

Viewpoint

AI-Driven Digital Twin Architecture for Multimodal Prediction and Adaptive Intervention in Cognitive Aging

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Abstract

Age-related cognitive dysfunction, including mild cognitive impairment and dementia, underscores the need for scalable and personalized predictive models. We present a conceptual artificial intelligence-driven digital twin framework to support early detection, real-time monitoring, and adaptive intervention. The system is structured around 4 core processes: perception, analytics, decision-making, and adaptive feedback, and is organized across 5 functional layers: data acquisition, integration, modeling, reasoning, and application. Multimodal behavioral, physiological, and clinical data are harmonized using Fast Healthcare Interoperability Resources and Observational Medical Outcomes Partnership standards. Predictive modeling uses convolutional and recurrent neural networks, gradient boosting, and reinforcement learning. The framework is designed for cloud-based deployment on platforms that support HIPAA-aligned implementation, including Amazon Web Services and Microsoft Azure, with 7 application modules spanning signal-based and pose-based assessment, personalized mind-body training, cognitive rehabilitation, and disease trajectory simulation. This architecture offers a foundation for precision cognitive care in aging populations.

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KEYWORDS

digital twin; cognitive aging; multimodal prediction; machine learning; adaptive intervention

Introduction

Rapid demographic aging is reshaping global health landscapes, with the number of individuals aged 60 years and older projected to increase from 901 million in 2015 to 2.1 billion by 2050 [1]. As life expectancy rises, the burden of age-related cognitive dysfunction, including mild cognitive impairment (MCI) and dementia, is increasing sharply, undermining individual quality of life and placing mounting pressures on health care infrastructures worldwide [2]. A systematic review of global studies reports that the prevalence of cognitive impairment

among older adults ranges from 5.1% to 41%, with a median of 19% [1].

Despite growing demands, current health care models remain poorly equipped to manage the dynamic, heterogeneous, and progressive nature of cognitive dysfunction. Conventional care approaches, often episodic and clinic-centered, lack the capacity for continuous longitudinal monitoring, personalized risk stratification, or timely intervention [3]. This limitation frequently results in delayed detection of cognitive deterioration, missing the optimal window for early-stage intervention where preventive strategies may be most effective. Addressing these

gaps requires innovative frameworks capable of enabling continuous surveillance, individualized cognitive modeling, and adaptive, real-time care strategies across diverse aging populations [4].

Recent advances in artificial intelligence (AI), machine learning (ML), and digital twin (DT) technologies offer promising avenues to meet these emerging needs [5]. AI and ML algorithms have demonstrated considerable capacity to extract latent patterns from complex, high-dimensional health data, supporting early detection of cognitive decline and the development of personalized intervention pathways [6]. Simultaneously, the adaptation of DT frameworks, originally conceived for engineering and industrial systems, into health care settings enables the creation of dynamic, real-time virtual representations of individual patients [7]. These models can continuously simulate health trajectories, forecast risks, and optimize care strategies based on evolving multimodal inputs [8].

Here, we present an AI-driven multimodal DT framework designed to enable continuous, dynamic, and personalized management of cognitive health in aging populations. By integrating real-time physiological, behavioral, and environmental data with adaptive ML-driven modeling and secure, scalable cloud infrastructures, the framework aspires to facilitate early identification of cognitive risk, dynamic intervention refinement, and proactive resilience building. Moving beyond reactive and episodic care models, this conceptual architecture represents a critical step toward establishing precision, sustainable, and equitable cognitive health care for an increasingly aging global society.

Conceptual Framework

Overview

DT technology, originally developed for engineering and industrial applications, has increasingly attracted attention in

health care for its potential to enable dynamic [9], personalized [10], and predictive management of patient health [8]. In the context of cognitive health, a DT is conceptualized as a continuously evolving, real-time virtual representation of an individual's physiological, behavioral, and environmental states, constructed through multimodal data acquisition, integration, and computational modeling [11]. The AI-driven DT framework proposed in this study is structured around four interdependent core processes: perception [12], analytics [13], decision-making [14], and adaptive feedback [15]. Each process plays a critical role in creating an individualized, dynamic, and responsive model of cognitive function and its evolution over time (Table 1 and Figure 1 [16]).

Figure 1 presents the proposed multimodal digital twin framework, which integrates real-time physiological, behavioral, and environmental data with large-scale clinical and research datasets to enable early detection, continuous monitoring, and adaptive intervention for cognitive decline in older adults. The system is structured around four core processes: perception, analytics, decision-making, and adaptive feedback, operationalized through five technical layers: data acquisition, integration, modeling, reasoning, and application. This structure is consistent with the canonical DT architecture, in which perception aligns with the physical entity, analytics and decision-making are instantiated in the virtual twin, and adaptive feedback is operationalized through the bidirectional communication channel to sustain a closed-loop workflow. Seven functional modules support dynamic, individualized care, including mind-body exercise recommendations, cognitive rehabilitation, lifestyle coaching, disease trajectory simulation, and health economic evaluation. The framework is designed for scalable deployment using cloud-native, vendor-agnostic architectures.

Table 1. Core processes of the artificial intelligence-enabled digital twin framework for cognitive health management^a.

Architecture	Core	Function	Representative components and methods
Physical entity	Perception	Captures and integrates multimodal physiological, behavioral, and environmental data	EEG ^b , HRV ^c , gait, speech, sleep, facial expressions, and environmental sensors; EHRs ^d , ADNI ^e , and UKB ^f ; data cleaning, temporal alignment, and FHIR ^g and OMOP ^h -based harmonization
Virtual twin	Analytics	Extracts latent features and predicts cognitive risk trajectories	CNNs ⁱ , LSTMs ^j , and autoencoders; multimodal fusion; few-shot learning; uncertainty estimation with Monte Carlo dropout
Virtual twin	Decision-making	Generates individualized intervention strategies based on predictive and causal inference models	Reinforcement learning, Bayesian inference, and propensity score matching; anomaly monitoring; intervention simulation; SHAP ^k and LIME ^l ; personalized mind-body, cognitive, and behavioral recommendations
Bidirectional communication channel	Adaptive feedback	Dynamically updates models and interventions based on new data and user responses	Federated and incremental learning; real-time tracking; edge computing; adaptive tuning of intervention intensity and content; mobile and wearable interfaces

^aThe framework comprises four synergistic processes that transform real-time data into personalized, adaptive interventions for cognitive decline in aging populations.

^bEEG: electroencephalography.

^cHRV: heart rate variability.

^dEHR: electronic health record.

^eADNI: Alzheimer's Disease Neuroimaging Initiative.

^fUKB: UK Biobank.

^gFHIR: Fast Healthcare Interoperability Resources.

^hOMOP: Observational Medical Outcomes Partnership.

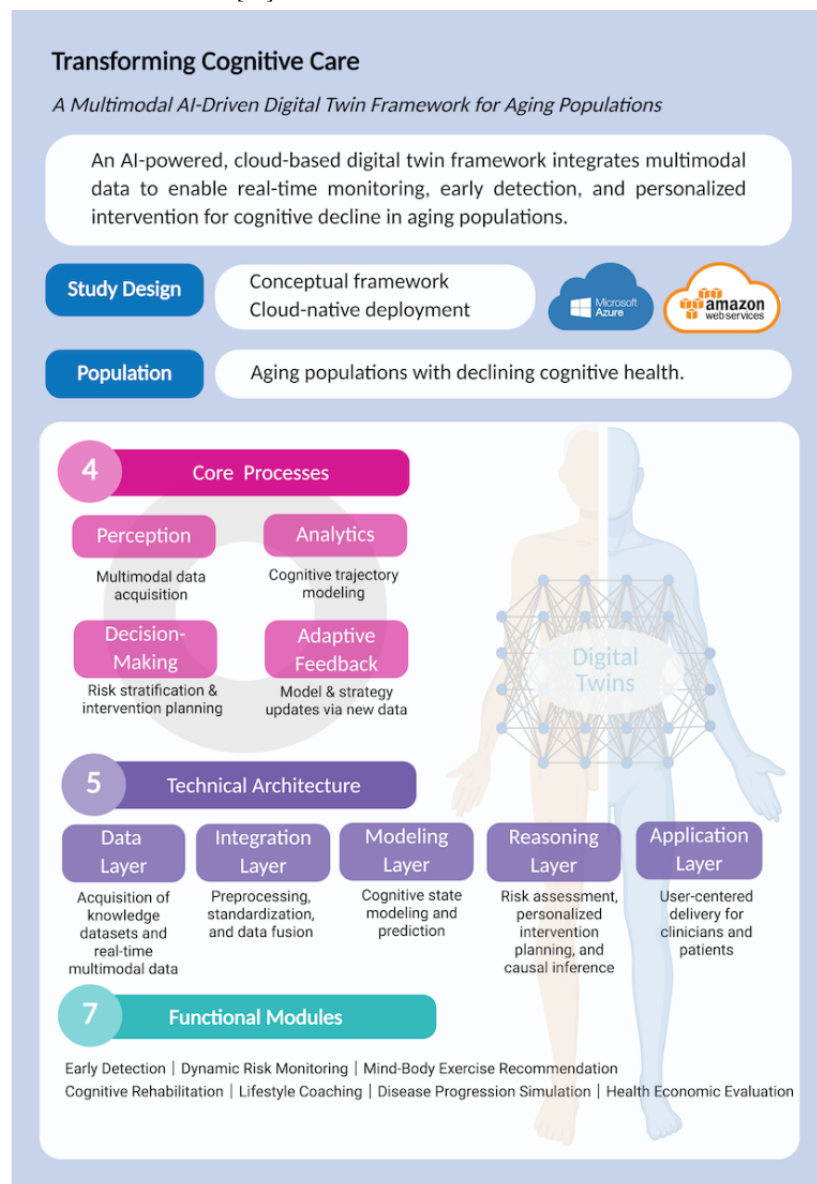
ⁱCNN: convolutional neural network.

^jLSTM: long short-term memory.

^kSHAP: SHapley Additive exPlanations.

^lLIME: Local Interpretable Model-Agnostic Explanations.

Figure 1. AI-enabled multimodal digital twin framework for personalized cognitive health management in aging populations. AI: artificial intelligence. Created in BioRender [16], licensed under CC BY 4.0 [17].



Perception

Perception involves the continuous acquisition and preprocessing of diverse multimodal data streams to construct a comprehensive and high-resolution representation of an individual's cognitive health status [18,19]. Data sources include physiological signals (eg, electroencephalography [EEG] [20], heart rate variability [HRV], heart rate, brain imaging (functional magnetic resonance imaging or magnetic resonance imaging, and positron emission tomography) [21]; cerebrospinal fluid and blood markers, genetic testing [22], behavioral indicators (eg, gait patterns, speech dynamics, and sleep architecture) [23]; facial expression imaging; and environmental exposures (eg, ambient light and noise) [24], collected via wearable devices, mobile apps, and electronic health records. In parallel, knowledge datasets, such as the Alzheimer's Disease Neuroimaging Initiative [23], UK Biobank [25], peer-reviewed publications, meta-analyses, clinical guidelines, and expert consensus statements, are incorporated to inform normative baselines and support population-level generalizability. All data

undergo standardized preprocessing pipelines to ensure quality, semantic harmonization, and interoperability across downstream analytical processes.

Analytics

Analytics focuses on the extraction of relevant features, detection of subtle cognitive anomalies, and prediction of future cognitive risks based on synthesized multimodal inputs [26]. Advanced ML models are applied, including lightweight convolutional neural networks (CNNs) for image and speech feature extraction [27], long short-term memory (LSTM) networks for modeling sequential physiological data [28], and autoencoders for unsupervised anomaly detection [29]. The analytics engine constructs individualized cognitive trajectories, enabling early identification of deviations from normative baselines and informing timely, proactive intervention planning.

Decision-Making

Decision-making transforms predictive insights into dynamic and personalized intervention strategies [30]. Leveraging a

combination of short-term and long-term reinforcement learning (RL) algorithms [30], Bayesian probability estimation frameworks [31], and causal inference techniques such as propensity score matching [31], the system stratifies cognitive risks, simulates potential intervention outcomes, and generates individualized recommendations. These recommendations may include targeted mind-body exercises, cognitive rehabilitation programs, or behavioral and lifestyle modifications tailored to each individual's evolving cognitive needs [32-36].

Adaptive Feedback

Adaptive feedback closes the learning loop by continuously assimilating new data, recalibrating cognitive state models, and refining intervention strategies based on individual responses over time [37]. Federated learning and incremental learning techniques are incorporated to support dynamic model updates while preserving data privacy and minimizing the need for centralized raw data aggregation [38]. This continuous adaptation mechanism ensures that cognitive care remains responsive, personalized, and aligned with real-world changes in patient health status [39].

To align our functional workflow with the canonical DT architecture, we explicitly map the DT's three structural components: (1) the physical entity, (2) the virtual twin, and (3) the bidirectional communication channel, to the four core processes proposed in this study. Specifically, perception primarily occurs at the physical entity level, where multimodal data are acquired from older adults and their context and undergo initial quality control. Analytics and decision-making are implemented within the virtual twin, which maintains an up-to-date computational representation of an individual's cognitive and health state for inference, prediction, and intervention selection. Adaptive feedback is enabled by the bidirectional channel that securely transmits state updates and model outputs from the virtual twin back to real-world actions.

Technical Architecture of the Personalized Cognitive DT Framework

Overview

To operationalize the AI-driven DT framework for cognitive dysfunction management, we developed a 5-layer technical architecture, encompassing the data layer [40], integration layer [41], modeling layer [42], reasoning layer [43], and application layer [44]. Each layer was designed to perform distinct yet synergistic functions, supporting continuous multimodal monitoring, predictive modeling, individualized intervention optimization, and dynamic adaptation based on real-time feedback (Figure 1).

Data Layer: Integration of Multimodal Data for Cognitive Health Modeling

The Data Layer enables acquisition, aggregation, and secure management of real-time multimodal data and knowledge datasets critical for constructing individualized cognitive health representations [11]. Real-time data streams are continuously captured across physiological, behavioral, and environmental domains [45]. Physiological signals include EEG, HRV, brain

imaging (magnetic resonance imaging, functional magnetic resonance imaging, and positron emission tomography), and heart rate, while behavioral data encompass gait trajectories, speech characteristics, sleep patterns, and facial expression imaging [18]. These data are collected through wearable sensors, IoT devices, and mobile health apps [46].

Brain imaging data, such as hippocampal atrophy, white matter hyperintensities, and resting-state connectivity, provide both structural and functional insights. Cerebrospinal fluid and blood-based biomarkers, including amyloid- β 42 (A β 42), total tau, phosphorylated tau (p-tau181/217), and neurofilament light chain, offer mechanistic specificity. Genetic risk factors, such as the apolipoprotein E epsilon 4 (APOE ϵ 4) genotype, are incorporated to stratify individual risk and inform longitudinal modeling [22]. EEG signals are processed to extract not only conventional event-related potentials but also higher-order complexity metrics, including permutation entropy and spectral entropy, which have demonstrated predictive value for cognitive impairment [47]. HRV features are computed to assess autonomic nervous system function, known to correlate with executive performance and cognitive resilience [48]. Gait variability, a well-established early biomarker of cognitive decline, is monitored using wearable inertial sensors [49]. Speech parameters, including articulation rates, pauses, and prosody, are extracted to detect subtle neurodegenerative changes [50]. Sleep architecture, including sleep efficiency and fragmentation, is captured to evaluate memory consolidation and overall cognitive status [51].

In parallel, knowledge datasets complement real-time acquisitions and include structured outpatient and inpatient electronic health records, large-scale clinical databases such as the Alzheimer's Disease Neuroimaging Initiative and UK Biobank, as well as peer-reviewed publications, meta-analyses, clinical guidelines, and expert consensus statements [50]. All sources are harmonized through standardized frameworks, including the Fast Healthcare Interoperability Resources (FHIR) and the Observational Medical Outcomes Partnership (OMOP) data models [52]. FHIR primarily supports operational interoperability and clinical data exchange, whereas OMOP is commonly used for harmonized observational analytics. A practical workflow is to ingest clinical data via FHIR, transform to OMOP for modeling, and expose DT outputs back to clinical systems through FHIR resources. To ensure analytical readiness, rigorous data quality assurance procedures, including data cleaning, temporal synchronization, and missing value imputation, are applied across modalities [53]. Privacy and security are safeguarded using differential privacy in aggregation workflows, edge computing for local preprocessing of sensitive data, and end-to-end encrypted transmission protocols to protect information exchange across networks [54] (Figure 1). Required sample size depends on modality coverage, label frequency, and model complexity; the framework supports starting with simpler models in smaller cohorts and scaling to higher-capacity models as longitudinal data accumulate.

Integration Layer: Standardization and Fusion of Heterogeneous Cognitive Health Data

The Integration Layer enables the standardization, synchronization, and fusion of heterogeneous multimodal data streams into coherent and interoperable feature representations [55]. Temporal synchronization ensures that physiological, behavioral, and environmental data streams are chronologically aligned, preserving the temporal context critical for dynamic modeling [56]. High-dimensional raw signals undergo feature standardization and extraction to transform them into semantically meaningful embeddings [57]. Data fusion is performed at multiple levels: early fusion strategies integrate features at the input stage; late fusion aggregates predictions from independent models; and hybrid fusion merges intermediate latent features for enhanced robustness [58]. Cross-modal autoencoders are used to compress multimodal inputs while preserving critical cross-domain relationships [59]. Feature concatenation techniques further enable unified feature spaces that retain the unique contributions of each modality [60]. Through these processes, heterogeneous data sources are effectively unified to facilitate downstream predictive analytics (Figure 1). Wearable-derived activity features and computerized digital cognitive biomarkers have each been systematically reviewed as feasible, clinically informative signals in older adults, motivating DT fusion pipelines that align heterogeneous modalities on event time and accommodate irregular observation intervals.

Modeling Layer: Multimodal Predictive Modeling for Personalized Cognitive Trajectories

The modeling layer enables the construction of individualized cognitive profiles and predictive models by synthesizing multimodal information into dynamic risk trajectories [61]. CNNs are deployed to extract spatially localized features from image-like data structures, including EEG topographies, facial expression maps, gait spectrograms, and sleep hypnograms [62]. LSTM networks are used to capture temporal dependencies in physiological time series such as HRV variations and sleep cycle dynamics [63]. Structured tabular data, comprising clinical laboratory results and self-reported cognitive assessments, are analyzed using extreme gradient-boosted trees and support vector machines (SVMs), with SVMs offering advantages for high-dimensional, small-sample settings such as daily cognitive diaries [64]. Multimodal feature fusion is accomplished through cross-modal autoencoders and feature concatenation pipelines, supporting comprehensive cognitive state modeling. Few-shot learning approaches, including Siamese and prototypical networks, facilitate rapid adaptation to novel individuals with minimal labeled data [65]. To address model uncertainty, Monte Carlo Dropout is applied, providing predictive confidence intervals that enhance reliability and support clinician trust [66] (Figure 1).

Reasoning Layer: Intelligent Decision-Making for Cognitive Intervention Optimization

The Reasoning Layer enables the transformation of predictive insights into dynamic, personalized intervention strategies through adaptive and explainable decision-making processes [67]. Short-term RL algorithms are used to dynamically optimize

immediate intervention plans based on real-time DT feedback, while long-term RL models evolve personalized intervention trajectories to maximize cognitive resilience over extended time horizons [68]. Bayesian probability estimation frameworks adjust risk stratification dynamically by incorporating model uncertainty [69]. Causal inference engines, using methods such as propensity score matching, infer the causal effectiveness of different intervention strategies, supporting evidence-based personalization [70]. Anomaly detection modules continuously monitor physiological and behavioral feature streams to identify early warning signs of cognitive decline, prompting timely interventions [71]. To enhance transparency and clinical interpretability, explainable AI techniques, specifically Shapley additive explanations and local interpretable model-agnostic explanations, are integrated to elucidate both global model behavior and individualized risk predictions [72] (Figure 1).

Application Layer: Real-Time Cognitive Health Management Through User-Centered Interfaces

The Application Layer enables the delivery of real-time cognitive health insights and intervention guidance to clinicians and patients through intuitive, user-centered interfaces [73]. For health care providers, the system offers interactive dashboards presenting real-time cognitive risk assessments, predictive trajectories, and personalized intervention recommendations [74]. Simulation tools enable clinicians to explore the potential effects of various intervention strategies on cognitive outcomes [75]. For patients, mobile health apps dynamically deliver customized mind-body exercise programs, including Baduanjin, Tai Chi, and Yoga, along with cognitive rehabilitation modules targeting memory, attention, and executive functioning [32-36,76]. Intelligent lifestyle coaching interventions are personalized to optimize sleep hygiene, dietary habits, physical activity, and psychological resilience [77]. Wearable device interfaces facilitate continuous remote monitoring, deliver anomaly alerts, and track adherence to prescribed interventions, closing the feedback loop between prediction, intervention, and outcome [78]. Through these user-centered interfaces, the DT framework enables dynamic, evidence-informed, and individualized cognitive health management across diverse care settings [79] (Figure 1).

Cloud-Native Infrastructure for Scalable DT Deployment

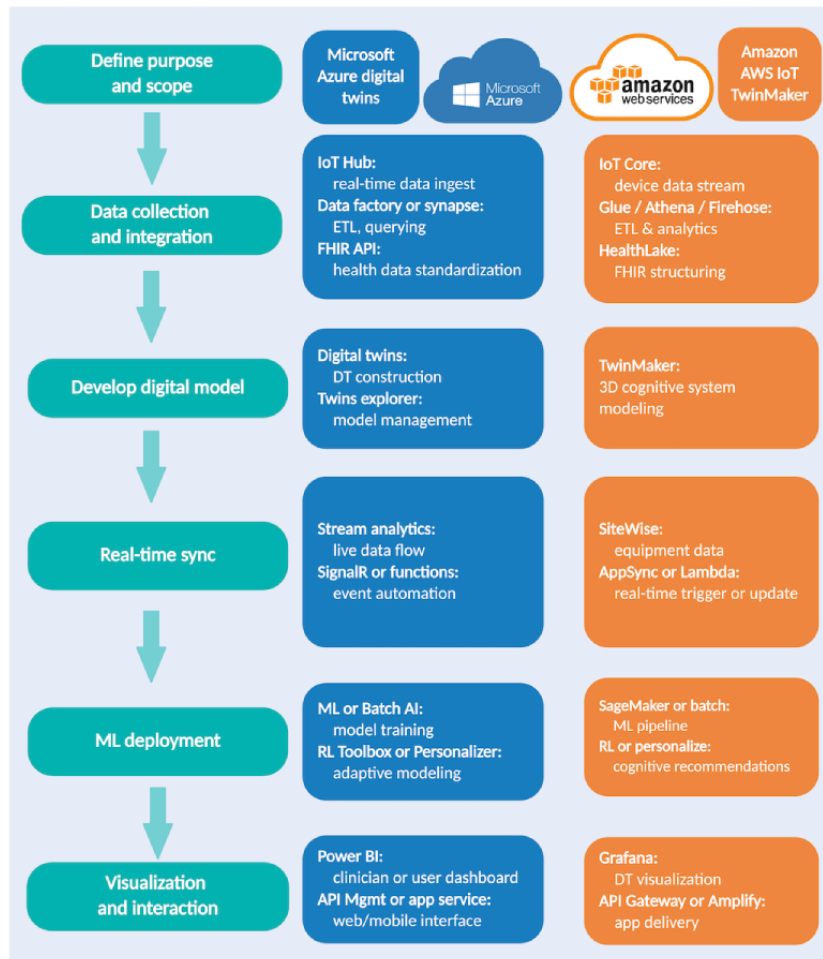
Overview

The Cloud-Native Infrastructure enables scalable, secure, and real-time deployment of cognitive DTs across diverse health care settings by leveraging advanced cloud computing services and architectures [80]. To achieve this, we implemented DT deployments on 2 leading cloud platforms, Amazon Web Services (AWS) and Microsoft Azure, and integrated advanced services to support real-time cognitive simulation and decision-making (Figure 2 [81]). The platform-specific services are provided to make the architecture operationally concrete; the core contribution is the vendor-agnostic design pattern (event-driven orchestration, state management, and closed-loop feedback), which can be implemented on either cloud ecosystem.

Figure 2 [81] outlines the stepwise architecture for digital twin development using cloud-based platforms. Azure and AWS are presented as alternative reference implementations to illustrate platform-to-function mapping, rather than as prescriptive recommendations. There are six modules: defining purpose and scope, data collection and integration, digital model development, real-time data synchronization, machine learning

model deployment, and visualization and interaction. Azure-based services are shown in blue, and AWS-based services are shown in orange. IoT-based device integration is supported by Azure IoT Hub and AWS IoT Core. Real-time analytics are enabled by Azure Stream Analytics and Amazon Kinesis. Interactive dashboards for clinicians and patients are built using Power BI and Amazon Managed Grafana.

Figure 2. Modular Pipeline for Cloud-Based DT Architecture Using Microsoft Azure and Amazon AWS. Created in BioRender [81], licensed under CC BY 4.0 [17]. AWS: Amazon Web Services; BI: business intelligence; DT: digital twin; IoT: Internet of Things; ML: machine learning.



AWS-Based DT Architecture

The AWS-based DT architecture leverages a modular suite of cloud services to support real-time data ingestion, cognitive modeling, and intervention optimization [82]. AWS IoT Core manages secure device connectivity and streaming of physiological and behavioral data [83]. Amazon SageMaker facilitates the training, deployment, and continuous updating of ML models, including CNNs [84], LSTMs [85], and RL agents [86]. AWS Lambda supports event-driven serverless computation, enabling dynamic model updating and real-time anomaly response [87]. Amazon HealthLake structures heterogeneous health data within a FHIR-compatible schema, promoting interoperability across systems [88]. Streaming analytics through Amazon Kinesis enables the continuous monitoring of multimodal data flows and supports immediate recalibration of DT models in response to evolving cognitive states [89] (Figure 2).

Azure-Based DT Architecture

The Azure-based DT architecture provides an integrated environment for real-time cognitive health management through Azure DTs, Azure IoT Hub, Azure Synapse Analytics, and Azure ML [90]. Azure DTs facilitates the construction of dynamic cognitive health graphs, mapping real-time changes in physiological, behavioral, and environmental states [91]. Azure IoT Hub ensures secure, scalable ingestion of real-time sensor and mobile app data. Azure Synapse Analytics consolidates large-scale multimodal datasets, supporting complex queries and feature extraction workflows. Azure ML orchestrates the training, serving, and retraining of cognitive state prediction models [66]. Additionally, Azure Stack Edge enables edge computing at the point of care, ensuring data preprocessing and privacy preservation close to the data source [92] (Figure 2).

Advanced Cloud Services for Real-Time Cognitive Simulation

Both AWS and Azure infrastructures integrate real-time streaming services to enable continuous cognitive state simulation and immediate intervention adjustment [93]. AWS Kinesis Data Streams and Azure Event Hubs provide scalable, low-latency data streaming capabilities essential for updating cognitive models in real time [94]. These services support anomaly detection, dynamic recalibration of RL agents, and deployment of adaptive intervention recommendations without delay [95]. In both environments, comprehensive security frameworks, encompassing encryption at rest and in transit, identity and access management, and audit trails, are enforced to protect patient data integrity [17,96] (Figure 2).

Cloud-Native Compliance Control and Governance

To ensure regulatory alignment and operational transparency, the digital twin architecture can integrate compliance-management tools from AWS and Azure. AWS Security Hub provides a centralized view of security and compliance posture across services and accounts, supporting automated checks against HIPAA-related and other industry standards [97]. On Azure, Microsoft Defender for Cloud offers a unified compliance dashboard that evaluates resources against HIPAA-aligned controls, provides remediation guidance, and supports audit readiness [98]. These governance tools enable

continuous compliance monitoring, reduce audit burden, and help ensure that cognitive-health applications operate within a secure and compliant environment.

Application Scenarios

Early Detection and Real-Time Risk Monitoring in Cognitive Decline

Early recognition of cognitive vulnerability and continuous dynamic monitoring are critical to preventing progression toward overt cognitive impairment [99]. The early detection module proactively identifies individuals at heightened risk by continuously analyzing multimodal physiological and behavioral signals. By detecting deviations from personal baselines before the emergence of clinical symptoms, the system issues timely alerts, enabling clinicians to initiate preventive strategies during the most responsive stages of cognitive decline [100]. The dynamic risk monitoring module ensures real-time surveillance of cognitive status and associated physiological behaviors [101]. Upon detection of significant risk elevation, the system prompts adaptive modifications to cognitive training intensity, exercise prescriptions, or lifestyle interventions, aiming to stabilize cognitive function and prevent crisis events [102]. This integrated approach supports proactive, longitudinal risk management across diverse aging populations (Table 2 and Figure 1).

Table 2. Functional modules of the digital twin framework across application domains.

Application domain, functional module ^a	Core objective
Early detection and continuous risk monitoring	
Early detection module	Identify early signs of cognitive decline through anomaly detection and predictive modeling.
Dynamic risk monitoring module	Continuously track cognitive and physiological indicators in real time to enable proactive interventions.
Personalized intervention and adaptive care optimization	
Mind-body exercise recommendation module	Dynamically recommend personalized mind-body interventions (eg, Baduanjin, Tai Chi, and Yoga) based on real-time assessments.
Cognitive rehabilitation module	Deliver individualized cognitive training programs targeting memory, attention, and executive function.
Lifestyle coaching module	Provide real-time personalized guidance on sleep, nutrition, physical activity, and psychological resilience.
Predictive simulation and value-based cognitive care planning	
Disease progression simulation module	Simulate cognitive disease trajectories under different intervention scenarios to support personalized care planning.
Health economic evaluation module	Evaluate the cost-effectiveness of intervention strategies to support value-based decision-making.

^aThis table summarizes the seven functional modules of the cognitive digital twin framework, grouped by three major application domains. Modules support early risk detection, real-time intervention adaptation, and predictive planning for value-based cognitive care in aging populations.

Personalized Cognitive Intervention and Adaptive Mind-Body Care for Aging Populations

Sustaining cognitive resilience requires interventions that are not only individualized but dynamically adaptable to changing cognitive and physiological states [103]. The Mind-Body Exercise Recommendation Module delivers personalized programs, including Baduanjin, Tai Chi, and Yoga, tailored to the user's real-time cognitive and physical profile [32,34-36]. Engagement, physiological responses, and health trends

continuously inform adjustments to optimize adherence and maximize neuroprotective benefits [104]. The Cognitive Rehabilitation Module offers targeted cognitive training exercises that adapt in difficulty and focus based on ongoing cognitive assessments, aiming to enhance memory, attention, and executive functioning in a progressive, individualized manner [105]. The lifestyle coaching module continuously integrates behavioral data to deliver tailored advice on sleep hygiene, nutritional optimization, physical activity enhancement, and psychological resilience, fostering a holistic approach to

cognitive and emotional well-being [106]. Together, these modules form a closed-loop, adaptive system that continuously refines intervention strategies, ensuring dynamic alignment with individual trajectories over time [107] (Table 2 and Figure 1).

Predictive Trajectory Simulation and Value-Based Planning for Cognitive Disease Management

Beyond day-to-day management, the DT framework empowers strategic cognitive health planning through predictive modeling and economic evaluation [108]. The Disease Progression Simulation Module enables users and clinicians to visualize projected cognitive trajectories, particularly transitions from MCI to dementia, under alternative intervention strategies, facilitating personalized, evidence-driven decision-making [109]. The Health Economic Evaluation Module assesses the cost-effectiveness of different cognitive health pathways, generating metrics such as incremental cost-effectiveness ratios and quality-adjusted life years [110]. These evaluations support health care providers and policymakers in prioritizing interventions that maximize clinical benefit while ensuring sustainable resource use [111] (Table 2 and Figure 1).

Ethical Considerations

The continuous cognitive and emotional monitoring enabled by DTs raises profound ethical and privacy challenges [112]. While technical safeguards such as differential privacy, encrypted local processing, and decentralized federated learning are embedded within the framework, true ethical assurance demands more than technical compliance [113]. Transparent, dynamic consent models must be established, empowering individuals to control the collection, use, and sharing of their cognitive data over time [114]. Algorithmic fairness audits and explainability measures must be incorporated to ensure that adaptive decision-making processes are understandable and trustworthy [115]. Furthermore, equitable access to cognitive DT technologies must be proactively designed [116]. Without deliberate attention to cultural sensitivity, digital literacy support, and accessibility accommodations, there is a significant risk that new disparities could emerge, disproportionately affecting marginalized or cognitively vulnerable populations [112]. Ensuring that the benefits of cognitive DTs are widely distributed remains a critical imperative.

Discussion

Principal Findings

This study proposes a conceptual AI-driven DT framework that integrates continuous multimodal data acquisition, predictive cognitive modeling, dynamic intervention optimization, and real-time adaptive feedback within a scalable cloud-native architecture. Structured across five synergistic layers, data acquisition, integration, modeling, reasoning, and application, the framework addresses major gaps in early cognitive risk detection, longitudinal surveillance, and individualized intervention in aging populations. Although currently conceptual, this architecture lays a technical and clinical foundation for transitioning cognitive health care from reactive, episodic models to proactive, precision-driven management,

positioning cognitive DTs as a transformative modality in future health care ecosystems.

Aging, Cognitive Health, and the Need for Innovation

The accelerating demographic shift toward aging societies underscores the urgent need for innovation in cognitive health care [117]. MCI and dementia represent leading contributors to disability and dependency among older adults, yet conventional health care models, often reactive and episodic, fail to address the heterogeneous progression and early warning signals of cognitive decline [118]. Fragmented service delivery, limited access to specialized care, and escalating health care costs further exacerbate these challenges [119]. Current interventions rarely incorporate continuous monitoring or real-time personalization, leading to missed opportunities for early intervention and prevention [120]. Emerging technologies such as AI, ML, and DT systems offer transformative opportunities to shift cognitive health care toward dynamic, individualized, and evidence-informed models [121]. By embedding real-time multimodal sensing, predictive analytics, and adaptive decision-making into a continuously evolving DT, our framework aspires to enable proactive cognitive health management at scale [122].

Transformative Potential of DTs in Cognitive Health and Remote Monitoring

The proposed framework advances the field by introducing several critical innovations. Multimodal data, including EEG, HRV, gait patterns, speech features, sleep architecture, and environmental exposures, are continuously captured through wearable sensors, IoT devices, and mobile apps [123]. These diverse signals are harmonized using FHIR and OMOP standards and integrated through sophisticated cross-modal autoencoders and feature concatenation pipelines, creating unified cognitive state representations [124]. Predictive models incorporate CNNs for spatial feature extraction, LSTM networks for temporal dynamics, and extreme gradient-boosted trees and SVMs for structured clinical data analysis [125]. Dynamic decision-making is achieved via short-term and long-term RL algorithms, enabling immediate adaptation and long-term trajectory optimization [126]. Uncertainty estimation and causal inference modeling further support clinical interpretability and evidence-based intervention planning [127].

Importantly, the system extends the concept of remote patient monitoring beyond traditional vital sign tracking [80]. By capturing dynamic cognitive and behavioral indicators in real-time, the DT continuously assesses cognitive resilience, predicts risk elevations, and recommends personalized adaptive interventions [122]. Cloud-native deployment leveraging federated learning and edge computing ensures that the framework is scalable, privacy-preserving, and responsive across diverse health care settings [128]. Collectively, these advances position cognitive DTs as a next-generation platform for remote monitoring, predictive simulation, and personalized cognitive health optimization [121].

Technical and Practical Challenges

While the conceptual architecture is robust, substantial technical barriers must be addressed for clinical translation. Seamless

multimodal data integration remains challenging, particularly given the asynchronous, noisy, and incomplete nature of real-world data [129]. Variability in device quality, user adherence, and environmental conditions introduces further complexity [80]. Real-time model updating through RL demands computational efficiency, low latency, and scalability across distributed cloud-edge infrastructures, requirements that are not yet fully met by existing health care AI pipelines [130]. Developing lightweight, resource-efficient online learning algorithms capable of dynamic personalization without compromising predictive accuracy will be essential [129]. Additionally, ensuring economic sustainability for continuous cognitive monitoring systems will require careful optimization of data synchronization intervals, computational resource allocation, and infrastructure costs. Real-world deployment in older adults is further constrained by systematic missingness and representativeness gaps and by methodological limits under highly heterogeneous (non-IID) data that motivate personalized federated learning in low-label longitudinal settings.

Limitations of the Present Framework

Several limitations should be noted. First, this work presents a conceptual and architectural framework, and it has not yet been tested in clinical trials or real-world deployment. As a result, its predictive performance, clinical usefulness, user engagement, and feasibility still need to be established. The models mentioned here, such as CNN, LSTM, and SVM, are included as examples rather than as definitive solutions. In reality, data collected in aging research and care are often messy and complicated, with irregular follow-up, missing values, multimorbidity, and multiple data types. Addressing these challenges will likely require more specialized modeling approaches than those briefly described here.

There are also important technical issues that remain unresolved, including how best to combine asynchronous multimodal data, handle missingness, and optimize RL strategies under real-world conditions. Interpretability will be equally important, and tools such as Shapley additive explanations and local interpretable model-agnostic explanations may need to be applied more

thoughtfully across the full modeling pipeline. In addition, the framework still needs to be tested across populations with different cognitive baselines, medical comorbidities, socioeconomic circumstances, and cultural backgrounds. Finally, although the current framework focuses on mind-body practices, cognitive rehabilitation, and lifestyle support, a more complete digital twin for cognitive care will likely need to incorporate broader treatment domains, including pharmacological and psychosocial interventions. Together, these limitations do not diminish the value of the framework, but instead point to the key areas that future work should address.

Future Directions

Looking ahead, future work should focus on building and testing cognitive digital twin systems step by step. This includes usability testing in diverse older adult populations, as well as longitudinal studies to determine whether these models can meaningfully predict outcomes and support adaptive interventions in real-world settings. Further technical development will also be needed to handle noisy, incomplete, and multimodal data while maintaining interpretability and efficiency.

Just as importantly, future research should address ethical and governance issues, including consent, privacy, fairness, and participant involvement in data use. Over time, it may also be valuable to expand cognitive digital twins beyond cognitive decline alone to include emotional well-being, frailty, multimorbidity, and social factors that shape aging and health.

Conclusions

In this study, we present a conceptual AI-driven, multimodal digital twin framework for precision cognitive care in aging populations. By supporting continuous monitoring, early risk detection, personalized intervention, and adaptive learning, the framework offers a proactive and patient-centered approach to cognitive health. Although empirical validation and further technical development are still needed, this work provides a useful foundation for future efforts to make cognitive care more personalized, responsive, and sustainable.

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Data Availability

This study is conceptual in nature and does not report or analyze any datasets. As no new data were generated, data sharing is not applicable.

Authors' Contributions

YL and KY conceptualized the study, designed the digital twin architecture, and drafted the manuscript. SM contributed to the cloud infrastructure architecture and interoperability strategy. HD provided clinical integration perspectives and critical revision. JK supervised the overall project, guided the clinical design, and revised the manuscript for important intellectual content. All authors reviewed and approved the final manuscript.

Conflicts of Interest

JK reports equity ownership in startup companies MNT and BTT, involvement in a granted patent related to ear vagus nerve stimulation (US 2018/0339148), and involvement in a pending patent. SM is employed by Microsoft. Microsoft had no role in

the study design, analysis, interpretation, manuscript preparation, funding, or material support. The other authors declare no competing interests.

References

1. World report on ageing and health. World Health Organization. 2015. URL: <https://www.who.int/publications/i/item/9789241565042> [accessed 2023-04-09]
2. Aliberti MJR, Avelino-Silva TJ, Suemoto CK. Maximizing early dementia detection through medicare annual wellness visits. *JAMA Netw Open*. 2024;7(10):e2437162. [FREE Full text] [doi: [10.1001/jamanetworkopen.2024.37162](https://doi.org/10.1001/jamanetworkopen.2024.37162)] [Medline: [39378039](https://pubmed.ncbi.nlm.nih.gov/39378039/)]
3. Marais L, Grootoank S, Leroi I, Hall J, Hill DL. TD - P - 016: Feasibility of real world continuous data collection from patients with cognitive impairment and their caregivers. *Alzheimer's & Dementia*. 2016;12(7S_Part_3). [doi: [10.1016/j.jalz.2016.06.262](https://doi.org/10.1016/j.jalz.2016.06.262)]
4. Ahmadzadeh M, Cosco TD, Best JR, Christie GJ, DiPaola S. Predictors of the rate of cognitive decline in older adults using machine learning. *PLoS One*. 2023;18(3):e0280029. [FREE Full text] [doi: [10.1371/journal.pone.0280029](https://doi.org/10.1371/journal.pone.0280029)] [Medline: [36867596](https://pubmed.ncbi.nlm.nih.gov/36867596/)]
5. Kale M, Wankhede N, Pawar R, et al. AI-driven innovations in alzheimer's disease: integrating early diagnosis, personalized treatment, and prognostic modelling. *Ageing Res Rev*. 2024;101:102497. [doi: [10.1016/j.arr.2024.102497](https://doi.org/10.1016/j.arr.2024.102497)] [Medline: [39293530](https://pubmed.ncbi.nlm.nih.gov/39293530/)]
6. Veneziani I, Grimaldi A, Marra A, et al. Towards a deeper understanding: utilizing machine learning to investigate the association between obesity and cognitive decline-a systematic review. *J Clin Med*. 2024;13(8):2307. [FREE Full text] [doi: [10.3390/jcm13082307](https://doi.org/10.3390/jcm13082307)] [Medline: [38673581](https://pubmed.ncbi.nlm.nih.gov/38673581/)]
7. Alimour SA, Alrabeei MA. A novel model for digital twins in mental health: the biopsychosocial AI-driven digital twin (BADT) framework. 2024. Presented at: 11th International Conference on Software Defined Systems (SDS); December 09-11, 2024:6-10; Gran Canaria, Spain. [doi: [10.1109/sds64317.2024.10883917](https://doi.org/10.1109/sds64317.2024.10883917)]
8. Vallée A. Digital twin for healthcare systems. *Front Digit Health*. 2023;5:1253050. [FREE Full text] [doi: [10.3389/fdgh.2023.1253050](https://doi.org/10.3389/fdgh.2023.1253050)] [Medline: [37744683](https://pubmed.ncbi.nlm.nih.gov/37744683/)]
9. Mulder ST, Omidvari A, Rueten-Budde AJ, et al. Dynamic digital twin: diagnosis, treatment, prediction, and prevention of disease during the life course. *J Med Internet Res*. 2022;24(9):e35675. [FREE Full text] [doi: [10.2196/35675](https://doi.org/10.2196/35675)] [Medline: [36103220](https://pubmed.ncbi.nlm.nih.gov/36103220/)]
10. Sarani Rad F, Hendawi R, Yang X, Li J. Personalized diabetes management with digital twins: a patient-centric knowledge graph approach. *J Pers Med*. 2024;14(4):359. [FREE Full text] [doi: [10.3390/jpm14040359](https://doi.org/10.3390/jpm14040359)] [Medline: [38672986](https://pubmed.ncbi.nlm.nih.gov/38672986/)]
11. Venkatesh KP, Raza MM, Kvedar JC. Health digital twins as tools for precision medicine: considerations for computation, implementation, and regulation. *NPJ Digit Med*. 2022;5(1):150. [FREE Full text] [doi: [10.1038/s41746-022-00694-7](https://doi.org/10.1038/s41746-022-00694-7)] [Medline: [36138125](https://pubmed.ncbi.nlm.nih.gov/36138125/)]
12. Xie H, Tan S, Ling F, et al. Digital twin enabled dual-system reinforcement learning method. 2022. Presented at: Proceedings of the 2022 IEEE Smartworld, Ubiquitous Intelligence & Computing, Scalable Computing & Communications, Digital Twin, Privacy Computing, Metaverse, Autonomous & Trusted Vehicles (SmartWorld/UIC/ScalCom/DigitalTwin/PriComp/Meta) 2218-2223 (2022); December 15-18, 2022; Haikou, China. URL: <https://ieeexplore.ieee.org/document/10189650> [doi: [10.1109/smartworld/uic/scalc56740.2022](https://doi.org/10.1109/smartworld/uic/scalc56740.2022)]
13. Gupta R, Dhasmana G, Lalitha T, Appalakonda V, Thacker C. AI-based cognitive twin models for software-defined IoT security and analytics. *IEEE*; 2024. Presented at: Proceedings of the 4th International Conference on Mobile Networks and Wireless Communications (ICMNWC); December 04-05, 2024; Tumkuru, India. URL: <https://ieeexplore.ieee.org/document/10872194> [doi: [10.1109/icmnwc63764.2024.10872194](https://doi.org/10.1109/icmnwc63764.2024.10872194)]
14. Rahimi SA, Baradaran A, Khameneifar F, Gore G, Issa AM. DECIDE-Twin: a framework for AI-enabled digital twins in clinical decision-making. *IEEE J Biomed Health Inform*. 2025;29(9):6332-6341. [doi: [10.1109/JBHI.2024.3521717](https://doi.org/10.1109/JBHI.2024.3521717)] [Medline: [40030650](https://pubmed.ncbi.nlm.nih.gov/40030650/)]
15. Pirbhulal S, Chockalingam S, Abie H, Lau H. Cognitive digital twins for improving security in IT-OT enabled healthcare applications. 2024. Presented at: Proceedings of the 6th International Conference, HCI-CPT 2024, Held as Part of the 26th HCI International Conference, HCII; June 29–July 4, 2024:153-163; Washington, DC, USA. [doi: [10.1007/978-3-031-61382-1_10](https://doi.org/10.1007/978-3-031-61382-1_10)]
16. Liu Y. AI-enabled multimodal digital twin framework for personalized cognitive health management in aging population. *BioRender*. 2026. URL: <https://BioRender.com/xtefd4f> [accessed 2026-06-22]
17. Attribution 4.0 International (CC BY 4.0). Creative Commons. URL: <https://creativecommons.org/licenses/by/4.0/> [accessed 2026-06-22]
18. Mo Y, Ma S, Gong H, et al. Terra: a smart and sensible digital twin framework for robust robot deployment in challenging environments. *IEEE Internet Things J*. 2021;8(18):14039-14050. [doi: [10.1109/jiot.2021.3068736](https://doi.org/10.1109/jiot.2021.3068736)]
19. El Mokhtari K, Panushev I, McArthur JJ. Development of a cognitive digital twin for building management and operations. *Front Built Environ*. 2022;8:856873. [doi: [10.3389/fbuil.2022.856873](https://doi.org/10.3389/fbuil.2022.856873)]

20. Khatun S, Morshed BI, Bidelman GM. A single-channel EEG-based approach to detect mild cognitive impairment via speech-evoked brain responses. *IEEE Trans Neural Syst Rehabil Eng.* 2019;27(5):1063-1070. [FREE Full text] [doi: [10.1109/TNSRE.2019.2911970](https://doi.org/10.1109/TNSRE.2019.2911970)] [Medline: [30998476](https://pubmed.ncbi.nlm.nih.gov/30998476/)]
21. Ahn JW, Ku Y, Kim HC. A novel wearable EEG and ECG recording system for stress assessment. *Sensors (Basel).* 2019;19(9):1991. [FREE Full text] [doi: [10.3390/s19091991](https://doi.org/10.3390/s19091991)] [Medline: [31035399](https://pubmed.ncbi.nlm.nih.gov/31035399/)]
22. Alzheimer's Association. 2025 Alzheimer's disease facts and figures. *Alzheimer's & Dementia.* 2025;21. [doi: [10.1097/00002093-199601010-00011](https://doi.org/10.1097/00002093-199601010-00011)]
23. Chauvin A, Baum S, Phillips NA. Individuals with mild cognitive impairment and Alzheimer's disease benefit from audiovisual speech cues and supportive sentence context. *J Speech Lang Hear Res.* 2021;64(5):1550-1559. [doi: [10.1044/2021_JSLHR-20-00402](https://doi.org/10.1044/2021_JSLHR-20-00402)] [Medline: [33861623](https://pubmed.ncbi.nlm.nih.gov/33861623/)]
24. Ogurtsova K, Soppa VJ, Weimar C, et al. Association of long-term air pollution and ambient noise with cognitive decline in the Heinz Nixdorf recall study. *Environ Pollut.* 2023;331(Pt 1):121898. [FREE Full text] [doi: [10.1016/j.envpol.2023.121898](https://doi.org/10.1016/j.envpol.2023.121898)] [Medline: [37244536](https://pubmed.ncbi.nlm.nih.gov/37244536/)]
25. Gadewar S, Zhu AH, Somu S, Ramesh A, Gari GB. Normative aging for an individual's full brain MRI using style GANs to detect localized neurodegeneration. 2023. Presented at: Proceedings of the International Workshop on Machine Learning in Medical Imaging; October 8, 2023:387-397; Vancouver, BC, Canada. [doi: [10.1007/978-3-031-45676-3_39](https://doi.org/10.1007/978-3-031-45676-3_39)]
26. Tam A, Dansereau C, Iturria-Medina Y, et al. A highly predictive signature of cognition and brain atrophy for progression to Alzheimer's dementia. *Gigascience.* May 01, 2019;8(5). [FREE Full text] [doi: [10.1093/gigascience/giz055](https://doi.org/10.1093/gigascience/giz055)] [Medline: [31077314](https://pubmed.ncbi.nlm.nih.gov/31077314/)]
27. Wubet YA, Lian KY. Voice conversion based augmentation and a hybrid CNN-LSTM model for improving speaker-independent keyword recognition on limited datasets. *IEEE Access.* 2022;10:89170-89180. [doi: [10.1109/access.2022.3200479](https://doi.org/10.1109/access.2022.3200479)]
28. Wang K, Chen Y, Bo D, Wang S. A novel multi-user collaborative cognitive radio spectrum sensing model: based on a CNN-LSTM model. *PLoS One.* 2025;20(1):e0316291. [FREE Full text] [doi: [10.1371/journal.pone.0316291](https://doi.org/10.1371/journal.pone.0316291)] [Medline: [39813223](https://pubmed.ncbi.nlm.nih.gov/39813223/)]
29. Coelho G, Matos LM, Pereira PJ, et al. Deep autoencoders for acoustic anomaly detection: experiments with working machine and in-vehicle audio. *Neural Comput & Applic.* 2022;34(22):19485-19499. [doi: [10.1007/s00521-022-07375-2](https://doi.org/10.1007/s00521-022-07375-2)]
30. Datta S, Li Y, Ruppert MM, et al. Reinforcement learning in surgery. *Surgery (United States).* 2021;170(1):329-332. [FREE Full text] [doi: [10.1016/j.surg.2020.11.040](https://doi.org/10.1016/j.surg.2020.11.040)] [Medline: [33436272](https://pubmed.ncbi.nlm.nih.gov/33436272/)]
31. Li L, Donnell ET. Incorporating Bayesian methods into the propensity score matching framework: a no-treatment effect safety analysis. *Accid Anal Prev.* 2020;145:105691. [doi: [10.1016/j.aap.2020.105691](https://doi.org/10.1016/j.aap.2020.105691)] [Medline: [32711214](https://pubmed.ncbi.nlm.nih.gov/32711214/)]
32. Tao J, Liu J, Chen X, et al. Mind-body exercise improves cognitive function and modulates the function and structure of the hippocampus and anterior cingulate cortex in patients with mild cognitive impairment. *Neuroimage Clin.* 2019;23:101834. [FREE Full text] [doi: [10.1016/j.nicl.2019.101834](https://doi.org/10.1016/j.nicl.2019.101834)] [Medline: [31128522](https://pubmed.ncbi.nlm.nih.gov/31128522/)]
33. Wells R, Yeh GY, Kerr CE, et al. Meditation's impact on default mode network and hippocampus in mild cognitive impairment: a pilot study. *Neurosci Lett.* Nov 27, 2013;556:15-19. [FREE Full text] [doi: [10.1016/j.neulet.2013.10.001](https://doi.org/10.1016/j.neulet.2013.10.001)] [Medline: [24120430](https://pubmed.ncbi.nlm.nih.gov/24120430/)]
34. Liu J, Tao J, Liu W, et al. Different modulation effects of tai chi chuan and baduanjin on resting-state functional connectivity of the default mode network in older adults. *Soc Cogn Affect Neurosci.* 2019;14(2):217-224. [FREE Full text] [doi: [10.1093/scan/nsz001](https://doi.org/10.1093/scan/nsz001)] [Medline: [30690554](https://pubmed.ncbi.nlm.nih.gov/30690554/)]
35. Tao J, Chen X, Egorova N, et al. Tai chi chuan and baduanjin practice modulates functional connectivity of the cognitive control network in older adults. *Sci Rep.* 2017;7:41581. [FREE Full text] [doi: [10.1038/srep41581](https://doi.org/10.1038/srep41581)] [Medline: [28169310](https://pubmed.ncbi.nlm.nih.gov/28169310/)]
36. Tao J, Liu J, Egorova N, et al. Increased hippocampus-medial prefrontal cortex resting-state functional connectivity and memory function after tai chi chuan practice in elder adults. *Front Aging Neurosci.* 2016;8:25. [FREE Full text] [doi: [10.3389/fnagi.2016.00025](https://doi.org/10.3389/fnagi.2016.00025)] [Medline: [26909038](https://pubmed.ncbi.nlm.nih.gov/26909038/)]
37. Gu Y, Li S, Qi J, et al. A cognitive digital twin approach to improving driver compliance and accident prevention. *Accid Anal Prev.* 2025;211:107913. [doi: [10.1016/j.aap.2024.107913](https://doi.org/10.1016/j.aap.2024.107913)] [Medline: [39778287](https://pubmed.ncbi.nlm.nih.gov/39778287/)]
38. Ramu SP, Boopalan P, Pham Q, et al. Federated learning enabled digital twins for smart cities: concepts, recent advances, and future directions. *Sustainable Cities and Society.* 2022;79:103663. [doi: [10.1016/j.scs.2021.103663](https://doi.org/10.1016/j.scs.2021.103663)]
39. Qu Z, Li Y, Liu B, Gupta D, Tiwari P. DTQFL: a digital twin-assisted quantum federated learning algorithm for intelligent diagnosis in 5g mobile network. *IEEE J Biomed Health Inform.* 2026;30(1):17-26. [doi: [10.1109/JBHI.2023.3303401](https://doi.org/10.1109/JBHI.2023.3303401)] [Medline: [37552590](https://pubmed.ncbi.nlm.nih.gov/37552590/)]
40. Ren Z, Shi J, Imran M. Data evolution governance for ontology-based digital twin product lifecycle management. *IEEE Trans Ind Inf.* 2023;19(2):1791-1802. [doi: [10.1109/tii.2022.3187715](https://doi.org/10.1109/tii.2022.3187715)]
41. Padovano A, Sammarco C, Balakera N, Konstantinidis F. Towards sustainable cognitive digital twins: a portfolio management tool for waste mitigation. *Computers & Industrial Engineering.* 2024;198:110715. [doi: [10.1016/j.cie.2024.110715](https://doi.org/10.1016/j.cie.2024.110715)]
42. Zheng X, Lu J, Kiritsis D. The emergence of cognitive digital twin: vision, challenges and opportunities. *International Journal of Production Research.* 2021;60(24):7610-7632. [doi: [10.1080/00207543.2021.2014591](https://doi.org/10.1080/00207543.2021.2014591)]

43. D'Amico RD, Sarkar A, Karray MH, Addepalli S, Erkoyuncu JA. Knowledge transfer in digital twins: the methodology to develop cognitive digital twins. *CIRP Journal of Manufacturing Science and Technology*. 2024;52:366-385. [doi: [10.1016/j.cirpj.2024.06.007](https://doi.org/10.1016/j.cirpj.2024.06.007)]
44. Alimam H, Mazzuto G, Tozzi N, Emanuele Ciarapica F, Bevilacqua M. The resurrection of digital triplet: a cognitive pillar of human-machine integration at the dawn of industry 5.0. *Journal of King Saud University - Computer and Information Sciences*. Dec 2023;35(10):101846. [doi: [10.1016/j.jksuci.2023.101846](https://doi.org/10.1016/j.jksuci.2023.101846)]
45. D'Amico S, Sauta E, Asti G, Delleani M. A comprehensive, artificial intelligence, digital twin platform based on multimodal real-world data integration for personalized medicine in hematology. *Blood*. 2024;144:2221-2221. [doi: [10.1182/blood-2024-209634](https://doi.org/10.1182/blood-2024-209634)]
46. Shui X, Xu H, Tan S, Zhang D. Depression recognition using daily wearable-derived physiological data. *Sensors (Basel)*. 2025;25(2):567. [FREE Full text] [doi: [10.3390/s25020567](https://doi.org/10.3390/s25020567)] [Medline: [39860935](https://pubmed.ncbi.nlm.nih.gov/39860935/)]
47. Gong Z, Ji J, Tong P, et al. Smart urban planning: intelligent cognitive analysis of healthcare data in cloud-based IoT. *Computers and Electrical Engineering*. 2023;110:108878. [doi: [10.1016/j.compeleceng.2023.108878](https://doi.org/10.1016/j.compeleceng.2023.108878)]
48. Moon E, Sharifuzzaman Sagar ASM, Kim HS. Multimodal daily-life emotional recognition using heart rate and speech data from wearables. *IEEE Access*. 2024;12:96635-96648. [doi: [10.1109/access.2024.3427111](https://doi.org/10.1109/access.2024.3427111)]
49. Poor FF, Dodge HH, Mahoor MH. A multimodal cross-transformer-based model to predict mild cognitive impairment using speech, language and vision. *Comput Biol Med*. 2024;182:109199. [doi: [10.1016/j.combiomed.2024.109199](https://doi.org/10.1016/j.combiomed.2024.109199)] [Medline: [39332117](https://pubmed.ncbi.nlm.nih.gov/39332117/)]
50. Campbell LM, Delgadillo JD, Paolillo EW, et al. TD - P - 01: mobile monitoring of cognition in middle - aged and older adults with and without amnesic mild cognitive impairment: Implications for alzheimer's disease clinical trials. *Alzheimer's & Dementia*. 2019;15(7S_Part_3):P153-P154. [doi: [10.1016/j.jalz.2019.06.4312](https://doi.org/10.1016/j.jalz.2019.06.4312)]
51. Champetier P, André C, Rehel S, et al. Multimodal neuroimaging correlates of spectral power in NREM sleep delta sub-bands in cognitively unimpaired older adults. *Sleep*. 2024;47(4):zsae012. [FREE Full text] [doi: [10.1093/sleep/zsae012](https://doi.org/10.1093/sleep/zsae012)] [Medline: [38227830](https://pubmed.ncbi.nlm.nih.gov/38227830/)]
52. Mateus P, Moonen J, Beran M, et al. Data harmonization and federated learning for multi-cohort dementia research using the OMOP common data model: a Netherlands consortium of dementia cohorts case study. *J Biomed Inform*. 2024;155:104661. [FREE Full text] [doi: [10.1016/j.jbi.2024.104661](https://doi.org/10.1016/j.jbi.2024.104661)] [Medline: [38806105](https://pubmed.ncbi.nlm.nih.gov/38806105/)]
53. Jin H, Chien S, Meijer E, Khobragade P, Lee J. Learning from clinical consensus diagnosis in india to facilitate automatic classification of dementia: machine learning study. *JMIR Ment Health*. 2021;8(5):e27113. [FREE Full text] [doi: [10.2196/27113](https://doi.org/10.2196/27113)] [Medline: [33970122](https://pubmed.ncbi.nlm.nih.gov/33970122/)]
54. Lyu M, Ni Z, Chen Q, Li F. Edge-DPSDG: an edge-based differential privacy protection model for smart healthcare. *IEEE Trans Big Data*. 2025;11(1):21-34. [doi: [10.1109/tbdata.2024.3366071](https://doi.org/10.1109/tbdata.2024.3366071)]
55. Xu X, Tu W, Yang Y. Efficient audio-visual information fusion using encoding pace synchronization for audio-visual speech separation. *Information Fusion*. 2025;115:102749. [doi: [10.1016/j.inffus.2024.102749](https://doi.org/10.1016/j.inffus.2024.102749)]
56. Aminosharieh Najafi T, Affanni A, Rinaldo R, Zontone P. Drivers' mental engagement analysis using multi-sensor fusion approaches based on deep convolutional neural networks. *Sensors (Basel)*. 2023;23(17):7346. [FREE Full text] [doi: [10.3390/s23177346](https://doi.org/10.3390/s23177346)] [Medline: [37687801](https://pubmed.ncbi.nlm.nih.gov/37687801/)]
57. Huang S, Wu X, Yang Y, Wan W, Wang X. A dual-encoder network based on multi-layer feature fusion for infrared and visible image fusion. *Int J Mach Learn & Cyber*. 2024;15(10):4511-4520. [doi: [10.1007/s13042-024-02162-y](https://doi.org/10.1007/s13042-024-02162-y)]
58. Susan S, Malhotra J. Learning image by-parts using early and late fusion of auto-encoder features. *Multimed Tools Appl*. Jul 03, 2021;80(19):29601-29615. [doi: [10.1007/s11042-021-11092-8](https://doi.org/10.1007/s11042-021-11092-8)]
59. Zhang M, Cui Q, Lü Y, Li W. A feature-aware multimodal framework with auto-fusion for Alzheimer's disease diagnosis. *Comput Biol Med*. 2024;178:108740. [doi: [10.1016/j.combiomed.2024.108740](https://doi.org/10.1016/j.combiomed.2024.108740)] [Medline: [38901184](https://pubmed.ncbi.nlm.nih.gov/38901184/)]
60. Liu S, Peng W, Liu Y, et al. AFCANet: an adaptive feature concatenate attention network for multi-focus image fusion. *Journal of King Saud University - Computer and Information Sciences*. 2023;35(9):101751. [doi: [10.1016/j.jksuci.2023.101751](https://doi.org/10.1016/j.jksuci.2023.101751)]
61. Atitallah SB, Driss M, Boulila W, Koubaa A. Enhancing early Alzheimer's disease detection through big data and ensemble few-shot learning. *IEEE J Biomed Health Inform*. 2025;29(9):6451-6462. [doi: [10.1109/JBHI.2024.3473541](https://doi.org/10.1109/JBHI.2024.3473541)] [Medline: [39356607](https://pubmed.ncbi.nlm.nih.gov/39356607/)]
62. Khan MS, Salsabil N, Alam MGR, Dewan MAA, Uddin MZ. CNN-XGBoost fusion-based affective state recognition using EEG spectrogram image analysis. *Sci Rep*. 2022;12(1):14122. [FREE Full text] [doi: [10.1038/s41598-022-18257-x](https://doi.org/10.1038/s41598-022-18257-x)] [Medline: [35986065](https://pubmed.ncbi.nlm.nih.gov/35986065/)]
63. Niu K, Lu G, Peng X, Zhou Y, Zeng J, Zhang K. CNN autoencoders and LSTM-based reduced order model for student dropout prediction. *Neural Comput & Applic*. 2023;35(30):22341-22357. [doi: [10.1007/s00521-023-08894-2](https://doi.org/10.1007/s00521-023-08894-2)]
64. Taparhudee W, Jongjaraunsuk R, Nimitkul S, Suwannasing P, Mathurossuwan W. Optimizing convolutional neural networks, XGBoost, and hybrid CNN-XGBoost for precise red tilapia (*Oreochromis niloticus* linn.) weight estimation in river cage culture with aerial imagery. *AgriEngineering*. 2024;6(2):1235-1251. [doi: [10.3390/agriengineering6020070](https://doi.org/10.3390/agriengineering6020070)]

65. Feng K, Chaspari T, Chaspari T. Few-shot learning in emotion recognition of spontaneous speech using a siamese neural network with adaptive sample pair formation. *IEEE Trans Affective Comput.* Apr 1, 2023;14(2):1627-1633. [doi: [10.1109/taffc.2021.3109485](https://doi.org/10.1109/taffc.2021.3109485)]
66. Wu Y, Cao H, Lai Y, Zhao L, Deng X, Wan S. Edge computing and few-shot learning featured intelligent framework in digital twin empowered mobile networks. *IEEE Trans Netw Serv Manage.* 2024;21(6):6505-6514. [doi: [10.1109/tns.2024.3450993](https://doi.org/10.1109/tns.2024.3450993)]
67. Valverde G, Quesada D, Larrañaga P, Bielza C. Causal reinforcement learning based on Bayesian networks applied to industrial settings. *Engineering Applications of Artificial Intelligence.* 2023;125:106657. [doi: [10.1016/j.engappai.2023.106657](https://doi.org/10.1016/j.engappai.2023.106657)]
68. Park H, Sim MK, Choi DG. Twin-system recurrent reinforcement learning for optimizing portfolio strategy. *Expert Systems with Applications.* 2024;253:124193. [doi: [10.1016/j.eswa.2024.124193](https://doi.org/10.1016/j.eswa.2024.124193)]
69. Ruah C, Simeone O, Al-Hashimi BM. A Bayesian framework for digital twin-based control, monitoring, and data collection in wireless systems. *IEEE J Select Areas Commun.* 2023;41(10):3146-3160. [doi: [10.1109/jsac.2023.3310093](https://doi.org/10.1109/jsac.2023.3310093)]
70. Méndez-Molina A, Morales EF, Sucar LE. CARL: a synergistic framework for causal reinforcement learning. *IEEE Access.* 2023;11:126462-126481. [doi: [10.1109/access.2023.3331728](https://doi.org/10.1109/access.2023.3331728)]
71. Raz AK, Mall K, Nolan SM, et al. Explainable AI and robustness-based test and evaluation of reinforcement learning. *IEEE Trans Aerosp Electron Syst.* 2024;60(5):6110-6123. [doi: [10.1109/TAES.2024.3403078](https://doi.org/10.1109/TAES.2024.3403078)]
72. Ahmed S, Kaiser MS, Shahadat Hossain M, Andersson K. A comparative analysis of LIME and SHAP interpreters with explainable ML-based diabetes predictions. *IEEE Access.* 2025;13:37370-37388. [doi: [10.1109/access.2024.3422319](https://doi.org/10.1109/access.2024.3422319)]
73. Adibi S, Rajabifard A, Shojaei D, Wickramasinghe N. Enhancing healthcare through sensor-enabled digital twins in smart environments: a comprehensive analysis. *Sensors (Basel).* 2024;24(9):2793. [FREE Full text] [doi: [10.3390/s24092793](https://doi.org/10.3390/s24092793)] [Medline: [38732899](https://pubmed.ncbi.nlm.nih.gov/38732899/)]
74. Wang KJ, Lee TL. Designing a digital-twin based dashboard system for a flexible assembly line. *Computers & Industrial Engineering.* 2024;196:110491. [doi: [10.1016/j.cie.2024.110491](https://doi.org/10.1016/j.cie.2024.110491)]
75. Yao Z, Wu H, Song Y, et al. Surrogate model-based cognitive digital twin for smart remote maintenance of fusion reactor: modeling and implementation. *Nucl Fusion.* 2024;64(12):126007. [doi: [10.1088/1741-4326/ad7b56](https://doi.org/10.1088/1741-4326/ad7b56)]
76. Liu Y, Hodges S, Wu J, Siegel B. Telehealth-delivered multimodal mind-body intervention for mild cognitive impairment: a randomized feasibility trial toward scalable dementia prevention. *npj Dementia.* 2026;2(1):39. [doi: [10.1038/s44400-026-00090-y](https://doi.org/10.1038/s44400-026-00090-y)] [Medline: [42238806](https://pubmed.ncbi.nlm.nih.gov/42238806/)]
77. Straand IJ, Baxter KA, Følstad A. Remote inclusion of vulnerable users in mHealth intervention design: retrospective case analysis. *JMIR Mhealth Uhealth.* 2024;12:e55548. [FREE Full text] [doi: [10.2196/55548](https://doi.org/10.2196/55548)] [Medline: [38875700](https://pubmed.ncbi.nlm.nih.gov/38875700/)]
78. Rashid Z, Folarin AA, Zhang Y, et al. Digital phenotyping of mental and physical conditions: remote monitoring of patients through RADAR-base platform. *JMIR Ment Health.* 2024;11:e51259. [FREE Full text] [doi: [10.2196/51259](https://doi.org/10.2196/51259)] [Medline: [39441952](https://pubmed.ncbi.nlm.nih.gov/39441952/)]
79. Zhang S, Song J. An empirical investigation into the preferences of the elderly for user interface design in personal electronic health record systems. *Front Digit Health.* 2023;5:1289904. [FREE Full text] [doi: [10.3389/fdgth.2023.1289904](https://doi.org/10.3389/fdgth.2023.1289904)] [Medline: [38348367](https://pubmed.ncbi.nlm.nih.gov/38348367/)]
80. Brahmi R, Boujnah N, Ejbali R. Elaboration of innovative digital twin models for healthcare monitoring with 6g functionalities. *IEEE Access.* 2024;12:109608-109624. [doi: [10.1109/access.2024.3439269](https://doi.org/10.1109/access.2024.3439269)]
81. Liu Y. Modular Pipeline for Cloud-Based DT Architecture Using Microsoft Azure and Amazon AWS. *BioRender.* 2026. URL: <https://BioRender.com/2ljk78> [accessed 2026-06-22]
82. Wang Z, Gupta R, Han K, et al. Mobility digital twin: concept, architecture, case study, and future challenges. *IEEE Internet Things J.* 2022;9(18):17452-17467. [doi: [10.1109/jiot.2022.3156028](https://doi.org/10.1109/jiot.2022.3156028)]
83. Dineva K, Atanasova T. Design of scalable IoT architecture based on AWS for smart livestock. *Animals (Basel).* 2021;11(9):2697. [FREE Full text] [doi: [10.3390/ani11092697](https://doi.org/10.3390/ani11092697)] [Medline: [34573662](https://pubmed.ncbi.nlm.nih.gov/34573662/)]
84. Khan A, Nawaz U, Ulhaq A, Robinson RW. Real-time plant health assessment via implementing cloud-based scalable transfer learning on AWS deepLens. *PLoS One.* 2020;15(12):e0243243. [FREE Full text] [doi: [10.1371/journal.pone.0243243](https://doi.org/10.1371/journal.pone.0243243)] [Medline: [33332376](https://pubmed.ncbi.nlm.nih.gov/33332376/)]
85. Saheed YK, Salau-Ibrahim TT, Abdulsalam M, Adeniji IA, Balogun BF. Modified bi-directional long short-term memory and hyperparameter tuning of supervised machine learning models for cardiovascular heart disease prediction in mobile cloud environment. *Biomedical Signal Processing and Control.* 2024;94:106319. [doi: [10.1016/j.bspc.2024.106319](https://doi.org/10.1016/j.bspc.2024.106319)]
86. Qin H, Zawad S, Zhou Y, et al. Reinforcement-learning-empowered MLaaS scheduling for serving intelligent internet of things. *IEEE Internet Things J.* 2020;7(7):6325-6337. [doi: [10.1109/jiot.2020.2965103](https://doi.org/10.1109/jiot.2020.2965103)]
87. Giménez-Alventosa V, Moltó G, Caballer M. A framework and a performance assessment for serverless MapReduce on AWS Lambda. *Future Generation Computer Systems.* 2019;97:259-274. [doi: [10.1016/j.future.2019.02.057](https://doi.org/10.1016/j.future.2019.02.057)]
88. Cao M, Ramezani R, Katakwar VK, et al. Developing remote patient monitoring infrastructure using commercially available cloud platforms. *Front Digit Health.* 2024;6:1399461. [FREE Full text] [doi: [10.3389/fdgth.2024.1399461](https://doi.org/10.3389/fdgth.2024.1399461)] [Medline: [39568539](https://pubmed.ncbi.nlm.nih.gov/39568539/)]

89. Barika M, Garg S, Chan A, Calheiros RN, Ranjan R. IoTSim-stream: modelling stream graph application in cloud simulation. *Future Generation Computer Systems*. 2019;99:86-105. [doi: [10.1016/j.future.2019.04.004](https://doi.org/10.1016/j.future.2019.04.004)]
90. Bozkaya-Aras E, Onel T, Eriskin L, Karatas M. Intelligent human activity recognition for healthcare digital twin. *Internet of Things*. 2025;30:101497. [doi: [10.1016/j.iot.2025.101497](https://doi.org/10.1016/j.iot.2025.101497)]
91. Xu R, Park C, Khan S, Jin W, Moe SJS, Kim DH. Optimized task scheduling and virtual object management based on digital twin for distributed edge computing networks. *IEEE Access*. 2023;11:114790-114810. [doi: [10.1109/access.2023.3325475](https://doi.org/10.1109/access.2023.3325475)]
92. Li Y, Kong Q, Xiong B, Chi F, Qu Y, Wang C. Edge-fog-cloud-based digital twin network for autonomous and distributed structural health monitoring of a mega dam cluster. *Automation in Construction*. 2025;172:106050. [doi: [10.1016/j.autcon.2025.106050](https://doi.org/10.1016/j.autcon.2025.106050)]
93. Ward R, Choudary R, Jans Singh M, et al. The challenges of using live-streamed data in a predictive digital twin. *Journal of Building Performance Simulation*. 2023;16(5):609-630. [doi: [10.1080/19401493.2023.2187463](https://doi.org/10.1080/19401493.2023.2187463)]
94. Tudoran R, Costan A, Nano O, Santos I, Soncu H, Antoniu G. JetStream: enabling high throughput live event streaming on multi-site clouds. *Future Generation Computer Systems*. 2016;54:274-291. [doi: [10.1016/j.future.2015.01.016](https://doi.org/10.1016/j.future.2015.01.016)]
95. Xu Q, Yue T, Ali S, Arratibel M. Pretrain, prompt, and transfer: evolving digital twins for time-to-event analysis in cyber-physical systems. *IEEE Trans Software Eng*. Jun 2024;50(6):1464-1477. [doi: [10.1109/tse.2024.3388572](https://doi.org/10.1109/tse.2024.3388572)]
96. Harode A, Thabet W, Dongre P. A tool-based system architecture for a digital twin: a case study in a healthcare facility. *ITcon*. 2023;28:107-137. [FREE Full text] [doi: [10.36680/j.itcon.2023.006](https://doi.org/10.36680/j.itcon.2023.006)]
97. Compliance validation for AWS Security Hub. Amazon Web Services. 2025. URL: <https://docs.aws.amazon.com/securityhub/latest/userguide/securityhub-compliance.html> [accessed 2026-04-09]
98. Regulatory compliance standards in Microsoft Defender for Cloud. Microsoft. 2025. URL: <https://learn.microsoft.com/en-us/azure/defender-for-cloud/concept-regulatory-compliance-standards#default-compliance-standards> [accessed 2026-04-09]
99. Rampal S. Early cognitive decline assessment via the synergy of machine learning algorithms and cognitive proficiency examination. 2023. Presented at: IEEE International Conference on ICT in Business Industry & Government (ICTBIG); December 8–9, 2023; Indore, Madhya Pradesh, India. [doi: [10.1109/ictbig59752.2023.10456082](https://doi.org/10.1109/ictbig59752.2023.10456082)]
100. Revathi A, Kaladevi R, Ramana K, Jhaveri RH, Rudra Kumar M, Sankara Prasanna Kumar M. Early detection of cognitive decline using machine learning algorithm and cognitive ability test. *Security and Communication Networks*. 2022;2022:4190023. [doi: [10.1155/2022/4190023](https://doi.org/10.1155/2022/4190023)]
101. Comai S, Masciadri A, Zuccarello D, Salice F. NeeMAS: a need-based multi-agent simulator of human behavior for long-term drifts in smart environments. In: *Lecture Notes in Networks and Systems 842 LNNS*. Cham. Springer; 2023:88-99.
102. Tranchant C, Gallibois M, Handrigan G, Omar H. 2788 Exercise trainers as key enablers in the remote delivery of dementia prevention interventions in the homes of older adults. *Age Ageing*. 2025;54(Supplement_1):afae277.105. [doi: [10.1093/ageing/afae277.105](https://doi.org/10.1093/ageing/afae277.105)]
103. Feng J, Tang H, Zhou S, Cai Y, Zhang J. Cognitive digital twins of the natural environment: framework and application. *Engineering Applications of Artificial Intelligence*. 2025;139:109587. [doi: [10.1016/j.engappai.2024.109587](https://doi.org/10.1016/j.engappai.2024.109587)]
104. Yang Y, Shi H, Liu J. Baduanjin qigong exercise intervention improves subjective and objective cognitive functioning: the moderation and mediation effects of sleep. *Alzheimer's & Dementia*. 2025;20(S7):e093211. [doi: [10.1002/alz.093211](https://doi.org/10.1002/alz.093211)]
105. Li F, Wang L, Qin Y, Liu G. Combined tai chi and cognitive interventions for older adults with or without cognitive impairment: a meta-analysis and systematic review. *Complement Ther Med*. 2022;67:102833. [FREE Full text] [doi: [10.1016/j.ctim.2022.102833](https://doi.org/10.1016/j.ctim.2022.102833)] [Medline: [35439549](https://pubmed.ncbi.nlm.nih.gov/35439549/)]
106. Bunyan M, Irving J, Barnett JH, et al. Assessing a digital lifestyle intervention to reduce dementia risk in older adults. *Alzheimer's & Dementia*. 2025;20(S10):e094330. [doi: [10.1002/alz.094330](https://doi.org/10.1002/alz.094330)]
107. Gámez Díaz R, Yu Q, Ding Y, Laamarti F, El Saddik A. Digital twin coaching for physical activities: a survey. *Sensors (Basel)*. 2020;20(20):5936. [FREE Full text] [doi: [10.3390/s20205936](https://doi.org/10.3390/s20205936)] [Medline: [33096595](https://pubmed.ncbi.nlm.nih.gov/33096595/)]
108. Wang D, Florian H, Yu Lynch S, et al. Assessment of AI - generated digital twin (DT) methodology on reduction of treatment effect variance and potential clinical trial sample size saving using a Phase 2 trial dataset from patients with Alzheimer's disease (AD). *Alzheimer's & Dementia*. 2024;20(S6):e090685. [doi: [10.1002/alz.090685](https://doi.org/10.1002/alz.090685)]
109. van der Veere PJ, Hoogland J, Visser LN, et al. Predicting cognitive decline in amyloid-positive patients with mild cognitive impairment or mild dementia. *Neurology*. 2024;103(3):e209605. [doi: [10.1212/WNL.0000000000209605](https://doi.org/10.1212/WNL.0000000000209605)] [Medline: [38986053](https://pubmed.ncbi.nlm.nih.gov/38986053/)]
110. Nosheny RL, Jin C, Neuhaus J, et al. Study partner-reported decline identifies cognitive decline and dementia risk. *Ann Clin Transl Neurol*. 2019;6(12):2448-2459. [FREE Full text] [doi: [10.1002/acn3.50938](https://doi.org/10.1002/acn3.50938)] [Medline: [31721455](https://pubmed.ncbi.nlm.nih.gov/31721455/)]
111. Sanjay AB, Sun L, Shokeen D, Isacson O, Shin S, Latourelle J. Investigating the ATN (Amyloid, Tau, Neurodegeneration) framework in Alzheimer's disease and its causal genetic - drivers using digital - twins. *Alzheimer's & Dementia*. 2024;20(S2):e091647. [doi: [10.1002/alz.091647](https://doi.org/10.1002/alz.091647)]
112. Vallée A. Envisioning the future of personalized medicine: role and realities of digital twins. *J Med Internet Res*. 2024;26:e50204. [FREE Full text] [doi: [10.2196/50204](https://doi.org/10.2196/50204)] [Medline: [38739913](https://pubmed.ncbi.nlm.nih.gov/38739913/)]
113. Sun K, Wu J, Bashir AK, et al. Personalized privacy-preserving distributed artificial intelligence for digital-twin-driven vehicle road cooperation. *IEEE Internet Things J*. 2024;11(22):35902-35916. [doi: [10.1109/jiot.2024.3389656](https://doi.org/10.1109/jiot.2024.3389656)]

114. Favela LH, Amon MJ. The ethics of human digital twins: counterfeit people, personhood, and the right to privacy. 2023. Presented at: Proceedings of the 2023 IEEE 3rd International Conference on Digital Twins and Parallel Intelligence (DTPI); November 7–9, 2023:1-6; Orlando, Florida, USA (UCF Campus). [doi: [10.1109/dtpi59677.2023.10365409](https://doi.org/10.1109/dtpi59677.2023.10365409)]
115. Ren C, Dong ZY, Yu H, Xu M, Xiong Z, Niyato D. ESQFL: digital twin-driven explainable and secured quantum federated learning for voltage stability assessment in smart grids. *IEEE J Sel Top Signal Process.* 2024;18(5):964-978. [doi: [10.1109/jstsp.2024.3485878](https://doi.org/10.1109/jstsp.2024.3485878)]
116. Nazarenko A, Marcelino-Jesus E, Sarraipa J, Gutiérrez y Restrepo E, Zamiri M, Flynn T. Inclusive sustainability: strategies for sustainable digital solutions in the twin transition for vulnerable communities. *IEEE*; 2024. Presented at: IEEE International Conference on Engineering, Technology, and Innovation (ICE/ITMC); June 24-28, 2024:1-9; Funchal, Portugal. [doi: [10.1109/ice/itmc61926.2024.10794329](https://doi.org/10.1109/ice/itmc61926.2024.10794329)]
117. Pires LR, Costa MV, de Oliveira Hansen E, et al. Analysis of clinical and sociodemographic factors involved in older adults' cognition. *Alzheimer's & Dementia.* Feb 2022;17(S7):e056471. [doi: [10.1002/alz.056471](https://doi.org/10.1002/alz.056471)]
118. Sepehry AA, Schultz IZ, Cohen DA, Greer S. From subjective cognitive decline to mild cognitive impairment to dementia: clinical and capacity assessment considerations. *Psychol Inj and Law.* 2022;16(3):273-287. [doi: [10.1007/s12207-022-09456-y](https://doi.org/10.1007/s12207-022-09456-y)]
119. Kang Y, Feng Z, Zhang Q, et al. Identification of circulating risk biomarkers for cognitive decline in a large community-based population in Chongqing China. *Alzheimers Dement.* 2025;21(2):e14443. [doi: [10.1002/alz.14443](https://doi.org/10.1002/alz.14443)] [Medline: [39713874](https://pubmed.ncbi.nlm.nih.gov/39713874/)]
120. Lin Y, Fuh J. Identifying cognitive trajectories and predicting rapid decline of cognitive function in early Alzheimer's disease. *Alzheimer's & Dementia.* 2021;17(S6):e050874. [doi: [10.1002/alz.050874](https://doi.org/10.1002/alz.050874)]
121. Wickramasinghe N, Ulapane N, Nguyen TA, et al. Towards discovering digital twins of dementia patients: matching the phases of cognitive decline. *Alzheimer's & Dementia.* 2022;18(S2):e066336. [doi: [10.1002/alz.066336](https://doi.org/10.1002/alz.066336)]
122. Hews E. From twins to digital twins: LLM-driven cognitive performance prediction. *Innov Aging.* 2024;8:1314. [doi: [10.1093/geroni/igae098.4197](https://doi.org/10.1093/geroni/igae098.4197)]
123. Alqahtani A, Alsubai S, Bhatia M. Digital-twin-assisted healthcare framework for adult. *IEEE Internet Things J.* 2024;11(8):14963-14970. [doi: [10.1109/jiot.2023.3345331](https://doi.org/10.1109/jiot.2023.3345331)]
124. Bolat-Akça B, Bozkaya-Aras E. Digital twin-assisted intelligent anomaly detection system for internet of things. *Ad Hoc Networks.* 2024;158:103484. [doi: [10.1016/j.adhoc.2024.103484](https://doi.org/10.1016/j.adhoc.2024.103484)]
125. An NY, Yang JH, Song E, Hwang S, Byun H, Park S. Digital twin-based hydrogen refueling station (HRS) safety model: CNN-based decision-making and 3D simulation. *Sustainability.* 2024;16(21):9482. [doi: [10.3390/su16219482](https://doi.org/10.3390/su16219482)]
126. Mortlock T, Muthirayan D, Yu SY, Khargonekar PP, Abdullah Al Faruque M. Graph learning for cognitive digital twins in manufacturing systems. *IEEE Trans Emerg Topics Comput.* 2022;10(1):34-45. [doi: [10.1109/tetc.2021.3132251](https://doi.org/10.1109/tetc.2021.3132251)]
127. Lim KYH, Yosai TS, Chen C, Zheng P, Wang L, Xu X. Graph-enabled cognitive digital twins for causal inference in maintenance processes. *International Journal of Production Research.* 2023;62(13):4717-4734. [doi: [10.1080/00207543.2023.2274335](https://doi.org/10.1080/00207543.2023.2274335)]
128. Zhang R, Xie Z, Yu D, Liang W, Cheng X. Digital twin-assisted federated learning service provisioning over mobile edge networks. *IEEE Trans Comput.* 2024;73(2):586-598. [doi: [10.1109/tc.2023.3337317](https://doi.org/10.1109/tc.2023.3337317)]
129. Diniz P, Grimm B, Garcia F, et al. Digital twin systems for musculoskeletal applications: a current concepts review. *Knee Surg Sports Traumatol Arthrosc.* 2025;33(5):1892-1910. [doi: [10.1002/ksa.12627](https://doi.org/10.1002/ksa.12627)] [Medline: [39989345](https://pubmed.ncbi.nlm.nih.gov/39989345/)]
130. Bellavista P, Bicocchi N, Fogli M, Giannelli C, Mamei M, Picone M. Exploiting microservices and serverless for digital twins in the cloud-to-edge continuum. *Future Generation Computer Systems.* 2024;157:275-287. [doi: [10.1016/j.future.2024.03.052](https://doi.org/10.1016/j.future.2024.03.052)]

Abbreviations

- AI:** artificial intelligence
- AWS:** Amazon Web Services
- CNN:** convolutional neural network
- DT:** digital twin
- EEG:** electroencephalography
- FHIR:** Fast Healthcare Interoperability Resources
- HIPAA:** Health Insurance Portability and Accountability Act
- HRV:** heart rate variability
- MCI:** mild cognitive impairment
- ML:** machine learning
- OMOP:** Observational Medical Outcomes Partnership
- LSTM:** long short-term memory
- RL:** reinforcement learning
- SVM:** support vector machine

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