AI is about to help us design even more valuable clinical trials

Early-Phase AI Impact

Shaan C. Gandhi, MD, DPhil
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AI optimizes around the objectives you give it.

For clinical development, those objectives should include commercial.

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Trials have historically targeted approvability

Clinical trials have historically been designed to clear the regulator's bar: an approvable profile of safety and efficacy.

Safety

Adverse events and tolerability at the proposed dose and regimen.

Efficacy

Primary endpoints the regulator accepts, such as response rate or survival.

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The example of aducanumab

2021 FDA Approval	Jan 2022 CMS proposal	Apr 2022 Coverage decision	2024 Discontinued
FDA accelerated approval on basis of surrogate biomarker (amyloid plaque) reduction	Further coverage limited to trial participants, a mechanism usually used for devices	No broad coverage without further evidence, e.g. additional post-approval confirmatory trials	Biogen discontinues commercialization

<$10M

in sales after approval

>$1B in R&D expense

Payers and major health systems all elected not to cover or offer aducanumab

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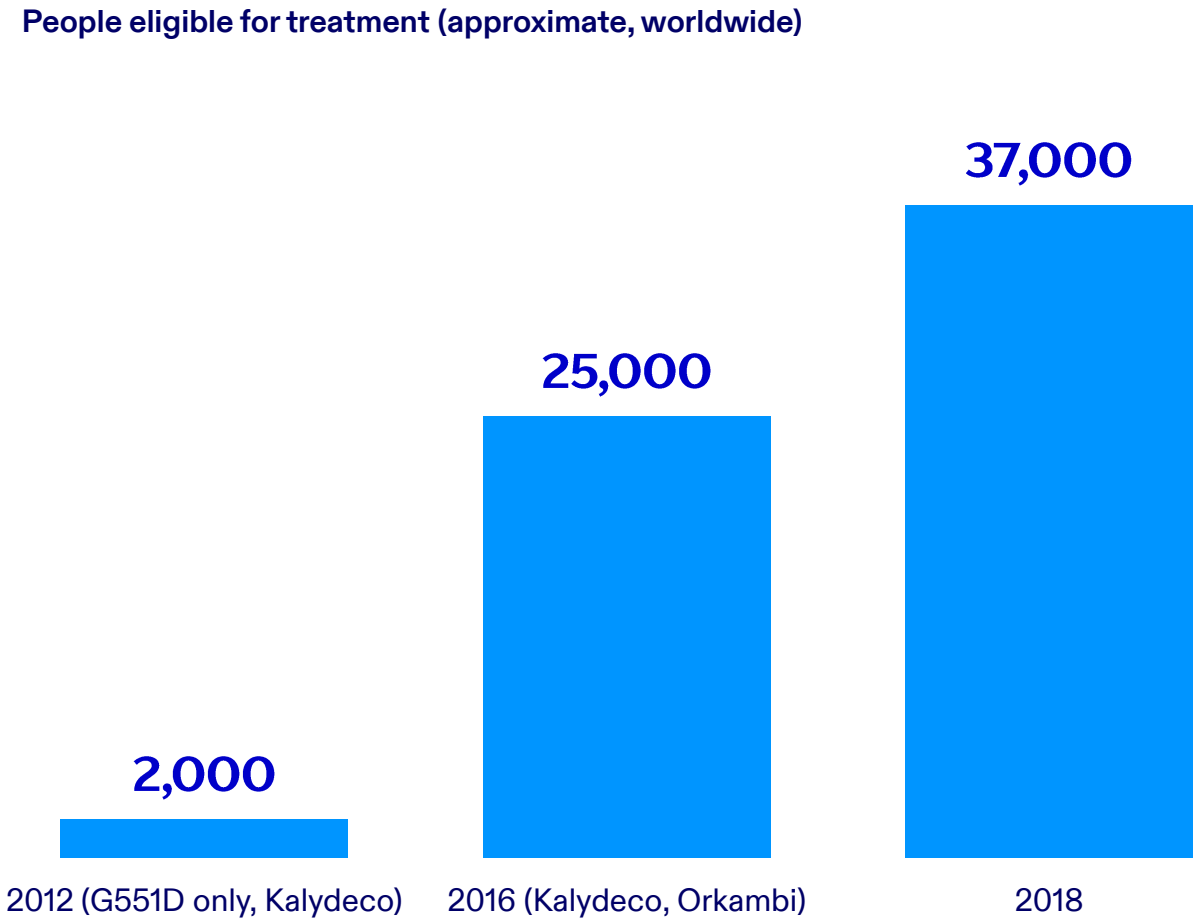
The example of cystic fibrosis

One small market, sequenced into a franchise.

- Kalydeco, 2012: one mutation, about 2,000 patients worldwide
- Label expansions, then Orkambi (2015) and Symdeko (2018)
- Orkambi needed country-by-country reimbursement; Vertex helped payers size eligible patients



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Commercial objectives belong in early trial design

A successful trial does not necessarily guarantee a commercially-viable product. Both objectives matter from the first protocol.

Approvable

Meets the regulator's bar: efficacy and safety. Evidence built for that bar alone may not satisfy anyone else, including investors and partners.

Viable

Clears the payer, the prescriber, and the competitive landscape. Each applies a different test of value.

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Using AI in clinical trial design

AI protocol tools optimize trial design and operations for approval. The market term is missing.

Optimized today

- Enrollment and retention forecasts
- Cost and timeline
- Site and patient burden
- Similar-study benchmarks

The missing term: market viability

- Patient: how many are eligible and treated
- Prescriber: what makes them switch
- Payer: what evidence unlocks coverage
- Competitor: what comparator proves the claim

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Framework

Work backward from the target product profile.

Patient

Who is treated, and how many?
Lever: population and biomarker
Evidence: real-world prevalence and testing rates

Prescriber

What makes them switch?
Lever: dose, regimen, tolerability
Evidence: tolerability and dosing convenience

Payer

What evidence unlocks coverage?
Lever: endpoints and duration
Evidence: outcomes tied to coverage criteria

Competitive landscape

What comparator proves the claim?
Lever: comparator and confirmatory path
Evidence: head-to-head or indirect comparison

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Designing the iterative loop

Add a market term, keep a human at the decision.

01 Inputs

- Real-world data (claims, EHR)
- Payer policies and HTA decisions
- Competitor pipelines and registries

02 Models

- Population sizing
- Trial emulation and digital twins
- Payer-evidence prediction

03 Scorecard

- Design options compared on operational and market terms together
- Shows trade-offs across options, not a single score

04 Human decision

- A named owner
- Documented assumptions
- Specific commercial criteria

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AI: sizing

Size it before protocol lock

Today

- **Estimate eligible populations under different definitions:** researchers sized how many Medicare beneficiaries would newly qualify for semaglutide, and the answer moved with the definition
- Use it to test definitions before you lock the population

Tomorrow

- **Fill gaps in real-world data:** 71% of NSCLC patients in one registry study were missing variables of interest, and the lack of data was itself prognostic
- Check data completeness before trusting a forecast

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AI: simulate

Illustrative uses: test design choices before you fund them.

Eligibility
Who should qualify?

Question: how many real patients would the criteria exclude?

AI: emulate the trial on real-world data

Decision: match criteria to the patients prescribers will treat

Comparator
What will payers expect?

Question: which comparator will payers expect?

AI: simulate alternative comparators and external controls

Decision: pick the one that best supports the label

Feasibility
Can we afford it?

Question: can the better design run within budget?

AI: simulate enrollment, duration, and cost

Decision: fund the best balance of evidence and cost

>2×

eligible pool when restrictive criteria were broadened

published NSCLC trial emulation, Nature 2021

Simulation shows what could happen. It does not guarantee regulatory acceptance.

Illustrative examples. Evidence: Liu et al., Nature 2021 (emulation of completed NSCLC trials in real-world data)

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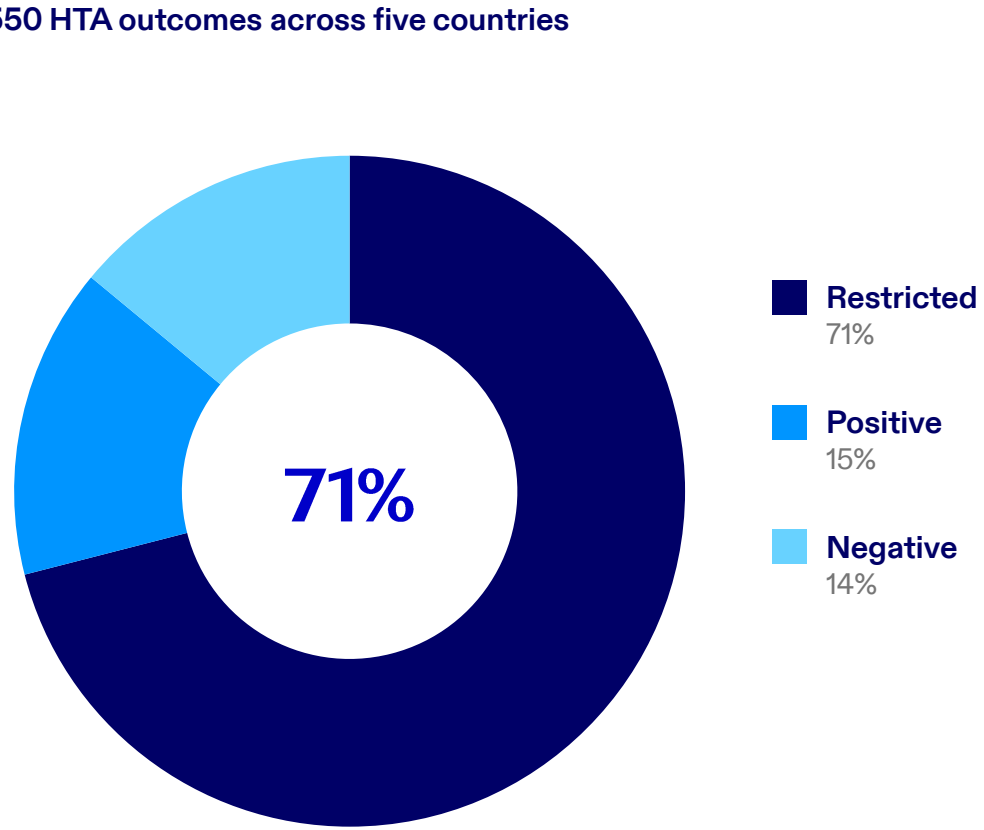
AI: payer

Restricted access is the base case, so design for it.

- Extract the evidence criteria payers applied to comparable indications
- Estimate how endpoint, population, and comparator choices change the odds of restriction
- Flag evidence gaps before protocol lock
- Prediction studies are early and mostly non-US: a direction, not a validated tool



Sources: ISPOR Europe 2024 (Lin et al.); LSE / Value in Health 2025 (McIntyre et al.); ISPOR (Wang et al.)

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Drug X

Hypothetical example

- Oral targeted agent for a biomarker-defined subset
- Second-line metastatic NSCLC
- Biomarker present in a minority of patients
- Competitors: an approved targeted agent, and chemo-immunotherapy as standard of care
- Decision: which Phase 2 design best supports a viable label

Same molecule. Two Phase 2 designs. Which would you fund?

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Drug X designs

One design for the regulator. One for the market.

Lever	Design 1: regulator-only	Design 2: market-aware
Trial design	Single-arm, response rate primary (FDA disfavors; justification required)	Randomized, with a time-to-event signal alongside response
Confirmatory trial	Planned for “later”	Enrolling at approval
Dose	Randomized dose comparison is now expected by FDA: table stakes for both designs	
Population and assay	Narrow criteria, ex-US sites, trial-specific assay	US-representative, including brain metastases; assay payers already reimburse
Tolerability	Omitted	Patient-reported tolerability included

Design 1: faster to a readout. Design 2: faster to commercial value.

AI in practice: size the population, simulate the randomized design against budget, test which evidence payers weight.

Hypothetical example.

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AI: coverage

Illustration: design for the coverage decision.

Ask
What unlocks coverage?

Which evidence would make payers cover a drug like this one for this indication?

Mine
What did payers require?

Use AI to read payer policies and coverage decisions for comparable drugs and extract the criteria they applied

Design
Build for both

Choose endpoint, population, and duration to answer the payer's question alongside the regulator's

Design the trial for the reimbursement question, not just the scientific one.

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Two questions

A readout rewards the stock.

A label rewards the company.

Role of commercial?

Should commercial have a formal voice, in clinical trial design?

Funding plan?

Should clinical trial funding depend on a named payer-evidence plan?

Thank you