

The Digital Frontier: A Narrative Review of Bio-Digital Twins, AI-Driven Orthodontics, and Ethical Clinical Integration

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Abstract

The transition from static digital records to dynamic Bio-Digital Twins is reshaping orthodontics by combining anatomical and functional data to simulate physiological behavior and improve diagnostic accuracy. This narrative review examines how artificial intelligence, including dynamic Bio-Digital Twins, can predict treatment duration, identify patients at risk of unplanned prolongation, and support personalized decision-making. A search of PubMed, ScienceDirect, Scopus, and Google Scholar was performed, focusing on digital workflows, precision orthodontics, aligner biomaterials, patient-reported outcomes, teleorthodontics, and the ethics of explainable AI. The evidence indicates that dynamic twins are more informative than conventional images because they integrate functional and biological data, while machine learning models estimate treatment time from clinical, imaging, and behavioral variables. Genetic, epigenetic, and multi-omics data further advance precision orthodontics. Successful implementation depends on high-quality data, explainable AI, reduction of algorithmic bias, and continued clinician oversight so that computational tools support rather than replace clinical judgment.

Keywords: Precision, orthodontics; tooth movement; multi-omics; genomics; epigenetics; systems biology; artificial intelligence; machine learning; bone remodeling; personalized orthodontics.

INTRODUCTION

One of the biggest conceptual changes in modern orthodontics is the move from snapshot-based digital dentistry to dynamic Bio-Digital Twins. Static records such as CBCT scans, intraoral scans, cephalometric radiographs, and photographs have been used for decades to diagnose malocclusions and plan treatment [1]. They provide detailed anatomical information, but they capture the patient at a single moment and do not account for the variable functional loads, mandibular movements, and muscle activity that influence tooth position throughout the day [2]. By incorporating multimodal, time-dependent physiological data into a dynamic, adaptive digital model of

the patient, emerging Bio-Digital Twin frameworks aim to overcome this limitation. This represents a paradigm shift from static imaging toward dynamic simulation grounded in real functional behavior rather than theoretical assumptions. [3]

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Several studies have demonstrated the potential of digital twin systems to transform orthodontic diagnostics and treatment planning. Olawade et al. describe a digital twin as a virtual replica that is continuously updated using patient-specific biological and mechanical data, allowing the clinician to simulate how a patient will respond under realistic functional conditions [4]. Digital twins are not limited to anatomical models; they can also incorporate dynamic inputs such as electromyography (EMG), mandibular motion tracking, and bite-force distribution [5]. This integration allows orthodontists to model tooth movement as it would occur in vivo, according to the forces applied during mastication, swallowing, and parafunction, a capability that Bhardwaj et al. also emphasize. [6]

The advantages of Bio-Digital Twins become increasingly apparent as CBCT, and intraoral scan datasets grow more complex and higher in resolution [3]. Traditional imaging stores only morphology, with no information about function, such as how occlusal contacts evolve during mastication or how the mandible moves according to muscle-activation patterns [7]. As Duggal et al. explain, digital twin systems address these limitations by blending imaging with real-time functional data streams, producing a model that not only looks like the patient but behaves like the patient. This functional fidelity is important for predicting tooth movement in multifactorial cases involving asymmetry, temporomandibular disorders, or muscular imbalance. [8]

The quality and integration of the underlying datasets are critical to the accuracy of digital twins. Combining more than one dentition model with CBCT has been shown to improve the accuracy of digital twin construction. Anatomical accuracy alone, however, is not sufficient [5]. To move from static to dynamic modeling, orthodontic systems must incorporate kinesigraphic records of mandibular movement, EMG signals reflecting muscle activation, and spatiotemporal occlusal metrics [8]. These functional datasets allow the Bio-Digital Twin to simulate tooth movement under actual forces rather than idealized vectors, producing more reliable movement trajectories [9].

Emerging computational frameworks facilitate this process. Machine learning-based biomechanical models allow the digital twin to be dynamically adapted as treatment progresses, and simulation environments that integrate physiological signals into anatomical models provide a framework for developing dynamic orthodontic twins that evolve during treatment [2]. Together, these innovations move orthodontics from a static toward a dynamic field of biological modeling, and the overall workflow, from static records to a functionally driven twin, is summarized in Figure 1 [10]. Understanding patients as dynamic systems, rather than as isolated snapshots, offers a more individualized, accurate, and physiologic basis for diagnosis and treatment planning, and points toward more predictable outcomes in digital orthodontics [11].

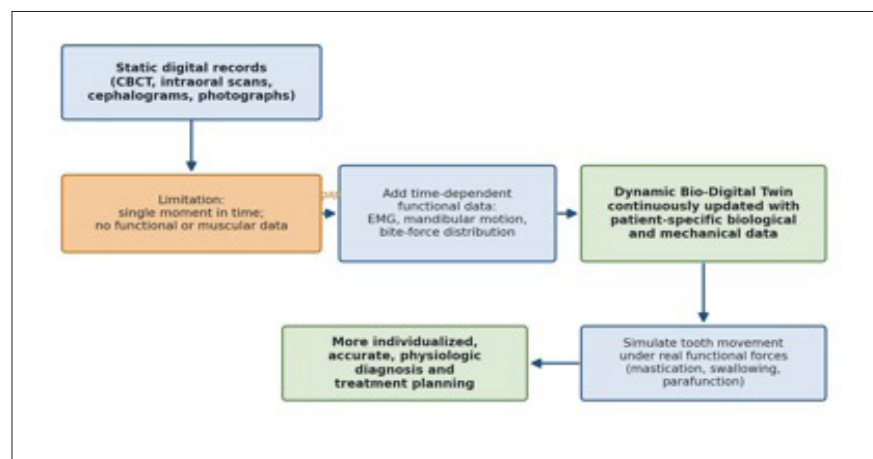


Figure 1. Conceptual shift from static imaging to a dynamic Bio-Digital Twin. Static records capture anatomy at a single moment; adding time-dependent functional data (EMG, mandibular motion, bite-force distribution) yields a continuously updated model that simulates tooth movement under real functional forces and supports more individualized diagnosis and treatment planning. [1,3]

AI-DRIVEN PREDICTIVE ANALYTICS FOR TREATMENT DURATION

Treatment duration is one of the most important factors patients consider when deciding whether to undergo orthodontic treatment. An accurate prediction of overall

treatment time helps motivate patients, prepares them for what to expect, and provides a realistic estimate that allows orthodontists to improve comprehensive treatment planning and appointment scheduling [12]. Before initiating treatment, clinicians must accurately diagnose

the patient and develop an individualized plan with objectives directed at the highest standards of esthetics, occlusion, and long-term stability. [13,14]

A realistic and credible estimate of treatment length is essential because it forms part of the informed consent process and of orthodontic financial planning, and it significantly influences patient satisfaction [12]. Estimating duration begins with the patient's diagnostic records, including dental models, clinical photographs, and radiographs such as cephalometric and panoramic images. From these records, a wide range of quantitative measurements can be obtained, including cephalometric values, tooth size-arch length discrepancy (TSALD), molar classification, and other clinical parameters. [15,16]

The application of artificial intelligence (AI) is transforming healthcare through the growing availability of health data and the rapid advancement of analytical techniques [14]. Machine learning (ML), a subset of AI, is used to build complex predictive models and extract clinically meaningful knowledge [17]. In clinical practice, ML-based models can assist clinicians in making individualized decisions, including predicting orthodontic treatment duration. AI encompasses systems capable of collecting and analyzing large volumes of data to generate information that supports and enhances human decision-making. [18]

In recent years, the application of AI and ML in dentistry, and particularly in orthodontics, has grown rapidly. These technologies have been used to analyze radiographic images, predict craniofacial growth, estimate age and sex, determine facial type and oral hygiene indices, and optimize treatment planning and clinical decision-making [19]. Additional variables incorporated into AI models include dental crowding, overjet, overbite, crossbite, the need for extractions, and even the potential requirement for orthognathic surgery. [21]

According to studies by Volović and colleagues, applying AI to predict treatment duration requires identifying patients at high risk for prolonged treatment and implementing predictive models that estimate treatment length while alerting clinicians when actual progress deviates from the original plan [17]. This approach helps prevent treatment creep by prompting timely corrective interventions. These models also consider the number of activations required and can recommend the most appropriate appliances, including conventional brackets, self-ligating brackets, clear aligners, and temporary anchorage devices [22]. They further incorporate variables such as poor attendance, inadequate elastic wear, and insufficient torque control, and they recognize that treatments involving serial or indicated extractions generally require longer treatment times. [23]

Current evidence suggests that the American Board of Orthodontics Discrepancy Index (ABO-DI) is a valuable tool for estimating treatment complexity because it relies on clinical parameters such as overjet, overbite, crowding, open bite, crossbite, occlusal relationships, and skeletal discrepancies [10]. AI models, particularly Random Forest and Deep Learning algorithms, provide more accurate predictions of duration because they integrate a broader range of clinical and behavioral variables, including cephalometric measurements, demographic information, extraction requirements, use of auxiliary appliances, patient compliance, missed-appointment history, three-dimensional intraoral scans, and longitudinal treatment data [15]. Integrating these variables enables AI to identify cases at risk of treatment creep at an early stage, as summarized in Table 1, making it a more efficient and reliable alternative to traditional prediction methods. [22]

Table 1. Comparison of methods for estimating orthodontic treatment duration. [22,24]

Approach	Basis and inputs	Strengths and limitations
ABO Discrepancy Index (ABO-DI)	Overjet, overbite, crowding, open bite, crossbite, occlusal relationships, skeletal discrepancies	Standardized, simple index of case complexity; estimates complexity rather than duration directly and omits behavioral data
Naive Bayes (machine learning)	Classification features from patient records	Simple probabilistic classifier for continuation versus discontinuation; lower accuracy than Random Forest in comparative testing
Random Forest and Deep Learning (machine learning)	Cephalometric, demographic, extraction, auxiliary appliances, compliance, missed appointments, 3D scans, longitudinal data	Higher accuracy (about ± 7.27 months) and early detection of treatment-creep risk; requires large, high-quality, representative datasets

Figure 1. Dharmasena et al. used two machine learning algorithms, Naive Bayes and Random Forest, to predict the likelihood of orthodontic treatment continuation or discontinuation. Their analysis of 310 patient records showed that Random Forest achieved the highest predictive accuracy and that an active treatment duration exceeding five years was the primary predictor of discontinuation. Overall, the ML models predicted actual treatment duration with an accuracy of approximately ± 7.27 months. Establishing appropriate clinical benchmarks remains essential for evaluating the predictive performance of these models. [15-16,24] Orthodontic treatment duration is influenced by multiple factors, including measurable pretreatment variables as well as events occurring during treatment. Pretreatment clinical examinations and cephalometric analyses contribute to case complexity and ultimately influence duration. Additional factors arising during treatment, including patient compliance, orthodontic emergencies, and missed appointments, can significantly affect the overall treatment time. Beckwith and colleagues demonstrated that bracket failures, poor oral hygiene, and missed appointments significantly prolonged treatment duration. [16,25-26]

Using Historical Data Patterns to Identify Early Warning Signals

Machine learning models can analyze historical patterns from large orthodontic databases to identify early warning signs associated with prolonged treatment [18]. Variables such as tooth extractions, occlusal complexity, impacted maxillary canines, auxiliary appliance use, and cephalometric characteristics can be recognized from the earliest stages, facilitating preventive interventions aimed at avoiding treatment creep [23]. Rather than relying solely on an initial estimate, AI systems continuously monitor patient progress and detect when a case begins to deviate toward an unplanned extension of treatment. [27]

Historical treatment data allow construction of a typical treatment trajectory that incorporates total duration, stage-specific tooth movement, the number of appointments and rescheduled visits, bracket or aligner failures, elastic-wear compliance, treatment-plan modifications, extractions or additional procedures, and digital progress assessed through three-dimensional scans [20,21]. Against this trajectory, modern AI models identify deviations from expected progress in clinically similar cases, and the

Table 2. Early warning signals of treatment creep detected by AI-based monitoring, grouped by type. [18,23]

Signal type	Representative indicators
Clinical	Delayed alignment during early phases; persistence of malocclusions that should have improved; repeated appliance adjustments
Behavioral	Poor compliance with elastics or aligners; missed or delayed appointments; frequent appliance failures
Mechanical	Repeated rebonding or recementation; frequent archwire-sequence changes; prolonged intermediate phases without measurable progress

recurring warning signals they detect are grouped in Table 2 [23].

By learning from thousands of previous cases, machine learning models detect deviations between actual progress and the expected trajectory for similar patients, providing clinicians with valuable decision-support tools for personalized treatment management. [18,21,23]

BIOMATERIAL INTEGRATION AND ALIGNERS 2.0

The success of orthodontic treatment planned with artificial intelligence depends not only on accurate digital planning but also on the properties of the material used to manufacture clear aligners. Although AI can predict tooth movement, it is the aligners themselves that must deliver the forces required to achieve it [28]. Advances in biomaterials and manufacturing have produced a new generation of aligners, often called Aligners 2.0, that offer

more stable force delivery, superior mechanical properties, and greater treatment customization. [29,30]

Aligners are manufactured primarily from thermoplastic polymers such as polyethylene terephthalate glycol (PETG) and thermoplastic polyurethane (TPU) [31]. Material composition directly influences behavior in the oral environment. Traditional single-layer materials tend to lose force rapidly because of their viscoelastic properties, whereas multilayer and hybrid materials better retain elasticity, recover their shape more readily, and maintain more constant force throughout treatment [32]. SmartTrack, for example, provides better adaptation to the tooth and more uniform force delivery, which supports more predictable tooth movement. [33]

A central challenge in aligner therapy is maintaining adequate force across the recommended wear period. Because of viscoelastic behavior, force decreases

progressively after the aligner is seated, a phenomenon known as stress relaxation [30]. From a biomechanical standpoint, force depends on material stiffness and deformation, expressed as $F = k \cdot x$, so both the material and the aligner thickness determine the magnitude of the applied force and how long it is sustained across the approximately 14 days of clinical use. [34,35]

Recent evidence indicates that the greatest loss of force occurs during the first few hours of wear, after which it tends to stabilize [34]. Materials such as F22 Evoflex and Erkoloc-Pro retain force better than conventional materials, promoting more predictable tooth movement and reducing the need for refinements [35]. Factors such as intraoral temperature, saliva, and aligner design also influence performance: elevated temperatures accelerate force decay, whereas saliva has a minor effect. Thicker aligners generate greater forces, and stiffer materials

facilitate more controlled tooth movement while reducing the risk of unwanted tipping. [36]

Experimental findings also indicate that biomechanical behavior depends primarily on material properties rather than attachment design. The thermoforming process can alter the thickness and certain physical properties of PETG, so both the material and the manufacturing technique influence the stability of the applied forces [33]. Three-dimensional printing represents a further advance in Aligners 2.0, since it enables fabrication of customized aligners with variable thickness and shape-memory materials [37]. The main material families and their force-delivery behavior are compared in Table 3, and together these innovations combine digital planning with more advanced biomaterials to achieve treatments that are more precise, predictable, and tailored to each patient. [38]

Table 3. Clear aligner materials and their force-delivery behavior. [28,38]

Material or system	Type	Force-retention behavior	Clinical implication
PETG (single-layer)	Thermoplastic polyester	Rapid force decay from viscoelasticity; thermoforming alters thickness and properties	Baseline material; less constant force across wear period
TPU, multilayer and hybrid (e.g., SmartTrack)	Thermoplastic polyurethane or layered	Better elastic recovery; more uniform, sustained force	More predictable movement; improved fit
F22 Evoflex, Erkoloc-Pro	Advanced thermoplastics	Superior force retention after the first hours	Fewer refinements; more predictable movement
3D-printed, shape-memory	Printed customizable polymers	Variable thickness; programmable force profile	Patient-specific force delivery; emerging option

QUANTIFYING PATIENT-REPORTED OUTCOME MEASURES (PROMS)

Patient-reported outcome measures (PROMs) have become an important part of healthcare because they allow clinicians to understand how patients feel during treatment. Clinical examinations provide essential information, but they do not always capture the patient's daily experience [39]. PROMs add another perspective by measuring pain, comfort, quality of life, and treatment satisfaction, and they help determine whether the changes seen after treatment are meaningful in the patient's everyday life. [40,41]

When patients regularly share their symptoms and concerns, clinicians gain a better understanding of progress and can respond more effectively [41]. PROM scores should nevertheless be interpreted carefully, because not every change represents a real clinical improvement. Considering these results alongside the patient's clinical

condition allows clinicians to make better decisions and provide more personalized care. [42,43]

Digital technology has changed how orthodontic care can be delivered. Teleorthodontics allows orthodontists to stay connected with patients between appointments through virtual consultations, smartphone photographs, and other digital tools [44]. This approach makes follow-up more convenient and helps identify possible problems before the next office visit. Although remote care offers many advantages, it is designed to support conventional treatment rather than replace direct clinical evaluation. [45-46]

Artificial intelligence has expanded the possibilities of teleorthodontics by making remote monitoring more effective. AI-based platforms can review patient-submitted images, evaluate aligner tracking, monitor oral hygiene, and alert clinicians when additional attention may be needed [46,47]. These systems also encourage patients

to participate more actively by sending regular updates throughout treatment; even so, the orthodontist remains responsible for the final clinical decisions. [48]

Recent evidence supports the use of teledentistry for orthodontic follow-up. Studies have shown that remote monitoring can reduce unnecessary office visits without

compromising the quality of care, and more frequent interaction allows clinicians to identify concerns earlier and provide guidance when needed [48]. The way these elements connect the clinician's plan to the patient's reality is illustrated in Figure 2, creating a more efficient follow-up process while helping patients stay engaged. [49,50]

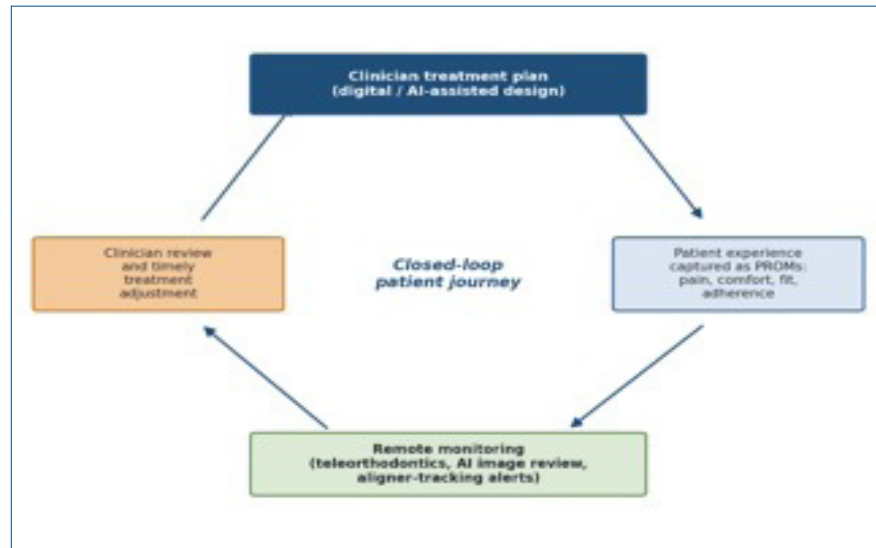


Figure 2. Closed-loop patient journey in digital orthodontics. The clinician's plan is delivered, the patient's experience is captured as PROMs (pain, comfort, fit, adherence), remote monitoring through teleorthodontics and AI review returns that information to the clinician, and timely adjustments feed back into the plan. [45,49]

Taken together, these studies show that PROMs and digital technologies complement each other in support of patient-centered orthodontic care. PROMs provide valuable information about the patient's experience, while teleorthodontics, artificial intelligence, and teledentistry make it possible to collect that information during treatment [39,40]. By combining patient feedback with continuous remote monitoring, orthodontists can identify concerns earlier, make timely adjustments, and maintain closer communication with their patients [41]. This ongoing exchange creates a closed-loop patient journey in which the patient's experience becomes an integral part of every clinical decision. [42,43]

GENETIC AND EPIGENETIC FACTORS IN PRECISION ORTHODONTICS

From Conventional to Precision Orthodontics

Traditional orthodontics relies primarily on clinical, radiographic, and biomechanical parameters to plan tooth movement, on the assumption that similar patients respond similarly to the forces applied. Clinical experience shows otherwise: the rate of tooth movement varies considerably between individuals, results are not uniformly stable, and side effects occur [51]. These observations indicate that conventional planning does not account for the

full range of biological factors involved [52]. Precision orthodontics aims to integrate biological information with biomechanical principles so that treatment can be predicted and tailored more effectively. [53]

Genetic and Epigenetic Basis of Orthodontic Tooth Movement

Orthodontic forces produce mechanical stress that initiates an inflammatory cascade and a coordinated remodeling of the periodontal ligament and alveolar bone that allows teeth to move [54]. Osteoclast activation and bone resorption are governed by cytokines such as IL-1 β , TNF- α , and IL-6, and mechanical stimuli are coupled to bone remodeling through the RANK/RANKL/OPG signaling pathway. Genetic differences among individuals influence this response; polymorphisms in genes involved in inflammatory signaling, such as IL1, and in mechanosensitive pathways, such as P2RX7, have been associated with differences in the rate of tooth movement and in susceptibility to external apical root resorption [55]. Epigenetic regulation, including microRNAs such as miR-21, DNA methylation, and histone modifications, also shapes gene expression, and unlike fixed genetic variants it is dynamic and responds to mechanical loading; the principal factors are summarized in Table 4. [56]

Table 4. Key genetic and epigenetic factors influencing orthodontic tooth movement. [57-59]

Factor or pathway	Type	Role in tooth movement	Clinical relevance
IL-1β, TNF-α, IL-6	Pro-inflammatory cytokines	Drive osteoclast activation and bone resorption	Modulate rate of tooth movement
RANK / RANKL / OPG	Signaling pathway	Couples mechanical stimuli to bone remodeling	Central control of resorption-formation balance
IL1 polymorphism	Genetic variant	Alters inflammatory signaling	Variation in movement rate
P2RX7 polymorphism	Mechanosensitive genetic variant	Modifies mechanotransduction	Movement rate and root-resorption risk
miR-21	Epigenetic regulator (microRNA)	Promotes osteoclast differentiation and remodeling	Dynamic marker responsive to loading
DNA methylation, histone modifications	Epigenetic regulation	Adjust gene expression under mechanical load	Potential treatment-responsive markers

Multi-Omics Integration and Artificial Intelligence

Characterizing this biology at scale generates genomic, transcriptomic, and epigenomic datasets that are too large and interdependent for conventional statistical methods. Artificial intelligence and machine learning are well suited to deriving predictive models from molecular information, clinical data, and imaging [11,20]. These methods can detect complex interactions between biological and biomechanical variables, helping to anticipate treatment outcomes and to plan care on a biological basis rather than on morphology alone. [27]

Clinical Translation Toward Personalized Care

Translated into practice, these tools point toward decision-support systems that treat biological markers as dynamic variables [17,52]. Cytokine expression and epigenetic activity, for example, could inform patient-specific estimates of the optimal activation interval, allowing force application to be timed to each patient's biological response rather than to a fixed schedule. Realizing this potential depends on combining multi-omics profiles with clinical and imaging data within validated computational models. [53]

Future Perspectives

The integration of multi-omics profiling, artificial intelligence, and computational modeling into clinically applicable decision-support systems is likely to underpin future advances in precision orthodontics [11]. As these technologies mature, they could enable continuous monitoring of the biological response to treatment and adaptive care over the course of therapy. Prospective trials are needed to validate these approaches clinically, and biological databases must be collected and standardized

before they can be used routinely [17]. Together, these advances represent an important step toward more predictive, adaptive, and patient-centered orthodontic treatment. [51]

ETHICAL CONSIDERATIONS AND ALGORITHMIC BIAS

The use of artificial intelligence in orthodontics raises several ethical concerns, including algorithmic bias and the black-box nature of many algorithms [4]. As AI is increasingly incorporated into digital workflows and simulation tools such as digital twins, clinicians' ethical duties expand to include critically appraising algorithmic recommendations rather than simply accepting them [27]. Digital twin technology should support decision-making, not replace it; the orthodontist's role is to use AI to enhance care while safeguarding patient safety. The broader ethical discussion emphasizes transparency, accountability, and informed consent regarding how and why decisions are made during treatment. [60]

One response to the black-box problem is the development of explainable artificial intelligence (XAI), which aims to make machine learning models clinically interpretable [10]. XAI techniques seek to reveal how a system reaches a prediction, to identify the factors that most influence it, and to let clinicians judge the validity of a recommendation in context [61]. In dentistry and orthodontics, methods such as SHAP values and saliency maps have been used to characterize the decision pathways of AI models and to improve trust in the resulting recommendations. Even so, most current models remain only partially transparent, which limits the clinician's ability to fully verify their outputs. [62]

AI-based treatment-planning systems depend heavily on machine learning and deep learning models trained

on large clinical datasets. These systems can achieve high diagnostic accuracy and outcome prediction, but their performance depends on the quality and representativeness of the training data [63]. When datasets are incomplete or do not reflect the diversity of the patient population, algorithmic bias can arise and affect patient groups differently; population imbalance, inconsistent labeling, and variation in clinical protocols during data collection can all introduce bias [64]. The result may be recommendations that are valid for some groups but not others, raising questions about the equity and generalizability of AI-supported orthodontic care. [65]

These issues have direct implications for patient management. AI can aid diagnosis, treatment planning, and prediction, but there is a risk that recommendations are accepted without understanding how or why they were generated [21]. A model trained on a skewed population might, for instance, propose a treatment that is not optimal for a patient with different characteristics or age, leading to suboptimal results [27]. This is why human oversight is essential: clinicians must evaluate AI outputs carefully and confirm that they are accurate and appropriate for each patient's circumstances, treating AI as an aid to clinical judgment rather than a replacement. The principal concerns and their mitigations are consolidated in Table 5. [66]

Table 5. *Principal ethical concerns in AI-supported orthodontics and corresponding mitigation strategies. [60-61]*

Ethical concern	Description	Mitigation strategy
Black-box opacity	Reasoning behind AI recommendations is not visible	Explainable AI (SHAP values, saliency maps)
Algorithmic bias	Skewed or incomplete training data disadvantage some groups	Diverse, representative datasets; fairness auditing
Data representativeness	Population imbalance, inconsistent labeling, protocol variation	Standardized, well-labeled multi-center data
Transparency and accountability	Unclear how and why decisions are reached	Documentation, clinician appraisal, informed consent
Human oversight	Risk of accepting outputs uncritically	Clinician verification; AI as decision support, not replacement

CONCLUSION

In summary, the ethical use of AI in orthodontics rests on transparency, interpretability, and accountability. Explainable AI can address the black-box problem by helping clinicians understand how an algorithm reaches its recommendations, while awareness of algorithmic bias and data variability underscores the need to validate and critically evaluate AI-generated information. Upholding these principles depends on the continued involvement of clinicians in decision-making, maintaining a balance between technology and human judgment while keeping patient-centered care at the forefront.

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