How regulatory science can fasten innovation in digital pathology and ML/AI

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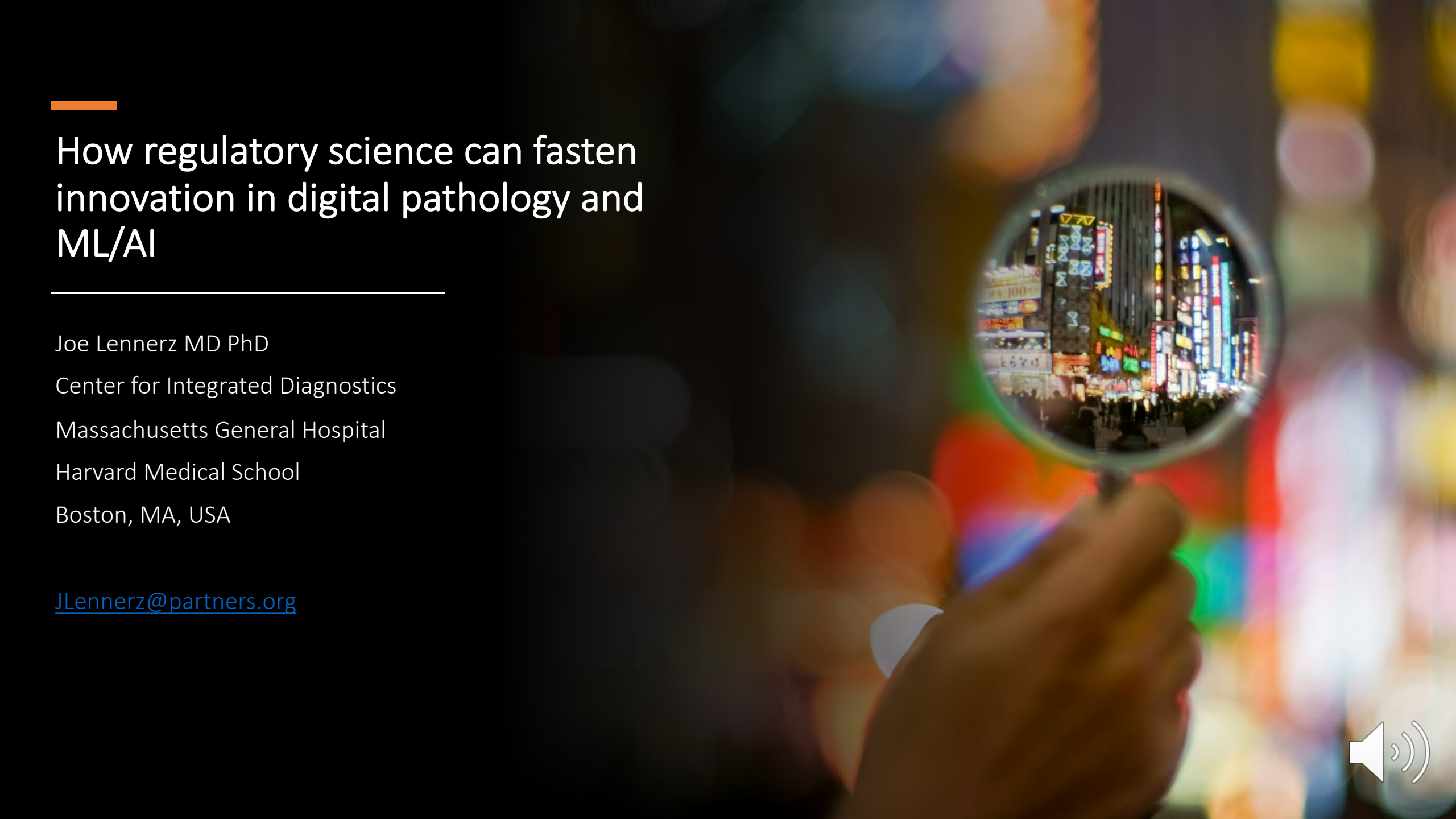


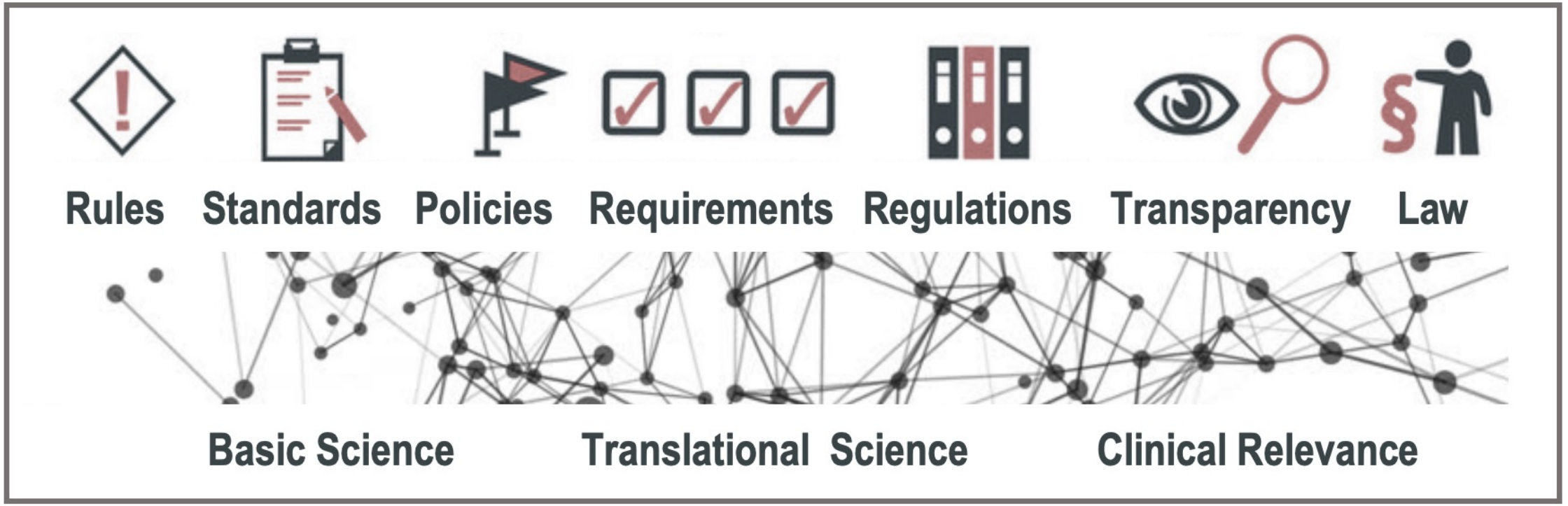
Promises of AI…

AI has the potential to unlock the full potential of digital pathology.

Research studies propose added value; however, clinical integration is lagging.

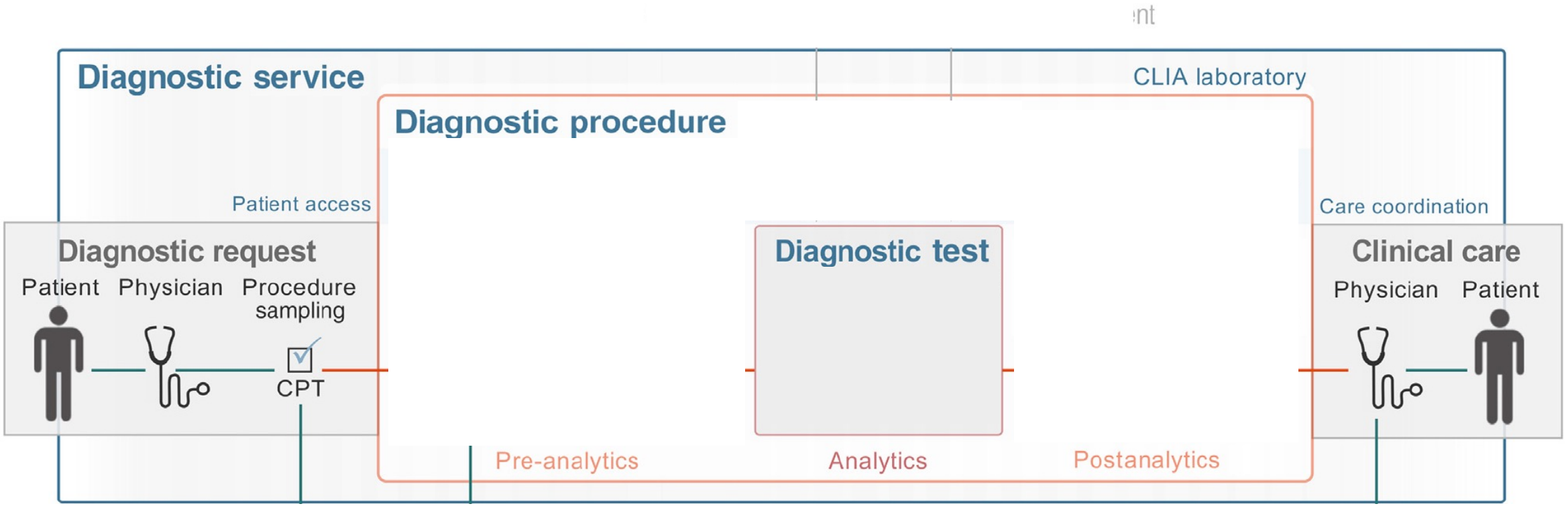
Faster innovation is contrasting with risks of bias, privacy issues, operational challenges, ethical responsibilities, and explainability.

...


Rules
Standards
Policies
Requirements
Regulations
Transparency
Law
Basic Science
Translational Science
Clinical Relevance

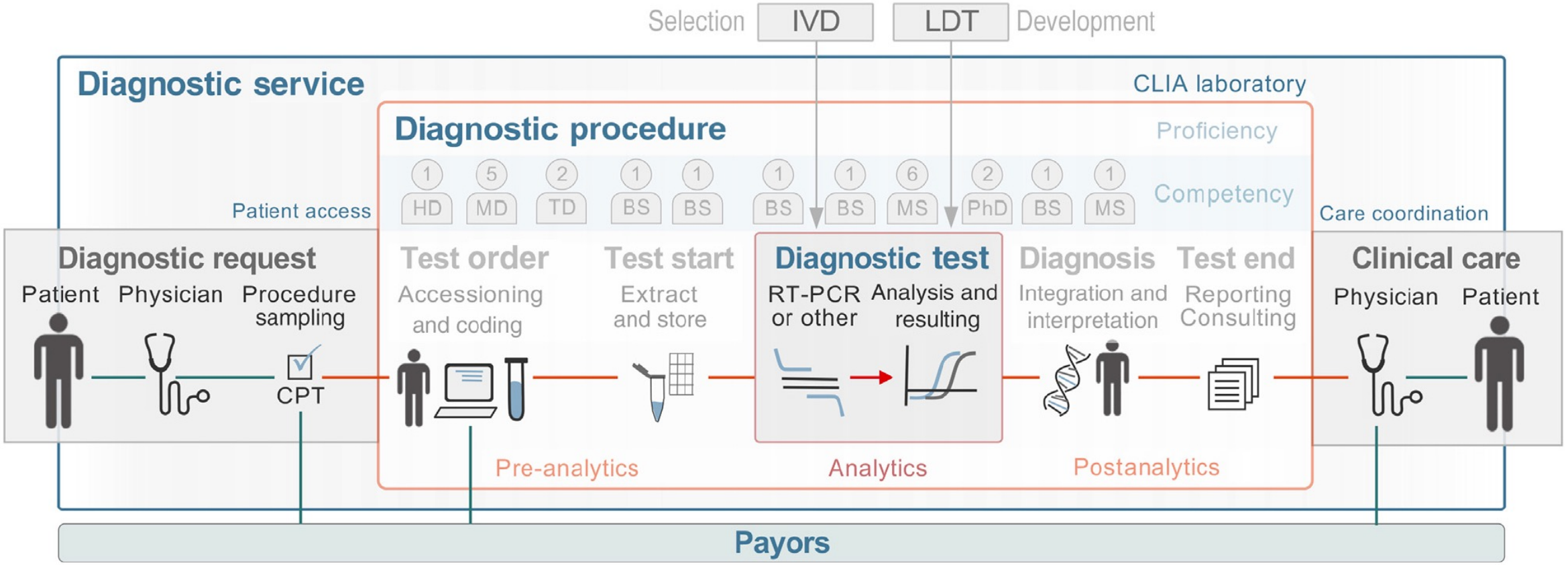
The Setting

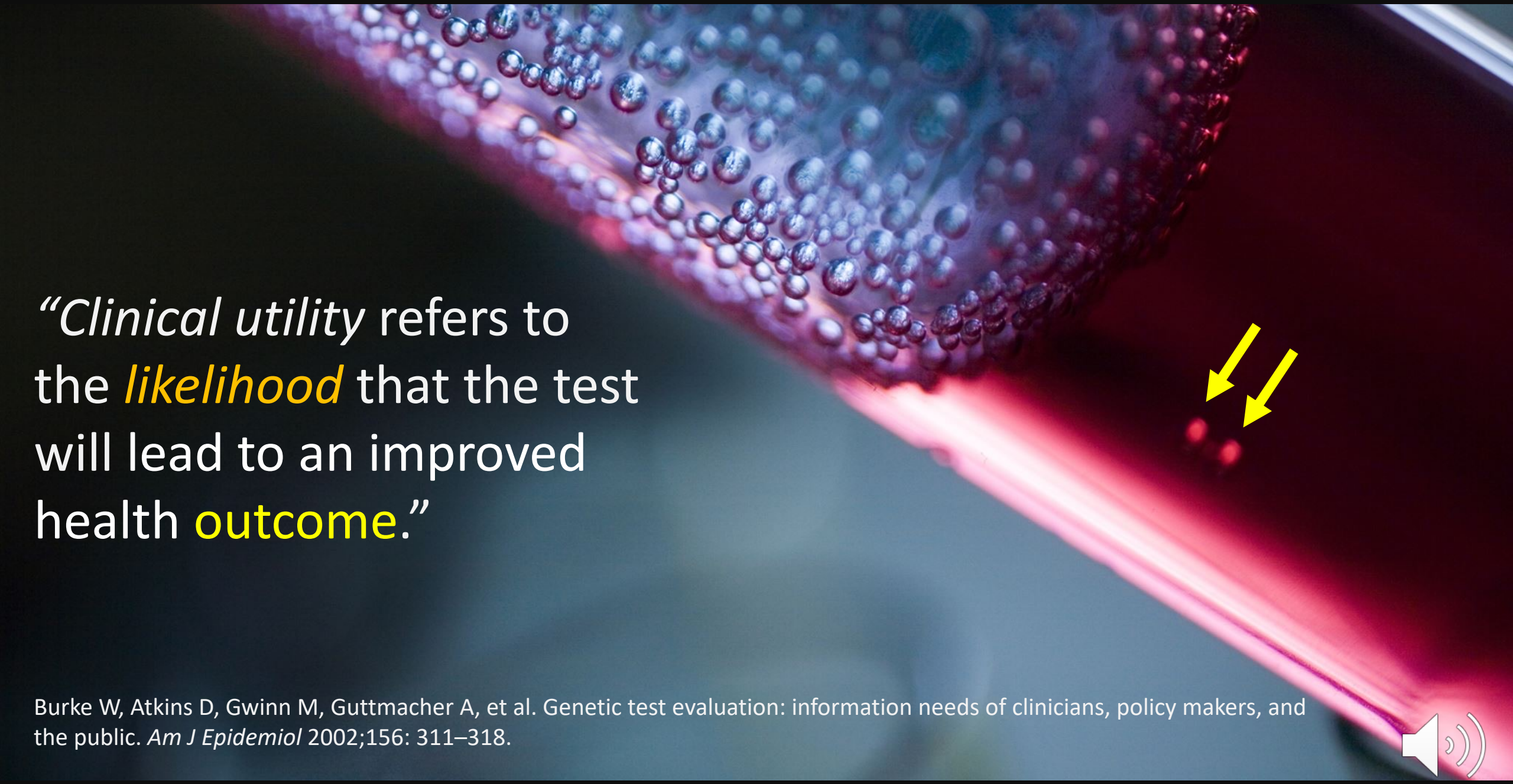
Context Laboratory Diagnostics



Marble et al., 2021 J Mol Diagnostics

Context Laboratory Diagnostics

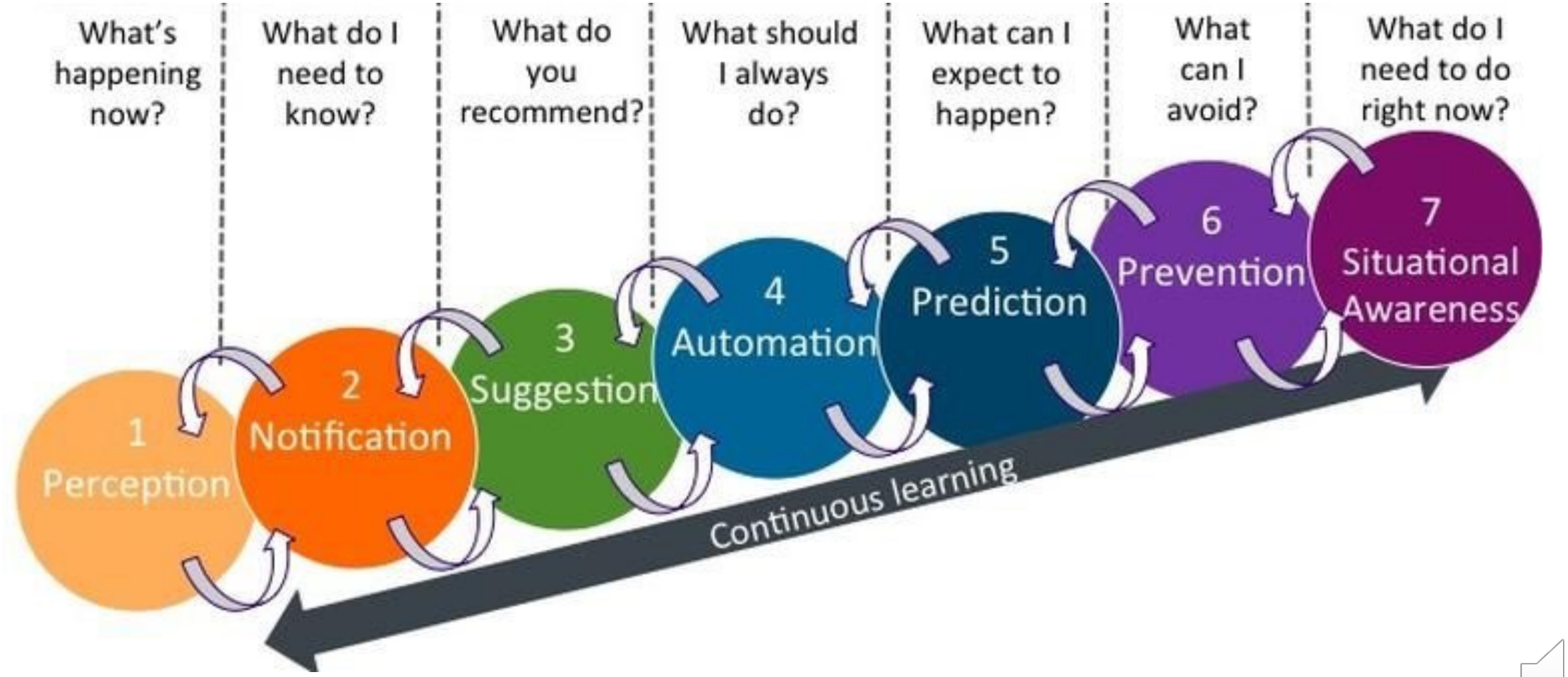




Burke W, Atkins D, Gwinn M, Guttmacher A, et al. Genetic test evaluation: information needs of clinicians, policy makers, and the public. *Am J Epidemiol* 2002;156: 311–318.

Synthesize

“Outcomes” of AI



MACHINE LEARNING IN LABORATORY MEDICINE

J. Lennerz

1 Applications

6 Data Model

RESULTS 5

Performance, test, transferability, **decision-support tool**

4 MODEL

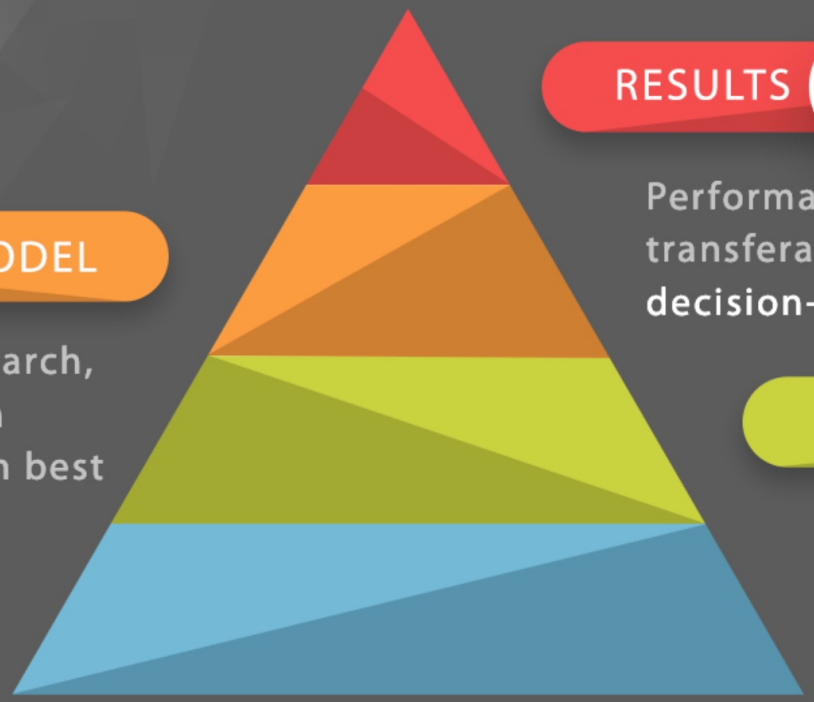
Classifier, grid search, data scaling, dim reduction, search best

DATA 3

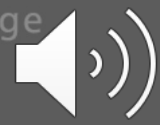
Source, combine, data types, label, missing, visualize, analyze, **cleansing/formatting**, encoding,

2 LIBRARIES

Python (scipy numpy matplotlib pandas sklearn etc...)



Define a problem. Framework:
What is the problem? I need to => TEP
Why does the problem need to be solved? Motivation – function vs. non-fct.
How would I solve the problem? map out idea, flush our domain knowledge



Major Challenges

Risk Awareness Model

Supposed AI function

Achieves function

Fails to achieve

Awareness

Yes

“Utility”
e.g., sensitivity

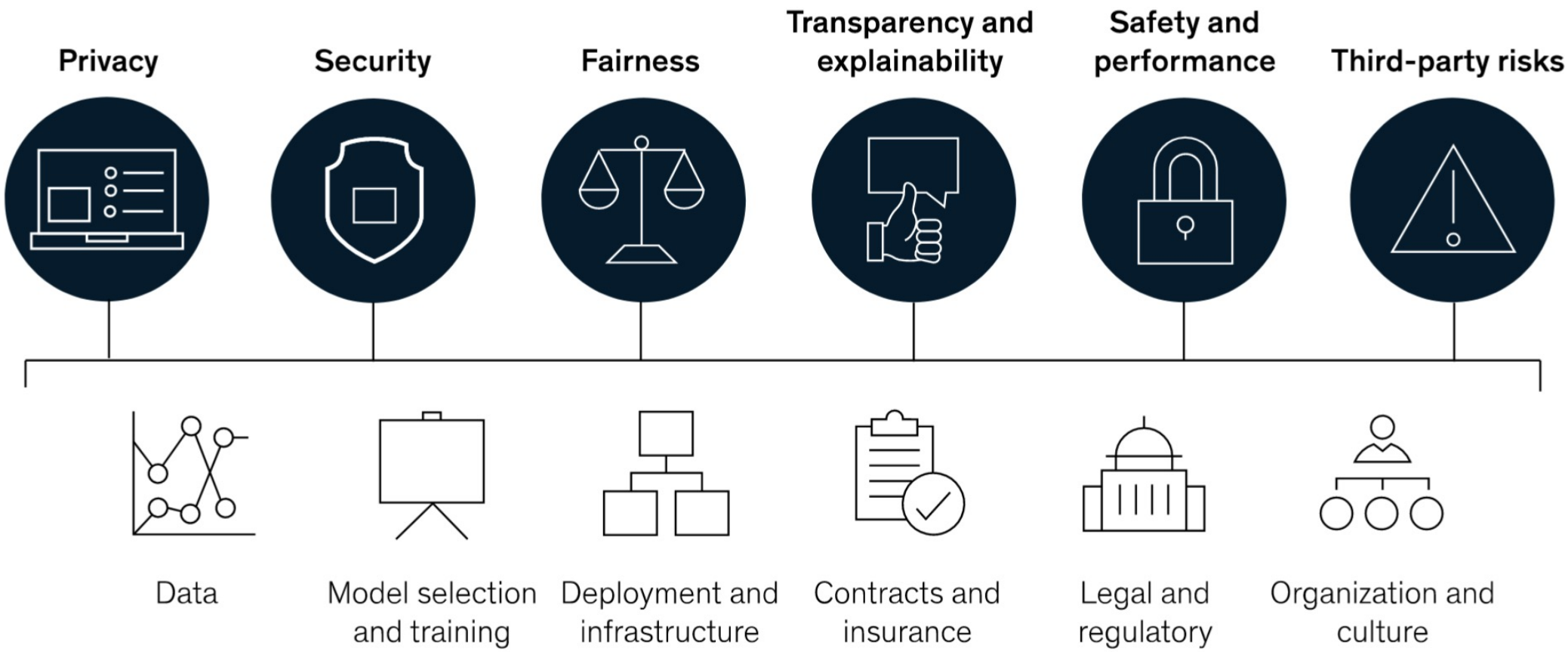
“Risk”
e.g., specificity

No

“missed opportunity”

“Seemingly Unexplainable errors”

A systematic approach to identifying AI risks examines each category of risk in each business context.



McKinsey & Company

Regulation

LAWS Establish requirements or prohibitions

Regulations Clarify how the law will be implemented

Instruments to further clarify laws and regulations

Guidances	***Policies***	***Standards***	***Procedures***
General recommendation, nonmandatory	*Specific in scope, mandatory*[a]	*Acceptable levels and controls*	*Detailed steps and components*

Huang et al., 2021 JCO OP

regulatory science Terminology

- “intended use” (what)
- “indication of use” (who and why),
- “context of use” (where)
- “instructions of use” (how)

- can help to communicate precisely

H. Indications for use:

1. Indications for use:

   Paige Prostate is a software only device intended to assist pathologists foci that are suspicious for cancer during the review of scanned whole s from prostate needle biopsies prepared from hematoxylin & eosin (H& fixed paraffin embedded (FFPE) tissue. After initial diagnostic review pathologist, if Paige Prostate detects tissue morphology suspicious for coordinates (X,Y) on a single location on the image with the highest lik cancer for further review by the pathologist.

   Paige Prostate is intended to be used with slide images digitized with P Scanner and visualized with Paige FullFocus WSI viewing software.

   Paige Prostate is an adjunctive computer-assisted methodology and its used as the primary diagnosis. Pathologists should only use Paige Prost with their complete standard of care evaluation of the slide image.

2. Special conditions for use statement(s):

   For prescription use only

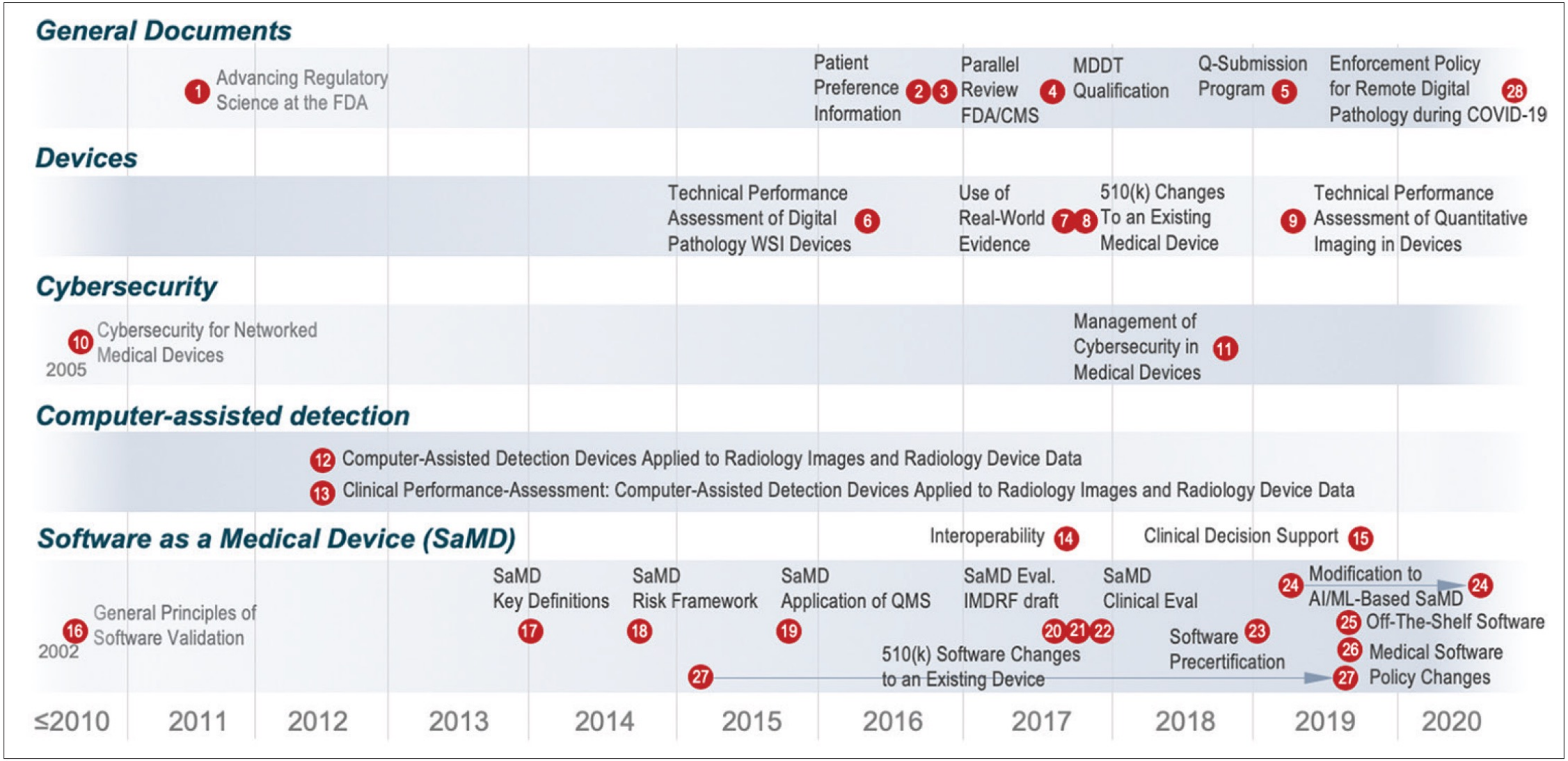


Figure 1: Overview of selected FDA guidance documents. Four of the authors (HM, RH, EA, and JKL) performed a meta-review of selected FDA guidance

Marble et al., 2020 J Pathol Informatics

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ICS › 35 › 35.020

ISO/IEC 23053

Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)

GENERAL INFORMATION

Status : Under development **Publication date :** 2022-05

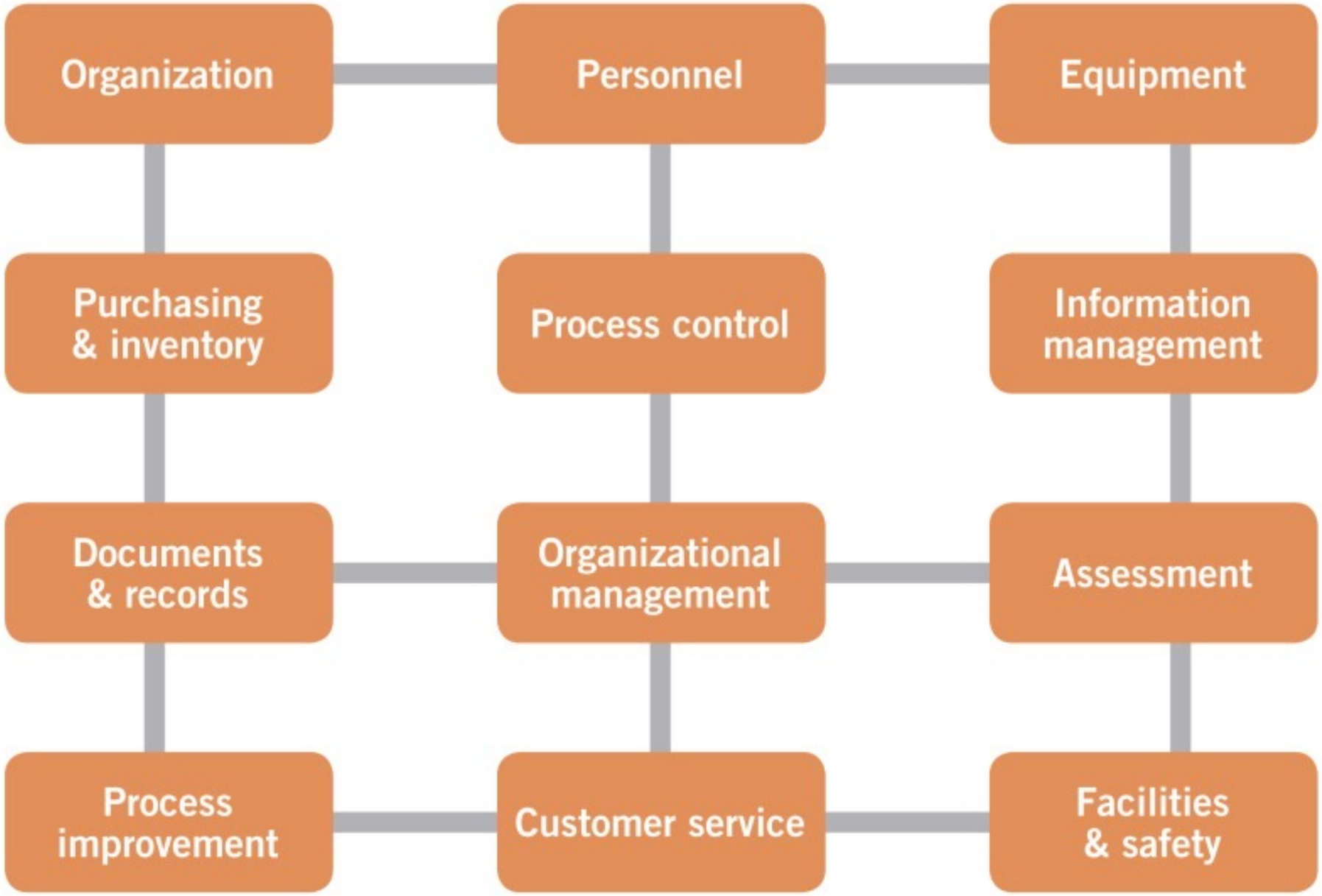
Edition : 1

Technical Committee : ISO/IEC JTC 1/SC 42 Artificial intelligence

ICS : 35.020 Information technology (IT) in general

WORKING GROUPS	
ISO/IEC JTC 1/SC 42/AG 3	AI standardization roadmapping
ISO/IEC JTC 1/SC 42/AHG 1	Dissemination and outreach
ISO/IEC JTC 1/SC 42/AHG 2	Liaison with SC 38
ISO/IEC JTC 1/SC 42/AHG 4	Liaison with SC 27
ISO/IEC JTC 1/SC 42/AHG 5	AI standardization landscape and roadmap
ISO/IEC JTC 1/SC 42/JWG 1	Joint Working Group ISO/IEC JTC1/SC 42 - ISO/IEC JTC1/SC 40: Governance implications of AI
ISO/IEC JTC 1/SC 42/JWG 2	Joint Working Group ISO/IEC JTC1/SC 42 - ISO/IEC JTC1/SC 7 : Testing of AI-based systems
ISO/IEC JTC 1/SC 42/WG 1	Foundational standards
ISO/IEC JTC 1/SC 42/WG 2	Data
ISO/IEC JTC 1/SC 42/WG 3	Trustworthiness
ISO/IEC JTC 1/SC 42/WG 4	Use cases and applications
ISO/IEC JTC 1/SC 42/WG 5	Computational approaches and computational characteristics of AI systems

STANDARD AN?POR PROJECT	
ISO/IEC DTS 4213.2	Information technology — Artificial Intelligence — Assessment of machine learning classification perfo
ISO/IEC AWI 5259-1	Artificial intelligence — Data quality for analytics and machine learning (ML) — Part 1: Overview, term
ISO/IEC AWI 5259-2	Artificial intelligence — Data quality for analytics and machine learning (ML) — Part 2: Data quality me
ISO/IEC AWI 5259-3	Artificial intelligence — Data quality for analytics and machine learning (ML) — Part 3: Data quality ma
ISO/IEC AWI 5259-4	Artificial intelligence — Data quality for analytics and machine learning (ML) — Part 4: Data quality pro
ISO/IEC AWI 5259-5	Artificial intelligence — Data quality for analytics and machine learning (ML) — Part 5: Data quality go
ISO/IEC CD 5338	Information technology — Artificial intelligence — AI system life cycle processes
ISO/IEC AWI 5339	Information Technology — Artificial Intelligence — Guidelines for AI applications
ISO/IEC AWI 5392	Information technology — Artificial intelligence — Reference architecture of knowledge engineering
ISO/IEC AWI TR 5469	Artificial intelligence — Functional safety and AI systems
ISO/IEC AWI TS 5471	Artificial intelligence — Quality evaluation guidelines for AI systems
ISO/IEC AWI TS 6254	Information technology — Artificial intelligence — Objectives and approaches for explainability of ML m
ISO/IEC CD 8183	Information technology — Artificial intelligence — Data life cycle framework
ISO/IEC AWI TS 8200	Information technology — Artificial intelligence — Controllability of automated artificial intelligence sys
ISO/IEC AWI TS 12791	Information technology — Artificial intelligence — Treatment of unwanted bias in classification and reg
ISO/IEC AWI 12792	Information technology — Artificial intelligence — Transparency taxonomy of AI systems
ISO/IEC FDIS 22989	Information technology — Artificial intelligence — Artificial intelligence concepts and terminology
ISO/IEC FDIS 23053	Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)
ISO/IEC DIS 23894	Information technology — Artificial intelligence — Risk management
ISO/IEC CD 24029-2	Artificial intelligence (AI) — Assessment of the robustness of neural networks — Part 2: Methodology
ISO/IEC AWI TR 24030	Information technology — Artificial intelligence (AI) — Use cases
ISO/IEC DTR 24368	Information technology — Artificial intelligence — Overview of ethical and societal concerns
ISO/IEC DIS 24668	Information technology — Artificial intelligence — Process management framework for big data analyt
ISO/IEC CD 25059	Software engineering — Systems and software Quality Requirements and Evaluation (SQuaRE) — Qu
ISO/IEC AWI TS 29119-11	Information technology — Artificial intelligence — Testing for AI systems — Part 1
ISO/IEC FDIS 38507	Information technology — Governance of IT — Governance implications of the [illegible] intellige
ISO/IEC CD 42001	Information Technology — Artificial intelligence — Management system


Organization
Personnel
Equipment
Purchasing & inventory
Process control
Information management
Documents & records
Organizational management
Assessment
Process improvement
Customer service
Facilities & safety

- Access control
- Two-factor authentication
- Encryption

- Network/application firewalls
- Two-factor authentication
- Intrusion detection

- Encryption
- Access controls
- Network/application firewalls

- Performance monitoring
- Disaster recovery
- Security incident handling

- Quality assurance
- Processing monitoring

Regulation
is made

Regulatory science is the scientific discipline that evaluates and challenges current regulation, benefit vs. risk assessments, and submission/approval strategies.

It is the application of the scientific method to enable evidence-based improvements of regulation…

By developing new tools, standards and approaches…
we can affect and improve safety and efficacy assessments

FDA

Search Menu

IN THIS SECTION: CDRH Strategic Priorities And Updates

← CDRH Strategic Priorities and Updates

Collaborative Communities: Addressing Health Care Challenges Together

Collaborative Communities with CDRH Participation

The FDA currently participates as a member of these collaborative communities, which have been established and are managed and controlled by external stakeholders.

- Collaborative Community on Ophthalmic Imaging
- National Evaluation System for health Technology Coordinating Center (NESTcc) Collaborative Community
- Standardizing Laboratory Practices in Pharmacogenomics Initiative (STRIPE) Collaborative Community
- International Liquid Biopsy Standardization Alliance (ILSA)
- Xavier Artificial Intelligence (AI) World Consortium
- Case for Quality Collaborative Community
- Heart Valve Collaboratory (HVC)
- Wound Care Collaborative Community
- Pathology Innovation Collaborative Community (PICC)
- RESCUE (REducing SuiCide Rates Amongst IndividUals with DiabEtes) Collaborative Community)

https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together

Pathology Innovation Collaborative Community

PIcc

The Alliance for Digital Pathology

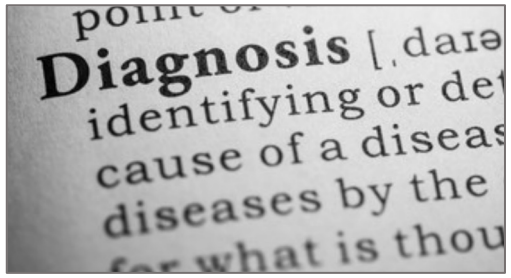
www.pathologyinnovationcc.org

Pathology Innovation Collaborative Community PIcc

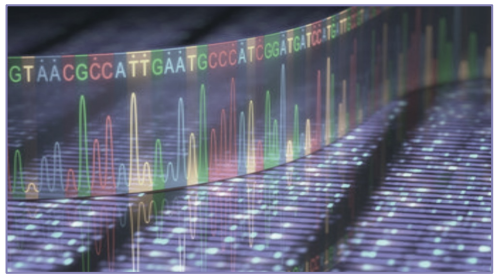
- Regulatory science initiative
- Facilitate Innovation
- Advance safety and effectiveness evaluations
- Harmonize approaches to speed delivery to patients
- Collaboration in the **pre-competitive space**
- Open to all stakeholders

What's next in Laboratory Medicine

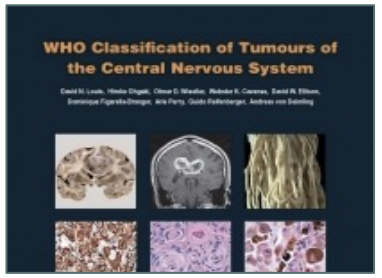
Diagnosis



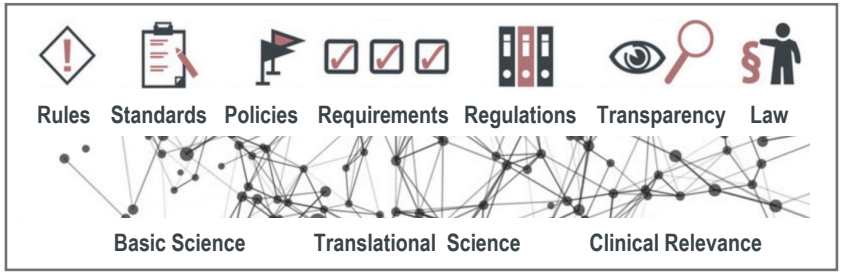
Technologies



Data Science



Regulatory Sciences



J. Lennerz 2022

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	Boston, Belgium, NY, Ulm, Heidelberg, Hamburg, London, Korea, and Japan

Funding: NIH Grant No. R01 CA225655 (Naxerova/Lennerz)

Partners Innovation Discovery Grant

Thank you

What's next?

Center for Integrated Diagnostics

Interested?

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