Detailed Summary of the Report to Congressional Requesters of the United States Government Accountability Office and National Academy of Medicine on *Artificial Intelligence in Health Care – Benefits and Challenges of Machine Learning Technologies for Medical Diagnostics (Sept. 29, 2022)*

Part One: Artificial Intelligence in Health Care: Benefits and Challenges of Machine Learning Technologies for Medical Diagnostics

Machine learning ("ML") is a subfield of artificial intelligence ("AI") whereby technologies are trained "by processing data to identify patterns that may be hidden or complex."[1] These technologies "could revolutionize diagnosis by augmenting clinical diagnostics practice resulting in earlier and better diagnoses, lives saved, and avoided costs of time and money.[2] Still, ML technology may raise important technological, economic, and regulatory questions.

There are several ML technologies available in the United States to assist in diagnostic processes, with benefits including (1) earlier detection of diseases; (2) more consistent analysis of medical data; and (3) increased access to care, particularly for underserved populations.[3] Most ML-based technologies rely on data from imaging such as x-rays or magnetic resonance imaging ("MRI").[4] "These technologies typically do not provide a diagnosis; rather, they typically augment the decision-making process of medical professionals. While some of these technologies can suggest a specific diagnosis, they are not intended or use[d] to determine a final diagnosis."[5] Despite their promise, these ML-based technologies have not been widely adopted by the medical community.[6]

Our Perspective: For the foreseeable future, industry will adopt ML-based technologies as a form of "augmented intelligence" rather than artificial intelligence. It is also likely that regulators will provide increased scrutiny to any ML-based health software claiming to remove a human from the decision-making loop.

1. Application to five select diseases.

GAO focused its report on ML-based technologies available for five diseases, including certain cancers, diabetic retinopathy, Alzheimer's disease, heart disease, and COVID-19.[7]

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[1] U.S. Gov't Accountability Off., GAO-22-104629, Artificial Intelligence in Health Care: Benefits and Challenges of Machine Learning Technologies for Medical Diagnostics (Sept. 29, 2022) at 7.
[2] *Id*. at 1.
[3] *Id*. at ix.
[4] *Id*.
[5] *Id*. at 10.
[6] *Id*. at ix.
[7] *Id*.

1. Cancer. "Available ML technologies for cancer diagnosis use data from images . . . to help specialists detect, measure, and analyze tumors."[8] "[T]he ability to validate ML technologies for diagnosing cancer varies by the type of cancer."[9]

Our Perspective: Industry continues to migrate image analysis algorithms from detection to diagnosis, while continuing to keep clinicians in the loop.

2. Diabetic Retinopathy. "Available ML technologies can detect signs of diabetic retinopathy by interpreting retinal images captured by a specialty camera. The technologies also recommend a diagnosis to medical professionals."[10]

3. Alzheimer's Disease. "Available ML technologies augment a clinician's process for diagnosing Alzheimer's disease by analyzing brain images. These analyses, based on MRI, are intended to help clinicians distinguish changes to brain structure resulting from normal aging and those resulting from Alzheimer's disease."[11] Some "interviewees stated that it can be difficult to validate technologies to detect and diagnose Alzheimer's disease, in part because of the disease's ambiguous clinical definition and diagnostic criteria."[12]

4. Heart Disease. "Available technologies include devices, sold directly to consumers, which track an individual's electrocardiogram (ECG) to detect conditions such as atrial fibrillation. . . . These technologies are not intended for consumers to self-diagnose specific medical conditions but rather to help medical professionals better diagnose patients by providing ECG information between visits."[13] In addition, "FDA has authorized devices that examine radiological images, score the amount of calcification in blood vessels, segment the amount of plaque buildup within blood vessels, and provide an early alert to radiologists that a patient may have a pulmonary embolism . . . ."[14]

Our Perspective: Particularly as it relates to cardiac medicine, the line between health applications and medical devices continues to be challenged especially in the field of monitoring and wearables. This technology is also increasingly migrating from clinical environments to consumer environments, which challenges existing considerations of safety, efficacy, and regulatory compliance.

5. COVID-19. "Technology developers are marketing ML technologies to help improve COVID-19 detection methods."[15]

2. Emerging Technologies.

"Academic, government, and private sector organizations continue to research improvements in AI and ML technologies that would enhance or expand upon available capabilities to diagnosing select diseases."[16] GAO identified three emerging approaches: (1) autonomous; (2) adaptive; and (3) consumer-oriented ML diagnostics.[17]

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[8] *Id*. at 12.
[9] *Id*.
[10] *Id*.
[11] *Id*. at 12–13.
[12] *Id*. at 13.
[13] *Id*.
[14] *Id*.
[15] *Id*.
[16] *Id*. at 16.
[17] *Id*.

1. Autonomous Technologies. "Technologies that independently interpret images or other patient data to render a diagnosis."[18]

    a. Benefits: "Fast and consistent information at the point of care"; "[i]mproved clinician capacity and patient access"; "[e]arlier and more accurate detection."[19]

    b. Potential Limitations: "Developers may not be able to create these technologies"; "[m]edical professionals may not adopt algorithms that can diagnose certain diseases automatically."[20]

Our Perspective: Autonomous technologies provide tremendous potential for more efficient and effective diagnosis and treatment, but the countervailing safety, regulatory, and legal risk may limit ready adoption.

2. Adaptive Algorithms. "Technologies that update their algorithms by incorporating new patient data."[21]

    a. Benefits: "May provide more accurate diagnoses or information by incorporating additional population or individual data"; FDA "may be able to streamline its regulatory review of adaptive algorithms by reviewing potential changes to an algorithm during the initial review phase, rather than reviewing individual updates to algorithms" which "could allow for rapid improvements in algorithms" and "[c]ould expand or improve features for users."[22]

    b. Potential Limitations: "Changes in the algorithm data may lead to adverse outcomes such as inconsistent or poorer algorithmic performance."[23]

Our Perspective: To date FDA has cleared few devices using adaptive algorithms, and the creation of clear regulatory standards will be important to facilitate development and uptake of this technology.

3. Consumer-Oriented Technologies. "Technologies such as wearables and at-home devices that are marketed to consumers and may assist medical professionals in monitoring a patient's medical conditions."[24]

    a. Benefits: "Can give medical professionals more information about patients to improve diagnosis and treatment"; "[m]ay increase access to care for consumers, particularly in underserved areas, such as rural settings, that lack specialists."[25]

    b. Potential Limitations: "Need further research to understand whether some devices improve patient outcomes"; "[e]ffectiveness may depend on patient's ability to understand or willingness to accept the health information presented."[26]

Our Perspective: Although less than 10% of 510(k)s submitted for FDA clearance have been consumer devices, we see this growing at a rapid pace in the next few years.

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[18] *Id*. at 18.
[19] *Id*.
[20] *Id*.
[21] *Id*.
[22] *Id*.
[23] *Id*.
[24] *Id*.
[25] *Id*.
[26] *Id*.

3. Challenges.

GAO "identified several challenges affecting the development and adoption of ML in medical diagnostics[,]" including: (1) "Demonstrating real-world performance across diverse clinical settings and in rigorous studies"; (2) "Meeting clinical needs, such as developing technologies that integrate into clinical workflows"; and (3) "Addressing regulatory gaps, such as providing clear guidance for the development of adaptive algorithms."[27] "These challenges affect technology developers, medical providers, and patients and may slow the adoption of these technologies."[28]

1. Demonstrating Real-World Performance. "Medical providers may be reluctant to adopt ML technologies until its real-world performance has been adequately demonstrated in relevant and diverse clinical settings, according to experts, stakeholders, and literature."[29] Unfortunately, "many available technologies have not been adequately tested or validated across generalizable data sets and settings and, as a result, may not transfer from development to adoption in clinical environments."[30] Further, performance can vary widely across different settings among ML technologies that have been externally validated.[31] Another barrier to adoption may be that prospective studies, meaning "those where the outcome has not occurred when the study starts and participants are followed over time to track eventual outcomes", have been limited.[32] "[S]takeholders will not know how well AI can predict key outcomes in the health care setting until there is robust validation in prospective studies with rigorous statistical methodology and analysis."[33] Challenges to evaluating and validating ML diagnostic technologies include that "developers have difficulty accessing high-quality representative data to train and validate their technologies."[34] A primary challenge is "access to sufficient amounts of nonbiased, ethnically diverse, real-world training data," in part because partnering with hospitals and academic centers takes time and institutions are often reluctant to share data due to privacy concerns and fears that doing so could hurt their competitive advantage.[35]

Our Perspective: We see data used to train and validate algorithms often dependent on individual relationships between AI/ML developers and clinical researchers. There is also an increased push for the development and dissemination of synthetic data to resolve some of the issues noted in the GAO report.

2. Meeting Clinical Needs. "Medical providers are less likely to adopt ML technologies that do not address a clear clinical need, and many ML diagnostic technologies do not progress from development to adoption for this reason."[36] Further, "providers and professionals are more likely to adopt technologies that integrate into existing health care systems and clinical workflows . . . ."[37] Last, "providers and professionals are also more likely to adopt technologies that they can

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[27] *Id*. at ix.
[28] *Id*. at 23.
[29] *Id*.
[30] *Id*.
[31] *Id*.
[32] *Id*. at 24.
[33] *Id*. (citing Topol, Eric J. "High-performance medicine: the convergence of human and artificial intelligence". Nature Medicine vol. 25 (2019): 49).
[34] *Id*. at 24.
[35] *Id*.
[36] *Id*. at 25.
[37] *Id*.

understand," and technologies where "they can verify its findings or recommendations."[38] "However, certain information – such as how the technology works – may be confidential, unknown, or unexplainable."[39]

Our Perspective: The debate between explainability and transparency continues, where transparency proponents argue that explainability in some AI/ML-based decisions is impractical or even impossible and transparency of the development, training, and validation methods and models may provide an adequate level of confidence.

3. Addressing Regulatory Gaps. "Regulatory requirements and standards for demonstrating real world performance and clinical validity are insufficient for wide clinical adoption . . . ."[40] "FDA reviews medical devices for safety and effectiveness. However, reviews do not always include comprehensive information on real world performance, clinical outcomes or other information that users may deem relevant to their adoption decisions."[41] However, according to an AI/ML action plan released by FDA in January 2021, the Agency "recognizes the need for more evidence of the real world performance of these technologies . . . ."[42] The plan identifies a need "for improved methods to evaluate bias, generalizability, and robustness, as well as the need for clearer guidance on real world performance monitoring."[43] Further, "existing regulations may also limit the development of emerging types of ML diagnostic technologies" and "may impact the development of adaptive algorithms" because "[c]hanges or modifications to a device may require additional review and authorization by FDA," limiting "their ability to improve by learning from real-world use and experience.[44] While FDA is working to update its regulatory guidance, including by issuing a discussion paper in 2019 on a proposed regulatory framework that would include a "Predetermined Change Control Plan" which "could allow devices to learn and iteratively improve after they are in use[,]" the draft guidance has not yet been published.[45]

Our Perspective: Other than Singapore, whose support of adaptive algorithms is purely theoretical at this point, FDA's proposed Pre-determined Change Control Plan draft guidance will likely provide the world's first articulated regulatory standards for this technology. Although the MDUFA commitment letter set a 2027 deadline for this guidance, we anticipate a draft as early as 2023, consistent with FDA's current guidance agenda.

4. Policy Options.

GAO developed three policy options to help address these challenges or enhance the benefits of ML-based diagnostic technologies.

1. Evaluation. "Policymakers could create incentives, guidance, or policies to encourage or require the evaluation of ML diagnostic technologies across a range of deployment conditions and

[38] *Id*. at 26.
[39] *Id*.
[40] *Id*.
[41] *Id*. at 27.
[42] *Id*. (citing Food and Drug Administration, Artificial Intelligence/ Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan (January 12, 2021)).
[43] *Id*. at 27.
[44] *Id*.
[45] *Id*. (citing FDA, "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)," Washington, D.C.: Apr. 2, 2019).

demographics representative of intended use."[46] For example, policymakers could provide funding or other incentives for more rigorous evaluations, create guidance, standards, or best practices for evaluation of ML technologies, or require post-adoption evaluation under certain conditions.[47]

a. Opportunities: "More comprehensive evaluation could help developers, providers, and policymakers better understand the performance of ML technologies across a diverse spectrum of patients, providers, and other factors."[48] "Evaluation could inform providers' adoption decisions" and a better understanding of ML technologies could lead to increased adoption.[49] "Information from evaluations can help inform the decisions of policymakers, such as decisions about regulatory requirements."[50]

b. Considerations: "Rigorous evaluations can be time-intensive and require collaboration between stakeholders that may already have limited time"; this could cause delays in the development of technologies and process of adoption by practitioners.[51] "More rigorous evaluation will likely lead to increased costs" and "developers may not be incentivized to conduct these evaluations if it could show their products in a negative light . . . ."[52] "[P]olicymakers could consider whether evaluations should be conducted or reviewed by independent parties . . . ."[53]

2. Data Access. "Policymakers could develop or expand access to high-quality medical data to develop and test ML medical diagnostic technologies.[54] "Policymakers can explore opportunities to make data sharing easier, faster, or cheaper" and "could also increase data access by, when appropriate, creating and participating in mechanisms for data sharing, such as data commons – cloud-based platforms where users can store, share, access, and interact with data and other digital objects."[55] Incentives such as grants or access databases could also be used to encourage data sharing.[56]

a. Opportunities: "Developing or expanding access to high-quality datasets could help facilitate training and testing ML technologies across diverse and representative conditions, which could improve their performance and generalizability," potentially "help[ing] developers and other stakeholders understand the performance of these technologies under varied conditions, identify[ing] biases or limitations, and identify[ing] opportunities for improvements.[57] "Expanding access could enable developers to save time in the development process, which could shorten the time it takes for these technologies to be available for adoption."[58]

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[46] *Id*. at 28.
[47] *Id*.
[48] *Id*. at 28–29.
[49] *Id*. at 29.
[50] *Id*.
[51] *Id*.
[52] *Id*.
[53] *Id*.
[54] *Id*.
[55] *Id*.
[56] *Id*.
[57] *Id*.
[58] *Id*. at 30.

b. Considerations: Entities that own data may hesitate to share because they may consider data to be valuable or proprietary or they may be concerned about patient privacy and the intended use and security of the data.[59] Depending on the quality and interoperability of the data, data sharing could be of limited use to researchers and developers.[60] Further, "curating and storing data could be expensive and may require public and private resources."[61]

3. Collaboration. "Policymakers could promote collaboration among developers, providers, and regulators in the development and adoption of ML diagnostic techniques."[62] "This policy option could help address the challenges of meeting medical needs and addressing regulatory gaps."[63] "Policymakers could convene multidisciplinary experts together in the design and development of these technologies."[64]

   a. Opportunities: "Collaboration between ML developers and providers could help ensure that the technologies address clinical needs" and "could help in the creation and access of ML ready data . . . ."[65]

   b. Considerations: "[P]roviders may not have time to both collaborate with developers and treat patients; however, organizations can provide protected time for employees to engage in innovation activities such as collaboration."[66] Further, "if developers only collaborate with providers in specific settings, their technologies may not be usable across a range of conditions and settings, such as across different patient types or technology systems."[67]

Part Two: Meeting the Moment: Addressing Barriers and Facilitating Clinical Adoption of Artificial Intelligence in Medical Diagnosis

Part two of the report, authored by NAM, discusses "the factors influencing the adoption of non-autonomous point-of-care AI technology that can assist in the diagnosing of a disease."[68]

Current AI techniques possess remarkable processing power, speed, and the ability to link and organize large volumes of multimodal data, and additionally have the ability to learn and adjust based on novel inputs building upon prior knowledge to generate new insights.[69] AI approaches, specifically ML, are particularly well-suited to problems related to clinical diagnosis, including the potential to shorten the time for disease detection, improve diagnostic accuracy, and reduce medical errors.[70] AI diagnostic decision support ("AI-DDS") tools "could reduce the cognitive burden on providers, mitigate burnout, and further enhance care quality."[71] Still, current concerns hampering the adoption of AI-DDS tools include concerns about their development, interoperability, workflow integration, maintenance, sustainability,

[59] *Id*.
[60] *Id*.
[61] *Id*.
[62] *Id*.
[63] *Id*.
[64] *Id*.
[65] *Id*. at 30–31.
[66] *Id*. at 31.
[67] *Id*.
[68] *Id*. at 34.
[69] *Id*. at 36.
[70] *Id*.
[71] *Id*.

and workforce requirements. Further, "the black box' nature of some AI systems poses liability and reimbursement challenges that can affect provider trust and adoption."[72]

Part two begins as a primer on AI-DDS tools. It then considers key factors related to the successful adoption of AI-DDS tools, considered in four parts: (1) reason to use; (2) means to use; (3) method to use; and (4) desire to use.[73] Further this part considers "crosscutting issues of bias and equity as they relate to provider trust and adoption of these tools."[74] Finally, this part considers policy implications surrounding adoption of AI-DDS systems and proposes action priorities for stakeholders.[75]

1. A Primer on AI-Diagnostic Decision Support Tools.

This part focuses on assistive AI-DDS tools, which involve a natural person to some degree in the analysis and decision-making process, unlike autonomous AI tools, which operate independently of human control.[76] NAM focused on tools designed to support health care professions, rather than consumer-facing tools.[77] Current AI-DDS tools "are designed to address specific clinical issues related to a prescribed range of clinical data" and do not, nor are they intended to, "comprise omniscient, science-fiction-like algorithmic interfaces that can span all disease contexts."[78] "Ultimately, the purpose of AI-DDS tools is to augment provider expertise and patient care rather than dictate it."[79]

"Generally, assistive AI-DDS tools currently use a combination of computer vision and ML techniques such as deep learning,[80] working to identify complex non-linear relationships between features of image, video, audio, in vitro, and/or other data types, and anatomical correlates or disease labels."[81] Assistive AI-DDS tools are most prominently found in the field of diagnostic imaging due to the highly digital and increasingly computational nature of the field.[82] The field of radiology, for example, has more FDA-authorized AI tools than any other medical specialty.[83]

2. Facilitating Provider Adoption of AI-Diagnostic Decision Support Tools.

NAM outlines eight major determinants for clinical adoption of AI-DDS tools across four interrelated core domains.

1. Domain 1. "***Reason to use*** explores the alignment of incentives, market forces, and reimbursement policies that drive health care investment in AI-DDS."[84]

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[72] *Id*.
[73] *Id*.
[74] *Id*.
[75] *Id*.
[76] *Id*. at 37 (citing Bitterman, D. S., H. J. W. L. Aerts, and R. H. Mak. 2020. Approaching autonomy in medical artificial intelligence. The Lancet Digital Health 2(9):e447-e449. https://doi.org/10.1016/S2589-7500(20)30187-4).
[77] *Id*. at 37.
[78] *Id*. at 38.
[79] *Id*.
[80] Deep learning is a "subset of ML consisting of multiple computational layers between the input and output that form a 'neural network' used for complex feature learning." *Id*. at 37.
[81] *Id*. at 39.
[82] *Id*.
[83] *Id*. (citing Benjamens, S., P. Dhunnoo, and B. Meskó. 2020. The state of artificial intelligence-based FDA-approved medical devices and algorithms: an online database. npj Digital Medicine 3(118). https://doi.org/10.1038/s41746-020-00324-0).
[84] *Id*. at 41 (emphasis in original).

a. Alignment with providers' and health systems' missions: This factor contemplates the ability of a tool to address a pressing clinical need and improve patient care and outcomes.[85] "AI-DDS tools must facilitate the goals and core objectives of the health care institution and care providers they serve, although the specific impetus and pathway for AI-DDS tool adoption can vary by organization."[86] It is important to establish and validate the accuracy of new AI-DDS tools at the start of the adoption process and through its use.[87] "[T]here are often discrepancies between AI-DDS developers' scope and the realities of clinical practice, resulting in tools that can be either inefficient or only tangentially useful."[88] To reassure providers that these tools are "optimized for clinical effectiveness, health system leaders must be committed to regular evaluations of AI-DDS models and performance, as well as efficient communication with developers and companies to update algorithms based on changes like diagnosis prevalence and risk-factor profiles."[89]

b. Incentives and reimbursements: AI-DDS tools require sufficient financial investment for deployment and maintenance. Thus the "tool's affordability both to the patient and the health system, including the incentives for the provider, patient, and health system to justify the costs of acquiring the tool and the investments needed to implement it" are highly relevant.[90] Because many health care systems operate on thin financial margins,[91] robust insurance reimbursement programs for the purchase and use of AI-DDS tools will be critical to promoting greater adoption of these technologies by providers and health systems.[92] "However, incentive structures and payer reimbursement protocols for AI-DDS systems, are particularly complex in the U.S. . . ."[93] In our current fee-for-service environment, the trend is generally that the Centers for Medicare and Medicaid Services ("CMS") is the first to establish payment structures for new technologies, with private payers then emulating the standards set by CMS.[94] "In determining whether to reimburse for the use of a novel AI-DDS tool (and to what extent), a primary consideration for payers, regardless of type, is to assess whether the technology in question pertains to a condition or illness that falls under the coverage benefits of the organization" as well as whether there is "an adequate evidentiary basis for the utility and safety of the new tool."[95] The safety and effectiveness assessment often requires data similar to what FDA would require for premarket approval of a device, which developers who bring new AI-DDS systems to market through FDA's

[85] *Id*. at 42.
[86] *Id*.
[87] *Id*.
[88] *Id*.
[89] *Id*. at 42–43.
[90] *Id*. at 42.
[91] *Id*. at 43 (citing Kaufman Hall & Associates. 2022. National Hospital Flash Report. Available at: https://www.kaufmanhall.com/sites/default/files/2022-03/National-Hospital-Flash-Report-March-2022.pdf (accessed May 25, 2022)).
[92] *Id*. at 43 (citing Chen, M. M., L. P. Golding, and G. N. Nicola. 2021. Who Will Pay for AI? Radiology: Artificial Intelligence 3(3). https://doi.org/10.1148/ryai.2021210030).
[93] *Id*. at 43.
[94] *Id*. (citing Clemens, J., and J. D. Gottlieb. 2017. In the Shadow of a Giant: Medicare's Influence on Private Physician Payments. Journal of Political Economy 125(1):1-39. https://www.journals.uchicago.edu/doi/10.1086/689772).
[95] *Id*. at 43.

other market authorization pathways may lack.[96] Further, experts highlight two additional "components of AI-DDS evaluation that are of particular interest to payers: potential algorithm bias and product value."[97]

2. Domain 2. "***Means to use*** reviews the data and human infrastructure components as well as the requisite technical resources for deploying and maintaining these tools in a clinical environment."[98]

    a. Infrastructure: "Building the necessary infrastructure to deploy AI-DDS tools relies on developing the hardware and software capabilities to support a range of functions beginning with data processing and curation[,]" as well as "developing and implementing a working AI-DDS pipeline" requiring "several health IT infrastructure and data flow steps . . . to support the implementation and sustainment of an AI-DDS tool."[99] A working AI-DDS pipeline would require (1) data ingestion, i.e. linking a data producer into a data collection and processing workflow; and (2) determining where and how the raw data is stored.[100] These considerations are constrained in practice by "the specific clinical problem being addressed" and by "the extent to which the available resources can accommodate the complexity of the pipeline."[101] "Some clinical problems may require more frequent data updates or 'data meals' to ensure that adaptive AI systems can appropriately address rapidly evolving issues with a nascent foundation of data."[102] Further, "health care AI needs to be deployed in clinical workflows" where the demand for "near real-time data can result in added hardware complexity, expense and risk.[103] Storage (AI-DDS tools may require the ability to access storage on the terabyte or even petabyte scale) and processing power (deep learning-based models may require the use of graphical processing units as opposed to central processing units) are also major considerations in any data plan.[104] It is also critical that institutions consider HIPAA compliance in their data plan when seeking to develop and deploy AI-DDS tools.[105] Lastly, there must be a local solution that allows mission-critical AI-DDS tools to continue to function in the face of potential internet connectivity disruptions.[106] A few potential sticking points must be considered, including incompatible systems which cannot "speak to one another," the need to access data stored on multiple different servers, or systems that "require harmonization of different sensors into the same repository[,]" as well as sticking points during the data cleaning/data curation stage.[107]

    b. Resources: Data and computational infrastructure must be developed and there are also significant human capital requirements to develop, implement, and maintain a health care AI-DDS solution.[108] Practices and health systems often do not have "the required human

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[96] *Id*.
[97] *Id*. at 44.
[98] *Id*. at 41 (emphasis in original).
[99] *Id*. at 45.
[100] *Id*.
[101] *Id*.
[102] *Id*.
[103] *Id*. at 46.
[104] *Id*.
[105] *Id*.
[106] *Id*.
[107] *Id*. at 47.
[108] *Id*. at 48.

resources to run a minimum data infrastructure that can support AI-powered applications."[109] Key requirements include, but are not limited to, frontline IT staff, data architects, AI-machine learning specialists, information security and data privacy officers, legal and industrial contract officers for business and data use agreements, and IT educators to train and retrain providers and staff.[110] Ensuring that the tools meet the clinical needs of the institution while maintaining alignment with best practice guidelines requires a governance process in the health care system, with time investments from executive leadership and sponsorship as well as committee and oversight mechanisms to provide regular review.[111] Direct clinical champions must "have dedicated time to interface between front-line clinicians and the leadership, informatics, and data science teams."[112]

3. Domain 3. "***Method to use*** discusses the workflow considerations and training requirements to support clinicians in using these tools."[113] "Operationalizing and scaling innovations within the health care delivery system is costly and challenging. This is partly due to the heterogeneity of clinical workflows across and within organizations, medical specialties, patient populations, and geographic areas."[114] A solution lies in "plugging into key process steps that are universally shared."[115] Yet, "a weakness that limits options for reshaping physician workflows is the still nascent implementation science for deploying interventions that change provider behavior as well as the non-modularity and non-modifiability of extant, sometimes antiquated point-of-care software, including EHRs[.]"[116] In addition to these workflow challenges, it is important that these tools are developed and deployed "in a manner that improves *efficiency of practice* and frees up cognitive and emotional space for providers to interact with their patients."[117]

    a. Workflow: "AI-DDS tools must be effectively integrated into clinical workflows to impact patient care. Unfortunately, many integrations of AI solutions into clinical care fail to improve outcomes because context-specific factors limit efficacy when tools are diffused across sites."[118] Three key insights have emerged from experiences integrating AI and ML tools into practice, including (1) "health systems looking to use AI-DDS tools must recognize the factors that shape adoption and be willing to restructure roles and responsibilities to allow these tools to function optimally"; (2) "health systems must closely examine the unique impacts of AI integration on different stakeholders along the care continuum and balance stakeholder interests"; and (3) "workflows should be continuously monitored and adapted to respond to optimize the labor effort required to effectively use AI tools."[119]

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[109] *Id*.
[110] *Id*.
[111] *Id*. (citing Sutton, R. T., D. Pincock, D. C. Baumgart, D. C. Sadowski, R. N. Fedorak, and K. I. Kroeker. 2020. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digital Medicine 3(17). https://doi.org/10.1038/s41746-020-0221-y).
[112] *Id*. at 48.
[113] *Id*. at 41 (emphasis in original).
[114] *Id*. at 49.
[115] *Id*.
[116] *Id*. (citing Mandl, K. D., and I. S. Kohane. 2012. Escaping the EHR Trap - The Future of Health IT. New England Journal of Medicine 366(24):2240-2242. https://doi.org/10.1056/NEJMp1203102).
[117] *Id*. at 49.
[118] *Id*.
[119] *Id*. at 49–50.

b. Efficiency of Practice: While the "impact of AI-DDS tools and systems on the cognitive and clerical burdens of health care providers remains unclear[,]" "[s]uccessful tools would ideally reduce both burdens by delivering just-in-time diagnostic assistance in the most unobtrusive manner to providers while minimizing clerical tasks that might be generated by their use . . . ."[120] One major barrier is "the high degree of difficulty integrating new software with vendor EHR products."[121] Still, "[t]he 21st Century Cures Act ("Cures Act") specifies a new form of health IT interoperability underpinning the redesign of provider-facing applications as modular components that can be launched within the context of the EHR, and which may be instrumental in delivering AI capabilities to the point of care[.]"[122] Further, top EHR vendors have all incorporated common [application programming interface] standards into their products, which creates a substantial opportunity for innovation in software and data-assisted health care delivery.[123] To avoid problems similar to EHR alert fatigue, diagnostic outputs by AI-DDS tools "should be specific, and clinically inconsequential information should be reduced or eliminated. Outputs should be tiered according to severity with any alternative diagnoses presented in a way that signals providers to clinically important data."[124] Further, alerts should be designed with human factors principles in mind and only the most important, high-level, or severe alerts should be made interruptive.[125] In addition to these human-centered design considerations, health care provider training will be required to ensure necessary competencies.[126] Rapid-paced technological changes require a nimble educational infrastructure.[127] CAM identified 5 core areas as essential to any educational infrastructure: (1) Foundational knowledge; (2) Critical appraisal; (3) Clinical decision making; (4) Technical use; and (5) Addressing unintended consequences.[128]

4. Domain 4. "***Desire to use*** considers the psychological aspects of provider comfort with AI, such as the extent to which the tools alleviate clinician burnout, provide professional fulfillment, and engender overall trust. This section also examines medicolegal challenges, one of the biggest hurdles to fostering provider trust in and the adoption of AI-DDS."[129]

    a. Professional Fulfillment: Alignment of AI technology with the aim to improve the work-life balance of health care professionals is an indispensable aspect of the potential success and adoption of AI tools.[130] "Health care providers report high levels of burnout, partially attributable to EHRs and related technologies[.]"[131] Providers are deeply reluctant to adopt new technologies where they have already seen an exponential rise in digital work since

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[120] *Id*. at 51.
[121] *Id*.
[122] *Id*.
[123] *Id*.
[124] *Id*. at 52.
[125] *Id*.
[126] *Id*.
[127] *Id*.
[128] *Id*.
[129] *Id*. at 41 (emphasis in original).
[130] *Id*. at 53.
[131] *Id*. (citing Melnick, E. R., L. N. Dyrbye, C. A. Sinsky, M. Trockel, C. P. West, L. Nedelec, M. A. Tutty, and T. Shanafelt. 2020. The association between perceived electronic health record usability and professional burnout among US physicians. Mayo Clinic Proceedings 95(3):476-487. https://doi.org/10.1016/j.mayocp.2019.09.024).

the onset of the COVID-19 pandemic.[132] "Successful AI-DDS tools will need to overcome this hesitancy and tap into positive sources of fulfillment for providers, including facilitating professional pride, autonomy, and security; reassessing or expanding their scope of practice; and augmenting their sense of proficiency and mastery."[133] "AI-DDS tools hold the potential to greatly improve diagnostic accuracy and reduce medical errors" and "[i]f seamlessly integrated, they could also unburden providers of rote tasks, enabling them to allocate more attention to engaging and establishing meaningful bonds with patients[,]" a great source of professional fulfillment.[134] However, deferring some higher-order data analysis and synthesis tasks to an AI-based system could cause providers to experience a sense of detachment from their work or even "erode the provider-patient relationship if patients begin to preferentially value the diagnostic recommendation of an AI system."[135]

b. Trust: "Trust within human-AI-diagnostic partnerships requires a human willingness to be vulnerable to an AI system."[136] Distrust can result from an AI-DDS tool whose recommendations are contrary to a provider's intuitive conclusions, if the user finds faults in the development process of the tool, or from concerns that the "tool's development and use is motivated by profits over people or a lack of professional values alignment[.]"[137] Key drivers of trust "can include positive past experiences with a particular manufacturer or service provider, seamless interoperability of a new application with an existing suite of tools from a familiar and currently trusted company or product, or company reputation among the professional health care community[.]"[138] Two significant sources of distrust with AI-DDS products were identified by NAM as particularly relevant to the adoption of these technologies by clinicians: (1) bias (real or perceived; and (2) liability.[139] In terms of bias, it is critical to design and monitor AI tools with an eye to preventing, detecting, and correcting bias and disclosing the tools' limitations to providers.[140] In terms of liability, a regulatory framework that prospectively aims to prevent injuries, coupled with accountability and compensation mechanisms should problematic outcomes occur is necessary.[141] Compensating patients for injuries could be done through medical malpractice, implying that that provider has ultimate responsibility, or through products liability, implying that developers and manufacturers have ultimate responsibility.[142]

    i. Tools to Promote Trust: Thoughtful regulation and governance from all levels of the U.S. government can reassure providers that they can trust available AI-DDS tools

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[132] *Id*. at 53.
[133] *Id*.
[134] *Id*.
[135] *Id*.
[136] *Id*. at 54.
[137] *Id*. (citing Rodin, J., and S. Madsbjerg. 2021.Making Money Moral : How a New Wave of Visionaries Is Linking Purpose and Profit. Wharton School Press).
[138] *Id*. at 54 (citing Adiekum, A., A. Blasimme, and E. Vayena. 2018. Elements of Trust in Digital Health Systems: Scoping Review. J Med Internet Res 2012:e11254. doi:10.2196/11254; High-Level Expert Group on AI (AI HLEG). 2019. Ethics Guidelines for Trustworthy AI; Benjamins, R. 2021. A choices framework for the responsible use of AI. AI and Ethics 1(1):49-53. https://doi.org/10.1007/s43681-020-00012-5)).
[139] *Id*. at 55.
[140] *Id*.
[141] *Id*.
[142] *Id*.

and move forward with implementation.[143] "A potential concern is that some, but not necessarily all, AI-DDS software is subject to FDA medical device regulation under the Cures Act. It remains difficult for providers to intuit whether a given type of AI-DDS tool is or is not likely to have received oversight under FDA's medical device regulations."[144] "The Cures Act authorizes the FDA to regulate only some of the software that might fit into the broader, more common conception of AI-DDS systems just described. Thus, FDA lacks authority to regulate all of the tools that clinicians might think of as being DDS/CDS tools."[145] This uncertainty likely fuels provider discomfort with using AI-DDS tools.[146] "Apart from the regulatory framework, another mechanism to instill trust is through increased and consistent collaboration among developers, ethicists, and clinical diagnosticians during various phase of the AI lifecycle."[147]

3. Ensuring and Promoting Health Equity in the Deployment of AI-Assisted Diagnostic Tools.

"While there is excitement and demonstrated benefits to bringing AI-DDS tools into clinical practice, poor data quality, prevalent biases in health care, and a lack of structural supports available to end users jeopardize progress toward achieving health equity and fuel ongoing uncertainties and hesitancies about adopting these tools."[148] "AI/ML algorithms are often developed using limited data samples that may not represent the people they are meant to impact[.]"[149] "Furthermore, social determinants of health data are generally not well captured in data sets used to train these algorithms."[150] Where there is inaccurate representation in training, testing, and validation data sets, the development of flawed models results.[151] Further, "[m]odels not accurately trained in the context that they are intended for may also have difficulty performing when there is a shift in population demographics."[152] "AI tools rely on human interaction from their inception to deployment, and AI algorithms can replicate explicit and implicit biases in human decision making in health care settings[.]"[153] "Inherent discrimination occurring within care delivery can be challenging to predict and uncover, and biases could easily transfer over into the design and use of AI algorithms[.]"[154]

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[143] *Id*. at 57–58.
[144] *Id*. at 58.
[145] *Id*.
[146] *Id*.
[147] *Id*. at 62.
[148] *Id*. at 64.
[149] *Id*. (citing Zou, J. and L. Schiebiner. 2021. Ensuring that biomedical AI benefits diverse populations. eBioMedicine 67:1-6. https://doi.org/10.1016/j.ebiom.2021.103358).
[150] *Id*. at 64.
[151] *Id*.
[152] *Id*.
[153] *Id*. (citing Char, D., N. Shah, and D. Magnus. 2018. Implementing machine learning in health care – addressing ethical challenges. New England Journal of Medicine 378(11):981-983. https://doi.org/10.1056/NEJMp1714229).
[154] *Id*. at 64 (citing Leslie, D., A. Mazumder, A. Peppin, M. K. Wolters, and A. Hagerty. 2021. Does "AI" stand for augmenting inequality in the era of covid-19 healthcare? BMJ 372:1-5. https://doi.org/10.1136/bmj.n304; Char, D., N. Shah, and D. Magnus. 2018. Implementing machine learning in health care – addressing ethical challenges. New England Journal of Medicine 378(11):981-983. https://doi.org/10.1056/NEJMp1714229).

"In addition to the adverse effects of incorrect data usage and biases, the absence of infrastructure to support equitable AI in developing and deploying AI-DDS tools will ultimately widen disparities. The digital gap perpetuates inequities through many social factors that may intertwine, including a lack of broadband internet access across regions and an inability to purchase up-to-date and well-equipped devices[.]"[155]

4. A Path Forward – Policy Implications and Action Priorities.

"Fostering provider adoption of novel AI-DDS systems will require broad infrastructural support, beginning with robust tool evaluations by health systems and payers, clear commitments from health systems and developers to regular monitoring and updating of algorithms, and training care teams to effectively interpret and implement changes based on AI-DDS outputs."[156] Stakeholders are becoming increasingly aware of issues of potential bias in AI algorithms and their deployment, making data representativeness and robust model training, as well as data integrity and reliability, top priorities for algorithm development and deployment.[157] "[C]ollaborative efforts aimed at curating rich and multimodal patient data—including crucial social determinants information—will be paramount."[158] In addition, excellent model development will require "robust and consistent standards for data access, sharing, harmonization, and interoperability, while simultaneously prioritizing data privacy and security . . . ."[159] Similarly, increasing provider comfort with the technology, which may drive provider adoption, may also depend on model transparency.[160] Part two concludes with presenting key action priorities related to provider adoption of AI-DDS tools in each of the four domains touched on earlier: (1) reason to use; (2) means to use; (3) method to use; and (4) desire to use.

1. <u>Reason to use</u>

    a. "Data representativeness and robust model training and testing must be the top priority in algorithm development in efforts to increase trust and adoption among all relevant stakeholders."[161]

    b. "Collaborative efforts among multiple health care systems aimed at curating rich and multimodal patient data—including essential social determinants information—will be paramount. Such efforts need to be coupled with robust and consistent standards for data access, sharing, and interoperability, while simultaneously prioritizing data privacy and security, to ultimately drive excellent model development."[162]

    c. "[A]lgorithm developers must design AI-DDS tools to integrate seamlessly into existing care team infrastructures, ensuring that their product value is not diminished by logistical inefficiency and cognitive burden."[163]

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[155] *Id*. at 64 (citing Ramsetty, A., and C. Adams. 2020. Impact of the digital divide in the age of COVID-19. Journal of American Medical Informatics Association 27(7):1147-1148. https://doi.org/10.1093/jamia/ocaa078).
[156] *Id*. at 66.
[157] *Id*.
[158] *Id*.
[159] *Id*.
[160] *Id*.
[161] *Id*.
[162] *Id*.
[163] *Id*.

2. Means to use:
    a. “Policy makers and payers should consider promoting sustainability through reimbursement to create a sustainable environment for the adoption and continual use of AI-DDS tools and to further promote capital infrastructure investments by health systems to facilitate this goal.”[164]
    b. “If consensus-based standards do not emerge, ensuring interoperability could require a “top-down” regulatory approach.”[165]
    c. “Policy makers and payers should consider using incentives to encourage the use of evidence-based AI-DDS in clinical practice.”[166]
3. Method to use:
    a. “Public and private research funders should increase focus and funding opportunities to advance the still nascent implementation science of AI-DDS . . . .”[167]
    b. “Institutions of medical education and accreditation organizations should review emerging competencies for the use of AI-DDS and consider how to integrate these into the current training and certification ecosystem to adapt to the rapidly changing needs of the clinical front line.”[168]
    c. “Professional societies, trade associations, and health care quality organizations should identify diagnostic centers of excellence that specialize in AI-DDS to facilitate the surfacing and effective diffusion of best practices through interdisciplinary learning networks and capacity-building programs.”[169]
    d. “Software and algorithm designers of point-of-care AI-DDS for providers and patients at home should leverage the public SMART on FHIR and SMART/HL7 Bulk FHIR APIs regulated under the ONC 21st Century Cures Act Rule, so that algorithms can be widely and uniformly integrated into care across EHR vendor products and other IT tools.”[170]
    e. “Regulators should monitor, for example through the 21st Century Cures Act EHR Reporting Program, EHR vendor implementation of public FHIR APIs to ensure their turnkey use by apps made accessible at the point of care.”[171]
4. Desire to use:
    a. “Professional societies, trade associations, and health care quality organizations should center AI-related efforts to promote clinician well-being through human-centered design in AI technology, aligned with the work-life balance of health care professionals . . . FDA should offer guidance and/or other communications, specifically tailored to health care providers

[164] *Id*. at 67.
[165] *Id*.
[166] *Id*.
[167] *Id*.
[168] *Id*.
[169] *Id*.
[170] *Id*.
[171] *Id*.

tasked with using AI/DDS tools, to aid their understanding of the types of software are – and are not – likely to receive FDA oversight under 21 U.S.C. § 360j(o)(1)(E)."[172]

b. "FDA should continue to explore the special considerations affecting design, validation review, market authorization, and post marketing oversight for AI-DDS tools, offering timely guidance while recognizing that, over the long term, notice-and-comment rulemaking may offer advantages over the continued use of guidance documents – for example – to enhance developers' access to HIPAA-protected real-world data for use in regulatory compliance activities, and to provide needed clarity and stability to foster development of state regulations and common law addressing clinical use of AI-DDS systems."[173]

c. "Professional medical, nursing, and other health care societies should develop clinical practice guidelines for AI system applications."[174]

d. "FDA, CDC, and ONC should ensure transparency and publicly accessible reporting for flaws and safety incidents related to AI-DDS tools, malfunctions, and patient harm."[175]

e. "Software developers should integrate human clinical diagnosticians at all phases of software development, design, validation, implementation, and iterative improvements."[176]

[172] *Id*. at 67–68.
[173] *Id*. at 68.
[174] *Id*.
[175] *Id*.
[176] *Id*.