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Strategic management of cancer progression: Novel approaches and the role of AI and modeling in treatment and crisis management

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Abstract

Cancer progression is increasingly recognized as a complex, multilevel process shaped by biological heterogeneity, treatment-induced evolution, and constraints at the organizational and health-system levels. Conventional, episode-based decision-making struggles to keep pace with expanding therapeutic options, growing data volumes, and recurrent crises such as pandemics that disrupt cancer pathways. This narrative review proposes a strategic framework for managing cancer progression that integrates novel clinical approaches with artificial intelligence (AI) and modeling across the entire cancer care trajectory and across micro (patient), meso (service), and macro (system) decision levels. We first conceptualize cancer care as a longitudinal continuum, spanning prevention and early detection, diagnosis and staging, primary treatment, surveillance and survivorship, management of recurrence or advanced disease, and palliative and end-of-life care, and argue that progression management requires anticipatory planning across this continuum rather than reactive choices at isolated time points. Within this structure, three pillars are examined in detail: novel therapeutic and organizational approaches (including precision oncology, immunotherapy, advanced radiotherapy, and pathway-based care), AI methods for prediction and decision support, and mechanistic and simulation-based models, including digital twins, for treatment optimization and scenario analysis. We then highlight how AI and modeling can be combined to support crisis management, for example by forecasting backlogs, guiding triage, and testing mitigation strategies during system shocks. Finally, we discuss ethical, legal, and organizational challenges and outline a research agenda for hybrid AI–mechanistic platforms and dynamic digital twins that could shift cancer care from reactive to strategic, learning system management of progression.

Keywords: Cancer progression, Strategic management, Artificial intelligence, Mathematical modeling, Crisis management.

Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide and continues to place an increasing burden on patients, health systems, and societies. Strategic management of cancer progression is critical because patient outcomes depend not only on selecting effective therapies, but on anticipating evolutionary resistance, coordinating sequencing decisions across the care continuum, and aligning limited diagnostic and treatment capacity, so that delays and suboptimal choices do not translate into avoidable progression and mortality. In 2020, the Global Cancer Observatory (GLOBOCAN) estimates indicated approximately 19.3 million new cancer cases and almost 10 million cancer-related deaths globally, with projections suggesting a substantial rise in incidence over the coming decades as populations age and risk factors accumulate.[1] These numbers underscore that cancer is not only a clinical problem at the level of tumor biology, but also an organizational and system-level challenge that unfolds over time horizons and across multiple layers of the healthcare system.[2]

Beyond its sheer burden, cancer is characterized by profound biological complexity. Tumors are

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heterogeneous, evolving ecosystems in which malignant cells interact dynamically with stromal, vascular, and immune components across multiple spatial and temporal scales. Complex-systems and dynamical-systems approaches have reframed cancer networks as highly nonlinear, adaptive systems whose behavior can be difficult to predict using purely intuitive or static models.[3] Mathematical and computational oncology have emerged in response, integrating biology, physics, and mathematics to describe tumor growth kinetics, intratumoral heterogeneity, clonal evolution, and tumor–immune dynamics.[4,5] These modeling frameworks reveal that treatment responses and resistance patterns arise from the interplay of evolutionary and ecological processes, implying that managing cancer progression effectively requires strategies that anticipate and steer these dynamics rather than reacting to them only after progression has occurred.[3-5]

In parallel, the therapeutic landscape of oncology has undergone a rapid transformation. Precision oncology efforts, driven by molecular profiling, novel biomarkers, and advances in drug development, have enabled more tailored treatment strategies that match specific genomic or phenotypic vulnerabilities.[6,7] Immunotherapies, including immune checkpoint inhibitors and cell-based therapies, have produced durable responses in subsets of patients across a range of malignancies and are increasingly integrated into multimodal treatment algorithms.[8] At the same time, adaptive and evolutionary-informed treatment concepts seek to modulate therapy intensity and sequencing to delay resistance and maintain long-term control of disease, rather than aiming solely for maximal short-term tumor reduction.[9] The proliferation of such novel approaches expands the decision space for clinicians and health systems, amplifying the need for structured, "strategic" management of cancer progression over the full trajectory of care.[10]

Artificial intelligence (AI) has simultaneously emerged as a powerful enabler of data-driven decision-making in oncology. Recent reviews highlight how machine learning and deep learning methods are improving cancer diagnostics and risk prediction across radiology, pathology, genomics, and multimodal data integration.[11,12] AI-based systems have achieved high performance in tumor detection, segmentation, and classification, as well as in predicting outcomes and treatment responses in diverse cancer types.[12, 3] In digital pathology, AI tools support automated tumor grading, biomarker quantification, and quality assurance, with potential to reduce interobserver variability and workload.[14] Beyond diagnostic tasks, AI-driven clinical decision support systems are being developed to aid treatment selection, toxicity prediction, trial matching, and longitudinal monitoring, with the ambition of delivering more precise, consistent, and efficient care across the cancer continuum.[11-14] Nevertheless, challenges related to data quality, bias, generalizability, interpretability, and workflow integration remain major barriers to realizing AI's full potential in routine cancer care.[11,12]

Alongside purely data-driven AI approaches, mechanistic mathematical models and digital twins (DTs) offer complementary tools for understanding and managing cancer progression. Mathematical models can simulate tumor growth, metastatic spread, and treatment response under different therapeutic scenarios, providing a quantitative basis for exploring "what-if" strategies that would be infeasible or unethical to test extensively in patients.[4,5] Building on these foundations, digital twin concepts aim to create virtual representations of individual patients by integrating clinical, imaging, molecular, and treatment data into continuously updated models.[15,16] In oncology and radiation oncology, such digital twins are being explored for personalized dose optimization, adaptive radiotherapy, and treatment replanning, with the goal of maximizing tumor control while limiting toxicity.[15,17] If successfully implemented, model-informed and AI-augmented digital twins could turn cancer care into a more anticipatory, strategy-driven process in which clinicians continuously adjust plans based on predicted trajectories rather than only on observed disease progression.[16,17]

The COVID-19 pandemic starkly illustrated why such strategic and predictive capabilities are urgently needed, not only at the level of individual patients but also at the level of health systems. Multiple systematic reviews have

documented substantial global disruptions to cancer screening, diagnosis, and treatment during the pandemic, including marked declines in screening uptake, delayed diagnoses, treatment postponements, and reallocation of oncology resources.[18-20] These disruptions are expected to translate into excess avoidable morbidity and mortality over the coming years as cancers are detected at more advanced stages and treatment backlogs accumulate.[19,20] At the same time, the pandemic catalyzed rapid experimentation with telemedicine, virtual tumor boards, and new triage protocols, while drawing renewed attention to the concepts of health-system resilience and crisis management.[21] Emerging resilience frameworks emphasize proactive preparedness, flexible resource allocation, learning systems, and robust decision-support tools as key components for navigating shocks while maintaining essential cancer services.[22] AI and modeling are natural candidates to support these functions by forecasting demand, simulating alternative policies, and identifying risk-prioritized patient cohorts during crises.

Despite these converging developments, much of the current literature remains siloed. Reviews of precision oncology and immunotherapy tend to focus on molecular targets and trial results without deeply engaging with system-level planning or crisis preparedness.[6-8] AI-focused reviews often emphasize technical performance and narrow clinical use cases, with relatively less attention to multilevel strategic management questions such as resource allocation, care pathway redesign, or resilience under stress.[11-13] Conversely, work on health-system resilience and crisis management rarely considers the specific complexities of cancer progression or the unique opportunities offered by AI and mechanistic modeling in oncology.[21, 22] There is therefore a need for an integrative narrative that explicitly frames cancer progression as a strategic management problem spanning patient-level treatment decisions and system-level crisis response, and that situates novel therapies, AI, and modeling within a single conceptual framework.

This narrative review seeks to address that gap by proposing a strategic management perspective on cancer progression that links novel clinical approaches with AI and modeling at both the patient and system levels. It aims to characterize cancer progression and its management across the full trajectory of care, synthesize current and emerging roles of AI in supporting strategic decisions, review mathematical modeling and digital twin approaches that can inform treatment planning and crisis preparedness, and discuss how these elements can be integrated into resilient, crisis-ready cancer care systems. In doing so, it provides a conceptual scaffold to guide future research, implementation efforts, and policy initiatives at the interface of oncology, data science, and health-system management.

2. Strategic framework for integrating AI and modeling in cancer progression management

2.1. Cancer progression as a multilevel strategic management problem

Cancer care is increasingly understood as a multilevel process in which patient outcomes are shaped by interacting factors at the clinical, organizational, and policy levels across the entire cancer care continuum.[23-25] Building on multilevel frameworks from cancer control and health services research, decisions relevant to cancer progression can be conceptualized at three nested levels: micro, meso, and macro.[23-27] At the micro level, decisions focus on the individual patient, including the choice, sequencing, and intensity of systemic therapies, radiotherapy, and surgery, as well as surveillance strategies and symptom management. At the meso level, oncology services and institutions design clinical pathways, allocate staff and infrastructure, and organize multidisciplinary tumor boards that determine how evidence and technologies are translated into routine practice. At the macro level, health systems and payers set reimbursement models, define national guidelines, and establish crisis protocols that shape access to diagnostics, treatment, and supportive care.[24, 25, 27-29]

These levels are tightly interdependent: micro-level clinical choices are constrained or enabled by meso-level organizational capabilities and macro-level policy decisions, while patient-reported outcomes and real-world evidence feed back into institutional learning and health-system reforms.[23-27] As the therapeutic and technological landscape in oncology has expanded, the number of

potential management strategies for any given patient has increased substantially, making intuitive decision-making alone insufficient for consistently high-quality care. This has led to calls for more explicit strategic management of cancer care that is forward-looking, data-informed, and aligned across micro, meso, and macro levels rather than fragmented or reactive.[24, 25, 28-30]

2.2. Cancer care trajectory as the temporal backbone of the framework

The conceptual framework proposed in this review is organized along the cancer care trajectory, which provides the temporal backbone for strategic management. Work from the National Cancer Institute and the Institute of Medicine describes the cancer care continuum as a sequence of interconnected phases: prevention and early detection, diagnosis and staging, primary treatment, surveillance and survivorship, management of recurrence or advanced disease, and palliative and end-of-life care.[23,24, 26, 28, 29] At each phase, patients face different risks, needs, and decision points, while health systems must balance finite resources against competing priorities.

Recent frameworks for integrated and supportive cancer care emphasize that planning across this continuum should be proactive, evidence-based, and patient-centered, with supportive care and coordination embedded from diagnosis through survivorship and bereavement rather than being confined to isolated stages.[26,29,31,32] For the purposes of strategic management of progression, this continuum is not only a clinical trajectory but also a planning horizon: decisions made at early phases (for example, choice of neoadjuvant therapy or extent of surgery) influence downstream treatment options, cumulative toxicity, and the feasibility of later interventions in recurrent or metastatic settings. A conceptual framework for strategic management must therefore explicitly address how decisions and information propagate along the trajectory over months and years, not just within a single episode of care.[23,26,28,29,31]

2.3. Three pillars of the strategic management framework

Within this multilevel and longitudinal context, we propose that the strategic management of cancer progression can be organized around three interlinked pillars: 1) novel clinical approaches, 2) AI, and 3) modeling and simulation.

2.3.1. Pillar 1 – Novel clinical approaches

Advances in precision oncology, targeted therapies, and immunotherapies have transformed the therapeutic landscape and expanded the set of plausible strategies for controlling cancer progression.[30, 31, 33-35] High-throughput molecular profiling and improved understanding of oncogenic signaling networks allow clinicians to select targeted agents based on actionable mutations, rearrangements, or pathway alterations.[30,31,36] Parallel progress in immunotherapy, including immune checkpoint inhibitors, CAR T-cell therapies, and next-generation cancer vaccines, has enabled durable disease control in subsets of patients who historically had poor prognoses.[33,34] Combination regimens and adaptive treatment concepts that modulate intensity or switch mechanisms of action in response to emerging resistance further enlarge the decision space.[31,33-35,37] These innovations provide the content of strategic management by creating new levers (e.g., treatment sequences, de-escalation and escalation strategies) through which clinicians and systems can attempt to steer tumor evolution and clinical outcomes over time.[30,31,33-37]

2.3.2. Pillar 2 – Artificial intelligence

AI methods, particularly machine learning and deep learning, supply the informational infrastructure for strategic management. Recent reviews describe how AI systems are being developed to improve risk stratification, early detection, prognostication, and treatment selection across multiple tumor types.[4,5,34,38] AI models can integrate high-dimensional data from imaging, pathology, genomics, and electronic health records to predict progression, treatment response, and toxicity, sometimes exceeding traditional statistical approaches in accuracy.[4,5,38,39] In addition to patient-level predictions, AI-enabled clinical decision support systems can help standardize complex treatment decisions, highlight deviations from guidelines, and identify patients who may benefit from clinical trials or intensified follow-up.[4,5,38,40] When deployed at scale, AI tools also generate new forms of real-time population-level intelligence, for example, signals about changing incidence patterns, service bottlenecks, or disparities in care, that can inform meso-

and macro-level strategic decisions. Recent work has emphasized that such systems must be implemented in ways that preserve safety, fairness, and transparency, but their potential to support multilevel oncology decision-making is substantial.[5, 38-40]

2.3.3. Pillar 3 – Modeling and simulation

Mechanistic mathematical models and digital twins provide the planning and experimentation layer of the framework. Mathematical oncology uses ordinary and partial differential equations, agent-based models, and hybrid approaches to capture tumor growth, treatment response, and tumor–immune interactions at different scales.[4,5,39,40] In radiotherapy, modeling has been used to optimize fractionation schemes, predict normal tissue complications, and design advanced techniques such as stereotactic body radiotherapy, spatially fractionated radiotherapy, and emerging FLASH regimens.[4,16,39] More recently, digital twin concepts in oncology and radiation oncology have been proposed, in which virtual replicas of individual patients, built from clinical, imaging, and molecular data, are continually updated to simulate alternative treatment strategies and predict likely trajectories.[15,16,41,42] These tools enable in silico experimentation with treatment sequences, dose adaptations, and supportive-care strategies under varying constraints, which can then inform both micro-level clinical decisions and meso-/macro-level policies such as pathway design or resource allocation for particular patient segments.[4,5,39,40]

2.4. Operationalizing the framework across the trajectory and decision levels

In the proposed framework, the cancer care trajectory runs on the horizontal axis, while the vertical axis represents micro, meso, and macro decision levels. Each cell in this conceptual grid corresponds to a set of strategic decisions that can be informed by one or more of the three pillars. For example, at the micro level during primary treatment, precision-oncology testing and novel regimens define the range of clinical options; AI models estimate progression risk and likely treatment response; and mechanistic or digital twin models simulate alternative sequences or dose adaptations, supporting a personalized treatment plan that aims to delay resistance and maintain long-term control. At the meso level during the same phase, institutions may use AI-derived risk scores to design triage rules and pathway variants, while simulation models of clinic workflows and patient flows help ensure that high-risk patients receive timely access to complex therapies. At the macro level, health authorities can use aggregated prediction outputs and scenario models to plan investment in diagnostic capacity, negotiate coverage for expensive novel agents, and develop contingency plans for crises (for example, pandemic-related disruptions) that might otherwise accelerate uncontrolled cancer progression in vulnerable populations.[4,5,16,23-25, 28-31, 38-40, 42].

This integrated view reframes the management of cancer progression as a coordinated, system-wide strategy rather than a series of isolated treatment choices. Novel therapies, AI, and modeling are not independent trends but complementary components: novel therapies expand what can be done; AI clarifies when and for whom interventions are most valuable; and modeling and digital twins allow stakeholders to test and refine strategic options before and during implementation. The remainder of this review elaborates on each pillar in detail and illustrates how they can be combined to support resilient, crisis-ready cancer care.[31, 34, 38, 41]

3. Novel approaches in clinical and system-level management of cancer progression

Rapid advances in systemic therapy, radiotherapy technology, and service organization have fundamentally changed how cancer progression can be managed over time. Precision oncology, immunotherapy, and innovative radiotherapy techniques have expanded the therapeutic "toolbox," while multidisciplinary tumor boards and structured clinical pathways have reshaped how decisions are made and coordinated.[7,43-46] Together, these innovations enable a more strategic, longitudinal approach to cancer control, in which treatment intensity, sequencing, and modality choice are deliberately planned to delay resistance, reduce toxicity, and optimize use of limited resources [Table 1].

Table 1. Novel therapeutic and organizational approaches relevant to strategic management of cancer progression

Approach / domain	Primary level (micro / meso / macro)	Strategic objective for progression management	Example evidence
Precision oncology (NGS-based, biomarker-driven targeted therapy)	Micro, Meso	Match patients to effective targeted agents; avoid ineffective/toxic regimens; preserve later-line options	[7, 43]
Evolutionary-informed and adaptive systemic therapy	Micro, Meso	Delay or prevent resistance; maintain a controllable tumor burden; reduce cumulative dose	[44]
Immune checkpoint inhibitors (single-agent ICI)	Micro	Achieve deep and durable responses; convert some cancers to chronic controllable disease	[47-50]
ICI-based combination immunotherapy (e.g. ICI + RT, dual checkpoints, metabolic or microbiome modulation)	Micro, Meso	Overcome primary/acquired resistance; broaden benefit; prolong progression-free survival	[45, 51, 52]
Stereotactic radiosurgery (SRS) / SBRT	Micro, Meso	Ablate oligometastatic or oligoprogressive sites; prolong systemic therapy benefit; improve local control	[53]
Spatially fractionated RT (GRID / lattice SFRT)	Micro, Meso	Treat bulky or previously irradiated tumors; enable re-irradiation with acceptable toxicity	[54-56]
FLASH radiotherapy	Micro, Meso, Macro	Widen therapeutic window by sparing normal tissue; enable aggressive local control with less late toxicity	[45, 53, 54]
Multidisciplinary tumor boards (MTBs)	Meso	Coordinate complex decisions; improve guideline adherence; standardize long-term management strategies	[46, 57, 58]
Oncology clinical pathways	Meso, Macro	Reduce unwarranted variation; optimize resource use; embed crisis-ready and value-based care	[59-63]

3.1. Precision Oncology and Targeted Therapies

Precision oncology aims to tailor therapy to the molecular and phenotypic characteristics of an individual tumor, rather than relying solely on histology or anatomical site.[7,43] High-throughput next-generation sequencing (NGS), large gene panels, and increasingly integrated bioinformatics pipelines have made it feasible to identify actionable driver alterations and match patients to targeted agents in both common and rare cancers.[7,43] Large narrative and systematic reviews show that biomarker-driven matched therapy can improve response rates, progression-free survival, and sometimes overall survival in selected patient subsets, especially in tumors with oncogene addiction such as EGFR-mutant lung cancer, BRAF-mutant melanoma, and ALK/ROS1-rearranged malignancies.[7,43]

At the same time, the proliferation of targeted agents has increased the number of plausible strategic options for a given patient, multiple lines of therapy, combination regimens, and opportunities for treatment de-escalation in biomarker-defined low-risk groups.[7]

This has stimulated interest in evolutionary-informed approaches such as adaptive therapy, where dose and scheduling are dynamically adjusted to exploit competition between drug-sensitive and drug-resistant clones.[44] Adaptive therapy studies and modeling work suggest that maintaining a controlled tumor burden, rather than aiming for complete eradication at all costs, can delay the emergence of highly resistant populations and extend time to progression.[44]

From a strategic management perspective, precision oncology and adaptive treatment concepts provide levers

that can be pulled at the micro and meso levels (patient and institutional) to shape the temporal pattern of cancer progression. Clinicians can choose between aggressive debulking strategies and more conservative, control-oriented regimens based on molecular risk, host factors, and anticipated resistance pathways, while institutions must ensure access to molecular diagnostics, molecular tumor boards, and appropriate data infrastructure to support such decisions.[7, 43, 44]

3.2. Immunotherapy and Immune Checkpoint Inhibition

Immune checkpoint inhibitors (ICIs) targeting CTLA-4, PD-1, and PD-L1 have transformed outcomes in multiple solid tumors and hematologic malignancies, with a subset of patients achieving deep, durable responses that effectively convert previously lethal diseases into chronic conditions.[47-50] Comprehensive reviews highlight their broad approval spectrum, from melanoma and non-small cell lung cancer to renal, bladder, head and neck, and gynecologic cancers.[47-49]

However, only a fraction of patients derives long-term benefit, and both primary and acquired resistance are frequent.[49, 50]

This has led to intense work on predictive biomarkers, PD-L1 expression, tumor mutational burden, microsatellite instability, gene-expression signatures, and features of the tumor microenvironment, as well as on novel checkpoints and rational combination strategies.[51,52]

Combination regimens that integrate ICIs with radiotherapy, targeted therapies, metabolic modulators, or microbiome-modifying interventions are being evaluated to broaden the responding population and overcome resistance.[45, 51, 52]

For strategic progression management, immunotherapy introduces two key dimensions. First, ICIs can be positioned as early aggressive therapy for high-risk disease or reserved for later lines to preserve future options; second, their long-lasting immune-mediated effects and immune-related adverse events (irAEs) require long-range planning for toxicity monitoring, endocrine and autoimmune sequelae, and survivorship care.[45, 47-50]

At meso and macro levels, health systems must manage the substantial financial and infrastructural burden of ICI programs, implement pathways for early recognition and management of irAEs, and collect real-world data to refine patient selection and duration of therapy. These multilevel considerations are reflected in the "Immunotherapy" rows of Table 1.

3.3. Strategic Planning in Radiotherapy

Radiotherapy remains a cornerstone of cancer treatment, and technological advances now allow highly conformal and biologically innovative approaches. Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) deliver ablative doses to small targets with sub-millimeter precision and have become standard options for oligometastatic disease and oligoprogression.[53]

In this context, local ablation of limited progressing sites can prolong the benefit of otherwise effective systemic therapy, effectively "resetting the clock" on progression while avoiding wholesale regimen changes.

Spatially fractionated radiotherapy (SFRT), including GRID and lattice techniques, delivers a heterogeneous dose pattern with very high peaks and lower valleys across bulky tumors. Recent critical reviews and clinical series suggest that SFRT can achieve substantial symptom relief, tumor downsizing, and sometimes durable control in large or previously irradiated masses, though standardized dosimetry and prospective evidence are still evolving.[54-56]

FLASH radiotherapy, characterized by ultra-high dose rates delivered over milliseconds, has emerged as a potentially paradigm-shifting modality. Preclinical and early translational studies indicate that FLASH may spare normal tissues while maintaining tumor control, potentially widening the therapeutic window.[45, 53, 54]

Clinical implementation, however, remains in its infancy, with ongoing research on beam modalities, dosimetry, and long-term safety.

From a strategic perspective, these radiotherapy innovations enable targeted, high-impact interventions at key points in the disease trajectory, such as consolidating response in oligometastatic disease, salvaging limited local failures, or palliating bulky symptomatic lesions, while attempting to preserve systemic treatment options and minimize cumulative toxicity.[53-56] Their placement in the micro and meso rows of Table 1 reflects the need for individualized planning at the patient level and careful allocation of technically demanding resources at the

institutional level.

3.4. Organizational and Pathway-Based Management

Novel drugs and technologies can only realize their strategic potential if embedded in organizational structures that support consistent, evidence-based, and adaptive decision-making. Multidisciplinary tumor boards (MTBs) are now widely recognized as a core component of high-quality cancer care. An umbrella review of MTBs shows associations with improved staging accuracy, greater adherence to guidelines, changes in treatment recommendations, and, in some contexts, better survival.[46, 57]

More recent work has highlighted that MTBs can standardize the use of complex modalities such as immunotherapy and advanced radiotherapy, while also providing a natural locus for integrating molecular and imaging data.[58]

In parallel, clinical pathways in oncology have been developed to translate guideline recommendations into structured, locally implementable care processes. A meta-analysis of hospital-based clinical pathways across multiple conditions, including cancer, found that pathway implementation was associated with reduced complications, shorter length of stay, and improved documentation quality.[59]

Umbrella reviews and observational studies focused on oncology suggest that pathway concordance is associated with lower costs and, in some settings, with improved outcomes and more consistent use of evidence-based regimens.[60-62]

Expert commentaries from ASCO and others emphasize that well-designed oncology pathways should both standardize care and preserve room for justified, patient-specific deviation.[63]

Strategically, MTBs and oncology clinical pathways operate primarily at the meso and macro levels, ensuring that individual treatment plans (micro) are aligned with broader institutional and system priorities. They also provide a structured data backbone for future AI and modeling efforts by standardizing decision points, documenting rationales, and enabling long-term monitoring of concordance and outcomes. Their roles in reducing unwarranted variation, enhancing crisis responsiveness, and supporting the deployment of advanced therapies are summarized in Table 1.

4. Role of Artificial Intelligence in strategic management of cancer progression

AI has rapidly evolved from a primarily experimental technology to a practical tool that increasingly permeates the cancer care continuum, from risk assessment and early detection to treatment selection, monitoring, survivorship, and end-of-life care.[11,64,65] Recent narrative and systematic reviews emphasize that AI is particularly well suited to oncology because of the high dimensionality and heterogeneity of available data, ranging from imaging and pathology to genomics, electronic health records (EHRs), and patient-reported outcomes.[11,34,64,65] When strategically deployed, AI systems can enhance risk stratification, predict disease trajectories, support individualized treatment decisions, and inform resource allocation at micro, meso, and macro levels [Table 2, Figure 1]. However, their value depends critically on issues such as data quality, model transparency, clinical integration, and governance.[34, 37, 66-69]

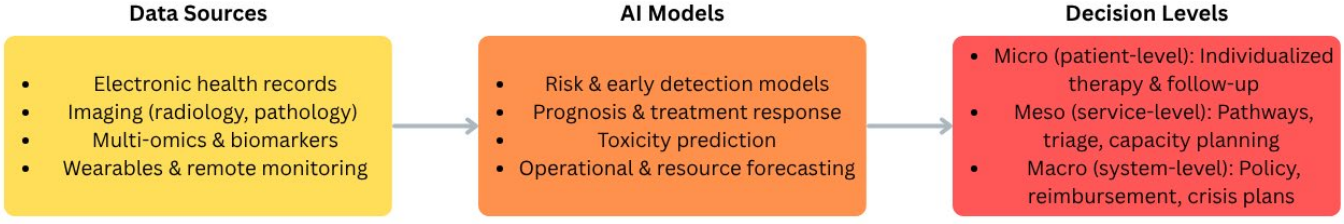

Figure 1. Conceptual data-to-decision pipeline for AI in strategic management of cancer progression.

Table 2. Key AI applications relevant to strategic management of cancer progression across the care trajectory

AI application	Dominant data sources	Main decision level(s)	Typical cancer-trajectory phase(s)	Strategic contribution to progression management
Risk stratification and early detection models	Claims/EHR data, screening images, genetics	Micro, Macro	Prevention & early detection	Identify high-risk individuals for intensified screening or prevention; enable targeted programs and efficient resource use.[11, 64, 65, 70]
Imaging-based tumor detection and staging (radiology, pathology)	CT/MRI/PET, digital slides, radiomics/pathomics	Micro, Meso	Diagnosis & staging	Improve diagnostic accuracy and staging; support timely, appropriate initiation of therapy.[11, 65]
Prognosis and recurrence prediction	Clinicopathologic data, radiomics, genomics	Micro, Meso, Macro	Diagnosis; primary treatment; surveillance	Estimate risk of progression and recurrence; tailor treatment intensity and follow-up intervals; inform population-level planning.[70-73]
Treatment-response prediction (systemic therapy, RT)	Baseline and on-treatment imaging, labs, genomics	Micro, Meso	Primary treatment; recurrence / advanced disease	Guide selection and sequencing of therapies; avoid futile regimens; support adaptive or response-driven strategies.[72-75]
Toxicity prediction and supportive-care optimization	EHR, prior treatments, comorbidities, dosimetry	Micro, Meso	Primary treatment; survivorship	Anticipate severe adverse events; personalize prophylaxis and monitoring; reduce unplanned hospitalizations and treatment breaks.[74, 75]
AI-enabled clinical decision support (regimen choice, guideline adherence, trial matching)	Structured EHR data, guidelines, trial databases	Micro, Meso	Diagnosis; treatment planning; recurrence management	Standardize complex decisions; highlight deviations from pathways; identify candidates for innovative therapies and clinical trials.[35, 38]
Operational and resource-forecasting models	Administrative data, scheduling, throughput	Meso, Macro	All phases	Anticipate demand for imaging, RT machines, infusion chairs; support capacity planning and crisis preparedness.[65, 70, 75]
AI-assisted digital twins and simulation of care scenarios	Multimodal longitudinal patient data	Micro, Meso, Macro	Treatment, surveillance, advanced disease	Virtually test alternative strategies, treatment sequences, and triage policies; anticipate long-term outcomes and system impact.[65,70, 74]
Trust and governance analytics (monitoring bias, drift, safety)	Model outputs, real-world outcomes, metadata	Meso, Macro	Implementation & monitoring across continuum	Ensure safe, equitable, and robust AI performance; support regulatory compliance and iterative model improvement.[37, 66-69]

4.1. AI across the cancer care continuum

Conceptually, AI applications in oncology can be mapped along the cancer care trajectory: risk prediction and early detection, diagnosis and staging, treatment planning and response monitoring, and survivorship and end-of-life care.[11, 64] Large reviews show that AI-based models are being developed for virtually every phase of this continuum. For example, deep learning applied to mammography, CT, and MRI has achieved performance comparable to or surpassing radiologists for certain detection tasks, while AI-enhanced liquid biopsy and multi-omics analysis support earlier identification of high-risk individuals and minimal residual disease.[11, 64, 65, 70]

In diagnosis and staging, AI has been used for automated tumor detection and segmentation in radiology, grading and biomarker quantification in digital pathology, and integration of imaging with genomic data to refine staging and molecular subtyping.[11, 65] At the treatment phase, AI tools increasingly aim to forecast progression, recurrence, and treatment-related toxicity, thereby informing the choice and sequencing of systemic therapies, radiotherapy, and surgical approaches.[65, 74, 75]

From a strategic management perspective, this breadth of applications means that AI can provide anticipatory information at multiple decision points, before cancer develops, at the moment of diagnosis, and during longitudinal follow-up, thereby supporting the design of long-term control strategies rather than short episodic decisions [Figure 1].

4.2. Predictive modeling for cancer progression and treatment response

A large body of work focuses on AI-based prediction of progression, recurrence, and response to therapy. Machine learning and deep learning models have been developed to predict outcomes in breast, colorectal, lung, and other cancers using combinations of clinical variables, radiomics features, gene-expression signatures, and treatment histories.[70-73, 75] For example, models in breast cancer that integrate imaging-derived biomarkers with clinicopathologic variables have shown improved discrimination of treatment response and survival compared with traditional prognostic tools.[72] Similarly, AI applied to colorectal cancer imaging has been used to predict short-term response to chemoradiotherapy and long-term survival, providing a basis for individualized treatment planning and surveillance intensity.[73]

Practical examples of this integration include AI radiomics and deep-learning models that use pretreatment CT/MRI/PET images to predict treatment response (e.g., pathological complete response in neoadjuvant settings) or to forecast benefit from immune-checkpoint inhibitors and identify patients more likely to require combination strategies.[76, 77] In parallel, AI applied to digital pathology and multimodal clinicogenomic data can generate complementary response scores or toxicity-risk estimates that are presented to clinicians as calibrated probabilities rather than binary outputs, supporting shared decision-making when standard biomarkers are inconclusive.[78, 79]

In radiotherapy, AI systems have been proposed to personalize dose distributions and fractionation by predicting tumor control probability and normal-tissue complication probability based on pretreatment imaging, dosimetry, and clinical factors.[74] Zwanenburg and colleagues describe successive "generations" of AI systems in radiotherapy: models based on baseline data, response-driven adaptive radiotherapy, and fully dynamic optimization that continuously updates predictions as new imaging and outcome data become available.[74]

These predictive tools serve strategic objectives at several levels. At the micro level, they enable refined counseling, shared decision-making, and the design of treatment pathways that balance potential benefit against toxicity and quality-of-life impact for individual patients. At the meso level, aggregated predictions can inform case-mix–adjusted benchmarking, capacity planning (e.g., anticipating demand for intensive care or advanced radiotherapy techniques), and prioritization of high-risk patients. At the macro level, robust risk models can support population-level screening strategies, reimbursement policies for expensive therapies, and scenario modeling during crises when resources are constrained.[64, 65, 70, 71]

4.3. AI-enabled clinical decision support and care coordination

Beyond stand-alone prediction models, AI is increasingly embedded into clinical decision support systems (CDSS).

A widely cited review on AI in oncology CDSS describes systems that generate treatment recommendations, flag potential deviations from guidelines, suggest trial eligibility, and assist with toxicity management by integrating real-time clinical and laboratory data.[35] Evaluation studies suggest that CDSS can improve guideline adherence, standardize complex decisions, and streamline care processes, although the impact on hard clinical outcomes remains variable.[35,75]

In real-world workflows, such tools are increasingly embedded into tumor-board deliberations and pathway-based order sets, where they can i) surface patient-specific evidence and guideline-concordant options, ii) flag contraindications and drug–drug interactions, iii) suggest dose modifications or supportive-care bundles based on predicted toxicity risk, and iv) support care coordination by identifying patients at high risk of deterioration who may benefit from earlier review or escalation.[80,81] The strategic value is not automation for its own sake, but faster, more consistent, and auditable decisions under uncertainty.

More recent work has explored autonomous or semi-autonomous AI agents that combine large language models with domain-specific tools. Ferber et al., reported an autonomous AI agent for precision oncology that integrates multimodal data and generates treatment suggestions, which are then reviewed by clinicians.[38] While such systems remain experimental, they illustrate the potential for AI to act as a continuous, context-aware assistant in tumor boards and multidisciplinary clinics.

At the organizational level, AI-driven CDSS can be linked to clinical pathways and electronic order sets, ensuring that evidence-based options are presented consistently while still allowing justified deviations. In addition, AI-powered operational tools, such as models that forecast clinic workload, radiotherapy machine utilization, or chemotherapy chair demand, help align resources with predicted patient flows.[65, 70, 75] As summarized in Table 2, this creates an integrated ecosystem in which predictive models support both clinical and logistical decisions across the cancer trajectory.

4.4. Trustworthy and strategically governed AI

As AI becomes more deeply embedded into oncology decision-making, the question is no longer whether AI can make accurate predictions, but whether these predictions can be trusted and governed responsibly. Ethical and policy-oriented reviews highlight several recurring challenges: bias arising from unrepresentative training data, lack of transparency in model development, limited external validation, and unclear accountability when AI recommendations influence patient care.[34, 37, 66-68]

At the same time, clinical deployment raises ethical issues that are particularly salient in cancer treatment. AI models often rely on large-scale EHR, imaging, and genomic data that are difficult to fully de-identify, increasing privacy and data-governance risks; informed-consent processes may not clearly cover secondary use, cross-institutional data sharing, or continuous model updating; and biased or non-representative training data can produce systematically different performance across patient groups or care settings, potentially amplifying disparities in access and outcomes.[34,82] Ethical implementation therefore requires explicit governance, data minimization, transparent consent and oversight, bias auditing, and monitoring for performance drift, alongside clinical validation.

Systematic reviews on trust in AI-based CDSS indicate that clinicians' willingness to use such systems depends on perceived accuracy, explainability, integration into workflow, and alignment with professional norms.[37,66] Frameworks such as FUTURE-AI and European and WHO guidelines for trustworthy medical AI articulate requirements including human oversight, technical robustness, privacy and data governance, transparency, fairness, and accountability.[67-69]

From a strategic-management viewpoint, these considerations mean that AI cannot be treated merely as a technical add-on. Instead, it must be embedded within governance structures that define roles and responsibilities, specify performance and monitoring standards, and ensure that AI outputs are interpreted within multidisciplinary contexts (e.g., tumor boards). Institutions and health systems need explicit strategies for model lifecycle management, covering development, validation, deployment, surveillance for performance drift, and retirement or updating of models, as well as for

transparent communication with patients about the role of AI in their care.

5. Modeling Approaches in Treatment and Crisis Management

Mathematical and computational models have become essential tools for understanding cancer dynamics and for designing treatment and system-level strategies that go beyond trial-and-error. Recent reviews emphasize that models can capture tumor growth, treatment response, clonal evolution, and host–tumor interactions across multiple scales, providing a structured way to explore "what-if" scenarios that would be infeasible or unethical to test directly in patients.[4,39,83] These models range from simple ordinary differential equation (ODE) systems to complex agent-based and multiscale hybrid frameworks, and they increasingly feed into digital twin architectures and health-system simulations.[4, 5, 39, 83, 84]

When aligned with clinical and organizational priorities, modeling can inform treatment optimization, adaptive therapy, triage, and crisis-response planning, complementing the AI-based approaches described in the previous section. Table 3 provides an overview of key model classes and their typical applications, while Figure 2 illustrates the generic pipeline that links clinical data, model construction, scenario simulation, and decision support.

Table 3. Comparison of modeling approaches in oncology relevant to treatment and crisis management

Model type	Typical scale	Main clinical or system questions addressed	Key strengths	Key limitations	References
Deterministic ODE tumor-growth models	Tumor cell populations, systemic therapy	Tumor growth under treatment; optimal dosing and scheduling; resistance dynamics	Mechanistically interpretable; relatively simple; amenable to optimal control	Often oversimplified biology; limited spatial detail; parameter uncertainty	[4, 39, 83, 84]
PDE and spatial diffusion models	Spatial tumor growth, drug/oxygen transport	Heterogeneous drug distribution; hypoxia; spatial patterns of response	Capture spatial gradients and microenvironmental effects	Mathematically and computationally more complex; harder to calibrate	[39, 83, 85]
Stochastic and branching-process models	Clonal evolution, resistance emergence	Probability and timing of resistance; evolutionary trajectories	Represent randomness and rare events; suited for evolutionary questions	Difficult to parameterize; often focus on simplified scenarios	[5, 84]
Agent-based and hybrid multiscale models	Single cells, microenvironment, tissues	Invasion, metastasis, microenvironmental interactions, spatial evolution	Capture heterogeneity and local interactions; highly flexible	Computationally intensive; many parameters; validation is challenging	[5, 39, 83, 86]
Radiotherapy and radionuclide models	Tumor and normal tissue under RT / RNT	Optimal fractionation; dose painting; scheduling of RT and radionuclide therapy	Directly linked to clinical dosimetry; support RT plan optimization	Require high-quality dose–response data; may be site-specific	[85-87]
System-dynamics /	Patient flow, resources, waiting lists	Backlogs, triage, capacity planning,	Ideal for crisis simulations and	Less detailed biology; require reliable administrative data	[39, 88, 89]

discrete-event models		effect of crises on access	policy testing; intuitive for managers		
Digital twins and virtual patients	Individual patients (biological + system)	Personalized treatment sequencing; comparative scenarios; long-term outcomes	Integrate multimodal data; enable rich what-if simulations for individuals	High data and computation demands; complex validation; fairness and bias concerns	[16, 90-92]

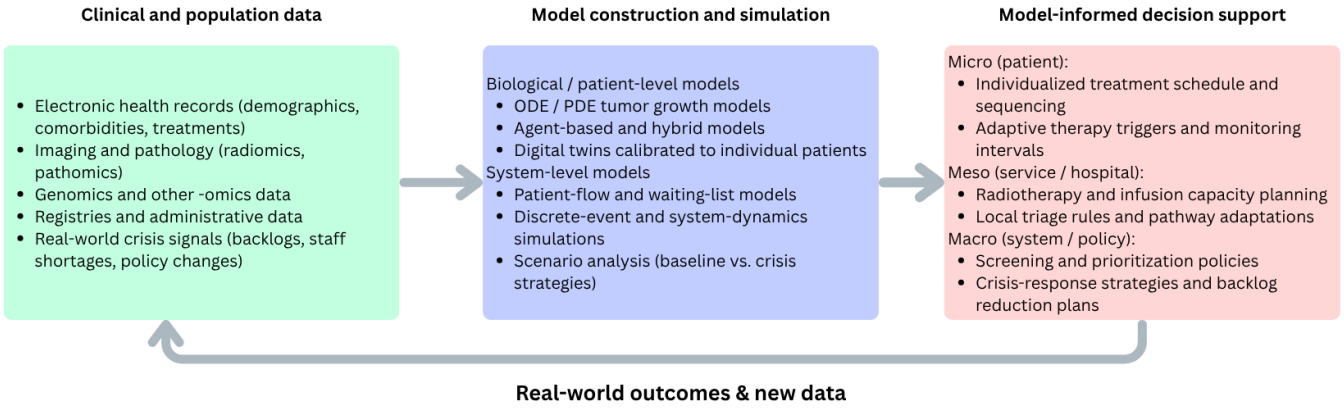

Figure 2. From data to model-informed decision support in cancer treatment and crisis management.

5.1. Types of models in oncology

Deterministic ODE and PDE models have a long history in oncology and remain the backbone of many mechanistic approaches. These models typically describe tumor cell populations, normal tissues, and sometimes immune or stromal compartments, with terms representing proliferation, death, treatment effects, and interactions.[4,83] They can be extended to include pharmacokinetics and pharmacodynamics (PK/PD) of systemic therapies, spatial diffusion of drugs or oxygen, and radiobiological effects such as repair and repopulation.[39,83] Azizi and colleagues summarized how such models can be used to represent different stages of cancer progression and to study how parameter changes, representing, for example, more aggressive clones or altered microenvironments, drive transitions between indolent and rapidly progressive disease.[4]

Stochastic and agent-based models (ABMs) add randomness and discrete cell-level rules, making them particularly suited to capturing heterogeneity and evolutionary dynamics. Recent work on the mathematical modeling of cancer cell evolution and plasticity illustrates how stochastic birth–death processes and ABMs can describe clonal selection, phenotypic switching, and microenvironmental influences on resistance emergence.[5] Hybrid models combine continuous and discrete elements, for example, ODEs for drug concentrations with ABMs for tumor cells, allowing exploration of how population-level pharmacology interacts with single-cell behavior.[5, 39, 83]

At a higher level of abstraction, system-dynamics and discrete-event simulation models are used to represent patient flows, waiting lists, and resource constraints within oncology services. These models support questions about capacity, backlogs, and the effects of changes in policy or staffing, especially during crises. Although they operate at a different scale from tumor-biology models, they are conceptually similar in that they use differential or difference equations and discrete events to project future states under alternative scenarios.[39, 84]

5.2. Modeling for treatment optimization

One of the most mature applications of mathematical oncology is treatment optimization. Deterministic and stochastic models have been used to design schedules for chemotherapy, targeted therapies, immunotherapies, and radionuclide treatments that balance tumor kill against toxicity and resistance.[4,39,83,84] For example, reviews on tumor growth models integrating treatment therapy

highlight how ODE systems with drug-effect terms can support identification of optimal dosing intervals, pulse schedules, and combination regimens.[39, 83]

In radiotherapy, Zheng et al. summarized applications of modeling for optimizing fractionation schemes, predicting tumor control probability, and estimating normal tissue complication probability using mechanistic and statistical models.[85] More specialized work has used fractional-order differential equations and other advanced operators to investigate the dynamics of novel radiation techniques and combined modality treatments.[86] Models have also been applied to optimize radionuclide therapies; for instance, mathematical models have been used to determine injection timing and activity in [177Lu]-based therapies so as to maximize tumor reduction while respecting organ-at-risk constraints.[87]

A growing subset of models explicitly focuses on treatment resistance and optimization under evolutionary constraints. Azizi's review on mathematical modelling of cancer treatments, resistance and optimization describes frameworks that consider sensitive and resistant subpopulations, drug cycling or mixing strategies, and multi-drug regimens aimed at delaying or preventing resistance.[84] These approaches align closely with adaptive and evolutionary-informed strategies described earlier in the article, but provide a quantitative substrate for testing competing hypotheses about dosing, sequencing, and treatment holidays before committing to specific clinical protocols.

5.3. Digital twins and predictive simulations

Digital twins represent a convergence of mechanistic modeling, AI, and rich longitudinal data. In a medical context, a digital twin can be defined as a virtual replica of an individual patient that is continually updated with clinical, imaging, omics, and treatment data, and that can be used to simulate alternative care strategies.[16,90,91] In oncology, scoping reviews show that digital and virtual twins have been proposed for breast, lung, and gastrointestinal cancers, as well as for radiotherapy and pain management.[16, 90]

Giansanti et al. reviewed digital twins in cancer treatment and highlighted their potential for optimized regimen design, trial simulation, and economic forecasting, while also emphasizing challenges related to data integration, biological model complexity, and computational demands.[16] Stefănigă and colleagues mapped advances in digital and virtual twins for precision oncology, noting that most published prototypes remain at early technological maturity and often lack fairness and external validation.[90] Saratkar et al., and Tortora et al., described broader frameworks for medical digital twins, including technical architectures, calibration and validation strategies, and potential governance models that are also applicable to oncology.[91, 92]

Within a strategic management framework, oncology digital twins can support patient-level (micro) decisions by simulating alternative sequences of surgery, radiotherapy, systemic therapy, and supportive care; meso-level decisions by aggregating results for typical patient archetypes to inform pathway design; and macro-level decisions by exploring the impact of new technologies or policies on population outcomes and costs. As shown schematically in Figure 2, data from clinical practice and trials feed into model construction and calibration, which in turn enables simulation of diverse "what-if" scenarios whose results can be presented to clinicians, managers, and policymakers as decision support.

5.4. Modeling for crisis management in cancer care

The COVID-19 pandemic highlighted the vulnerability of cancer care systems to disruptions in capacity, diagnostics, and treatment pathways. Early analyses documented widespread delays in diagnosis, interruptions in therapy, and changes in treatment patterns across multiple tumor types and jurisdictions.[88, 93-95] Several studies used modeling to estimate the impact of these delays on survival and mortality; for example, Maringe et al., projected additional cancer deaths due to diagnostic delays in the United Kingdom using stage-shift and survival models.[95] OECD analyses similarly synthesized modeling work across countries to estimate backlogs and to assess policy options for mitigating their long-term consequences.[89]

From a strategic-management standpoint, many COVID-19 responses can be interpreted through crisis-management and resilience frameworks that emphasize preparedness, rapid reconfiguration, and recovery

learning cycles. During pandemic surges, oncology programs implemented formal triage criteria to prioritize curative-intent and time-sensitive treatments, adopted hypofractionated radiotherapy schedules to reduce visits, and reorganized staffing and workflows to preserve throughput while minimizing infection risk.[96,97] In the recovery phase, health systems faced large diagnostic and treatment backlogs; here, system-dynamics and discrete-event simulation models have been used to estimate accumulated waiting lists, test capacity-expansion scenarios, and evaluate prioritization policies that balance delay-related harm against limited resources.[98,99] These practical examples show how strategic frameworks translate into concrete allocation decisions under crisis conditions, deciding not only what is clinically best, but what is feasible and fair when capacity is constrained.

In radiation oncology, Rivera et al. discussed triage frameworks and hypothetical decision trees for managing patients requiring radiotherapy in the context of COVID-19 risk, effectively illustrating how algorithmic approaches can prioritize cases when capacity is constrained.[93] Subsequent modeling studies have used discrete-event simulation and system-dynamics models to explore strategies such as expedited short-course regimens, centralized referral to higher-capacity centers, and extended hours of operation to reduce backlogs.[39, 89]

These experiences suggest a broader role for modeling in crisis management, beyond pandemics. Natural disasters, cyberattacks, workforce shortages, or major policy changes can all create sudden mismatches between demand and capacity. Models of patient flow, waiting lists, and resource allocation can help health systems test triage rules, reconfiguration of services, and surge-capacity strategies before implementing them. When linked with tumor-progression and outcome models, they can also estimate the trade-offs between delays for different patient groups and overall survival or quality-adjusted life years, thus providing a transparent basis for ethically sensitive decisions.

6. Crisis Management in Cancer Care: Role of AI and Modeling

Crises such as pandemics, natural disasters, cyberattacks, and workforce shortages expose structural vulnerabilities in cancer care systems and can accelerate uncontrolled cancer progression by disrupting screening, diagnosis, and treatment. Traditional crisis management frameworks in healthcare emphasize phases of mitigation or prevention, preparedness, response, and recovery.[100,101] In oncology, these phases must be interpreted through the lens of time-sensitive disease trajectories, where delays of weeks or months can translate into shifts in stage distribution and avoidable mortality.[19,95,102,103] AI and modeling provide complementary capabilities to anticipate, absorb, and adapt to such shocks, both at the level of individual patients and at the level of services and health systems [Table 4, Figure 3].

Table 4. Crisis scenarios in cancer care and potential AI- and modeling-based strategies

Crisis type	Level	Main impact on cancer care	AI-based tools	Modeling-based tools	Strategic recommendations
Global pandemic (e.g., COVID-19)	System	Reduced screening and diagnosis, treatment delays, capacity constraints, infection risk	Forecasting of infections and hospital demand; triage and risk models; AI-supported telemedicine and monitoring	Stage-shift and survival models; discrete-event simulation of backlogs; RT pathway and capacity simulations	Prioritize high-benefit treatments; use hypofractionation and streamlined regimens; aggressive backlog recovery plans.
Natural disaster (earthquake, flood)	System	Damage to facilities, temporary loss of services, disrupted supply chains	Rapid capacity and logistics forecasting; geospatial AI to identify affected populations	Network models of patient redirection; simulations of regional referral patterns	Pre-agreed diversion pathways; regional mutual-aid agreements; stockpiles of critical oncology supplies.

Cyberattack on hospital IT	System	Loss of EHR access, scheduling disruption, communication failures	Anomaly detection for early warning; AI-assisted manual triage from partial data	Workflow simulations for downtimes; scenario analysis of manual vs. electronic operations	Incident-response playbooks; analogue backup procedures; periodic drills integrating modeling insights.
Acute workforce shortage	System	Reduced clinic slots, delayed RT and systemic therapy, burnout	AI-based scheduling and load balancing; prediction of staffing shortages; decision support for task shifting	Capacity and queueing models to test staffing configurations and extended hours	Cross-training and role substitution; dynamic prioritization rules; proactive recruitment and retention policies.
Drug or radioisotope shortage	System	Inability to deliver standard regimens or radionuclide treatments	AI tools to optimize allocation to highest-benefit patients; prediction of near-term demand	Optimization models for allocation and regimen modification; scenario analysis of alternative protocols	Transparent prioritization criteria; alternative protocols validated through models; regional and international pooling.
Rapid disease progression or emergency presentation	Patient	Acute instability, need for urgent intervention and re-planning	AI-based early-warning scores from symptoms/labs; ED triage support	Individual-level digital twins to simulate alternative urgent strategies (e.g., RT vs. surgery vs. systemic therapy)	Embed fast-track emergency oncology pathways; integrate model-informed options into crisis tumor boards.
Severe treatment-related toxicity	Patient	Treatment interruption, hospitalization, risk of death	Toxicity prediction models; real-time monitoring via apps and wearables	Models linking interruptions and dose reductions to progression risk, to guide restarting or modifying therapy	Proactive supportive care; risk-adapted follow-up; protocols balancing toxicity management with disease control.

Figure 3. Crisis management loop in oncology.

6.1. Types of crises in cancer care

Crises affecting cancer care can be broadly classified into system-level and patient-level events. System-level crises include global health emergencies (e.g., COVID-19), natural disasters, major cyber-incidents, prolonged supply-chain failures, and acute workforce shortages. These events disrupt infrastructure, capacity, staffing, supply of drugs and radioisotopes, and patient access to diagnostic and treatment facilities. Disaster medicine literature consistently describes healthcare crises in terms of phases, mitigation, preparedness, response, and recovery, requiring coordinated planning across institutions.[100, 101]

Patient-level crises include rapid disease progression, emergent complications (e.g., spinal cord compression, obstructive syndromes, sepsis), and severe treatment-

related toxicities requiring urgent intervention. While these are not "disasters" in the classic sense, they are acute instability points in an individual's cancer trajectory that demand rapid triage and re-optimization of treatment. Both categories of crises interact: system-level disruptions can increase the frequency and severity of patient-level crises by delaying care or constraining the range of feasible interventions.[19, 95, 102, 103]

Table 4 summarizes typical crisis scenarios in oncology and maps potential AI- and modeling-based strategies to mitigate their impact on cancer outcomes.

6.2. Conceptual frameworks for crisis management in health systems

Generic emergency management frameworks emphasize an iterative cycle of preparedness, response, recovery, and mitigation, supported by surveillance, risk assessment, and continuous learning. In healthcare, these phases are operationalized through emergency plans, surge capacity arrangements, stockpiling, staff training, and incident command systems.[100,101] Recent work on resilient healthcare systems extends this logic by highlighting the importance of data infrastructure, real-time situational awareness, and adaptive governance to manage complex, prolonged crises.[101]

When applied to oncology, this implies that cancer networks should not only react to acute shocks but also maintain crisis-ready pathways and analytical tools that explicitly consider how disruptions in screening, staging, radiotherapy, surgery, and systemic therapy propagate into later-stage presentations and excess mortality. Modeling and AI are natural candidates to provide the anticipatory intelligence required in the preparedness and mitigation phases, while also supporting real-time response and post-crisis recovery planning [Figure 3].

6.3. COVID-19 as a case study of systemic disruption

The COVID-19 pandemic provides a paradigmatic example of crisis-induced disruption in cancer care. An umbrella review of systematic reviews by Muka et al., showed consistent evidence of reductions and delays in screening, diagnosis, and treatment across many cancer types, along with increased psychosocial burden and rapid expansion of telemedicine.[102] Patt et al., described substantial decreases in new cancer diagnoses and delays in care in the United States during the early phase of the pandemic.[19]

Modeling studies have quantified the likely impact of these disruptions. Maringe et al., estimated additional cancer deaths in England due to diagnostic delays using a national population-based modeling approach, predicting substantial excess mortality over the subsequent years [95]. Ward et al. similarly projected worse stage distribution and survival outcomes resulting from diagnostic delays.[103] Analyses of radiotherapy capacity showed deferral of non-urgent treatments and modifications of fractionation schedules to reduce visits, with modeling of different triage and scheduling strategies to maintain essential services.[104, 105]

These studies collectively demonstrate that during a crisis, time becomes a critical strategic resource in oncology: delays in access and changes in practice patterns translate into measurable shifts in progression and survival. They also illustrate the role of modeling as an ex-ante and ex-post tool to estimate the consequences of alternative policies (e.g., prioritizing certain tumor types, using hypofractionation, or aggressively reducing diagnostic backlogs).

6.4. Role of AI in crisis management

AI contributes to crisis management in at least three domains: epidemiologic and operational forecasting, clinical triage, and virtualization of care. Reviews of AI in pandemic responses highlight models for predicting infection dynamics, hospital admissions, ICU occupancy, and resource needs using machine learning and deep learning applied to surveillance, mobility, and clinical data.[105-108]

At the hospital level, AI systems have been used to optimize operations by forecasting patient arrivals, bed occupancy, and staff or supply requirements, enabling more efficient allocation of constrained resources.[107,109,110] In oncology, such tools can support decisions on when to postpone elective procedures, which patients to prioritize for in-person visits or radiotherapy slots, and how to schedule high-risk treatments during surges. AI-based risk stratification models can also help identify cancer patients at greatest risk of severe outcomes from concurrent infections (such as COVID-19) and inform shielding or

vaccination strategies.[105, 107]

AI-enabled telemedicine, automated symptom monitoring, and natural-language–based triage bots played an important role during the pandemic in maintaining contact with patients while minimizing physical visits.[19,102,109] Strategically, this allowed some aspects of cancer care (toxicity assessment, psychosocial support, survivorship follow-up) to be decoupled from physical infrastructure, increasing resilience.

6.5. Role of modeling in crisis scenarios

Modeling and simulation provide a complementary scenario-planning and experimentation layer for crisis management. In radiation oncology, pathway simulations and discrete-event models have been used to replicate real-world workflows and test the impact of alternative triage rules, scheduling policies, and capacity expansions.[104,105,111]. "Modeling approaches to radiotherapy in the era of COVID-19" illustrate how patient-level risk of infection, treatment benefit, and resource constraints can be combined to prioritize cases and design contingency regimens.[105, 111]

At a broader system level, models of cancer pathways have been used to estimate the cumulative burden of diagnostic and treatment backlogs and to evaluate mitigation strategies such as extended clinic hours, additional imaging capacity, or temporary centralization of complex treatments.[95,103,104,112] These models help policymakers understand trade-offs between different patient groups and tumor sites, enabling decisions that minimize overall harm rather than simply restoring pre-crisis volumes.

7. Challenges, ethical and organizational considerations

The strategic use of novel therapies, AI, and modeling for cancer progression management is constrained by a number of technical, ethical, and organizational challenges. Recent reviews on AI in oncology and across the cancer care continuum emphasize that issues such as data quality, bias, interpretability, legal accountability, and organizational readiness are now as important as algorithmic performance.[12,34,64] Addressing these challenges is essential if AI- and model-informed strategies are to be safely deployed at scale and to support crisis-ready cancer care rather than amplifying existing inequities.

7.1. Data quality, bias, and generalizability

Most AI and modeling approaches in oncology are trained and calibrated on data from specific institutions, regions, or health systems. Reviews of AI across the cancer care continuum and in general cancer applications highlight that training datasets often over-represent patients from high-income countries, large academic centers, and majority ethnic groups, while under-representing low-resource settings, minorities, older adults, and patients with multimorbidity.[12,64] This limits external validity and raises concerns that models may systematically underperform in precisely those populations that already face barriers to cancer care.

Data quality problems are also common: missing data, inconsistent coding, non-standard imaging protocols, and outcome misclassification can all degrade model performance and lead to spurious associations.[12,34] In oncology specifically, temporal dataset shifts are frequent because diagnostic technologies, treatment standards, and staging systems evolve rapidly; models trained on historical cohorts may not reflect current therapeutic options or patterns of progression. Reviews on ethical and legal aspects of AI in oncology explicitly warn that uncorrected dataset bias and poor documentation of data provenance can translate into discriminatory recommendations and opaque risk stratification tools.[34]

Consensus guidelines such as the FUTURE-AI framework call for systematic bias assessment, careful documentation of inclusion/exclusion criteria, transparent reporting of data pipelines, and extensive external validation across diverse populations as preconditions for trustworthy deployment.[69] For mathematical and simulation models, analogous concerns arise around parameter uncertainty and structural assumptions; if key parameters are inferred from limited or biased evidence, projected benefits of novel strategies or crisis policies may be overly optimistic for some groups and pessimistic for others.[12, 34]

7.2. Interpretability and trust in AI-assisted decision-making

Even when model performance is adequate, adoption in clinical practice depends heavily on trust and perceived interpretability. A recent systematic review on trust in AI-CDSS among healthcare workers identified eight thematic areas that influence trust, including perceived usefulness, reliability, explainability, workflow integration, training, and organizational support.[66] A broader 30-year review of trust in medical AI similarly concludes that clinicians are more likely to rely on systems that provide understandable rationales, align with professional norms, and allow for human override.[113]

Systematic reviews of AI-CDSS show that many published tools are "black boxes" from the user's perspective: they provide risk scores or recommendations without clear indication of which features drive the output or how uncertainty is quantified.[114] This is particularly problematic in oncology, where decisions often involve trade-offs between progression control, toxicity, and quality of life, and where patients may ask clinicians to justify why a given regimen or triage decision was recommended. Lack of transparency can lead to automation bias (over-reliance without adequate scrutiny) or, conversely, complete rejection of the system.

Frameworks for trustworthy AI emphasize that interpretability is not only a technical property but also a socio-technical one: explanations must be calibrated to user roles (oncologists, nurses, managers) and integrated into existing decision structures such as tumor boards and clinical pathways.[65,66,69,113] Narrative reviews on AI in oncology further note that large language models and other generative systems require additional safeguards to avoid hallucinations and to ensure that generated text (e.g., draft notes or patient information) does not mislead clinicians or patients.[37, 65]

7.3. Integration into clinical workflow and strategic decision processes

Another recurrent challenge is the gap between prototype performance and real-world impact. Reviews and case studies across oncology emphasize that many AI tools remain confined to research environments because they are not embedded into routine workflows, electronic health record interfaces, or strategic decision processes.[64,65] A systematic review of AI-based CDSS highlights issues such as alert fatigue, poor usability, misalignment with local guidelines, and lack of clarity on who is responsible for acting on AI outputs.[114]

In strategic management terms, AI and modeling must align with micro-level point-of-care decisions, meso-level processes such as tumor boards and pathway management, and macro-level planning for capacity and crisis response. This includes defining when AI is consulted (e.g., automatically for all cases versus selectively for high-risk patients), how its recommendations are documented, and how disagreements between AI suggestions and clinician judgment are resolved. Reviews on AI as a strategic enabler in health systems argue that organizations need explicit governance structures to prioritize high-value use cases, retire low-impact tools, and avoid a proliferation of poorly coordinated pilots.[65,115]

Large language models introduce additional workflow questions: for example, whether they should be used for summarizing records, generating draft tumor-board notes, or assisting with patient communication, and how such use should be supervised and logged. Position papers from oncology societies and regional guidance documents stress that such tools must complement, not replace, multidisciplinary deliberation and evidence-based guidelines.[37,65,115]

7.4. Ethical, legal, and regulatory issues

The deployment of AI and digital twins in oncology raises complex ethical and legal questions that extend beyond traditional concerns about informed consent and confidentiality. A dedicated review on artificial intelligence and decision-making in oncology outlines challenges related to consent for secondary uses of data, risk of re-identification with high-dimensional datasets, algorithmic bias and discrimination, opaque liability chains, and the potential dehumanization of care if AI is perceived as substituting clinical judgment.[34]

Papers on language models in oncology highlight further risks, including hallucinated or outdated recommendations, subtle misinformation, and the possibility of generating persuasive but misleading explanations for complex treatment choices.[37,65] ESMO's (European Society for Medical Oncology) recent guidance on the use of large language models in clinical practice

emphasizes that such systems must be used under human supervision, with strict controls on data input, clear documentation that AI was involved, and prohibition of unsupervised patient-facing use in high-stakes contexts.[115]

The FUTURE-AI consensus guideline proposes six overarching principles, fairness, universality, traceability, usability, robustness, and explainability, and translates them into 30 best practices covering the entire lifecycle of healthcare AI, from design and validation to deployment and post-market surveillance.[69] These principles are highly relevant to oncology digital twins and simulation tools, which may eventually be used to test treatment strategies virtually before exposing real patients to them. Ensuring that digital twins are scientifically credible, transparently validated, and equitably deployed is central to maintaining public trust.

7.5. Organizational readiness and change management

Finally, successful implementation of AI and modeling for cancer progression management depends on organizational readiness and effective change management. Early conceptual work on organizational readiness for AI in health care argued that many hospitals focus primarily on technology acquisition while underestimating the importance of leadership engagement, culture, clinical champions, and alignment with strategic goals.[116] More recent empirical studies show that healthcare workers' readiness for medical AI is generally moderate to high, but that perceptions of organizational change, training opportunities, and communication strongly influence acceptance.[117]

A quantitative study in a university hospital found a positive association between readiness for medical AI and openness to organizational change, suggesting that investments in change management, education, and participatory governance can create a virtuous circle [117]. Analyses of AI adoption and satisfaction in healthcare organizations similarly highlight tensions between enthusiasm for innovation and concerns about workload, role changes, and loss of professional autonomy [118]. Reviews on AI as a strategic enabler in health systems recommend that organizations treat AI and modeling as part of broader digital-transformation and resilience strategies, rather than as isolated technical projects.[115,119]

For oncology specifically, this implies establishing clear ownership of AI and modeling initiatives (e.g., within cancer centers or regional networks), aligning them with existing quality-improvement and crisis-preparedness programs, and embedding continuous training and evaluation. Organizational maturity for AI should include not only technical infrastructure and data governance, but also mechanisms for ethical oversight, patient involvement, and rapid-learning cycles that connect model performance to real-world outcomes.

8. Future Directions and Research Agenda

Although the integration of novel clinical approaches, AI, and modeling into cancer progression management has advanced rapidly, the field is still in an early translational phase. Current systems are often fragmented point solutions, single predictive models, local digital-twin prototypes, or one-off crisis simulations, rather than fully integrated, learning health systems. Future research needs to move from proof-of-concept tools towards hybrid, multi-level, and prospectively evaluated platforms that can sustainably support clinical and policy decisions in routine and crisis settings.[65,120-123]

8.1. Hybrid AI–mechanistic modeling platforms

One important direction is the development of AI–mechanistic hybrid platforms, sometimes referred to as mechanistic learning, that combine the explanatory power of mathematical models with the pattern-recognition capabilities of machine learning.[120-122] Mechanistic learning frameworks use mechanistic models as structural priors or constraints while allowing parts of the system, such as unknown parameters, functional relationships, or stochastic terms, to be learned from data.[120,121]

Recent reviews highlight several strategies for hybridization: i) using ML to estimate parameters or initial conditions for ODE/PDE models; ii) embedding differentiable mechanistic modules inside neural networks; and iii) learning low-dimensional surrogates of complex simulations that can be evaluated in real time.[121,122,124] In oncology, proof-of-concept studies have shown that combining mechanistic tumor-immune models with deep learning can improve prediction of

survival or response under immune checkpoint inhibitors compared with either approach alone.[122] Hybrid pharmacometric–machine learning models have been proposed for oncology drug development to better capture nonlinear PK/PD relationships, inter-patient variability, and high-dimensional covariates.[124]

A concrete research agenda includes:[120-122, 124]

- systematically comparing purely data-driven, purely mechanistic, and hybrid approaches for key tasks (e.g., progression and toxicity prediction, optimal scheduling of combined radiotherapy–systemic regimens);
- developing benchmarking datasets and standardized reporting for hybrid oncology models; and
- exploring how mechanistic constraints can reduce overfitting and improve extrapolation when clinical data are sparse or evolving (for example, after the introduction of new therapies or fractionation schemes).

8.2. Dynamic, real-time digital twins across the cancer trajectory

DTs are increasingly viewed as a key vehicle for implementing strategic, model-informed management of cancer progression.[15,16,42,125] Most current oncology DTs are still early prototypes, often static or semi-static models calibrated at baseline or at a small number of time points. Future research needs to move towards dynamic, real-time digital twins that are continuously updated with clinical, imaging, and -omics data and that can simulate alternative scenarios over the entire cancer care trajectory.

Recent narrative and systematic reviews argue that oncology digital twins could support treatment sequencing, adaptive radiotherapy, toxicity mitigation, and trial design by enabling in silico exploration of strategies before implementation.[15,16,125] Position papers in biomedical informatics similarly describe medical digital twins as core infrastructure for precision medicine, emphasizing the need for robust synchronization between the twin and the patient over time.[42] A very recent contribution on dynamic digital twins for adaptive oncology outlines architectures in which multimodal streams (EHR, imaging, molecular data, wearables) update a patient-specific model after each treatment cycle, with predicted trajectories feeding into adaptive protocols.[125]

Future work should address:[15,16,42,125,126]

- technical challenges in multimodal data integration, real-time updating, and uncertainty quantification;
- clinical questions about when and how often the twin should be re-calibrated (e.g., after each cycle, imaging exam, or major event);
- regulatory and ethical aspects of using DTs to support high-stakes decisions (for example, de-escalation or radical changes in therapy); and
- scaling from single-patient twins to twin networks representing populations or service-level pathways for strategic planning.

8.3. Multi-level and crisis-aware decision-support architectures

Another research priority is the design and evaluation of multi-level decision-support architectures that explicitly connect micro (patient), meso (service), and macro (system) decisions in both routine and crisis conditions. Existing AI-enabled clinical decision support systems in oncology mainly target micro-level decisions, such as regimen selection or risk prediction, and are often not integrated with operational and policy-level tools.[35, 123]

Future systems should combine:

- patient-level AI/CDS and digital twins embedded in electronic health records and tumor boards;
- service-level simulation models for capacity planning, radiotherapy and infusion scheduling, and backlog management;
- system-level tools for scenario analysis during crises (e.g., pandemics, workforce shocks, supply disruptions).

Concept papers on responsible AI governance in oncology emphasize that such architectures require clear role definitions, oversight mechanisms, and integration into existing decision forums.[126] Early work on autonomous AI agents for precision oncology suggests that multi-tool agents can orchestrate guideline retrieval, risk modeling, and trial matching; extending these approaches to include simulation and crisis modules is a natural next step.[65]

Research questions include how to design interfaces that communicate model outputs appropriately to different

user groups (clinicians, managers, policymakers), how to propagate uncertainty information across levels, and how to align micro-level recommendations with macro-level constraints in crisis triage protocols. There is also a need to explore ethical frameworks for reconciling individual and population-level objectives when AI and models inform rationing or prioritization decisions.[126]

8.4. Prospective trials, implementation science, and consortia

Finally, a major gap is the lack of prospective, adequately powered trials and robust implementation studies that measure the real-world impact of AI- and modeling-based strategies on outcomes and costs. Most published AI and modeling work in oncology consists of retrospective validation, simulation-only studies, or small pilot implementations.[35,65,123] Large trials and quasi-experimental studies are now emerging, for example, the NHS trial of AI-supported breast cancer screening, which will evaluate diagnostic performance, workflow effects, and patient outcomes at scale.[127] However, similar prospective efforts are rare for integrated AI–modeling platforms or digital twins.

Future research should prioritize:[38, 128, 129]

- pragmatic clinical trials comparing AI/model-informed strategies versus standard care, with endpoints that include survival, progression-free survival, quality of life, costs, and equity impacts;
- stepped-wedge and cluster-randomized designs for evaluating system-level interventions such as AI-based triage and capacity management tools;
- implementation-science studies that characterize barriers, facilitators, and organizational readiness, building on frameworks that have been proposed for AI in radiotherapy and broader oncology.

International and national consortia will be crucial. Initiatives such as EuCanImage, which develops data standards and shared infrastructures for AI in imaging and precision oncology, demonstrate the value of common data models and interoperability for multi-center research.[129] Large digital-oncology programs (for example, the German Cancer Research Center's cross-topic "Digital Oncology") are building integrated teams of data scientists, clinicians, and modelers to accelerate translation.[130] Professional societies are also beginning to shape the agenda; for instance, the ESMO has launched a dedicated Congress on Artificial Intelligence and Digital Oncology to coordinate research, policy, and education in this field.[131]

Conclusions

This review reframes the management of cancer progression as a strategic, system-wide challenge rather than a sequence of isolated clinical decisions. By organizing decisions along the cancer care trajectory and across micro, meso, and macro levels, the proposed framework clarifies how novel therapeutic approaches, AI, and modeling can function as complementary pillars of a unified strategy. Novel clinical and organizational innovations, such as precision oncology, immunotherapy, advanced radiotherapy techniques, and structured pathways, expand the feasible decision space for controlling tumor evolution over time. AI contributes real-time, data-driven intelligence for risk stratification, treatment selection, toxicity prediction, operational forecasting, and crisis triage. Mechanistic models, simulation tools, and digital twins add an experimentation and planning layer, enabling in silico exploration of treatment sequences and system-level scenarios, including those arising during crises such as pandemics, workforce shortages, or supply disruptions. At the same time, the review underscores substantial challenges: biased and fragmented data, limited external validation, opaque models, regulatory uncertainty, and variable organizational readiness. Addressing these requires robust governance, transparency, and systematic evaluation in real-world settings, ideally through multicenter consortia and prospective studies. Future work on hybrid AI–mechanistic platforms, dynamic digital twins, and multi-level decision-support architectures could help embed strategic thinking directly into clinical workflows and health-system planning. If developed and implemented responsibly, the integration of AI and modeling with novel clinical strategies offers a path to transform cancer care from reactive management of events into proactive, learning and crisis-resilient management of progression.

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Competing interests

The authors declare that they have no competing interests.

Abbreviations

Artificial Intelligence: AI; Global Cancer Observatory: GLOBOCAN; Digital Twins: DTs; Immune Checkpoint Inhibitors: ICIs; Immune-Related Adverse Events: irAEs; Stereotactic Radiosurgery: SRS; Stereotactic Body Radiotherapy: SBRT; Spatially Fractionated Radiotherapy: SFRT; Multidisciplinary Tumor Boards: MTBs; Next-Generation Sequencing: NGS; Electronic Health Records: EHRs; Computed Tomography: CT; Magnetic Resonance Imaging: MRI; Positron Emission Tomography: PET; Clinical Decision Support Systems: CDSS; Ordinary Differential Equation: ODE; Partial Differential Equation: PDE; Agent-Based Models: ABMs; Pharmacokinetics and Pharmacodynamics: PK/PD; Tumor Control Probability: TCP; Normal Tissue Complication Probability: NTCP; Emergency Department: ED; European Society for Medical Oncology: ESMO; Intensive Care Unit: ICU; National Health Service: NHS.

Authors' contributions

All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

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