THE TRIAL READINESS INDEX

A Predictive Operating Framework for Patient Readiness in Clinical Trials

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Executive Summary

Clinical trials measure medical eligibility, enrollment, retention, protocol adherence, site performance, and study completion. What they generally lack is a comparable leading measure of whether an eligible patient is prepared to sustain the demands of participation.

That gap matters because many of the conditions that determine trial success emerge outside traditional eligibility criteria. Patients must understand the study, decide with confidence, manage travel and scheduling, accommodate procedures and treatment burden, engage caregivers where necessary, maintain motivation, and continue participating as burden accumulates over time.

The Trial Readiness Index, or TRI, is designed to measure that execution risk before it becomes visible through lagging indicators such as screen failure, missed visits, withdrawal, enrollment delay, or rescue activity.

TRI evaluates readiness through the interaction of the patient, the protocol, and time. It uses readiness intelligence across Social, Behavioral, and Protocol-Fit domains. Those signals are consolidated into Primary Frictions that explain where participation is likely to break down and what type of intervention may improve the patient's ability to progress.

TRI provides the baseline assessment. Targeted interventions address the relevant frictions. Readiness Gain measures subsequent improvement. Longitudinal reassessment identifies Readiness Decay before it becomes dropout.

TRI is designed as a predictive framework whose weights, thresholds, and progression probabilities are calibrated and refined against observed study outcomes. Until prospective validation is established for a specific use case, outputs should be treated as modeled estimates with explicit confidence and coverage measures.

Baseline TRI → Friction Diagnosis → Intervention → Reassessment → Readiness Gain → Progression Monitoring → Readiness Decay Detection

1. The Measurement Gap

Clinical development organizations already measure protocol feasibility, site capacity, patient prevalence, medical eligibility, recruitment velocity, investigator performance, treatment adherence, protocol deviations, retention, and study completion.

Patient readiness is less systematically measured. A medically eligible patient may satisfy every protocol requirement while carrying meaningful risk related to comprehension, trust, logistics, cost, caregiver support, scheduling, treatment burden, uncertainty, fear, motivation, follow-through, or fatigue.

These factors influence whether the patient can successfully participate, yet they are often discovered only after significant sponsor and site resources have already been committed. TRI is intended to provide earlier visibility while there is still time to intervene.

2. What TRI Predicts

TRI is intended to estimate successful progression across the major milestones of clinical trial participation.

Outcome	TRI Question
Activation	How likely is the patient to engage with the study opportunity and take the next step?
Prescreen Progression	How likely is the patient to complete early qualification activities?

Outcome	TRI Question
Consent	How likely is the patient to understand the study, evaluate its burden, and make a durable participation decision?
Randomization	How likely is the patient to move from consent into active participation?
Persistence	How likely is the patient to sustain the requirements of the study over time?
Completion	How likely is the patient to remain sufficiently ready through study closeout?

3. Patient × Protocol × Time

Patient

Behavioral tendencies, social circumstances, treatment history, support systems, preferences, functional capacity, prior adherence patterns, and decision-making characteristics.

Protocol

Visit frequency, duration, procedures, sample collection, placebo design, washout requirements, hospitalization, dosing burden, travel requirements, and informed consent complexity.

Time

Readiness can improve or decline as motivation, caregiver capacity, logistics, confidence, burden, and life circumstances change.

> **Readiness is protocol-specific and longitudinal.**

4. The TRI Readiness Architecture

TRI is supported by three major readiness domains.

Domain	Purpose	Examples
Social	Practical ability to participate	Transportation, site distance, employment flexibility, caregiver support, language, material hardship, provider continuity, functional status
Behavioral	How the patient understands, evaluates, decides, and follows through	Trust, health literacy, cognitive load, planning, adherence history, resilience, decision confidence, treatment fatigue
Protocol Fit	Compatibility between protocol demands and patient capacity	Placebo concern, washout, visit frequency, duration, procedures, sample collection, dosing burden, hospitalization, time off work

Protocol Fit is central to the TRI concept because it prevents readiness from being treated as a static patient attribute. A patient may be highly ready for one protocol and poorly matched to another because the demands differ.

5. From Models to Primary Frictions

The full readiness architecture is analytically useful, but study teams need a smaller operational layer. TRI therefore consolidates predictive model signals into 19 Primary Frictions.

Operational Domain	Primary Frictions
Understand and Decide	Trust; Comprehension; Cognitive Load; Decision Confidence; Protocol Design Fear
Access and Activate	Transport; Cost; Digital Access and Skill; Language; Care Continuity
Sustain Participation	Schedule Burden; Caregiving Burden; Support System; Functional Limitation
Persist and Complete	Motivation; Execution Pattern; Treatment Fatigue; Emotional and Mood; Material Hardship

The four-domain structure provides an executive view. The 19 individual frictions provide operational detail.

6. Why Primary Frictions Matter

Predictive models identify signals. Primary Frictions translate those signals into actionable participation risk.

Illustrative Signals	Primary Friction	Example Intervention
Limited transportation access; long site distance; low local healthcare density	Transport Friction	Travel planning, ride coordination, reimbursement support, decentralized options where permitted
Limited health literacy; weak risk comprehension; high protocol complexity	Comprehension Friction	Plain-language education, visual explanation, teach-back, simplified trial expectations

Model Signal → Primary Friction → Intervention

7. TRI Construction Principles

Model Relevance

Not every model matters equally for every protocol.

Milestone Relevance

The importance of a friction changes over time.

Evidence Strength

Signals supported by several recent and consistent sources should carry greater confidence.

Protocol Interaction

Protocol-Fit measures should reflect the interaction between patient capacity and study burden.

Missing Data

Missing information should lower confidence rather than automatically lower readiness.

Dynamic Weighting

Weights may vary by therapeutic area, protocol, milestone, cohort, and observed predictive performance.

TRI should not be constructed as a simple arithmetic average of readiness variables. Weighting should be empirically calibrated.

8. Interpreting TRI

TRI is expressed on a normalized 0 to 100 scale, with higher values representing greater assessed readiness for the specific protocol and milestone being evaluated. The score should be interpreted together with its readiness band, Primary Frictions, Model Coverage, Assessment Confidence, and milestone-specific progression risk.

A numerical TRI alone should not determine patient eligibility or access to participation.

TRI Output	Meaning
TRI Score	Overall protocol-specific readiness
Readiness Band	Operational risk classification
Primary Frictions	Factors suppressing readiness
Model Coverage	How much relevant evidence is available
Assessment Confidence	Reliability of the estimate
Milestone Risk	Where progression is most vulnerable

Numerical cutoffs for readiness bands should be calibrated empirically rather than published as universal thresholds.

9. Baseline TRI

The first readiness assessment establishes Baseline TRI. It should identify overall readiness, milestone-specific progression probabilities, highest-risk Primary Frictions, assessment confidence, model coverage, and intervention priorities.

10. The TRI Operating Model

Step	Purpose
1. Baseline TRI	Establish initial readiness.
2. Friction Diagnosis	Identify the Primary Frictions suppressing progression.
3. Targeted Intervention	Deploy support aligned to the friction.
4. Reassessment	Measure the updated readiness state.
5. Readiness Gain	Quantify improvement.
6. Progression Monitoring	Observe whether readiness improvement translates into actual advancement.
7. Readiness Decay Detection	Continue reassessing during participation and intervene when readiness deteriorates.

11. Intervention

Primary Friction	Example Intervention
Trust	Transparent education, trusted-source communication
Comprehension	Plain-language education, teach-back
Transport	Travel planning and transportation support
Cost	Financial navigation and reimbursement education
Support System	Caregiver onboarding and family support
Decision Confidence	Values clarification and decision support
Protocol Design Fear	Procedure, placebo, or washout preparation
Schedule Burden	Scheduling assistance and visit planning
Execution Pattern	Behavioral reminders and follow-through support
Treatment Fatigue	Persistent education and pacing support

Intervention should remain traceable to the friction that triggered it, the underlying models, the milestone at risk, and the subsequent change in readiness.

12. Readiness Gain

Readiness Gain = Current TRI - Baseline TRI

The score change alone is insufficient. The more important analytical question is whether Readiness Gain changes actual progression probability.

- Engagement
- Prescreen completion
- Clinical screening progression
- Consent
- Randomization
- Visit adherence
- Persistence
- Completion

Risk Identified → Intervention → Readiness Gain → Observed Progression

13. Readiness Decay

Readiness can deteriorate after randomization as visit burden, travel fatigue, caregiver strain, treatment frustration, anxiety, work disruption, expense, and motivation change.

Readiness Decay represents a meaningful decline relative to the patient's prior state. Its purpose is to identify deterioration before missed visits, protocol deviations, nonadherence, disengagement, or withdrawal become visible.

14. TRI Across Trial Milestones

Trial Stage	Primary TRI Role
Identification	Estimate baseline readiness among medically eligible patients
Engagement	Identify likely activation barriers
Prescreen	Assess readiness to continue qualification
Clinical Screening	Surface behavioral and logistical risk before greater investment
Consent	Evaluate expectation alignment and decision confidence
Randomization	Establish participation baseline
Active Study	Detect Readiness Decay
Completion	Identify remaining persistence risk

15. Study-Level and Site-Level TRI

Individual readiness assessments can be aggregated into study and site intelligence.

- Mean and distribution of Baseline TRI
- Current TRI and Readiness Gain
- Patients by readiness band
- Primary Friction prevalence and severity
- Milestone-specific progression risk
- Site-level readiness variation
- Cohort-level readiness variation
- Model Coverage
- Assessment Confidence

At the site level, a readiness summary can provide current TRI, high-priority frictions, interventions already delivered, remaining support requirements, expectation risks, probability of progression, and emerging Readiness Decay.

16. TRI as a Predictive Measure

TRI becomes operationally valuable when it predicts outcomes with sufficient accuracy to influence decisions.

Potential TRI Band	Operational Interpretation
High Readiness	Strong expected progression and persistence
Moderate Readiness	Likely progression with identifiable support needs
Low Readiness	Material readiness barriers requiring intervention
Critical Readiness Risk	High probability of near-term progression failure

Thresholds should emerge from observed outcomes and should not be treated as universal constants.

17. Validation and Calibration

Discrimination

Can TRI distinguish patients who progress from patients who do not? Potential measures include AUROC, sensitivity, specificity, precision, and recall.

Calibration

Do predicted progression probabilities correspond with observed outcomes?

Incremental Predictive Value

Does TRI improve prediction beyond medical eligibility, conventional demographic variables, historical recruitment signals, site performance, and standard engagement metrics?

Intervention Response

Does Readiness Gain predict better subsequent progression?

Longitudinal Performance

Does Readiness Decay predict missed visits, nonadherence, withdrawal, or other downstream participation risk?

Generalizability

Does TRI remain useful across therapeutic areas, disease complexity, phases, sites, and geographies?

Fairness

Does model performance remain sufficiently consistent across relevant patient populations?

The framework should be recalibrated continuously as evidence accumulates.

18. Evidence Coverage and Confidence

Model Coverage

The proportion of relevant readiness dimensions for which sufficient evidence is available.

Assessment Confidence

The strength of the readiness estimate based on evidence volume, source quality, recency, consistency, patient confirmation, behavioral observations, and protocol completeness.

Identical TRI scores may carry different levels of certainty. A TRI of 70 with broad, recent, consistent evidence carries more decision value than a TRI of 70 based on limited data.

19. Governance and Fairness

Readiness intelligence should support participation and intervention. It should not create inappropriate exclusion.

- Low transportation access should trigger transportation support.
- Limited digital access should trigger technical support or alternative participation methods.
- Caregiver burden should trigger support planning.
- Low comprehension should trigger improved education.

Sensitive dimensions such as experiences of discrimination, stigma, anxiety, or depression burden require additional safeguards, including appropriate consent, source provenance, role-based visibility, restricted use, auditability, retention controls, transparent model documentation, and ongoing fairness review.

20. TRI and Economics

> **TRI → Readiness Gain → Changed Progression Probability → Investment Protected**

The full financial framework is addressed in the companion paper, The Economics of Patient Readiness. Maintaining this separation improves conceptual clarity. TRI is the operating measure. Readiness Gain is the change measure. Investment Protected is the financial measure.

21. TRI as a Clinical Development Operating Metric

Many clinical trial performance measures are lagging. Enrollment reveals who entered. Screen failure reveals who failed. Missed visits reveal deterioration after behavior changes. Withdrawal reveals loss after it occurs.

TRI provides a leading measure that supports a different operating cadence.

- Which patients are most likely to struggle?
- Which milestones are most exposed?
- Which frictions are creating the risk?
- Which intervention should be deployed?
- Did readiness improve?
- Is readiness beginning to decay?
- Is progression probability improving?

This allows readiness to be governed alongside enrollment, site performance, protocol compliance, retention, and operational risk.

Conclusion

Clinical trial execution depends on the ability of patients to understand, decide, activate, navigate, persist, and complete.

Those capabilities are influenced by social conditions, behavioral patterns, support systems, treatment experience, and protocol demands. They also change throughout participation.

The Trial Readiness Index provides a structured framework for measuring these conditions before they become operational failures.

Primary Frictions make readiness risk interpretable. Targeted interventions make the intelligence actionable. Readiness Gain measures improvement. Readiness Decay provides an early-warning signal during participation. Outcome calibration establishes predictive credibility.

The broader opportunity is to make readiness governable. TRI makes patient readiness measurable, comparable, longitudinal, and actionable. It gives study teams a leading indicator that can be managed alongside other core execution variables.

> **Where is readiness likely to fail, what is driving that risk, and what can be done before the failure affects enrollment, retention, or study completion?**

Appendix A. PRISM Readiness Model Architecture

The TRI architecture comprises 62 readiness models across Social, Behavioral, and Protocol-Fit domains. These models roll up into the 19 Primary Frictions described in the body of the paper.

Social Models (21)

- Transportation Access Model
- Distance to Study Site Model
- Housing Stability Model
- Food Security Model
- Insurance and Coverage Model
- Out-of-Pocket Cost Capacity Model
- Employment Flexibility Model
- Caregiver Availability Model
- Caregiver Trial-Task Support Model
- Caregiver Approval of Participation Model
- Family and Community Approval Model
- Childcare and Dependent-Care Burden Model
- Utilities and Material Hardship Model
- Broadband and Device Access Model
- Language Access Model
- Education Attainment Model
- Neighborhood Deprivation Model
- Rurality and Healthcare Density Model
- Community Support Density Model
- Provider Continuity Model
- Disability and Functional Status Model

Behavioral Models (29)

- Trust in the Care Team Model
- Trust in Clinical Research Model
- Experience of Discrimination Model
- General Literacy Model
- Health Literacy Model
- Numeracy and Risk Comprehension Model
- Cognitive Load Model
- Self-Confidence to Complete the Trial Model
- Expected Personal Benefit Model
- Tolerance for Uncertainty Model
- Short-Term Focus Model
- Planning and Follow-Through Model
- Treatment Adherence History Model
- Appointment Attendance History Model
- Persistence and Resilience Model
- Stated Commitment to Trial Model
- Goal Commitment Model
- Prior Trial Experience Model
- Information-Seeking Behavior Model
- Treatment Fatigue Model
- Coping Style Model
- Social Influence Model
- Decision Confidence Model
- Disease-Specific Stigma Model
- Anxiety and Depression Burden Model

- Perceived Disease Severity Model
- Confidence with Digital Tools Model
- Decision Autonomy Model
- Treatment Preference Strength Model

Protocol-Fit Models (12)

- Placebo Assignment Concern Model
- Washout Period Concern Model
- Visit Frequency Tolerance Model
- Trial Duration Tolerance Model
- Procedure Tolerance Model
- Sample Collection Tolerance Model
- Side Effect Concern Model
- Hospitalization or Overnight Stay Tolerance Model
- Informed Consent Document Readability Match Model
- Protocol Complexity Comprehension Match Model
- Pill Burden and Dosing Schedule Tolerance Model
- Time Off Work for Visits Tolerance Model

Appendix B. The 19 Primary Frictions

- Trust Friction
- Comprehension Friction
- Cognitive Load Friction
- Transport Friction
- Cost Friction
- Material Hardship Friction
- Support System Friction
- Caregiving Burden Friction
- Digital Access and Skill Friction
- Language Friction
- Care Continuity Friction
- Motivation Friction
- Decision Confidence Friction
- Emotional and Mood Friction
- Protocol Design Fear Friction
- Schedule Burden Friction
- Execution Pattern Friction
- Treatment Fatigue Friction
- Functional Limitation Friction

About the Author

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John brings 30 years of experience building categories, products, brands, and growth engines around emerging technology, including executive leadership roles at Medidata, conversationHEALTH, and Swoop. At Jumo Health, he helps define patient readiness as measurable infrastructure for recruitment, retention, completion, capital efficiency, and more credible forecasting.