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Digital twin in medical device and regulatory overview of USA and India

Authors information
Boin Poojitha[1], Alekula Reshma[1], Imran Shareef[1] Dr. A. Ravi Kiran[1]
Affiliations:
1. Department of Regulatory Affairs
G. PULLA REDDY COLLEGE OF PHARMACY, Mehdipatnam, HYDERABAD, TELANGANA

CORRESPONDING AUTHORS:
BOIN POOJITHA, Department of Regulatory Affairs
G. PULLA REDDY COLLEGE OF PHARMACY,
Email id: boinpoojitha@gmail.com,

ABSTRACT:

Digital twins [DT] are real-time virtual replicas of patients, organs, or healthcare systems, built by integrating diverse data sources including electronic health records, genomics, wearables, imaging, and lifestyle data. Powered by artificial intelligence, machine learning, and the Internet of Things, these dynamic models are transforming healthcare delivery by enabling personalized, proactive, and data-driven clinical decision-making. Unlike traditional population-based approaches, digital twins generate patient-specific simulations that predict disease progression, assess individual risk, and evaluate treatment outcomes virtually before real-world application. The technology offers multiple healthcare benefits, including personalized care planning, early detection of high-risk conditions, real-time health monitoring, optimized hospital resource allocation, and safe clinical training through virtual simulations. Evolving from industrial machine replicas, digital twins now model complex biological systems at cellular and organ levels, continuously learning through feedback loops. Their integration into personalized medicine marks a paradigm shift, moving from standardized interventions to tailored therapeutic strategies based on each patient's unique biological, genetic, and physiological profile. Four key implementation steps are required to embed this technology into routine clinical practice. As rich health data continues to grow alongside advancing AI capabilities, digital twins hold significant promise for improving diagnostic accuracy, reducing medical errors, preventing health crises, and ultimately enhancing long-term patient outcomes.

KEYWORDS: Artificial intelligence, genomics, internet of things (IoT), software as medical device (SaMD), personalised medicine

INTRODUCTION:

1. DIGITAL TWINS:

Digital twins are virtual copies of real things, like products, organs, or even patients, that update in real time. They are gaining a lot of attention from researchers and companies because technologies like sensors, IoT (Internet of things), big data, AI, and simulations have greatly improved their capabilities.

This technology is changing healthcare by creating virtual copies of patients or systems. It uses real-time data, smart analysis, and simulations to improve care, predict problems, streamline operations, and train staff.[1]

Benefits of Digital Twin in the healthcare system

- **Personalized Care**: It creates custom treatment plans using full patient data from records, wearables, and devices for faster diagnoses and real-time monitoring.
- **Patient Empowerment**: It lets patients actively join their care journey with clear, ongoing insights.
- **Predictive Power**: It uses AI to forecast disease progression, spot high-risk people early, and suggest preventive steps.
- **Better Safety and Outcomes**: It improves long-term health results by acting proactively.
- **Smarter Resources**: It optimizes operations, cuts waste and allocates staff/tools efficiently.
- **Training Boost**: It offers safe virtual simulations for doctors to practice and improve skills.[1]

Evolution of digital twins:

They started as digital versions of machines and their connections. Now, they are smart replicas of living things, such as organs and cells, as well as non-living things. They learn from data, predict problems like failures or diseases, and optimize everything through constant feedback loops. [1]

The Core Tech Behind:

- Data-driven: It uses the statistical models from sensors provide quick insights.
- Knowledge-based: They combine physics simulations, AI, and multi-scale data

Importance in healthcare system:

Major companies use them for efficiency across industries and healthcare is next field. In this field, a digital twin reflects a patient, a body part, or a hospital. It uses health records, genetics, wearables, lifestyle data, and more. AI and IoT make it dynamic, allowing it to predict health changes and enhance diagnosis and treatment. The amount of rich data now available is driving rapid growth in this area. [1,2]

Working:

Digital twins supercharge risk assessment in healthcare by feeding AI and machine learning algorithms a patient's full data profile—like genes, daily habits (diet, exercise), surroundings (pollution, stress), and health history from wearables or records. [1]

How It Works Step-by-Step process:

- Data crunching: The twin builds a live model of you; spotting patterns others miss. For example, it might flag "high diabetes risk" from your family DNA plus sedentary job and poor sleep.[1]
- Smart Prediction**:** AI runs simulations to score risks accurately like say, 75% chance of heart issues in 5 years and way better than generic checks or the physical examination. [2]
- Custom Action Plans: Doctors get precise recommendations: "Prescribe this med, add walking goals, or screen early for cancer." It prevents crises, not just treats them.

This makes healthcare proactive and personal like a crystal ball tuned to your life cutting emergencies and improving long-term health. [1,2,3]

1.1 Digital Twins in Personalized Medicine:

In contemporary to the healthcare system, personalized medicine is currently one of the most significant trends, signalling a dramatic change from population-based treatment plans to patient-specific care. Instead of employing standardized interventions based on average responses, it seeks to tailor diagnosis, treatment options, and follow-up plans to everyone's unique biological, physiological, and genetic profile.[4]

Tracking Health Live

They make it simple for doctors to watch your health 24/7, spot how diseases worsen (like cancer spreading), and check if treatments work (say, if chemo shrinks a tumor). It's all updated instantly for spot-on monitoring.

Personalized Medicine Magic

DTs predict your disease path, test "what if" treatments virtually (e.g., "Will this drug help your heart without side effects?"), and map the best care plan just for you. Doctors try options risk-free, cut errors, and track long-term.

Data Powerhouse

They blend AI, sensors, imaging, and EHRs into one hub—like a bridge from complex biology to everyday doctor visits. This drives true custom care: proactive, patient-focused, and data-smart for better results [5]. The fig 1 explains that by combining various medical data sources, doctors can create a virtual replica of a patient to make better medical decisions, and it maps out the four steps needed to make this technology a standard part of healthcare.

This technology is changing healthcare by creating virtual copies of patients or systems. It uses real-time data, smart analysis, and simulations to improve care, predict problems, streamline operations, and train staff.[1]

The fig- 1 states the pipeline of the digital twins:

It starts with the patient: Their health data is collected, like heart rate, blood pressure, or medical history.

- That information flows into real-time monitoring, almost like a smartwatch keeping track of their health every second.
- The system then aligns the real person with their digital twin—a virtual version of them that mirrors their health status.
- Doctors can use this twin to simulate treatments, testing “what if” scenarios safely before trying them in real life.
- Finally, the twin becomes a decision-support partner, helping clinicians choose the best treatment plan tailored to that patient.

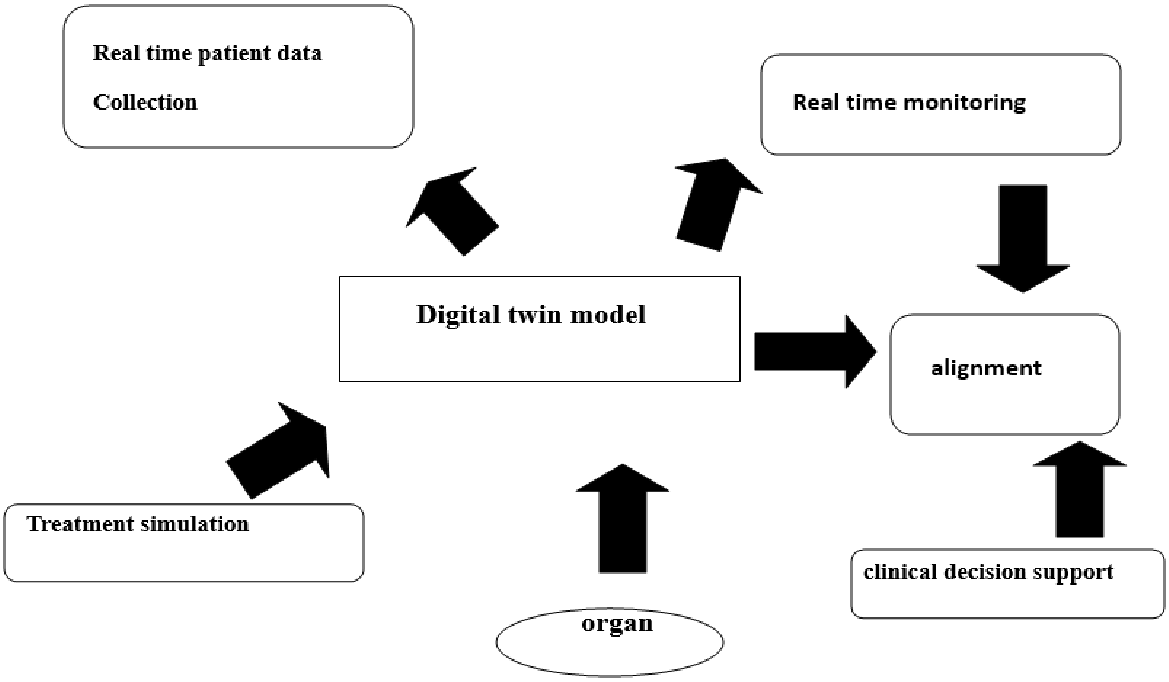

Fig 1 Digital twins’ pipeline in real time applications

1.2. Clinical Applications of Digital Twins in Personalized Medicine

From the measuring planes or buildings as engineering concepts, digital twins (DTs) have transformed into service instruments in healthcare. In the fig-2 explains the clinical application of the digital twins in cardiology, oncology, neurology, pharmacogenomics, rare disease etc. It includes diagnostics now, then treatment planning, training and trial of new devices blending patient geometric form physiology, drug response and actual environmental data; this can help insure safe care delicate disease conditions.

1.2.1. Radiation Therapy Features Digital twins (DTs)

Most forms of heart care rely now on DTs, its only exception being in an ambivalent function which has yet to produce noticeable results. Yes, from scans simulating both electrical/mechanical behaviour and treatment device effectiveness in CRT custom tailored to the patient's unique body shape and size. Drugs and Surgery Get a Boosts DTs help you with drugs (for example, modifying beta blockers to treat heart failure, taking into account the living blood flowrate of your heart) and risk judgement for surgery.[4]

2. Translational Gap in Digital Twins:

Digital Twins (DTs) remain rare in everyday clinical practice, despite growing evidence supporting their role in personalized medicine. While pilot projects and proof-of-concept studies demonstrate technical feasibility in areas like neurology, cardiology, oncology, and pharmacogenomics, transitioning to real-world clinical settings has been slow, fragmented, and inconsistent.

This gap underscores a key challenge: the difference between DTs' theoretical potential in research literature and their use as reliable, validated tools for daily clinical decision-making. Addressing this disparity is essential to advancing the field. The translational gap for Digital Health Twins (DHTs) goes beyond technical hurdles it's a complex interplay of culture, policy, ethics, and infrastructure that tests real-world healthcare adoption.

Future DHT (Digital Health Twins) development must prioritize co-design with clinicians, patient validation, health system alignment, and transparent governance to bridge this divide. Only then can these tools evolve from promising concepts into everyday clinical assets across technical, regulatory, ethical, organizational, computational, and equity fronts and several barriers in clinical application as discussed below.[4]

2.1. The main barriers in the clinical translation of digital twins (DT):

1. Technical

- Description: Lack of interoperability between hospital systems
- Clinical Impact: Fragmented data, outdated models
- Real-World Example: EHRs are incompatible with sensors

2. Regulatory

- Description: Absence of specific guidelines for DT approval
- Clinical Impact: Delayed certification and institutional trust
- Real-World Example: No legal framework for hybrid models

3. Validation

- Description: Lack of standardized validation frameworks
- Clinical Impact: Lack of clinical trust, delays in adoption of the method
- Real-World Example: No agreed endpoints for in silico validation

4. Ethical

- Description: Dynamic consent and continuous use of patient data
- Clinical Impact: Risk of unauthorized or opaque use
- Real-World Example: Updates without renewed patient consent

5. Trust / Explainability

- Description: Limited explainability and unclear decision accountability
- Clinical Impact: Low clinician confidence, reluctance to use in practice
- Real-World Example: Opacity of AI-driven DT predictions in oncology/neurosurgery

6. Organizational

- Description: Staff resistance and lack of training
- Clinical Impact: Low adoption despite availability of tools
- Real-World Example: Clinicians ignoring DT-generated alerts

7. Computational

- Description: Insufficient infrastructure for real-time data processing
- Clinical Impact: Inability to update the model dynamically

- Real-World Example: Hospitals lacking adequate servers or cloud resources

8. Equity / Inclusion

- Description: Models trained on non-representative populations
- Clinical Impact: Risk of algorithmic bias and errors in vulnerable populations
- Real-World Example: Underrepresentation of genetic and socioeconomic minorities. [6,7,8,9,10 – 17]

3. Digital Twin Validation advancement over the conventional trials

Limitations of Traditional RCTs in the Digital Twin Context:

Randomized controlled trials (RCTs) remain the gold standard for assessing clinical interventions. However, their rigid, population-based framework often clashes with the personalized, adaptive nature of digital twin (DT) technologies. Several fundamental mismatches create challenges as mentioned in the table [1]

Challenge	Explanation
Static vs. Dynamic Design	RCTs rely on fixed protocols, whereas DTs operate through continuous, real-time feedback loops that evolve with patient data.
Control Arm Ethics	When DT-guided simulations demonstrably outperform standard care, maintaining a conventional control group may become ethically questionable or scientifically redundant.
Blinding Difficulties	Clinicians interacting directly with DT outputs cannot be easily blinded, potentially introducing bias into outcome assessment.
Attribution Complexity	Disentangling the specific contribution of a DT recommendation from the clinician's own judgment complicates causal inference and outcome attribution.
Limited Real-World Evidence	Few DT applications have undergone full-scale RCTs; existing studies are often single-centre or confined to narrow clinical scenarios.

Table -1 It shows the outweighs the conventional trials over the digital twins [4]

To address the limitations of conventional Randomized Controlled Trials (RCTs) in validating Digital Twins (DT), the medical and regulatory communities are shifting toward adaptive, data-driven, and continuous validation frameworks. By solving the challenges as mentioned in tab 1 we can validate the data correctly. [4]

3. Regulatory overview of the DTs in USA and INDIA:

4.1. USA (FDA):

- It is regulated as Software as a Medical Device (SaMD) if used for diagnosis/treatment
- The approach is based on the risk-based and higher patient impact = more evidence required
- The only benefit is Precent Program allows faster updates for trusted developers
- The Evidence needed is the validation testing, AI explainability, post-market monitoring
- Privacy: HIPAA [Health Insurance Portability and Accountability Act] compliance required [19,20,21]

Regulatory oversight for digital twins in medical devices primarily falls under FDA guidelines for Software as a Medical Device (SaMD) and computational modeling, emphasizing credibility, validation, and risk-based assessments. Agencies like FDA, EMA, and NIH/NSF support their use in trials to reduce animal/human testing while requiring transparency in data inputs, model performance, and real-world evidence.

FDA's 2023 guidelines on computational modelling endorse digital twins for device submissions, listed in the Regulatory Science Tools Catalog for credibility in simulations. High-risk models undergo stringent reviews on "model influence" and "decision consequence," as in a sponsor's Phase 2/3 trial where twins predicted placebo responses. [20,21]

3.2. India (CDSCO)

India lacks specific regulations for digital twins as medical devices; they fall under the Medical Devices Rules (MDR) 2017, enforced by CDSCO, treating them as Software as a Medical Device (SaMD) if diagnostic, monitoring, or therapeutic.

- It is Regulated as SaMD under Medical Devices Rules, 2017
- The Approach is based on the Clear risk matrix (Class A–D) based on condition severity × tool function
- The benefit is new 2025 rules streamline approvals and exports
- Evidence required: Technical documentation, safety proof, cybersecurity plans
- Privacy: It is done through Digital Personal Data Protection Rules (2025) and strict consent & encryption. [23,24, 25, 26]

Digital twins are risk-classified (A-D) per First Schedule of MDR 2017, typically Class C/D for predictive analytics (e.g., cardiology twins), requiring CDSCO registration, clinical evaluation, and ISO 13485 QMS. Import licenses need Form MD-14/15; reliance on USFDA/EMA approvals expedites via abridged pathways if no global safety issues. [27,28,29,30]. There is the comparison of the regulatory overview of the digital twins in the (table 2) which states different parameters in both the countries.

Dimension	**USA (FDA)**	**India (CDSCO)**
Primary Framework	SaMD via IMDRF alignment; Cures Act exclusions	Medical Devices Rules, 2017 + Draft SaMD Guidance (2025)
Risk Classification	IMDRF-based (A–D); context-dependent enforcement discretion	Explicit matrix linking clinical impact × condition severity → Class A–D
AI/Digital Twin Specifics	Risk-based credibility assessment; draft AI guidance (2025)	Draft guidance references AI standards (ISO/IEC 23894, ISO 42001)
Clinical Trial Use	Accepted for exploratory analyses; validation required for primary endpoints	Emerging; MedTech Mitra handbook supports IVD/digital innovation pathways
Data Governance	HIPAA + state privacy laws; FDA focuses on data integrity for submissions	DPDP Rules 2025; encryption, consent, and processor obligations
Post-Market Oversight	Real-world performance monitoring (Precert pilot); adverse event reporting	Mandatory PMS, 15-day adverse event reporting, periodic safety updates
Regulatory Certainty	Evolving guidance; case-by-case review common.	Draft guidance improving predictability; full adoption pending stakeholder feedback

Table – 2 [comparison of core regulatory framework of USA and INDIA [20,21,24,25,26,27]

4. VALIDATION OF DIGITAL TWINS:

Researchers are actively developing novel validation methodologies to address the unique challenges of evaluating digital health technologies. Among the most promising approaches are in silico clinical trials and computational studies that leverage virtual patient cohorts to simulate disease progression and treatment responses. The phases involved in this are stated below: [32,33,34]

Phase 1: Planning

- Define Question of Interest – What decision will the twin support?
- Define Context of Use – What are the boundaries (patient type, conditions, device state)?
- Assess Model Risk – Rate Model Influence × Decision Consequence to determine validation rigor.

Phase 2: Verification (Code Check)

- Code Review & Unit Testing – Ensure software is bug-free.
- Solution Verification – Confirm numerical accuracy (mesh convergence, time-step stability).

Phase 3: Validation (Reality Check)

- Calibrate Model – Tune parameters using a training dataset.

- Test Against Independent Data – Validate predictions using a held-out test dataset.
- Quantify Uncertainty – Calculate confidence intervals (e.g., Monte Carlo, sensitivity analysis).
- Compute Accuracy Metrics – Measure error (RMSE, R^2, Bland-Altman, Clarke Error Grid).

Phase 4: Continuous Validation (Post-Market)

- Monitor Drift – Track prediction error in real-world use
- Trigger Recalibration – Auto-alert when error exceeds predefined threshold.
- Periodic Re-assessment – Annual review of model credibility and applicability.

Regulatory Alignment (If Applicable)

- Early FDA/EMA Engagement – Use Q-Submission to align on validation strategy.
- Submit Credibility Report – Document risk assessment, verification, validation, and uncertainty.
- Plan for Updates – Use Predetermined Change Control Plan (PCCP) for adaptive models.

Note: Validation is risk-proportional, evidence-based, and continuous but not a one-time checkbox (continuous process).

Examples of some tools used to validate the data Dakota (Sandia Labs), sim vascular and V&V manager etc. [32,33,34,35,36]

They help businesses by allowing them to monitor performance, predict problems before they happen, and test changes safely in a virtual space and all of which can save time and money. However, creating and maintaining digital twins can be expensive and technically challenging. They also require large amounts of accurate, up-to-date data, and if that data is compromised, it could lead to security risks. In short, while digital twins offer powerful tools for improvement, they also demand careful planning and strong data protection so the table 3. states the pros and cons of the digital twins and their net assessment in 2026.

Table 3 DIGITAL TWINS PRO'S AND CON'S (2026 OUTLOOK) [37,38,39]

Category	Advantages	Disadvantages	Net Assessment (2026)
Patient Outcomes	- Personalized treatment plans - Predictive alerts forearly intervention - Preventive care via simulations - Safer virtual therapy testing	- Over-reliance on imperfect models - Alert fatigue -False positives/negatives	Strong positive with safeguards (ASME V&V 40, monitoring)
Research Efficiency	- Accelerated trials via in silico screening - smaller samples with synthetic controls - rare disease research via virtual cohorts - Rapid hypothesis testing	- Resource-intensive validation - Model drift without recalibration - Biased conclusions from undiverse cohorts	Growing FDA/EMA acceptance with evidence standards
Cost & Access	- Long-term savings from prevention - Reduced readmissions via monitoring - Lower trial costs with virtual screening	- High upfront investments - Widens digital divide - Ongoing data/compute costs	Concentrated in well-resourced centers; needs equity policies
Regulatory Pathway	- Clearer FDA/EMA guidance (2023 CM&S) - Reduced testing for low-risk apps - PCCP for model updates	- Uncertainty for adaptive twins - Heavy documentation - Incomplete global harmonization	Positive with early Q-Submission and alignment
Ethical & Social	- Equitable access via virtual cohorts	- Bias amplification from poor data	Needs bias testing, federated learning, governance

	- Less placebo exposure - Transparent decisions via documentation	- Privacy concerns - Unclear liability	

These are the few examples of the machine learning application in the healthcare system:

- **Cancer Analyses (2022)**: Used natural language processing labeling with CNN, recurrent neural networks, and TF-IDF ensemble models on CT scans (2009-2021). Achieved 93.8% accuracy for lung cancer, 92.5% for liver cancer, and 96.1% for adrenal cancer with TF-IDF; up to 96.8-99.7% with augmented CNN in validation.
- **Personal Health Care with Emotion Recognition (2022)**: Automatic emotion detection from EEG signals using gradient boosting, k-nearest neighbors, and random forest models on EEG images. Reached 99.9% accuracy with gradient boosting, 98.6% with decision trees, 99.7% with k-NN, and 99.6% with random forest.
- **Prostate Cancer Progression (2022)**: Predicted biochemical recurrence and seminal vesicle involvement using SVM, random forest, neural networks, RNN, and LSTM on clinical data warehouse. Delivered 82.7% accuracy for recurrence and 83.9% for seminal vesicle.
- **Abdominal Aortic Aneurysm Severity (2021)**: Employed inverse analysis with CNN and LSTM on digital patient datasets. Attained 99.91% for detection and 97.79% for severity.
- **Stroke Prevention and Poststroke Treatment (2021)**: Applied SVM on EEG datasets. Yielded 76% accuracy and 0.84 performance metric.
- **Fault Diagnosis Pattern (2019)**: Utilized deep neural networks and deep transfer learning (DFDD) on digital patient datasets. Achieved 98% accuracy with DFDD and 91.5% with standard DNN.
- **Ischemic Heart Disease Detection (2019)**: Implemented deep neural models on pulmonary tuberculosis diagnostic ECG database. Produced 85.8% of the data accuracy. [40,41,42,43,44,45,46]

The utilisation of AI algorithms and machine learning techniques, digital twins can analyse patient data to assess an individual's risk factors for specific diseases or health conditions with high levels of performance. This personalized risk assessment considers a patient's genetic profile, lifestyle choices, environmental factors, and other relevant data. With this information, health care providers can offer targeted preventive measures, early detection strategies, and personalized interventions to mitigate the identified risks. [45, 46]

5. CONCLUSION:

Digital twins represent a groundbreaking advancement in modern healthcare, bridging the gap between complex biological data and practical clinical decision-making. By integrating electronic health records, genomics, wearables, imaging, and real-time sensor data through artificial intelligence and machine learning, digital twins enable a shift from reactive, population-based medicine to proactive, personalized patient care. Their ability to simulate disease progression, predict individual health risks, and virtually test treatment options before clinical application significantly reduces medical errors and improves patient outcomes. Beyond individual care, they optimize hospital operations, enhance resource allocation, and provide safe training environments for healthcare professionals. While challenges surrounding data privacy, standardization, and regulatory frameworks remain, continued technological advancement and interdisciplinary collaboration will accelerate their integration into routine clinical practice. Ultimately, digital twins hold transformative potential to revolutionize healthcare delivery, making it smarter, safer, and deeply personalized for every patient.

7. ETHICAL APPROVAL

Not applicable

8. CONSENT TO PARTICIPATE

Not applicable

9. CONSENT TO PUBLISH
Not applicable

10. DATA AVAILABILITY STATEMENT
The data that supports findings are openly available

11. Authors contributions:
Dr. A. Ravi Kiran has contributed in design and review of the work. Boin Poojitha has been instrumental in collection of the data and preparation of the article. Alekula Reshma has given suggestion and contributed in article work. Imran has contributed in collection the data and suggestions for final work.

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