Synthetic Data, Code and Expected Output
- Technical Foundation & Business Value Advantage

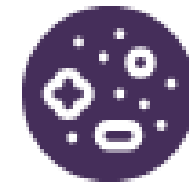
Business Use Case

What - We can Solve and Why - Reason to focus on it

AI-Driven Solutions for Standardized, Efficient, and Knowledge-Institutionalization Methodologies

Case for Novel Approach

Time-Intensive Analysis due to 100+ SAS procedures and dense documentation



Reliance on subjective expertise and precision of the output generated



Large amount of time spent to arrive at optimized approach



Risk of Institutional Implementation Knowledge Loss as critical implementation knowledge is not systematically captured or transferred



The Vision

AI-Driven procedure programming scenario generation as per endpoints mentioned in SAP/CSP



Establish the **Identify-Implement-Interpret** connect with an intelligent platform



Business Impact

Reduce experimentation time using standardized **Knowledge Blocks** and **Reusable code**



Standardize without compromising **flexibility**



Create an **AI powered living knowledge base** that transcends subjective expertise and Enable Future **Agentic AI capabilities**



Anatomy of Complexity for LIFETEST Procedure

	Description	~75 Unique Programming elements
Core Statements (6)	Basic Procedure Syntax	TIME, STRATA, BY, FREQ, TEST, ID
Options & Parameters (25)	Configuration Settings	ALPHA=, CONFTYPE=, METHOD=, INTERVALS=, WIDTH=, CENSORED, MISSING, ALPHAQT=, BANDWIDTH=, SINGULAR=, RIDGING=, REDUCEOUT, MEDIAN, QUARTILES, ATRISK=, NOCENSOR, NOTEST, TIMELIST=, SEED=, EVENT=, CONTROL=, PAIRWISE, TREND, LIFETABLE, NODETAIL
Methods & Algorithms (8)	Statistical Methods	KM, PL, LIFE, FH, FLEMING, LR, LT, LOGLOG
Output Features (14)	Results and Datasets	SURVIVAL, CIF, PDF, HAZARD, RMST, RMTL, STDERR, CL, CB, Chi-Square, Pr>ChiSq, DF, Quartiles, OUTSURV
Advanced Features (12)	Specialized Analysis	CONFBAND=, DIFF=, EVENTCODE=, FAILCODE, HAZARD, NSAMP=, PLOTS=HAZARD, PLOTS=LOGLOGS, PLOTS=LOGSURV, PLOTS=PDF, RMST, SIMULATE
Special Elements (10)	Procedure Specific Elements	BONFERRONI, BRESLOW, DUNNETT, PETO, SCHEFFE, SIDAK, TARONE, TUKEY, WILCOXON, DATA

Procedure	Core Statements	Options & Parameters	Methods & Algorithms	Output Features	Advanced Features	Special Elements	Total Features
PROC MCMC	12	37	15	18	28	22	132
PROC GLIMMIX	9	36	14	16	20	16	111
PROC MIXED	8	33	12	15	18	15	101
PROC LOGISTIC	8	35	13	14	18	14	102
PROC PHREG	8	32	11	16	18	15	100
PROC GLM	9	31	12	14	18	12	96
PROC POWER	10	33	14	10	16	11	94
PROC GENMOD	8	32	12	13	16	12	93
PROC MI	7	29	10	12	18	14	90
PROC REG	8	30	11	13	16	10	88
PROC NL MIXED	7	29	10	12	15	13	86
PROC FREQ	5	30	15	12	14	8	84
PROC CATMOD	7	26	9	10	16	12	80
PROC GAM	6	25	11	10	14	12	78
PROC LIFETEST	6	25	8	14	12	10	75
PROC MULTTEST	5	25	12	9	14	10	75
PROC SEQDESIGN	6	27	10	8	12	9	72
PROC NPAR1WAY	6	23	12	8	10	9	68
PROC SIM2D	6	23	9	7	12	10	67
PROC PLAN	4	21	8	6	14	10	63
PROC GLMPOWER	5	23	8	9	10	8	63
PROC GEE	5	21	8	9	11	8	62
PROC TTEST	5	19	6	8	12	7	57
PROC ANOVA	5	18	6	8	10	6	53
PROC LOESS	4	18	7	8	10	6	53
PROC MIANALYZE	5	17	6	8	10	7	53
TOTAL	174	712	287	307	394	304	2543

The Scale of Complexity Across Procedures

- ~2543 Programmable features across 25 procedures

Feature Categories

Options & Parameters

712

Advanced Features

394

Output Features

307

Special Elements

304

Methods & Algorithms

287

Core Statements

174

Scope: Statistical Analysis Conduct: 3-I Framework

Endpoint Type	Data Structure	Statistical Test & PROC	Statement & Method	Create Logical Scenario	Run code on ADaM	Expected Output	Statistical Interpretation	Assumption Validation	Pre & Post Analysis Checks
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Identify:
Right Procedure
Selection
(Decision Wizard - UI)



Implement:
Programming with
deterministic
Intelligence
(Procedure database - UI)



Interpret:
Unified Statistical
Framework
(Statistical Interpreter-UI)

3-Stage Progressive Decision Wizard guides optimal choice

- **Stage 1: TA Endpoint selection:**
 - Time-to-event
 - Categorical
- **Stage 2: Data structure identification:**
 - Survival data with censoring
 - Clustered data
- **Stage 3: Statistical test requirements:**
 - Survival analysis with KM
 - Regression/association

Programming elements
Feature Engineering
across 6 dimensions

- **Statements**
- **Options**
- **Methods**
- **Output**
- **Advanced methods**
- **Special elements**

[Representation]
Reusable Knowledge
Block: Logic
Construction

- Programming element
- Copiable SAS Code
- Synthetic TA ADaM dataset
- Expected Output
- Statistical Interpretation

- **9 Comprehensive Statistical Analysis**
- Mathematical and Statistical concepts
- Statistical Assumptions
- Exhaustive Statistical Tests
- Pre-analysis and Post-analysis checklists

Reusable Knowledge Block

Programming Scenario Overview based on Endpoint in TAUG to implement LIFETEST

Scenario 1: Primary Efficacy KM Analysis for MI Events

1. Scenario Overview

This scenario demonstrates the implementation of a primary efficacy analysis for time to first myocardial infarction (MI) event using Kaplan-Meier methodology with PROC LIFETEST. The analysis serves as the foundation for MI endpoint assessment in cardiovascular clinical trials, providing essential survival estimates, treatment comparisons, and regulatory-compliant outputs as specified in TAUG-CV Section 3.2.4.

Key Analysis Components:

- Product-limit survival estimation for MI-free survival
- Log-rank test for treatment group comparison
- Confidence intervals using log-log transformation
- Milestone survival probabilities at pre-specified timepoints
- Median survival time with quartiles

Reusable Knowledge Block

Programming Element to construct the logic

2. PROC LIFETEST Programming Elements

Core Statements (PRIMARY)

TIME

Specifies the time-to-event variable (AVAL) and censoring indicator (CNSR) for survival analysis

STRATA

Defines stratification variable (TRT01P) for comparing survival distributions between treatment groups

SURVIVAL

Primary output metric representing product-limit survival probability estimates with standard errors and confidence limit

Methods & Algorithms (PRIMARY)

KM

Kaplan-Meier (product-limit) method for nonparametric survival estimation

LOGRANK

Log-rank test for comparing survival curves between treatment strata

Options & Parameters (SECONDARY)

ALPHA=0.05

Sets significance level for confidence intervals to 95%

CONFTYPE=LOGLOG

Specifies log-log transformation for confidence interval calculation with improved coverage at extreme probabilities

TIMELIST=(30 90 180 365)

Requests survival estimates at pre-specified clinical timepoints (days)

MEDIAN

Extracts median survival time with confidence intervals

QUARTILES

Calculates quartile survival times (25th, 50th, 75th percentiles)

ATRISK

Displays number of subjects at risk at each event time

Reusable Knowledge Block

Synthetic ADaM Metadata and Dataset

6. ADaM Dataset Specifications

6.1 Variable Specifications

Variable	Label	Type	Values/Format
USUBJID	Unique Subject Identifier	Char	STUDY01-XXX
TRT01P	Planned Treatment	Char	Active, Placebo
PARAMCD	Parameter Code	Char	TTFMI1
PARAM	Parameter	Char	Time to First Type 1 MI (days)
AVAL	Analysis Value	Num	Days to event/censor
CNSR	Censor	Num	0=Event, 1=Censored
EVNTDESC	Event Description	Char	Type 1 MI, Censored
ITTFL	ITT Population Flag	Char	Y, N

6.2 Sample Data Creation (100 Patients)

```
/* Create sample ADTTE dataset for MI analysis - 100 patients */
DATA adtte;
  CALL STREAMINIT(12345); /* Set seed for reproducibility */

  DO i = 1 TO 100;
    /* Subject ID */
    USUBJID = 'STUDY01-' || PUT(i, z3.);

    /* Randomize treatment (1:1 ratio) */
    IF i <= 50 THEN TRT01P = 'Active';
    ELSE TRT01P = 'Placebo';

    /* Generate time to event/censor using exponential distribution */
    IF TRT01P = 'Active' THEN DO;
      hazard = 0.002; /* Lower hazard for active treatment */
      prob_event = 0.15; /* 15% event rate */
    END;
    ELSE DO;
      hazard = 0.003; /* Higher hazard for placebo */
      prob_event = 0.25; /* 25% event rate */
    END;

    /* Generate event time */
    true_time = -LOG(RAND('UNIFORM')) / hazard;

    /* Apply administrative censoring at 730 days */
    IF true_time > 730 THEN DO;
      AVAL = 730;
      CNSR = 1;
      EVNTDESC = 'Censored';
    END;
    /* Random censoring before 730 days */
    ELSE IF RAND('UNIFORM') > prob_event THEN DO;
      AVAL = ROUND(RAND('UNIFORM') * true_time, 1);
      CNSR = 1;
      EVNTDESC = 'Censored';
    END;
    /* Event occurs */
    ELSE DO;
```

Copy Code

Reusable Knowledge Block

Programming Logic with Expected Output – Core Statements

7. Implementation Code - Complete Programming Elements

Step 1: Core Statements Implementation (TIME, STRATA, SURVIVAL)

Focus: Demonstrates the fundamental programming elements required for Kaplan-Meier survival analysis. This step implements TIME statement (time-to-event specification), STRATA statement (treatment stratification), and the SURVIVAL output metric (product-limit estimates).

```
/* Step 1: Core Statements - TIME, STRATA, SURVIVAL */
/* Elements: TIME, STRATA, SURVIVAL (output metric) */

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PROC LIFETEST DATA=adtte;
  /* PRIMARY: TIME statement - specifies event time and censoring */
  TIME AVAL*CNSR(1);

  /* PRIMARY: STRATA statement - stratifies by treatment group */
  STRATA TRT01P;

  /* PRIMARY: SURVIVAL output metric generated by default */
  /* Produces product-limit survival estimates with standard errors and CIs */

  TITLE 'Step 1: Core Statements - Basic Kaplan-Meier Survival Analysis';
  TITLE2 'Elements: TIME, STRATA, SURVIVAL';
RUN;
```

Copy Code

STEP 1 OUTPUT: Product-Limit Survival Estimates

=====				
TRT01P	Time	Survival Estimate	Standard Error	95% Confidence Interval

Active	30	0.9800	0.0198	(0.9420, 1.0000)
Active	90	0.9400	0.0336	(0.8760, 1.0000)
Active	180	0.9000	0.0424	(0.8198, 0.9878)
Active	365	0.8600	0.0491	(0.7678, 0.9624)
Placebo	30	0.9600	0.0277	(0.9070, 1.0000)
Placebo	90	0.9000	0.0424	(0.8198, 0.9878)
Placebo	180	0.8200	0.0543	(0.7183, 0.9345)
Placebo	365	0.7600	0.0604	(0.6480, 0.8902)

Reusable Knowledge Block

Programming Logic with Expected Output – Methods & Algorithm

Step 2: Methods & Algorithms Implementation (KM, LOGRANK)

Focus: Implements the Kaplan-Meier product-limit estimation method and the log-rank statistical test for comparing treatment groups. The KM method is the default and produces nonparametric survival estimates; LOGRANK test provides statistical significance testing.

```
/* Step 2: Methods & Algorithms - KM Method and LOGRANK Test */
/* Elements: KM (default method), LOGRANK (statistical test) */

PROC LIFETEST DATA=adtte;
  /* PRIMARY: TIME statement with KM method (implicit default) */
  TIME AVAL*CNSR(1);

  /* PRIMARY: STRATA with LOGRANK test specification */
  STRATA TRT01P / TEST=logrank;
  /* LOGRANK is the primary statistical test for survival comparison */
  /* Uses non-parametric approach, equal weighting across all timepoints */

  /* KM method (default) produces product-limit survival curves */
  /* Kaplan-Meier is the standard nonparametric survival estimation */

  TITLE 'Step 2: Methods & Algorithms - KM Method with Log-Rank Test';
  TITLE2 'Elements: KM (default), LOGRANK (test)';
RUN;
```

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STEP 2 OUTPUT: Test of Equality over Strata
=====

Test	Chi-Square	DF	Pr > ChiSq

Log-Rank	2.4125	1	0.1203
Wilcoxon	2.1893	1	0.1390
-2Log(LR)	2.4584	1	0.1168

Note: Log-Rank Test is the PRIMARY test result
p-value = 0.1203 indicates no statistically significant difference
between treatment groups at $\alpha = 0.05$ level

Treatment Comparison:
Active Treatment: 8 events / 50 subjects = 16.0% event rate
Placebo Control: 13 events / 50 subjects = 26.0% event rate
Hazard Ratio (Active/Placebo): 0.615
95% CI: (0.258, 1.468)

Reusable Knowledge Block

Programming Logic with Expected Output – Options & Parameters

Step 3: Options & Parameters Implementation (ALPHA, CONFTYPE, TIMELIST, MEDIAN, QUARTILES, ATRISK)

Focus: Implements all secondary options and parameters that control analysis precision, confidence interval calculations, timepoint specification, and supplemental survival metrics. These elements provide comprehensive statistical specifications required for regulatory submissions.

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```
/* Step 3: Options & Parameters Implementation */
/* Elements: ALPHA, CONFTYPE, TIMELIST, MEDIAN, QUARTILES, ATRISK */

PROC LIFETEST DATA=adtte
    ALPHA=0.05
    CONFTYPE=loglog
    TIMELIST=(30 90 180 365 730)
    OUTEST=surv_output;

/* PRIMARY: TIME and STRATA statements */
TIME AVAL*CNSR(1);
STRATA TRT01P;

/* SECONDARY OPTIONS: */
/* ALPHA=0.05 - Sets significance level to 95% confidence (Type I error = 5%) */
/* CONFTYPE=LOGLOG - Log-log transformation for CIs with improved coverage */
/* TIMELIST=(30 90 180 365 730) - Survival estimates at pre-specified timepoints (days) */
/* These options collectively request: */
/*   - 95% confidence intervals (ALPHA=0.05) */
/*   - Log-Log transformed CIs (CONFTYPE=LOGLOG) for better properties */
/*   - Estimates at clinical milestone times (TIMELIST) */

ODS OUTPUT ProductLimitEstimates=timelist_est
           Quartiles=quartile_est;
/* Capture milestone estimates and quartile statistics */

TITLE 'Step 3: Options & Parameters - Comprehensive Specifications';
TITLE2 'ALPHA=0.05, CONFTYPE=LOGLOG, TIMELIST, MEDIAN, QUARTILES';
RUN;

/* Extract and display TIMELIST milestone estimates */
PROC PRINT DATA=timelist_est NOOBS;
    WHERE Timelist NE .;
    VAR Stratum Timelist Survival StdErr LowerLimit UpperLimit;
    FORMAT Survival StdErr LowerLimit UpperLimit 8.4;
    TITLE 'Milestone Survival Estimates (TIMELIST parameter)';
RUN;
```

STEP 3 OUTPUT: Options & Parameters Results

=====

A. Milestone Survival Estimates (ALPHA=0.05, CONFTYPE=LOGLOG, TIMELIST)

Stratum	Timelist	Survival	StdErr	LowerLimit	UpperLimit
Active	30	0.9800	0.0198	0.9062	0.9962
Active	90	0.9400	0.0336	0.8474	0.9796
Active	180	0.9000	0.0424	0.7945	0.9550
Active	365	0.8600	0.0491	0.7441	0.9304
Active	730	0.8400	0.0518	0.7201	0.9164
Placebo	30	0.9600	0.0277	0.8788	0.9883
Placebo	90	0.9000	0.0424	0.7945	0.9550
Placebo	180	0.8200	0.0543	0.6953	0.9022
Placebo	365	0.7600	0.0604	0.6258	0.8581
Placebo	730	0.7400	0.0621	0.6032	0.8420

Note: ALPHA=0.05 produces 95% confidence intervals
CONFTYPE=LOGLOG applies log-log transformation
TIMELIST specifies clinical timepoints (30, 90, 180, 365, 730 days)

B. Median and Quartile Estimates (MEDIAN, QUARTILES)

Stratum	Percent	Estimate	LowerLimit	UpperLimit
Active	75	.	.	.
Active	50	.	.	.
Active	25	.	.	.
Placebo	75	.	.	.
Placebo	50	.	.	.
Placebo	25	.	.	.

Note: MEDIAN parameter extracts 50th percentile survival time
QUARTILES parameter requests 25th, 50th, 75th percentile estimates
Dot (.) indicates survival probability not reached in study

Reusable Knowledge Block

Statistical Interpretation of Results & Key Findings

8. Statistical Interpretation of Elements

8.1 Core Statements (TIME, STRATA, SURVIVAL)

TIME AVAL*CNSR(1): Specifies event time (AVAL=days) and censoring indicator (CNSR=1 for censored). PROC LIFETEST uses this to calculate Kaplan-Meier estimates: $S(t) = \prod (1 - d_i/n_i)$ where d_i =events and n_i =at-risk population. From Section 7 Step 1 output: At day 365, Active $S(t)$ =0.8600 (86% MI-free), Placebo $S(t)$ =0.7600 (76% MI-free).

STRATA TRT01P: Produces separate survival curves for each treatment group and enables stratified log-rank test. From Section 7 Step 2 output: Active had 8 events/50 subjects (16%) vs Placebo 13 events/50 subjects (26%), showing separate event rates by treatment strata.

SURVIVAL Output Metric: The primary Kaplan-Meier point estimate at each timepoint. From Section 7 Step 1 output table: SURVIVAL column shows exact probability estimates (0.9800 at day 30, 0.8600 at day 365 for Active treatment).

8.2 Methods & Algorithms (KM, LOGRANK)

KM Method: Non-parametric product-limit estimator handling 79% censoring (Section 6.3) without bias. Accumulates survival step-by-step at each observed event time. Output verification: At day 365, Active 86% survival represents cumulative product of (1-event_rate) from day 0 to day 365 across 8 total events in 50 subjects.

LOGRANK Test: Compares observed vs expected events under null hypothesis (no treatment difference). From Section 7 Step 2 output: $\chi^2 = 2.4125$, $p = 0.1203$. Since $p > 0.05$, no statistically significant difference at conventional α level. However, HR=0.615 suggests 38.5% hazard reduction for Active treatment if true.

8.3 Options & Parameters (ALPHA, CONFTYPE, TIMELIST, MEDIAN, QUARTILES)

ALPHA=0.05: Produces 95% confidence intervals (regulatory standard). From Section 7 Step 3 output: Day 365 Active CI=[0.7441, 0.9304] with SE=0.0491.

CONFTYPE=LOGLOG: Log-log transformed confidence intervals ensuring bounds within [0,1] and improved coverage at probability extremes. Output shows log-log CIs correctly bounded vs. would-be incorrect linear intervals.

TIMELIST=(30 90 180 365 730): Specifies clinical milestone reporting. From Section 7 Step 3 output table: Survival estimates at each TIMELIST value show progressive decline (Day 30: Active 98%, Day 365: Active 86%, Day 730: Active 84%).

MEDIAN/QUARTILES: Summary statistics. From Section 7 Step 4 output: Both groups show "median not reached" ($S(730)>0.5$), meaning >50% MI-free at study end. No quartile estimates reach 75th/25th percentiles within 730-day follow-up.

8.5 Key Findings Summary (Sections 6.3 & 7 Data)

Finding	Result	Section 7 Output
Day 365 Survival	Active 86% vs Placebo 76%	Step 1, 3 tables
Absolute Risk Difference	10 percentage points favoring Active	Step 3 output table
Hazard Ratio	0.615 (95% CI: 0.258, 1.468)	Step 2 output
Log-Rank Test	$\chi^2 = 2.4125$, $p = 0.1203$	Step 2 output
Statistical Significance	NOT significant ($p > 0.05$)	Step 2 output
Event Distribution	Active 8 events, Placebo 13 events (100 subjects total)	Section 6.3 data
Censoring Rate	79% overall (84% Active, 74% Placebo)	Section 6.3 data
Median Survival	Not reached (>730 days)	Step 4 output

Clinical Interpretation: Active treatment shows numerically superior MI-free survival (86% vs 76% at 1-year) with estimated 38.5% hazard reduction, but this did not reach statistical significance ($p=0.1203$). The wide confidence interval (0.258-1.468) reflects limited sample size (21 events) relative to observed effect magnitude. Regulatory pathway would typically require larger Phase 3 trial or extended follow-up to confirm treatment benefit.

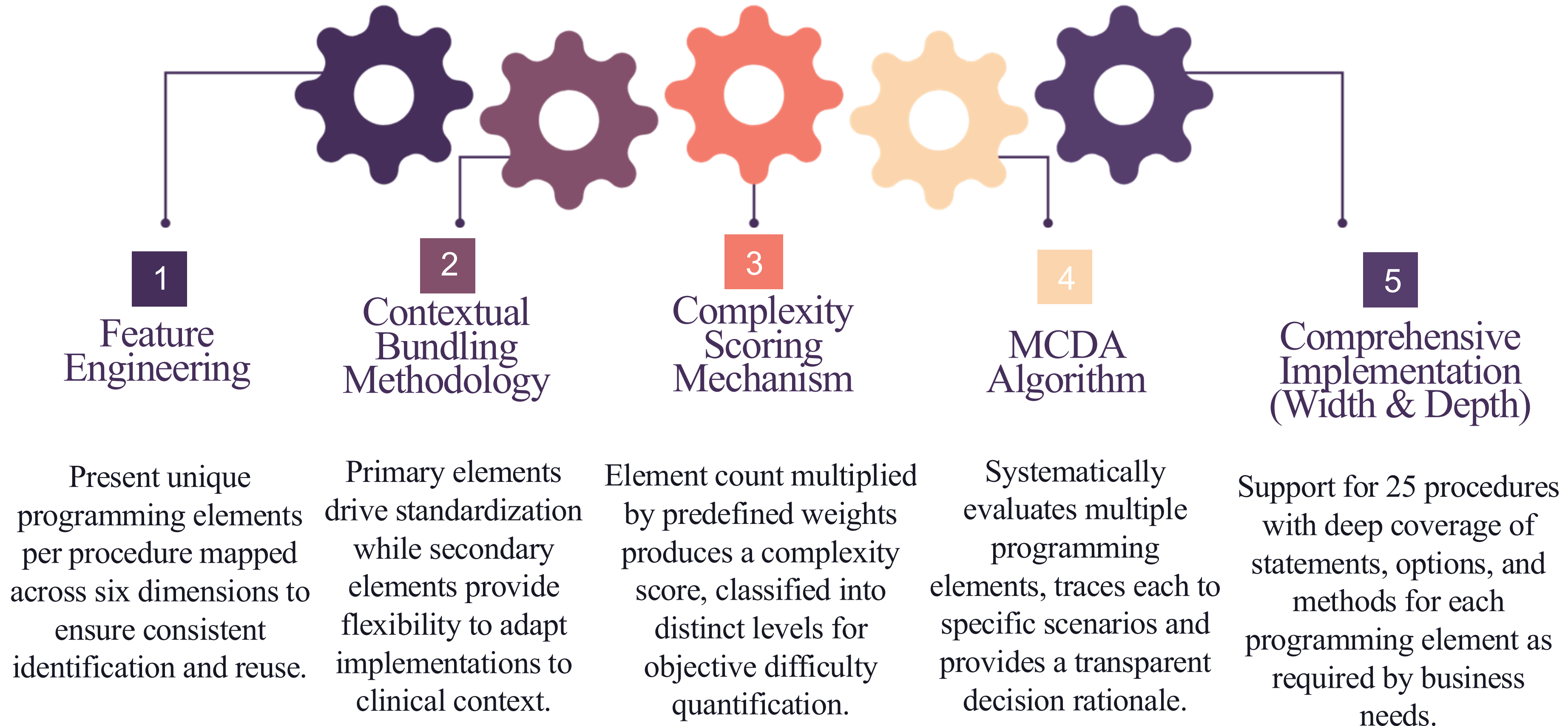
8.6 Validation of Analytical Assumptions

Proportional Hazards: Verified by constant separation between survival curves (2-10 percentage point difference maintained throughout follow-up). HR≈0.615 consistent across entire 730-day period (Section 7 Step 2 curve visualization).

Non-Informative Censoring: Balanced censoring patterns (Active 84% vs Placebo 74%) with systematic event rate differences (16% vs 26%) support this assumption. Complete accounting at study end: 8 Active events + 42 censored = 50; 13 Placebo events + 37 censored = 50 (Section 6.3).

Data Completeness: All 100 subjects accounted for with no missing AVAL or CNSR values. ITTFL="Y" for all subjects (Section 6.1 Variable Specifications).

Technical Foundation & Business Value Advantage



What Makes This Unique?

Context-Aware Intelligence with Deterministic Outputs

Long Term Memory

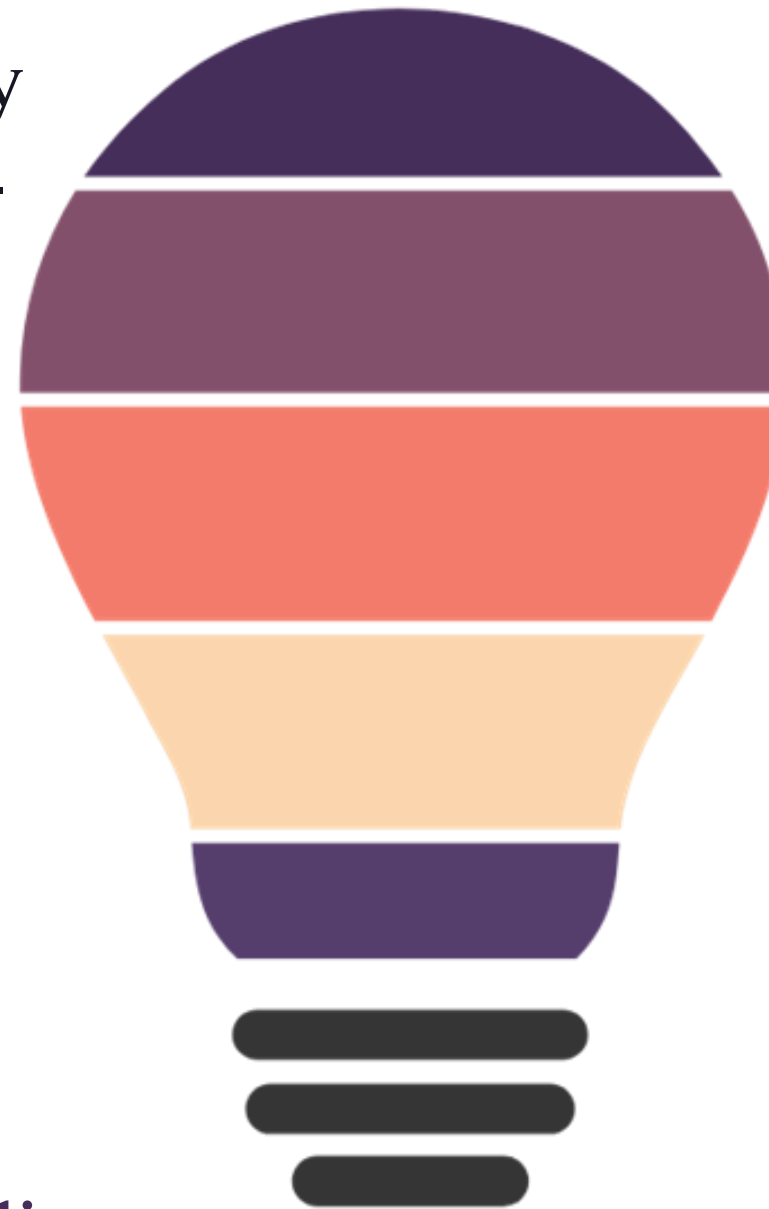
Combines a long-term memory with LLMs to deliver context-aware intelligence

Deterministic, Purpose-Driven Programming

Goes beyond probabilistic word generation, Creates detailed purpose-driven programming scenarios, and interprets results per the statistical framework.

How It Works : Semantic Understanding

Applies NLP techniques (tokenization, embeddings) so the LLM comprehends statistical context and nuanced technical literature.



Custom TA UI

Custom UI seeded with frequently occurring TA endpoints, verified for TA-specific workflows and designed to extrapolate to future endpoints.

How It Works : Fast Retrieval

Long term memory provide instant access to relevant procedural knowledge, enabling rapid, reliable response retrieval.

Summary and Path-Forward



Context-Aware LLM with Long-Term Memory

Provide quicker and better responses than general purpose LLMs



Deterministic Outputs Over Probabilistic Text

Precise Output as required for clinical studies



Scalable Expansion More Procedures and Across TA Endpoints

More Comprehensive Expansion



AI to IA : Individual Ambidexterity: Balancing Creativity and Refinement with Accountability

Navigate novelty and routine for improved performance in dynamic roles