

Opportunities to Leverage Electronic Health Records in Clinical Evidence Generation

Incorporating Integrated Diagnostics
into Precision Oncology Care: A Workshop
National Cancer Policy Forum

Neal J. Meropol, MD
Vice President, Research Oncology
Flatiron Health
March 6, 2023

Disclosures

Employment by Flatiron Health, Inc., an independent subsidiary of the Roche Group

Equity interest in Roche

The Problem for Diagnostics

- **Research:** Diagnostic modalities historically lack investment to ensure optimal evidence generation
- **Complexity:** Advances in technology are driving a wealth of new diagnostic tools
- **Decision making:** These tools often enter the clinic with incomplete guidance for their use
 - Clinicians may not know what to order
 - Clinicians may not know how to interpret results

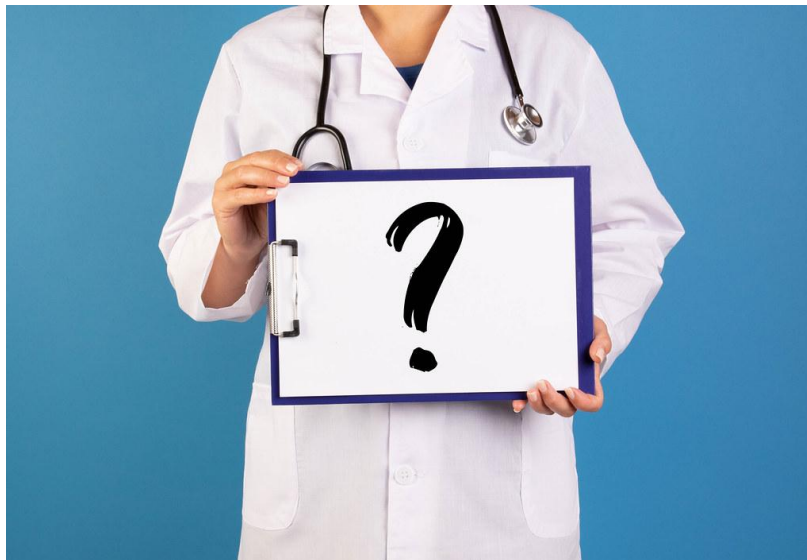
For every patient...

Screening

Who should I screen?
How should I screen
them?

Diagnosis

What is the best test?



Treatment

What biomarker can
guide therapy?

Follow Up

What is the best
surveillance strategy?

Test Performance

Sensitivity/Specificity/PPV/NPV

Cost

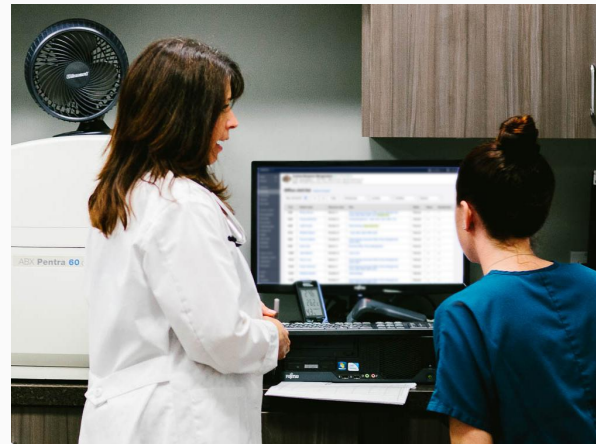
Convenience

Interpretability

Then



Now



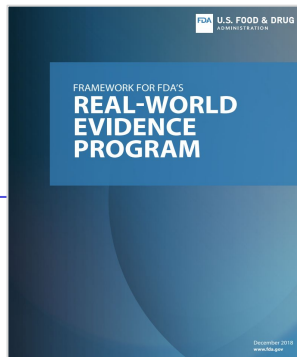
EHRs were
not built
for research

However...

- ✓ **Rich source** of patient-level data
- ✓ **Integrate** multiple data sources
- ✓ **Real-time** documentation
- ✓ **Digital** information
- ✓ Key component of **point-of-care workflow**
- ✓ **Representative** of all patients

Recent FDA Draft Guidances Outline Key Considerations in Using EHR/Real-World Data for Research

2018



Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

July 2018
Prefinal

2021

Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment. Comments and suggestions regarding this draft document should be submitted to the Federal Register of the notice announcing the availability of this document. Submit electronic comments to <https://www.regulations.gov>. For questions regarding this draft document or the Real-World Evidence Program, please email CDER@FDA.HHS.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

September 2021
Real-World Data/Real-World Evidence (RWD/RWE)

Data Standards for Drug and Biological Product Submissions Containing Real-World Data

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only. Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of this draft guidance. Submit electronic comments to <https://www.regulations.gov>. For questions regarding this draft document or the Real-World Evidence Program, please email CDER@FDA.HHS.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2021
Real-World Data/Real-World Evidence (RWD/RWE)

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only. Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of this draft guidance. Submit electronic comments to <https://www.regulations.gov>. For questions regarding this draft document or the Real-World Evidence Program, please email CDER@FDA.HHS.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

September 2021
Real-World Data/Real-World Evidence (RWD/RWE)

Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry

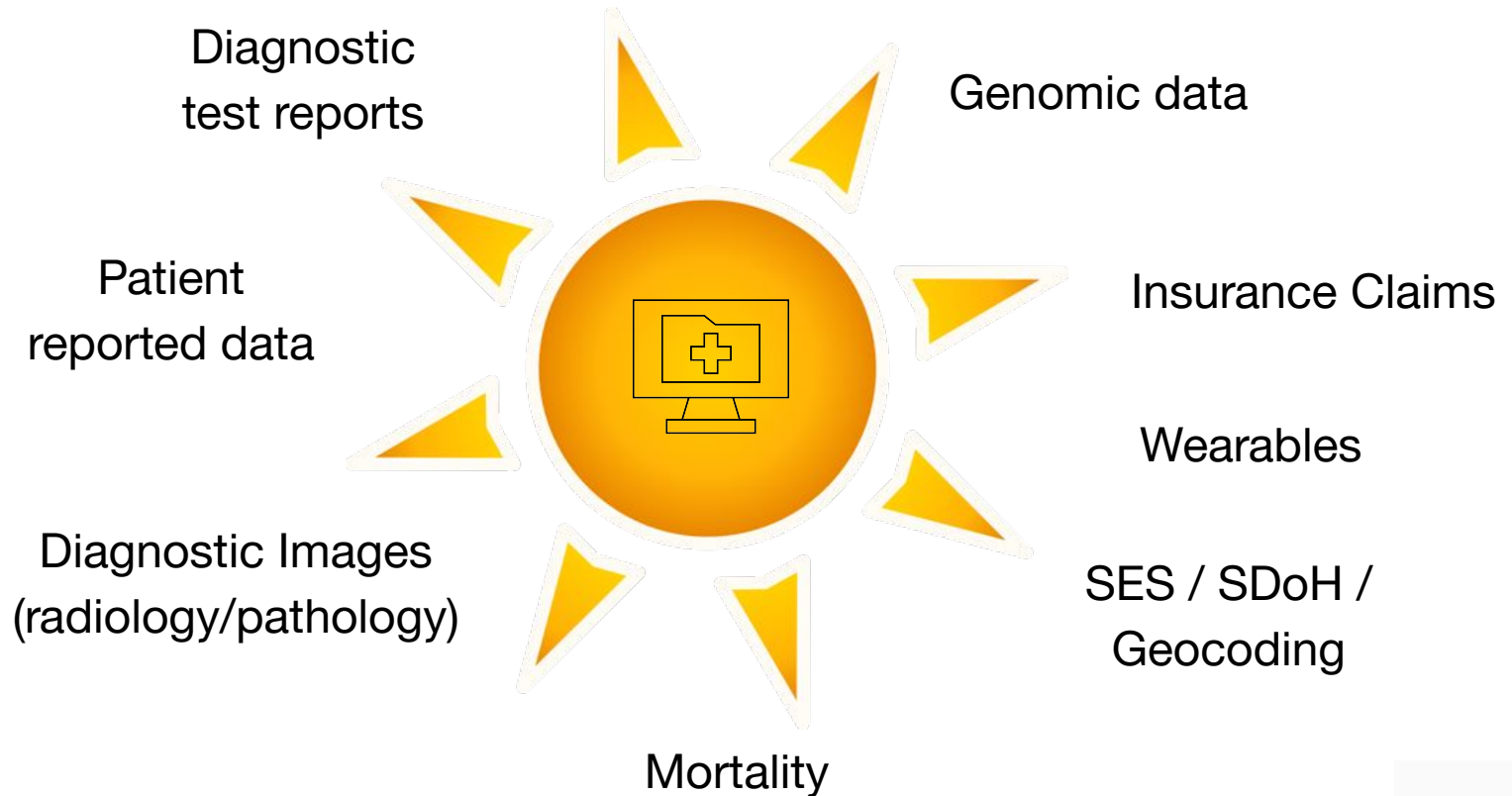
DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only. Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of this draft guidance. Submit electronic comments to <https://www.regulations.gov>. For questions regarding this draft document or the Real-World Evidence Program, please email CDER@FDA.HHS.gov.

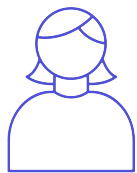
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

September 2021
Real-World Data/Real-World Evidence (RWD/RWE)

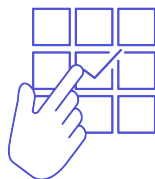
The EHR as a Platform for Integrating Evidence



“Table Stakes” for use of EHRs in Integrating Evidence



Privacy framework that respects patients



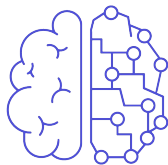
Curation capabilities for structured & unstructured data



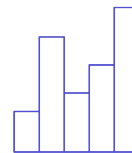
Real-time EHR data access



Linkage / tokenization for data not documented in the EHR



Careful application of ML and NLP

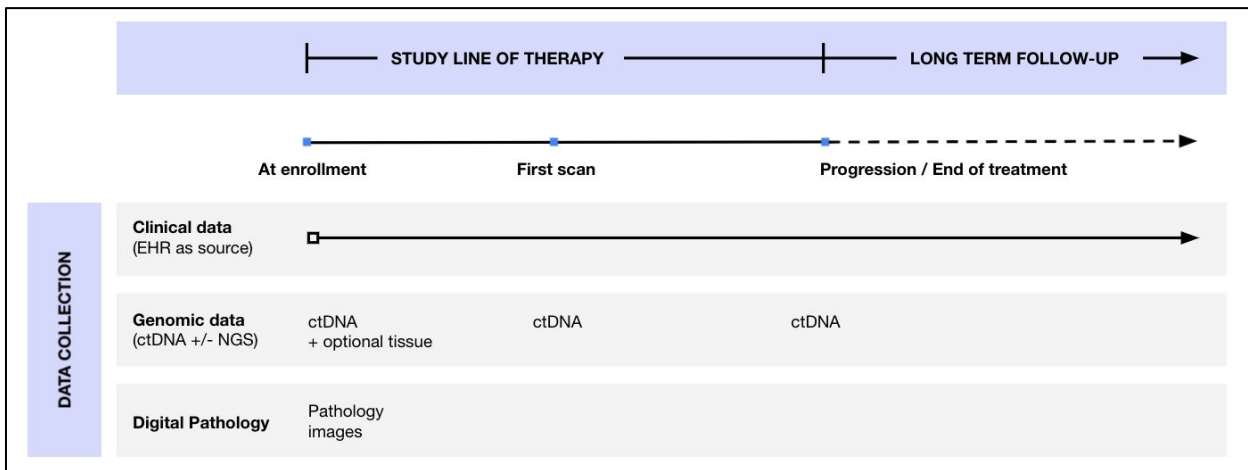


Relentless appetite for context-specific characterization of data quality and fitness-for-purpose

“Passively” collected data is not always enough

- **Routinely collected** data may not be fit-for-purpose to address all evidence gaps
 - Missingness, selection / confounding biases, causal inference, outcome measurement, exposure variability
- **Intentionally collected** data can be implemented to support specific research questions, e.g.
 - Non-routine diagnostic / monitoring tests
 - Prespecified testing modalities or intervals
 - Patient-reported outcomes

Case Study: A Prospective Clinico-genomic Study in Patients with Advanced Lung Cancer

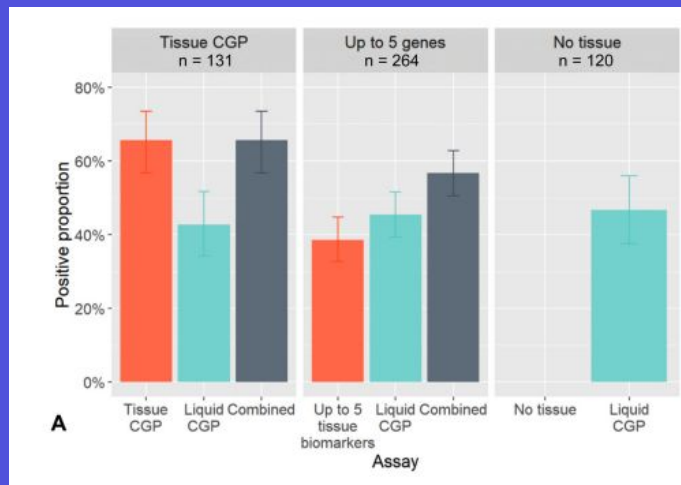


- ~1000 patients enrolled to “low interventional” study
- Tech-enabled ascertainment
- Centralized EHR-based data collection and processing
- Routine + intentional data collection

Lu MW et al. ASCO 2020; Schwartzberg LS et al. J Thoracic Oncol, Chiang A et al. WCLC, 2022; Bourla A. J Precision Med, 2022

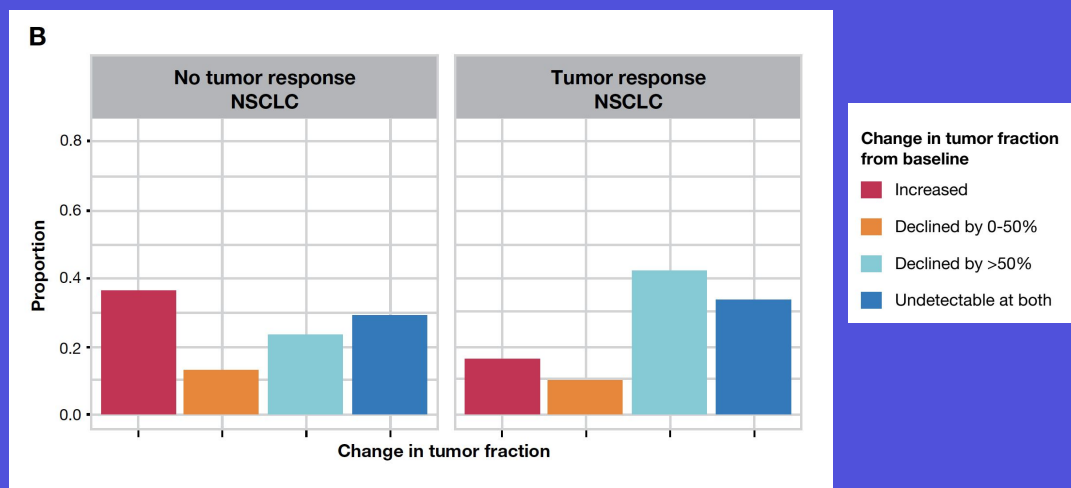
Insights from a Prospective Real-World Study on an EHR-Based Platform in Patients with NSCLC

Complementary Roles for Tissue- and Blood-Based Genomic Profiling



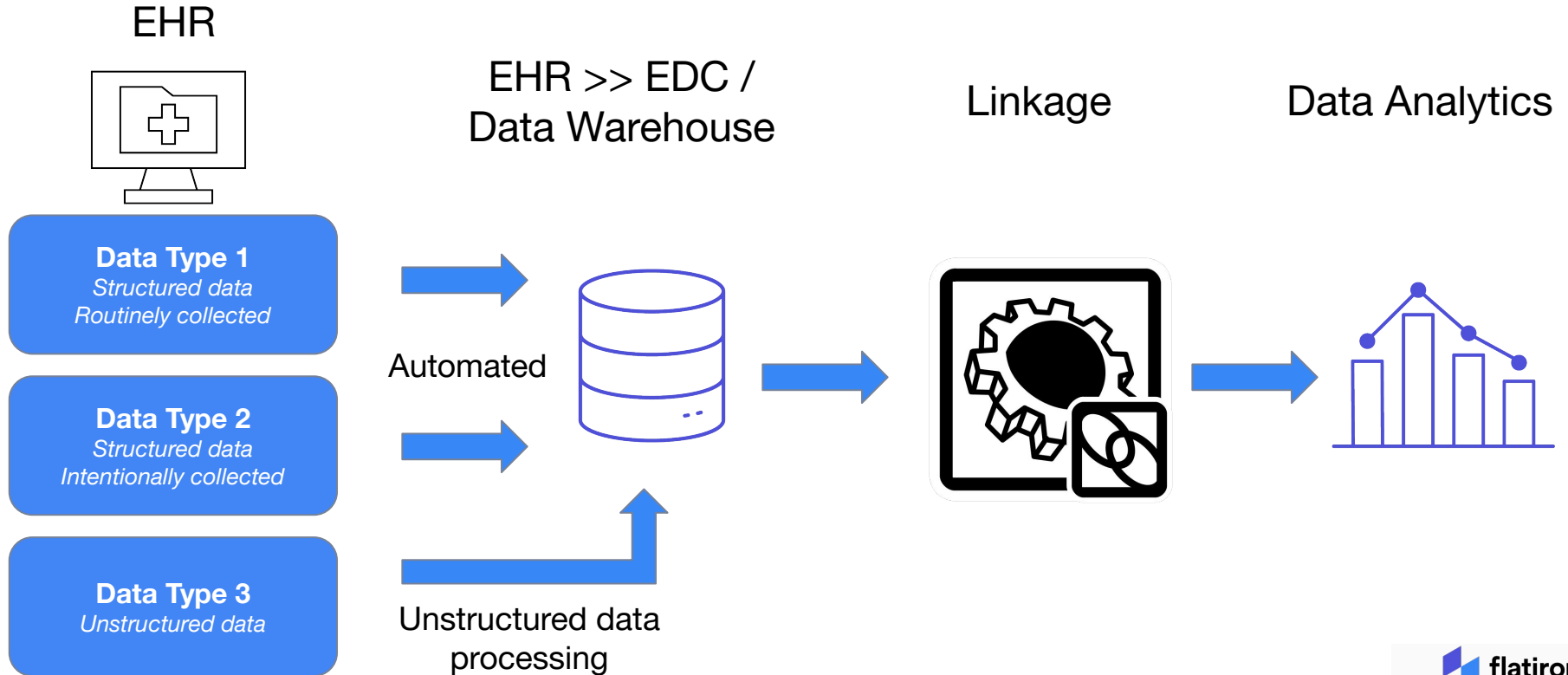
LS Schwartzberg et al. JTO Clinical and Res Reports, 2022

Association of ctDNA with rwResponse

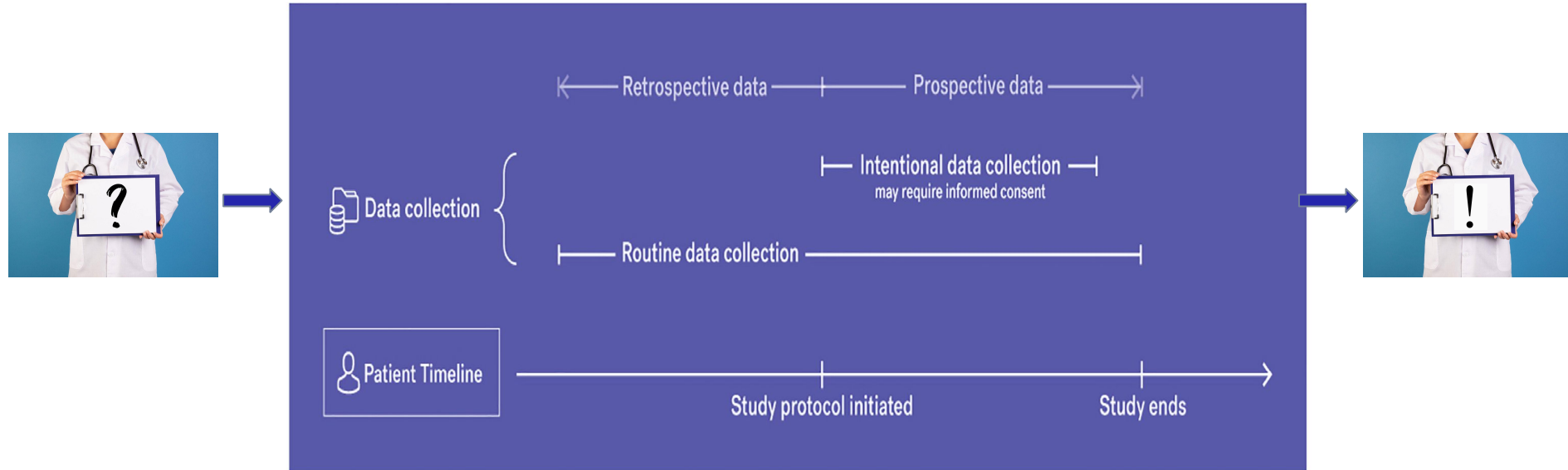


Chiang AC et al, WCLC, 2022

Getting from EHR to Evidence: *What does this mean operationally?*



A platform for real-time learning



Bourla and Meropol, Digital Health, 2021

Tools Exist Today

- ML-based cohort selection / automated patient ascertainment
- Structured and unstructured data processing
- Research-oriented data collection tools embedded in EHR
- Automated transfer of EHR > EDC
- Tokenization and linkage of EHR-based data with external sources

A modern, open-plan office space with a high ceiling, exposed ductwork, and large white pendant lights. In the foreground, a woman sits on a dark grey sofa, working on a laptop. To her right, two men sit on a blue armchair, engaged in conversation. Further back, a woman sits at a desk in a cubicle. The office is furnished with various seating options, including sofas, armchairs, and cubicles with wooden desks. Potted plants are placed throughout the space, adding a touch of greenery. The overall atmosphere is bright and professional.

Thank You
nmeropol@flatiron.com