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Digital twins in oncology: From predictive modelling to personalised treatment strategies

David B. Olawade [a,b,c,*], Emmanuel O. Oisakede [d,e], Oluwakemi Jumoke Bello [f], Claret Chinenyenwa Analikwu [g], Eghosasere Egbon [h], Adeyinka Ojo [i]

[a] Department of Allied and Public Health, School of Health, Sport and Bioscience, University of East London, London E16 2RD, UK
[b] Department of Research and Innovation, Medway NHS Foundation Trust, Gillingham, Kent ME7 5NY, UK
[c] Department of Public Health, York St John University, London E14 2BA, UK
[d] Department of Clinical Oncology, Leeds Teaching Hospitals Trust, Leeds, UK
[e] Department of Health Research, University of Leeds, Leeds, UK
[f] The Clinical Research Centre, The London Clinic, 20 Devonshire Place, London W1G 6BW, UK
[g] Department of Microbiology, University Hospital Southampton NHS foundation Trust, Hampshire SO16 6YD, UK
[h] Department of Tissue Engineering and Regenerative Medicine, Faculty of Life Science Engineering, FH Technikum, Vienna, Austria
[i] Department of Artificial Intelligence and Data Factory, Capgemini plc, London EC4V 4HN, UK

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ABSTRACT

The digital twin (DT) concept, originating from engineering disciplines, has emerged as a transformative technology in healthcare, particularly in oncology. A digital twin creates a dynamic, virtual replica of a patient's physiological and pathological state, integrating multi-dimensional data to enable personalised cancer care. Despite growing interest, comprehensive reviews examining the breadth of DT applications in oncology remain limited. This narrative review aims to synthesise current evidence on digital twin applications in oncology, evaluate their potential to transform cancer care delivery, and identify challenges hindering clinical translation. A comprehensive literature search was conducted across PubMed, Scopus, Web of Science, and IEEE Xplore databases from inception to September 2025. Studies describing DT development, validation, or application in any cancer type were included. Grey literature, conference proceedings, and expert commentaries were also reviewed to capture emerging trends. Digital twins demonstrate applications across the cancer care continuum, including precision treatment selection, radiotherapy optimisation, drug development, immuno-oncology modelling, surgical planning, and survivorship care. Integration of multi-omics data, imaging biomarkers, and artificial intelligence enables dynamic simulation of tumour behaviour and treatment response. However, challenges persist in data integration, model validation, computational scalability, and ethical governance. Digital twin technology holds substantial promise for advancing precision oncology through predictive, personalised, and adaptive care strategies. Addressing current limitations through interdisciplinary collaboration and regulatory framework development is essential for clinical implementation.

1. Introduction

The heterogeneous nature of cancer characterised by diverse molecular profiles, varying treatment responses, and unpredictable disease trajectories, presents significant challenges in clinical management. Traditional one-size-fits-all treatment approaches have gradually given way to precision oncology, which seeks to tailor interventions based on individual patient characteristics. However, despite advances in molecular diagnostics and targeted therapies, predicting treatment outcomes and optimising therapeutic strategies remain formidable challenges in contemporary oncology practice.

The advent of digital health technologies has revolutionised healthcare delivery, with data-driven approaches increasingly informing clinical decisions. The integration of genomics, proteomics, radiomics, and electronic health records has generated unprecedented volumes of patient data. Yet, translating these complex, multi-dimensional datasets into actionable clinical insights remains a bottleneck for clinicians (Matheny et al., 2020). Conventional predictive

* Corresponding author at: Department of Allied and Public Health, School of Health, Sport and Bioscience, University of East London, London E16 2RD, UK.
E-mail address: d.olawade@uel.ac.uk (D.B. Olawade).

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models, whilst useful, are often static and fail to capture the dynamic nature of cancer progression and treatment response (Olawade et al., 2025). There is an urgent need for innovative computational frameworks that can synthesise diverse data streams, simulate disease trajectories, and enable real-time adaptation of treatment strategies.

Digital twin (DT) technology, originally developed in aerospace and manufacturing industries, has emerged as a promising solution to these challenges. A digital twin is defined as a dynamic, virtual representation of a physical entity in this case, a cancer patient that evolves in parallel with its real-world counterpart (Jones et al., 2020; Katsoulakis et al., 2024). In oncology, DTs aim to integrate multi-omics data, clinical history, imaging findings, and lifestyle factors to create patient-specific models that simulate tumour growth, predict therapeutic responses, and enable scenario testing. Unlike traditional predictive models, oncology DTs have the potential to continuously update based on new patient data, offering a dynamic framework for personalised cancer care (Jones et al., 2020). This paradigm shift from static prediction to dynamic simulation represents a fundamental advancement in precision oncology.

Recent years have witnessed growing interest in DT applications across medical specialties, with oncology emerging as a particularly promising domain. The complexity and heterogeneity of cancer, combined with the availability of rich multi-modal datasets, make oncology an ideal testing ground for DT technology. Pilot and proof-of-principle studies (especially in breast cancer) have demonstrated the feasibility of tumour- or patient-specific digital twins in predicting treatment responses and optimising treatment schedules (Wu et al., 2025). Artificial intelligence (AI) and machine-learning methods enhance the predictive capabilities of such DTs by enabling integration of imaging, mathematical modelling, and sometimes early-treatment data. However, evidence is limited for their use across all common cancer types, especially in terms of toxicity mitigation, and their translation into routine clinical practice remains constrained by technical, ethical, regulatory, and data challenges.

Current oncology practice lacks comprehensive, dynamic tools that can integrate diverse patient data to predict treatment outcomes and optimise therapeutic strategies in real time. Whilst precision medicine has made significant strides, most predictive models remain static and fail to capture the evolving nature of cancer. Digital twin technology offers a novel solution by creating dynamic, patient-specific models that aim to continuously update based on new data. However, evidence on DT applications in oncology is scattered across multiple disciplines, and a comprehensive synthesis of current applications is lacking. This narrative review addresses this gap by systematically examining DT applications across the cancer care continuum, from diagnosis to survivorship. The novelty of this review lies in its comprehensive coverage of diverse DT applications, critical evaluation of technical and ethical challenges, and identification of pathways for clinical translation. The primary aim is to synthesise evidence on digital twin applications in oncology, evaluate their transformative potential, and identify barriers to implementation. Specific objectives include: (1) describing the conceptual framework of oncology DTs; (2) reviewing current applications across cancer care domains; (3) analysing technical, ethical, and regulatory challenges; and (4) proposing future directions for research and clinical implementation.

2. Methods

2.1. Search strategy

A comprehensive literature search was conducted across four major databases: PubMed/MEDLINE, Scopus, Web of Science, and IEEE Xplore. The search covered all publications from database inception to September 2025. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to digital twins and oncology. The core search string was: ("digital twin*" OR "virtual patient*" OR "in silico model*" OR "computational model*" OR "patient-specific model*") AND ("oncology" OR "cancer" OR "neoplasm*" OR "tumour" OR "tumor" OR "malignancy") AND ("precision medicine" OR "personalised medicine" OR "treatment planning" OR "predictive model*").

2.2. Inclusion and exclusion criteria

Studies were included if they: (1) described the development, validation, or application of digital twin technology in any cancer type; (2) reported on computational modelling approaches for patient-specific cancer care; (3) discussed integration of multi-omics, imaging, or clinical data for cancer prediction; or (4) addressed technical, ethical, or regulatory aspects of DT implementation in oncology. Both original research articles and review papers were included. Exclusion criteria comprised: (1) studies focusing solely on population-level models without patient-specific components; (2) articles describing only general computational techniques without oncology applications; and (3) publications not available in English.

2.3. Data extraction and synthesis

Following duplicate removal, titles and abstracts were screened for relevance. Full-text articles of potentially eligible studies were retrieved and assessed against inclusion criteria. Given the narrative nature of this review, a qualitative synthesis approach was employed. Data extracted included: study design, cancer type, DT components (data sources, computational methods), clinical applications, validation approaches, reported outcomes, and identified challenges. Grey literature, including conference proceedings, technical reports, and expert commentaries, was also reviewed to capture emerging trends and ongoing initiatives. Thematic analysis was used to organise findings into coherent domains of DT application in oncology.

3. Concept and framework of digital twin in oncology

3.1. Defining digital twin in cancer care

The digital twin concept in oncology extends beyond simple predictive modelling to create a comprehensive, dynamic virtual representation of an individual patient's cancer journey. An oncology DT aims to integrate multiple data layers, genomic and molecular profiles, tumour histopathology, radiological imaging, clinical history, treatment records, and lifestyle factors, into a unified computational framework. This integration has the potential to enable the simulation of tumour behaviour under various scenarios, including different treatment regimens, timing of interventions, and disease progression pathways (Jones et al., 2020).

Central to the DT paradigm is the concept of bidirectional data flow. Unlike conventional models that provide one-time predictions, DTs aim to continuously receive real-world data from the patient and update their internal representations accordingly (Katsoulakis et al., 2024). When a patient undergoes imaging, receives treatment, or experiences disease progression, these data are fed back into the DT, refining its accuracy and enabling more precise predictions over time. This iterative refinement process mirrors the biological evolution of cancer and creates a learning system that becomes increasingly personalised to the individual patient. Fig. 1 illustrates the conceptual framework of digital twin technology in oncology, demonstrating how diverse data streams are integrated to create a dynamic virtual patient representation.

3.2. Technical architecture and data integration

The technical architecture of an oncology DT typically comprises three core components: the data layer, the computational layer, and the interface layer. The data layer aggregates information from electronic

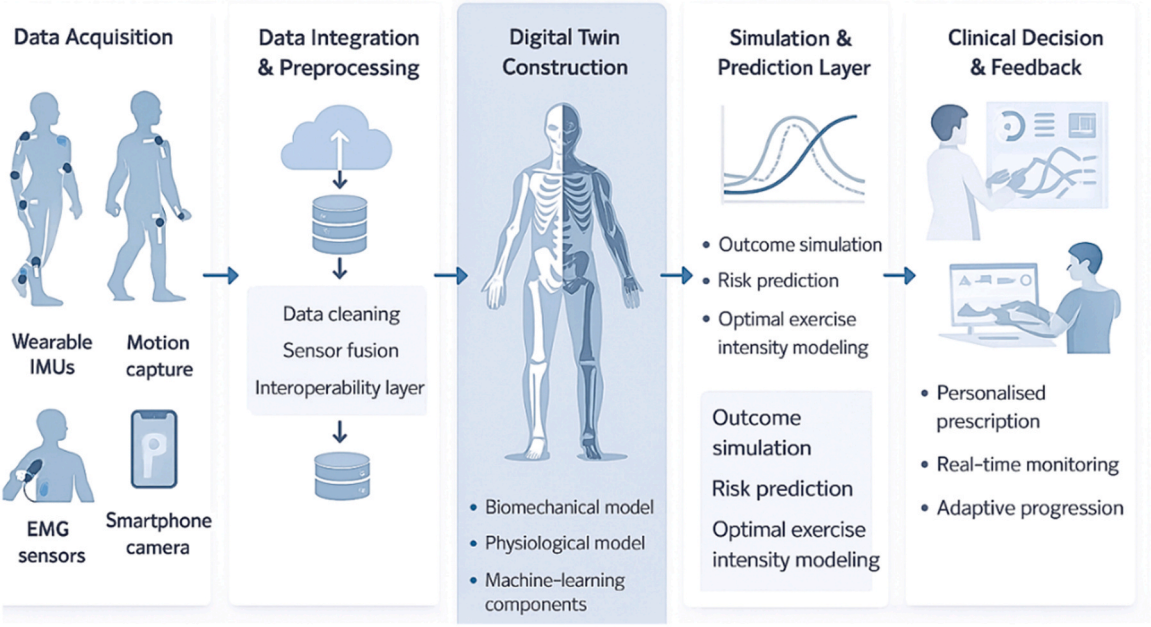

Fig. 1. Conceptual framework of digital twin technology in oncology showing bidirectional data flow between the real patient and virtual representation. The system integrates multi-omics data, clinical records, imaging, and lifestyle factors through computational layers to enable predictive modeling and personalized treatment optimization. Not all components are currently implemented in all oncology digital twin platforms; the figure represents an aspirational integrated framework.

health records, laboratory information systems, picture archiving and communication systems (PACS), genomic databases, and patient-reported outcomes. Data harmonisation and standardisation are critical at this stage, as information originates from heterogeneous sources with varying formats and quality (Mollica et al., 2024).

The computational layer employs a hybrid approach combining mechanistic modelling and machine learning. Mechanistic models, based on biological principles and differential equations, simulate tumour growth dynamics, drug pharmacokinetics, and radiation dose-response relationships (Laubenbacher et al., 2024; Kolokotroni et al., 2024; Coveney et al., 2025). Machine learning algorithms, including deep neural networks and ensemble methods, complement mechanistic models by identifying complex patterns in high-dimensional data and making predictions where biological mechanisms are incompletely understood (Mollica et al., 2024; Ștefănigă et al., 2024). The integration of these approaches aims to create a robust framework capable of both interpretable simulation and accurate prediction.

A critical consideration in DT architecture is uncertainty quantification and error propagation. Given that digital twins integrate data from diverse sources, each with inherent measurement errors, missing values, and variability, understanding how uncertainties propagate through the computational models is essential for reliable clinical decision-making (Kemkar et al., 2024; Giansanti and Morelli, 2025). Probabilistic methods, Bayesian inference frameworks, and ensemble modelling approaches are increasingly being incorporated to characterise prediction uncertainty and provide confidence intervals alongside point estimates (Dhiman et al., 2022; Amasiadi et al., 2025). Without explicit uncertainty quantification, clinicians may be unable to assess the reliability of DT predictions, potentially leading to inappropriate clinical decisions. Future DT systems must implement robust uncertainty propagation methods to ensure that confidence in predictions aligns with their actual accuracy.

The interface layer provides clinicians with intuitive visualisations and decision-support tools. Interactive dashboards display tumour progression trajectories, treatment response predictions, and risk stratification results. Scenario-testing modules allow oncologists to explore "what-if" questions, such as the predicted outcome of delaying surgery or switching from chemotherapy to immunotherapy (Wentzel et al., 2024). This layer translates complex computational outputs into actionable clinical insights, facilitating shared decision-making between healthcare providers and patients.

3.3. *Multi-omics integration and systems biology*

Modern oncology DTs increasingly aim to incorporate multi-omics data, reflecting the multi-layered complexity of cancer biology (Kolokotroni et al., 2024; Moztarzadeh et al., 2023). Genomic, transcriptomic, proteomic, and metabolomic data each contribute distinct biological insights: genomic data identify driver mutations, copy number variations, and mutational signatures that influence therapeutic vulnerability, whilst transcriptomic analysis reveals gene expression patterns associated with treatment response and resistance mechanisms (Kolokotroni et al., 2024). Proteomic and metabolomic data provide insights into functional consequences of genetic alterations and metabolic reprogramming within tumours (Aghamiri and Amin, 2025).

Integrating these diverse omics layers requires systems biology approaches that model molecular interactions, signalling pathways, and regulatory networks. Pathway analysis tools identify dysregulated biological processes, whilst network modelling reveals potential therapeutic targets and combination strategies (Aghamiri and Amin, 2025). The incorporation of single-cell sequencing data has added another dimension, enabling DTs to capture intra-tumoural heterogeneity and predict the emergence of resistant subclones under therapeutic pressure (Li et al., 2022a). These advances are exemplified by recent AI-driven Molecular Twin platforms that integrate multi-omic data to predict outcomes and therapeutic responses in cancer (Osipov et al., 2024).

4. Applications of digital twins in oncology

The following sections examine how digital twin technology is being applied across different stages of cancer care, from initial treatment selection through long-term survivorship monitoring. Digital twins demonstrate applications across the cancer care continuum (Fig. 2), with the potential to enable precision medicine approaches from initial diagnosis through long-term survivorship.

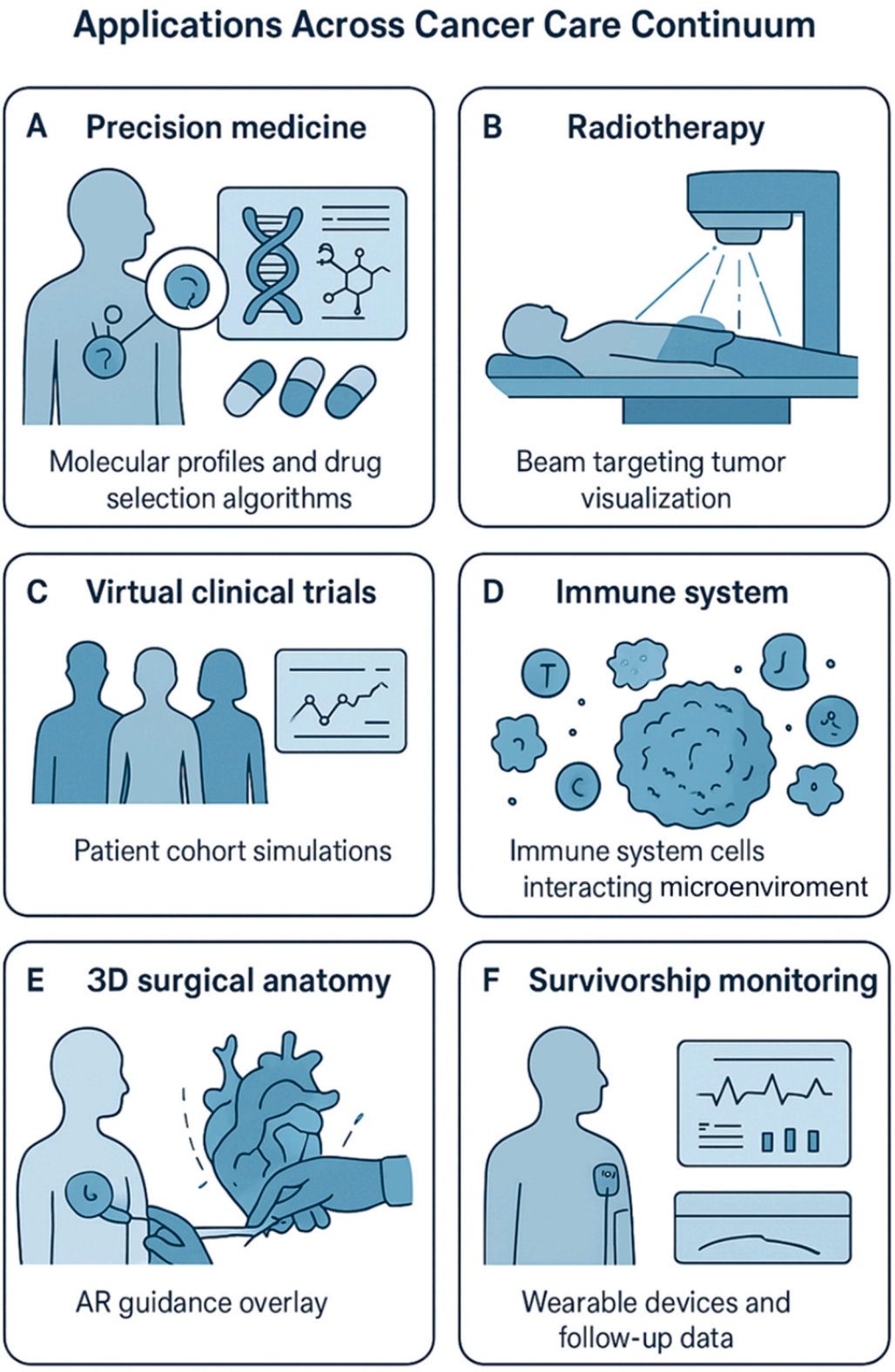

Fig. 2. Digital twin applications across the cancer care continuum. Six key application domains are illustrated: (A) Precision treatment selection with drug response prediction, (B) Radiotherapy planning and dose optimization, (C) Drug development through in silico trials, (D) Immuno-oncology modeling of tumor microenvironment, (E) Surgical planning with 3D visualization, and (F) Survivorship care with long-term monitoring. The figure illustrates potential applications currently at varying stages of development and clinical validation.

4.1. Precision oncology and personalised treatment selection

One of the most promising applications of DT technology lies in precision treatment selection, where virtual simulations aim to guide therapeutic decision-making. By integrating a patient's molecular profile with tumour growth kinetics and treatment response data, DTs have the potential to predict the efficacy and toxicity of various therapeutic options. In breast cancer, DTs have been developed to simulate responses to different chemotherapy regimens and targeted agents. For example, an MRI-based digital twin calibrated to individual imaging data predicted pathological complete response (pCR) in triple-negative breast cancer and was used to optimise neoadjuvant chemotherapy schedules for each patient (Wu et al., 2025). These models typically incorporate tumour receptor status, genomic alterations, and clinical covariates to rank treatment options by predicted outcome (Mollica et al., 2024).

In lung cancer, DTs are being explored for modelling response to targeted therapies (e.g., EGFR inhibitors) by integrating mutation profiles, imaging, and resistance mechanisms (Gevaert et al., 2017; Wang et al., 2019). Preliminary systems point toward the ability to anticipate treatment failure or suggest optimal sequencing of lines of therapy. However, large prospective validations comparing DT-guided selection versus standard care remain scarce.

Beyond regimen selection, DTs also have the potential to enable dose optimisation by simulating relationships between drug exposure, organ function, and therapeutic effect. For patients with renal or hepatic impairment, DT-based pharmacokinetic models aim to personalise dosing schedules to maintain efficacy while minimising toxicity, particularly for narrow-therapeutic-index drugs such as platinum-based agents and combination therapies (Prunella et al., 2025).

A landmark adaptive clinical trial in metastatic castrate-resistant prostate cancer (mCRPC) illustrated how DT-inspired adaptive therapy principles can improve outcomes. During this trial, abiraterone treatment was halted once prostate-specific antigen (PSA) levels decreased by 50 % and restarted when PSA levels returned to baseline (Zhang et al., 2022). This cyclical, feedback-controlled approach maintained competition between drug-sensitive and resistant tumour populations, delaying resistance and extending disease control. This finding demonstrates how mechanistic evolutionary DT models could capture individual tumour growth dynamics, interactions with therapy, and simulation of retreatment timing.Tables 1–3

4.2. Radiotherapy planning and optimisation

Radiation oncology has emerged as a frontrunner in clinical DT implementation, given its quantitative nature and reliance on imaging and computational dose calculation. Modern DTs in radiotherapy integrate anatomical imaging (CT, MRI), functional imaging (PET), tumour delineation, and normal tissue constraints to optimise treatment planning (Chaudhuri et al., 2023). By simulating thousands of potential dose distributions, these systems identify plans that maximise tumour coverage whilst sparing critical organs such as the heart, lungs, and spinal cord.

Adaptive radiotherapy, a key application of DT technology, enables real-time plan modification based on changes in tumour size, shape, or position during treatment. For patients with head and neck cancer, significant weight loss during radiotherapy can alter the relationship between the tumour and surrounding anatomy (Noble et al., 2019). DTs continuously monitor these changes through repeat imaging and automatically generate revised treatment plans that maintain optimal dose distribution. This approach has been shown to reduce acute toxicity and improve local control rates.

DTs also have the potential to facilitate prediction of radiation-induced toxicity by modelling dose-response relationships for normal tissues (Chaudhuri et al., 2023). For breast cancer patients receiving radiotherapy, cardiac dose is a critical concern for long-term cardiovascular health. DTs aim to estimate the lifetime risk of coronary events based on individualised heart dose distributions, patient age, and cardiovascular risk factors (Thangaraj et al., 2024). This enables clinicians to balance oncological benefit against potential late toxicity, particularly in young patients with excellent prognosis.

4.3. Drug development and in silico clinical trials

The pharmaceutical industry faces escalating costs and prolonged timelines in oncology drug development, with the average cost of bringing a new cancer drug to market exceeding $2 billion, which may even fail to reach the market (Austin and Hayford, 2021). DT technology offers a paradigm shift by enabling in silico clinical trials, where virtual patient cohorts are used to test drug efficacy and toxicity before progressing to human trials. These virtual cohorts are generated by sampling from distributions of patient characteristics derived from real clinical data, creating diverse populations that reflect the heterogeneity encountered in actual practice (Surendran et al., 2023).

In silico trials allow rapid exploration of multiple scenarios: different dosing schedules, combination regimens, and patient selection criteria. For example, DTs have been used to optimise the design of immunotherapy trials by identifying biomarkers that predict response to certain chemotherapeutic agents (Giansanti and Morelli, 2025; Moingeon et al., 2023). By simulating trial outcomes across various patient stratification strategies, pharmaceutical companies can design more efficient trials with higher success rates and smaller sample sizes. Regulatory agencies, including the FDA and EMA, are increasingly receptive to incorporating

Table 1
Applications of Digital Twins Across the Oncology Care Continuum.

Clinical Domain	Specific Applications	Key Data Inputs	Computational Methods	Clinical Outcomes
Precision Treatment Selection (Bordukova et al., 2023)	Drug response prediction, regimen ranking, dose optimization	Genomics, drug levels, tumour kinetics, comorbidities	Machine learning, pharmacokinetic models, response prediction algorithms	Improved progression-free survival, reduced toxicity
Radiotherapy Planning (Sumini et al., 2024)	Dose distribution optimisation, normal tissue sparing, adaptive planning	CT/MRI imaging, tumour geometry, tissue density, organ motion	Monte Carlo simulation, dose-volume modelling, optimisation algorithms	Reduced radiation toxicity, improved local control
Drug Development (Jiang et al., 2023; Chasseloup et al., 2023; Kleeberger, 2025)	Virtual clinical trials, biomarker identification, patient stratification	Multi-omics data, clinical trial databases, drug properties	Population modelling, Bayesian inference, virtual cohort generation	Accelerated drug approval, reduced trial costs
Immuno-oncology (Wang et al., 2024)	Checkpoint inhibitor response prediction, combination therapy design	Tumour microenvironment profiling, immune markers, imaging	Agent-based modelling, immune system simulation, network analysis	Enhanced immunotherapy response rates
Surgical Planning (Mekki et al., 2025; Shu et al., 2023)	Resection boundary planning, complication prediction, operative guidance	3D imaging, tumour vasculature, organ anatomy	Computational fluid dynamics, biomechanical modelling, augmented reality	Reduced surgical complications, improved precision
Survivorship Care (Sarp et al., 2023)	Recurrence/progression risk assessment, toxicity monitoring, quality of life prediction	Follow-up imaging, biomarkers, patient-reported outcomes	Longitudinal modelling, risk prediction algorithms, symptom tracking	Early response tracking, improved quality of life

Table 2
Major Challenges in Digital Twin Implementation and Potential Solutions.

Challenge Domain	Specific Issues	Technical Barriers	Potential Solutions	Timeframe
Data Integration (Mollica et al., 2024; HL7 International, 2024)	EHR fragmentation, format heterogeneity, missing data	Limited interoperability, inconsistent standards	FHIR/HL7 standard adoption, federated learning, automated data pipelines	2–5 years
Model Validation (Rudin, 2019; Fuse et al., 2025)	Lack of prospective trials, black-box algorithms, regulatory uncertainty	Computational cost, limited interpretability	Explainable AI, adaptive licensing, prospective RCTs	5–10 years
Computational Resources (Es-haghi et al., 2024)	High processing demands, long runtimes, infrastructure costs	Scalability limitations, cloud security concerns	High-performance computing, reduced-order models, edge computing	3–7 years
Ethical Governance (Huang et al., 2022)	Data privacy, algorithmic bias, informed consent	Regulatory compliance, representation gaps	Diverse training data, continuous bias monitoring, dynamic consent frameworks	Ongoing
Clinical Acceptance (Zackoff et al., 2024; Jawad et al., 2022)	Healthcare providers and Patient acceptance, workflow integration, training needs	Change management, workforce capacity	User-friendly interfaces, clinical champion programmes, education initiatives	3–5 years
Equity and Access (Strigari et al., 2025)	Resource-limited settings, digital divide, cost barriers	Infrastructure gaps, affordability	Open-source platforms, simplified models, capacity-building programmes	10 + years

Table 3
Cancer-Specific Digital Twin Applications and Maturity Levels.

Cancer Type	Primary DT Applications	Key Biomarkers Integrated	Validation Status	Clinical Implementation	Maturity Level
Breast Cancer (Wu et al., 2025)	Treatment-response prediction during neoadjuvant chemotherapy using MRI-based digital twins that model tumour growth dynamics and optimise dosing schedules	MRI imaging, tumour volume kinetics, regimen type, treatment cycles	Retrospective / proof-of-concept validation in triple-negative breast cancer; AUC ≈ 0.82	Pilot programmes in research settings	Intermediate
Glioblastoma (High-Grade Glioma) (Chaudhuri et al., 2023)	Predictive DTs for radiotherapy optimisation under uncertainty, integrating patient-specific growth models and imaging data	MRI features, tumour heterogeneity, mechanistic growth equations	*In silico* cohort validation; demonstrates feasibility and clinical potential	Research / academic centres	Early-Intermediate
Colorectal Cancer (Li et al., 2022b)	Deep-learning prognostic "molecular twin" models predicting survival benefit from adjuvant chemotherapy in stage II/III CRC	Histology (H&E), clinical variables, survival outcomes	Retrospective internal/external validation on multi-institutional datasets	Research setting	Early-Intermediate
Prostate Cancer (Camacho-Gomez et al., 2025)	Physics-informed ML DT reconstructing tumour growth trajectories from PSA kinetics for therapy monitoring	PSA kinetics, tumour vascularity, patient-specific parameters	Retrospective validation in clinical PSA datasets	Early adopter institutions	Early
Melanoma (Gschwind and Ossowski, 2025; Abbott et al., 2021)	Multi-omics and radiomic twin-like models predicting immune-checkpoint inhibitor response	TMB, PD-L1 expression, neoantigen burden, radiomic features	Retrospective cohorts; early prospective studies underway	Academic oncology centres	Early-Intermediate
Pancreatic Cancer (Osipov et al., 2024)	"Molecular twin" platform integrating multi-omic profiles to simulate therapy outcomes and survival prediction	Genomic and transcriptomic signatures, CA19–9, clinical outcomes	Proof-of-concept; validated retrospectively on trial datasets	Research programmes	Early-Intermediate
Ovarian, Pancreatic or Breast Cancer (Cavallo, 2024; Griffiths et al., 2024)	Simulation of therapeutic responses to chemotherapy using FarrSight®-Twin across historical trial data	Clinical data, large gene panels, whole-exome and transcriptome sequencing	Retrospective validation using blinded and unblinded simulations across 8 phase II/III trials	Research / pilot phase; simulation-based validation only	Early

in silico evidence into drug approval pathways, particularly for rare cancers where large-scale trials are infeasible (Pappalardo et al., 2019).

Beyond clinical trial design, DTs have the potential to accelerate biomarker discovery by identifying molecular signatures associated with treatment response (Rodriguez et al., 2021). Machine learning models analyse multi-omics data from virtual patient cohorts to predict which genetic alterations, pathway activations, or immune profiles correlate with drug sensitivity (Liu et al., 2025). These biomarkers can then be validated in smaller, focused clinical studies, streamlining the path to personalised therapy.

4.4. Immuno-oncology and tumour microenvironment modelling

The complexity of immune system-tumour interactions presents both opportunities and challenges for DT development. Immunotherapy response depends on multiple factors: tumour mutational burden, neoantigen presentation, immune cell infiltration, checkpoint molecule expression, and immunosuppressive signals within the tumour microenvironment. DTs in immuno-oncology aim to integrate these elements to predict which patients will benefit from checkpoint inhibitors, adoptive cell therapies, or cancer vaccines.

Agent-based modelling, a technique where individual cells (tumour cells, T cells, macrophages) are simulated as discrete entities, has proven valuable for immuno-oncology DTs. These models capture spatial relationships, cell-cell interactions, and temporal dynamics of the immune response. By simulating the effects of checkpoint inhibitors on the tumour microenvironment, DTs have the potential to predict response likelihood and optimal treatment timing. For example, Mongeon et al. (2024) used a spatial agent-based model (ABM) initialised with patient-derived data, oncolytic virus, and combination therapies/immune checkpoint inhibitors to model immune responses in glioblastoma. Their simulations identified factors that influenced the success of immune checkpoint inhibitors and suggested how spatial immune cell density could impact treatment efficacy. Other multiscale ABMs have been developed to capture how neoantigen expression, immune checkpoint signalling (e.g., PD-1/PD-L1), and tumour growth affect response to immunotherapy. These models can also simulate the effects of combination strategies, such as checkpoint inhibitors with chemotherapy or oncolytic viruses (Gong et al., 2017; Norton et al., 2019). Such modelling approaches offer a promising direction for rational design of immuno-oncology trials by narrowing down treatment combinations and patient selection strategies prior to human studies.

4.5. Surgical oncology and operative planning

Surgical oncology has benefited from DT technology through enhanced preoperative planning and intraoperative guidance. Patient-specific 3D models, reconstructed from CT or MRI imaging, allow surgeons to visualise tumour location, size, and relationship to critical structures such as blood vessels and nerves. For hepatobiliary cancers, where tumour proximity to vascular structures determines resectability, DTs enable detailed assessment of surgical anatomy and prediction of postoperative liver complications (Golse et al., 2021).

Augmented reality (AR) integration with DTs has revolutionised intraoperative navigation. Surgeons wearing AR headsets can visualise the patient's digital twin superimposed on the operative field, providing real-time guidance during tumour resection. This technology has proven particularly valuable in minimally invasive surgery (Doornbos et al., 2024), where tactile feedback is limited and spatial orientation challenging. Future applications in surgery could explore AR-guided DT navigation with a view to improving resection margins and reducing operative time.

Predictive modelling of surgical complications represents another application domain. DT frameworks are being proposed that could integrate patient comorbidities, tumour characteristics, and surgical complexity to simulate or predict postoperative physiological outcomes and risks of complications. For example, DT models have been used to forecast post-hepatectomy portal hypertension (Golse et al., 2021). Similarly, deep learning models combining multidimensional patient data accurately predict complication risk across different types of liver pathology including liver malignancy following major liver resection (Xu et al., 2023). This information facilitates shared decision-making, allowing patients to make informed choices about surgical versus non-surgical treatment options based on personalised risk assessments.

4.6. Survivorship care and long-term monitoring

The growing population of cancer survivors, especially those living beyond five years after diagnosis, faces ongoing risks of recurrence, secondary malignancies, and treatment-related late effects. DTs and related AI/digital health technologies are being investigated to support survivorship care via integration of imaging biomarkers, clinical and biomarker data, and patient-reported outcomes in order to improve detection of relapse or complications.

Wearable devices and mobile health applications have demonstrated benefits in survivorship care in areas such as increasing physical activity, improving quality of life, and monitoring symptoms, though real-time incorporation into DTs to detect recurrence has not yet been robustly validated. For instance, wearable physical activity trackers in breast cancer survivors improve activity levels and health-related outcomes (Pan et al., 2023). More sophisticated models have been developed to track the risk of breast cancer recurrence. For example, radiomics models using mammography (and combining imaging features with clinical risk factors) have been developed to predict recurrence risk (Mao et al., 2021), though not yet in a framework clearly labelled as a "digital twin" integrating continuous wearable / patient-reported outcome (PRO) data with imaging and biomarkers.

Similarly, in colorectal cancer surveillance, AI-aided detection (AIAD) methods during colonoscopy increase adenoma detection rates, which could influence the timing of subsequent surveillance intervals (Ashat et al., 2021). However, evidence of DTs incorporating serial biomarker (carcinoembryonic antigen) (CEA) measurements plus colonoscopy findings explicitly predicting new lesions is not yet clearly established.

Quality of life (QoL) prediction is being explored: digital health tools are being used to track patient-reported outcomes, treatment side effects, fatigue, and physical function in survivorship (Pan et al., 2022), but modelling trajectories for specific toxicities (e.g., neuropathy after chemotherapy or radiotherapy) within DT systems remains underexplored.

5. Challenges and limitations in digital twin implementation

The implementation of digital twins in oncology faces multiple interconnected challenges (Fig. 3), requiring coordinated technical, regulatory, and organisational solutions across different timeframes.

5.1. Data integration, quality, and interoperability

The promise of oncology DTs hinges on seamless integration of diverse data sources, yet significant barriers impede this goal. Electronic health record (EHR) systems remain fragmented, with limited interoperability across institutions and countries. Data formats vary widely: genomic data may be stored in VCF files, imaging data in DICOM format, and clinical data in proprietary EHR schemas. Harmonising these heterogeneous data streams requires substantial computational infrastructure and adherence to data standards such as Fast Healthcare Interoperability Resources (FHIR) and Health Level Seven (HL7).

Data quality poses an equally significant challenge. Missing data are ubiquitous in clinical datasets, with incomplete follow-up, inconsistent recording practices, and variable data capture across institutions. Oncology DTs are sensitive to data quality issues, as missing or erroneous inputs can propagate through computational models and generate inaccurate predictions (Katsoulakis et al., 2024). Rigorous data curation, validation protocols, and imputation strategies are essential but resource-intensive. Furthermore, historical biases in clinical data, such as underrepresentation of certain ethnic groups or socioeconomic strata, can be perpetuated by DT models, raising concerns about equitable access to precision oncology.

Real-time data capture presents additional technical hurdles. For DTs to function as truly dynamic systems, they must receive continuous updates from multiple sources: imaging scans, laboratory results, patient-reported symptoms, and wearable device outputs. Establishing automated data pipelines that feed information into DT platforms in real time requires investment in information technology infrastructure and integration with existing clinical workflows. Many healthcare institutions, particularly in resource-limited settings, lack the technical capacity to implement such systems.

5.2. Model validation and clinical acceptance

A critical barrier to DT adoption in clinical oncology is the lack of robust validation frameworks. Whilst many DT models demonstrate impressive performance on retrospective datasets, their accuracy in prospective, real-world settings remains uncertain. Clinical validation requires demonstrating that DT-guided decisions improve patient outcomes compared to standard care, a time-consuming and expensive process. Randomised controlled trials comparing DT-guided treatment selection against conventional approaches are scarce, and those that exist have shown mixed results (Wu et al., 2025; Kovatchev et al., 2025).

Clinicians remain cautious about adopting DT recommendations without understanding the underlying reasoning. Black-box machine learning models, whilst often accurate, lack transparency and input from experts, making it difficult for oncologists to trust their predictions (Mohamed et al., 2024). Explainable AI (XAI) techniques, which aim to provide interpretable explanations for model outputs, are increasingly being integrated into DTs to enhance clinical acceptance. However, balancing model accuracy with interpretability remains a fundamental trade-off in DT design.

Regulatory pathways for DT systems are still evolving. In practice, DTs and other AI/machine learning (ML)-driven clinical decision-support tools are generally treated under existing Software as a Medical Device (SaMD) framework, which requires risk classification, clinical evaluation, and post-market surveillance. Regulators are increasingly emphasising total-product-lifecycle approaches (including pre-market

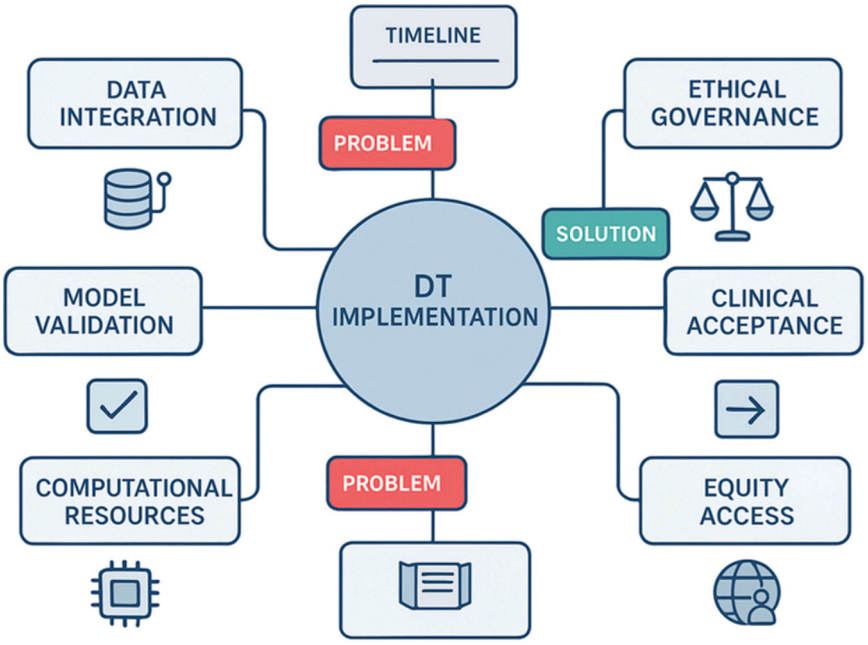

Fig. 3. Major challenges in digital twin implementation and potential solution pathways. The framework categorises barriers into six domains: data integration and interoperability, model validation and clinical acceptance, computational complexity, ethical governance, clinical workflow integration, and equity considerations. Each challenge domain is paired with corresponding technical and organisational solutions, with implementation timelines indicated. Current implementation maturity varies significantly across domains.

evidence plus post-market monitoring and change-control plans) for AI-enabled software rather than a single, one-time approval. For example, the U.S. FDA has issued draft guidance on AI-enabled device software functions that stresses lifecycle management and marketing-submission recommendations, while international bodies and national agencies (EMA, IMDRF, MHRA) have published reports and position papers calling for iterative evaluation, good machine-learning practice, and stronger post-market oversight of continuously updating algorithms (FDA, 2024; European Medicines Agency, 2025; Dubowik, 2024). Nevertheless, no single consensus standard yet exists for validation of continuously learning DTs (e.g., how to demonstrate ongoing safety/effectiveness after model updates), and regulators continue to refine expectations for change control, transparency, and real-world performance monitoring.

5.3. Computational complexity and scalability

The computational demands of patient-specific oncology DTs are substantial. High-fidelity simulation of tumour growth, treatment response, and immune interactions requires significant processing power, memory, and storage capacity. For institutions serving large patient populations, creating and maintaining individualised DTs for every cancer patient is computationally prohibitive. Cloud computing and high-performance computing clusters offer potential solutions, but concerns about data security and privacy in cloud environments (Sun et al., 2014) have slowed adoption.

Model complexity also affects runtime, a critical consideration for clinical decision-making. Clinicians require timely predictions ideally within hours or days to inform treatment planning. However, detailed mechanistic models incorporating multi-omics data and spatiotemporal tumour dynamics may take days or weeks to run. Balancing model fidelity with computational efficiency is an ongoing challenge. Reduced-order models and surrogate modelling techniques offer compromise solutions by simplifying complex simulations whilst retaining predictive accuracy (Es-haghi et al., 2024).

Scalability extends beyond computation to encompass personnel requirements. Developing, maintaining, and interpreting DTs demands expertise in oncology, computational biology, data science, and software engineering (Giansanti and Morelli, 2025). Few institutions possess the multidisciplinary teams needed to support DT initiatives, and training programmes to build this workforce capacity are nascent. Without addressing these human resource challenges, widespread DT implementation will remain limited to a handful of well-resourced academic centres.

5.4. Ethical, legal, and governance considerations

The use of DTs in oncology raises complex ethical questions around data privacy, informed consent, and algorithmic bias. Patient data used to construct DTs are highly sensitive, encompassing genomic information, medical history, and lifestyle factors. Ensuring robust data protection mechanisms that comply with regulations such as the General Data Protection Regulation (GDPR) in Europe and the Health Insurance Portability and Accountability Act (HIPAA) in the United States is paramount (Shah, 2023). However, the dynamic nature of DTs, where data are continuously updated and shared across platforms complicates traditional consent frameworks, which assume static data collection at a single time point.

Algorithmic bias represents another ethical concern (Huang et al., 2022). If training datasets used to develop DT models disproportionately represent certain demographics, the resulting systems may perform poorly for underrepresented groups. For example, if a DT is trained primarily on data from Caucasian patients, its predictions may be less accurate for patients of African, Asian, or Hispanic descent. This could exacerbate existing health disparities rather than alleviate them. Ensuring diverse and representative training datasets, along with ongoing monitoring for bias, is essential for equitable DT implementation.

Liability issues arise when autonomous systems like DT-guided decisions influence patient care (Vellinga, 2023). If a DT recommends a treatment that results in adverse outcomes, determining responsibility is complex. Is the clinician liable for following the DT's recommendation? Is the institution responsible for deploying an insufficiently validated system? Or does liability rest with the DT developers or algorithm

providers? Legal frameworks have not kept pace with these technological advances, creating uncertainty that may discourage DT adoption.

6. Future directions and emerging trends

6.1. Integration with advanced artificial intelligence

The next generation of oncology DTs will leverage cutting-edge AI architectures, including transformer models, graph neural networks, and reinforcement learning. Transformer models, which have revolutionised natural language processing, are being adapted for analysing sequential clinical data such as longitudinal imaging and treatment histories (Nerella et al., 2024). These models can identify subtle patterns in disease progression that escape traditional statistical methods. Graph neural networks excel at modelling molecular interactions and biological pathways, making them ideal for integrating multi-omics data into DTs (Isah et al., 2024).

Reinforcement learning, where algorithms learn optimal strategies through trial-and-error simulation, holds particular promise for treatment optimisation. A reinforcement learning-based DT could simulate thousands of treatment scenarios, learning which sequences of therapies maximise survival whilst minimising toxicity. For example, a study developed a DT model for head-and-neck cancer that utilised sequential deep reinforcement learning to personalise treatment plans, balancing tumour control and toxicity risk (Wentzel et al., 2024). Additionally, another study applied deep Q-network-based reinforcement learning to automate proton therapy replanning for head-and-neck cancer patients, achieving improved plan quality compared to manual methods (Madondo et al., 2025). As these technologies mature, their integration into clinical DTs will enable more sophisticated decision support.

Federated learning represents another transformative development. This approach allows DT models to be trained across multiple institutions without sharing raw patient data, addressing privacy concerns whilst enabling learning from diverse populations (Sheller et al., 2020). Federated oncology DTs could aggregate knowledge from thousands of patients across different hospitals and countries, improving model generalisability and reducing bias.

6.2. Real-world data and continuous learning systems

Future DTs will increasingly aim to incorporate real-world data from sources beyond traditional clinical systems. Wearable devices that monitor heart rate, activity levels, and sleep patterns have the potential to provide continuous physiological data that reflect treatment tolerance and recovery. Smartphone applications enable patient-reported outcome capture, documenting symptoms, functional status, and quality of life in real time. Social determinants of health, such as housing stability, nutrition access, and environmental exposures, are increasingly recognised as critical factors influencing cancer outcomes and should be integrated into comprehensive DTs.

Population cancer registries and observational databases offer valuable real-world evidence for DT training and validation. These datasets capture outcomes from diverse patient populations treated in routine practice, complementing the highly selected cohorts typical of clinical trials. Linkage between DT platforms and national cancer registries could enable continuous model refinement as new treatment patterns and outcomes emerge.

The vision of a continuously learning DT system, one that improves its predictions as it accumulates experience, requires careful governance. Mechanisms for version control, model retraining triggers, and re-validation thresholds must be established to ensure that model updates enhance rather than degrade performance. Regulatory frameworks that accommodate continuous learning whilst maintaining patient safety are essential for realising this vision.

6.3. Standardisation, interoperability, and regulatory pathways

Achieving wider uptake of DTs depends on establishing shared standards for data representation, device/software attributes, digital endpoints, and model performance metrics. For example, the Clinical Data Interchange Standards Consortium (CDISC) is developing standards for digital health technologies in clinical research and has partnered with the Digital Medicine Society (DiMe) to standardise device attributes, endpoints, and related best practices (CDISC, 2024).

Regulatory agencies face the challenge of evaluating technologies that evolve over time. Traditional regulatory models, based on fixed versions of medical devices or drugs, are ill-suited to adaptive DT systems. The FDA's Digital Health Center of Excellence and the EMA's Innovation Task Force are exploring frameworks for continuous oversight, including post-market surveillance mechanisms that monitor DT performance in real-world use (Gilroy et al., 2024). Collaborative approaches involving regulators, healthcare providers, and DT developers will be essential for establishing efficient yet rigorous approval pathways.

Intellectual property considerations also merit attention. As DT technology matures, questions arise about ownership of patient-specific models, algorithm licensing, and data rights. Clear frameworks that balance innovation incentives with patient autonomy and data sovereignty will facilitate sustainable DT ecosystem development.

6.4. Equity, access, and global health perspectives

Ensuring equitable access to DT technology is a moral imperative and practical necessity. Currently, DT development is concentrated in high-income countries with advanced research infrastructure. However, the global cancer burden disproportionately affects low- and middle-income countries (LMICs), where resources for cancer care are limited and mortality rates higher. Adapting DT frameworks for resource-constrained settings requires consideration of available infrastructure, data availability, and local capacity.

Simplified DT models that require less computational power and fewer data inputs may be more appropriate for LMICs. Mobile health platforms can facilitate data collection in settings where EHR systems are absent. Capacity-building initiatives that train local data scientists and clinicians in DT methodology will foster sustainable implementation. International partnerships and open-source DT platforms can democratise access, ensuring that precision oncology benefits are not confined to affluent populations.

Addressing the digital divide within high-income countries is equally important. Vulnerable populations, including rural residents, elderly patients, and socioeconomically disadvantaged groups, may lack access to the technologies that enable DT-based care, such as smartphones, internet connectivity, and digital literacy. Health equity considerations must be embedded in DT design and deployment strategies to prevent technology from exacerbating existing disparities.

7. Limitations of this review

This narrative review has several limitations that should be acknowledged. First, the narrative review methodology, whilst appropriate for synthesising broad and heterogeneous literature, lacks the systematic rigour and predefined protocols of systematic reviews. Selection bias may have influenced which studies were included, and the absence of quantitative synthesis limits the ability to draw definitive conclusions about DT effectiveness. Future systematic reviews with meta-analyses would provide more robust evidence on specific DT applications.

Second, the rapidly evolving nature of DT technology means that recent developments may not yet be reflected in published literature. Conference proceedings, preprints, and grey literature were included to capture emerging trends, but these sources may lack the peer-review

scrutiny of journal articles. Additionally, proprietary DT systems developed by commercial entities may not be fully described in the public domain, limiting a comprehensive assessment of the field's state.

Third, the review's scope, covering applications across the entire cancer care continuum, necessitated breadth over depth. Each application domain (radiotherapy, drug development, surgical planning, etc.) could warrant dedicated in-depth reviews. The high-level synthesis provided here may not capture all nuances and technical details relevant to specialists in each subdomain.

Fourth, most studies reviewed were retrospective or proof-of-concept investigations conducted in research settings. Evidence from prospective clinical trials demonstrating improved patient outcomes with DT-guided care remains limited. The translation gap between research prototypes and clinically validated systems is substantial, and this review cannot fully address whether DT technology will deliver on its promise in routine practice.

Fifth, the review focused predominantly on literature from high-income countries, reflecting the current geographical distribution of DT research. Perspectives from LMICs and underserved populations are underrepresented, limiting the generalisability of findings. Additionally, language restrictions (English-only publications) may have excluded relevant studies published in other languages.

Finally, the technical complexity of DT systems means that many implementation details, such as specific algorithms, validation methods, and computational architectures, were not fully accessible from published literature. This limits the ability to critically evaluate model robustness and reproducibility. Greater transparency in DT methodology, including code and data sharing, would enhance future reviews.

8. Conclusion

Digital twin technology represents a paradigm shift in oncology, offering a dynamic, personalised framework for cancer care that extends from diagnosis through treatment to long-term survivorship. By integrating multi-dimensional patient data, genomics, imaging, clinical history, and real-time monitoring with advanced computational modelling, DTs have the potential to enable predictive, adaptive, and participatory medicine. Industrial and research platforms such as SOPHiA DDM™ are already incorporating multimodal biological and clinical data to generate patient-specific digital twin models for simulating potential therapies and outcomes, illustrating the practical feasibility of this approach. The applications reviewed span the cancer care continuum: precision treatment selection that aims to optimise therapeutic efficacy whilst minimising toxicity, radiotherapy planning that balances tumour control against normal tissue sparing, accelerated drug development through in silico trials, immuno-oncology modelling that aims to predict immunotherapy response, surgical planning that enhances operative precision, and survivorship care that aims to detect recurrence early whilst monitoring quality of life.

Despite this transformative potential, substantial challenges must be addressed before DTs become integral to routine oncology practice. Data integration remains hampered by fragmented electronic health systems, inconsistent standards, and quality concerns. Model validation requires prospective clinical trials demonstrating improved outcomes, yet few such studies exist. Computational demands pose scalability barriers, particularly for resource-limited institutions. Ethical considerations around data privacy, informed consent, and algorithmic bias demand robust governance frameworks. Clinical acceptance depends on explainable models that enhance rather than replace clinical judgement, and regulatory pathways must evolve to accommodate continuously learning systems.

The path forward requires interdisciplinary collaboration among oncologists, data scientists, engineers, ethicists, and policymakers. Standardisation efforts must establish common frameworks for data representation and model validation. Investment in computational infrastructure and workforce training will build capacity for DT implementation. Regulatory innovation that balances rigorous oversight with flexibility for adaptive technologies will facilitate clinical translation. Crucially, equity considerations must guide DT development to ensure that precision oncology's benefits reach all patients, regardless of geography or socioeconomic status.

As artificial intelligence continues to advance and real-world data sources proliferate, oncology DTs will become increasingly sophisticated and clinically valuable. The vision of a truly personalised, predictive, and participatory cancer care system, where each patient's unique biology, treatment response, and lived experience inform therapeutic decisions in real time, is within reach. Realising this vision demands sustained commitment, innovative thinking, and collaborative effort across the global oncology community. The digital twin may well become, in the coming decades, as fundamental to cancer care as molecular profiling and precision medicine are today.

CRediT authorship contribution statement

David B. Olawade: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Project Administration, Conceptualization. **Emmanuel O. Oisakede**: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. **Oluwakemi Jumoke Bello**: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Claret Chinenyenwa Analikwu**: Writing – review & editing, Writing – original draft, Methodology, Investigation, Software. **Eghosasere Egbon**: Writing – review & editing, Writing – original draft, Methodology, Investigation, Visualization. **Adeyinka Ojo:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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David B. Olawade (MPH, FRSPH, SFHEA): Senior Research and Innovation Project Facilitator in the UK (NHS), and a visiting university lecturer in the UK. His research expertise lies at the intersection of artificial intelligence, healthcare delivery, and health equity, with particular focus on AI implementation in clinical settings.

Emmanuel O. Oisakede, MBBS, M.Sc. (Human Physiology), MPH, PGDipMedEd, FHEA: Oncology resident doctor in the UK with research experience in Immunotherapy/radiotherapy modelling, AI in oncology, new advances in oncology, infectious disease preparedness and medical education.

Oluwakemi Jumoke Bello: PhD researcher with a background in healthcare and international business, bringing an interdisciplinary, systems-driven approach to health research. Experienced in healthcare environments and global organisational contexts, with developing specialist expertise in AI in healthcare, sustainable health systems, public health, and environmental epidemiology. Focused on bridging real-world healthcare practice with innovation, policy, and future-ready health solutions.

Claret Chinenyenwa Analikwu: PhD researcher with a degree in biomedical sciences and a background in medical microbiology. Experienced in cell culture, microbiological techniques, histology and haematology. Research interests focus on biogenesis, microbiome Engineering, global health challenges in health environment and ecological approaches in understanding pathogenic diseases.

Eghosasere Egbon: PhD researcher with degree in Tissue Engineering and Regenerative Medicine and a background in medical biochemistry. Experienced in cell biology, membrane and lipid biology, and advanced in vitro model systems. Research interests focus on lysosomal biogenesis, membrane dynamics, and translational mechanisms underlying human disease.

Adeyinka Ojo: Manager within the Analytics and AI practice at Capgemini Invent, with extensive experience designing and delivering Data and AI transformation programmes from early mobilisation through to go-live across both public and private sector organisations. I have led multidisciplinary teams delivering secure data platforms, AI, GenAI, and Agentic AI solutions, as well as AI ethics and Responsible AI initiatives. My focus is on driving practical, measurable impact GenAI, and Agentic AI solutions with health industry.