Artificial Intelligence and Health Care

Webinar
April 30, 2020 | 2:00 – 4:00 PM EST

Share your thoughts!

@theNAMedicine
Welcome & Introduction

Michael McGinnis  
National Academy of Medicine

Timothy Persons  
United States Government Accountability Office
Agenda

Welcome 2:00 – 2:10 PM

Michael McGinnis, National Academy of Medicine
Tim Persons, U.S. Government Accountability Office

Part I

AI in Health Care: An NAM Special Publication 2:10 – 2:25 PM

Michael Matheny, Vanderbilt University Medical Center
Sonoo Thadaney-Israni, Stanford University

Panel Discussion 2:25 – 2:50 PM

Jack Resneck, American Medical Association
Marelize Gorgens, World Bank
Gil Alterovitz, Veterans Affairs
Glenn Cohen, Harvard Law School
Part II

GAO Tech Assessment: AI in Drug Development 2:50 – 3:05 PM
Karen Howard, U.S. Government Accountability Office
Rebecca Parkhurst, U.S. Government Accountability Office

Panel Discussion 3:05 – 3:30 PM
Ken Getz, Tufts Center for the Study of Drug Development
M. Khair ElZarrad, FDA Center for Drug Evaluation and Research
Danielle Friend, Biotechnology Innovation Organization

Q&A 3:30 – 4:00 PM
Panelists to answer questions submitted by participants via Q&A box

Adjourn 4:00 PM
Closing remarks - Michael McGinnis & Tim Persons
Artificial Intelligence in Health Care

The Hope, the Hype, the Promise, the Peril

Michael Matheny, Sonoo Thadaney Israni, Mahnoor Ahmed, and Danielle Whicher, Editors

December 2019

United States Government Accountability Office
Science, Technology Assessment, and Analytics

TECHNOLOGY ASSESSMENT

Artificial Intelligence in Health Care

Benefits and Challenges of Machine Learning in Drug Development

With field background content from the National Academy of Medicine

GAO-20-215SP
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Artificial Intelligence in Health Care: The Hope, the Hype, the Promise, the Peril
An NAM Special Publication

Michael Matheny
Vanderbilt University Medical Center

Sonoo Thadaney Israni
Stanford University
Sonoo Thadaney Israni, MBA
Executive Director, Stanford University Presence Center (Stanford Medicine)
AI: The Hope, The Hype, The Promise, The Peril
Available for download:
“Humans were always far better at inventing tools than using them wisely.”
AI needs population representative data or GIGO

AI-triggered Healthcare Inequity
“AI Could Reinvent Medicine—Or Become a Patient's Nightmare

The Mayo Clinic will store health data in Google's cloud and use its AI expertise to unearth insights. But Google has made mistakes before...”
COVID-19 knows no “other” – we’re in this together

Most Americans have used email and messaging services to connect with others during the COVID-19 outbreak, while one-in-four have used video calling for work

<table>
<thead>
<tr>
<th>Used email or messaging services to communicate with others</th>
<th>Used social media to share or post information about the coronavirus</th>
<th>Used video calling or online conferencing services to attend a work meeting</th>
<th>Used the internet or email to connect with doctors or other medical professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>U.S. adults</strong> 76</td>
<td>76</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td><strong>Men</strong> 76</td>
<td>69</td>
<td>32</td>
<td>26</td>
</tr>
<tr>
<td><strong>Women</strong> 78</td>
<td>71</td>
<td>43</td>
<td>24</td>
</tr>
<tr>
<td><strong>Ages 18-29</strong> 60</td>
<td>62</td>
<td>34</td>
<td>25</td>
</tr>
<tr>
<td><strong>30-49</strong> 80</td>
<td>79</td>
<td>47</td>
<td>22</td>
</tr>
<tr>
<td><strong>50-64</strong> 71</td>
<td>64</td>
<td>34</td>
<td>22</td>
</tr>
<tr>
<td><strong>65+</strong> 72</td>
<td>62</td>
<td>26</td>
<td>19</td>
</tr>
<tr>
<td><strong>White</strong> 78</td>
<td>69</td>
<td>34</td>
<td>26</td>
</tr>
<tr>
<td><strong>Black</strong> 84</td>
<td>61</td>
<td>37</td>
<td>25</td>
</tr>
<tr>
<td><strong>Hispanic</strong> 77</td>
<td>76</td>
<td>48</td>
<td>23</td>
</tr>
<tr>
<td><strong>HS or less</strong> 85</td>
<td>87</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td><strong>Some college</strong> 87</td>
<td>83</td>
<td>38</td>
<td>21</td>
</tr>
<tr>
<td><strong>College+</strong> 91</td>
<td>97</td>
<td>46</td>
<td>19</td>
</tr>
<tr>
<td><strong>Rural</strong> 69</td>
<td>62</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td><strong>Suburban</strong> 80</td>
<td>72</td>
<td>36</td>
<td>20</td>
</tr>
<tr>
<td><strong>Urban</strong> 78</td>
<td>78</td>
<td>42</td>
<td>29</td>
</tr>
<tr>
<td><strong>Rep/Lean Rep</strong> 75</td>
<td>67</td>
<td>35</td>
<td>20</td>
</tr>
<tr>
<td><strong>Dem/Lean Dem</strong> 78</td>
<td>74</td>
<td>40</td>
<td>30</td>
</tr>
</tbody>
</table>

Note: Whites and blacks include only non-Hispanics, Hispanics are of any race. Those who did not give an answer are not shown. Source: Survey of U.S. adults conducted March 19-24, 2020.

Coronavirus deaths and race

COVID-19 is disproportionately killing black Americans, according to data released by several states.

Deaths per 100,000

<table>
<thead>
<tr>
<th>Race</th>
<th>Louisiana</th>
<th>Michigan</th>
<th>Illinois</th>
</tr>
</thead>
<tbody>
<tr>
<td>blacks</td>
<td>5.8</td>
<td>2.6</td>
<td>1.3</td>
</tr>
<tr>
<td>whites</td>
<td>27</td>
<td>21.6</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Total deaths

<table>
<thead>
<tr>
<th>State</th>
<th>Total deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Louisiana</td>
<td>407</td>
</tr>
<tr>
<td>Michigan</td>
<td>298</td>
</tr>
<tr>
<td>Illinois</td>
<td>129</td>
</tr>
<tr>
<td>North Carolina</td>
<td>13</td>
</tr>
</tbody>
</table>

Death totals as of Tuesday afternoon.
State governments, U.S. Census Bureau

Lorena Elebee / Los Angeles Times
Framework for implementing AI via lens of human rights values

Implementing AI through the lens of human rights values requires some ‘friction’.
Source: Judy Estrin, Technology Pioneer, Entrepreneur, & CEO, JLABS, LLC

What do we value?
How are we each responsible?
We can, but should we?

What does Human Centered mean?
To humans, for humans, by humans?

How do we define progress, quality of life, well-being?

Who knows, who decides, who decides who decides?
– Shoshana Zuboff
The Age of Surveillance Capitalism

Quintuple Aim

“That which is measured, improves.”

Karl Pearson
Statistician & founder of mathematical statistics

Thank you!

Sonoo Thadaney Israni, MBA
Executive Director, Stanford University
Presence Center (Stanford Medicine)
Michael Matheny, MD, MS, MPH
Co-Director, Center for Improving Patients’ Health Through Informatics, Vanderbilt University
Associate Director, VINCI, Department of Veterans Affairs
Michael.matheny@vumc.org, michael.matheny@va.gov, @MichaelEMatheny
Promise & Challenge of AI In Healthcare

Clinical Decision Support

https://simonsmarketing.com/robotics-ai-information-synthesis-professional-services

https://www.cdc.gov/media/subtopic/images.htm

Overview & Outbreak Detection Example

https://nam.edu/artificial-intelligence-special-publication/
https://apnews.com/100fbb228c958f98d4c755b133112582
Data Availability & Access Remain Challenges

The Cures Act Final Rule: Interoperability-Focused Policies that Empower Patients and Support Providers

Accelerating Data Infrastructure For COVID-19 Surveillance And Management

Monica Rogati’s Medium Post “The AI Hierarchy of Needs”
In order to assess the fair use of these technologies and support trust in users, it is important to assess the needs for transparency and how to best translate that.

• Assess context dependent requirements for **data, algorithmic, and performance** transparency
Focus Health Care-AI on Augmented Intelligence

Picture of health care data trend during covid, utilization or Other drasic change.. I have non-med, want med

https://medium.com/insight-io/extended-intelligence-not-ai-a209e15c626d
AI Lifecycle Excerpt: Monitor Performance

Susceptibility – ♦ High  ◇ Moderate  ▽ Low

<table>
<thead>
<tr>
<th>Model</th>
<th>Event Rate Shift</th>
<th>Association Shift</th>
<th>Case Mix Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic regression</td>
<td>♦</td>
<td>♦</td>
<td>♦</td>
</tr>
<tr>
<td>L1 penalized regression</td>
<td>♦</td>
<td>♦</td>
<td>♦</td>
</tr>
<tr>
<td>L2 penalized regression</td>
<td>♦</td>
<td>♦</td>
<td></td>
</tr>
<tr>
<td>L1-L2 penalized regression</td>
<td>♦</td>
<td>♦</td>
<td>♦</td>
</tr>
<tr>
<td>Random forest</td>
<td>♦</td>
<td>◇</td>
<td></td>
</tr>
<tr>
<td>Neural network</td>
<td>♦</td>
<td>◇</td>
<td>◇</td>
</tr>
</tbody>
</table>

https://nam.edu/artificial-intelligence-special-publication/
Davis SE, Lasko TA, Chen G, Matheny ME. Proceedings of the AMIA Annual Symposium. 2017
Thank You

• Publication Authors & Editors
  • Co-Editor Sonoo Thadaney-Israni
  • 28 Chapter Authors

• National Academy of Medicine
  • Michael McGinnis, Jonathan Perlin, and Reed Tuckson
  • Danielle Whicher & Mahnoor Ahmed
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Jack Resneck
American Medical Association
A.I. In Healthcare
NAM/GAO Joint Webinar

Jack Resneck, Jr., MD
Immediate-Past Chair, AMA Board of Trustees

April 2020
No Personal Financial Conflicts of Interest

Do Serve as Trustee and Immediate-Past Chair, AMA Board of Trustees
Physicians Embrace Innovation, but Want to Know:

• Will it work?
  • Clinically tested/validated? Published vs proprietary data?
  • Right choice of training data and validation for deployment setting
  • Can humans understand and trust its predictions?

• Will it work in my practice/population?
  • Addresses meaningful need or challenge?
  • User centered? Integrated into workflows? Actionable?
  • Does it re-engineer experiences to reduce friction and mitigate burnout?

• Will it reduce costs and improve value?

• Will I be sued for using it? (or not using it?)
  • Patient privacy protected?
  • Who is liable for unintended outcomes?

Thoughtful Design on the Front End (Including End Users) is Critical
Physicians and Patients Want to Know Which AI and Digital Health Tools Will Work

• Critical Factors for Quality:
  • Strong, Published Clinical Validation in Settings of Deployment
  • Right Training Data
  • Transparency or at Least Explainability -- so Humans can Understand and Trust Conclusions
Risk of Irreversible Privacy Loss

Need a National Discussion on Balancing Potential Benefits with Risks of Re-identifiable Data, and Opportunities for Meaningful Notice and Dynamic Consent by Patients

As Congress continues discussions around federal privacy legislation, the AMA seeks to ensure that resulting privacy law protects the sacred trust at the heart of the physician-patient relationship. Specifically, the AMA is working to ensure that as health information is shared—particularly outside of the health care system—patients have meaningful controls over and a clear understanding of how their data is being used and with whom it is being shared. Above all, patients must feel confident that their health information will remain private. Preserving patient trust is critical.

These principles, derived primarily from AMA HOD policy, will serve as the foundation for AMA advocacy on privacy. They are meant to apply to entities other than those already considered covered entities under HIPAA—in other words, physicians generally would not be subject to additional regulation. The principles take into consideration that some data historically not considered “personal” may in fact be personally identifiable (e.g., IP addresses, advertising identifiers from mobile phones). Accordingly, the Principles’ use of the term “data” includes information that can be used to identify an individual, even if it is not descriptive on its face.

The Principles provide individuals with rights and protections from discrimination and shift the responsibility for privacy from individuals to data holders other than HIPAA-covered entities (collectively referred to in this document as entities). In other words, third parties who access an individual’s data should act as responsible stewards of that information, just as physicians promise to maintain patient confidentiality. The Principles also call for robust enforcement of penalties for violation of rights to help patients develop and maintain trust in digital health tools, including the use of smartphone applications (apps) to access their own health information.

Individual Rights:

1. Individuals have the right to know exactly what data of theirs an entity is accessing, using, disclosing, and processing—and for what purpose—at or before the point of collection.
A.I. Regulatory Policy Lags Behind the Technology

• The Physician Approach to Right-Sizing Regulation based on Level of Risk
  • Use Case
    • Clinical Care (Assistive, Autonomous)
    • Patient-facing tools
    • Research
    • Administration / Operations
  • Scale/Scope of Deployment
    • Home-grown local system
    • Commercialized
  • Type of Machine Learning
    • Locked vs Continuous
    • Supervised (labelled training data) vs Unsupervised
• Recent FDA guidance suggests low risk systems not subject to FDA regulation
  • IMDRF risk model only accounts for disease seriousness & use case
Liability Should be Assigned to Those Knowledgeable about a System’s Design and Validation and Best Positioned to Mitigate Risk and Avert Harm

New York is investigating UnitedHealth's use of a medical algorithm that steered black patients away from getting higher-quality care

Aliana Akhtar Oct 28, 2019, 8:02 AM

RESEARCH ARTICLE

ECONOMICS

Dissecting racial bias in an algorithm used to manage the health of populations

Ziad Obermeyer, Brian Powers, Christine Vogeli, Sendhil Mullainathan

© 2018 American Medical Association. All rights reserved.
Physicians Embrace Innovation, but Want to Know:

• Will it work?
  • Clinically tested/validated? Published vs proprietary data?
  • Right choice of training data and validation for deployment setting
  • Can humans understand and trust its predictions?

• Will it work in my practice/population?
  • Addresses meaningful need or challenge?
  • User centered? Integrated into workflows? Actionable?
  • Does it re-engineer experiences to reduce friction and mitigate burnout?

• Will it reduce costs and improve value?
• Will I be sued for using it? (or not using it?)
  • Patient privacy protected?
  • Who is liable for unintended outcomes?

Thoughtful Design on the Front End (Including End Users) is Critical
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Marelize Gorgens
World Bank
Improve or Impair?

The Promise and Perils of the use of AI in Developing Countries

Marelize Gorgens Prestidge
mgorgens@worldbank.org
The Promise to **Improve**

- Create **electronic health records** – rapid transition from paper-based to electronic-based
- Potential for **increases in efficiency** – technical, production and allocative efficiency
- Digital task shifting and addressing **severe staff shortages**, e.g. radiology
- **Population-health** perspectives: micro targeting and differentiated care services for different patients and clients not yet seeking care
- **Non-traditional health sector data** for early warning signs and sentiment analyses
The Perils to Impair

• Exponential increase in ‘pilot-itis’
  • Partial, siloed, systems
  • 228 in Ethiopia

• As long as data access is not universal and data costs prohibitive, potential to exacerbate inequality in service quality

• Disproportionate focus on the highest hanging fruit: clinical decision support systems

• Patient confidence – lack of understanding of ‘augmented intelligence’
Eight Imperatives to Make Lasting Progress

1. Digital health bouquets, not a thousand flowers – also funding for integration of existing solutions
2. Evaluations and cost effectiveness: just because it is new, it is not necessarily better
3. Consider system disruptions and linkage to existing systems
4. Digitization then AI, or designed with embedded AI?
5. Patient and health care worker confidence
6. Regulation and governance
Zoom Instructions

General
• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A
• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Gil Alterovitz
Veterans Affairs
National Academy of Medicine Recommendations and Implementation at the National AI Institute

Artificial Intelligence in Health Care
The Hope, the Hype, the Promise, the Peril

Gil Alterovitz, PhD, FACMI, FAMIA
Director

National Artificial Intelligence Institute
7 NAM Recommendations

1. Population-representative data accessibility, standardization, quality is vital
2. Ethical health care, equity, and inclusivity should be prioritized
3. The dialogue around transparency and trust should change to be domain- and use-case differential
4. Near-term focus should be on augmented intelligence rather than full automation
5. Develop and deploy appropriate training and educational programs to support health care AI
6. Leverage existing frameworks and best practices within the learning health care system, human factors, and implementation science
7. Balancing degrees of regulation and legislation of AI to promote innovation, safety, and trust
7 NAM Recommendations

1. Population-representative data accessibility, standardization, quality is vital
2. Ethical health care, equity, and inclusivity should be prioritized
3. The dialogue around transparency and trust should change to be domain- and use-case differential
4. Near-term focus should be on augmented intelligence rather than full automation
5. Develop and deploy appropriate training and educational programs to support health care AI
6. Leverage existing frameworks and best practices within the learning health care system, human factors, and implementation science
7. Balancing degrees of regulation and legislation of AI to promote innovation, safety, and trust
Collaborations with Researchers

- Predict Acute Kidney Injury (AKI) 48 hours in advance
- Early warning enables time to take preemptive action
- Helps prevent kidney injury
7 NAM Recommendations

1. Population-representative data accessibility, standardization, quality is vital
2. Ethical health care, equity, and inclusivity should be prioritized
3. The dialogue around transparency and trust should change to be domain- and use- case differential
4. Near-term focus should be on augmented intelligence rather than full automation
5. Develop and deploy appropriate training and educational programs to support health care AI
6. Leverage existing frameworks and best practices within the learning health care system, human factors, and implementation science
7. Balancing degrees of regulation and legislation of AI to promote innovation, safety, and trust
Rapid Prototyping

Through our tech sprints and flexibility to work collaboratively with academics, we are in the process of identifying projects for rapid prototyping.

- Identify areas with specific pain points for veterans and work collaboratively to pilot a use case.
- Leverage the vast amount of VA data to bring perspective.
AI Tech Sprints

Clinical Trials Selector

<table>
<thead>
<tr>
<th>Lab Results</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>Leukocytes</td>
<td>Platelets</td>
</tr>
<tr>
<td>10.53 L</td>
<td>3.85 10^3/μL</td>
<td>14.21 g/dL</td>
</tr>
</tbody>
</table>

Filter trials by inclusion criteria

There are 40 trials for 4 conditions

- Trials for condition: Osteoporosis (C3298)
- Trials for condition: Cardiac Arrest (C50479)
- Trials for condition: Myocardial Infarction (C27966)
- Trials for condition: Grade III Prostatic Intraepithelial Neoplasia (C3842)

Courtesy: Girls Computing League

Courtesy: Composite Apps
7 NAM Recommendations

1. Population-representative data accessibility, standardization, quality is vital
2. Ethical health care, equity, and inclusivity should be prioritized
3. The dialogue around transparency and trust should change to be domain- and use- case differential
4. Near-term focus should be on augmented intelligence rather than full automation
5. Develop and deploy appropriate training and educational programs to support health care AI
6. Leverage existing frameworks and best practices within the learning health care system, human factors, and implementation science
7. Balancing degrees of regulation and legislation of AI to promote innovation, safety, and trust
Pioneering New and Representative Data

Given that veterans face physical and mental health challenges at disproportionate rates, we leverage existing frameworks from AI/ML and to understand the quality of life determinants for vulnerable populations.

- Leverage non-traditional health information. Makridis, et. al. (2020) showed that socio-economic factors matter much more than demographics and geographic factors at predicting physical well-being for veterans.

- Results highlight the importance of human factors for health care.
Questions?

Web: research.va.gov/naii
Contact: gil.alterovitz@va.gov
Glenn Cohen
Harvard Law School
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Part II

GAO Tech Assessment: AI in Drug Development 2:50 – 3:05 PM

Karen Howard, U.S. Government Accountability Office
Rebecca Parkhurst, U.S. Government Accountability Office

Panel Discussion 3:05 – 3:30 PM

Ken Getz, Tufts Center for the Study of Drug Development
M. Khair ElZarrad, FDA Center for Drug Evaluation and Research
Danielle Friend, Biotechnology Innovation Organization

Q&A 3:30 – 4:00 PM

Panelists to answer questions submitted by participants via Q&A box

Adjourn 4:00 PM

Closing remarks - Michael McGinnis & Tim Persons
AI in Health Care: Benefits and Challenges of Machine Learning in Drug Development

Karen Howard, Director
Rebecca Parkhurst, Senior Physical Scientist

Science, Technology Assessment, and Analytics (STAA)

April 2020
About GAO

The U.S. Government Accountability Office (GAO) is an independent, nonpartisan agency that works for Congress.

Often called the "congressional watchdog," GAO examines how taxpayer dollars are spent and provides Congress and federal agencies with objective, reliable information to help the government save money and work more efficiently.
STAA’s Work

Technology Assessment
Provides foresight on key technologies and the policy implications for the federal government.

Science and Technology Auditing
Handles oversight of research programs, intellectual property protections, innovation programs.

Engineering Sciences
Provides best practices, including for cost, schedule, earned value, and technology readiness assessment.

Innovation Lab
Explores, pilots, and deploys advanced analytics, information assurance auditing, and emerging technologies to improve auditing practices.

Across our work we aim to augment our core products with a range of timely, high-value technical assistance services for our congressional clients.
Technology Assessments

STAA provides foresight, oversight, and insight on science and technology issues to Congress and the public.

- Each TA is a robust assessment of a crosscutting technology that impacts many sectors.
- TAs include policy options, similar to recommendations.
TECHNOLOGY ASSESSMENT

Artificial Intelligence in Health Care

Benefits and Challenges of Machine Learning in Drug Development

With field background content from the National Academy of Medicine

The drug discovery, development, and approval process

Drug Discovery
Researchers may screen thousands of compounds in the laboratory to identify a few promising candidates.

Preclinical Research
Drugs undergo laboratory and animal testing to answer basic questions about safety and dosing ranges on 20 to 80 patients.

Clinical Trials
- Phase I: Drugs tested for safety and dosing ranges on 20 to 80 patients
- Phase II: Drugs tested for efficacy on a few dozen to hundreds of patients
- Phase III: Drugs tested for efficacy on hundreds to thousands of patients

FDA Drug Review and Approval
Approximately 1 in 10 compounds entering clinical trials receives FDA approval.

Source: GAO analysis of Food and Drug Administration (FDA) and Pharmaceutical Research and Manufacturers of America (PhRMA) documentation. | GAO-20-215SP

Note: IND=investigational new drug application, NDA=new drug application.
Examples of machine learning in drug development

**Drug discovery**
- Identifying new targets
- Screening known compounds for new therapeutic applications
- Designing new drug candidates

**Preclinical research**
- Augmenting preclinical testing
- Predicting toxicity before testing potential drugs in humans

**Clinical trials**
- Selecting and recruiting patients for clinical trials
- Moving clinical research towards precision medicine
Potential benefits of machine learning in drug development

Machine learning is used throughout the drug development process and could increase its efficiency and effectiveness, decreasing the time and cost required to bring new drugs to market.

Source: GAO. | GAO-20-215SP
## Challenges hindering the use of machine learning in drug development

### Gaps in Research
Research gaps present a significant challenge to advancing the use of machine learning in drug development.

- Gaps exist in fundamental biology and chemistry research needed to develop machine learning models, such as understanding mechanisms of disease.
- Gaps in domain-specific machine learning research, such as how to represent molecules to machine learning algorithms, also exist.

### Data Quality
A shortage of high-quality data is a major challenge for machine learning in drug development.

- Much of the data available were not collected for machine learning purposes.
- Biases in data, such as an underrepresentation of certain populations, may limit machine learning’s effectiveness.

### Data Access and Sharing
Accessing and sharing data can be difficult due to cost, legal issues, and reluctance from some companies.

- Acquiring, curating, and storing data is expensive, and uncertainty around data privacy laws hinders sharing.
- Data sharing may be limited by a lack of economic incentives for certain organizations to share.

Source: GAO analysis of expert discussions, interviews, and the scientific literature. | GAO-20-215SP
Challenges hindering the use of machine learning in drug development

**Workforce**
A shortage of skilled and interdisciplinary workers makes hiring and retention difficult for drug companies and regulators.

- Workers with advanced skills in these areas command a higher salary than some companies or agencies may be able to pay.
- Bridging the cultural divide between biomedical and data scientists is also challenging.

**Regulatory Challenges and Federal Commitment**
Uncertainty about regulation and federal commitment may hamper adoption.

- Drug companies expressed confusion about regulatory requirements, which may limit investment in machine learning in drug development.
- Other countries’ support of machine learning in drug development may create a competitive disadvantage for the U.S.

Source: GAO analysis of expert discussions, interviews, and the scientific literature. | GAO-20-215SP
**Policy options**

**Research:** Policymakers could promote basic research to generate more and better data and improve understanding of machine learning in drug development.

- **Potential opportunities**
  - Could increase scientific and technological output.
  - Could generate additional high-quality, machine readable data.

- **Considerations**
  - Benefits of basic research are uncertain.
  - Would likely require assessment or reallocation of available resources.
Policy options

Data access: Policymakers could create mechanisms or incentives for increased sharing of high-quality data held by public or private actors, while also ensuring protection of patient data.

- Potential opportunities
  - Could shorten the length of the process and reduce costs.
  - Could help companies identify unsuccessful drug candidates sooner.

- Considerations
  - Would likely require coordination and costs.
  - Could have legal consequences.
  - Cybersecurity risks could increase.
  - Organizations could be reluctant to participate.
Policy options

**Standardization**: Policymakers could collaborate with relevant stakeholders to establish uniform standards for data and algorithms.

- **Potential opportunities**
  - Could improve interoperability.
  - Could increase explainability, transparency, and benchmarking.

- **Considerations**
  - Could be time- and labor-intensive.
Policy options

Human capital: Policymakers could create opportunities for more public and private sector workers to develop appropriate skills.

• Potential opportunities
  – Could provide a larger pool of skilled workers.
  – Interdisciplinary teamwork could improve.

• Considerations
  – Data science-trained workers could seek higher-paying opportunities.
  – Would likely require an investment of time and resources.
Policy options

**Regulatory certainty:** Policymakers could collaborate with relevant stakeholders to develop a clear and consistent message regarding regulation of machine learning in drug development.

- **Potential opportunities**
  - Could increase the level of public discourse.
  - Drug companies could better leverage the technology.

- **Considerations**
  - Would likely require coordination within and among agencies and other stakeholders.
  - If new regulations are promulgated, compliance costs and review times could increase.
**Status quo:** Policymakers could maintain the status quo (i.e., allow current efforts to proceed without intervention).

- **Potential opportunities**
  - Challenges may be resolved through current efforts.
  - Companies are already using machine learning and may not need action from policymakers to continue expanding its use.

- **Considerations**
  - The challenges described in this report may remain unresolved or be exacerbated.
Thank you.

Feel free to follow up with any questions.
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Ken Getz
Tufts Center for the Study of Drug Development
Reactions to Report

Kenneth Getz, MBA
Deputy Director, Professor
Tufts Center for the Study of Drug Development

617-636-3487, Kenneth.getz@tufts.edu
Challenges Hindering Use of ML in Drug Development

- Thoughtful
- Insightful
- Useful

- Other Considerations:
  - Data Uses; Fragmentation; Leadership and Culture
  - Point to more practical and actionable strategic opportunities
Data Volume, Sources and Uses

### Reported Data Sources Used

- **Electronic Data Capture (EDC)**: 100.0%
- **Randomization and Trial Supply Management**: 77.4%
- **Safety/Pharmacovigilance**: 70.4%
- **Electronic Trial Master File (eTMF)**: 69.7%
- **Clinical Trial Management System (CTMS)**: 61.1%
- **eCOA / ePRO**: 49.4%
- **Investor Grant Payments**: 26.5%
- **Electronic Medical Record (EHR/EMR)**: 19.5%
- **Electronic source data capture (eSource)**: 18.3%
- **Study start-up**: 14.0%
- **Other (please specify)**: 3.1%

### Source: Tufts CSDD 2018 and 2019; N=257 and N=114 major and mid-sized pharmaceutical and biotechnology companies

### Top ‘Desires’ for Machine Learning and AI

- **Improve Patient Safety**: 73%
- **Accelerate Decision Making**: 69%
- **Achieve Cost Efficacy and Streamline Business...**: 68%
- **Improve Market Access**: 64%
- **Improve and Develop New Drugs**: 57%
- **Expand Scope of Automation**: 51%
Organizational Fragmentation

63% of sponsor companies report having no centralized function

Source: Tufts CSDD 2019; N=114 major and mid-sized pharmaceutical and biotechnology companies
Organizational Leadership and Culture

Percent of companies reporting

- Have a formal data strategy: 32%
- Have a formal data governance policy: 21%
- Currently establishing data scientist role and responsibility: 74%
- Offer ML/AI training: 28%
- Staff who possess skills to use ML/AI: 24%

Source: Tufts CSDD 2019; N=182 major and mid-sized pharmaceutical and biotechnology companies
Six Policy Options

- Greater emphasis on collaboration and open innovation
- High visibility use cases with measurable ROI
- Opportunity to transform culture and corporate leadership
  - Analogs and digital thinking principles and competencies
  - Encouragement of data strategy and governance
  - Hiring guidelines
  - Expansive candidate identification
  - Address competitive threat from the tech sector

- RESEARCH
- DATA ACCESS
- STANDARDIZATION
- HUMAN CAPITAL
- REGULATORY CERTAINTY
- STATUS QUO
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
AI in Drug Development

M. Khair ElZarrad, PhD, MPH

Deputy Director
Office of Medical Policy
Center for Drug Evaluation and Research

The views and opinions expressed in the following slides are those of the presenter and may not reflect the views and opinions of the U.S. FDA or HHS.

No conflicts to declare
AI for Drug Development

- Mechanisms of Disease
- Biomarkers Identification
- Repurposing Existing Drugs
- Identify Novel Drug Candidates
- Compound Design
- Toxicity Prediction
- Design and Run Preclinical Experiments
- Design Clinical Trials
- Optimize Clinical Trials
- Recruit and Retain for Clinical Trials
- Organize and Analyze Real World Data
- Many others
Potential for Faster Drug Development

Developing a New Medicine Takes an Average of 10-15 Years

Examples of machine learning in the early stages of drug development include:

- **Drug Discovery**: Researchers are applying data science tools to identify new drug targets and screen known compounds for potential therapeutic applications.
- **Preclinical Research**: Researchers are augmenting preclinical testing and predicting toxicity before moving potential drugs to human trials.
- **Clinical Trials**: Researchers are applying machine learning to improve clinical trial design, a point where many drug candidates fail. Their efforts include applying machine learning to patient selection, recruitment, and stratification.

Source: GAO | GAO-20-215SP

http://blogs.nature.com/news/2012/09/pharma-comes-together-over-clinical-trials.html - From the Pharmaceutical Research and Manufacturers of America

Evolving Evidence Generation Paradigm

https://www.fda.gov/media/120060/download
Regulatory Considerations in an Increasingly Digital World

Examples of current work streams

- The use of EHR and claims data
- Digital health tools
- Decentralized clinical trials
- Data standards
- Collaborations on AI for health

Discussion paper Published April 2019
What is needed? - Multifaceted Approach

• Understanding the functions that lend themselves to AI adoption
  o AI is not necessarily the silver bullet for everything

• Shared understanding of principles for designing AI systems
  o The need a benchmarking framework(s)
  o What will transparency, audit trail, validation, etc., look like for AI?
  o Early engagement with regulatory agencies

• A convergence of multidisciplinary expertise
  o We need educational and training programs connecting essential disciplines
  o Modifying business processes and staff management- Think teams
  o Understanding ethical implications (are IRBs and DMCs ready?)

• Pilots to explore the utility of AI - Evaluate successes and failures
  o Failure here is not the standard concept we are used to— failure is an integral part of machine learning/training.
Prediction algorithms predict the most likely outcome/decision based on input data - not necessarily the accurate answer.

AI may produce unpredictable or unconventional “solutions”.

Sometimes, the ways algorithms work can have unexpected and disastrous consequences. In 2013, M.I.T. researchers trained an algorithm that was supposed to figure out how to sort a list of numbers. The humans told the algorithm that the goal was to reduce sorting errors, so the program deleted the list entirely, leaving zero sorting errors. And in 1997, another algorithm was supposed to learn to land an airplane on an aircraft carrier as gently as possible. Instead, it discovered that in its simulation it could land the plane with such huge force that the simulation couldn’t store the measurement, and would register zero force instead.
Zoom Instructions

General

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video, click the ‘start video’ option at the bottom left of your screen

Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Danielle Friend
Biotechnology Innovation Organization
Artificial Intelligence in Healthcare: Benefits and Challenges of Machine Learning in Drug Development

Danielle Friend, Ph.D.
Senior Director, Science and Regulatory Affairs
Biotechnology Innovation Organization

April 30, 2020
Who is BIO?

- **BIO is the world's largest trade association.**

- BIO’s members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place.

- **BIO’s Mission** is to advance biotechnology innovation by promoting sound public policy and fostering collaboration, both locally and globally.
Report clearly outlines key challenges and potential policy solutions for AI in drug development:

- Research
- Data access
- Standardization
- Human capital
- Regulatory certainty

Other Key Challenges:
- Timing of access to data
COVID-19 Treatments and Vaccines
- Data and AI approaches can aid in answering questions regarding
  - Factors that may predict worse outcomes
  - Identification of vulnerable populations
  - Factors that influence recovery duration or use of ventilators
  - Identification of patients for specific trials

Non-COVID-19 Treatments:
- Increased consideration for the use of digital technologies and associated AI approaches to support continued data collection and monitoring of clinical trials.
Key Considerations and Next Steps for Advancing Utility of Artificial Intelligence Moving Forward

- BIO supports proactive policy development and discussions around the use of AI for drug development and review
  - Public forums to discuss use cases, benefits and challenges of AI approaches, concerns from the public
  - Issuance of guidance

- Need to ensure that drug developers, regulators, and other key stakeholders keep pace to help realize the full potential of AI in drug development.

- Need to ensure that AI addresses inefficiencies in drug development.
Q&A Session

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name
  • To whom?
  • Question?
Artificial Intelligence and Health Care

Webinar
April 30, 2020 | 2:00 – 4:00 PM EST

Share your thoughts!

@theNAMedicine

NATIONAL ACADEMY OF MEDICINE

U.S. GOVERNMENT ACCOUNTABILITY OFFICE
Closing Remarks

Thank you for joining!

For more information about the National Academy of Medicine’s initiatives, please visit us at: nam.edu