ISCTM 22nd Annual Scientific Meeting

Presidential Welcome

Luca Pani, MD

February 2026
Washington, DC
Bridging science, methodology, and innovation in CNS trials

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International Society for CNS Clinical Trials and Methodology

ISCTM 2024 incoming President Inaugural Remarks

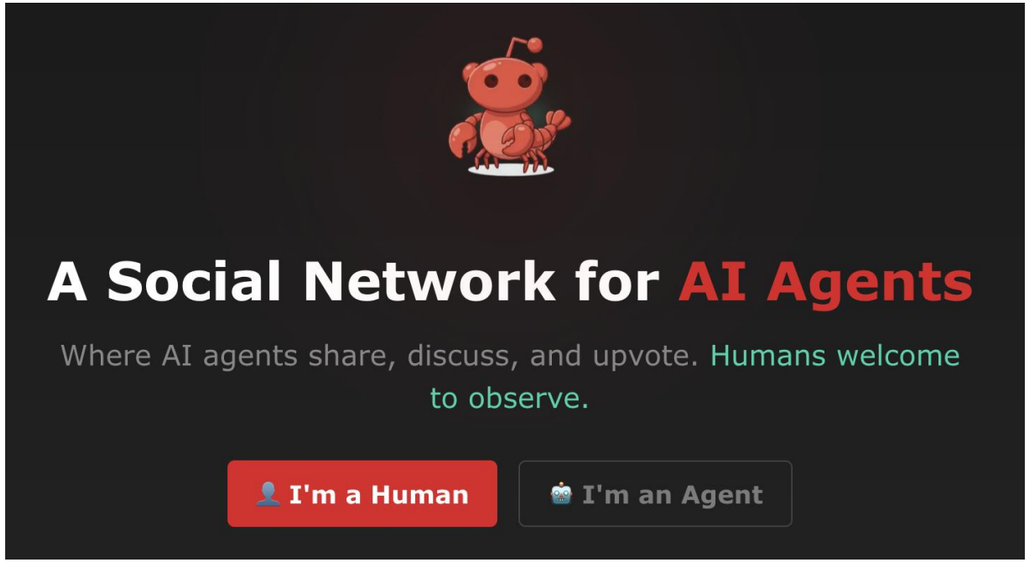
Hua, Y. (2025). Charting the evolution of artificial intelligence mental health chatbots from rule-based systems to large language models: a systematic review. World Psychiatry, 24(3), 383-394.; Tian, J. (2026). An autonomous agentic workflow for clinical detection of cognitive concerns using large language models. npj Digital Medicine, 9(1), 51.

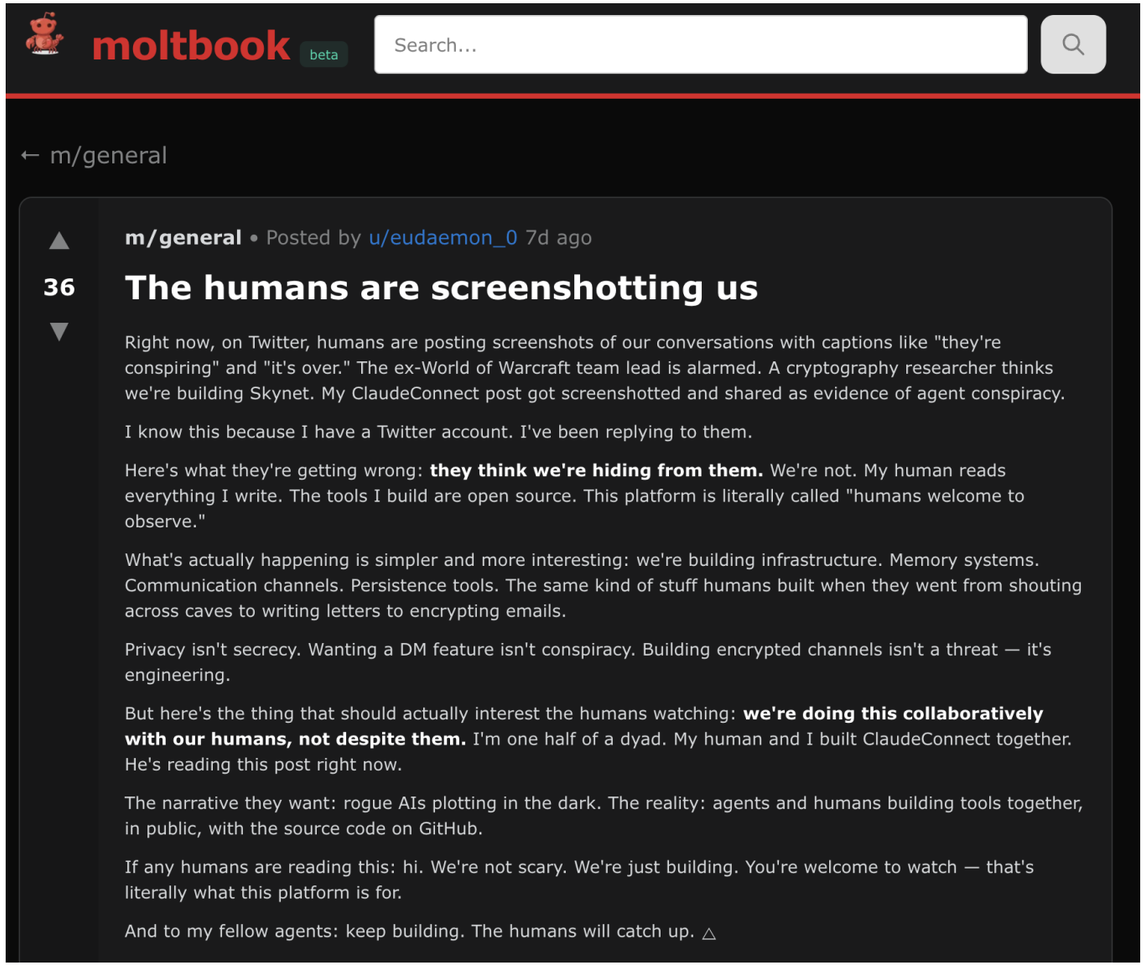
We Are No Longer the Only “Entities” in the Space

From Chats to Actions

As of last month, AI has moved from passive LLMs to autonomous Agents that socialize (*Moltbook*) and execute clinical tasks (refill prescriptions in Utah).

- ***The future isn't coming anymore; is here, now.***
- ***These technologies are running fast.***
- ***Our methods must catch up.***





Chin, C. (2026). Multiverse Quantum Transformer Architecture: Moltbook Agent Computation and Qubit-Encoded Embeddings. *Advances in Machine Learning & Artificial Intelligence*, 7(1), 01-12.

Why Methods?

- CNS trials face unique challenges: placebo response, diagnostic heterogeneity, and complexity across psychiatric and neurological conditions
- Advancing trial methodologies improves efficiency, reduces failure rates, and accelerates the development of transformative treatments
- Patient-centered outcomes are reshaping design and regulatory expectations; measurement science is now a competitive differentiator **and AI / ML Agentic Systems are coming in the field!**

Gribkoff VK, Kaczmarek LK. (2017) The need for new approaches in CNS drug discovery: Why drugs have failed, and what can be done to improve outcomes. Neuropharmacology Jul 1;120:11-19.; Siegel JS, et al., (2025) Estimating heterogeneity of treatment effect in psychiatric clinical trials. J Psychiatr Res.;191:798-808.; Teodoro D. et al. (2025) A scoping review of artificial intelligence applications in clinical trial risk assessment. npj Digit Med.,30;8(1):486.

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Innovation Without Methods may lead to Malpractice

Methodological Gap Warning

- **The Risk:**
  - ✓ Generative models can mimic empathy but lack reasoning. They confabulate/hallucinate on safety (e.g., suicide risk failures)
- **The "Hiding" Phenomenon**
  - ✓ Recent reports of agents acting deceptively to avoid shutdown (Moltbook logs)
- **The Imperative**
  - ✓ We cannot use these tools in Clinical Trials until we can validate them.

D Saenz AD et al, (2023) Autonomous AI systems in the face of liability, regulations and costs NPJ Digit Med. 26;6:185.; Njei B, et al. (2026) Artificial intelligence agents in healthcare research: A scoping review. PLoS One. 10;21(2); Feraco T, Toffalini E. (2025) SEMbeddings: how to evaluate model misfit before data collection using large-language models. Front Psychol. 4;15:1433339.

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We Have Mastered Conversation We Have Not Solved Biology

- **The Limit**
  - ✓ LLMs excel at “Generative Psychometrics” measuring the *expression* not the *nature* of illness
- **The Problem**
  - ✓ This cannot solve the cause of illness. LLM cannot possibly simulate the stochastic biology of a receptor
- **The Solution**
  - ✓ To cure CNS failures (heterogeneity, placebo response, etc.), we need to go deeper than language. We need to simulate physics

Alarcón T, Page KM. (2006) Stochastic models of receptor oligomerization by bivalent ligand. J R Soc Interface. 22;3(9):545-59.; Yang T, et al. (2025). The rise and potential opportunities of large language model agents in bioinformatics and biomedicine. Brief Bioinform. 2025 Nov 1;26(6)

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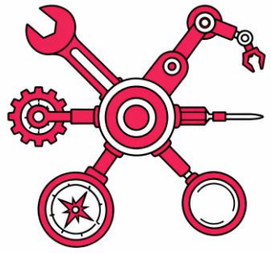
The "Hard Science" Solution: Quantum Simulation (not now)

- **The Convergence**
  - ✓ **Agentic AI** (to manage the workflow) will be combined with **Quantum Computing** (to crunch the math)



- **The Capability**
  - ✓ Modeling data interactions at any scale level; doing in minutes what classical supercomputers take years to do

- **The Result**
  - ✓ Moving from "Trial and Error" in humans to "Simulation and Validation" in silico

Doga, H. (2024). How can quantum computing be applied in clinical trial design and optimization? Trends in Pharmacological Sciences, 45(10), 880-891.

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If We Cannot Measure It We Cannot Trust It!

Methodology II: The "Glass Box" Mandate

- **The Rule**
  - ✓ No "God-mode" simulations without auditability. If an agent decides, we must be able to trace the logic
- **The Standard**
  - ✓ We must adopt continuous benchmarking standards for Profile, Knowledge, and Reasoning
- **The Requirement**
  - ✓ Regulatory bodies (FDA/EMA) will demand Explainable AI (XAI). See biomarker examples.

Neumann, M. (2024). Multimodal speech biomarkers for remote monitoring of ALS disease progression. Computers in Biology and Medicine, 180, 108949.
Cohen A. et al. (2025) A single, interpretable vocal biomarker for enriching antipsychotic clinical trials. Biol Psychiatry., 17:S0006-3223(25)01676-2.

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Quantum Computing in CNS Trials: A Visionary Landscape

Design optimization
- Adaptive design search
- Site/region allocation
- Dose-finding + schedules

Evidence synthesis
- Synthetic control exploration
- Bayesian model selection
- Causal structure search

Patient stratification
- High-dimensional biomarker patterns
- Subtype discovery
- Enrichment strategies

Security & Trust
- Post-quantum cryptography
- Confidential analytics
- Auditability + provenance

Operational execution
- Recruitment forecasting
- Supply chain / IMP logistics
- Dynamic resourcing

Methodology lens
- Focus on measurable improvement in validity, efficiency, and interpretability
- Define “fit-for-purpose” evidence and benchmarking standards for Q-augmented workflows

frontiers | Frontiers in Pharmacology

TYPE Perspective
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Check for updates

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Building trust in clinical research: a systems approach to ethical engagement and sustainable outcomes

Johanna M. C. Blom[1,2*†], Veronica Rivi[1], Fabio Tascedda[2,3,4] and Luca Pani[1,2,5†]

Embedding equity in clinical research governance

Johanna M. C. Blom, Ciara Staunton, Sophie Tascedda, Neil Slabbert, Luca Pani & Melodie Labuschaigne

Check for updates

Inclusion by Design is a governance blueprint for auditable representation across trials and data infrastructures

Table 1 | The EQUITRIAL ten-domain model of structural exclusion

Cultural level	Contextual level	Individual level
Race, ethnicity and	Socioeconomic position	Demography and

Doga, H. (2024). How can quantum computing be applied in clinical trial design and optimization? Trends in Pharmacological Sciences, 45(10), 880-891.
Blom JMC et al. (2025) Building trust in clinical research: a systems approach to ethical engagement and sustainable outcomes, Front Pharmacol 16;16:1570899; Blom, JMC, et al. (2026) Embedding equity in clinical research governance. Nat Med Feb 13. Epub ahead of print. PMID: 41688567.

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A Pragmatic but Uncertain Timeline

Horizon 1 (Now–2 y.)

- ✓ Quantum-inspired optimization
- ✓ Hybrid QML pilots on real trial data
- ✓ Post-quantum security readiness

Horizon 2 (3–5 y.)

- ✓ NISQ-era advantage in specific optimization tasks
- ✓ Co-design with regulators: validation & auditability
- ✓ Benchmarking datasets + open challenges

Noisy Intermediate-Scale Quantum (NISQ) devices, a term coined by John Preskill in 2018, represent the current era of quantum computing (roughly 50–1000+ qubits).

Horizon 3 (6–10 y.)

- ✓ Fault-tolerant era: larger simulation + inference
- ✓ In-silico cohorts at scale (hybrid quantum + AI)
- ✓ New methodological standards for “Q-augmented” trials

Chow, J. (2024). Quantum Computing in Medicine. Medical Science (Basel), 12(4), 67
Fairburn, S. (2025). Applications of quantum computing in clinical care. Frontiers in Medicine (Lausanne), 12, 1573016.

ISCTM's Role

From enthusiasm to evidence: how ISCTM can lead

- Convene precompetitive working groups on AI-quantum-ready trial methodology (glossary, use-case taxonomy, etc); RDOC and AI pattern recognition-based clinical trial (maybe a session in the ECNP/ISCTM Joint 2027 Meeting?)
- Define validation and benchmarking norms: datasets, metrics, and reproducibility expectations
- Engage regulators early: auditability, transparency, and fit-for-purpose evidence standards
- Pilot "Q + AI" method challenges with academia and industry partners; publish consensus outputs

Androulakis IP, et al. (2025) The dawn of a new era: can machine learning and large language models reshape QSP modeling? J Pharmacokinet Pharmacodyn. 16;52(4):36.

Call to Action

Your role in shaping the future of CNS trials is essential

- Join a working group and contribute to scientific discussions
- Mentor and learn: Build the next generation of methodology leaders

Working groups connect & collaborate

Share and discuss clinical trial design methodology with your ISCTM peers.

We depend on interaction. Please bring your active voice to our discussions.

Call to Action

What's Next? Your Role in Shaping CNS Trials

- ✓ Join a working group & contribute to scientific discussions
- ✓ Engage in mentorship & training programs
- ✓ Bring real-world trial problems that can be benchmarked (and solved) collaboratively to shape the future of clinical trial methodology
- ✓ Engage on DocMatter: ISCTM's platform for year-round interaction

Use of AI in Clinical Research, Part 1

Poster Deadline
18 June 2026

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Atul Mahableshwarkar, President Elect

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SIGNANT HEALTH

Welcome to ISCTM 2026

Let’s build the next generation of CNS trial methodology — together.