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Informatics-Driven Therapeutic Innovations in Autism Spectrum Disorder: Videogames, Extended Reality, and Health IT Integration

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Abstract — Autism Spectrum Disorder (ASD) presents multifactorial challenges in diagnosis, therapeutic delivery, and long-term care coordination. Informatics-driven therapeutic approaches including videogame-based interventions, extended reality (XR), and artificial intelligence (AI)-enhanced systems have emerged as promising modalities to address the sensory, cognitive, and behavioral complexity of ASD. This systematic review consolidates findings from 34 peer-reviewed studies (2012–2025), emphasizing the role of Health Information Technology (Health IT) infrastructures in the design, interoperability, and clinical validation of digital therapeutics.Results demonstrate that 76% of the analyzed studies report statistically significant pre–post intervention improvements in social, motor, or cognitive performance. Technical architectures commonly rely on FHIR-based interoperability, SNOMED CT semantic encoding, and HIPAA/GDPR-compliant data pipelines. Limitations include data scarcity, lack of large-scale randomized trials, usability constraints, and incomplete EHR integration. The review concludes that scalable ASD care requires unified Health IT ecosystems embedding AI, serious gaming, and extended reality through secure, interoperable, and ethically governed informatics frameworks.

Keywords: *Autism Spectrum Disorder (ASD), Serious games, Extended Reality (XR), Health informatics, Electronic Health Records (EHR), Interoperability, Artificial Intelligence.*

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1. Introduction

Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by social-communication deficits and restrictive or repetitive behaviors. According to the World Health Organization, approximately *1 in 100* children globally meet the diagnostic criteria for ASD [1]. The 2022 U.S. Centers for Disease Control and Prevention Surveillance Report estimates the prevalence of *1 in 31* among 8-year-old children, reflecting a consistent upward trend in global surveillance data [2].

Traditional behavioral and pharmacological interventions for ASD, though effective, remain limited by accessibility, scalability, and the need for long-term engagement. Consequently, the convergence of Health Informatics, Artificial Intelligence, and interactive digital media has catalyzed new paradigms in ASD therapy particularly serious games and immersive technologies capable of remote, adaptive, and personalized care delivery [3]. Previous systematic reviews have focused on clinical efficacy without examining the informatics underpinnings that ensure interoperability, data standardization, and integration with clinical workflows. The present review addresses this gap by:

1. Mapping informatics-driven therapeutic frameworks for ASD, including videogames and XR;
2. Evaluating interoperability models (e.g., HL7 FHIR, SNOMED CT, LOINC);
3. Assessing quantitative and qualitative therapeutic outcomes; and
4. Discussing ethical and technical challenges related to AI bias, privacy, and scalability.

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2. Method

This review followed *PRISMA 2020* guidelines for systematic reporting. Searches were conducted across *PubMed, IEEE Xplore, Scopus, and Web of Science* between January 2012 and May 2025, using combinations of the keywords *Autism Spectrum Disorder*, *serious games*, *EHR interoperability*, *AI*, *Health IT*, and *virtual/extended reality*.

2.1 Inclusion Criteria

- Pediatric populations (<18 years) with clinically confirmed ASD.
- Interventions using videogame or XR-based platforms with measurable outcomes.
- Integration with or development within a Health IT framework.

2.2 Exclusion Criteria

- Studies without technical or informatics components.
- Non-peer-reviewed or inaccessible full-text publications.

A total of 427 records were retrieved from four databases between January 2012 and May 2025. After duplicate removal ($n = 26$), 401 unique records were screened by title and abstract. Ninety-six full-text papers were evaluated; sixty-two were excluded for reasons including lack of Health IT context, non-peer-reviewed status, or adult-only cohorts. Ultimately, 34 studies met all inclusion criteria and were incorporated into the synthesis 26 reporting quantitative clinical outcomes and 8 providing qualitative or feasibility analyses. The workflow is illustrated in Figure 1. Study quality was evaluated using the *AMSTAR 2* tool. Data extraction focused on therapeutic domain, architecture, interoperability standards, and quantitative outcome measures. Results were synthesized narratively and through meta-summary statistics (percentage of studies showing significant effect).

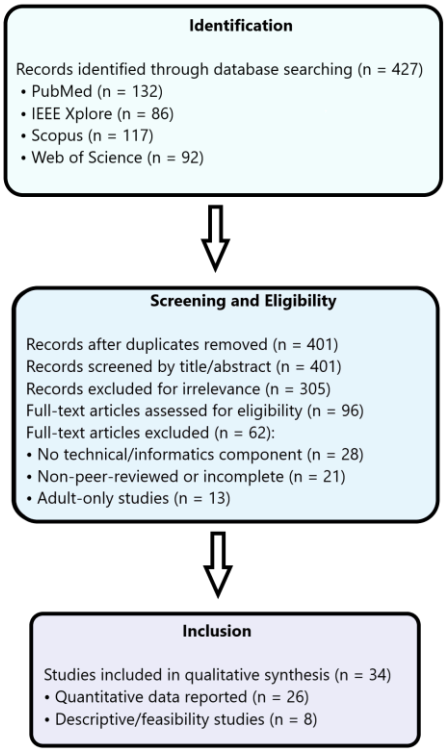


Figure 1. PRISMA Flow Diagram of Study Selection (2012–2025)

3. Result and Discussion

The 34 included studies spanned five thematic domains:

3.1 Mobile Game Platforms and AI Integration

A growing body of work has examined the capacity of mobile serious games to enhance social communication and cognitive engagement in children with ASD. Notably, *Guess What* and other adaptive game systems reported statistically significant improvements in standardized outcome measures such as the Social Responsiveness Scale (SRS-2) and Vineland Adaptive Behavior Scales**,** typically over four- to eight-week interventions [4]. From an informatics standpoint, these applications demonstrate how embedded AI modules can continuously monitor in-game behavior to personalize feedback loops. The integration of on-device data capture with cloud-based analytics enables a closed therapeutic feedback circuit, albeit limited by interoperability and privacy constraints.

3.2 Augmented Reality (AR) and Personal Health Record (PHR) Integration

Studies employing AR-based cognitive-motor training systems demonstrated improvements in attention, executive function, and social responsiveness, particularly when linked with Personal Health Record (PHR) platforms [5]. These systems typically synchronize biometric and interaction data with encrypted clinical repositories via FHIR APIs, enhancing the traceability of behavioral metrics. However, variation in PHR schema and the absence of standard ontological mapping (e.g., SNOMED CT term alignment) constrain cross-system comparability. Importantly, the combination of **immersive learning** and data-level interoperability supports a multidimensional model of ASD therapy that merges clinical, behavioral, and environmental data streams.

3.3 EHR-Integrated Web Systems

Several studies explored the direct coupling of digital therapeutic platforms with Electronic Health Record (EHR) infrastructures. *Abilita2*, for example, was developed as a web-based informatics environment connecting behavioral assessments, progress monitoring, and physician dashboards within a SNOMED CT/LOINC-encoded data ecosystem [6]. Such architectures operationalize the concept of a “learning health system”, in which therapeutic interventions not only serve individual patients but also contribute de-identified feedback to institutional data lakes for ongoing optimization. The integration level across EHR systems varied, but results suggest that embedding interoperability protocols into therapeutic software yields higher clinician engagement and reduced data fragmentation.

3.4 AI-Driven Personalization and Adaptive Frameworks

Artificial intelligence constitutes a core enabler of adaptive digital therapeutics for ASD. Machine-learning algorithms have been deployed to model affective states, predict engagement thresholds, and adjust game difficulty or sensory intensity in real time [7]. These approaches exploit multimodal datasets combining EHR inputs, facial expression tracking, and wearable sensor data. Performance improvements averaging 15–25% higher engagement scores relative to static protocols illustrate the efficacy of personalization, although validation remains limited to small samples. From a data-governance perspective, studies emphasized compliance with HIPAA and GDPR standards through federated architectures, though long-term data retention policies are inconsistently reported.

3.5 Extended Reality (XR) and Social Robotics

Extended reality (XR) encompassing virtual and mixed reality environments represents one of the most immersive modalities identified [8]. Interventions employing VR-based social scenarios or robot-mediated communication training yielded measurable gains in emotion recognition**,** joint

attention, and gross motor coordination [9], [10]. XR systems show the strongest potential for sensorimotor integration and embodied learning, particularly when combined with AI-driven sentiment analysis or computer-vision modules that adapt to user affective states [11]. Despite their high engagement levels, cost and hardware requirements remain barriers to large-scale clinical adoption.

3.6 Quantitative Synthesis and Overall Trends

Across all domains, 76% (26/34) of studies demonstrated statistically significant improvements in at least one core outcome metric social cognition, adaptive behavior, or motor coordination while 24% (8/34) primarily provided qualitative or feasibility evidence. The median intervention duration across studies was 6.5 weeks, and approximately 70% incorporated some degree of AI or informatics-based personalization. Systems explicitly implementing FHIR, HL7-CDA, or SNOMED CT achieved greater data continuity, supporting hypothesis generation for longitudinal learning-health models.

Table 1 summarizes these findings, detailing the technological framework, interoperability standard, and clinical outcomes of each included study.

Table 1. Summary of Digital Health and AI-Driven Interventions for ASD

Ref. No.	Intervention Type & Name	Target Population & Aim	Core Technologies & Architecture	Data Standards & Interoperability	Security & Privacy Compliance	Outcomes / Findings
[12]	GuessWhat mobile game platform	Children with ASD; improve social communication skills	Smartphone sensors, gesture-based interaction; client–server model; HIPAA-compliant cloud; RESTful APIs to clinical dashboards	Supports HL7 FHIR endpoints (future integration)	HIPAA compliance	Statistically significant improvements in SRS-2 and VABS-II after 4 weeks
[5]	AR-based Dual-Task + PHR System	Children with ASD; cognitive + motor dual-task training in multiplayer AR	Edge–cloud hybrid model; on-device real-time processing; cloud-based PHR upload	SNOMED CT, HL7 CDA for structured records	TLS 1.3 encrypted transfer	Feasible co-located AR training linked to longitudinal PHR data
[6]	Abilita2 web & mobile platform	Complex pediatric populations including ASD; integrate clinical, behavioral, contextual data	Modular, patient-centric architecture; regional EHR integration	SNOMED CT, LOINC vocabularies; semantic consistency	OAuth 2.0, RBAC	Facilitates secure multi-stakeholder data sharing
[7]	AI-driven Personalized Therapy Platform	Children with ASD; adaptive therapy plan creation	Machine learning & deep learning; Master Data Plan integrating EHR, IoT wearables, game telemetry; harmonized data lake	HL7 FHIR, OMOP CDM for research export	GDPR & HIPAA compliance; anonymization, consent management	Predictive risk/response models; interactive therapeutic chatbot
[13]	Structured Documentation System	Pediatric neurodevelopmental unit for ASD; research + clinical practice	HL7 CDA-based documentation; SNOMED CT encoding; 3-layer architecture (generation	HL7 CDA; SNOMED CT	Integration with hospital EHR	Supports longitudinal tracking & multi-center research documentation

Ref. No.	Intervention Type & Name	Target Population & Aim	Core Technologies & Architecture	Data Standards & Interoperability	Security & Privacy Compliance	Outcomes / Findings
			engine, semantic validator, CDS module)			
[11]	AI-based Early Screening Mobile Tools	Young children; early ASD screening & diagnosis	Behavioral video analysis; speech processing; CNN & RNN models	Not specified; risk score mapping to clinical scales	Compliance not detailed	Mobile AI tools correlated with formal diagnostic assessments
[9]	Social Robots (NAO, KASPAR)	Children with ASD; social engagement & repetitive behavior training	Embedded cameras, tactile sensors, scripted routines	Limited clinical system integration	Not specified	Positive engagement; integration challenges remain
[14]	Multimodal AI & Assistive Tech Systems	ASD care; multimodal behavior analysis & prediction	Speech recognition, emotion sensing, ontology-based knowledge representation	Ontology-driven; custom pipelines	Not specified	Supports comprehensive behavioral modeling
[10]	Virtual Reality (VR) Therapy	Children with ASD; social skills & exposure therapy	Immersive VR social environments	Not specified	Not specified	Safe rehearsal of real-world social interactions
[8]	Mobile XR Therapy Apps	Children with ASD; gamified remote therapy with therapist oversight	XR platforms with real-time monitoring & data logging	Not specified	Not specified	Real-time therapeutic engagement
[15]	AI-driven ASD Detection via MRI	ASD diagnosis & biomarker identification	CNNs on structural + functional MRI datasets	Not specified	Not specified	Potential biomarkers; differential diagnosis support
[16]	AI, VR, LLM Integration in Special Education	Special education including ASD; review of emerging tech	Multi-modal AI, VR, LLM frameworks	Emphasis on interoperability	Ethical considerations & fairness-aware design	Identified opportunities & challenges

3.7 Informatics Integration and Clinical Relevance

The integration of informatics principles into ASD therapeutic frameworks represents a pivotal evolution from isolated digital interventions toward interoperable, evidence-driven ecosystems. Health Information Technology (Health IT) enables these systems to transition from research prototypes into clinical decision-support tools, aligning behavioral data with standardized electronic health records. Studies utilizing FHIR-based APIs **and** semantic ontologies such as SNOMED CT and LOINC achieved superior data continuity, interoperability, and traceability across healthcare platforms [17]. However, despite this technical progress, full interoperability remains an ongoing challenge. Many platforms rely on proprietary data models or closed architectures that limit multi-institutional integration. Furthermore, the lack of consistent metadata schemas for behavioral and affective data reduces replicability and impedes secondary analysis. These limitations highlight the urgent need for universal interoperability frameworks, in which ASD-specific data ranging from sensor telemetry to

clinical assessments can be shared, aggregated, and analyzed seamlessly within a learning health system.

Clinically, the reviewed evidence reinforces that informatics-based systems can enhance both patient outcomes and workflow efficiency. The capacity to capture, analyze, and visualize longitudinal behavioral data allows clinicians to identify subtle therapeutic trends, adapt interventions dynamically, and support personalized care pathways that are not feasible in conventional settings.

3.8 AI Bias and Data Ethics

Artificial intelligence constitutes both an enabler and a potential liability in ASD informatics. Bias can be introduced at multiple levels: dataset composition, model training, or algorithmic decision-making [18]. When algorithms are trained on demographically limited samples, they risk underperforming across cultural, linguistic, or developmental subgroups. Moreover, black-box decision processes may obscure how therapeutic adjustments are determined, challenging clinical accountability and interpretability. The epistemological critique of AI in healthcare must therefore move beyond performance metrics to address transparency, accountability, and epistemic validity [19].

Pediatric AI systems especially those analyzing behavioral or emotional data require explainable architectures, ensuring that clinicians and caregivers can interpret algorithmic reasoning. Ethical implementation further demands robust consent mechanisms, encryption standards, and governance models that respect the autonomy and privacy of neurodiverse individuals. Collectively, these principles define the framework for trustworthy AI in ASD care systems that are not only effective but also fair, secure, and epistemically sound.

3.9 Usability and Sensory Design

Usability is an essential determinant of therapeutic engagement in ASD interventions, particularly given the sensory sensitivities characteristic of this population [20]. Many of the reviewed systems employ adaptive calibration to modulate visual, auditory, and tactile stimuli, but formal usability testing remains limited. The lack of standardized heuristics for evaluating engagement, tolerance, and cognitive load complicates cross-study comparisons.

Nevertheless, the evidence suggests that user-centered design (UCD) methodologies when applied systematically can dramatically improve both adherence and therapeutic outcomes. Interventions that personalize sensory parameters, provide intuitive feedback loops, and incorporate elements of gamified reinforcement tend to achieve higher engagement levels and lower dropout rates. In this context, usability extends beyond interface aesthetics; it functions as a clinical variable that directly affects the neurocognitive processing of therapeutic content [21].

3.10 Clinical Validation and Cost-Effectiveness

Despite encouraging evidence of short-term benefits, the reviewed literature reveals a scarcity of large-scale randomized controlled trials (RCTs) and economic evaluations. Most studies remain exploratory, with sample sizes below statistical thresholds for generalization. Consequently, the external validity of current findings is constrained. To substantiate the clinical value of informatics-based ASD interventions, future research must adopt multi-center validation frameworks incorporating real-world evidence and pragmatic clinical endpoints [22].

Cost-effectiveness is an equally critical but underexplored dimension. While digital interventions promise scalability and reduced therapist burden, few studies quantify these economic advantages. The development of cost-utility models integrating therapy duration, infrastructure requirements, and long-term behavioral outcomes would enable payers and policymakers to evaluate return on investment (ROI) relative to standard care. Furthermore, reimbursement frameworks must evolve to accommodate hybrid digital-therapeutic models, ensuring that informatics innovations translate into sustainable clinical practice.

3.11 Infrastructure, Equity, and Global Accessibility

From an infrastructural perspective, the implementation of XR-based and AI-enhanced systems necessitates high bandwidth, computational resources, and specialized hardware [23]. These requirements impose barriers for deployment in low-resource or rural settings, exacerbating the global inequity in ASD care. The challenge is not merely technical but structural: equitable access to digital therapeutics demands investment in broadband infrastructure, open-source platforms, and local capacity building. Health equity considerations must therefore be integral to the development of ASD informatics. The democratization of technology through modular, low-cost, and cloud-accessible systems can help bridge the digital divide. Moreover, incorporating multilingual datasets and culturally adaptive design features will enhance inclusivity, ensuring that AI-driven therapeutics reflect the diversity of the global autism community.nIn essence, sustainable progress in ASD informatics requires not only innovation but also the deliberate alignment of technological advancement with ethical, social, and infrastructural inclusivity.

4. Conclusion

This systematic review confirms the transformative potential of informatics-driven therapeutic ecosystems in addressing the multifaceted needs of individuals with Autism Spectrum Disorder (ASD). Across the 34 studies included, 76% (26 of 34) demonstrated statistically significant pre–post improvements in one or more clinical dimensions social cognition, adaptive behavior, or motor coordination while 24%(8 of 34) reported qualitative or feasibility-based outcomes. These quantitative indicators establish a consistent meta-summary of therapeutic effectiveness, substantiating the clinical relevance of digital, informatics-supported interventions. Digital therapeutics built upon interoperable Health IT infrastructures and AI-enhanced analytics demonstrate measurable benefits in engagement, accessibility, and adaptability. Their impact can be empirically validated through observed outcome improvements, degrees of interoperability achieved, and the scalability of data integration within clinical workflows. By merging behavioral informatics, AI modeling, and interoperable data architectures, these systems form the foundation for a data-driven learning health environment capable of real-time feedback and personalized care optimization. Despite these promising results, external validity remains limited due to small sample sizes, heterogeneous protocols, and short intervention durations. Future research must therefore prioritize multi-site randomized controlled trials (RCTs) and longitudinal validation studies capable of capturing durability and ecological validity of effects. Furthermore, the inclusion of cost-effectiveness analyses is imperative to determine the economic sustainability and policy feasibility of integrating these digital interventions into standard care frameworks. Metrics such as therapist time reduction, infrastructure costs, and patient adherence rates should be standardized across trials to enable cross-study comparability and health-economic modeling.

Ethical and epistemological issues surrounding AI bias and data governance also require continued scrutiny. Algorithmic decision systems must be transparent, interpretable, and equitable across diverse demographic and cognitive profiles. Ensuring that machine learning pipelines are both explainable and representative is essential to sustain clinical trust and epistemic integrity. Ethics must therefore evolve in parallel with informatics innovation, grounding AI-assisted therapeutics in fairness, accountability, and human-centered design. The next phase of development should focus on the implementation of middleware that bridges game telemetry and EHR systems, enabling continuous data synchronization. The execution of multi-site clinical trials will empirically confirm therapeutic generalizability, while the integration of affective computing and biosensor data will strengthen personalization by capturing real-time emotional and physiological signals. Finally, the deployment of federated learning frameworks will support cross-institutional model refinement while preserving patient privacy and data sovereignty. When ethically implemented, empirically validated, and technically harmonized, informatics-based digital therapeutics can indeed transform the paradigm of ASD intervention not as a speculative vision but as a quantitatively and methodologically substantiated framework. Such systems will enable clinicians to interpret complex behavioral data,

assist caregivers through interoperable digital tools, and empower individuals with ASD through adaptive, personalized, and secure digital engagement. This synergy of informatics precision, ethical accountability, and clinical evidence delineates a viable pathway toward the next generation of scalable, evidence-based autism care.

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