AI/ML to guide 21st Century Clinical Trial Enrollment: are we there yet?

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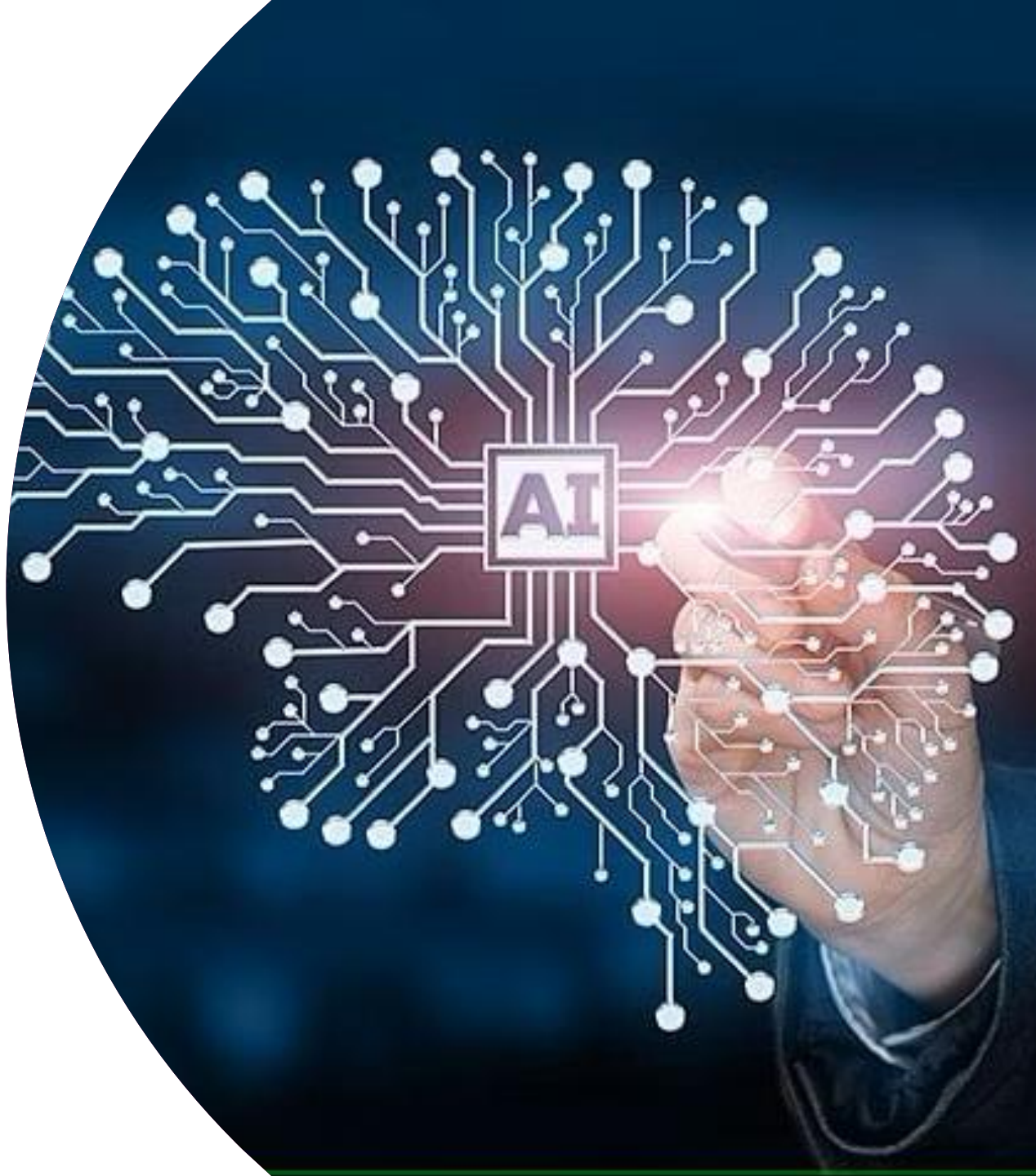
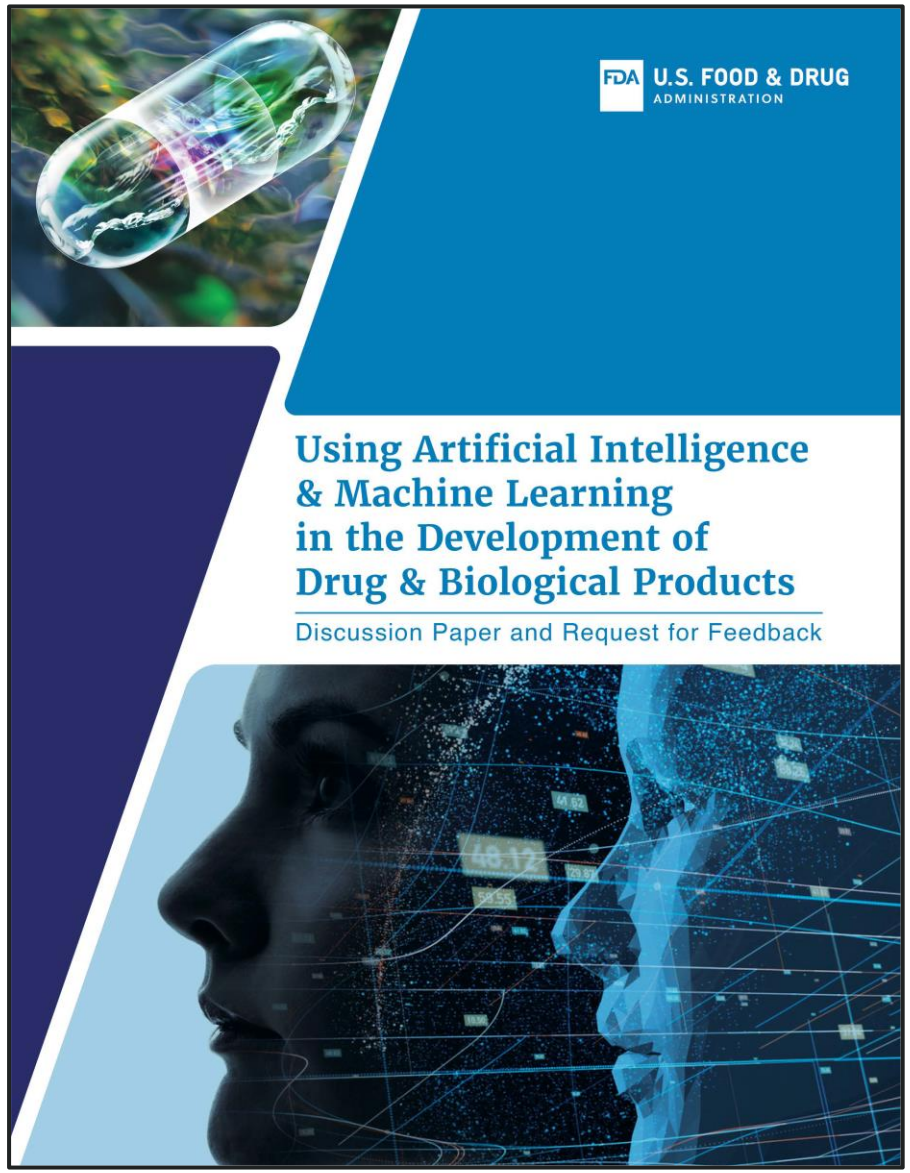


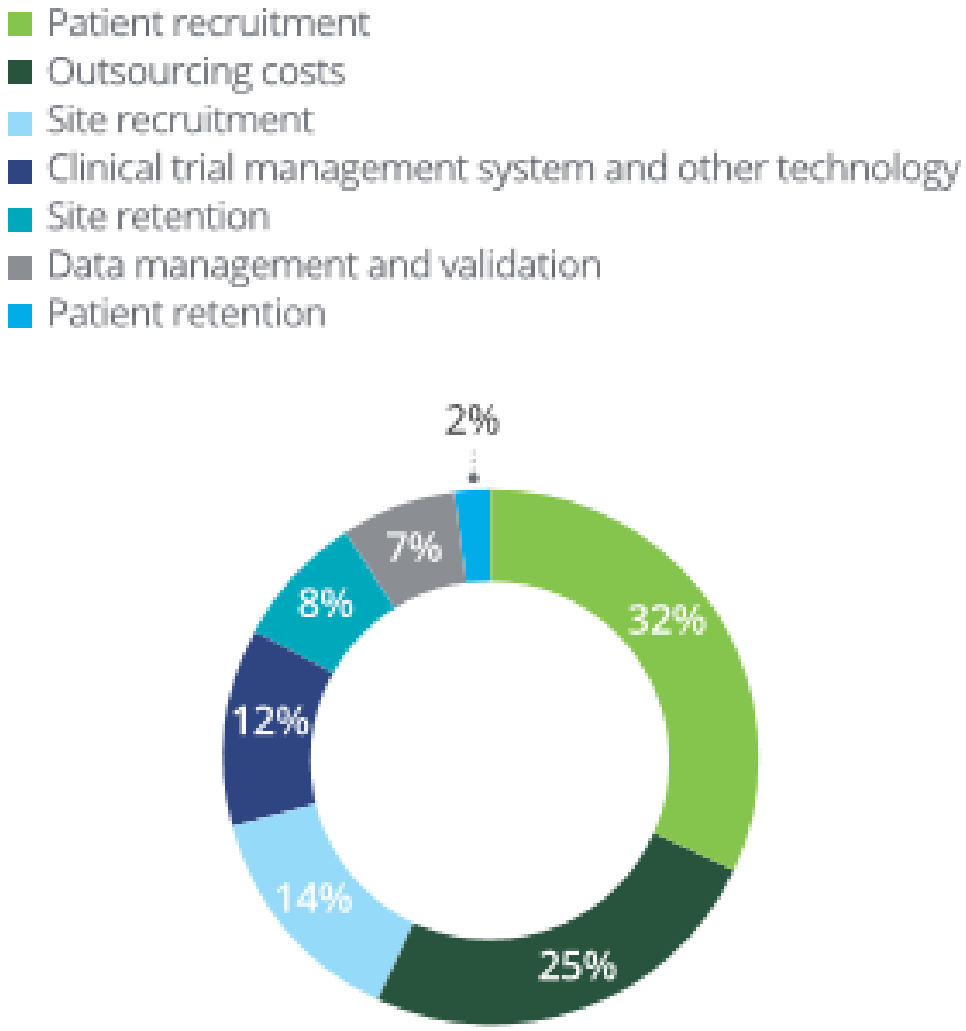


https://www.fda.gov/science-research/science-and-research-special-topics/artificial-intelligence-and-machine-learning-aiml-drug-development

The traditional approach to trial recruitment

- Hospital/clinic site(s) selected for specific trial protocol
- Investigators at site trained and signed off
- Patients identified in clinic or as inpatient *opportunistically*
- Patient approached by junior member of team
- If patient consents, then enrolled
- Multiple site visits over (many) months – patient hopefully remains engaged
- Once site recruits one patient, likely to recruit (a few) more patients
- Site monitoring ongoing, and multiple touch points re data collection & quality control
- Site eventually closed down after queries answered and database locked

Cost drivers in clinical trials

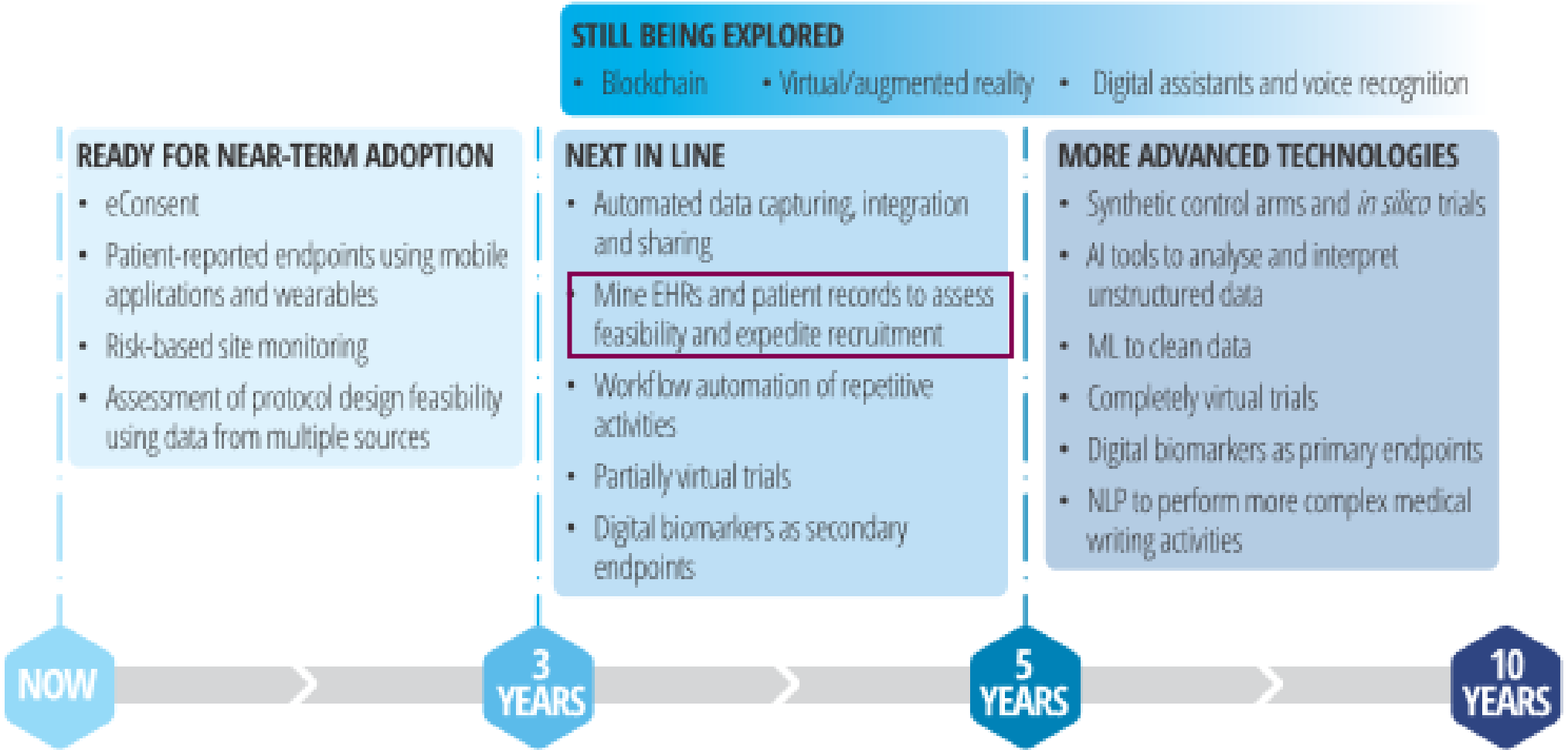


Source: Deloitte analysis.

Patients and (good) sites are the most precious resource

https://www2.deloitte.com/us/en/insights/industry/life-sciences/artificial-intelligence-in-clinical-trials.html

Expected timeline for the adoption of AI-enhanced digital technologies at scale



Source: Deloitte US Center.

AI areas of interest in AstraZeneca Clinical Operations

AstraZeneca is currently engaged in multiple exploratory projects for harnessing AI in our trial delivery. Areas of learning, automation and the patient experience are key.

Recruitment

- EMR integrated machine learning and predictive analytics to identify prospective volunteers
- Generative AI models to create plain language patient-facing materials at scale
- Chatbot technology to conduct trial pre-screening and answer volunteer questions
- Predictive volunteer scoring for trial suitability (i.e. how likely to randomise?)
- Automated trial and site recommendation engine

Feasibility and site selection

- Predictive site-level recruiting models based on past performance data
- Multi-layered heat-mapping harnessing patient, Rx, site and public health data
- Automated site / protocol optimisation recommendations

Protocols

- Automated protocol document creation
- Predictive success modelling based on I/E, site/patient burden data

Accelerate recruitment rates and strengthen site relationships with algorithmic patient identification & novel data partnerships

Goal: Create end-to-end data interrogation offerings to bolster recruitment rates for high-priority CVRM Disease Areas

1. Identify data partners (e.g., EHR, pharmacy, remote patient monitoring) that enable identification and access to target patient populations + readiness to participate in clinical research

2. Develop data-driven approaches to non-invasively identify and screen for i/e criteria

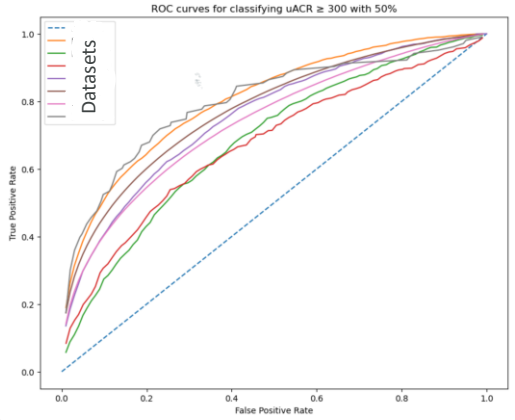
3. Ensure simple and intuitive interface for end users (e.g. site study coordinators) to query data, interpret actionable outputs, and enable fit-for-purpose patient outreach to maximize trial conversion rates

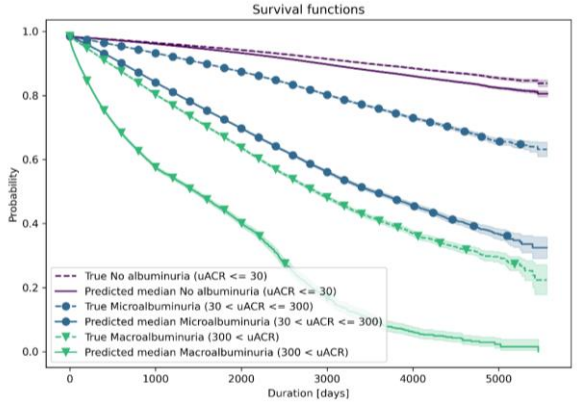
Project Examples with applications in CKD, rHTN, and HF

Algorithmic Patient Identification: machine learning models to identify at-risk patients for recruitment to our trials

USE CASE: CKD Albuminuria Threshold Prediction

- AZ's data science team developed an Albuminuria prediction model to detect individuals with undiagnosed CKD
- Model is based on patient level data (demographics, vitals, labs) and predicts actual uACR thresholds, undiagnosed CKD, risk of progression and outcomes.
- Model was developed and internally validated on 3 RWE and 4 retrospective clinical studies/biobank datasets
- **Next Steps:** external validation on retrospective data and deployment testing in partnership with leading US healthcare system; site and patient journey mapping





Innovative partnerships: pharmacies, data aggregators and remote patient monitoring companies have access to well characterized patient populations

USE CASE: Exploring recruitment opportunities beyond the clinical site to expand trial access and participant diversity.

Pharmacy/prescription data

- **Who:** Community pharmacy networks with access to well defined patient populations consented to participate in research; healthcare companies with direct access to pharmacy distribution data and simple search
- **Opportunity:** Geolocation of pharmacy and trial sites to accelerate patient identification and site referrals meeting pre-screening i/e criteria.

Remote patient monitoring (RPM) and digital therapeutics companies

- **Who?:** Technology companies with EHR-integrated RPM solutions (e.g. blood pressure cuff, digital scales, vitals, med adherence, 24/7 virtual care teams)
- **Opportunity:** Leverage RPM digital solutions and healthcare system relationships to accelerate recruitment rates and establish 'high-performing' sites

Innovative Recruitment and RPM: HCPs and patients are still at the center of this model

Using social media to reach potential study participants

80% of USA adults < 50y use social media

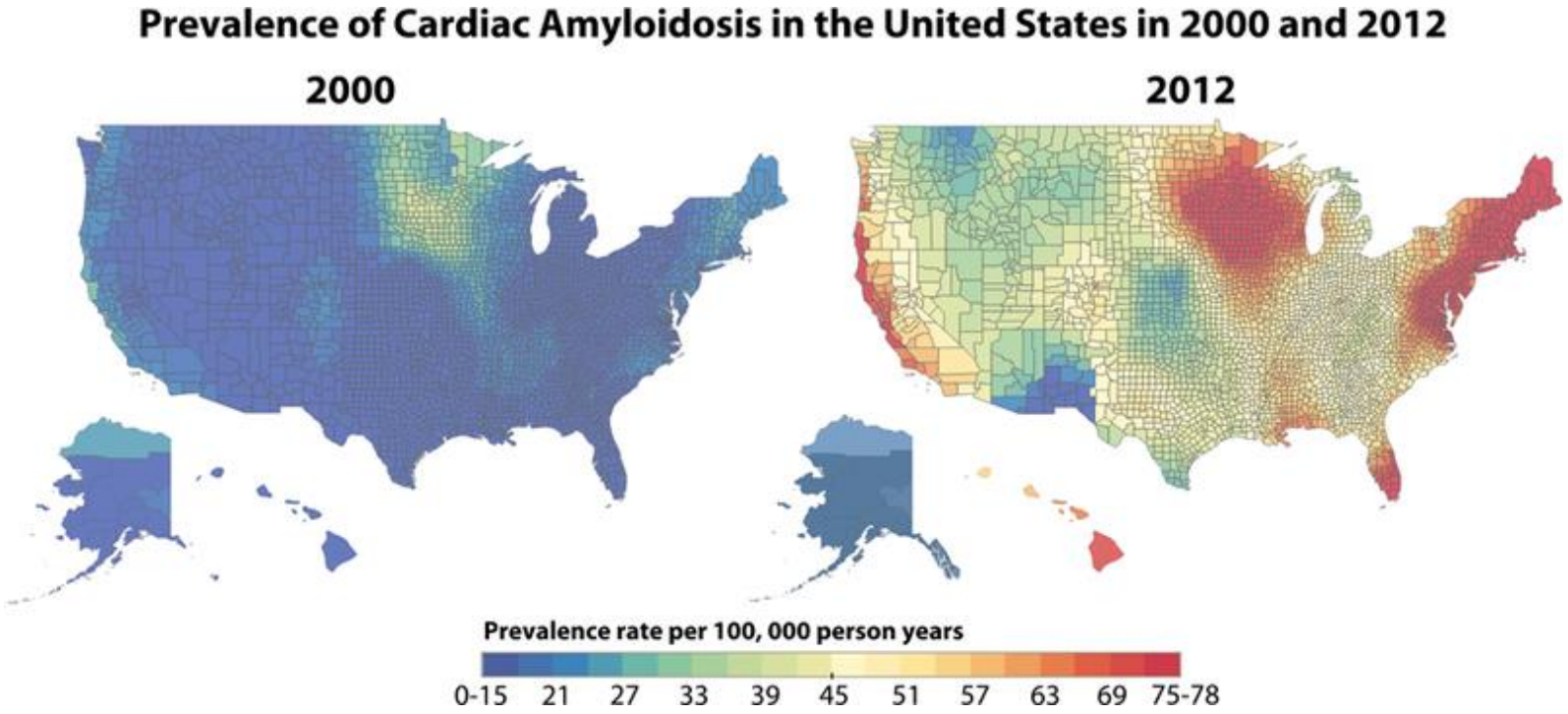
Venue for volunteer engagement

Low or no cost “venue” for recruitment

Greater generalisability as can access diverse or marginalised communities

[10] Goldberg EM et al. J Med Internet Res 2022; 24: e350804

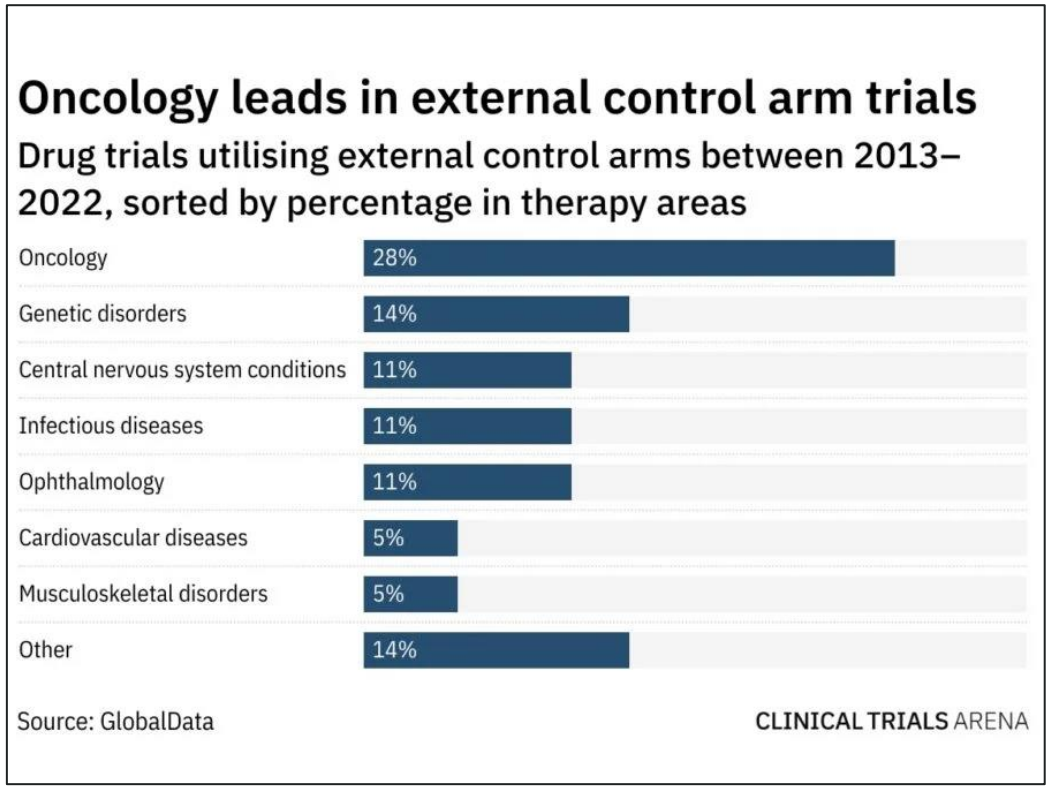
Where are those we are trying to recruit?



[11] Gilstrap LG et al. Circ Heart Fail 2019; 12(6): e005407

AI to create synthetic control arms

- Using RWE to construct a “synthetic” control group so all patients entering a trial receive active therapy
- Popular with patients!
- Not protected by randomisation, but can match against measured features and use a wide source of data
- Currently used more in oncology & rare disease trials
- ?faster more efficient trials
- ?earlier access to innovation
- ?no issue of unintentional unblinding



https://www.clinicaltrialsarena.com/features/external-control-arms/

AIDA – Automated Identification, Detection & Adjudication

from **4 months** *to* **4 minutes**

Event Sniffer

Geotagged Visits

Study team follow-up with patient

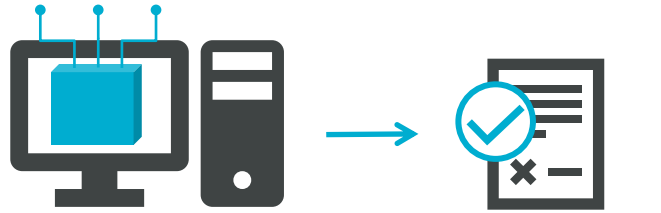
Harmonizer

Electronic Health Records

Additional data collection

Data harmonization

Classifier



Human assessment for some cases

Automated collection and harmonization of data + Automated clinical event classification using Machine Learning = Reduced trial time of 3-4 months with Adjudication ready in minutes

Conclusions

- Optimal patient and site identification is crucial to clinical trial success
- Operationally, the traditional model is already changing, including the use of AI-informed approaches
- Should be viewed in the wider context of increasingly decentralised trials that need to recruit individuals more typical of those affected by the condition
- Progress is currently rather plodding, but likely to accelerate
- Challenges should be discussed including data interoperability, biases, consent, and variable data privacy concerns and legislation across geographies
- Beware “magic dust” approach to AI – use-cases need to prove its worth

Further Reading

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9414344/

https://www.clinicaltrialsarena.com/features/ai-clinical-trial-recruitment/

https://www2.deloitte.com/us/en/insights/industry/life-sciences/artificial-intelligence-in-clinical-trials.html