SCIENTIFIC COMPANION • RESEARCH FRAMEWORK • AUGUST 2026

RESTORE

When symptom control is not the same as functional recovery

A function-centered, hypothesis-generating framework examining psychiatric medication burden, perceived functional restoration, and methamphetamine use after incarceration

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STATUS AND SCOPE

Read this first

RESEARCH STATUS

RESTORE is a clinical observation and research framework in development. This booklet does not report a completed trial, does not present patient-level study results, and does not establish that psychiatric medications cause methamphetamine use or relapse.

The central proposition is narrower than a medication-reduction campaign: among some people returning to the community, medication-related sedation, cognitive slowing, motivational blunting, or regimen complexity may be one contributor to poor real-world function. Some individuals may perceive methamphetamine as restoring energy, alertness, focus, confidence, or capacity. Whether systematic reassessment and individualized optimization can improve function—and whether that reduces methamphetamine use—remains to be tested.

Clinical guardrails

- **Not blanket deprescribing.** Necessary treatment should be preserved. Medication changes require individualized diagnosis, shared decision-making, gradual planning when indicated, and monitoring for withdrawal, recurrence, mania, psychosis, suicidality, or other harm.
- **Not a substitute for stimulant-use treatment.** Contingency management is the current standard of care; evidence-based behavioral treatment, harm reduction, medical care, housing support, and indicated pharmacotherapy remain central. [18,19]
- **Not a claim about every patient.** The framework anticipates responders, nonresponders, and counterexamples. Social conditions, sleep, trauma, psychiatric illness, withdrawal, pain, ADHD, and other substances may better explain functional difficulty.
- **Not clinical advice.** The cases are educational composites and are not instructions for treating any specific person.

How the evidence is labeled

Label	Meaning in this booklet
DIRECT	The study examines substantially the same exposure, mechanism, or outcome as the RESTORE question.
ADJACENT	The study supports part of the pathway, but in another population, setting, or with a different exposure/outcome.
GAP	The proposed connection has not been adequately tested; this is where RESTORE contributes a research question rather than a conclusion.

EXECUTIVE BRIEF

The clinical signal, stated precisely

RESTORE asks whether psychotropic and sedative burden may contribute to functional impairment after incarceration and whether perceived functional restoration may be an underrecognized contributor to methamphetamine use. It then asks whether systematic reassessment and individualized optimization can improve function—and whether improved function is associated with less continued methamphetamine use or relapse.

The wording matters. RESTORE is about methamphetamine, not the broader category of 'stimulants.' It is about association and perceived function, not presumed causation. And it evaluates a whole pathway, not a single medication or receptor theory.

What the literature already advances

- **Medication burden → function:** Sedating adverse effects of antipsychotics are consistently associated with worse daily functioning in a small literature; anticholinergic burden is associated with broad cognitive impairment in schizophrenia. These studies do not establish the post-incarceration pathway. [3–5]
- **Methamphetamine → perceived function:** Qualitative and survey studies directly document motives including energy, alertness, concentration, productivity, mood regulation, trauma escape, and counteracting other drugs. They do not prove that psychiatric medication burden caused use. [9–11]
- **Optimization → function:** Small studies suggest that reducing unnecessary anticholinergic exposure may improve cognition, while antipsychotic dose-reduction trials show mixed functional findings and clinically important relapse risk. [6–8]
- **Function → methamphetamine outcome:** Executive dysfunction and altered risk processing are associated with relapse, and cognitive remediation has proof-of-concept results. The mediation chain from medication optimization to function to less methamphetamine use is untested. [12–14]

> **BOTTOM LINE**
>
> Yes—research has advanced major components of three questions and provides indirect support for the fourth.
> No—published evidence does not yet validate the complete RESTORE pathway or justify causal claims.

What this revised booklet adds

- A question-by-question evidence map with supportive, conflicting, and missing evidence.
- Four fictionalized composite cases, including a deliberate counterexample.
- A minimum data set and repeated-measures evaluation plan.
- A ladder for converting clinic impressions into a consecutive case series, registry, pilot, and comparative study.
- Safety, DEI, and interpretation guardrails designed to prevent overreach.

CONTENTS

A scientific companion for clinicians, researchers, and partners

Three questions to keep in view

1. What did the person experience before methamphetamine use: sedation, cognitive slowing, depression, withdrawal, sleep deprivation, untreated ADHD, trauma, social threat—or several at once?
2. What changed after a carefully documented intervention, and did the change precede any change in methamphetamine use?
3. What evidence would make us revise or reject the RESTORE explanation for this person?

PART I

The hypothesis

A testable pathway—not a conclusion

Precision protects both patients and the scientific integrity of RESTORE.

THE FOUR RESEARCH QUESTIONS

From burden to function to methamphetamine outcome

Question	Precise formulation	Current status
Q1	Is greater post-release psychotropic and sedative burden associated with impaired functional recovery?	Adjacent evidence; direct reentry evidence is sparse.
Q2	For some people, is methamphetamine use partly an attempt to restore perceived functioning?	Direct evidence for functional motives; the medication link is untested.
Q3	Can systematic reassessment and individualized medication optimization improve real-world function?	Plausible and partly supported; broad reduction findings are mixed.
Q4	When function improves, is continued methamphetamine use or relapse reduced?	Associative links exist; the full mediation pathway is untested.

The proposed pathway

1 • Exposure	2 • Experienced effect	3 • Behavioral meaning	4 • Outcome
Medication burden and contextual load	Sleepiness, slowing, low drive, poor concentration, or reduced role capacity	Methamphetamine is perceived as restoring energy, alertness, focus, confidence, or safety	Continued use or relapse may become more likely

RESTORE then introduces a proposed intervention at the first two links: a structured medication and diagnosis review, paired with measurement of function and evidence-based methamphetamine-use care. The hypothesis predicts that when modifiable burden improves, some—but not all—people will show better function and possibly less methamphetamine use.

NECESSARY CONDITION FOR CREDIBILITY

Every arrow must remain falsifiable. Improvement without medication change, medication change without functional improvement, and functional improvement without reduced methamphetamine use are all informative outcomes—not failures to be hidden.

EVIDENCE MAP

What is supported, what is indirect, and what is missing

Link	Evidence presently available	RESTORE-specific gap
Burden → function	Sedation is associated with worse daily function; anticholinergic burden with worse cognition in schizophrenia. [3–5]	Post-release medication burden, daily function, and temporal change have rarely been studied together.
Meth → perceived function	People report energy, alertness, concentration, productivity, mental-health regulation, and escape as motives or perceived benefits. [9–11]	Few studies test whether those perceptions follow medication-related impairment, and perceptions can be inaccurate or short-lived.
Optimization → function	Anticholinergic taper studies show possible cognitive benefit; antipsychotic reduction studies are mixed and can increase relapse. [6–8]	No validated RESTORE optimization protocol or reentry trial exists.
Function → meth outcome	Executive dysfunction and risk-processing differences are associated with relapse; cognitive remediation is feasible. [12–14]	No study has demonstrated that medication-related functional improvement mediates lower methamphetamine use.

A disciplined interpretation

The first three questions are not appearing from nowhere. They sit beside established literatures on medication adverse effects, cognition in psychotic disorders, self-reported functions of methamphetamine use, and individualized medication review. The novel contribution is the proposed integration of those literatures in a high-risk reentry setting—and the explicit downstream hypothesis about methamphetamine outcomes.

That integration is scientifically valuable precisely because it is not yet proven. A credible booklet should make the seam visible rather than presenting adjacent studies as if they tested the entire pathway.

PART II

What the evidence says

Question-by-question support, contradiction, and uncertainty

The strongest version of RESTORE is the one that survives serious alternative explanations.

CLINICAL AND SOCIAL CONTEXT

Reentry is a high-risk transition, not a neutral laboratory

After release, people may face abrupt changes in medication supply, prescribers, housing, sleep, food, transportation, supervision requirements, employment expectations, family roles, and exposure to substances. Those forces can overwhelm or mimic a medication effect.

33,811 releases

Washington State cohort; overdose was the leading cause of death, with the greatest mortality risk in the first two weeks. Psychostimulant-related mortality was prominent. [1]

1 in 20

In one Australian cohort with significant mental-health needs and brief imprisonment, only one in 20 received a community mental-health-team referral. [2]

Why this matters for the hypothesis

- Medication lists at release may reflect acute custody management, historical diagnoses, or formulary decisions rather than a current community function target.
- Missed appointments, unstable housing, poor sleep, and role overload can independently impair concentration, motivation, and adherence.
- Methamphetamine exposure can itself worsen sleep, cognition, mood, psychosis, and function, creating reverse causation.
- The first weeks are too clinically risky for a single-cause explanation or rapid, poorly monitored medication changes.

RESTORE IMPLICATION

Reentry should be modeled as a dynamic context. Medication burden is one candidate exposure within a larger system of biological, psychiatric, social, and structural determinants.

QUESTION 1

May psychotropic and sedative burden impair functional recovery?

The answer from adjacent evidence is: sometimes, plausibly, and not in a way that can be inferred from pill count alone. Sedation, anticholinergic activity, dopamine blockade, orthostasis, metabolic effects, emotional blunting, and regimen complexity may each affect function differently. Illness severity and treatment indication can confound every association.

Evidence that supports the link

- **Sedation and daily function.** A 2025 systematic review found only 11 eligible peer-reviewed papers, but the available results consistently supported a negative effect of antipsychotic sedation on daily functioning and motivation; quality-of-life findings were also concerning. The limited evidence base is itself important. [3]
- **Anticholinergic burden and cognition.** In 1,120 outpatients with schizophrenia or schizoaffective disorder, higher modified Anticholinergic Cognitive Burden scores were associated with worse performance across cognitive domains after adjustment for demographic factors and proxies of illness severity. Cross-sectional design prevents causal inference. [4]
- **Cognition is not automatically restored by antipsychotic treatment.** A network meta-analysis of 68 studies involving 9,525 participants found few clear differences between antipsychotics and no individual agent clearly better than placebo for cognitive outcome; data were relatively sparse. [5]
- **Complexity may matter.** In a high-utilizer psychiatric cohort, greater psychotropic regimen complexity and psychotropic count were associated with shorter time between readmissions, though not readmission frequency. This is associative and not reentry-specific. [22]

What these studies do not show

- They do not show that the medication was inappropriate or that stopping it would improve net outcome.
- They do not separate illness-related cognitive impairment from medication-related impairment perfectly.
- They do not establish that impairment leads to methamphetamine use.
- Most do not measure reentry tasks such as attending supervision, securing identification, managing transportation, or returning to work.

Measure burden as more than medication count

Domain	Candidate indicator	Interpretation caution
Sedative load	Drug Burden Index or prespecified sedative classification; timing and dose; patient-reported sleepiness	DBI was developed in older adults and requires validation for this population. [17]
Anticholinergic load	ACB/ADS-type scale plus reason for each contributor	Scales disagree; burden score is not a treatment recommendation.
Dopamine-blocking exposure	Agent, route, timing, chlorpromazine-equivalent dose where appropriate	Dose equivalents do not capture individual response or all receptor effects.
Regimen complexity	Medication Regimen Complexity Index; dosing frequency; PRNs; refill burden	Complexity can reflect genuine clinical need.
Experienced effects	Sleepiness, concentration, slowed thinking, low drive, dizziness, emotional range	Patient experience is essential but may be influenced by symptoms and expectations.
Function	WHODAS-12 plus reentry-specific tasks and role goals	Self-report should be paired with objective or collateral indicators when consented.

Competing explanations to measure at the same visit

Clinical	Substance/sleep	Social/structural
Depression, negative symptoms, psychosis, mania, anxiety, PTSD, ADHD symptoms, pain, medical illness	Methamphetamine intoxication/withdrawal, opioids, alcohol, cannabis, sleep debt, sleep apnea, circadian disruption	Housing, food, transportation, work schedule, supervision demands, stigma, safety, family caregiving, digital access

TESTABLE PREDICTION

If medication-related burden contributes meaningfully, within-person improvement in burden should precede and correlate with improvement in prespecified functional outcomes—without unacceptable symptom recurrence or safety events.

QUESTION 2

May methamphetamine be perceived as functional restoration?

This is the portion of the framework with the clearest direct qualitative support. People who use methamphetamine do not describe a single motive. Alongside euphoria and social effects, studies document energy, alertness, concentration, productivity, confidence, mood regulation, trauma escape, and counteracting the effects of other substances. [9–11]

What the studies actually advance

Study	Design and signal	Limit
Hooten et al., 2025 [9]	Survey of 91 people reporting recent methamphetamine use; perceived benefits included energy, alertness, and productivity, with sex differences in some responses.	Convenience sample; perceived benefit is not objective function; no medication-burden test.
Fockele et al., 2023 [10]	Qualitative interviews with 20 adults at moderate/high risk described methamphetamine as enhancing function, regulating mental health, escaping hardship, and later producing serious harms.	Washington sample with recent ED care and phone access; findings are contextual, not prevalence estimates.
Hart et al., 2001 [11]	Controlled human self-administration study shows reinforcing effects and acute subjective/behavioral consequences of methamphetamine.	Laboratory behavior does not establish a real-world functional-restoration pathway.

The clinically important distinction

Perceived restoration is not the same as sustained restoration. A person may experience short-term alertness or productivity while sleep deprivation, compulsive use, paranoia, cardiovascular risk, cognitive disruption, and social consequences accumulate. The word ‘perceived’ belongs in the hypothesis because it respects the patient’s reported function without endorsing methamphetamine as an effective or safe treatment.

> **INTERVIEW STANCE**
>
> Ask what methamphetamine was doing for the person before asking only what it was doing to the person. The answer can reveal treatment targets without normalizing the harms of use.

A RESTORE Functional Effects Interview

The following prompts are proposed clinical-research questions, not a validated instrument. They should be asked nonjudgmentally and coded prospectively before outcome is known.

1. Before using methamphetamine, what were you trying to be able to do that felt difficult or impossible?
2. What changed in the first hours after use—energy, wakefulness, focus, confidence, anxiety, pain, mood, social connection, or feeling safe?
3. Which change mattered most in your decision to use again?
4. How long did the helpful effect last, and what happened afterward?
5. Did any prescribed medication feel connected to the problem you were trying to solve? What makes you think so?
6. Did the same difficulty exist before that medication, during incarceration, during withdrawal, or during periods without methamphetamine?
7. What would have to improve for methamphetamine to feel less necessary?
8. What are the harms or costs that make you want something different?

Predefined codes

Code family	Examples
Activation/function	Wakefulness, energy, concentration, task initiation, speed, productivity, work endurance
Affect/trauma	Mood lift, emotional numbing, confidence, escape, hypervigilance, perceived safety
Social/identity	Belonging, sexual connection, confidence, role performance, stigma avoidance
Drug interaction	Counteracting opioid/sedative effects, avoiding withdrawal, extending a binge
Harms	Sleep loss, paranoia, psychosis, anxiety, compulsive use, overdose, violence exposure, financial/legal consequences

A credible analysis reports all code families, including pleasure, craving, social reinforcement, and compulsivity. Selecting only ‘function’ statements would create confirmation bias.

QUESTION 3

Can individualized optimization improve real-world function?

The word ‘individualized’ is doing essential work. Medication review may confirm the need for current treatment, adjust timing, address adverse effects, remove an unnecessary contributor, simplify a regimen, treat an unrecognized condition, or recommend no medication change. Optimization is defined by net benefit, not by fewer medications.

Supportive evidence

- **Anticholinergic discontinuation.** In a 12-week study of 20 outpatients with schizophrenia or schizoaffective disorder, 18 discontinued an anticholinergic after a four-week taper and showed improvement in a cognitive composite; two could not discontinue because of akathisia. The sample was small and uncontrolled. [6]
- **Long-term first-episode follow-up.** At seven years, a dose-reduction/discontinuation strategy after remission was associated with higher recovery than maintenance in a follow-up of an earlier randomized trial. After the two-year trial, treatment was naturalistic, and the authors urged additional studies before practice change. [7]

Conflicting and safety-critical evidence

- **RADAR.** In 253 adults with recurrent psychotic disorders, gradual flexible antipsychotic reduction did not improve social functioning at 24 months. Serious adverse events, mainly admission for relapse, affected more people in the reduction group. [8]
- **Net outcome matters.** A person can feel less sedated yet experience symptom recurrence; another can remain stable with better cognition after removing an unnecessary anticholinergic. Averaging these trajectories can conceal clinically decisive differences.

RESTORE POSITION

Do not treat the framework as evidence for broad antipsychotic withdrawal. It supports structured reassessment, measurement of experienced burden and function, preservation of indicated treatment, and carefully monitored individualized change when clinically justified.

A safety-first decision sequence

Step	Core question	Document before change
1 • Reconstruct	What diagnoses, target symptoms, episodes, prior responses, and harms support each medication?	Records, collateral with consent, timeline, adherence, substance exposure
2 • Experience	What does the person report the regimen helps and hinders?	Benefits, side effects, timing, valued roles, preferences
3 • Measure	What is the baseline burden, symptom state, sleep, cognition, and function?	Prespecified scales and observable role tasks
4 • Decide	Is there a clinically justified, shared change—or is no change safer?	Rationale, alternatives, risk formulation, consent
5 • Change one thing	Can attribution be improved by limiting simultaneous changes?	Agent/timing/dose change, start date, expected effect
6 • Monitor	Did function improve without unacceptable recurrence or withdrawal?	Repeated outcomes, adverse events, rescue plan
7 • Integrate	How does this fit contingency management, psychotherapy, housing, sleep, medical, and peer supports?	Whole treatment plan and care coordination

Possible optimization actions

- Clarify or correct the diagnostic formulation.
- Confirm that each medication still has a current indication and measurable target.
- Address dose timing, duplication, PRN accumulation, interaction, or regimen complexity.
- Treat sleep disorder, depression, trauma, pain, ADHD, medical illness, or withdrawal when present.
- Use a gradual monitored change only when the anticipated net benefit exceeds risk.
- Choose no medication change when the current regimen is necessary and well tolerated.

QUESTION 4

If function improves, does methamphetamine use decrease?

This is the key outcome question and the least established link in the complete RESTORE pathway. Several literatures make it plausible, but none demonstrate the proposed mediation chain.

What is known

- **Executive dysfunction and relapse.** In a cross-sectional study of 168 men with methamphetamine use disorder, greater self-reported executive dysfunction was associated with repeated relapse. The design cannot establish direction or causation. [12]
- **Risk processing.** In early abstinence, attenuated insular activation during risky decision-making predicted relapse in a small prospective neuroimaging study. This supports the relevance of cognitive-neural processes, not a medication mechanism. [13]
- **Cognitive remediation.** A 36-person cluster-randomized crossover proof-of-concept trial found no advantage for self-reported executive function but suggested benefits on objective tasks and methamphetamine-dependence severity. It was not a definitive relapse trial. [14]

What must be demonstrated

1. A modifiable medication-related burden existed at baseline.
2. A documented intervention reduced that burden without unacceptable psychiatric harm.
3. Prespecified functional measures improved after the burden changed.
4. The change in methamphetamine outcome followed the functional change.
5. Alternative explanations—including contingency management exposure, housing, sleep, treatment engagement, and regression to the mean—were measured and addressed.

> **CAUSAL STANDARD**
>
> A reduction in methamphetamine use after a medication change is not enough. Timing, repeated measurement, negative cases, comparator data, and control of co-interventions are necessary before attributing outcome to functional restoration.

SYNTHESIS

The evidence supports a research program, not a verdict

Question	Evidence judgment	What would move it forward
Q1	Moderate adjacent evidence; limited direct reentry evidence	Prospective repeated measurement of burden and function from release forward
Q2	Moderate direct evidence for perceived functional motives; weak evidence for medication linkage	Interviews linked to medication timelines and objective function
Q3	Preliminary and mixed; intervention-specific	Safety-first pilot with individualized decisions and prespecified function outcomes
Q4	Plausible association; causal pathway not established	Longitudinal mediation analysis, then comparative pragmatic evaluation

RESTORE's defensible contribution

RESTORE can define a clinically recognizable but understudied pathway; establish a reproducible way to measure it; identify who appears to fit or not fit the pattern; test the feasibility and safety of individualized optimization; and generate effect-size estimates for a future controlled study. That would be a meaningful contribution even if the strongest version of the hypothesis is not supported.

PART III

Composite cases

How the hypothesis might appear—and how it might be wrong

Each case is fictionalized, combines common clinical patterns, and includes disconfirming evidence.

FICTIONALIZED COMPOSITE CASE 1

Marcus

Wakefulness, task initiation, and a crowded release regimen

SIGNAL UNDER EXAMINATION

Methamphetamine is described as making it possible to stay awake, travel across town, complete supervision tasks, and start job applications.

Scenario

Marcus is a 38-year-old man seen ten days after release. His discharge list includes a nighttime sedating antipsychotic started during a period of severe insomnia and paranoia, a scheduled gabapentinoid for anxiety and pain, an as-needed sedating antihistamine, and an anticholinergic continued from an earlier episode of stiffness. He reports sleeping nine to eleven hours, needing repeated alarms, missing a morning supervision appointment, and feeling 'under water' until afternoon. He used methamphetamine twice after release and says the immediate attraction was being awake enough to take buses, complete forms, and search for work.

His history also includes recurrent methamphetamine-related paranoia, chronic trauma symptoms, probable sleep apnea, unstable housing, and several nights of sleep deprivation before the use episodes. The antipsychotic may be preventing recurrence; methamphetamine itself may be driving the sleep-wake instability.

What supports the hypothesis

- A temporal report of sedation before the post-release use episodes.
- A specific functional motive rather than a generic statement of craving.
- Multiple contributors to sedative and anticholinergic burden.

What could falsify or weaken it

- Objective function was equally poor before the current regimen.
- Methamphetamine use preceded the daytime sleepiness or was primarily social/compulsive.
- Sleep apnea, withdrawal, depression, or homelessness explains more variance.
- Any reduction in protection from psychosis produces net harm.

Safe RESTORE response

Reconstruct the psychosis and medication timeline; assess current symptoms, sleep, withdrawal, and sleep-apnea risk; quantify sleepiness and function; review the continuing indication for each contributor; coordinate evidence-based methamphetamine-use treatment and housing support; and, only if clinically justified, make one carefully monitored change while preserving a rapid-response plan.

What would count as evidence in Marcus's case?

Before	During	After
Medication reconciliation; symptom and episode timeline; WHODAS-12; sleepiness; reentry task list; methamphetamine timeline; urine testing when clinically appropriate	Document exactly one change or no-change decision; weekly symptoms, sleepiness, task completion, craving, methamphetamine days, housing and treatment exposure	Assess whether burden changed first, function changed second, and methamphetamine outcome changed later—while documenting psychosis and adverse events

Potential outcome pattern

A supportive within-person pattern would be reduced daytime sleepiness and improved completion of prespecified morning tasks after a clinically appropriate burden change, without symptom recurrence, followed by reduced endorsement of 'needing methamphetamine to function.' Even that pattern would remain preliminary because housing stabilization, treatment engagement, and expectancy could explain change.

DO NOT CONCLUDE

'Sedating medication caused Marcus's relapse.' The case can generate a hypothesis and a measurement sequence; it cannot establish population-level causation.

FICTIONALIZED COMPOSITE CASE 2

Elena

Concentration, trauma, caregiving, and diagnostic uncertainty

SIGNAL UNDER EXAMINATION

Methamphetamine is described as improving concentration, emotional distance from trauma, confidence, and the ability to work and care for family—until use becomes destabilizing.

Scenario

Elena is a 31-year-old woman returning to the community after a short incarceration. Her record contains changing diagnoses of bipolar disorder, major depression, PTSD, and possible ADHD. Her current regimen includes a mood-stabilizing agent, a sedating antidepressant at night, and frequent as-needed antihistamine use for anxiety. She reports slowed thinking, difficulty organizing tasks, and intense fatigue. She began using methamphetamine years earlier while working nights and caring for a child, long before the present regimen. After release, she uses again and describes being able to 'hold the whole day in my head.'

Within hours, however, she becomes hyperfocused and misses meals; after two nights without sleep, she experiences panic and suspiciousness. She is living with a partner who uses methamphetamine. Her current functional impairment could reflect trauma, depression, ADHD, sleep disruption, social exposure, medication effects, or their interaction.

Why this case matters

- It supports the functional-motive question but weakens a simple medication-causation story because methamphetamine use predates the current regimen.
- It highlights sex- and caregiving-related contexts without assuming they apply to all women.
- It requires diagnostic reconstruction: treating unrecognized bipolar disorder, ADHD, PTSD, or depression carries different risks.

Safe RESTORE response

Build a longitudinal diagnostic and substance timeline; assess trauma, mood episodes, ADHD symptoms across settings and abstinent periods, sleep, caregiving demands, and intimate-partner safety; measure perceived benefit and actual next-day function separately; preserve evidence-based methamphetamine-use care; and make medication decisions only after the diagnostic and risk formulation is sufficiently stable.

Four explanations can be true at once

Model	Prediction	Data that would challenge it
Medication burden	Function improves after an indicated, safe burden change.	No functional change; deterioration; same difficulty predates exposure.
Untreated condition	Function improves when PTSD, depression, sleep disorder, ADHD, or another condition is accurately treated.	Symptoms/function do not track targeted treatment.
Social reinforcement	Use tracks partner/network exposure more closely than medication or function.	Use decreases despite unchanged exposure network.
Compulsive use	Craving, cue reactivity, and loss of control dominate regardless of perceived functional need.	Use falls when function improves despite persistent cues.

Outcome interpretation

If Elena's concentration improves after better sleep and trauma treatment without a medication reduction, RESTORE has still produced useful knowledge: the functional target was valid, but the initially suspected mechanism was wrong. The framework should reward correct mechanism discovery, not only confirmation of medication burden.

EQUITY LENS

Functional demands are not evenly distributed. Caregiving, unsafe housing, shift work, transportation, discrimination, and probation requirements can shape both perceived need for methamphetamine and the feasibility of treatment.

FICTIONALIZED COMPOSITE CASE 3

Darius

A necessary antipsychotic and a modifiable secondary burden

SIGNAL UNDER EXAMINATION

The primary treatment is protective; the question is whether a secondary contributor can be addressed without destabilizing psychosis.

Scenario

Darius is a 45-year-old man with well-documented schizophrenia and several severe relapses when a long-acting antipsychotic was interrupted. He is stable after release and wants to remain on it. He nevertheless reports slowed processing, dry mouth, constipation, and trouble remembering bus transfers. His list includes a daily anticholinergic that was started years ago for extrapyramidal symptoms but has never been reassessed. He has resumed intermittent methamphetamine use, describing a temporary sense of mental speed, while acknowledging that it has triggered paranoia in the past.

The case does not support reducing the medication that is preventing psychotic relapse. It does support asking whether the continuing indication for the anticholinergic, dose timing, untreated sleep disorder, or another contributor is modifiable.

Why this case protects the framework

- It separates necessary treatment from potentially unnecessary burden.
- It puts prior relapse history and patient preference ahead of a pill-count goal.
- It allows a narrow, reversible question with close movement-disorder monitoring.
- It treats methamphetamine-related psychosis risk as a major safety outcome, not a footnote.

Safe RESTORE response

Confirm current movement symptoms and indication for the anticholinergic; obtain baseline cognition, function, constipation, and movement ratings; discuss options and risks; if a gradual change is clinically chosen, monitor for akathisia or other recurrence; keep the protective antipsychotic plan intact; and integrate contingency management and harm reduction.

Optimization is not synonymous with reduction

Possible decision	Why it could be optimal
No medication change	Current treatment is indicated, benefits exceed burden, or instability risk is too high.
Reassess a secondary medication	Current indication is unclear and a monitored change could improve cognition or side effects.
Change timing or simplify administration	Function or adherence may improve without reducing total therapeutic exposure.
Treat another condition	Sleep apnea, depression, pain, medical illness, or withdrawal may better explain impairment.
Increase or restore treatment	Worsening psychosis, mania, depression, or another target may require more—not less—treatment.

Evidence pattern

A narrow improvement after safely removing an unnecessary anticholinergic would be consistent with the small discontinuation study and burden literature. [4,6] It would not show that antipsychotics generally impair recovery, nor that the change caused a methamphetamine outcome.

CLINICAL PRIORITY

The correct endpoint is better net health and function with psychiatric stability—not the lowest medication count.

FICTIONALIZED COMPOSITE CASE 4

Nia

A counterexample: function improves, methamphetamine use continues

SIGNAL UNDER EXAMINATION

The functional target responds, but relationship, cue exposure, reward, and compulsive use remain dominant.

Scenario

Nia is a 36-year-old woman whose daytime sleepiness improves substantially after treatment of obstructive sleep apnea and simplification of nighttime medications. She begins arriving on time, completes identification paperwork, and returns to part-time work. She no longer says she needs methamphetamine 'to wake up.' Yet she continues to use with a close social network on weekends and experiences escalating craving and loss of control.

This case is not a failure of RESTORE. It demonstrates that functional restoration may remove one motive without resolving reinforcement, cues, social belonging, trauma, or compulsive use. Her treatment must continue to center evidence-based stimulant-use care, safety, and her own goals.

What this case teaches

- Q3 can be supported while Q4 is not.
- Patient-reported motive can change without immediate behavior change.
- Methamphetamine use is multiply determined; a single pathway will never explain everyone.
- Negative and discordant cases are essential for estimating who the framework fits.

PRECOMMITMENT

RESTORE should publish or present counterexamples and adverse trajectories alongside supportive cases. Otherwise a flexible framework can become impossible to falsify.

CROSS-CASE SYNTHESIS

The same complaint can arise from different mechanisms

Case	Functional complaint	Leading candidates	Most informative next data
Marcus	Sleepiness; cannot start morning tasks	Sedative/anticholinergic load, sleep apnea, withdrawal, housing	Time-ordered sleepiness, symptoms, burden, and morning task completion
Elena	Focus and organization	Trauma, depression, ADHD, sleep, caregiving, medication, social exposure	Longitudinal diagnostic timeline and objective versus perceived function
Darius	Slowed processing and memory	Necessary antipsychotic exposure, secondary anticholinergic, sleep/medical	Movement ratings, burden, cognition, role task, psychosis stability
Nia	Sleepiness improves; use persists	Social reinforcement, craving, cues, compulsivity	Network exposure, craving, CM participation, use pattern, valued goals

What to look for across consecutive patients

- Recurring exposure patterns—not memorable anecdotes alone.
- Temporal ordering: what changed first?
- Specific functions that matter in reentry: waking, transportation, appointments, forms, work, caregiving, money, and social participation.
- Discordance between perceived short-term benefit and objective next-day or weekly function.
- Who does not fit, why, and whether the framework creates unintended harm.

PART IV

Evaluation blueprint

A minimum viable protocol for a hypothesis-generating program

The goal is to measure enough to learn—without pretending a clinic registry is a randomized trial.

DESIGN

Start with a prospective, consecutive, mixed-methods cohort

A practical first study is not a selective collection of success stories. Enroll consecutive eligible patients during a defined period, whether or not clinicians expect medication optimization to help. Collect a baseline before any RESTORE-attributed change when feasible, then repeat a compact outcome set.

Proposed phases

Phase	Purpose	Primary product
0 • Protocol	Define eligibility, exposures, outcomes, adverse events, interview codes, and analysis before reviewing results.	Preregistered protocol and data dictionary
1 • Feasibility cohort	Test recruitment, data completeness, measure burden, and characterize the four-question pathway.	Consecutive descriptive cohort
2 • Embedded optimization pilot	Evaluate safety, acceptability, and within-person functional change among those with a clinically indicated plan.	Effect-size and process estimates
3 • Comparative evaluation	Compare enhanced RESTORE review with usual evidence-based care using a pragmatic design.	Between-group effectiveness and safety

Eligibility concept for Phase 1

- Adult returning from incarceration or under community reentry care within a prespecified time window.
- Current or recent methamphetamine use, methamphetamine use disorder, or high relapse risk defined in advance.
- At least one prescribed psychotropic/sedating medication or a medication-transition question.
- Capacity for consent or appropriate ethics-approved process; language access provided.

AVOID SELECTION BIAS

Do not require the clinician to believe the medication caused impairment. That belief is an exposure to record—not an entry criterion.

MINIMUM DATA SET

Measure the pathway, alternatives, and safety

Domain	Core variables	Frequency
Medication exposure	Complete reconciliation; indication; dose/timing; PRNs; sedative, anticholinergic and regimen-complexity indicators; adherence	Baseline; every change; monthly
Experienced burden	Sleepiness, slowed thinking, concentration, motivation, dizziness, emotional range, patient-rated helpfulness/harm	Baseline; weekly during change; monthly
Psychiatric state	Psychosis, mania, depression, anxiety/PTSD, suicidality, withdrawal, ADHD symptoms as clinically indicated	Baseline; each contact; standardized monthly
Function	WHODAS-12; 2–3 patient-selected role goals; prespecified reentry task completion; attendance	Baseline; 2, 4, 8, 12 weeks
Methamphetamine	Timeline Followback days/quantity where feasible; craving; motive codes; urine results when clinically indicated and consented	Baseline; weekly/biweekly; 4, 8, 12 weeks
Co-interventions	Contingency management, psychotherapy, medications, peer care, housing, transport, employment, legal requirements	Every contact/monthly summary
Safety	Symptom recurrence, hospitalization, ED use, overdose, severe withdrawal, violence exposure, medication adverse events	Continuous capture; rapid review

Primary feasibility outcomes

- Percentage of eligible people approached and enrolled.
- Completion of baseline before an intervention-attributed medication change.
- Retention and outcome completion at 4 and 12 weeks.
- Percentage with sufficiently documented indication and medication timeline.
- Adverse-event rate and percentage requiring reversal or urgent escalation.

Define ‘function’ before looking at the result

Function should be broad enough to matter and specific enough to change. The 12-item WHODAS 2.0 is a defensible global measure with evidence of validity in psychotic-disorder outpatients, but it should be paired with reentry-specific indicators and patient-valued goals. [15,16]

Layer	Measure	Why include it
Global	WHODAS 2.0, 12-item	Brief, cross-domain disability measure; validated in psychotic-disorder outpatients. [15,16]
Experienced	0–10 ratings of sleepiness, concentration, drive, slowed thinking, and ability to start tasks	Captures the hypothesized effects; RESTORE-specific items require development and validation.
Goal-based	Two or three Goal Attainment Scaling-style reentry goals defined at baseline	Centers what the patient needs to do; scoring must be prespecified to reduce bias.
Objective/observable	Attendance, transport completion, forms/ID, medication access, work/school/caregiving milestones	Adds behavior to self-report; must not become punitive surveillance.
Cognitive	Brief processing-speed/executive task if feasible	Tests mechanism; practice effects and staffing burden require planning.

Methamphetamine outcomes

- Days of methamphetamine use in a fixed interval, reported with a calendar-based method.
- Time to first use after baseline or release, if timing is known.
- Heavy-use episodes or return to a participant-defined harmful pattern.
- Craving and perceived functional necessity.
- Treatment engagement and contingency-management participation.
- Urine testing only with transparent consent, clinical purpose, and protection against punitive misuse.

> **DO NOT COLLAPSE OUTCOMES**
>
> Abstinence, reduced days, reduced harm, lower craving, and no longer perceiving methamphetamine as necessary are related but distinct outcomes. Report them separately.

VISIT RHYTHM

A 12-week learning window

Time	What to capture
Baseline	Release/substance/diagnostic timeline; medication reconciliation; burden; symptoms; sleep; function; methamphetamine pattern and motives; social context
Week 1	Safety, withdrawal/recurrence, sleepiness, early function, use/craving, medication access and adherence
Week 2	Repeat compact pathway set; record any single change and co-interventions
Week 4	Full function and symptom set; interview perceived mechanism; review treatment plan
Week 8	Compact outcomes; confirm timeline; document discordant change
Week 12	Full outcomes; adverse events; qualitative interview; clinician and patient causal judgments recorded separately

Why repeated measures matter

A single before/after comparison is vulnerable to withdrawal, sleep recovery, regression to the mean, expectancy, housing change, and concurrent treatment. Repeated measures show trajectory and temporal ordering. They also reveal transient ‘activation’ that does not translate into durable function.

Record three causal judgments

Perspective	Question
Patient	What most explains the change in your ability to function?
Clinician	What mechanism best explains the observed trajectory, and with what confidence?
Independent review	Given blinded or structured timeline data, what explanations are supported, contradicted, or unresolved?

ANALYSIS

Separate description, association, and mediation

Question	Initial analysis	Claim ceiling
Who fits the pattern?	Prevalence of predefined burden, function, and motive indicators with confidence intervals	Descriptive; no cause
Does burden track function?	Within-person and longitudinal association with prespecified covariates	Association; residual confounding remains
Does optimization track function?	Interrupted time-series or repeated-measures change among clinically selected participants	Preliminary effectiveness; selection and co-intervention bias
Does function track meth outcome?	Lagged association: earlier functional change predicting later use outcome	Temporal association; not mediation proof
Is the full pathway causal?	Comparative design with adequate sample, prespecified mediation model, safety outcomes	Causal inference depends on design and assumptions

Confounders and effect modifiers

- Baseline illness severity, prior episodes, and indication bias.
- Methamphetamine intoxication, withdrawal, cumulative exposure, and time abstinent.
- Sleep duration/quality, sleep apnea, other substances, pain, and medical illness.
- Housing, social network, transportation, employment, family roles, and legal supervision.
- Contingency management and other treatment exposure.
- Race/ethnicity, gender, age, disability, language, and structural inequities as potential modifiers—not biological shortcuts.

PREANALYSIS DISCIPLINE

Specify the primary exposure, primary functional outcome, primary methamphetamine outcome, timing, and covariate set before examining change. Treat exploratory analyses as exploratory.

A monitoring plan is part of the intervention

Risk	Minimum safeguard
Psychosis or mania recurrence	Baseline risk formulation; early-contact schedule; explicit stop/reversal criteria; crisis access; collateral when consented
Withdrawal or rebound	Appropriate tapering when indicated; one change at a time where feasible; symptom-specific monitoring
Suicidality or severe depression	Routine assessment; escalation pathway; do not attribute all slowing to medication
Methamphetamine-related harm	Evidence-based treatment, contingency management access, harm reduction, overdose education, polysubstance assessment
Privacy/legal harm	Separate research and supervision data where possible; clear consent; minimum necessary data; no hidden punitive reporting
Therapeutic misconception	Explain that RESTORE is under study and may recommend no medication change

Governance roles

- Patient/community advisory group with lived experience of reentry and methamphetamine use.
- Independent psychiatric and addiction review of the protocol and adverse-event criteria.
- Statistician or methodologist involved before data collection.
- Clear quality-improvement versus research determination and IRB review where applicable.
- Transparent conflict-of-interest and funding statements.

PART V

From observation to evidence

How to show what the clinic is seeing without overclaiming

Clinical pattern recognition is the beginning of inquiry; reproducible measurement is what makes it shareable.

EVIDENCE LADDER

Five steps from signal to credible finding

Step	Action	Why it matters
1	Create a structured observation log for every eligible patient, including non-cases.	Tests whether the pattern is recurring or memorable.
2	Publish a consecutive case series with predefined variables and all trajectories.	Adds denominator, timing, counterexamples, and adverse events.
3	Build a prospective registry with repeated measures and patient interviews.	Tests associations and identifies candidate subgroups.
4	Run a safety/feasibility pilot of the full review process.	Shows whether the intervention can be delivered and measured.
5	Conduct a pragmatic comparative study with prespecified mediation analysis.	Tests whether RESTORE adds benefit beyond high-quality usual care.

What to collect tomorrow

- A one-page medication indication and experienced-effects grid.
- A release-to-present timeline with medications, sleep, methamphetamine, symptoms, housing, and major events on the same axis.
- Two patient-valued functional goals stated behaviorally.
- A standardized question about what methamphetamine is perceived to make possible.
- A field for ‘does not fit RESTORE’ and the alternative explanation.
- A weekly adverse-event and no-change record.

CONSECUTIVE CASE SERIES

Replace three persuasive stories with a denominator

The four composites in this booklet teach the logic. The first empirical report should instead include every consecutively eligible patient in a fixed period. That prevents a case series from becoming a collection of only the most compelling RESTORE-consistent stories.

Recommended case-series table

Field	Report
Denominator	Eligible, approached, enrolled, declined, lost to follow-up
Baseline	Medication burden, indications, symptoms, sleep, function, methamphetamine pattern, social context
Mechanism	Patient-perceived functional motive and clinician hypothesis, coded before outcome
Intervention	Exact decision: no change, timing/simplification, reduction, increase, alternate treatment, referral
Trajectory	Repeated function, symptoms, methamphetamine outcomes, co-interventions
Safety	Recurrence, withdrawal, hospitalization, ED visits, overdose, reversals
Fit	Supports, partly supports, contradicts, or cannot evaluate each RESTORE link

Better than clinician memory

A structured log can reveal whether sedation complaints cluster around specific exposure patterns, whether functional motives are common or rare, and how often the clinic chooses no medication change. It can also reveal clinician confirmation bias—for example, if ‘RESTORE-consistent’ cases are followed more closely than others.

> **PUBLISH THE DENOMINATOR**
>
> A small complete sample is more scientifically informative than a larger selective sample.

MIXED METHODS

Pair numbers with the patient's explanation

Quantitative measures can show that burden, function, or use changed. Interviews can reveal what changed first, what the person believed was helpful, and why an apparently successful medication adjustment did or did not alter methamphetamine use.

Suggested qualitative sampling

- RESTORE-consistent: burden decreases, function improves, methamphetamine outcome improves.
- Partial: burden decreases and function improves, but methamphetamine use persists.
- No functional response: burden changes without improved function.
- No medication change: function improves through another pathway.
- Adverse: symptom recurrence, withdrawal, or other harm.
- Declined: eligible patients who do not want the approach or research participation.

Analytic safeguards

- Use a codebook that includes nonfunctional motives and negative consequences.
- Double-code a subset and report how disagreements were resolved.
- Include lived-experience reviewers in code interpretation.
- Do not use isolated quotations as prevalence estimates.
- Report whether interviewers were involved in treatment decisions.

Five practical additions that would strengthen the booklet and project

1. A one-page deidentified clinic dashboard showing enrollment, data completeness, burden patterns, functional trajectories, methamphetamine outcomes, and adverse events—only after a protocol is active.
2. A timeline figure for each case that places medication changes, sleep, symptoms, function, methamphetamine use, and social events on the same axis.
3. A ‘what changed without medication change?’ panel to surface housing, sleep, trauma care, employment, transportation, and contingency management effects.
4. A patient-voice section developed through consented qualitative research or a lived-experience advisory group—not unattributed clinic quotations repurposed as evidence.
5. A quarterly hypothesis audit: list observations that support, weaken, or contradict each question and decide what the protocol should change.

A useful dashboard avoids premature success metrics

Show	Avoid
Enrollment denominator and missingness	Only completed or favorable cases
Function and safety together	Medication-count reduction as success
Co-interventions and context	Attributing all change to RESTORE
Counterexamples and reversals	Hiding adverse or discordant trajectories
Uncertainty intervals	Large percentages from very small samples without context

Function is socially situated

A reentry framework can inadvertently medicalize structural barriers. Missing an appointment may reflect sedation, but it may also reflect a two-hour bus route, unstable housing, phone loss, caregiving, parole requirements, disability, language barriers, or fear of stigmatizing care. Those explanations should be measured, not treated as noise.

Equity commitments

- Co-design measures and interpretations with people who have lived experience of incarceration and methamphetamine use.
- Provide language access and accessible consent; report who is excluded by the design.
- Do not use urine testing, attendance, or functional data as covert supervision tools.
- Examine whether medication burden, opportunity for review, and outcomes differ across race/ethnicity, gender, age, disability, and housing status—without implying biological causation from social categories.
- Include women, gender-diverse people, rural patients, people with psychotic disorders, and people with polysubstance use unless there is a defensible safety reason not to.
- Compensate advisory participants and research participants fairly when feasible.

> **EQUITY TEST**
>
> If the project only improves medication precision while ignoring transportation, housing, sleep, safety, and evidence-based stimulant treatment, it is not measuring functional recovery in the world patients actually inhabit.

PART VI

Practice implications

What can be done now—and what must remain research

The immediate clinical gain is better questioning and measurement, not proof of the pathway.

Take-home messages

1. Ask about function explicitly. Symptom stability and real-world capacity are related but not identical.
2. Use the word methamphetamine when that is the substance under study; do not obscure the question with a broader label.
3. Ask what methamphetamine is perceived to make possible, while also documenting pleasure, craving, cues, compulsivity, and harm.
4. Review the entire medication regimen—indication, benefit, burden, timing, complexity, interaction, and patient preference.
5. Optimization may mean preserving, increasing, simplifying, retiming, reducing, or replacing treatment; fewer medications is not the endpoint.
6. Never let medication review displace contingency management, harm reduction, psychiatric care, medical care, housing, and social support.
7. Measure before changing when feasible, change one thing at a time when clinically appropriate, and monitor early.
8. Treat counterexamples and adverse trajectories as central evidence.

A 60-second RESTORE screen

Ask	Listen for
What are you unable to do that matters most right now?	Specific role or reentry function
What helps or gets in the way?	Medication effects, illness, sleep, withdrawal, social/structural barriers
What does methamphetamine seem to make possible?	Energy, wakefulness, focus, affect, safety, belonging, pleasure, craving
What happens afterward?	Duration, crash, psychosis, anxiety, harm, actual task completion
What would make it feel less necessary?	Testable patient-defined target

LIMITATIONS

What RESTORE must not outrun

- The complete psychotropic-burden → function → perceived restoration → methamphetamine outcome pathway has not been directly established.
- Most medication-burden evidence comes from schizophrenia or older-adult populations, not people immediately after incarceration.
- Self-reported functional benefit from methamphetamine may reflect short-term subjective activation rather than durable objective function.
- Indication bias is profound: people with greater illness severity may receive more medication and also have worse function.
- Methamphetamine exposure can cause or worsen cognitive impairment, sleep disruption, depression, psychosis, and role failure, producing reverse causation.
- Medication reduction can cause withdrawal or recurrence and can increase severe relapse risk in some populations. [8]
- Clinic-based samples may not represent people disengaged from care, people in rural areas, or those excluded by consent and follow-up requirements.
- A local case series can estimate feasibility and generate hypotheses, but it cannot establish general effectiveness or causal mediation.

Claims appropriate for the present stage

Appropriate	Not yet appropriate
‘We observe a recurring clinical pattern.’	‘We have shown that medication burden causes methamphetamine relapse.’
‘Several literatures support components of the hypothesis.’	‘The literature proves the RESTORE pathway.’
‘We are developing a structured evaluation.’	‘RESTORE improves outcomes.’
‘Individualized optimization may be testable and clinically useful.’	‘Deprescribing is the solution.’

RESEARCH AGENDA

The next ten questions

1. How common is the proposed pattern among consecutive reentry patients with recent methamphetamine use?
2. Which burden construct—sedation, anticholinergic exposure, dose, timing, or regimen complexity—best tracks function?
3. Which patient-reported functional motives agree with objective or role-based measures?
4. Which alternative explanations most often account for impairment?
5. Can a brief RESTORE assessment be completed before treatment changes in routine care?
6. How often does review appropriately result in no medication change, an increase, or treatment of another condition?
7. What are the rates of symptom recurrence, withdrawal, hospitalization, and reversal during optimization?
8. Which functional domains change first, and are gains sustained?
9. Does functional improvement precede reduced perceived necessity, craving, days of methamphetamine use, or relapse?
10. Does an enhanced RESTORE review add benefit beyond high-quality usual care that includes contingency management and social support?

A publishable first aim

AIM 1

Estimate the prevalence and 12-week trajectories of prespecified medication-burden, functional-impairment, and perceived-functional-restoration indicators among consecutively enrolled adults receiving reentry care with recent methamphetamine use.

A publishable pilot aim

AIM 2

Evaluate the feasibility, acceptability, safety, and within-person functional outcomes of a structured, individualized medication-and-function review among participants for whom a treating clinician identifies a clinically justified optimization plan.

CONCLUSION

A careful hypothesis can change practice before it proves causation

RESTORE begins with a humane observation: some people tell us that they are stable enough to leave custody yet not functional enough to rebuild daily life, and some describe methamphetamine as temporarily restoring capacities they feel they have lost. That account deserves to be heard, measured, and tested.

The literature supports serious attention to sedating and anticholinergic burden, to patient-reported functional motives for methamphetamine use, and to cognition and executive function in relapse. It also warns against simplistic solutions. Necessary psychiatric treatment prevents devastating recurrence; medication reduction is not uniformly beneficial; and methamphetamine use is shaped by reinforcement, trauma, sleep, social networks, structural conditions, and compulsivity as well as perceived function.

The next step is therefore not to announce that RESTORE is correct. It is to define the pathway, enroll consecutive patients, measure function and alternatives over time, preserve evidence-based treatment, monitor harm, and publish the supportive and contradictory trajectories together.

RESTORE IN ONE SENTENCE

A hypothesis-generating research framework asking whether careful, individualized review of psychiatric medication burden can improve real-world function after incarceration—and whether that functional recovery changes the perceived need for, continued use of, or relapse to methamphetamine.

Research & collaboration: hughes@moodclinics.com • moodclinics.com/restore

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Selected scientific and clinical sources

Literature scan current through 23 August 2026. Reference selection prioritizes studies that directly test a RESTORE component, major adjacent studies, contradictory evidence, and practical measurement or treatment guidance.

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RESTORE

Restore function. Measure uncertainty. Protect stability.

A hypothesis-generating research framework in progress

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