Artificial Intelligence, Medical Devices & Soft Law Governance Adam Thierer, R Street Institute

"The faster cycles of innovation and the speed of change for medical device software would benefit from a new regulatory approach." – U.S. Food & Drug Administration (2022)¹

INTR	ODUCTION	2	
HOW	AI/ML POSES SPECIAL PROBLEMS FOR TRADITIONAL REGULATION	3	
А.	Information volume & pacing problems	3	
В.	Growing tech sophistication / interconnectedness problem	4	
C.	Consumer empowerment / democratization problem	4	
D.	Definitional / regulatory authority problem	5	
E.	Speech-related concerns	6	
F.	Inadequate resources problem	6	
EVOI	LUTION OF FDA'S APPROACH TO DIGITAL HEALTH & AI/ML GOVERNANCE	6	
А.	Basic FDA medical device authority	6	
В.	Early software/computing oversight (1981-2002)	8	
C.	Digital health & mobile medical oversight ramps up (2002-2019)	8	
D.	AI/ML-enabled devices become the focus (2019-present)	.11	
SOFT LAW ELEMENTS IN THE FDA'S APPROACH19			
А.	Continued reliance on guidance as primary governance tool	.15	
В.	Coordination with international NGOs & other governments	.16	
C.	Reliance on standard-setting bodies	.16	
D.	Public-private partnerships / multistakeholder meetings & workshops	.17	
RECO	OMMENDATIONS FOR EXPANDED USE OF SOFT LAW FOR AI/ML	17	
A.	AI Audits and Algorithmic Impact Assessments	.18	
В.	Expand enforcement discretion & rely on best practices	. 19	
C.	Expand the use of pilot programs / sandboxing	. 19	
D.	Rely on private AI registries & a more "distributed approach" to governance	. 19	
E.	Expansion of health education / literacy	.20	
CON	CLUSION	20	
APPE	NDIX: THE PROMISE OF AI/ML IN HEALTH CARE	21	
ENDN	NOTES	23	

INTRODUCTION

This paper considers how the continued rapid growth of artificial intelligence (AI) and machine learning (ML) systems create unique governance challenges as these technologies continue to revolutionize health care and the practice of medicine. While AI/ML will have important ramifications for drug discovery and development,² this paper primarily addresses how the U.S. Food & Drug Administration (FDA) has been trying to craft a new governance framework for AI/ML-enabled medical devices. This has proven to be a significant challenge for the agency over the past decade and regulators will likely continue to struggle with AI/ML governance as these technological capabilities expand faster and become even more sophisticated.

To address these challenges, the FDA has been considering the use of some non-traditional regulatory tools and approaches for AI/ML. These new efforts build on the agency's existing "hard law" regulatory tools (i.e., formal statutes and regulations), but also incorporate more flexible, experimental governance strategies. Some of these alternatives could be considered forms of "soft law," which is shorthand for more informal, decentralized, and often voluntary governance tools and strategies.³ Soft law incorporates a diverse range of governance options for emerging technologies, including agency guidance documents and consultations, multistakeholder processes, ongoing consultations, the formation of best practices, and educational efforts.⁴ Soft law approaches are being tapped or recommended increasingly as a way to address AI-related governance matters in many fields.⁵

Importantly, however, this hard law versus soft law distinction is often quite amorphous and varies widely by context and agency.⁶ It is best to think of soft law governance more as a fluid continuum of strategies than a set of rigid and distinct categories.⁷ Soft law typically unfolds in the shadow of hard law, and some agencies embrace these alternative governance tools and methods more robustly and creatively than others.

In the case of the FDA, hard law is still very much at the heart of the agency's approach to regulating digital health technologies, but the agency has shown more willingness to engage in experimental governance or "entrepreneurial administration" when approaching new technologies. The agency has often done so using enforcement discretion, regulatory forbearance, and nonbinding guidance documents.⁸ At all times, however, the potential for far-reaching regulation looms and influences private parties. As a group of leading medical legal experts observes, "[d]iscretionary forbearance from regulation under circumstances specified in nonbinding guidance documents may impress upon innovators a lurking possibility of regulation, allowing FDA to monitor new technologies informally without expending the administrative resources necessary for premarket approval or clearance of every product."⁹ Thus, the role soft law plays for AI/ML devices will always be somewhat more limited than it is in many other emerging technology sectors and contexts

This paper proceeds in four parts. The opening section explores some of the unique challenges and risks associated with algorithmic technologies that will strain traditional regulatory approaches and processes. The second section considers how the FDA has been responding to these challenges over the past decade as the agency has gradually expanded its approach to digital health and AI/ML-enabled medical devices. The third section summarizes the soft law elements of those FDA efforts. Finally, the paper discusses some potential ways that alternative governance approaches might help the FDA overcome the challenges identified herein. An appendix also identifies some

of the ways that AI/ML medical technologies are already being used to address various diseases, disabilities, or ailments.

Despite a professed willingness to consider new strategies, it remains to be seen whether FDA officials or congressional lawmakers are willing to embrace more soft law tools and approaches to keep pace with rapid-fire developments in the AI/ML medical space.

HOW AI/ML POSES SPECIAL PROBLEMS FOR TRADITIONAL REGULATION

Despite these many potential benefits, AI/ML technologies also raise some risks that regulators must address preemptively. The FDA possesses sweeping regulatory authority over medical devices under the Food, Drug & Cosmetic Act (FDCA) and many subsequent laws and regulations. This section briefly identifies some unique challenges the FDA faces when considering how to regulate AI/ML-enabled medical technologies while the next section discusses the FDA's approach to regulating digital health applications.

A. Information volume & pacing problems

Digital health devices and applications are witnessing explosive growth. The IQVIA Institute for Human Data Science estimates that over 90,000 new digital health apps were released in 2020.¹⁰ Meanwhile, the overall corpus of medical knowledge has been growing rapidly.¹¹ Seven thousand medical papers are now published *every day*.¹² In the closely related field of medical robotics, the number of scientific papers has grown exponentially from less than 10 published in 1990 to more than 5200 in 2020 according to a recent study in *Science*.¹³

On one hand, these are welcome developments. The combination of AI/ML technologies and expanding medical information will allow health researchers and practitioners to take better advantage of this explosion of knowledge. This same amazing potential poses serious challenges for regulators, however. Many health policy scholars refer to the "volume problem" surrounding these technologies.¹⁴ "Regulators are racing to keep up with a flood of applications for new AI programs," notes *NPR*.¹⁵

Beyond volume, the velocity of change matters, too. Many experts wonder how regulatory agencies like

Estimated Doubling Time of Medical Knowledge		
<u>1950</u> : 50 years		
<u>1980</u> : 7 years		
<u>2010</u> : 3.5 years		
<u>2020</u> : 0.2 years (77 days)		

the FDA will handle the so-called "pacing problem," or the notion that legal or regulatory regimes struggle to keep up with the fast-evolving nature of modern technological systems.¹⁶ "The pace of regulation is one of the central issues of our time," notes legal scholar Richard Epstein.¹⁷ He worries about how a failure to reform FDA policies could lead to "a long-term drag on innovation that could, if the trend is not abated, lead to long-term mediocrity, as inventors and scientists flee our shores for friendlier environments."¹⁸ Other scholars worry about the opposite concern, suggesting that "the FDA is not yet ready for health AI and that there are significant safety and effectiveness concerns associated with the current regulatory framework."¹⁹

Despite their different concerns, both these camps generally agree the FDA needs to utilize new governance approaches for modern digital health technologies. As Ariel Dora Stern of the Harvard Business School summarizes, "ongoing regulatory clarity and policy innovation will be necessary for regulation to keep pace with AI innovation in health care."²⁰

B. Growing tech sophistication / interconnectedness problem

Algorithmic technology is also growing increasingly sophisticated, multifaceted, and interdependent. AI/ML is powered by a combination of massive data sets, powerful computational systems, high-speed and ubiquitous mobile networks and applications, cloud-based systems, user-generated content, wearable devices, sensor technologies, and other technological tools and capabilities. Algorithms are also continuous learning systems that usually improve over time as all these technological capabilities work together and gain more widespread use. This creates an interconnectedness problem in that regulating AI/ML medical devices may necessitate some degree of oversight over upstream and downstream technologies and uses, especially as they evolve over time. There is also an obsolescence problem: Digital health devices and systems tend to evolve more rapidly than older medical systems, meaning newer systems might more quickly fall out of use or fail to be updated.

Many technology scholars have stressed the transparency problems associated with new algorithmic medical innovations. This is sometimes called "black box medicine," or "the use of opaque computational models to make decisions related to health care."²¹ "Blackbox medicine is an awkward fit for the FDA's typical regulatory paradigm," says digital health policy expert W. Nicholson Price.²² Others argue that this black-box nature of AI medical systems, "can present challenges in validating the outputs of the AI models," and make it harder to preemptively ensure the safety of a device.²³ The "lack of explainability affecting some algorithms" is a problem in this context because it "adds to regulatory complexity."²⁴

Meanwhile, expanded AI/ML medical device regulation may also in potential tension with some intellectual property or trade secrecy protections, although the scope of those protections could be somewhat more limited in this context than others because digital algorithms are harder to protect by their nature.²⁵

C. Consumer empowerment / democratization problem

Consumer empowerment and the democratization of medicine does not sound like something that would be considered a problem, but it represents a legitimate challenge for the FDA.²⁶ The internet gave rise to easily accessible health information and advice websites like Healthline, PatientsLikeMe, and WebMD that empowered individuals with health questions to come together and form communities of common interest where people could share advice. With 268 million monthly visits as of June 2023, Healthline is currently the most visited health-related website in the world, which puts it ahead of the NIH and the Mayo Clinic.²⁷ WebMD is fourth with 112 million monthly visits.

Meanwhile, many "biohackers" or "citizen scientists" are tapping new technological capabilities to pursue "open-source science."²⁸ Others refer to this movement as "patient-led research" or "citizen-driven biomedical research."²⁹ Regardless of what this movement is called, it appears to be growing and creating headaches for regulators as it does because more medical devices will be both developed for, and used by, people who are not traditional health care providers.

As online tools have empowered a generation of citizens with more information about health issues and technologies, it has also left them expecting greater personalized care.³⁰ Dr. Eric Topol has written about these trends in his books *The Creative Destruction of Medicine*³¹ and *The Patient Will See You Now*.³² The rise of AI-enabled medical tools and health-related capabilities will greatly exacerbate these challenges for the FDA. This is essentially the flipside of the pacing

problem, which is mostly driven by the *supply* of many new devices and capabilities. But the *demand* side matters, too, as more and more citizens come to expect more (and better) technological capabilities each passing year. This puts pressure on both industry and regulators to deliver results faster.

D. Definitional / regulatory authority problem

The problems discussed here also gives rise to another problem related to AI/ML systems: rapidly changing definitions of technologies, sectors, and even regulatory boundaries.

We can begin with a foundational question: What is artificial intelligence? Despite generating considerable attention in recent years, a clear definition of the term has proven remarkably elusive. "There is no single universally accepted definition of AI, but rather differing definitions and taxonomies," a U.S. Government Accountability Office report concludes.³³ This factor will complicate governance of AI/ML as the agency considers how to classify algorithmic medical inventions. "Health care stakeholders are yet to reach a consensus on the definition of AI and ML when it is applied to health care," note several medical practitioners.³⁴ Thus, while the FDA's regulatory authority is sweeping, it is not unlimited and many AI/ML technologies "may get less scrutiny from FDA, perhaps because they do not fit within the statutory definition of medical devices."³⁵ This definitional matter can be particularly tricky with algorithmic technologies because they are often just digital programs that do not have a physical manifestation.³⁶

This gives rise to another tricky question: Could some AI health applications be considered a doctor instead of a medical device? This is important because the FDA does not regulate the practice of medicine or some other important medical practices. Various scholars have noted how "many algorithms used for clinical decision support or for prioritizing access to specialized services may be outside the legislative governance purview of the [FDA]," because some healthcare uses or medical practices fall outside the FDA's statutory power, and "certain software is excluded from the definition of medical device."³⁷ Thus, if an AI-enabled chatbot is offering consumers medical opinions or advice via a simple textual search, that is not something that the agency has much say over relative to a new algorithmically-enabled tool sold to consumers or hospitals to directly evaluate or diagnose a medical problem. There may also be certain speech-related First Amendment considerations in play here that could limit the agency's authority anyway.³⁸

There are other definitional headaches. For example, "much biomedical innovation has routinely happened in the course of activities that are beyond FDA's reach,"³⁹ and the agency only exercises limited authority over compounding pharmacies, which are instead governed more closely by standards formulated by U.S. Pharmacopeia, which is the only independent, not-for-profit, nongovernmental pharmacopeia in the world.⁴⁰ Also, because the FDA's authority focuses on safety and efficacy of new drugs and devices that are introduced into the stream of interstate commerce, this means that hospitals or health systems that develop customized AI/ML products and services for internal purposes only (i.e., not for sale to others) will be mostly exempt from FDA regulations.⁴¹ Finally, health insurers are tapping AI/ML tools to address how care is provided or covered by their plans, but those insurance plans and innovations are largely beyond the reach of FDA authority.⁴²

The combined effect of these factors means that the FDA's oversight powers for AI/ML may end up being somewhat more constrained and complicated than traditional medical device oversight.

E. Speech-related concerns

Although it has not yet become an impediment for the FDA, the regulation of algorithms could give rise to some speech-related issues. "Software regulation also can implicate First Amendment free speech rights," observes health policy expert Nathan Cortez.⁴³ AI/ML-enable medical devices that collect and process information might find some level of First Amendment protection from regulation in the future.⁴⁴ However, as will be noted below, this has not yet become a problem for the agency primarily because it has generally not regulated less risky digital health devices—such as those that collect and process fitness or dietary information—as heavily as other devices.

F. Inadequate resources problem

A final potential problem beyond the scope of this study involves claims that the FDA lacks adequate resources to take on the many new challenges outlined above. A lack of resources or funding has been a long-standing complaint of the agency and some in the public health community, but AI/ML raises new technical challenges for the agency, thus potentially necessitating new knowledge and skills.

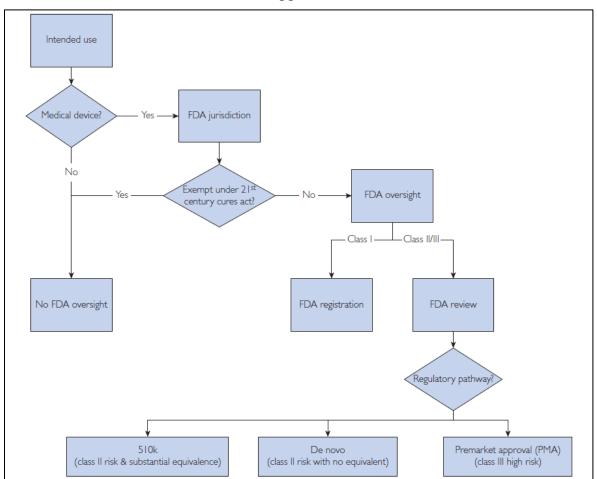
EVOLUTION OF FDA'S APPROACH TO DIGITAL HEALTH & AI/ML GOVERNANCE

This section discusses the FDA's approach to what the agency broadly refers to as "digital health," which includes AI/ML-enabled medical devices and mobile health information technology, wearable devices, telehealth and telemedicine, and personalized medicine.⁴⁵ Most of the FDA's AI/ML activity falls under their Software as a Medical Device (SaMD) and Software in a Medical Device (SiMD) initiatives. Most recently, the FDA has issued several notices pertaining to "AI/ML-Enabled Device Software Functions." But AI/ML functions and issues are also dealt with in some of the agency's work on mobile or wearable medical devices and various other digital health proceedings and guidance. These different monikers and classifications can make it difficult to track and analyze all the agency's activity in the field. Moreover, there are additional distinctions related to how these technological capabilities affect drug versus medical devices.

A. Basic FDA medical device authority

The Medical Device Amendments of 1976, the primary law governing how the FDA regulates medical devices, created a three-class, risk-based classification system for all medical devices.⁴⁶ Class I devices that pose lower risk only require general agency controls and oversight, while Class II and Class III devices that pose higher risk entail greater regulation.⁴⁷ Class III devices require premarket approval before they can be released. Most devices go through the so-called 510(k) process, which is "the mechanism by which a manufacturer seeks marketing authorization for a new device and by which FDA classifies devices into their appropriate regulatory category."⁴⁸

The agency's approach to medical device approval has been modified repeatedly over the years, but a particularly important change occurred in 2012 when the "Food and Drug Administration Safety and Innovation Act" passed.⁴⁹ That law created the *de novo* pathway process, which permits the classification of novel devices of low-to-moderate risk into Class I or II without being forced to automatically go through 510(k) process or premarket approval as a Class III device.⁵⁰ The 21st Century Cures Act and subsequent FDA guidance has also exempted some types of software from this process, including algorithmic applications that deal with more mundane matters such as medical billing and scheduling, or physical fitness and dietary tracking.



FDA Device Approval Flow Chart



Most of the FDA's activities on this front are coordinated through the Digital Health Center of Excellence, which is part of the agency's Center for Devices and Radiological Health. The agency's approach to device approval has drawn criticism for being slow and sometimes arbitrary or unpredictable, which can delay innovations by creating legal uncertainty and raising costs.⁵¹ On the other hand, the volume and sophistication of modern medical devices creates unavoidable complexities that defy easy solution. Unfortunately, these challenges are multiplying in the age of digital health and AI/ML-enabled devices for the reasons outlined above. The following three sections outline the FDA's approach to regulating these technologies.

Year	Major FDA Software / Digital Health-related developments		
1981	Task Force on Computers and Software as Medical Devices		
1984	Program Management Committee on Software and Computerized Devices		
1989	Draft Software Policy for the Regulation of Computer Products		
1997	General Principles of Software Validation		
2002	General Principles of Software Validation – Version 2.0		
2011	Draft Guidance on Mobile Medical Applications		
2013	Policy for Device Software Functions and Mobile Medical Applications		
2014	4 Cybersecurity in Medical Devices		
2016 21st Century Cures Act of 2016 passes			
2017	D17 Digital Health Innovation Action Plan		
2017	2017 Digital Health Software Precertification (Pre-Cert) Program		
2017	/ IMDRF Software as a Medical Device guidance		
2019	Clinical Decision Support Software guidance		
2019	Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine		
	Learning (AI/ML)-Based Software as a Medical Device (SaMD): Discussion Paper		
2021	1 Artificial Intelligence and Machine Learning (AI/ML) Software as a Medical Device Action Plan		
2021	Public Workshop on "Transparency of Artificial Intelligence/Machine Learning-enabled		
	Medical Devices"		
2021	Good Machine Learning Practice for Medical Device Development: Guiding Principles		
2023	Marketing Submission Recommendations for a Predetermined Change Control Plan		
	for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software		
	Functions		

B. Early software/computing oversight (1981-2002)

The FDA's digital health coverage can be traced back to 1981, when the agency created a Task Force on Computers and Software as Medical Devices and then a Program Management Committee on Software and Computerized Devices in 1984. A "Draft Software Policy for the Regulation of Computer Products" was also issued toward the end of the decade.⁵² It was withdrawn in 2005⁵³ because the agency determined the draft policy, "did not adequately address all of the issues related to the regulation of all medical devices containing software."⁵⁴

In 1997, the FDA released a draft guidance on "General Principles of Software Validation,"⁵⁵ that was replaced in 2002 by a newer guidance as "version 2.0."⁵⁶ The guidance recommended best practices for the "integration of software life cycle management and risk management activities" and further developed the agency's thinking on how it would regulate software relative to traditional medical hardware.⁵⁷

C. Digital health & mobile medical oversight ramps up (2002-2019)

After the turn of the century, the use of mobile services and digital applications grew rapidly, and the FDA took notice of how innovators were increasingly utilizing such capabilities in medical devices.

In 2011, the FDA issued "Draft Guidance on Mobile Medical Applications," which highlighted "the rapid pace of innovation in mobile apps" and outlined the agency's early approach to them.⁵⁸ It was followed by the 2013 "Policy for Device Software Functions and Mobile Medical Applications,"⁵⁹ which was then revised and reissued in 2019 and again in 2022.⁶⁰ The guidance sought to further clarify how the agency planned to regulate SaMD/SiMD technologies and again stressed that it would exercise enforcement discretion over lower-risk devices and instead focus on mobile or digital devices "whose functionality could pose a risk to a patient's safety if the device were to not function as intended."⁶¹ Thus, the agency would generally forebear from applying strict controls to less risky things like fitness or dietary applications, and instead evaluate whether to regulate mobile devices that might use sensors to monitor heart rate or blood pressure.⁶²

Even in these latter cases, the FDA can and has exercised some regulatory forbearance. While the 21st Century Cures Act of 2016 continued to grant the FDA broad discretion to regulate software and digital health services, Congress also encouraged the agency to pursue the "least burdensome" requirements necessary when regulating these technologies. The agency's subsequent guidance reflected this focus on finding less onerous approaches to device regulation, often through forbearance.

In 2017, for example, the FDA issued guidance for "Deciding When to Submit a 510(k) for a Software Change to an Existing Device," which sought to clarify certain types of updates that would not require new regulatory approvals, such as cybersecurity-related updates to the device software.⁶³ And in 2019, the FDA published "Clinical Decision Support Software" guidance (which was again updated in 2022), that clarified, "the types of clinical decision support software functions that are excluded from the definition of device."

FDA will exercise enforcement discretion for				
mobile apps or software that				
help patients with diagnosed psychiatric	offer checklist of common signs and			
conditions	symptoms to provide on when to consult a			
	health care professional			
offer periodic educational information,	recommend the type of health care facility			
reminders, or motivational guidance	most appropriate to their needs			
video and video games to motivate patients to	enable a patient or caregiver to create and			
exercise	send an alert or general emergency			
	notification to first responders			
aggregate and display trends in personal	keep track of medications and provide user-			
health incidents	configured reminders for improved			
	medication adherence			
track blood pressure data and share this data	provide oral health reminders or tracking			
with others	tools for users with gum disease			
offer prediabetes patients with guidance or	use images or other messages for a substance			
tools to help them develop better eating habits	abuser who wants to stop addictive behavior			
or increase physical activity	-			

In 2017, the FDA launched a "Digital Health Software Precertification (Pre-Cert) Program" as a pilot program.⁶⁵ The agency said it recognized that "the current device regulatory framework, enacted by Congress more than 40 years prior and incrementally updated since then, had not been optimized for regulating these devices."⁶⁶ "The pilot explored innovative approaches to regulatory

oversight of medical device software developed by organizations that have demonstrated a robust culture of quality and organizational excellence and who are committed to monitoring real-world performance of their products once they reach the U.S. market," the agency summarized.⁶⁷ The effort looked to create streamlined review processes and methods to evaluate real-world performance through in-person and remote interactions. The goal was "to assess the association between the organization's software design, development, verification, and validation processes and the organization's general business processes" using various performance indicators.⁶⁸

With only nine firms being invited to participate in the pilot program, however, the FDA admitted that the experiment "led to few devices being available for consideration under the pilot" and had other limitations.⁶⁹ The Pre-Cert program thus came to an end in late 2022. "The faster cycles of innovation and the speed of change for medical device software would benefit from a new regulatory approach," the FDA concluded when evaluating the pilot project results five years later. "Ultimately, the approach to regulating novel, swiftly-evolving medical device software must foster, not inhibit, innovation, while continuing to provide reasonable assurance of safety and effectiveness," the agency said.⁷⁰

In March 2020, the agency released a "Digital Health Innovation Action Plan" summarizing how it was working "to reimagine FDA's approach" to oversight of digital medical devices.⁷¹ Later, the agency released a "Digital Health Policy Navigator" online tool to assist developers when determining which regulatory policies apply to various digital tools or software functions.⁷² This online tool featured interactive drop-down menus that allowed developers to walk through a series of questions about their products and determine what steps they needed to take next.

For comprehensive policy feedback, complete the steps for EACH of your product's software functions:

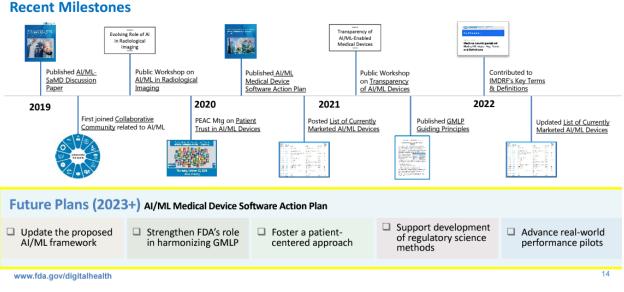


- <u>Step 2: Is the software function intended for administrative support of a health care facility?</u>
- <u>Step 3: Is the software function intended for maintaining or encouraging a healthy</u> <u>lifestyle?</u>
- Step 4: Is the software function intended to serve as electronic patient records?
- <u>Step 5:</u> Is the software function intended for transferring, storing, converting formats, or displaying data and results?
- Step 6: Is the software function intended to provide clinical decision support?
- <u>Step 7: Does the Device Software Functions and Mobile Medical Applications</u>
 <u>Guidance apply?</u>

Source: FDA, <u>https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-policy-navigator</u>

A Collaborative Approach to AI/ML-Enabled Devices





Source: FDA, https://ric.nrc.gov/docs/abstracts/forrests-hv-t6.pdf

D. AI/ML-enabled devices become the focus (2019-present)

Up to 2019, very few of the FDA's digital health guidance's or other policy documents had much to say specifically about artificial intelligence or machine learning. But that year the FDA made AI/ML-enabled medical devices a major priority with the publication of a discussion paper on the agency's "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)."⁷³ Building on its past approach to digital health more generally, the FDA began by admitting the need "to reimagine an approach to premarket review for AI/ML-driven software modifications," because of the way these technologies moved so fast and underwent continuous change.⁷⁴

The challenge for regulation, as the agency noted in this discussion paper, is that there are many different types of AI/ML medical devices along a spectrum from fully locked to continuously learning. Devices that are locked (i.e., which provide the same function/result each time they are used) are obviously somewhat easier for the FDA's regulatory process to handle. But those which evolve and engage in continuous learning (and whose functions could change over time) create problems for the old regulatory system. The agency admitted that:

"The traditional paradigm of medical device regulation was not designed for adaptive AI/ML technologies, which have the potential to adapt and optimize device performance in real-time to continuously improve healthcare for patients. The highly iterative, autonomous, and adaptive nature of these tools requires a new, total product lifecycle (TPLC) regulatory approach that facilitates a rapid cycle of product improvement and allows these devices to continually improve while providing effective safeguards."⁷⁵

The agency stressed that TPLC approach "allows FDA's regulatory oversight to embrace the iterative improvement power of AI/ML SaMD," but made it clear that ongoing algorithm changes

would need to be "implemented according to pre-specified performance objectives," and also, "follow defined algorithm change protocols," among other stipulations.⁷⁶ The agency's new approach relies on what it calls a "predetermined change control plan" (PCCP), which would ask developers to include the types of anticipated modifications they envision down the line. The PCCP model, which has become central to the agency's medical AI governance vision, will be discussed more below.

The FDA's discussion paper also made it clear it was aligning its approach with the four-part classification system for SaMD technologies developed by the International Medical Device Regulators Forum (IMDRF). The IMDRF, which was formed in 2011, brings together medical device regulators from 11 major nations who seek to voluntarily harmonize the regulatory treatment for medical products.⁷⁷ Under the IMDRF's risk classification scheme for SaMD, Category IV devices are the most sensitive and, therefore, subjected to the most scrutiny, while Category I devices are considered non-serious.⁷⁸ For example, under the IMDRF system, a SaMD device meant to diagnose and address different types of strokes would be a Category I device, whereas as a SaMD that merely stored blood pressure information would be a Category I device.

State of healthcare	Significance of information provided by SaMD to healthcare decision			
situation or condition	Treat or diagnose	Drive clinical management	Inform clinical management	
Critical	IV			
Serious	Ш	Ш	I	
Non-serious	II	I	I	

This discussion paper also pushed for the development of Good Machine Learning Practices (GMLP). This culminated in an October 2021 release of GMLPs through a joint effort with Health Canada and the United Kingdom's Medicines and Healthcare Products Regulatory Agency.⁷⁹ These regulatory agencies identified 10 guiding principles that can inform AI/ML device design and use and explained how these best practices could be further developed or refined in a multistakeholder fashion by the IMDRF, international standards organizations, and other collaborative bodies.

The GMLPs are interesting in that they are derived from best practices that transcend medical devices and which are often recommended (or already applied) in many other contexts. For example, one of these machine learning principles involves the idea of keeping "humans in the loop" at important stages of technological design and decision-making, while another focuses on providing user with clear and essential information to help them understand the nature of the technology and its risks. These are core best practices that are being utilized in various other fields where AI/ML are already having an impact.⁸⁰

FDA U.S. FOOD & DRUG	Health Santé Canada Canada Medicines & Healthcare products Regulatory Agency			
Good Machine Learning Practice for Medical Device Development: Guiding Principles				
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented			
Clinical Study Participants and Data Sets are Representative of the Intended Population	Training Data Sets are Independent of Test Sets			
Selected Reference Datasets are Based Upon Best Available Met	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device			
Focus is Placed on the Performance of the Human-Al Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions			
Users are Provided Clear, Essential Information	Deployed Models are Monitored for Performance and Re-training Risks are Managed			

Source: FDA

The FDA's 2019 discussion paper eventually led to the agency's 2021, "Artificial Intelligence and Machine Learning (AI/ML) Software as a Medical Device Action Plan," which identified upcoming steps needed to further harmonize the GMLPs, advance more real-performance pilot programs, and then updated PCCP guidance.⁸¹

These efforts eventually culminated in the April 2023, "Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions."⁸² In this draft guidance, the agency acknowledges that the development of these technologies "is an iterative process" and proposes a "least burdensome approach to support iterative improvement through modifications" to these technologies.⁸³ The agency argues that its guidance "demonstrates FDA's broader commitment to developing innovative approaches to the regulation of device software functions as a whole."⁸⁴

The agency defines a Predetermined Change Control Plan as "documentation describing what modifications will be made to the [ML device] and how the modifications will be assessed."⁸⁵ These plans are to be detailed explanations "describing the methods that will be followed when developing, validating, and implementing modifications."⁸⁶ Each PCCP is to be accompanied by an impact assessment weighing the benefits and risks of those anticipated modifications. The FDA hopes that, "[b]y including a PCCP in a marketing submission, manufacturers can proactively prespecify and seek premarket authorization for intended modifications," and then avoid the need to make additional marketing submissions prior to implementation of new function.⁸⁷

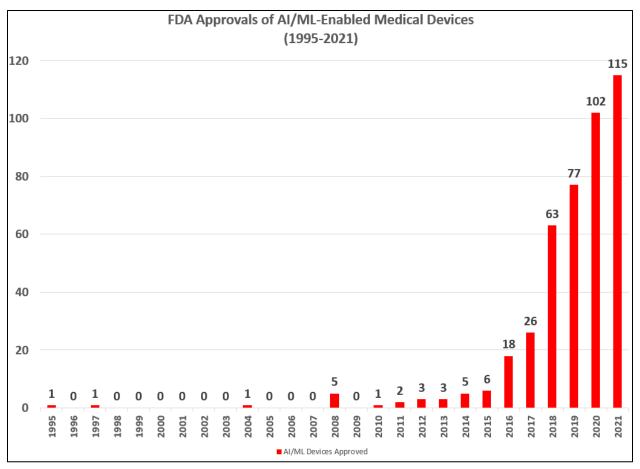
Many industry comments to the FDA in this proceeding requested that the agency offer additional guidance and provide more clarity about how it plans to implement and interpret this new authority in very specific circumstances. This gets to the fundamental problem with the PCCP idea: No one in either industry or government can accurately forecast the future course of AI/ML innovation. This creates an unavoidable challenge for developers when considering what information will be needed to convince the FDA that it has reasonably considered how their systems might evolve in the future. "To ensure an efficient review," the FDA, "recommends that a PCCP include only a limited number of modifications that are specific, and that can be verified and validated."⁸⁸ But

what sort of PCCP should a developer submit if there could be multiple potential future modifications as the system continuously learns. And how is that to be done when some future capabilities would be unknowable in advance? Finally, if a developer makes guesses about what those capabilities might be to play it safe, but then they fail to develop, will that open them to any blowback or liability (either from the FDA, investors, or consumers)?

Thus, while many commenters praised the FDA for proposing a more iterative and flexible approach, some worried how such uncertainties under this new approach might create a burden on innovation. Bradley Merrill Thompson, chief data scientist of EBG Advisors, said the proposal will require that "intricate plans" be prepared and that it "requires the companies to develop an enormous amount of documentation going forward."⁸⁹ The Consumer Technology Association argued that, "the amount of work and documentation required to comply with the guidance is substantial, and we believe may only be appealing in a more limited set of circumstances, where a manufacturer wishes to make changes to the device following clearance or approval."⁹⁰ The Digital Pathology Association worried about "the potential impact the implementation of PCCPs and modifications can have on the interoperability of downstream devices the software must interface with."⁹¹ That concern reflects the interconnectedness problem discussed earlier in this paper.

Several commenters also expressed concern about the potential can of worms the FDA opened with its inclusion of the concept of "social harm" in the guidance document's impact assessment language. The guidance suggested that PCCP impact assessments should, "discuss the benefits and risks, including risks of social harm, of each individual modification."⁹² This is important because concerns about algorithmic bias or discrimination have been the subject of intense academic scrutiny, and has prompted many calls for expanded regulation.⁹³

Going forward, the FDA will face a fundamental tension between flexibility and regulatory certainty as it is related to oversight AI/ML-related devices. While FDA approvals for such devices continue to expand, this tension will likely grow more acute and force the agency to consider how it might experiment with still other governance strategies for these devices.



SOFT LAW ELEMENTS IN THE FDA'S APPROACH

The FDA's recent digital health actions fit squarely within the FDA's hard law orientation, but also reflect a moderate change of approach to medical device regulation, at least for softwareenabled or AI/ML-enabled devices. The FDA's culture and governance approach remain firmly rooted in a precautionary hard law stance, but with a willingness to occasionally experiment with new approaches to address fast-moving developments and new technological capabilities. Some soft law elements are present in the agency's recent digital health actions.

A. Continued reliance on guidance as primary governance tool

As Cortez observes, "[t]he most striking feature of the FDA's traditional approach to software is its heavy reliance on nonbinding guidance."⁹⁴ Guidance documents "describe FDA's interpretation of our policy on a regulatory issue," and "represent FDA's current thinking on a topic," the agency notes, but "do not create or confer any rights for or on any person and do not operate to bind FDA or the public."⁹⁵ Guidance documents have long played a crucial role in the way the agency formulates policy, but they have featured particularly prominently in the governance of digital health technologies. This is consistent with a soft law approach to emerging technology governance.

Not all agency guidance documents are equal, however, and the FDA's might better be more akin to "hard law lite" than soft law. FDA guidance documents carry more weight than, say, a guidance document issued by an agency like the National Telecommunications and Information Administration (NTIA), which is part of the U.S. Department of Commerce. The NTIA has crafted

many best practice frameworks for emerging technology issues, including drones,⁹⁶ the Internet of Things,⁹⁷ and facial recognition.⁹⁸ Because the NTIA lacks formal regulatory authority over these technologies and sectors, however, its best practice guidance documents are more voluntary and nonbinding. By contrast, the FDA's recommended best practices all flow from underlying (and quite expansive) regulatory authority, and they carry the implied threat of potential agency sanction at every juncture.

B. Coordination with international NGOs & other governments

When formulating policy for AI/ML, the FDA is taking many of its cues from the International Medical Device Regulators Forum (IMDRF).⁹⁹ Such as their "Software Risk Categorization" framework, which has played an important role in aligning global standards around how SaMD is defined and governed across the globe.¹⁰⁰ The FDA uses this framework as the foundation for its new "total product lifecycle regulatory approach" and focus on a "Global Approach to Software as a Medical Device."¹⁰¹ While the IMDRF's members are traditional "hard law" regulators, the IMDRF produces a variety of documents that do not bind any member formally, but do come to influence how those individual members formulate their own policies, often in close collaboration with other members. This represents another common technique in global soft law efforts, where global officials and other stakeholders work together to better coordinate standards across jurisdictions. GMLP guiding principles represent an effort to coordinate global best practices and standards, which represents a sort of soft law approach to tech governance.

C. Reliance on standard-setting bodies

The FDA is also leaning on other stakeholders or professional bodies to assist their efforts on AI/ML-enabled devices and their governance. To formulate standards for advanced medical devices, the agency works with the Institute of Electrical and Electronics Engineers (IEEE) P2801 Artificial Intelligence Medical Device Working Group and the International Organization for Standardization (ISO) Joint Technical Committee 1/ Sub-Committee 42 (ISO/ IEC JTC 1/SC 42) - Artificial Intelligence.

Specifically, the FDA relies on specific standards developed by that ISO committee, including:

- ISO/IEC 23053 Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)
- ISO/IEC 24027 Bias in AI systems and AI aided decision making
- ISO/IEC 38507 Governance implications of the use of artificial intelligence by organizations
- ISO/IEC 23894 Artificial Intelligence: Risk Management
- ISO/IEC TR 24368 Artificial Intelligence (AI): Overview of ethical and societal concerns

The IMDRF has also relied on many ISO/IEC standards, which in turn influence FDA decision-making. Those standards include:¹⁰²

- IEC 62304:2006 Medical device software -- Software life cycle processes
- ISO/IEC 14764:2006 Software Engineering Software Life Cycle Processes Maintenance
- ISO 14971:2019 application of risk management to medical devices

- ISO/IEC 27000:2009 Information technology Security techniques Information security management systems
- IEC 62366:2007 Medical devices Application of usability engineering to medical devices

The FDA also relies on standards formulated by the Association for the Advancement of Medical Instrumentation, the primary source of consensus standards and guidance documents for the medical device industry.¹⁰³

Again, this represents another standard part of the soft law playbook. Non-governmental professional associations play a crucial role in many fast-moving and highly technical fields. "Such relationships are deeply important: (internationally recognized) standard setting organizations are known to be vital for identifying the most promising technologies and influencing the trajectory of technology adoption in other contexts," says Stern.¹⁰⁴

D. Public-private partnerships / multistakeholder meetings & workshops

The FDA's ongoing "collaborative communities" effort represents another creative governance tool that could play a bigger role in AI/ML policy. Collaborative communities are defined by the agency as, "a continuing forum in which private- and public-sector members, like the FDA, work together on medical device challenges to achieve common objectives and outcomes. They are convened by interested stakeholders and may exist indefinitely, produce deliverables as needed, and tackle challenges with broad impacts."¹⁰⁵ The agency says that these collaborative communities may develop for a number of reasons, including when, "challenges are ill-defined or there is no consensus on the definition of the challenge," "challenges and outcomes are complex," or "better outcomes could be achieved with integrating different perspectives, experiences, resources, and expertise.¹⁰⁶ An AI-related collaborative community formed as the Xavier Artificial Intelligence (AI) World Consortium and later transitioned to the Association of Food and Drug Officials/Regulatory Affairs Professionals Society (AFDO/RAPS) to be part of the AFDO/RAPS Healthcare Products Collaborative. Such efforts could be tapped going forward to address other AI/ML governance challenges using collaborative multi-stakeholder mechanisms.

Agency workshops have become another standard part of the soft law toolkit for many agencies that deal with cutting-edge tech issues like the FDA. In early 2020, the FDA convened a two-day public workshop to explore the use of AI in radiology featuring many practicing experts in the field.¹⁰⁷ In late 2020, the agency also held a meeting with the FDA's Patient Engagement Advisory Committee, which is a body that, "provides advice to the Commissioner or designee, on complex issues relating to medical devices, the regulation of devices, and their use by patients."¹⁰⁸ In that meeting, the FDA looked to "elicit input from a diverse group of patients on AI/ML technologies."¹⁰⁹ The following year, in October 2021, the FDA held a virtual public workshop on "Transparency of Artificial Intelligence/Machine Learning-enabled Medical Devices," to "gather input from various stakeholders on the types of information that would be helpful for a manufacturer to include in the labeling of and public facing information of AI/ML-enabled medical devices, as well as other potential mechanisms for information sharing."¹¹⁰

RECOMMENDATIONS FOR EXPANDED USE OF SOFT LAW FOR AI/ML

The FDA's recent actions represent a tacit acknowledgement that their traditional regulatory approach is poorly suited to fit fast-moving AI/ML-enabled medical technologies and that constant experimentation and reevaluation will be the new normal. The agency seems to now recognize

that, if algorithmic inventors must stop at every single stage to notify the FDA that an improvement has been made, many beneficial types of iterative innovation will be discouraged. That could have deleterious impacts on public health. Still, the agency remains more focused on the opposite problem of ensuring that those innovations do not create new risks. Therefore, effective AI/ML medical device governance will need to be a more iterative, experimental, and collaborative process. There are, however, some potential soft law strategies that the agency could consider utilizing to balance AI/ML innovation and safety.

A. AI Audits and Algorithmic Impact Assessments

In the broader field of AI policy, various analysts have suggested that some sort of mandatory algorithmic transparency will be needed to determine what is going on inside the proverbial "black box."¹¹¹ Others have recommended policymakers encourage or even mandate greater "explainable AI" as a way to generate more trustworthiness and accountability in algorithmic systems.¹¹² One way to accomplish this would be through the use of AI audits or algorithmic impact assessments, which are attracting widespread interest in the field of algorithmic governance today.¹¹³ AI audits and impact assessments would require those who develop or deploy algorithmic systems to conduct reviews to evaluate how well aligned the systems were with various ethical values or other commitments.¹¹⁴

The NTIA recently opened a proceeding on "AI Accountability Policy," which asked for public comment regarding how audits and impact assessments might play a role in broader algorithmic governance.¹¹⁵ This comes after the Biden administration's October 2022 release of a "Blueprint for an AI Bill of Rights," which floated the use of audits and impact assessments "to mitigate risks to the safety and efficacy of AI systems."¹¹⁶

AI audits and impact assessments have many tradeoffs,¹¹⁷ but they offer one way to advance a more transparency-oriented approach to algorithmic regulation. Some digital health scholars suggest that the FDA could, "implement a less centralized oversight regime based on as much transparency as possible."¹¹⁸ The FDA has already been heading down this path since 2019 when its Proposed Regulatory Framework for AI/ML-Based Software discussion paper outlined, under its TPLC approach, "manufacturers would be expected to commit to the principles of transparency and real-world performance monitoring for AI/ML-based SaMD," and that the agency "would also expect the manufacturer to provide periodic reporting to FDA on updates that were implemented" as part of its control plan.¹¹⁹ Subsequently, in its 2021 "AI/ML Action Plan, the agency noted that "[p]romoting transparency is a key aspect of a patient-centered approach, and we believe this is especially important for AI/ML-based medical devices, which may learn and change over time, and which may incorporate algorithms exhibiting a degree of opacity."¹²⁰

In October 2021, the agency also hosted held a Public Workshop on "Transparency of Artificial Intelligence/Machine Learning-enabled Medical Devices" to consider, "the types of information that would be helpful for manufacturers to include in the labeling and public facing information of AI/ML-enabled medical devices, as well as other potential mechanisms for information sharing."¹²¹

An oversight regime rooted in hyper-transparency could go further and, in theory, offer regulators a way to pursue safety goals without as much formal regulation of specific algorithmic technologies or practices. The regulatory focus could shift from pre-market to post-market oversight with transparency efforts and existing agency product recall authority being used to address problematic products in an *ex-post* fashion. Such a move would be controversial, of course,

because many would fear the risks of allowing harmful products to reach the market without enough preemptive oversight or approval. As noted below, this approach would also require greater reliance on third-party validators as well as greater public risk education.

B. Expand enforcement discretion & rely on best practices

Since the FDA will exercise enforcement discretion over lower-risk digital health devices and has creating a webpage on that lists examples of 19 specific software functions exempt from its regulation even if the apps or systems meet the definition of a medical device.¹²² It would not be surprising if the agency expanded its use of enforcement discretion as more AI/ML-enabled devices come to market.

If the FDA did so, some critics will likely be worried about what they may regard as deregulation through forbearance, but the FDA has repeatedly stressed that general controls apply to all medical devices it oversees and that it could always reconsider and reclassify devices later if needed due to new risks.¹²³ Moreover, if the FDA is to better focus its time and resources on riskier AI/ML-enabled apps and devices, then it will be forced increasingly to make some tough choices about what technologies and issues to regulate more aggressively. If the agency is wise, it would offload some of the oversight to third-parties (such as industry groups or NGO-led multistakeholder groups) to use best practices and technical standards to address less risky AI/ML apps and systems.

C. Expand the use of pilot programs / sandboxing

Some of the FDA's recent digital health initiatives, especially the Pre-Cert program, made the use of real-world performance monitoring a central part of the effort. The goal of Pre-Cert, for example, was to work with developers on a voluntary basis to engage in real-time learning as systems evolved and consider how regulation might be improved.

The FDA should consider expanding such experimental efforts with more ambitious pilot programs and "sandboxes," which are an increasingly popular soft law mechanism. Sandboxes are policy experiments that typically see policymakers temporarily relax or tweak certain regulations to determine whether alternative approaches might work better.¹²⁴ Such sandboxes efforts let both innovators and regulators learn what sort of guidelines do the best job balancing innovation and safety. Sandboxes are also a good way to make sure that policy changes on a more regular basis to keep up with the pacing problem. But the FDA would likely need Congressional approval to engage in greater experimentation of this sort because the Pre-Cert effort was haunted by questions of statutory authority.

D. Rely on private AI registries & a more "distributed approach" to governance

Price has suggested that "the FDA could rely more heavily on third party validation of black-box medicine techniques, either as a precondition of marketing or as a continuing evaluation after early limited market approval."¹²⁵ Others have floated similar ideas. A recent report in *PLOS Digital Health* from seven medical researchers called for a "distributed approach to the regulation of clinical AI" that would be "a hybrid model of regulation and oversight, building on the model of algorithmic stewardship."¹²⁶ Under this approach, "centralized regulation would only be required for the highest risk tasks," they say, "and "decentralized regulation is the default for most applications of clinical AI going forward."¹²⁷ They argue that this approach would involve:

"an accountability framework, as well as the development of open data assets, AI registries, and a robust process for public engagement. It will also require a shift in

regulatory mindset and an acceptance of changes in institutional responsibilities from existing regulatory organizations."¹²⁸

The FDA would likely respond that it is currently pursuing this sort of approach in some of its digital health efforts. The agency could go much further, however, by offloading more governance authority to non-governmental registries. The industry group Connected Health speaks of the need for "longer-term opportunities to reimagine certification and precertification roles and workflows to further leverage AI/ML innovations."¹²⁹ Details are murky here, but this general model could serve as the basis of future digital health governance if the FDA finds itself increasingly overwhelmed by the task at hand.

E. Expansion of health education / literacy

Educational strategies are a particularly important part of the soft law toolkit, and health literacy and risk communication efforts have long been a part of the FDA's mission. In its 2009 *Strategic Plan for Risk Communication*¹³⁰ and 2011 report on *Communicating Risks and Benefits: An Evidence-Based User's Guide*,¹³¹ the FDA offered a blueprint for expanded risk education. But this has always been a secondary part of the agency's mission.

Some analysts have explained how education and health literacy could play a larger role going forward, "to ensure patients receive the information they need to make informed and autonomous health choices."¹³² The focus here would be on identifying risk communication and mitigation strategies that can help the general public better understand the benefits and risks of the many new digital health devices flooding the market today. With the demand for personalized medicine options growing fast, the public needs to be better informed and empowered to make sensible wellness decisions.¹³³ Stepped-up risk education and health literacy efforts can begin in the classroom at a young age but should also be the focus of public service campaigns for the general public on an ongoing basis. Industry-backed educational efforts could complement those efforts.

CONCLUSION

For AI/ML-enabled medical devices, it is clear that "the complex regulatory landscape remains underdeveloped,"¹³⁴ and there is "some uncertainty as to what future regulation will look like."¹³⁵ Experts tend to agree that, "it is almost certainly the case that novel regulatory approaches are needed" for these medical technologies to, "take into account the specific and dynamic needs associated with software products."¹³⁶

Some of this uncertainty is the inevitable byproduct of both the complexity of the FDA's regulatory process as well as the inherent nature of algorithmic systems more generally. While the FDA continues to experiment with new approaches to algorithmic oversight and regulation, the agency should consider how it might tap additional governance tools and approaches outside its traditional wheelhouse.

Of course, such efforts would be controversial because of the safety-first ethos surrounding medical device regulation and the FDA's operating culture more generally. Opening the door to more soft law-oriented solutions could also lead to push back from some policymakers, public health and safety advocacy groups, and even some established industry players who benefit in different ways from the regulatory status quo. But the agency may have no choice but to explore those alternatives as artificial intelligence and machine learning medical technologies multiply rapidly and grow increasingly complex.

APPENDIX: THE PROMISE OF AI/ML IN HEALTH CARE

AI tools are allowing doctors and scientists to create highly personalized care options and develop new medical treatments tailored to the unique needs of each patient.¹³⁷ Here are some specific examples of how AI/ML-enabled technologies are already helping to improve health outcomes:

- *Organ donation*: AI can reduce human errors and increase matching speeds during the organ-patient matching process.¹³⁸
- *Heart attack detection & treatment*: AI and ML tools are helping detect and treat heart disease and heart attacks, ¹³⁹ improving personalized treatment for women who have had heart attacks, ¹⁴⁰ and being able to quantify coronary plaque buildup in five to six seconds compared to 25 to 30 minutes of humans.¹⁴¹
- *Cancers*: Despite major government efforts to pursue a national "war on cancer"¹⁴² and a "cancer moonshot,"¹⁴³ cancers unfortunately remain the second leading causes of death in the U.S.,¹⁴⁴ claiming 602,350 lives in 2020 alone.¹⁴⁵ AI and ML-enabled technologies are poised to help reduce that staggering death toll. Mayo Clinic researchers have shown how ML models can help diagnose and treat pancreatic cancer (the third leading cause of cancer death) at an earlier stage.¹⁴⁶ AI/ML techniques are also helping with early detection and treatment of lung cancer,¹⁴⁷ breast cancer,¹⁴⁸ brain cancer,¹⁴⁹ cervical cancer,¹⁵⁰ and many other types of cancer¹⁵¹ (including undiagnosable cancers¹⁵²), aided by increasingly personalized screening techniques.¹⁵³
- Sepsis & superbugs: Recent medical studies have also documented how AI-powered monitoring systems are helping to detect antibiotic-resistant "superbugs"¹⁵⁴ and sepsis,¹⁵⁵ and will save thousands of lives each year as a result. Roughly 1.7 million adults develop sepsis every year in the U.S. and more than 250,000 of them die.¹⁵⁶ The use of AI "dramatically cuts the time it takes to sort through thousands of promising compounds," to fight drug-resistant pathogens, researchers find.¹⁵⁷
- *Paralysis*: The Christopher & Dana Reeve Foundation has estimated that there are nearly 1 in 50 people living with paralysis in the United States.¹⁵⁸ The combination of artificial intelligence and robotic technologies hold out the hope of helping paralyzed individuals regain certain motor functions.¹⁵⁹ In May 2023, a man who had been paralyzed from the waist down for more than a decade regained his ability to walk thanks to brain and spine implants and an AI-enabled thought decoder that helped him translate electrical brain signals into muscle movement.¹⁶⁰ He is now able to walk around his own home and in get in and out of a car on his own. A paralyzed American man also regained a sense of touch and mobility thanks to similar AI-enabled brain implants.¹⁶¹
- Brain disease, mental health & drug addiction: Scientists are developing AI-driven methods to help better detect and diagnose degenerative brain disease, including Alzheimer's, dementia, and Parkinson's.¹⁶² AI can also help identify and address mental health problems through textual analysis, which can supplement human-based analysis at a time when there is a nationwide shortage of health care workers in this area.¹⁶³ AI tools are also being tapped to help find novel drugs that can help counter opioid addiction, which has become a chronic problem in recent years.¹⁶⁴

There are many other current or potential health-related applications for algorithmic technologies, including abnormal chest X-ray detection,¹⁶⁵ AI-powered ultrasounds,¹⁶⁶ detecting and addressing

eye disease and blindness,¹⁶⁷ and new drug and vaccine discovery.¹⁶⁸ AI will also become crucial for various surgeries in terms of both improving outcomes when operations are necessary (often through robotic assisted surgery)¹⁶⁹ or, better yet, avoiding the need for invasive procedures altogether.¹⁷⁰ Robotic surgery at a distance is now also becoming possible thanks to recent advances.¹⁷¹ In the process, AI/ML will also help share medical knowledge across far more institutions and reach more patients as a result. Meanwhile, AI assistants can help address the significant paperwork and filing burdens that doctors and nurses face today, which will help free up time for dealing with patients and research.¹⁷²

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