Exploring Applications of AI in Genomics and Precision Health

NASEM BOARD ON HEALTH SCIENCES POLICY
Roundtable on Genomics and Precision Health
Oct 28, 2025

Melissa Haendel, PhD, FACMI
University of North Carolina at Chapel Hill
Monarch Initiative

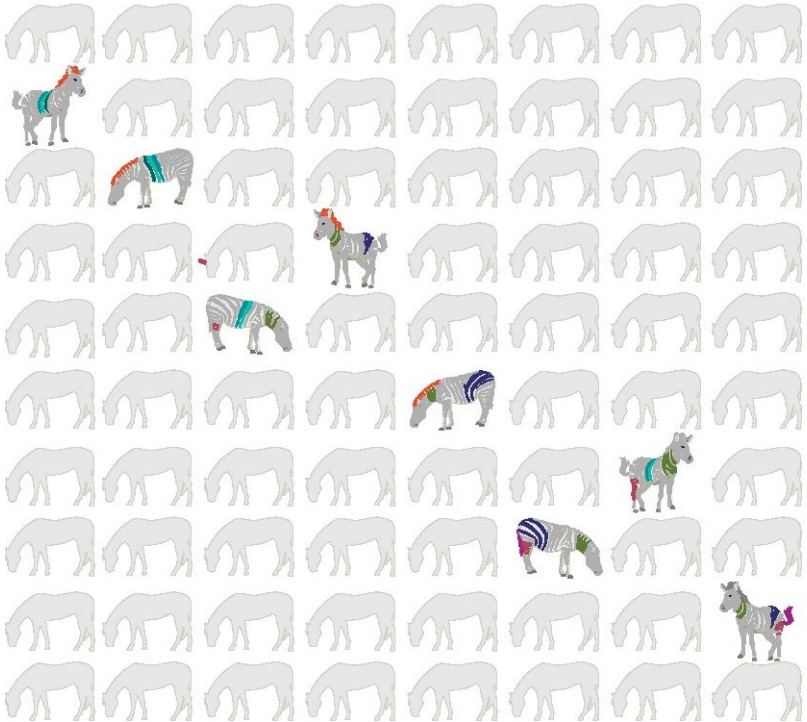
Slides available at: tislab.org/NASEM; image credits in speaker notes

Disclosures

Founder of **Alamya Health**, a genomics diagnostics B-corp dedicated to implementing genomic diagnostics labs in resource or expertise-poor settings.

1/10 americans (400M globally) affected

each patient's characteristics are akin to the variation in zebra stripes



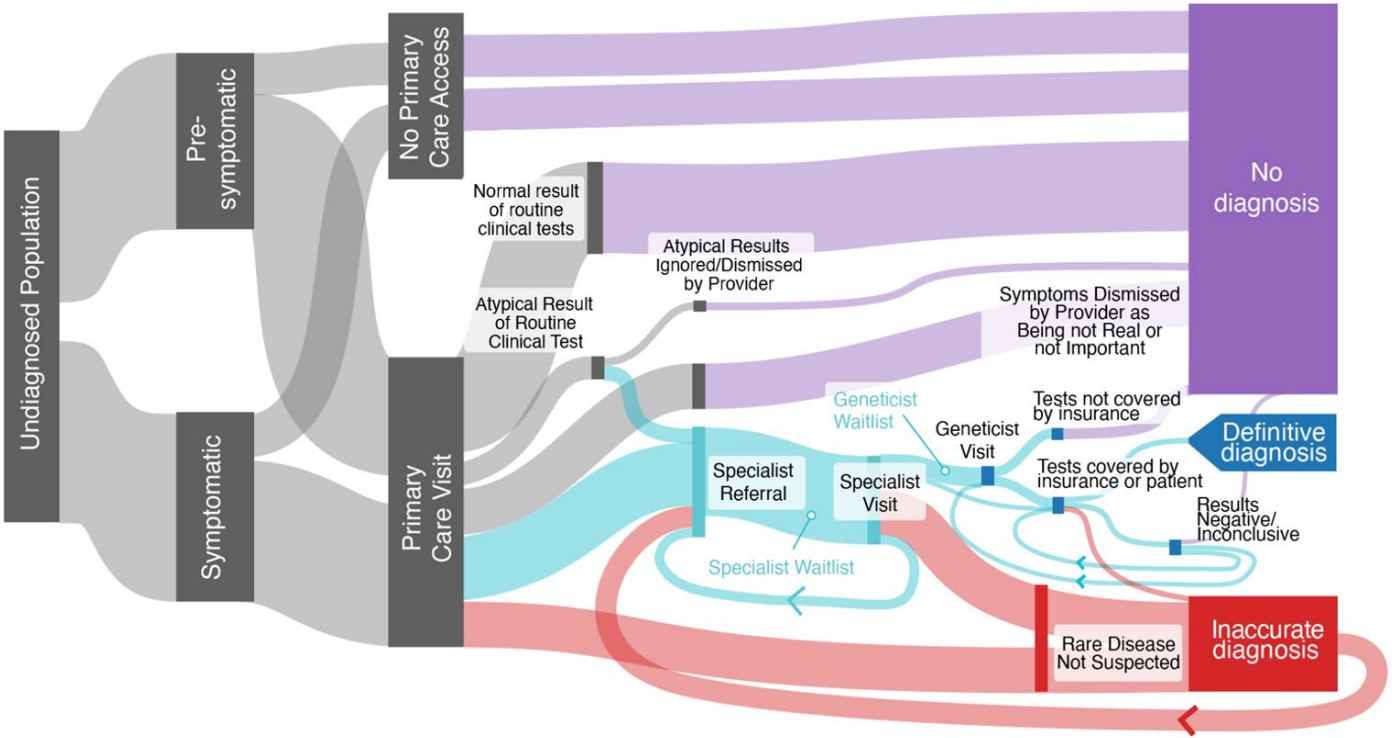
"When you hear hoof beats, think horses, not zebras."

"There are ~7000 rare diseases"

- per Orphan Drug Act (1983);

This number is demonstrably wrong.

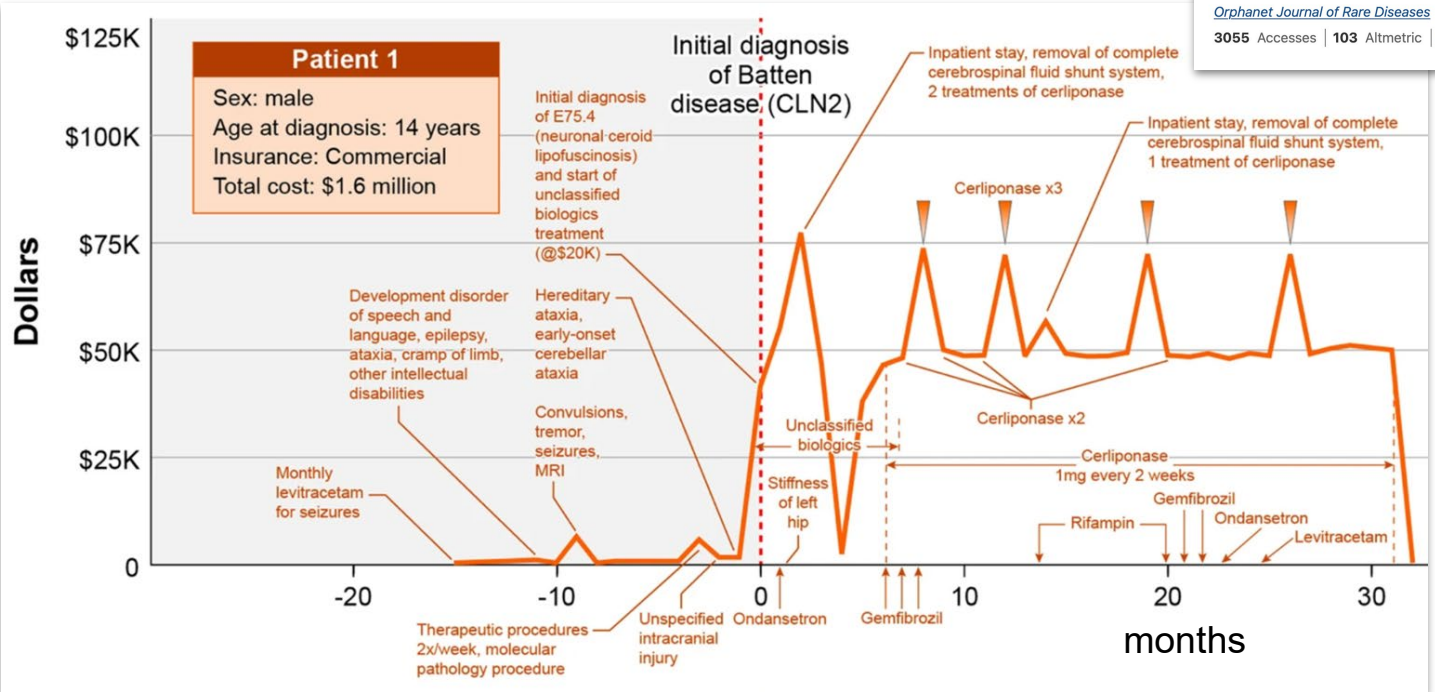
Rare disease: Key to solving numerous bottlenecks in precision med



Critical Bottlenecks in Rare Disease Research and Care: A Community Perspective
https://zenodo.org/records/14906644

Patient journeys differ across health care systems and d

…for diseases with ICD codes or that are easily phenotyped



Research | Open Access | Published: 22 October 2021

The IDeaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems

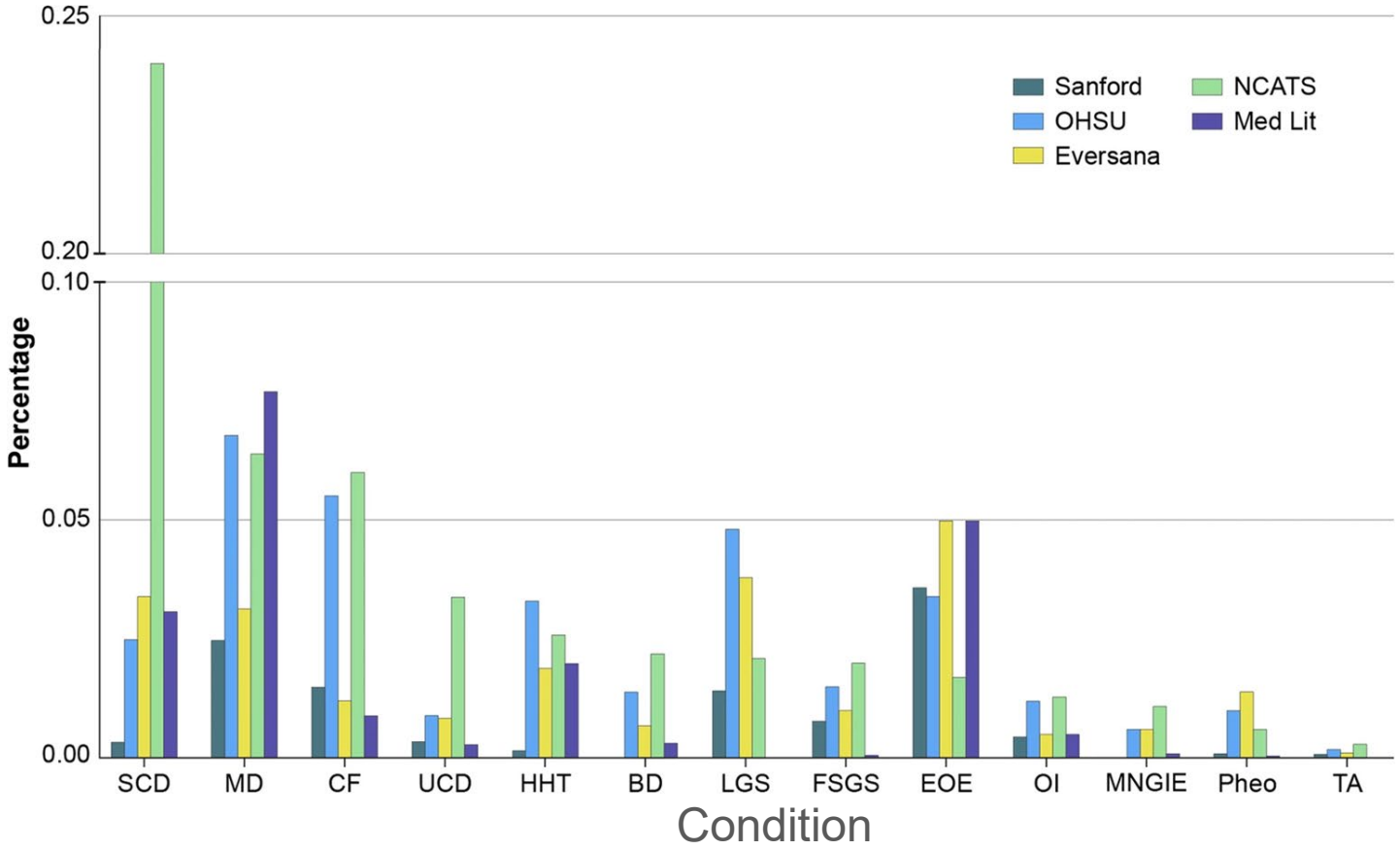
Ainslie Tisdale, Christine M. Cutillo, Ramaa Nathan, Pierantonio Russo, Bryan Laraway, Melissa Haendel, Douglas Nowak, Cindy Hasche, Chun-Hung Chan, Emily Griese, Hugh Dawkins, Oodaye Shukla, David A. Pearce, Joni L. Rutter & Anne R. Pariser

Orphanet Journal of Rare Diseases **16**, Article number: 429 (2021) | Cite this article

3055 Accesses | **103** Altmetric | Metrics

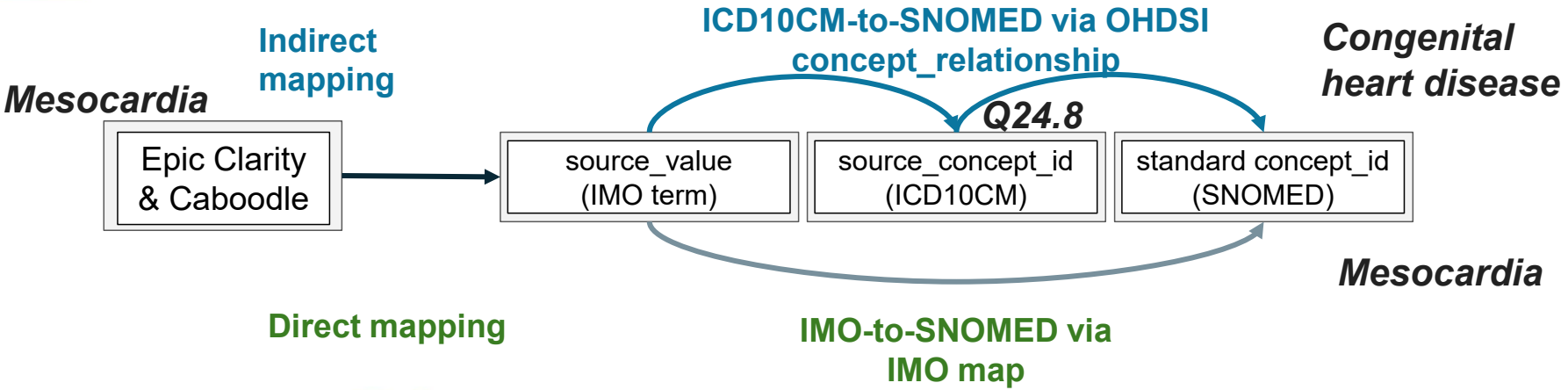
bit.ly/ideas-initiative-rd

Rare disease prevalence varies across healthcare systems & public sources



Differences in prevalence across healthcare systems are in part due to diagnostics, but also due to differences in coding and billing biases

One problem: what comes out of the EHR is lossy BUT it is what many AI models are based on



Melanie Philofsky, Katie Mullen
https://www.ohdsi.org/2025showcase-141/

AI alone can’t fix discordant or missing data / know

GENETICS

Mondo: Integrating Disease Terminology Across Communities

Vasilevsky et al October 2025

https://doi.org/10.1093/genetics/iyaf215

mondo
THE WORLD'S DISEASE CONCEPTS, UNIFIED

	Gene Association		Distinct Disease Record				
	ORPHA	OMIM	ORPHA	OMIM	MESH	ICD10	ICD11
Cardiomyopathy, dilated, 1S	52 genes	MYH7	○	■	✕	✕	✕
Cardiomyopathy, hypertrophic, 1	✕	3 genes	✕	●	✕	⬟	≠
Congenital myopathy 7A, myosin storage, autosomal dominant	MYH7	MYH7	○	●	✕	●	▲
Congenital myopathy 7B, myosin storage, autosomal recessive	MYH7	MYH7	●	●	✕	✕	✕
Laing distal myopathy	MYH7	MYH7	●	●	■	▲	✕
Left ventricular noncompaction 5	14 genes	MYH7	○	■	✕	✕	✕
Ebstein malformation of the tricuspid valve	MYH7	0 genes	●	○	●	●	●

LEGEND

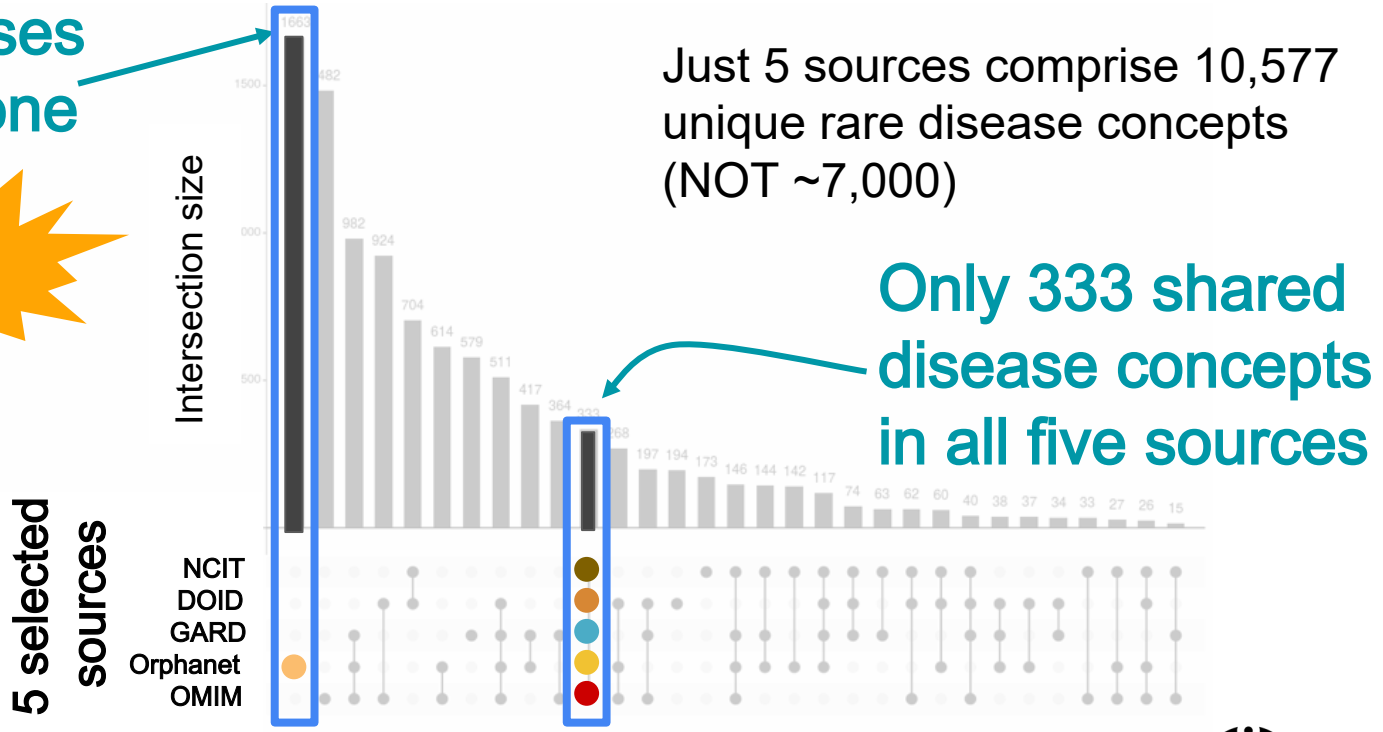
- ✕ Absent
- ● Present
- ⬟ Present but called something else
- ▲ Present but uninterpretable
- ○ Present but misrepresented; missing genes or mappings
- ■ Present but grouped or lumped with other term / gene
- ≠ Present based on ORPHA but absent from OMIM or unspecified

AI is already helping us reconcile disparate ge disease definitions

monarch INITIATIVE

Many diseases are in only one source

NEW! >10K!



Just 5 sources comprise 10,577 unique rare disease concepts (NOT ~7,000)

Only 333 shared disease concepts in all five sources

NIH FDA Global Genes® Allies in Rare Disease EVERYLIFE FOUNDATION FOR RARE DISEASES NORD® National Organization for Rare Disorders SANFORD RESEARCH

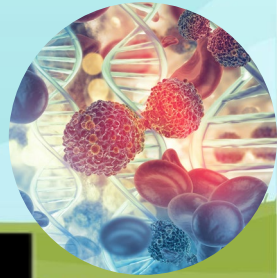
Nature Reviews Drug Discovery (bit.ly/nature -rare-diseases)
Genetics (https://doi.org/10.1093/genetics/iyaf215)

mondo THE WORLD'S DISEASE CONCEPTS, UNIFIED

Precision Medicine is here, but challenges aren't technical

✅ Newborn Screening

✅ Cancer

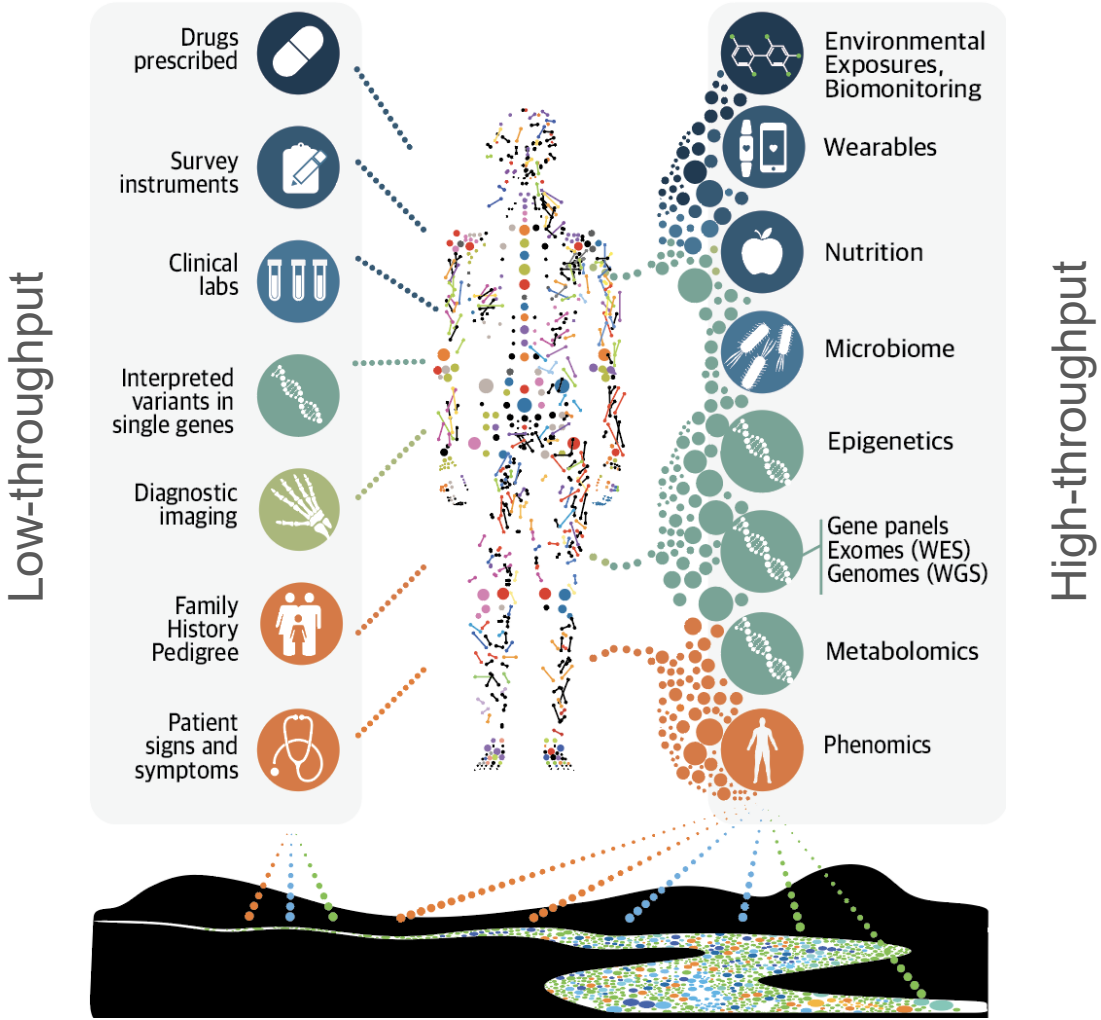


AI will make it easier/cheaper;
governance/policy needed to make implementation reality

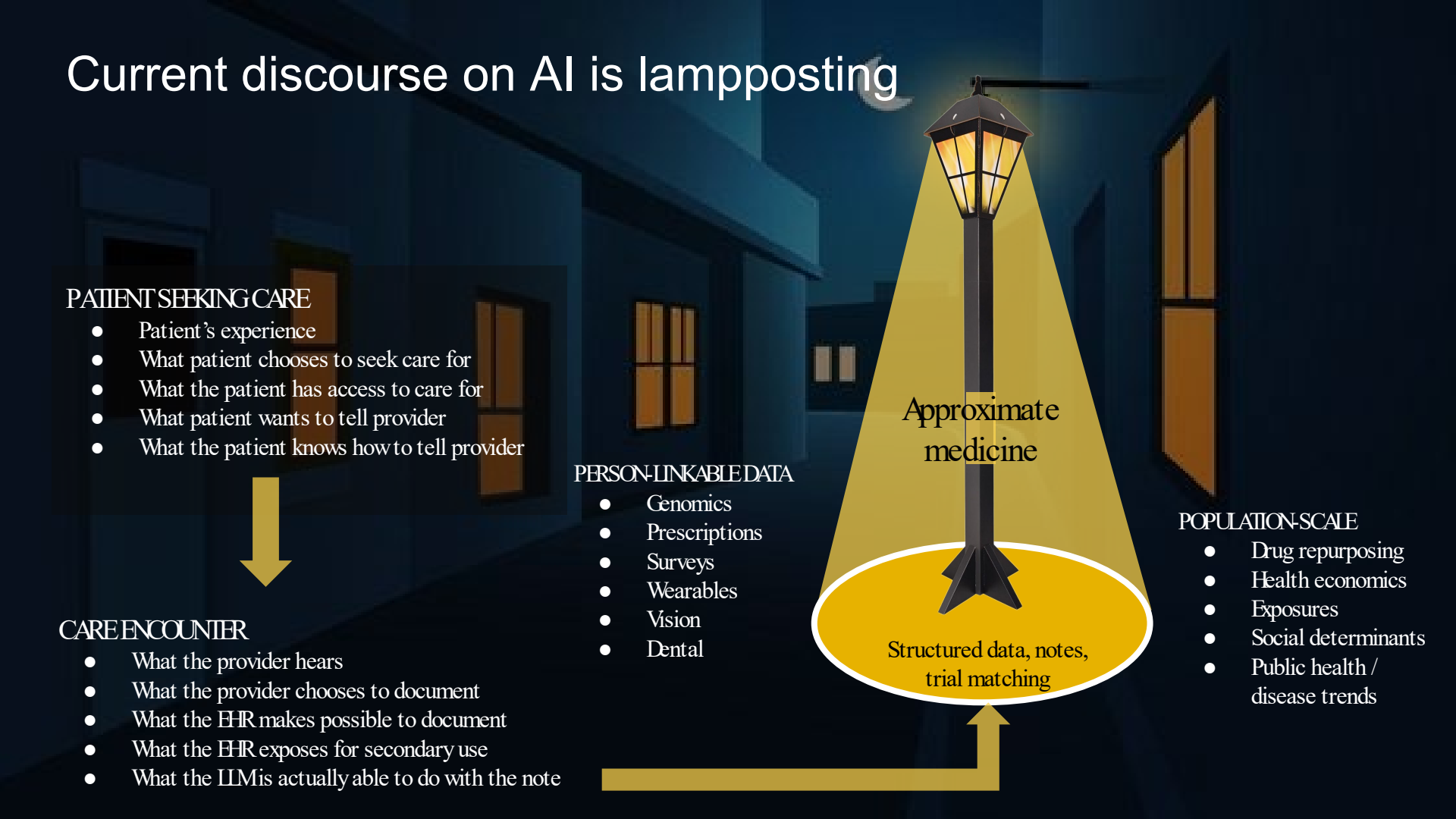
Chasm of Approximate Medicine:

Rare diseases, Chronic complex conditions, Mental health conditions, Autoimmune diseases, Environmental and occupational illnesses, Functional disorders (eg. IBS, fibromyalgia), Emerging diseases, Addiction and substance use disorders

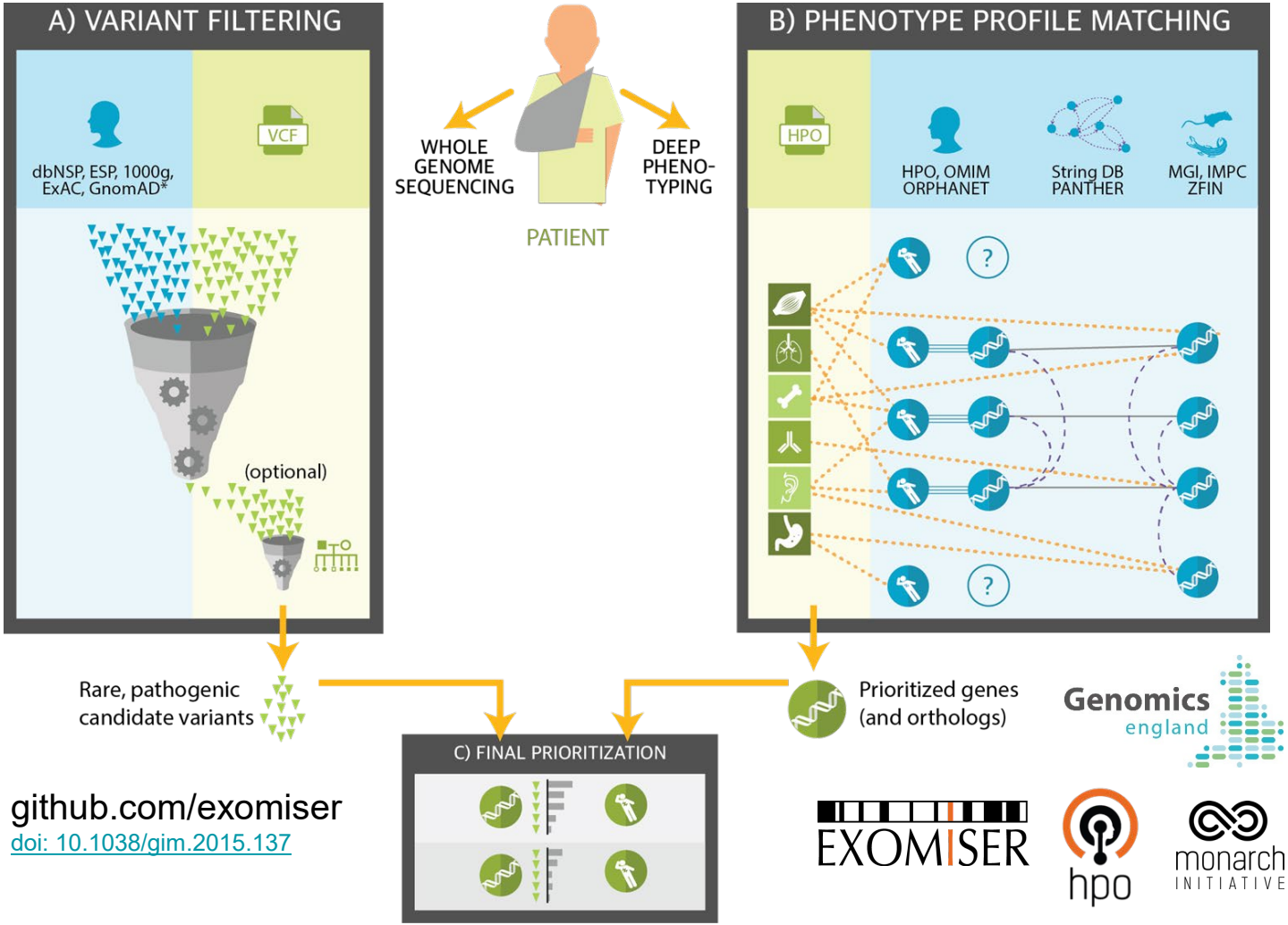
Data modalities relevant to health are increasingly high-throughput and must be analyzed in context of their temporal flow.



Current discourse on AI is lampposting



Good old fashioned AI can improve variant prioritization, leveraging multispecies knowledge



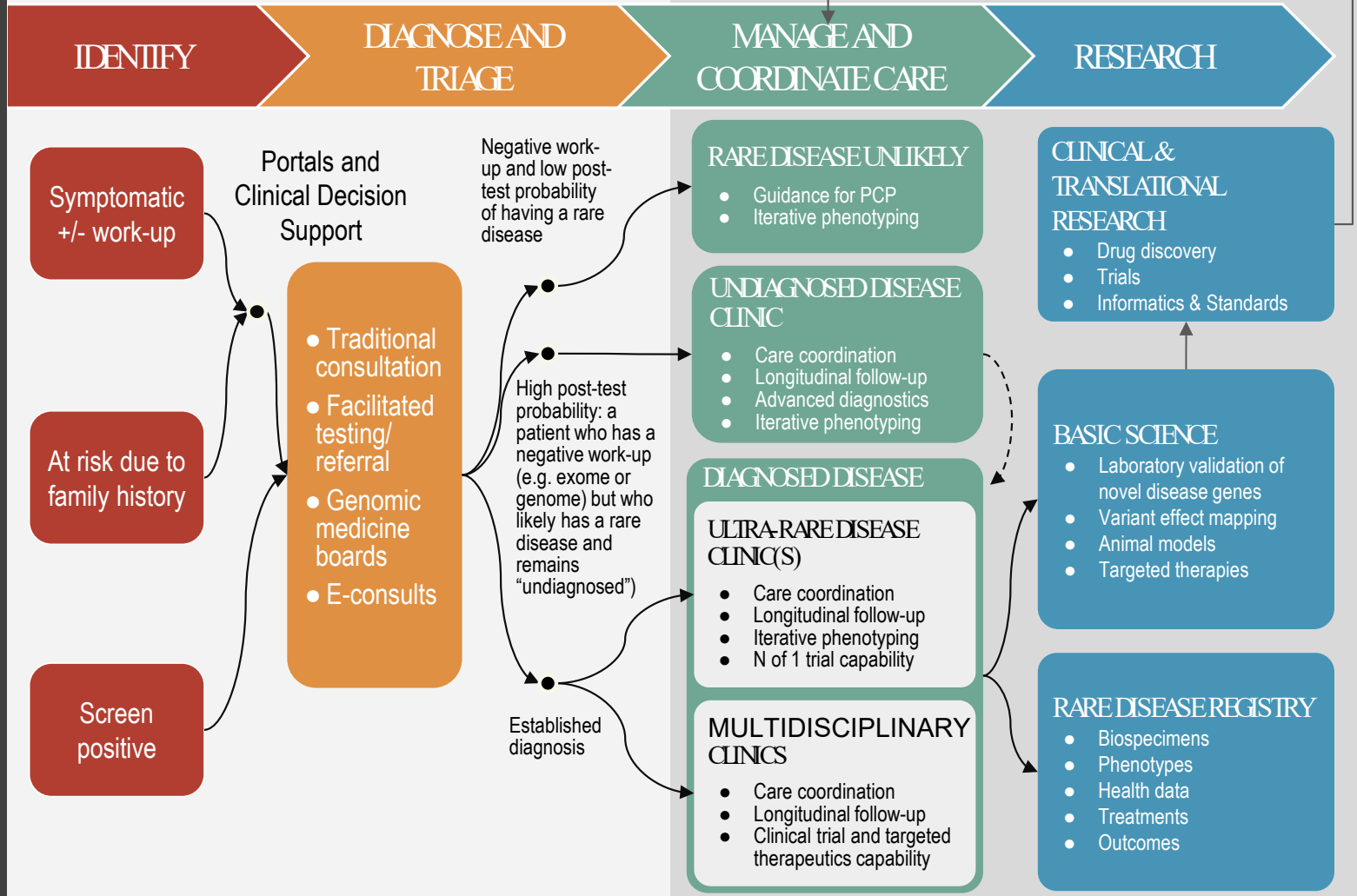
github.com/exomiser

doi: 10.1038/gim.2015.137

exomiser.readthedocs.io

nejm.org/doi/full/10.1056/NEJMoa2035790

There are many steps in the journey where AI can assist precision medicine and genomics



Takeaways to bridge the chasm of approximate m

Problem: AI models built on data that happens to be available; narrowly applied

Solution: Include more data types, integration, and linkage, and expand applications to more timepoints in the care journey

Problem: AI alone can't fix discordant or missing data / knowledge

Solution: Harden & leverage knowledgebases, deploy socio-technical engineering

Problem: Implementation trails far behind technology.

Solution: Modernize data governance, stewardship, and policies to bring all data to the point of care