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Identifying Illness Episode Misclassification in ADaM Using AI-Assisted Temporal Logic and Explainable Decision Tree Models

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The QC Problem

A new illness number does not always mean a new illness.

- Symptoms may be reported on several dates across a longitudinal study.
- ADaM derivations can create sequential records such as COVID_1_ILLNESS and COVID_2_ILLNESS.
- The QC question is whether the transition is consistent with the protocol/SAP temporal rule.
- Review becomes harder when similar derivations must be checked across multiple studies.

QC focus: identify transitions that deserve closer review — without changing the clinical rule.

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Protocol / SAP Rule → A Deterministic QC Screen

Example rule used in the synthetic SARS-CoV-2 scenario

Previous illness resolution

GAP_DAYS
Current onset − previous resolution

Current illness onset

GAP_DAYS ≤ 4

Temporal-review candidate

GAP_DAYS > 4

Four-day screening criterion not triggered

Important: GAP_DAYS is a screening variable — not the final clinical classification.

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Why Add an AI-Assisted QC Layer?

Deterministic SAS screen

- Transparent and traceable to the protocol/SAP
- Identifies the candidate population
- Consistent across records and studies
- Defines the screening boundary

Explainable ML layer

- Uses symptom-level evidence within candidates
- Organizes transitions by QC evidence
- Provides an interpretable if–then rule
- Helps prioritize human review

Protocol/SAP defines the rule → AI assists the reviewer

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Hybrid Protocol-Driven + AI-Assisted QC Framework

1. Protocol / SAP 4-day rule
2. SAS temporal screen
3. Symptom-level features
4. HPSPLIT explainable ML
5. QC review prioritization

Clinical rule remains authoritative.
Machine learning prioritizes candidate transitions for QC review.

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Synthetic Demonstration Design

30
synthetic illness transitions

20
GAP_DAYS ≤ 4 review candidates

10
GAP_DAYS > 4 not triggered

- SUBJ001–SUBJ030; two synthetic illness records per subject.
- 153 synthetic symptom-level records.
- 20 candidate transitions: 12 HIGH_CONFIDENCE and 8 REVIEW.
- No actual participant identifiers, study dates, or clinical outcomes.

Labels are synthetic QC reference labels — not clinical ground truth.

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What Evidence Does the Model See?

GAP_DAYS Current onset − previous resolution

PREVIOUS_DURATION Days in previous illness

CURRENT_DURATION Days in current illness

PREV_N_SYMPTOMS
Distinct symptoms in previous illness

CURRENT_N_SYMPTOMS
Distinct symptoms in current illness

N_SAME_SYMPTOMS
Shared symptom codes

SYMPTOM_CONTINUATION
Timing supports symptom continuation

The final model uses all seven predictors. SAME_SYMPTOM was omitted because it is redundant with N_SAME_SYMPTOMS > 0.

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Explainable HPSPLIT Model

20
candidate transitions

→

Entropy
tree growth

→

Cost-complexity
pruning

→

5-fold
random CV

Target: QC_REFERENCE HIGH_CONFIDENCE | REVIEW

Purpose: prioritize QC evidence within the protocol-defined candidate population

Sensitivity model: GAP_DAYS excluded to test whether symptom-level evidence retains discriminative value.

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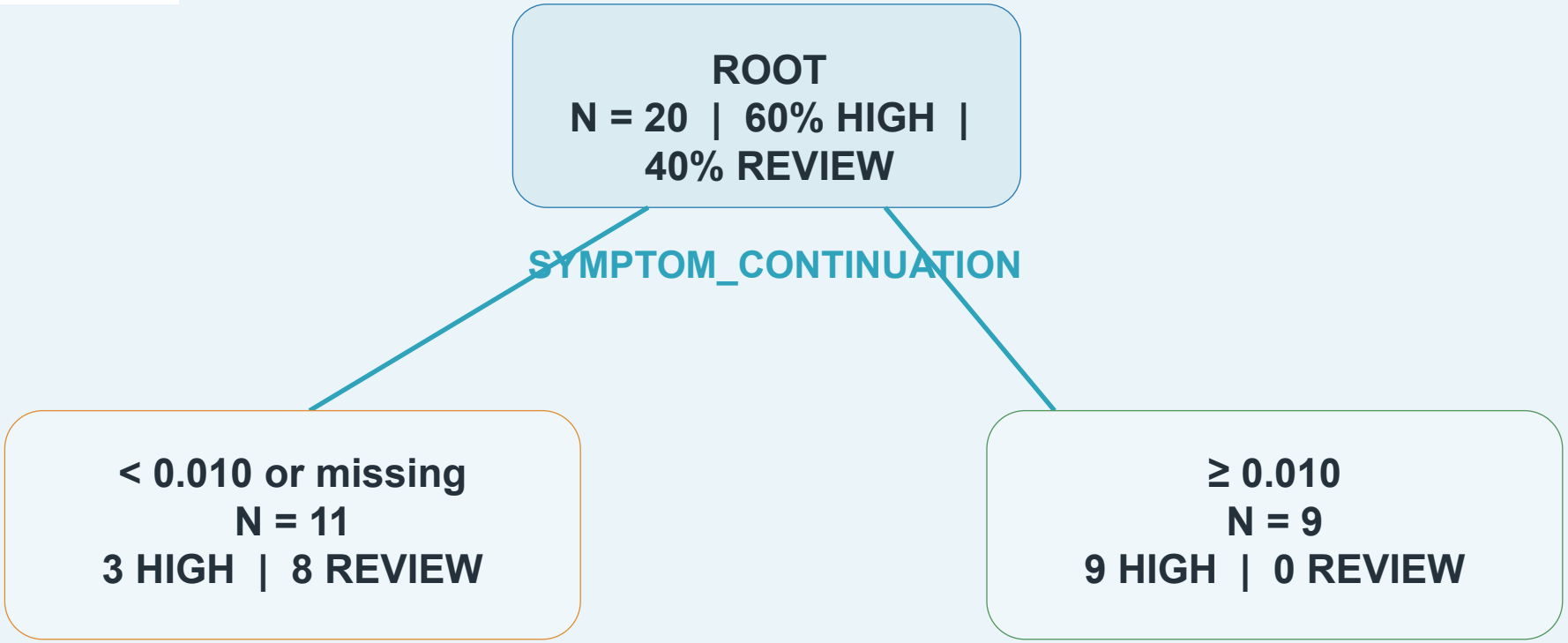
Selected Two-Leaf Tree: One Transparent Split



In this synthetic example, SYMPTOM_CONTINUATION is the dominant split.

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Model Performance: Illustrative, Not Generalizable

75.0%

CV accuracy

15 / 20

66.7%

CV sensitivity

HIGH_CONFIDENCE

87.5%

CV specificity

REVIEW

0.2300

CV misclassification

model assessment

Training AUC = 0.875

9 / 12 HIGH_CONFIDENCE correctly classified
8 / 8 REVIEW correctly classified

Because only 20 observations are modeled, these metrics demonstrate the workflow — not predictive performance in a real study.

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Two Transitions: Same Temporal Screen, Different Evidence

Example A — SUBJ007

GAP_DAYS = 0

SYMPTOM_CONTINUATION = 1

Temporal rule triggers review
+ symptom evidence supports continuity

Synthetic class: HIGH_CONFIDENCE

Example B — SUBJ014

GAP_DAYS = 4

SYMPTOM_CONTINUATION = 0

Temporal rule triggers review
+ symptom evidence is insufficient

Synthetic class: REVIEW

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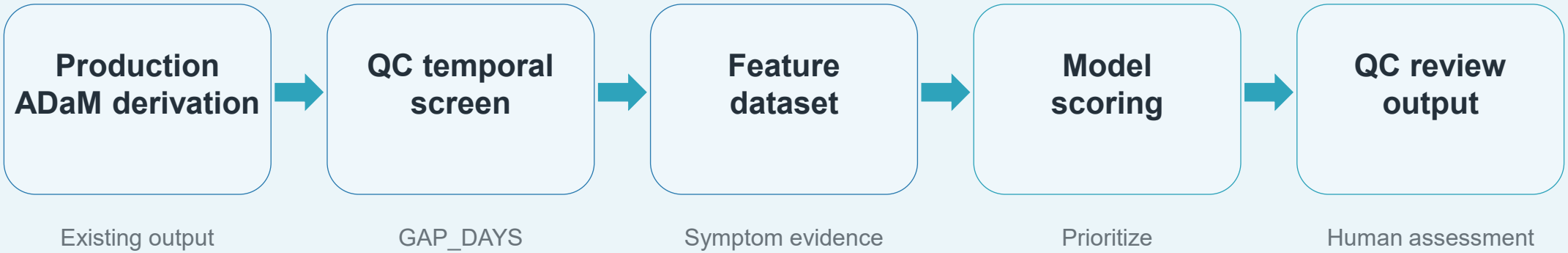
How This Fits Into a Real QC Workflow



Suggested QC dataset fields

Previous/current dates • GAP_DAYS • symptom features • model class • review status

The production derivation itself does not need to be changed for the QC demonstration.

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Governance: What the Model Does — and Does Not Do

DOES

- Prioritize temporal-review candidates
- Use traceable symptom-level features
- Provide an interpretable rule for review focus
- Support reproducible QC documentation

DOES NOT

- Redefine the protocol/SAP rule
- Override the clinical endpoint
- Make a diagnosis
- Establish clinical truth from synthetic labels

Human/QC assessment remains authoritative.

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Limitations and Next Steps

What limits this demonstration?

- Synthetic data and simulated QC reference labels
- Only 20 observations in the supervised population
- Decision-tree results may be unstable with small samples
- SYMPTOM_CONTINUATION is highly informative by construction

What would be needed next?

- Independent real study data
- Documented QC / clinical-adjudication labels
- Additional temporal and symptom-level predictors
- Assessment of impact on manual QC effort

Goal: scale the QC workflow without compromising traceability or clinical governance.

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Key Takeaways

1 Protocol/SAP defines the temporal boundary.

2 SAS makes the temporal screen and features reproducible.

3 Explainable ML helps prioritize candidate QC transitions.

4 In the synthetic demonstration, SYMPTOM_CONTINUATION was the sole split.

The model tells the reviewer where to look; it does not tell the reviewer what the clinical truth is.

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Thank You

Questions & Discussion

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