International Journal of Modern Scientific Discoveries
ISSN: 3107-9377 | Volume 2 Issue 3, 21-32, July-September 2026
DOI: https://doi.org/10.64137/31079377/IJMSD-V2I3P103

Received: 07/07/2026 Revised: 27/07/2026 Accepted: 31/07/2026 Published: 01/08/2026

Original Article

Explainable Multi-Agent Clinical Intelligence Framework for Advanced Healthcare Decision Support

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ABSTRACT: *Clinical reasoning in medicine must integrate increasing knowledge with established guidelines while considering patient-specific factors. AI, expert systems, and recommender systems support clinicians, but explaining the reasons for the computer's decision remains a major challenge. Simulation environments enable researchers to explore the potential of different Clinical Reasoning Models in a Multi-Agent System environment. Tests in simulated environments are supported by real-world trials in which agents collaborate, patients are modeled with knowledge and need representations, and preventive and therapeutic prescriptions constitute another dimension of the process. Most frameworks introduce Multi-Agent Clinical Reasoning Systems that are able to collaborate for Explainable Decision Intelligence in Healthcare. Roles are introduced together with the specific characteristics of the medical agents. Decision interpretation and explanation requirements are analyzed for a diagnostic use case supported by a differential framework, where a clinical hypothesis must be confirmed or refuted, taking into account all the evidence from available knowledge. Evaluation, planning, and recommendation agents reason concerning patient evolution through time and suggest preventive or therapeutic prescriptions.*

KEYWORDS: *Multi-Agent Clinical Reasoning, Explainable Artificial Intelligence (XAI), Healthcare Decision Intelligence, Clinical Decision Support Systems, Intelligent Healthcare Agents, Explainable Clinical Analytics, Collaborative AI in Healthcare, Medical Decision-Making, Human-Centered Healthcare AI, Trustworthy Clinical Intelligence Systems.*

1. INTRODUCTION

High-fidelity simulation environments offering strong realism can support medical training and educational experiences that improve knowledge and clinical skills, providing cost-effective alternatives to real-world trials and practical experience. However, the primary function of simulation environments as teaching tools can limit their broader applicability. Agent-based versions of medical simulation games that allow players to take on a variety of roles have demonstrated that simulation environments are in fact suitable for a diverse range of simulation tasks. With the same focus on flexibility, an agent-based multi-agent clinical reasoning system has been developed that supports a number of clinical use cases, including an extensive multiagent diagnostic support service set in a simulated hospital.

Despite the considerable resources devoted to the development of clinical decision-support applications, clinical reasoning tools that function at the level required to formally support clinical decisions remain elusive. Two limitations contribute to this lack: the requirement for explainable decision intelligence and the relatively limited scope of current decision-support applications. A crucial aspect of clinical decision-support systems is therefore that they be explainable. A well-established communication-centered perspective of clinical reasoning suggests that clinical reasoning support services should be agent-based, with multiple autonomous agents cooperating to complete the reasoning task. Within this perspective, the roles of the agents should be flexible and defined as the reasoning process unfolds.

Mathematical Formulas:

Eq. (1) Clinical Decision Score

$$CD = \sum E_i$$

Eq. (2) Diagnostic Confidence

$$DC = \frac{E_p}{E_t}$$

Eq. (3) Agent Trust Value

$$AT = \frac{S}{N}$$

Eq. (4) Evidence Weight

$$EW = R \times C$$

Eq. (5) Diagnosis Probability

$$DP = P(D \mid E)$$

Eq. (6) Recommendation Score

$$RS = B - R$$

Eq. (7) Agent Collaboration Index

$$ACI = \frac{M}{A}$$

Eq. (8) Clinical Risk Score

$$CRS = \sum W_i X_i$$

Eq. (9) Explainability Measure

$$EM = \frac{I}{T}$$

Eq. (10) Patient Health Status

$$PHS = H_b + H_c$$

Eq. (11) Decision Accuracy

$$DA = \frac{C}{T}$$

Eq. (12) Knowledge Coverage

$$KC = \frac{K_u}{K_t}$$

Eq. (13) Evidence Support Ratio

$$ESR = \frac{PE}{TE}$$

Eq. (14) Agent Reliability

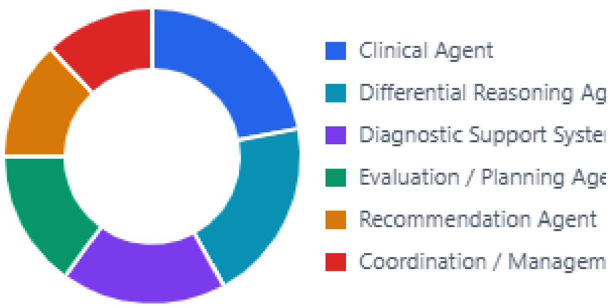
$$AR = \frac{A_c}{A_t}$$

Eq. (15) Treatment Effectiveness

$$TE = O_a - O_b$$

1.1. SIMULATION ENVIRONMENTS AND REAL-WORLD TRIALS

Patient modelling, training, and testing usually rely on expert-annotated clinical cases, spanning a range of clinical presentations, management options, and outcomes. The elaboration of synthetic populations, endowed with associated clinical cases, supports the simulation of the holistic interaction of multiple agents in a clinical environment, contributing to the generation of appropriate clinical reasoning frameworks. Target audiences can query patient models simulated as scenarios in open-world environments or as agents interacting in a multi-agent system framework. These technologies have been harnessed to perform proof-of-concept research projects in which the models were applied primarily for training or demonstration purposes. A logical next step is to deploy clinical reasoning systems comprising such patient models in a real-world environment.



FIGUER 1 Distribution of AI Agent Types in the Clinical Decision-Making Process

Agent Roles in the MAS (doughnut): Clinical, Differential Reasoning, Diagnostic Support, Evaluation/Planning, Recommendation, and Coordination agents.

The platforms allow the demonstration of ML-based agents with multimodal input and output. For interpretable and explainable clinical reasoning systems, human annotators provide information in a shared communication language to build structured agents endowed with specific reasoning capabilities. The recent proof-of-concept research projects have elucidated a broader, holistic approach to AIMED that encompasses not only diagnostic support, including differential reasoning, but also therapeutic recommendations and training tools for medical students. Such frameworks have also stimulated research on natural language generation and dialogue systems.

TABLE 1 Core Components of Multi-Agent Clinical Reasoning Systems

Components	Primary Function	Inputs	Outputs
Clinical Agent	Constructs patient profiles and captures clinical findings	Patient history, symptoms, examination data	Structured patient profile
Differential Reasoning Agent	Generates differential diagnoses	Patient profile, medical knowledge	Ranked diagnostic hypotheses
Diagnostic Support Agent	Provides evidence-based rationale	Diagnostic hypotheses, evidence repositories	Explainable diagnostic recommendations
Planning Agent	Coordinates reasoning workflows	Clinical objectives, agent capabilities	Task sequences and execution plans
Recommendation Agent	Suggests interventions	Diagnostic conclusions, guidelines	Preventive and therapeutic recommendations
Explaining Agent	Produces human-understandable explanations	Decision traces, reasoning paths	Natural-language explanations
Data Agent	Supplies patient and external data	EHRs, literature databases	Verified clinical evidence

2. FOUNDATIONS OF CLINICAL REASONING

A Multi-Agent Clinical Reasoning System mimics the medical decision-making processes of a group of experienced healthcare agents who clinical agencies share decision-making responsibilities associated with a specific use case. Communication protocols describe how agents share medical knowledge, while coordination mechanisms outline how agents share clinical domains and roles for the application of collective reasoning. For a medical use case like Differential Diagnosis, the system facilitates the interaction of three types of intelligent agents. A Clinical Agent takes the patient case and produces a patient profile; a Differential Reasoning Agent generates a set of differential diagnoses; and a Diagnostic Support System provides a diagnosis-supporting rationale without making the final decision.

James S. Gordon, an endodontist in private practice who received his DMD from the University of Pennsylvania School of Dental Medicine, observes that an exquisite awareness of the difficult differential diagnosis of teeth that hurt when chewing on them is characteristic of experience: “Teeth whose pulp has begun to necrose can often hurt on chewing or biting, where the pain is dull and slightly lingering. Pain is often limited to one tooth, perhaps with adjacent teeth being slightly exaggerated and perhaps with noticeable percussion tenderness; the diagnosis is the pulpless tooth and root canal therapy is performed.” The Differential-Reasoning Agent can generate groups of differential diagnoses for a group of Clinical-Agents' cases.

TABLE 2 Agent Roles and Responsibilities in Clinical Decision Intelligence

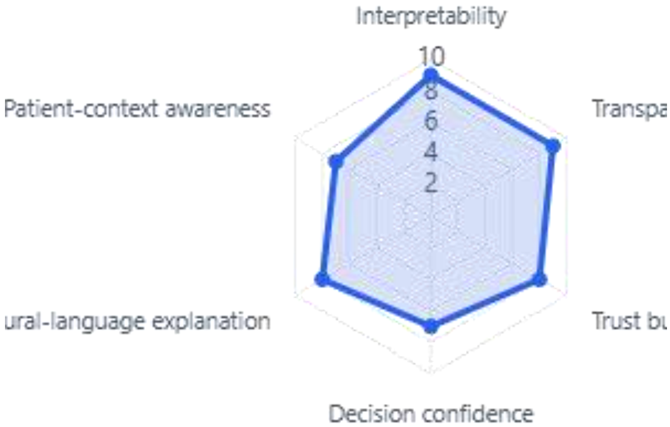
Agent Role	Responsibilities	Interaction Type
Clinical Agent	Patient assessment and information acquisition	Human–Machine
Differential Agent	Hypothesis generation and elimination	Machine–Machine
Diagnostic Agent	Diagnostic validation and evidence interpretation	Human–Machine
Coordination Agent	Synchronization of agent activities	Machine–Machine
Process Management Agent	Monitoring workflow execution	Machine–Machine
Recommendation Agent	Care planning and treatment suggestions	Human–Machine
Explanation Agent	Interpretation of outcomes	Human–Machine

2.1. COMMUNICATION PROTOCOLS AND COORDINATION

Multi-agent systems rely on communication protocols and coordination to fulfil the activities of the system's participating entities. In clinical settings, they can adopt clinical communication protocols and clinical coordination protocols. Clinical communication protocols describe the messages that can be exchanged between different agents at runtime and their respective contents. A communication protocol can use the general semantic approach of multi-agent systems, in which the performance of agents is based on the expressive power of epistemic logic to make inferences on the messages they receive from other agents.

A clinical coordination protocol describes the activities that agents must perform to achieve their goals. It includes the sequence of communicative acts that must be fulfilled in an interaction, indicating which agents must perform each act. A protocol is defined for each particular situation in which a group of clinical agents interacts to achieve a specific goal. A methodology can assist in the design and implementation of these protocols, enabling the activity of multiple agents in heterogeneous environments.

FIGUER 2 **Multi-Agent Clinical Reasoning Architecture**



FIGUER 3 **AI System Performance Across Key Clinical Decision-Making Dimensions**

Explainability & Interpretability Requirements (radar): interpretability, transparency, trust, decision confidence, NL explanation, patient-context awareness.

3. MULTI-AGENT SYSTEM ARCHITECTURES IN HEALTHCARE

Various distributed AI system architectures have been proposed in healthcare. These systems feature different underlying reasoning modalities, types of agents, roles, and usage scenarios.

Determining the roles of agents, depending on the clinical decision made, is the key. Healthcare systems generally involve two sides. On one side is the doctor, a human whose logical reasoning and expertise can be complemented by a clinical reasoning system. Well-known examples include systems that point doctors to potential errors in reasoning, such as TREC's textual entailment systems and Mississippi's Multi-Agent Clinical Reasoning and Decision-Support System (MACRDSS). These focus on distinguishing true from false clinical questions and identifying potential direct or indirect answers. MACRDSS connects human-level clinical reasoning and medical literature using multi-agent systems (MAS) technology. The system conveys the answer with clinical intuition and reasoning at a human level, while research supports it. Human understanding is enhanced using transparent and explainable systems such as the fuzzy backward chaining MACRDSS, which integrates and explains explicit knowledge using human-like clinical language.

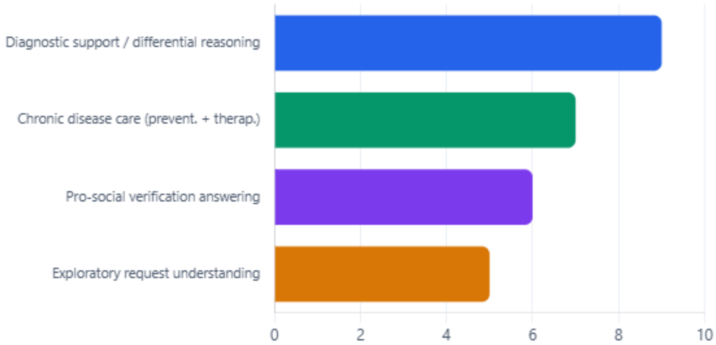
TABLE 3 **Explainability Requirements in Healthcare Decision Support**

Requirement	Description	Clinical Importance
Transparency	Visibility into reasoning mechanisms	Builds clinician trust
Interpretability	Human-readable explanations	Facilitates adoption
Decision Confidence	Assessment of certainty levels	Supports risk management
Traceability	Ability to reconstruct decisions	Improves accountability
Context Awareness	Incorporation of patient-specific factors	Enhances personalization
Reproducibility	Consistent reasoning outcomes	Enables validation
Natural Language Explanation	Clinician-friendly communication	Improves usability

3.1. AGENT ROLES AND INTERACTIONS

Unified communication protocols enable diverse multi-agent architectures in complex problem solving. Explanations for automated healthcare decision support systems require upper-level formalisms so that expert agents can develop human-interpretable knowledge. Multi-agent Clinical Reasoning Systems utilise the complementary strengths of artificial intelligence and human intelligence computers' rapid processing, memory, and information-sharing abilities, and the human ability to reason with sparse data and common-sense heuristics. These System-of-Systems architectures employ data from different environments across different agent interactions, both human machine and machine–machine.

In addition to intelligent agents and specialized expert agents that complete specific sub-tasks, other agents provide optimal control, coordination, and management for effective decision support. Agents assume collective roles during joint tasks: planning determines sub-task composition and order, identifies required agents, and specifies the communication prerequisites, whilst process management oversees completion. Coordination reduces the workload and resource usage of other roles. During multi-agent diagnosis support, planning computes the sequence of required descriptions from descriptions provided by patient agents. In a multi-agent approach to differential reasoning, functional description agents provide formal specifications that undergo specialized hazard-function evaluation; description subsumption and description distance minimize description-transformation overhead.



FIGUER 4 AI Applications Across Key Healthcare Use Cases

Clinical Use Cases Addressed (horizontal bar): diagnostic/differential, chronic care, pro-social verification, exploratory request understanding.

4. EXPLAINABLE DECISION INTELLIGENCE IN MEDICINE

Explainable, reproducible, and highly accurate decision-making capabilities required in safety-critical applications such as healthcare are achieved in agent-based clinical reasoning systems. The need for explainable intelligent systems stems from the lack of transparency in many deep learning models, as well as from high-profile failures of non-explainable learning systems. Recent studies have outlined the requirements for achieving explainable decision intelligence in medicine. Special requirements for interpretability and transparency of decision-making in health and for building trust between the intelligent system and the user are identified. Potential research directions include defining a specialized language for concepts in medicine, specializing neural-symbolic architecture for complex relations, developing new types of clinical case bases, explaining for both prediction and retrieval, achieving decision confidence, and working on the patient's health context.

The role of explaining-assisting agents in intelligent medical assistants is highlighted. The diagnoses supported by a diagnostic intelligent assistant equipped with a specialized neural-symbolic architecture, which can answer inquiries about the reasoning behind its predictions in natural language, are interpretable and transparent for medical doctors. Research on the development of a differential DX-based agent and the construction of an intelligent therapeutic assistant is outlined. A neuro-symbolic architecture for the differential DX process, in combination with a natural-language explaining agent, is also proposed.

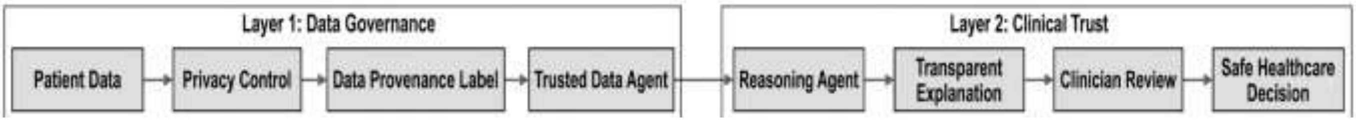
TABLE 4 Comparison Between Traditional CDSS and Multi-Agent Clinical Reasoning Systems

Features	Traditional CDSS	Multi-Agent Clinical Reasoning Systems
Architecture	Centralized	Distributed
Decision Making	Rule-based	Collaborative reasoning
Explainability	Limited	Built-in explanation mechanisms
Adaptability	Moderate	High
Coordination	Minimal	Extensive agent cooperation
Patient Personalization	Limited	Comprehensive
Learning Capability	Restricted	Integrates AI and knowledge reasoning
Scalability	Moderate	High

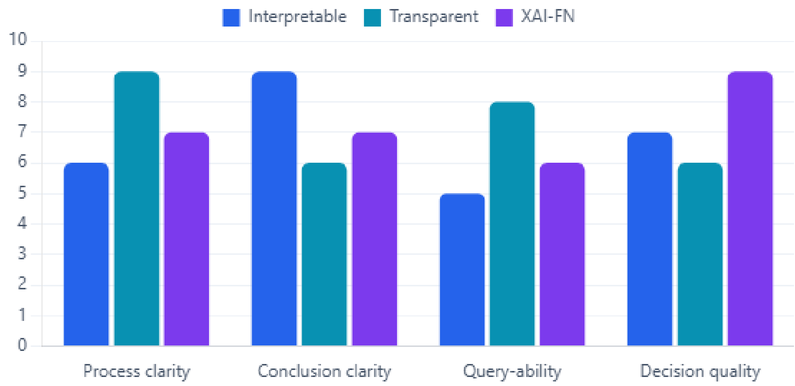
4.1. INTERPRETABILITY AND TRANSPARENCY REQUIREMENTS

The expansion of machine learning (ML) and deep learning (DL), particularly explainable AI (XAI), has produced a new generation of systems that can predict a range of events based on historical analysed data. Because predictions made by these systems can be complex and sometimes confound experts, XAI has been developed to interpret results in human-readable terms. While these systems can provide significant support, they differ from clinical reasoning and by themselves cannot replace clinical experts. Their decisions and explanations are based solely on the available data rather than inference and logical reasoning, making it crucial to understand the limits of ML, DL, and XAI in clinical systems. In medicine, the decision process often influences patient outcomes, and it is essential to demonstrate how a clinical expert reached the conclusion rather than simply showing the conclusion itself.

When using clinical DSS systems, doubts frequently arise, such as whether the recommendation is correct and whether different data would lead to more suitable decisions. Therefore, XAI should offer interpretable and transparent explanations to enable both clinicians and patients to understand the reasoning behind the provided conclusions. Clinical DSS should satisfy different interpretability requirements and combine transparent and interpretable approaches for additional clarity and understanding. An interpretable system generates an explanation directly or derives its operation from an interpretable knowledge base. Transparent systems provide a naturally comprehensible decision-making process based on their internal logic and are exploited through reasonable queries. XAI-FN systems seek to improve decision quality via internal examination, while transparent-and-interpretable systems guarantee the comprehension of both the process and the conclusion.



FIGUER 5 Data Governance and Trust Flow



FIGUER 6 Comparison of AI Explainability Approaches Across Key Clinical Decision Quality Metrics

Interpretable vs. Transparent vs. XAI-FN Systems (grouped bar): process clarity, conclusion clarity, query-ability, decision quality.

5. REASONING FRAMEWORKS FOR CLINICAL USE CASES

Multiple reasoning frameworks for selected clinical use cases highlight the diversity of temperaments among agents with heterogeneous knowledge representation. The first case illustrates a diagnosis-support assistant, focusing mainly on the differential reasoning of suspected diseases through explanations based on positive evidence. The second use case features a multi-agent chronic disease care system under an aggressive management policy and position, considering both preventive and therapeutic interventions. This agent coordination model promotes various parties and agents involved in comprehensive patient management and follow-up care, thus forming a chronic care ecosystem. The third underpinning explores a multi-agent semantics within a pro-social answering setting. Underlining positive answers to verification questions with consultation and language feedback to clarify the questions. Negative answers are inferred but not explicitly represented. Finally, an agent team for exploratory health-care request understanding assists in establishing a clear health-care request. The simulation and user-initiate-interaction in a 2-D visualized environment allow demonstration of virtual human viewpoints to assist in engaging agents' sub-agent deliberation–decision cycles.

TABLE 5 Communication and Coordination Protocols

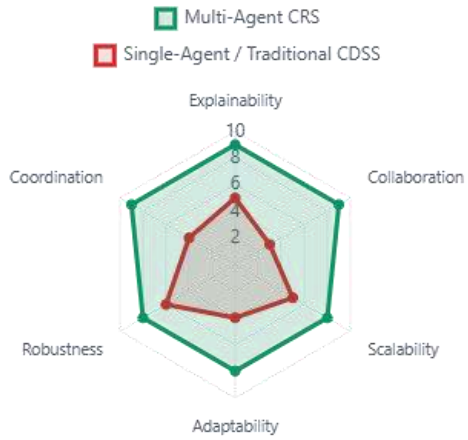
Protocol Type	Purposes	Example Activities
Communication Protocol	Defines message exchange formats	Sharing diagnoses
Coordination Protocol	Organizes task execution	Diagnostic sequencing

Negotiation Protocol	Resolves conflicting recommendations	Consensus formation
Query Protocol	Requests clinical evidence	Laboratory result retrieval
Explanation Protocol	Exchanges reasoning justifications	Decision clarification
Verification Protocol	Validates clinical conclusions	Cross-agent confirmation

5.1. DIAGNOSTIC SUPPORT AND DIFFERENTIAL REASONING

Simulated environments, such as Goal-Driven Simulation of Medical Diagnosis, and real-world deployments, like the LHS for Tuberculosis diagnostics, are key for testing new architectures and approaches. Open-Source Clinical Reasoning Systems are essential for the integration of diverse reasoning implementations and the orchestration of interactions across reasoning agents.

The analysis of causal relations links the possibility of causal inference to the applicability of the analysis. The study of agents that carry out differential reasoning unveils how a set of hypotheses is selected based on the patient's observations, and how the process can be organized. A multi-agent technology that solves a task by means of cooperation and negotiation towards a common goal, with foundations drawn from the Formal Theory of Communication, is also considered.



FIGUER 7 Comparison of Multi-Agent and Traditional Clinical Decision Support Systems Across Key Performance Dimensions

Multi-Agent vs. Single-Agent/Traditional CDSS (radar): explainability, collaboration, scalability, adaptability, robustness, coordination.

6. DATA GOVERNANCE, PRIVACY, AND SECURITY

Data governance obligations are heightened in the healthcare sector. As agent-based systems collect, analyze, and exploit a wider range of sensitive health-related patient data, privacy measures protecting these data must also expand. Data provenance preserves security measures while ensuring sensitive patient data are not mismanaged and meet their trust requirements. Data provenance serves different purposes for different agents; for example, protecting an agent while aiding the decisions of others. Data leading to a diagnostic conclusion must therefore be flagged with a special provenance label enabling a differential display, the goal being to show the grounds of the other agent's decision should this stumble into suspicion.

TABLE 6 Clinical Use Cases Supported by Multi-Agent Systems

Use Cases	Participating Agents	Outcomes
Differential Diagnosis	Clinical, Differential, Diagnostic Agents	Diagnostic support
Chronic Disease Management	Recommendation, Planning Agents	Longitudinal care optimization
Therapeutic Decision Support	Recommendation, Explanation Agents	Treatment planning
Medical Education	Simulation Agents	Clinical training
Diagnostic Dialogue Systems	Language and Reasoning Agents	Interactive consultations
Preventive Care Management	Evaluation and Recommendation Agents	Risk mitigation strategies

6.1. DATA PROVENANCE AND TRUST

When exploring data governance in healthcare, the focus is usually on meeting regulatory standards while ensuring adequate privacy and security measures. However, especially in the context of clinical decision systems, explainability and trust become fundamental issues. Explainable Healthcare encompasses the aspects of Explainable Artificial Intelligence (XAI), although it is not limited to machine-learning-based Clinical Decision Support Systems (CDSS). Any system offering a clinical recommendation or diagnosis should facilitate understanding of the input and output data and the reason for the recommendation. Trust is typically woven into the simulation component of a clinical reasoning system, even when no deontic logic is explicitly used. A single Agent can easily communicate the requisite diagnostic information to patients, physicians, and nursing staff.

Multi-Agent Clinical Reasoning Systems (MCRS), by nature, emphasize trust-building in the vast data exchanged and generated by the Agents. For example, in a diagnostic-activity MCRS, \({\mathcal{D}}\) is a composite Agent that recruits Data Agents when simulating un-DS or conditional DS data to support differential diagnosis. When Agent \({\mathcal{D}}\) requests help from DataAgent \(D\), it must check whether \(D\) is a trusted source of the requested disease condition for the simulated patient. Though trust requires a previously established baseline knowledge of a Data Agent, the mechanisms underlying this trust relationship, such as trust metrics or thresholds specific to different clinical contexts (e.g., reliability across time), vary traditionally with the reason used to access some data.

FIGUER 8 Evaluation of AI Clinical Systems Across Key Trust and Performance Dimensions

Data Governance, Privacy & Security (bar): privacy, security, provenance, trust, compliance, access tracking.

7. CONCLUSION

The synthesis of agent-based approaches for clinical reasoning into a generic multi-agent architecture, along with the explanation of the centralized coordination approach and the reflective diagnosis use-case enabled by the multi-agent clinical reasoning architecture, establishes a first step towards an efficient, robust, and adaptable logical multi-agent answer set architecture suited to clinical reasoning. Such multi-agent approaches are aligned with established clinical reasoning models and CR conversations. These models also enable the monitoring of CR conversations and embolden supporting agents to make differential inferences.

Furthermore, the development of MA-CRS should be complemented with appropriate protocols for agent interaction. Information from agents supporting the central reflective diagnosis agent should be confident and trustworthy, thus maintaining the confidentiality and privacy of patients and their data. The need for transparent systems is paramount in medicine, since erroneous adjudication of a medical concern has the potential to cost a patient's life. For this reason, patients' data provenance and governance must be appropriately managed. However, data usage and governance depend on the purpose and the agent type. Supporting agents providing diverse data services, such as a patient data agent or a literature-lookup agent, require very different data governance and provenance models.

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