Omics and AI from trial to practice

Actions: AI and omics current applications: practice impact and next steps

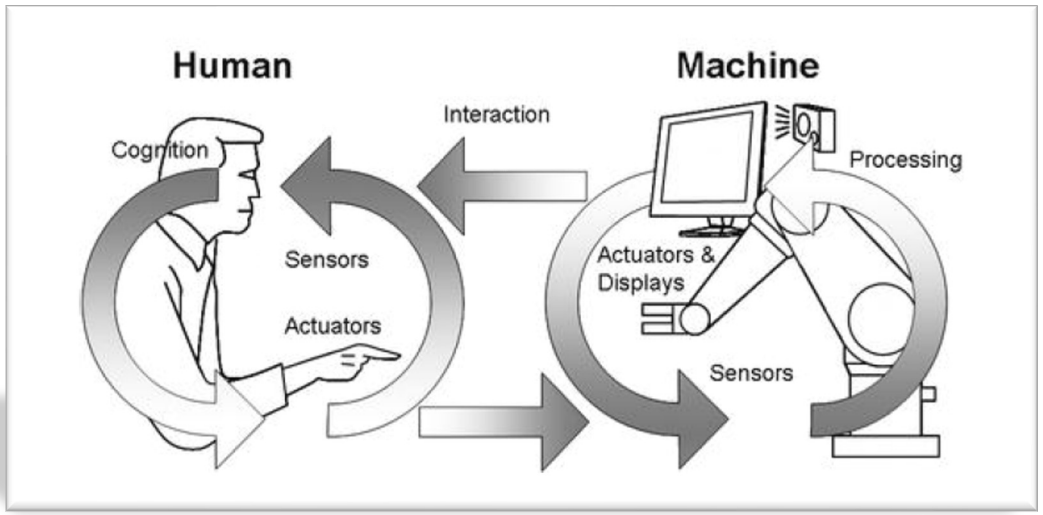
Prof. dr. Karin Haustermans
UZ Leuven, Belgium

Introduction

Modern radiation oncology

- Has become increasingly complex owing to technological advances

Near-complete reliance on human-machine interactions



Growing complexity of these human-machine interactions

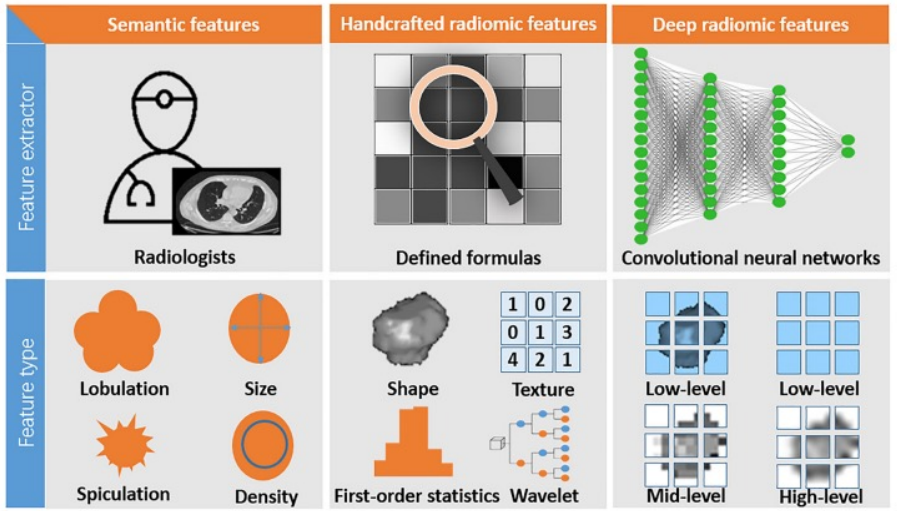


Fig. 2 A comparison of semantic, handcrafted radiomic, and deep radiomic features

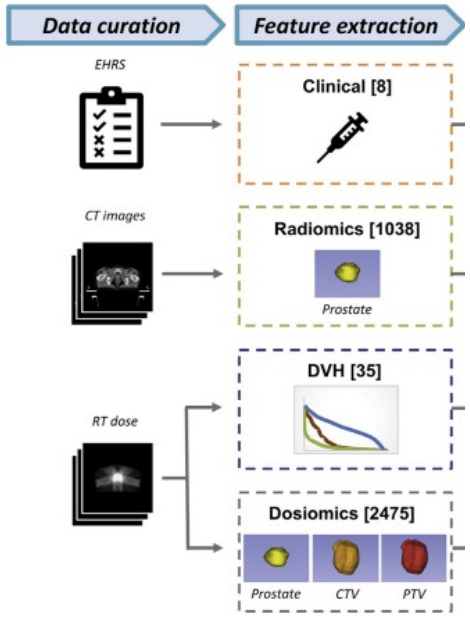
Huynh E et al Nat Rev Clin Oncol 2020
Razzaq M et al IJACSA 2017
Wu G et al Eur J Nucl Med Mol Imaging 2021

Modern radiation oncology

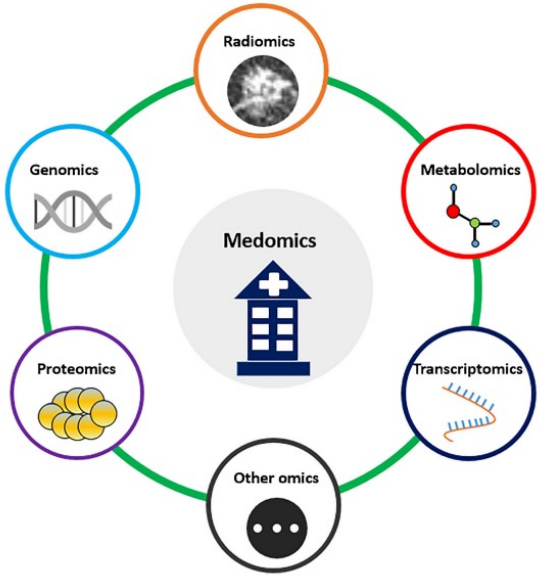
- Has become increasingly complex owing to multi-omics research

Molecular and non-molecular omics studies

FIGURE 1 | The complexity of multi-omics: merger of omics-driven biology, data science, informatics, statistics, and computational sciences.

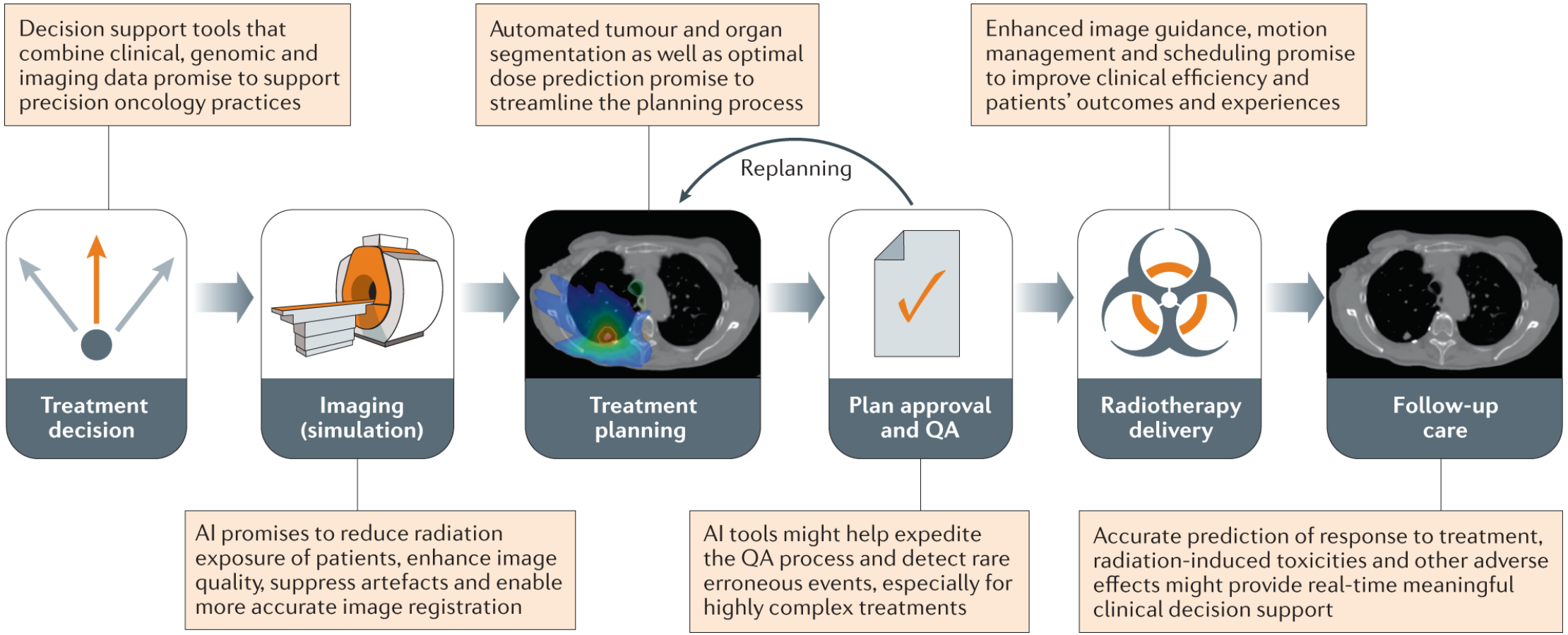


Rapid development of multi-discipline or multi-omics to form “Medomics”



Krassowski M et al Frontiers in Genetics 2020
Murakami Y et al Int J Radiat Oncol Biol Phys 2021
Wu G et al Eur J Nucl Med Mol Imaging 2021

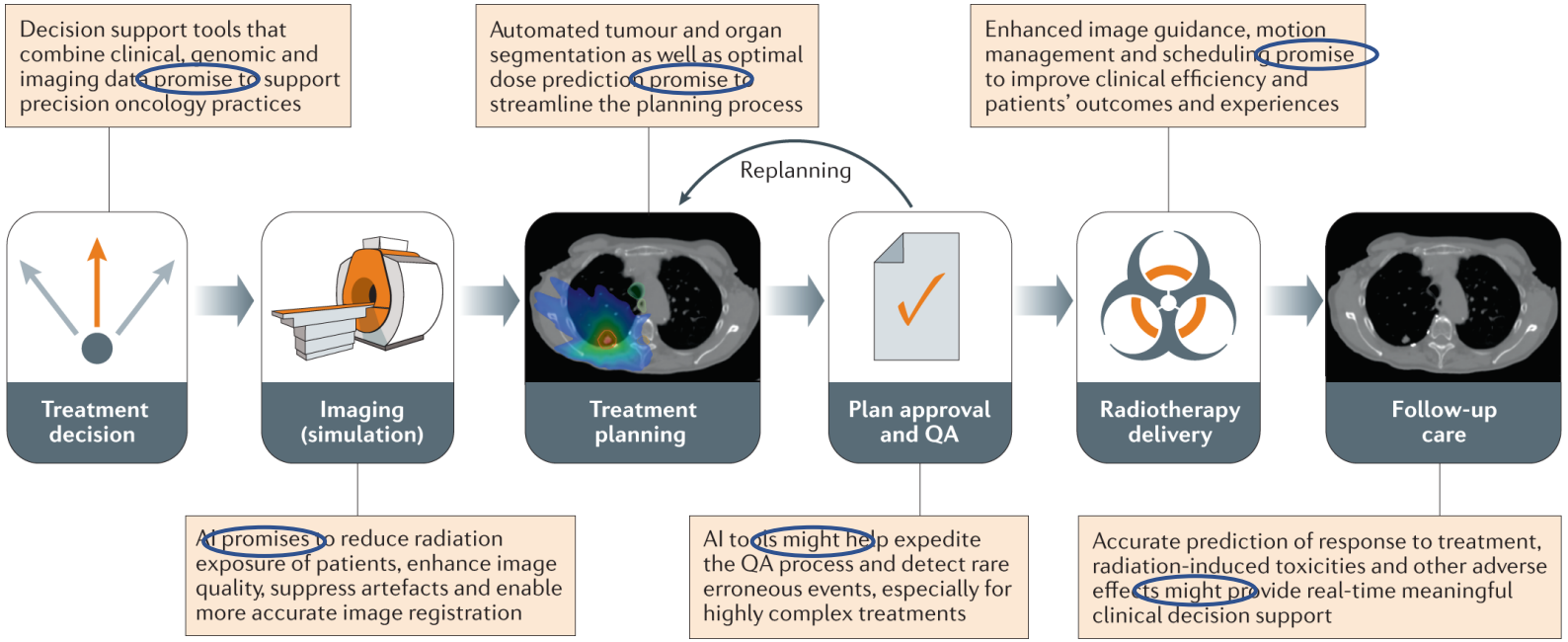
Applications of omics/AI in RT workflow



Huynh E et al Nat Rev Clin Oncol 2020

Omics and AI: from trial to clinic

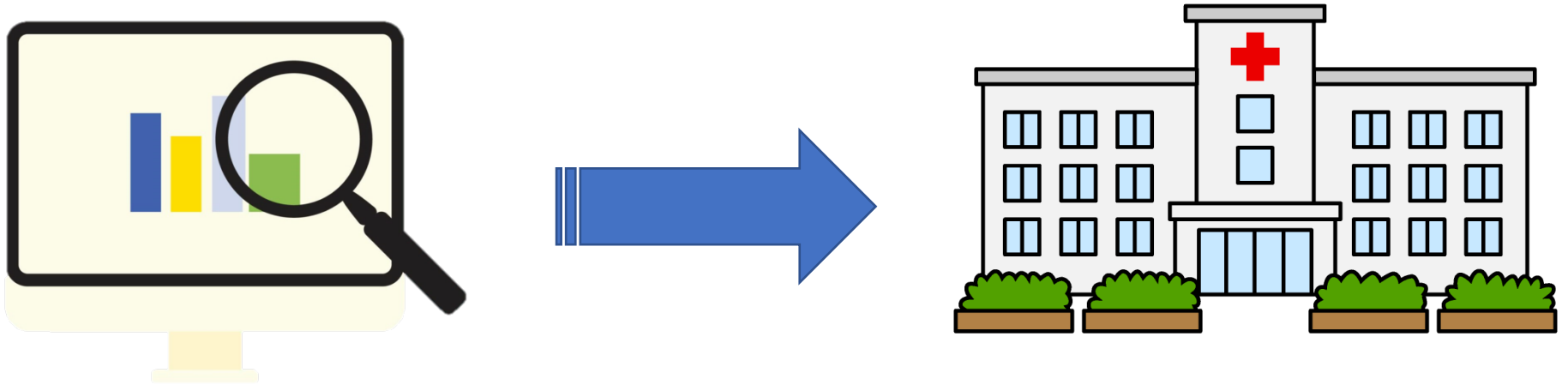
- Still some way to go….



Huynh E et al Nat Rev Clin Oncol 2020

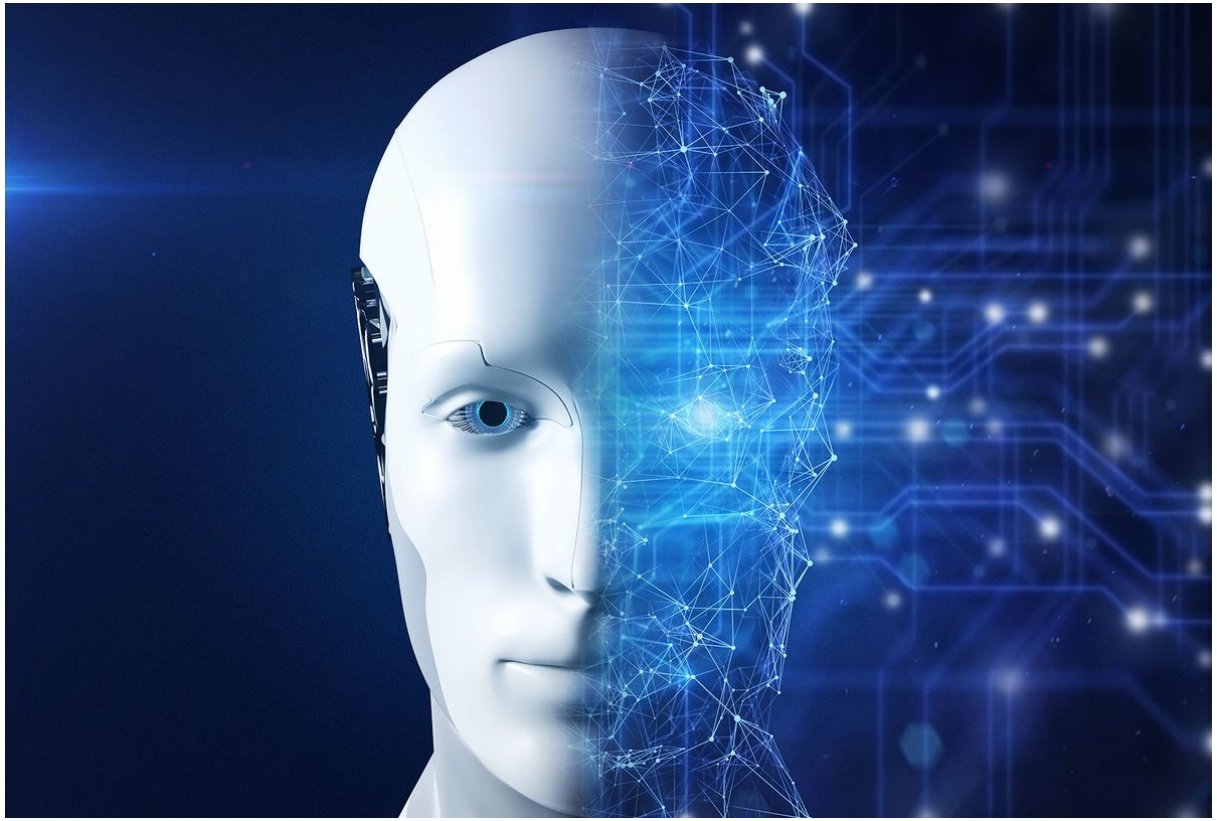
Omics and AI: from trial to practice

- How big is the gap we still need to bridge?



AI

From trial to practice



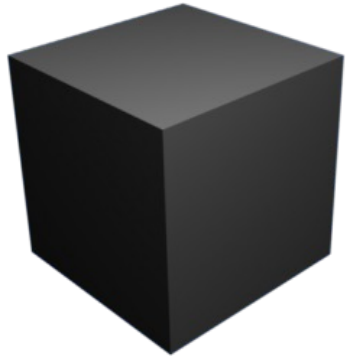
Challenges to clinical implementation of AI tools

- Availability of high-quality datasets for algorithm training and validation
- Lack of consistent standards in generation of these data hinders data sharing and aggregation accross institutions
- Collection of robust outcome & toxicity data continues to be a challenge
- Limited knowledge of optimization algorithms (due to proprietary nature TPS)
- External validation of AI tools to show generalizability and effectiveness

Huynh E et al Nat Rev Clin Oncol 2020

Challenges to clinical implementation of AI tools

- Key barrier to realizing the full potential of AI in radiation oncology is clinical adoption
- Will require
  - Upfront investment of time and resources
  - Efforts to understand the utility and limitations of clinical AI tools
- Establishing trust in AI systems
  - Interpretability and explainability of AI
  - Continuous assessment of training data
  - Actively monitoring AI performance



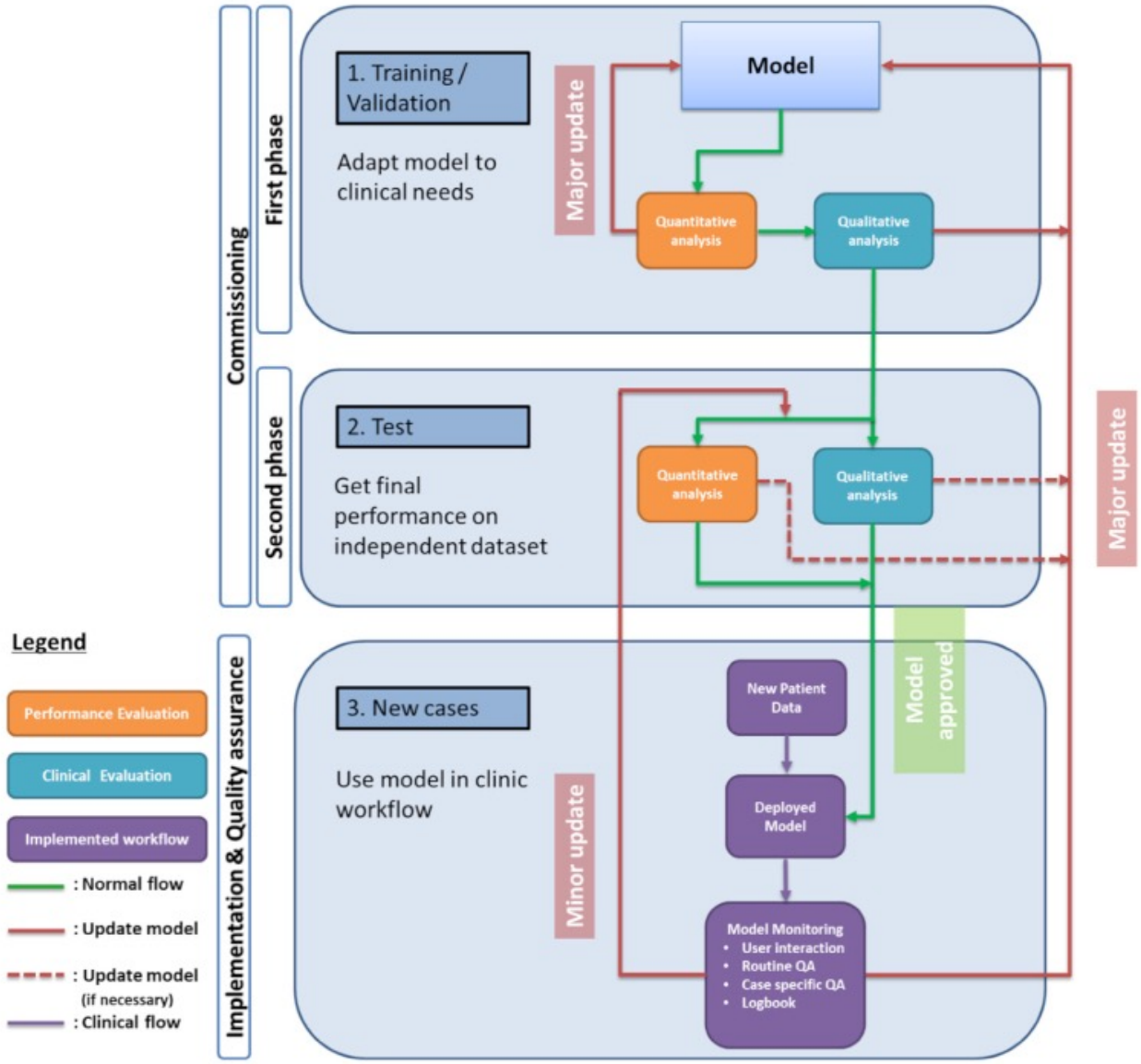
Huynh E et al Nat Rev Clin Oncol 2020

Criteria to evaluate clinical implementation potential of AI tools

- Time available for and the ability of the user to judge the accuracy of the result
- Whether erroneous results can be corrected
- Consequence of errors for a patient

Huynh E et al Nat Rev Clin Oncol 2020

Workflow for the commissioning, implementation and QA of a new AI model in the clinic



Vandewinckele L et al Radiother Oncol 2020

The EU MDR: implications for AI-based medical device software in medical physics

- EU medical device regulation (MDR)
  - Applies to processing software that is intended to provide information for one or more of the following purposes, such as diagnosis, prevention, monitoring, treatment or alleviation of a disease.
  - Also applies to software that merely provides information intended to inform a medical professional in making the final diagnostic or therapeutic decision

→ AI-tool = medical device software

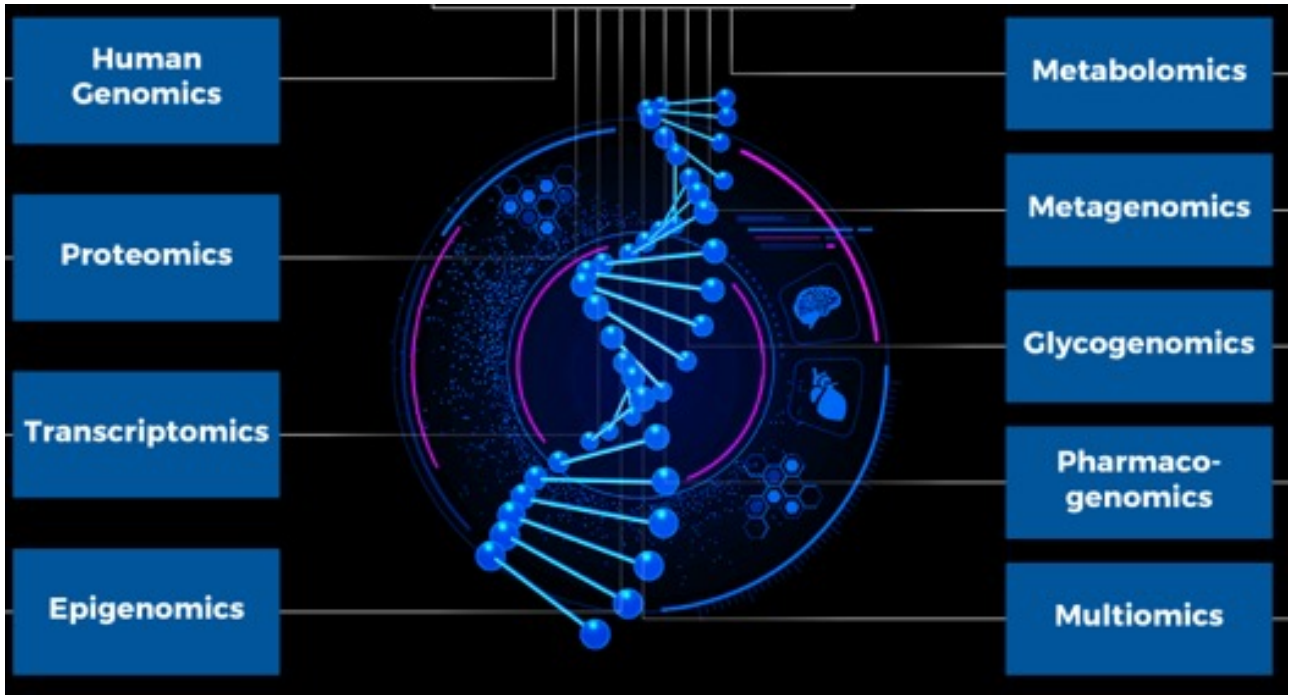
Table 1
Overview of relevant EU legislation applicable to medical device software.

Medical Devices	
Directive 93/42/EEC	Directive on Medical Devices (MDD). It will be repealed by the Medical Device Regulation (MDR).
Regulation (EU) 2017/745	MDR: it will be fully applicable from 26 May 2021.
Regulation (EU) 207/2012	Regulation on electronic instructions for use of medical devices.
MEDDEV 2.7/1 (rev. 4)	Guidance on the clinical evaluation of medical devices. Although this guidance is developed under the MDD and not legally binding, it offers detailed assistance and formulates strict requirements for clinical evaluation, matching these of the MDR.
MDCG 2019-11	Guidance on qualification and classification of Medical Device Software (MDSW). Not legally binding.
MDCG 2019-16	Guidance on cybersecurity for medical devices.
MDCG 2020-1	Guidance on clinical evaluation of MDSW. Intended to supplement MEDDEV 2.7/1 (rev. 4) for clinical evaluation of MDSW falling under EU MDR.
Data protection	
Regulation (EU) 2016/679	The General Data Protection Regulation (GDPR) on the protection of natural persons regarding the processing of personal data and on the free movement of such data. The regulation applies since 25 May 2018, repealing the previous Directive (95/46/EC).

Beckers R et al Physica Medica 2021

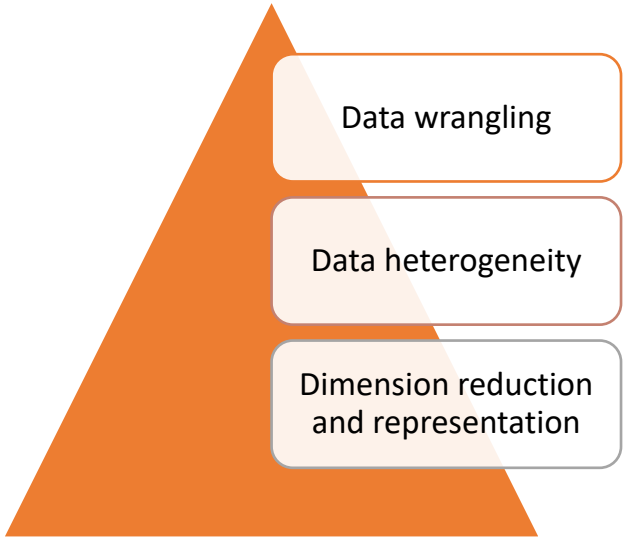
Omics

From trial to practice



Why is multi-omics challenging?

- Inherits challenges from single omics datasets
- Challenges for integration/fusion, clustering, visualization, and functional characterization
- Data harmonization
- Computational burden and storage space requirements



Krassowski M et al Frontiers in Genetics 2020

Challenges for clinical implementation of omics

- Key challenges in omics-scale benchmarking of computational tools
  - Acquisition of ‘gold standard’ datasets
  - Incorporating new methods for establishing benchmarks as they are published
  - Ensuring reproducibility in the context of increasing complexity of the software involved

Krassowski M et al Frontiers in Genetics 2020

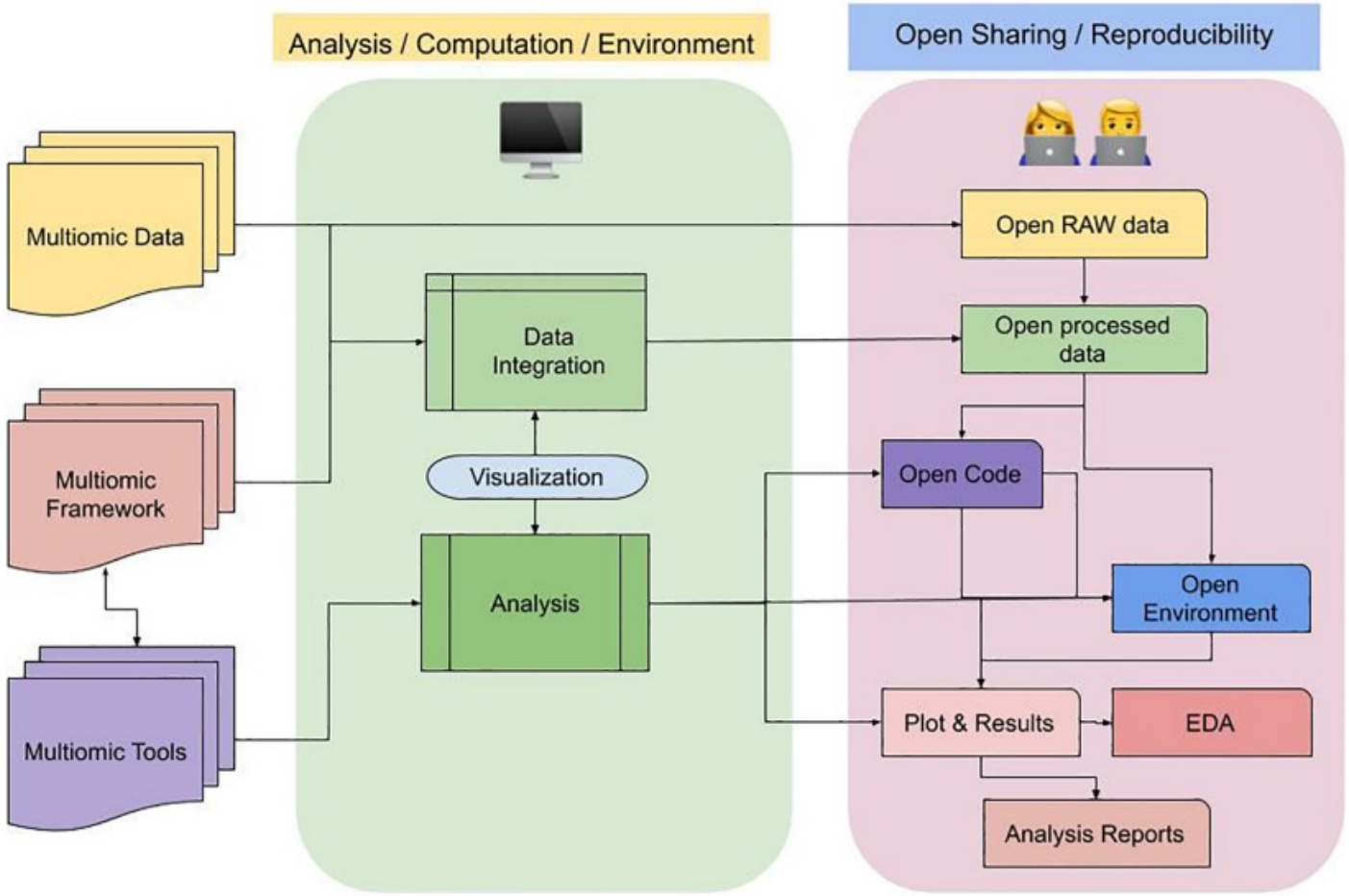
*FAIR*ification of multi-omics efforts

Findability, Accessibility, Interoperability, Reusability standards

Data sharing

Workflow & environment sharing

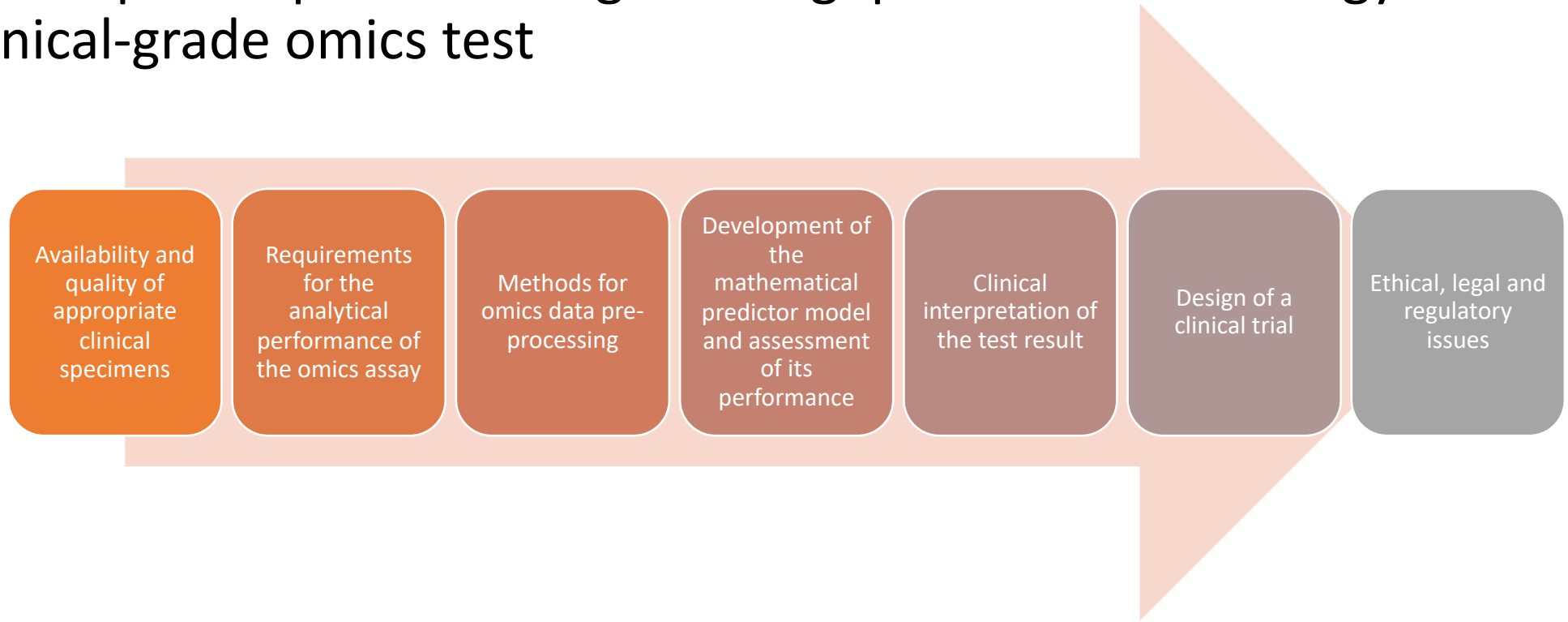
Code sharing



Krassowski M et al Frontiers in Genetics 2020

Criteria for the use of omics-based predictors in clinical trials

- Development path from high-throughput omics technology to a clinical-grade omics test



McShane L et al BMC Medicine 2013

Regulatory and Ethical, legal and social implications (ELSI) issues related to multi-omics

- Multi-omics allow researchers to make more inferences on individuals
- Labs/clinics that do translational research are often under regulatory compliances that restrict data upload to any server for analysis when patient information is involved

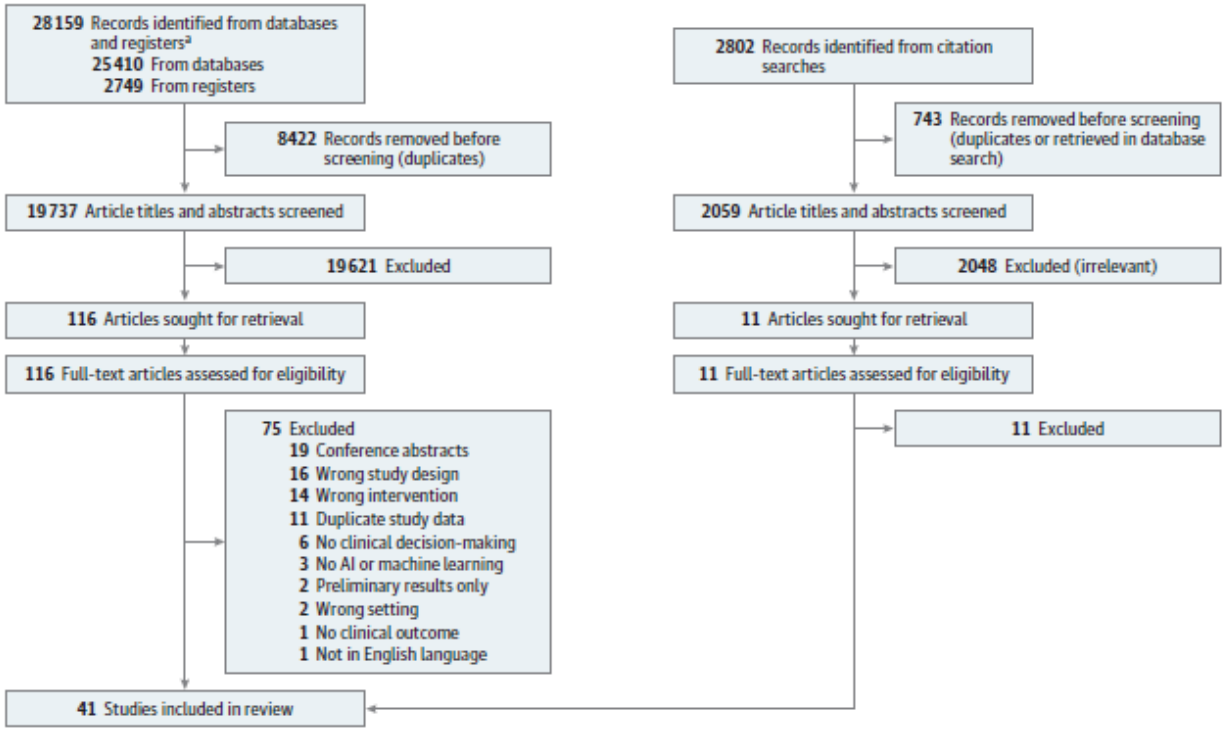
Krassowski M et al Frontiers in Genetics 2020

From trial to practice

AI and omics

Randomized clinical trials on ML interventions in health care

Figure 1. Screening and Selection of Randomized Clinical Trials



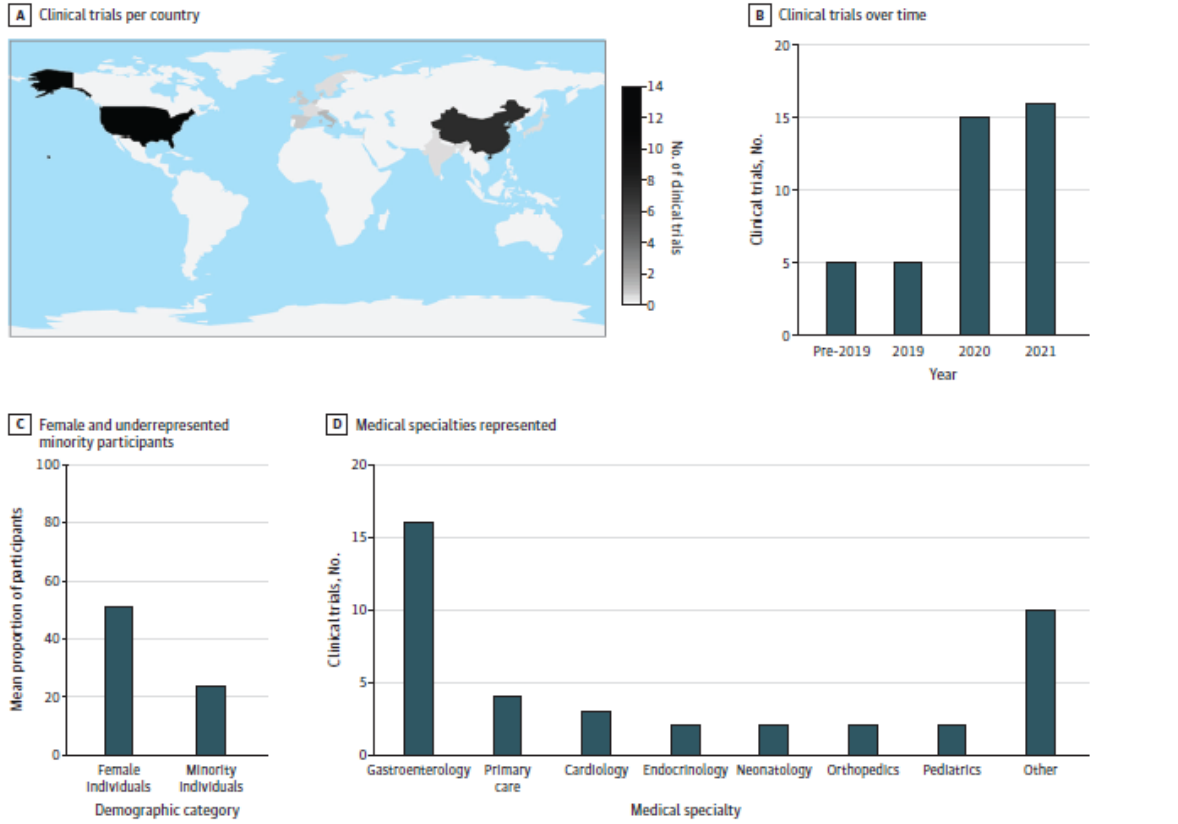
AI indicates artificial intelligence.

[a] Databases and registers included Cochrane Library, Google Scholar, Ovid Embase, Ovid MEDLINE, PubMed, Scopus, and Web of Science Core Collection.

Plana D et al JAMA Network Open 2022

Randomized clinical trials on ML interventions in health care

Figure 2. Characteristics of Randomized Clinical Trials



Plana D et al JAMA Network Open 2022

Randomized clinical trials on ML interventions in health care

Figure 3. Adherence to Consolidated Standards of Reporting Trials–Artificial Intelligence (CONSORT-AI) Extension Guideline

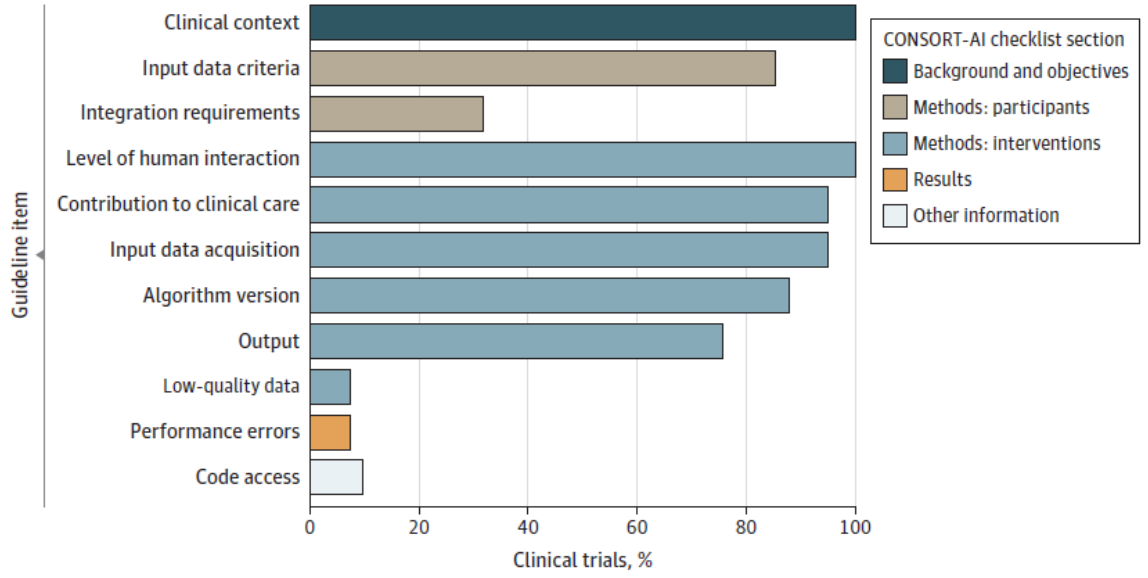
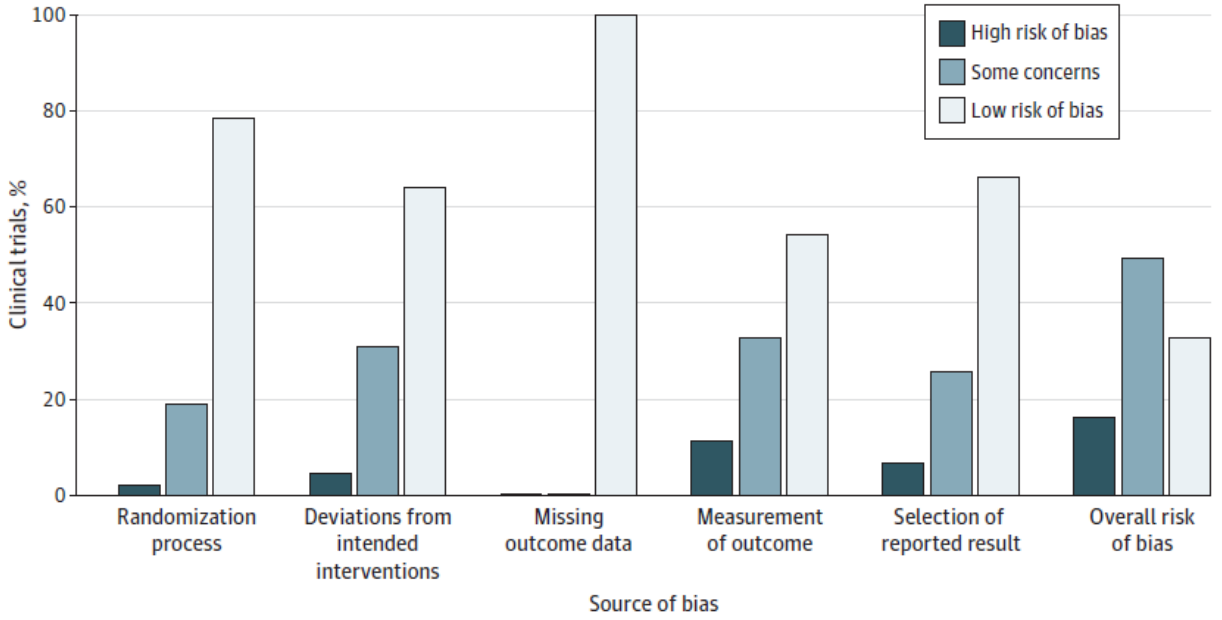


Figure 4. Risk of Bias in Randomized Clinical Trials



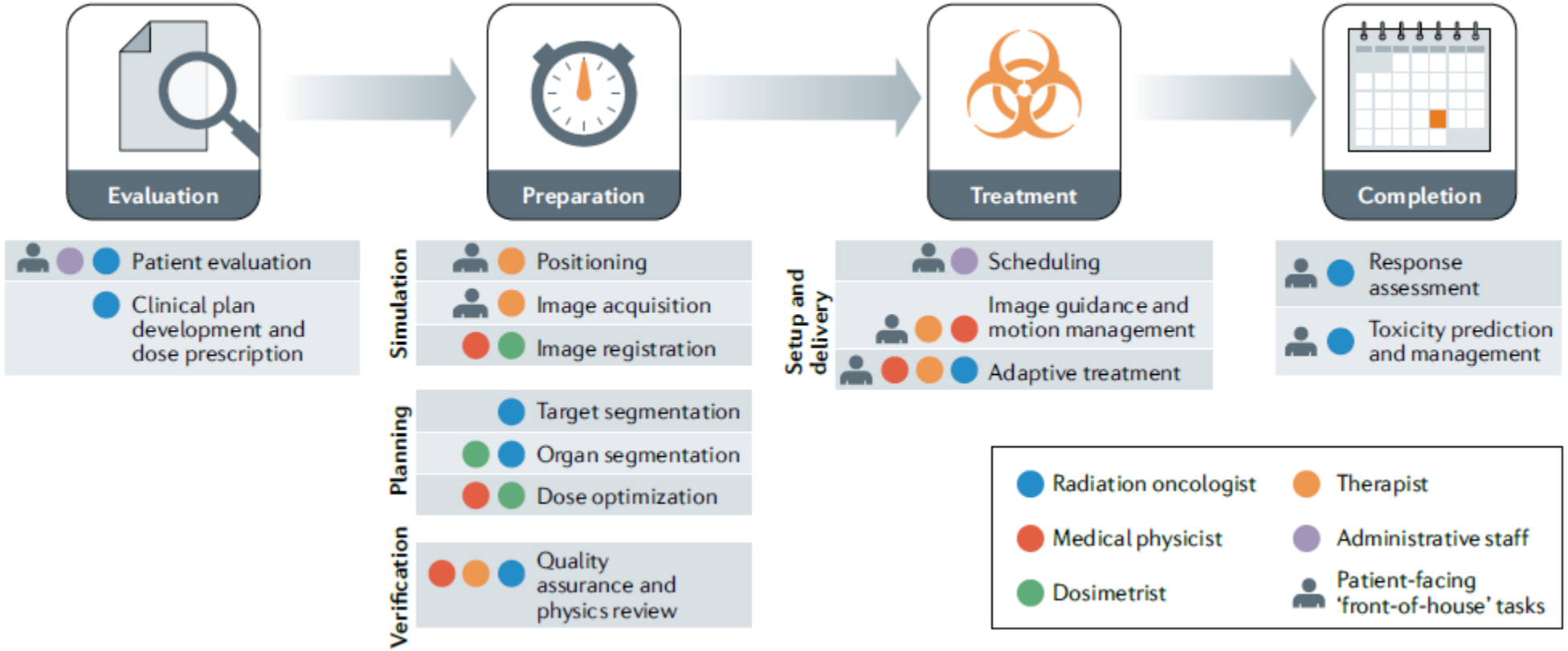
Plana D et al JAMA Network Open 2022

Time to reality check the promises of machine-learning powered precision medicine

- *"There is no question that the appearance of big data and machine learning offer an exciting chance for revolution, but revolutions demand greater scrutiny, not less. This scrutiny should involve a reality check on the promises of machine learning-powered precision medicine and an enhanced focus on the core principles of good data science—trained experts in study design, data system design, and causal inference asking clear and important questions using high-quality data."*

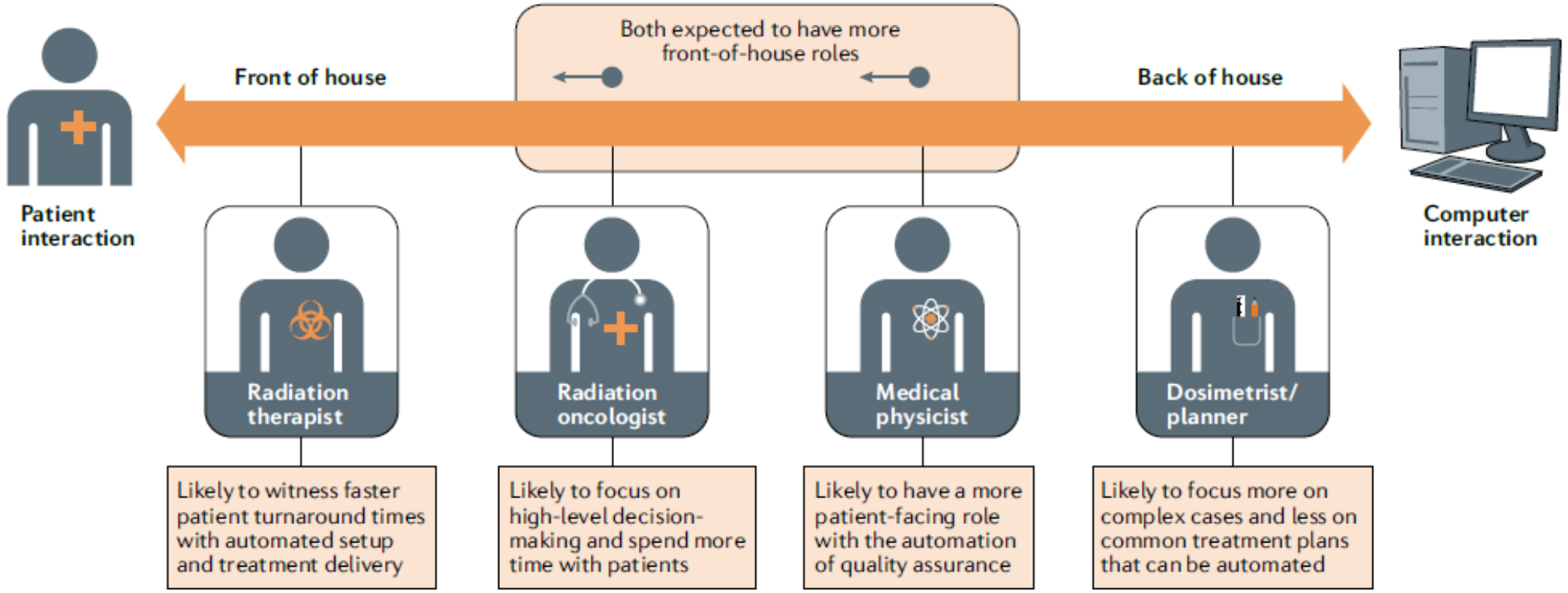
Wilkinson J et al The Lancet 2020

The radiation therapy workflow



Huynh E et al Nat Rev Clin Oncol 2020

Potential implications of applying AI for members of the radiotherapy workforce



Huynh E et al Nat Rev Clin Oncol 2020

Need for appropriate training

iGrad.com

Current training models

- Focus on memorizing clinical facts and lengthy apprenticeships to gain expertise in manual segmentation and evaluating treatment plans

Future training programmes

- Increased focus on instilling a deeper understanding of how to integrate and interpret information from large datasets in order to support clinical decision-making

Huynh E et al Nat Rev Clin Oncol 2020

Omics and AI: from trial to clinic and back

- Continuous interaction and improvements to allow better implementation