

Decentralized Trials: Naughty or Nice?

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@texhern



Duke Clinical Research Institute

FROM THOUGHT LEADERSHIP
TO CLINICAL PRACTICE

Disclosures

- Research: American Regent, Amgen, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Janssen, Merck, Novartis, Pfizer, Verily
- Consultant: Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Boston Scientific, Cytokinetics, Intercept, Merck, Myokardia, Nova Nordisk, Novartis



Agenda

Why?

What?

How?

Naughty or Nice?

Now what?



Decentralized, Remote, Virtual, Digitized Trials... New?

Review Article

Use of Mobile Devices to Measure Outcomes in Clinical Research, 2010–2016: A Systematic Literature Review

Brian Perry^{a,b} Will Herrington^c Jennifer C. Goldsack^{b,d}
Cheryl A. Grandinetti^e Kaveeta P. Vasisht^e Martin J. Landray^c
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Prader-Willi Research, Walnut, CA, USA; ⁿJanssen Research and Development,

Titusville, NJ, USA



npj | Digital Medicine www.nature.com/npjdigitalmed

PERSPECTIVE OPEN Check for updates

Digitizing clinical trials

O. T. Inan^{1,2}, P. Tenaerts², S. A. Prindiville³, H. R. Reynolds⁴, D. S. Dizon⁵, K. Cooper-Arnold^{6,21}, M. Turakhiya⁷, M. J. Pletcher⁸, K. L. Preston⁹, H. M. Krumholz^{10,11,12}, B. M. Marfin¹³, K. D. Mandl¹⁴, P. Klasnja¹⁵, B. Spring¹⁶, E. Iturriaga¹⁷, R. Campo¹⁷, P. Desvigne-Nickens¹⁷, Y. Rosenberg¹⁷, S. R. Steinhubl¹⁸ and R. M. Califf^{9,20}

Clinical trials are a fundamental tool used to evaluate the efficacy and safety of new drugs and medical devices and other health system interventions. The traditional clinical trials system acts as a quality funnel for the development and implementation of new drugs, devices and health system interventions. The concept of a “digital clinical trial” involves leveraging digital technology to improve participant access, engagement, trial-related measurements, and/or interventions, enable concealed randomized intervention allocation, and has the potential to transform clinical trials and to lower their cost. In April 2019, the US National Institutes of Health (NIH) and the National Science Foundation (NSF) held a workshop bringing together experts in clinical trials, digital technology, and digital analytics to discuss strategies to implement the use of digital technologies in clinical trials while considering potential challenges. This position paper builds on this workshop to describe the current state of the art for digital clinical trials including (1) defining and outlining the composition and elements of digital trials; (2) describing recruitment and retention using digital technology; (3) outlining data collection elements including mobile health, wearable technologies, application programming interfaces (APIs), digital transmission of data, and consideration of regulatory oversight and guidance for data security, privacy, and remotely provided informed consent; (4) elucidating digital analytics and data science approaches leveraging artificial intelligence and machine learning algorithms; and (5) setting future priorities and strategies that should be addressed to successfully harness digital methods and the myriad benefits of such technologies for clinical research.

npj Digital Medicine (2020)3:101; <https://doi.org/10.1038/s41746-020-0302-y>



What's the problem we're solving?

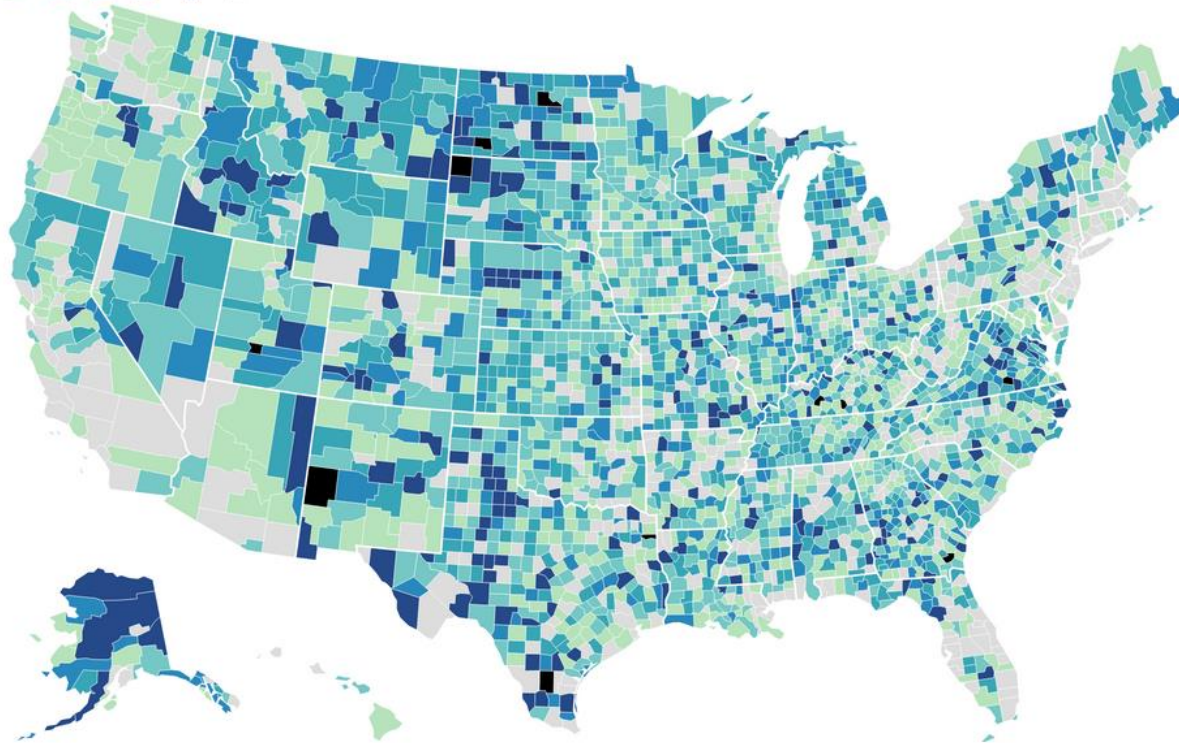


Covering Clinical Trial Deserts

Healthcare Deserts, County by County

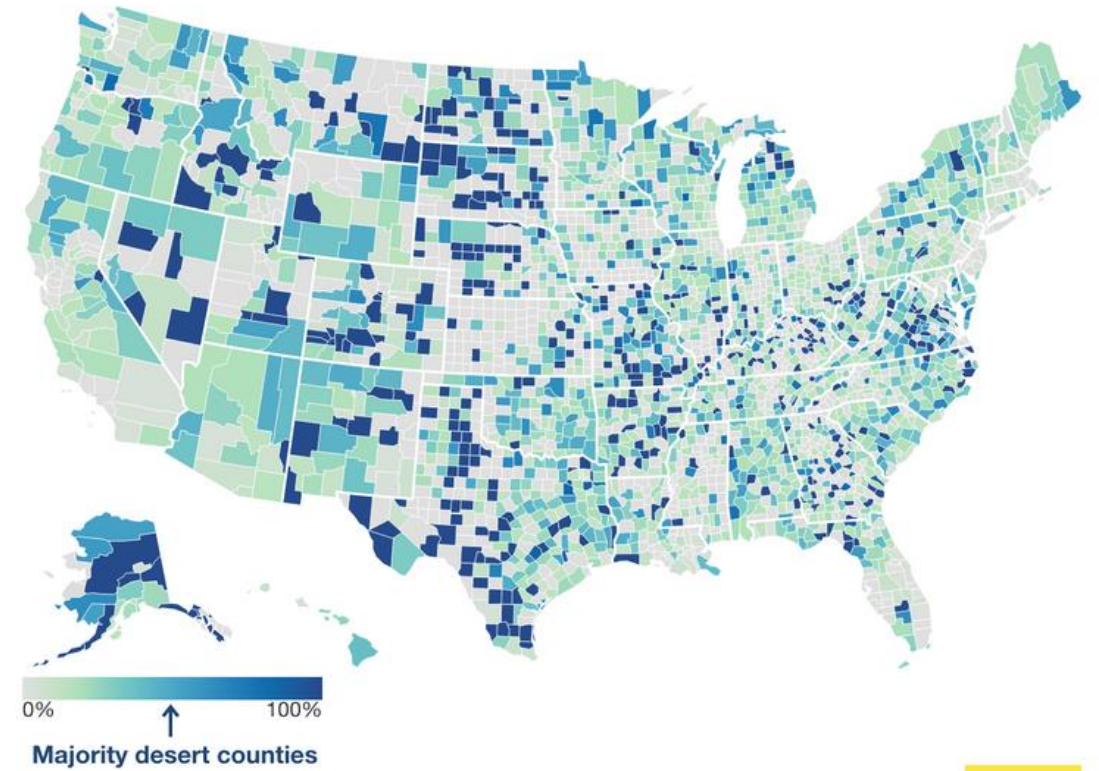
Counties where most people lack adequate access to pharmacies, primary care providers, hospitals, hospital beds, trauma centers, and/or low-cost health centers.

Number of healthcare deserts
1 2 3 4 5 6



Population Living in a Hospital Desert

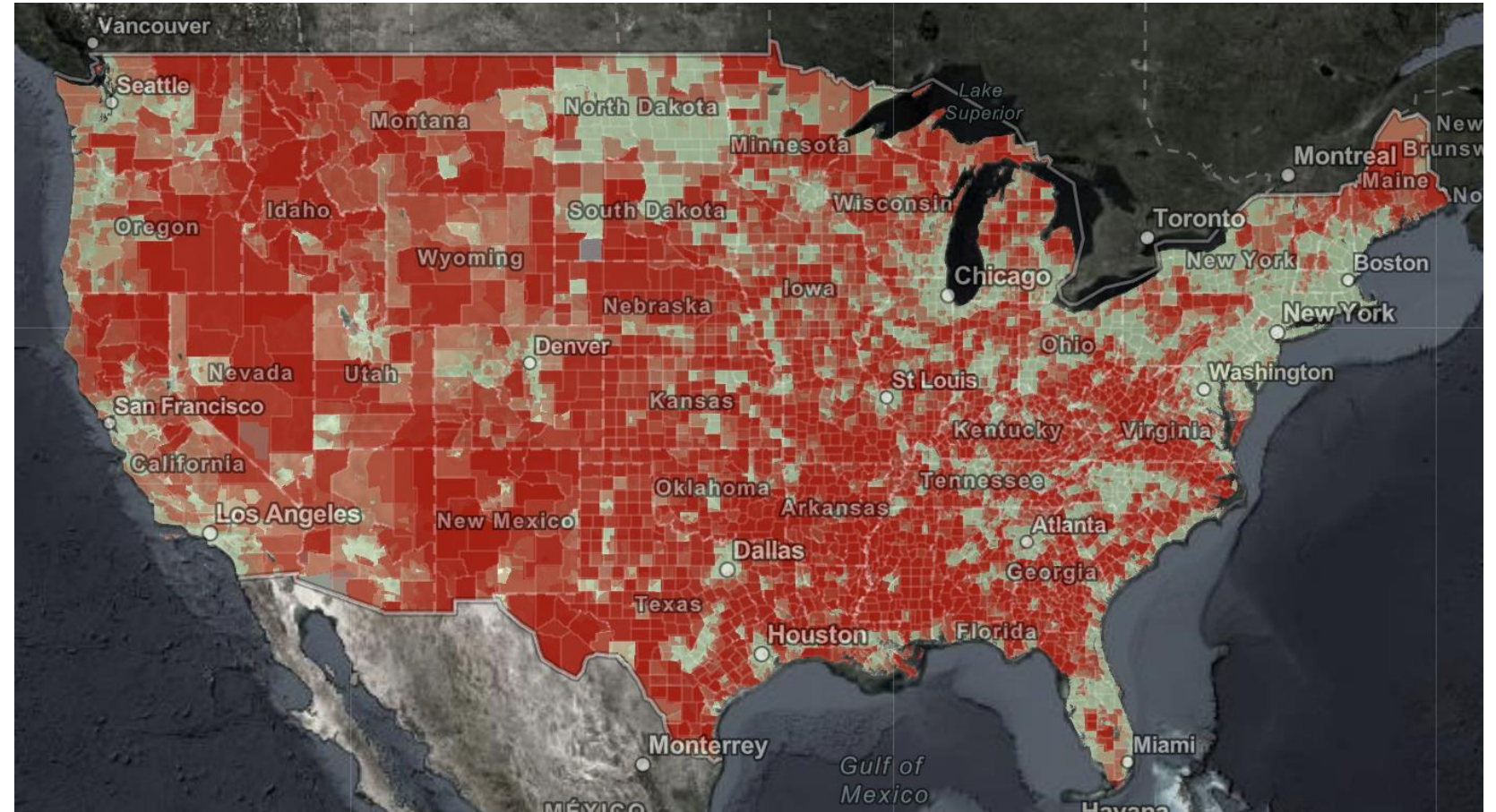
Percent of county's population living over 30 minutes from the closest hospital.



Digital Divide?



Indicators for Broadband Need



Let's consider a pandemic: Challenges vs. Opportunities

>49.6 Million
Covid Cases

>793,000
Deaths

- If 2%-4% of eligible participate in clinical trials
- For COVID-19, that could have been **~960K-1.9M** participants in a national, coordinated platform
- Why didn't that happen?



What if you enrolled...~1 million or so....



What would you rather get randomized in your stocking?



Any answer vs. the best answer

medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES



15,555

88

Observational vs. Prospective, Interventional Trials



Agenda

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How?

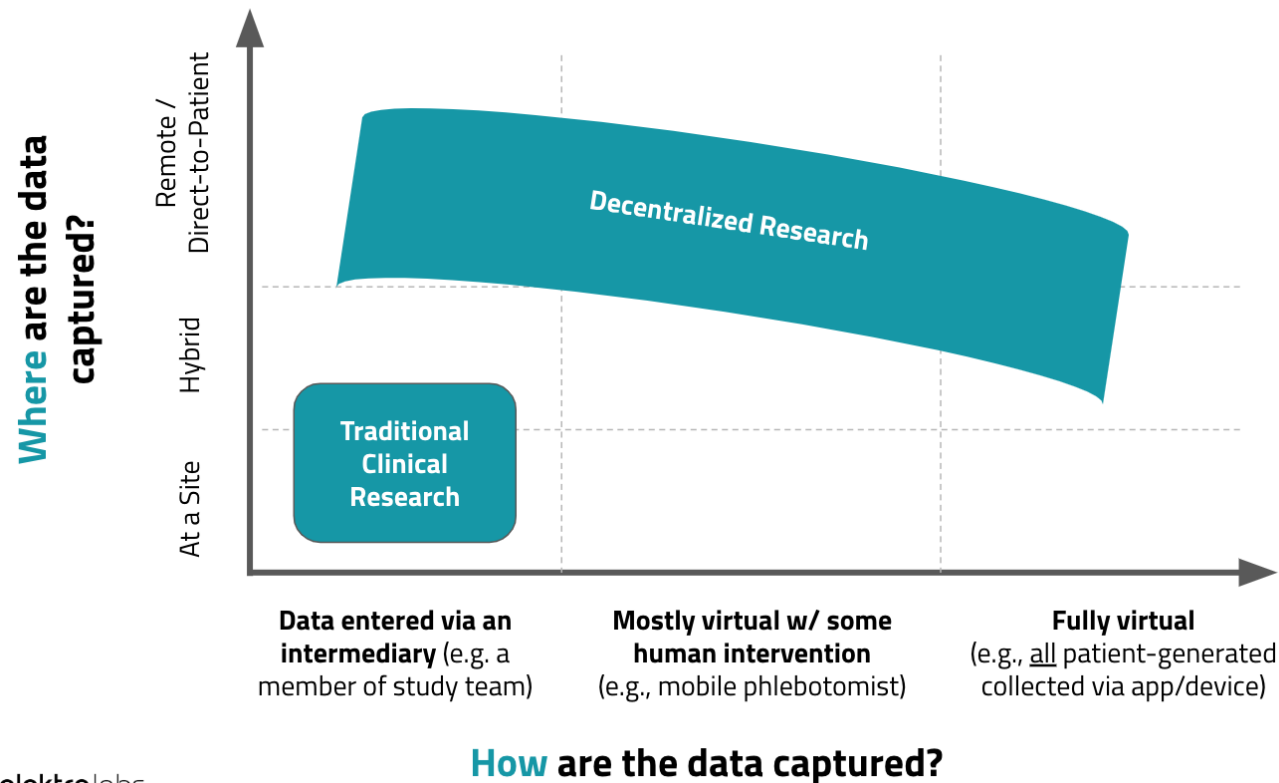
Naughty or Nice?

Now what?



Decentralize Research: A range!

Decentralized studies have two components: decreased reliance (1) on an intermediary and (2) on a physical location



elektralabs



McKinsey Review of the Market 2021

Fully decentralized ← Hybrid → Fully centralized



All trial procedures are conducted virtually, enabled by digital technologies and supply delivery

Less complex trial procedures that don't require in-person visits (eg, vital signs, electrocardiograms) are conducted via telehealthcare, remote data collection, or direct-to-patient supply

Less complex trial procedures that require in-person visits (eg, injections) are conducted via mobile clinicians or alternative sites (eg, mobile clinics, retail sites)

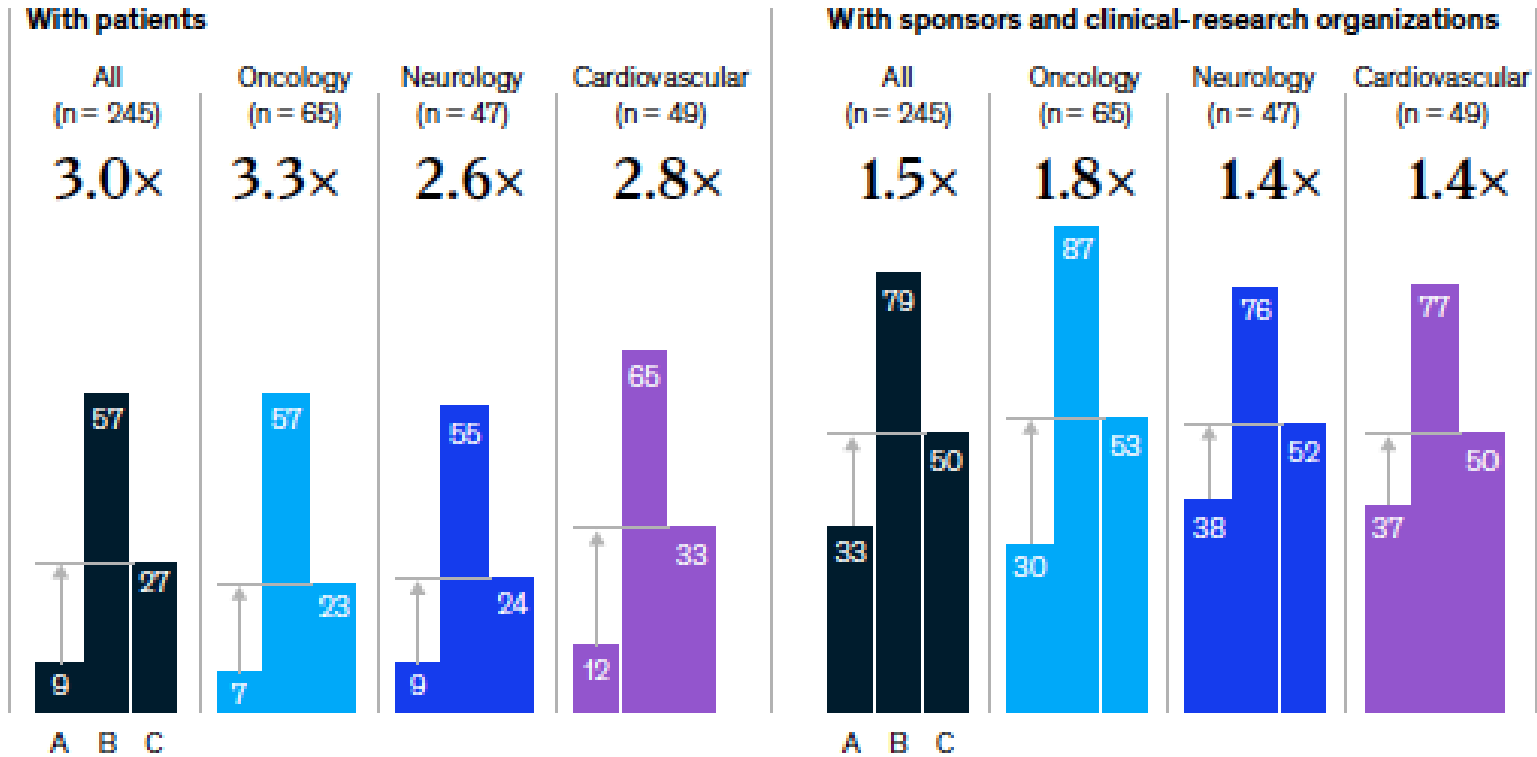
Complex trial procedures (eg, complex screening protocols, cell therapy, magnetic resonance imaging) are conducted via research sites (eg, academic medical centers) or local hospitals

All trial procedures are conducted at a research site (eg, academic medical center)

Components of remote rechnologies are here to stay

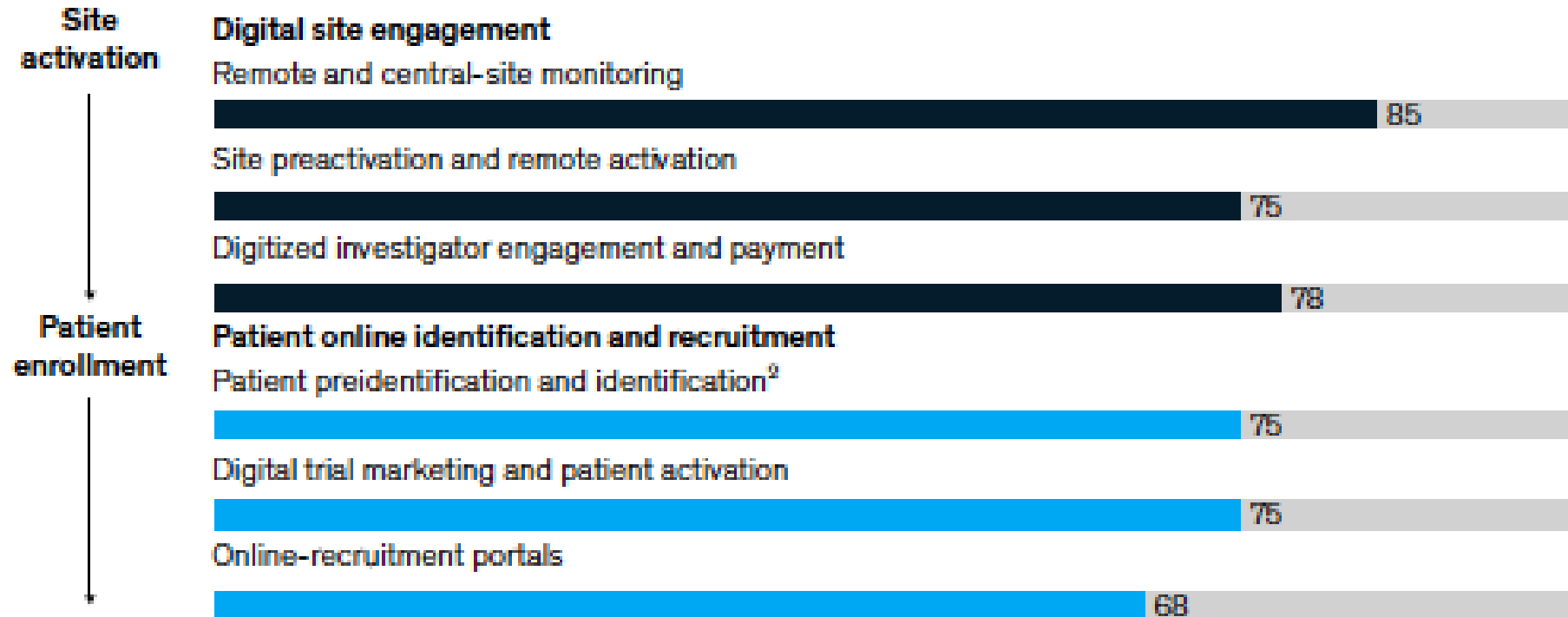
Physicians' comfort with remote technologies has increased as a result of the COVID-19 pandemic.

Clinical-trial investigators' share of virtual interactions, % of respondents¹ A. Pre-COVID-19 crisis B. At crisis peak C. 6 months postcrisis

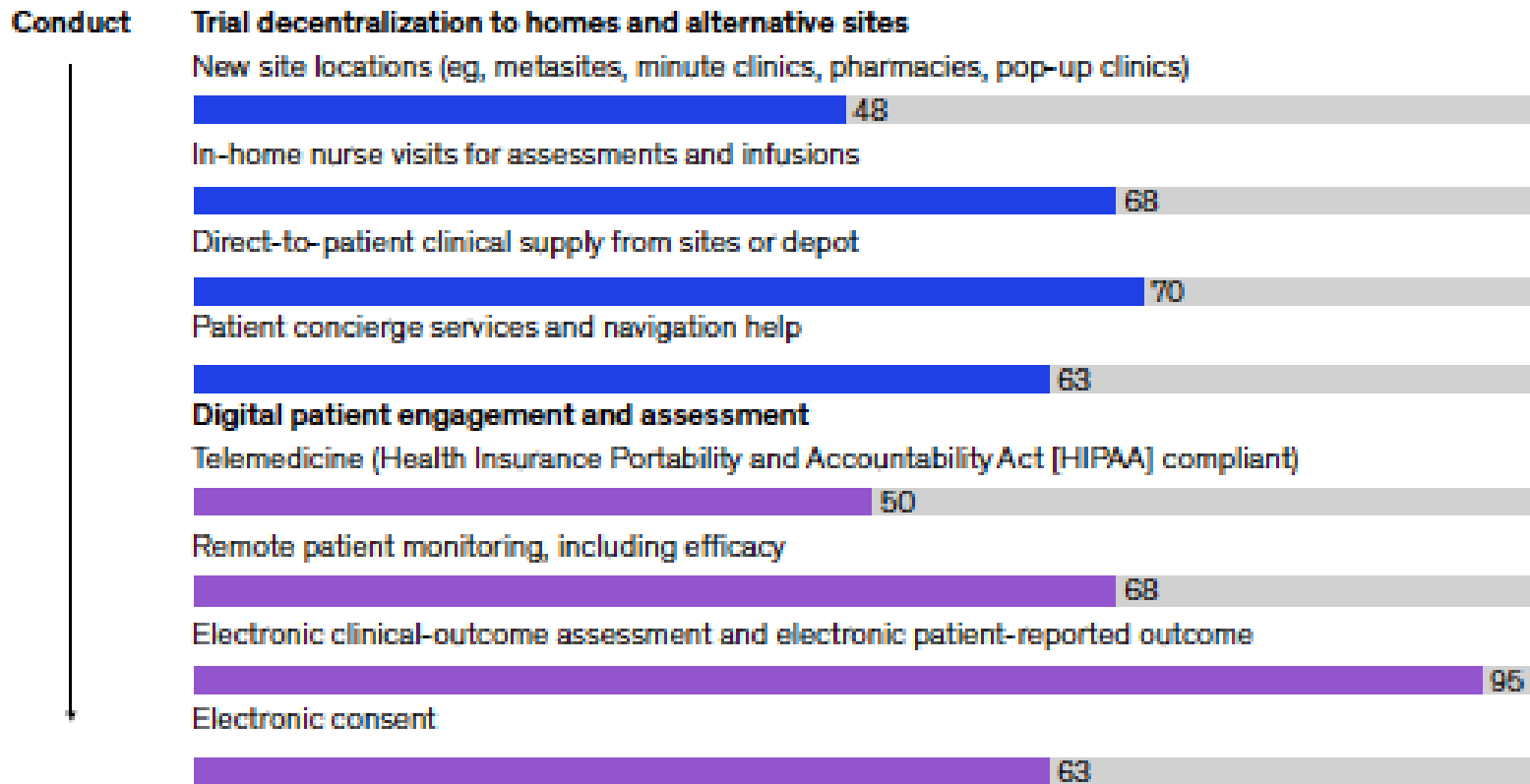


Most trials will not be fully decentralized

Activities that enable decentralized clinical-trial conduct, % of respondents¹



Most trials will not be fully decentralized



Question: Have you deployed these services in the past (pre-COVID-19 pandemic) in a Phase III trial?
For example, through digital and social media, patient communities, health records and testing, and consumer genomics.
Source: Crunchbase, McKinsey analysis

Agenda

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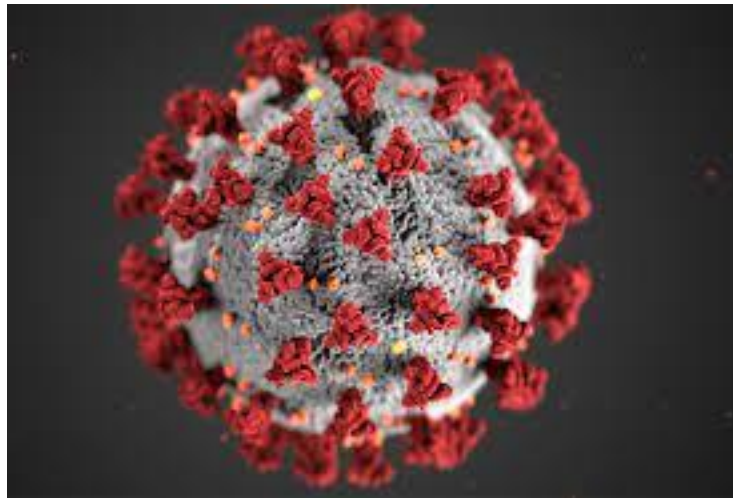
How?

Naughty or Nice?

Now what?



COVID as a change agent for Remote/Virtual Visits



Support study patients during COVID-19 lockdown & minimize exposure risk

Maintain study assessments for protocol compliance & trial integrity

Critical data collection if possible

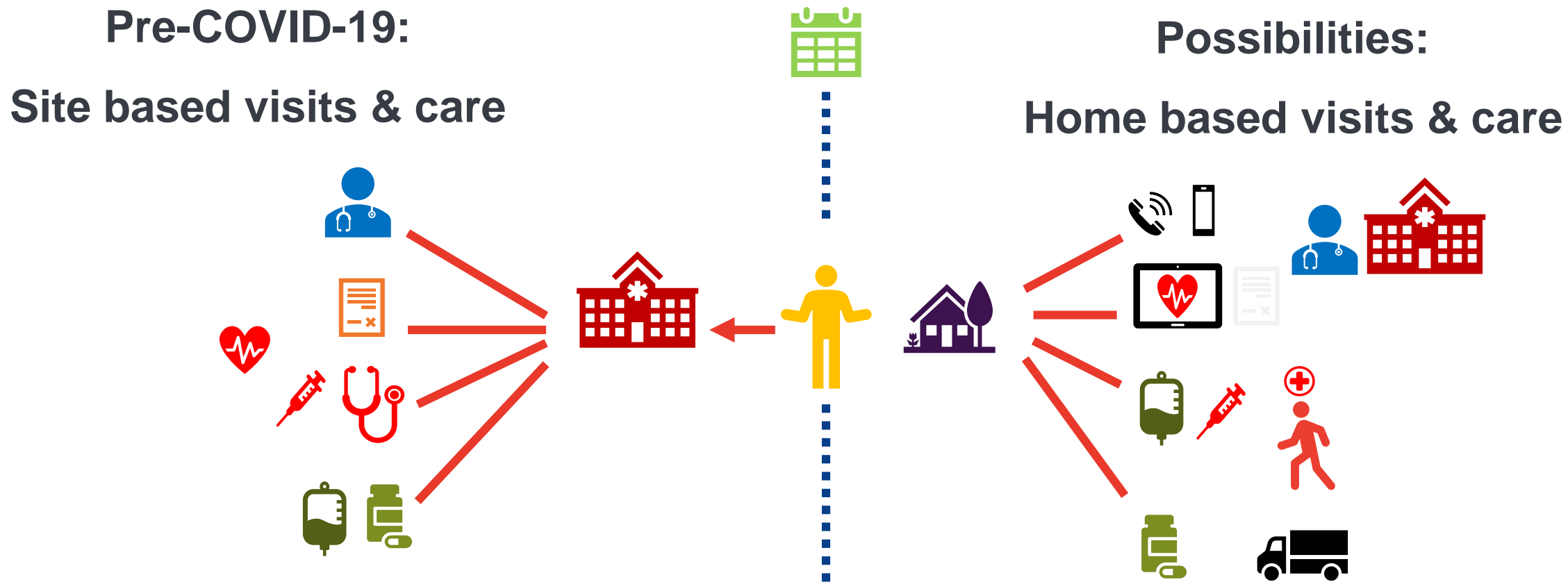
Efficacy assessments if feasible (indication dependent)

Maintain patient – physician engagement

Ensure uninterrupted study drug dosing



Going from Pre-Covid to Post COVID Clinical Trial Visits



Implementation Considerations



Case Examples on How



Duke Clinical Research Institute

FROM THOUGHT LEADERSHIP
TO CLINICAL PRACTICE

HeartLine Study (Pre-COVID)



[About the Study >](#) [Frequently Asked Questions >](#) [Our Team >](#) [For Providers >](#)

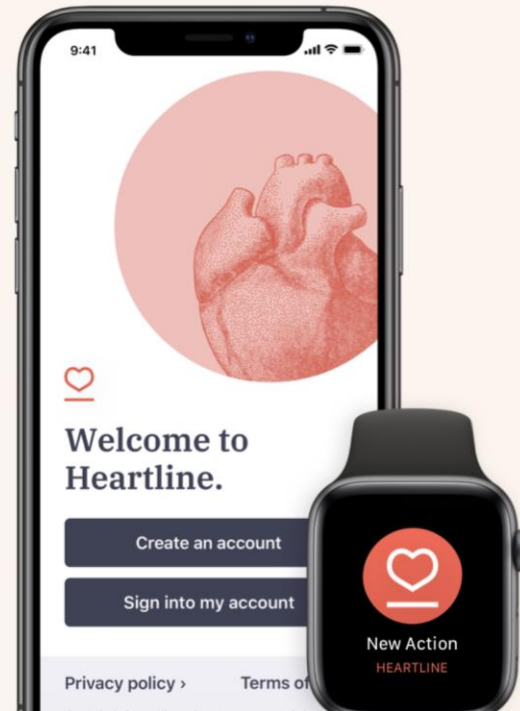


Learn about your heart health. Make a difference.

Johnson & Johnson, in collaboration with Apple, invites people 65+ to join Heartline, a heart health study on your iPhone.



A health study conducted by
Johnson & Johnson



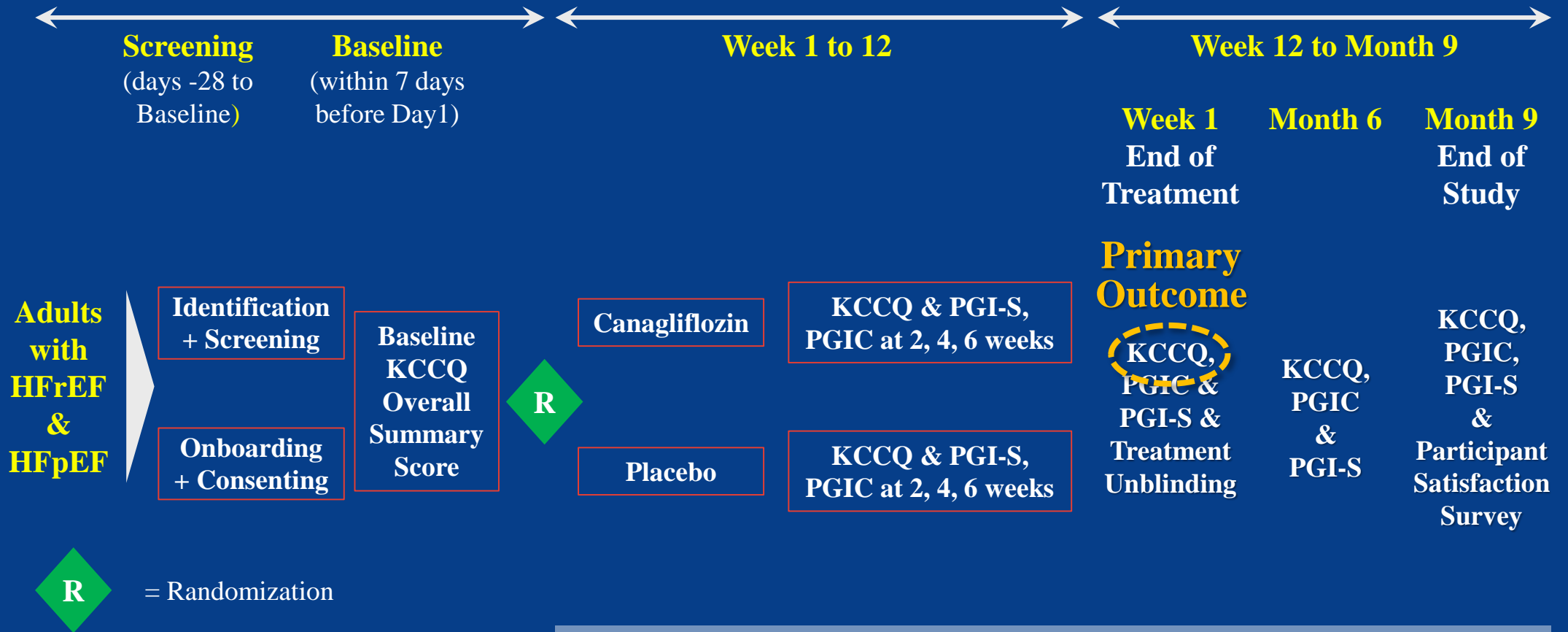
Primary objectives:

- identify and diagnose Atrial Fibrillation (AF)
- Evaluate improvement in cardiovascular (CV) outcomes
- improve direct oral anti-coagulant (DOAC) adherence and persistence
- Better characterize participants and identify predictors of disease.



An RCT without a Face-to-Face Visit

CHIEF-HF Study Schematic



*Actigraphy measures include step count, floors climbed

Claims Data Collection & Actigraphy Measures*



Healthcare Worker Exposure
Response & Outcomes

*A registry of healthcare workers impacted by COVID-19
and a platform for direct to participant studies*



STUDY SNAPSHOT

- A registry of over 50,000 diverse healthcare workers across the United States
- A platform to support studies to protect and support healthcare workers
- Rapid start-up for registry and trial

THE QUESTION

What therapeutic and psychosocial interventions can help protect and support healthcare workers at high risk of COVID-19 infection?

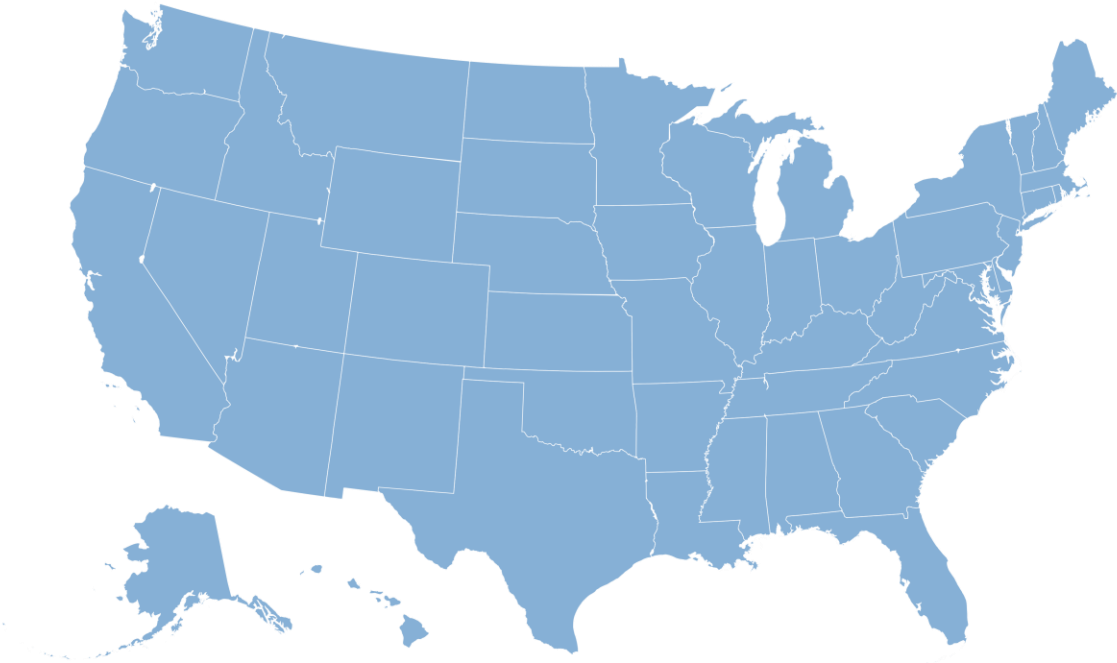
Decentralized Approach

- Platform permits participants to personalize their experience and express interest in trials and surveys, and be directed to trial sites
- Online consent and survey follow-up
- Serves as post-authorization safety study for COVID-19 Vaccine (n= 20,000)



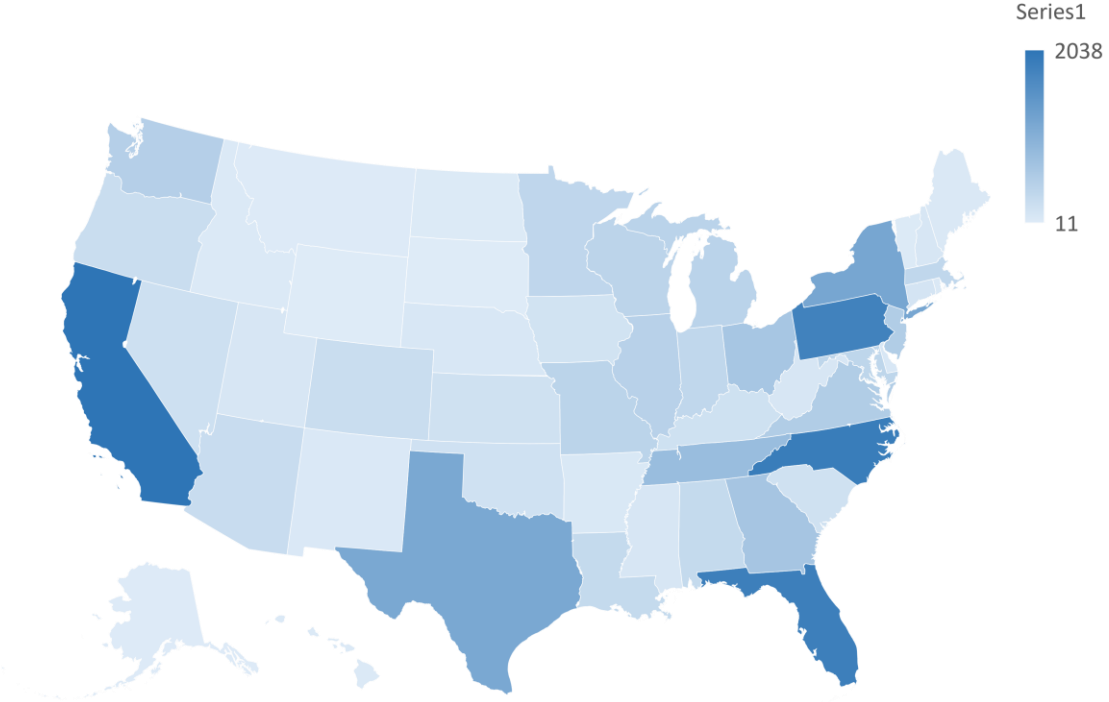
HERO-TOGETHER ENROLLMENT

Any enrollment



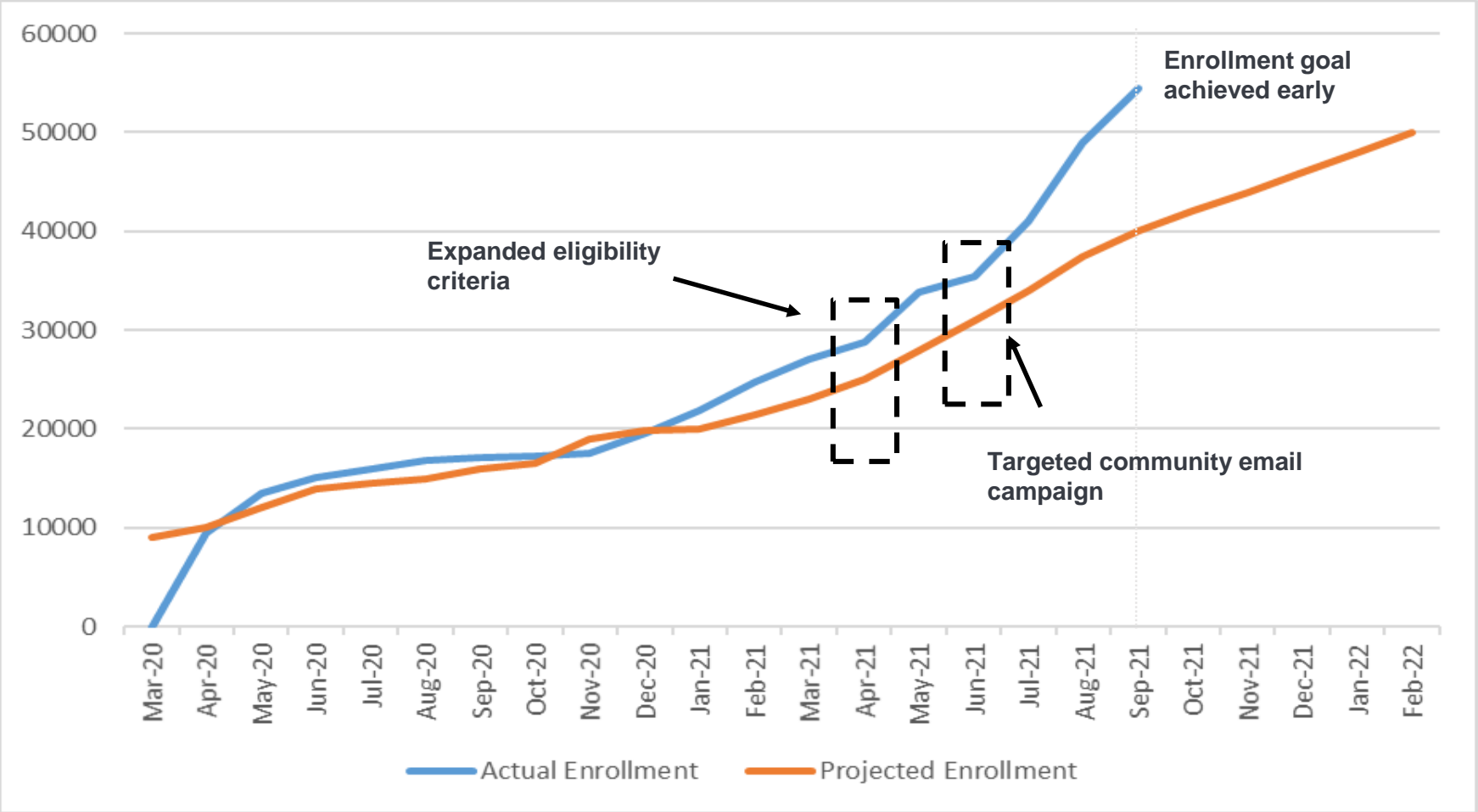
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Enrollment Density

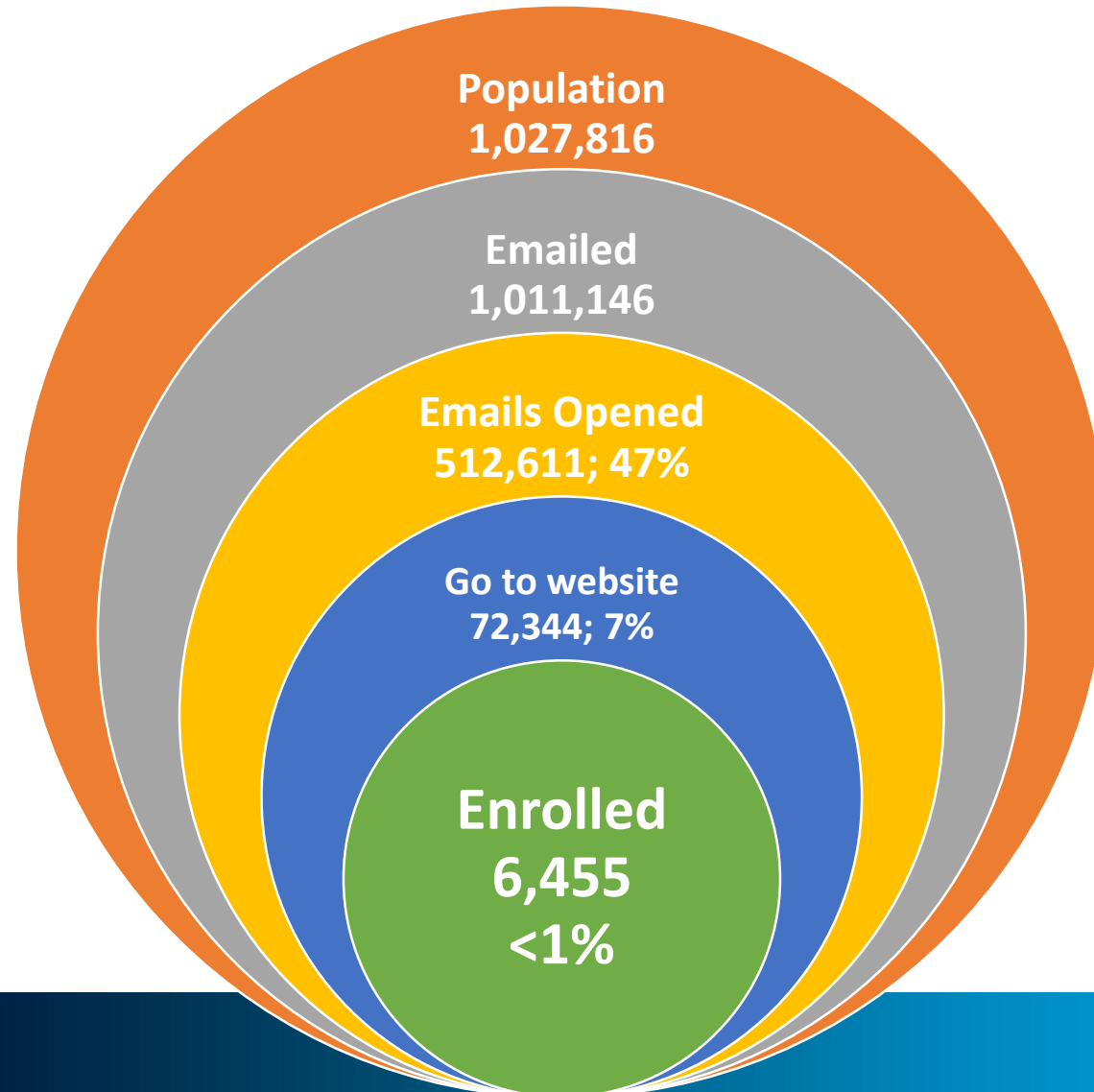


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A Challenge – Sustaining Enrollment Campaigns

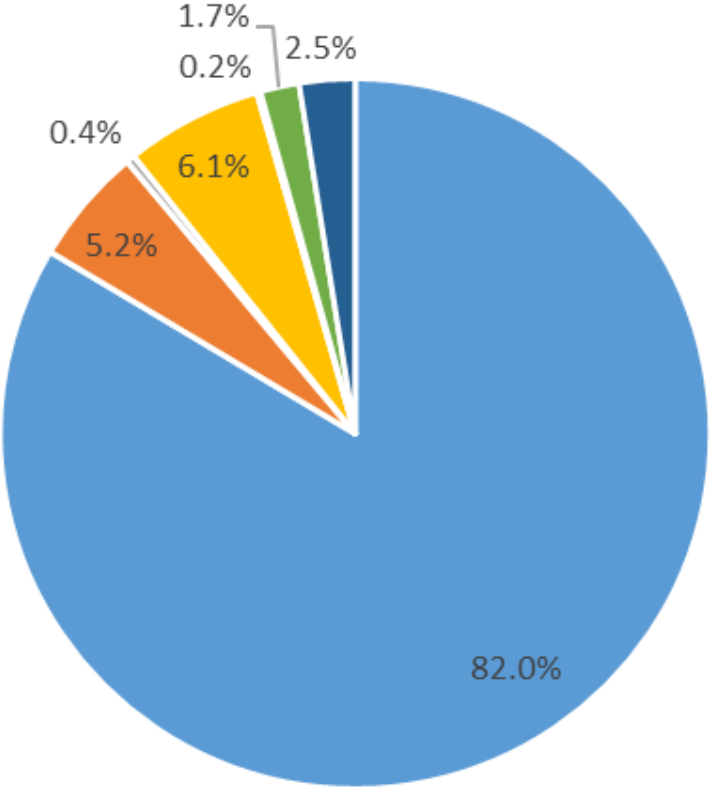


E-Touch Campaigns: Volume Matters



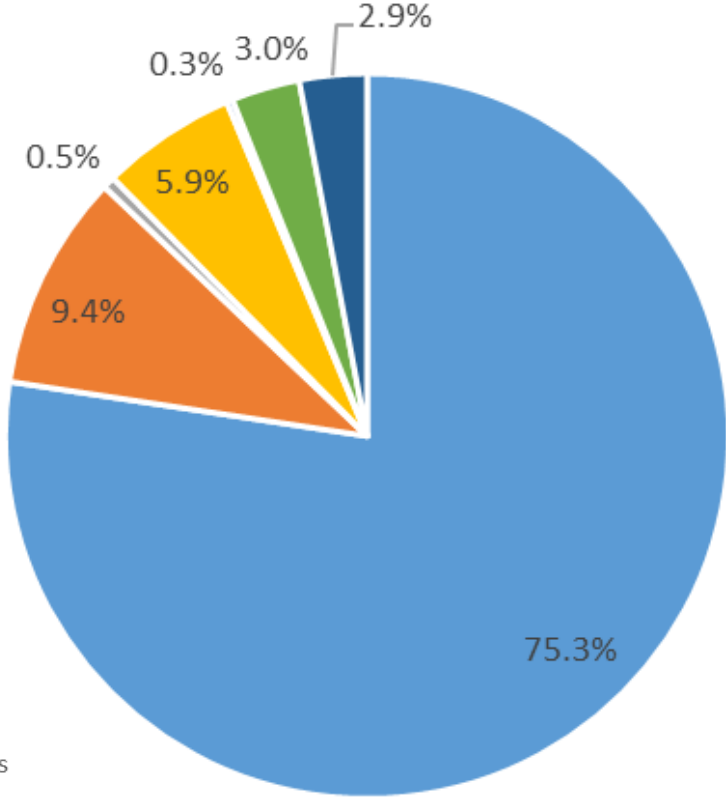
Reaching into Different Communities: Helpful?

Pre-campaign



8% Hispanic, Latino/a

Post-campaign



12% Hispanic, Latino/a

- White
- Black
- American Indian or Alaska Native
- Asian
- Native Hawaiian or Other Pacific Islanders
- Other
- Multi-race

ACTIV-6: COVID-19 Outpatient Randomized Trial to Evaluate Efficacy of Repurposed Medications

ACTIV-6 

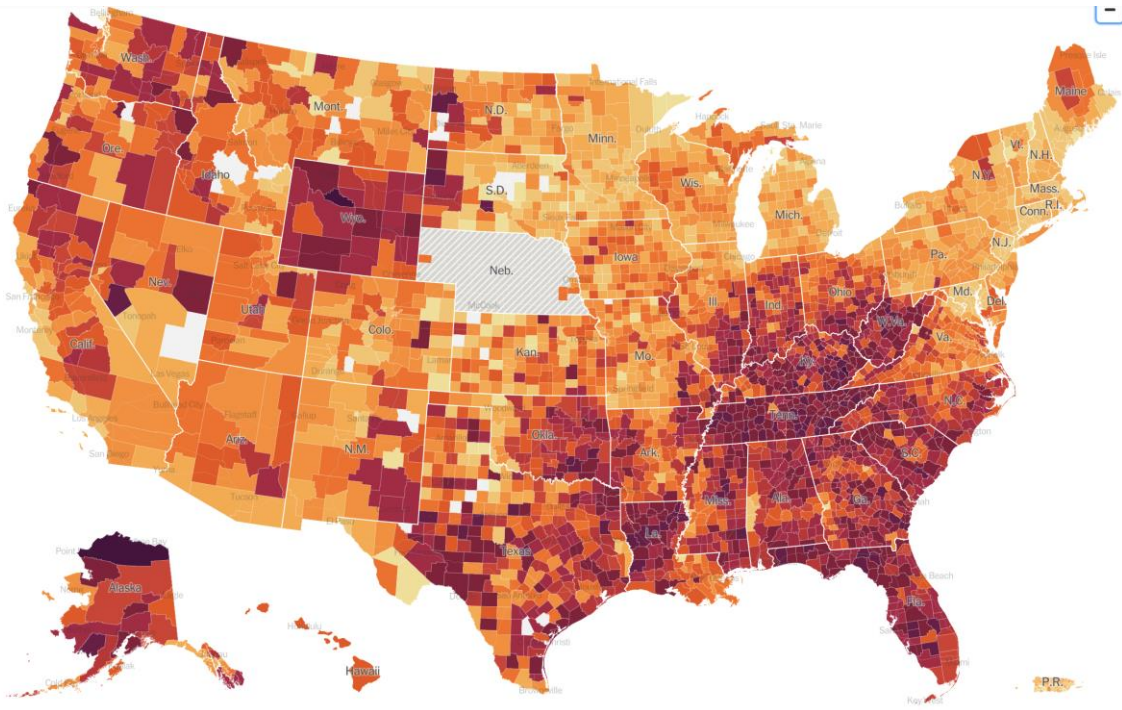
Key Questions Facing Clinicians, Patients and Caregivers

How to help people with newly diagnosed mild-moderate COVID-19 feel better faster?

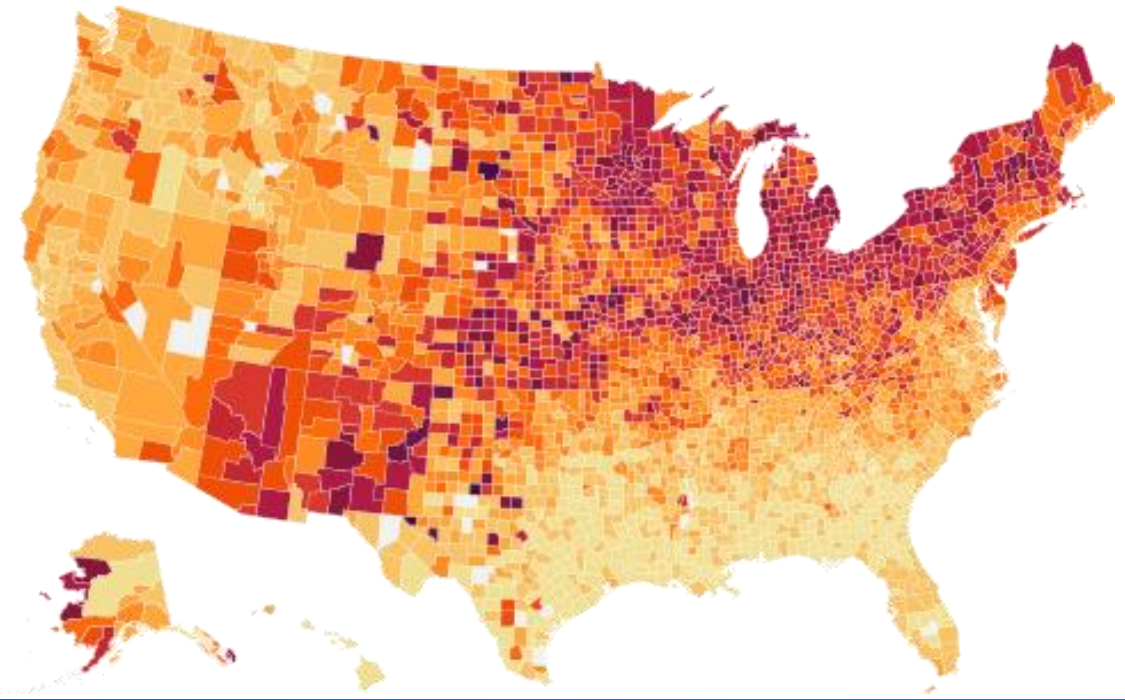
How to prevent hospitalizations or death in someone with newly diagnosed mild-moderate COVID-19?

United States Hot Spots

NY Times Sept 7, 2021



NY Times Dec 9, 2021



ACTIV-6 Hybrid Approach: Engagement, Recruitment and Follow-up

N = Tens of
thousands



ACTIV-6
eligible



Health
Systems

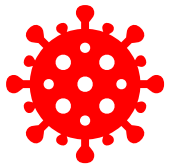


@Home

Click & Mortar

ACTIV-6 Hybrid Approach: Engagement, Recruitment and Follow-up

N = Tens of
thousands



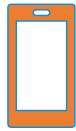
ACTIV-6
eligible



Health
Systems



@Home

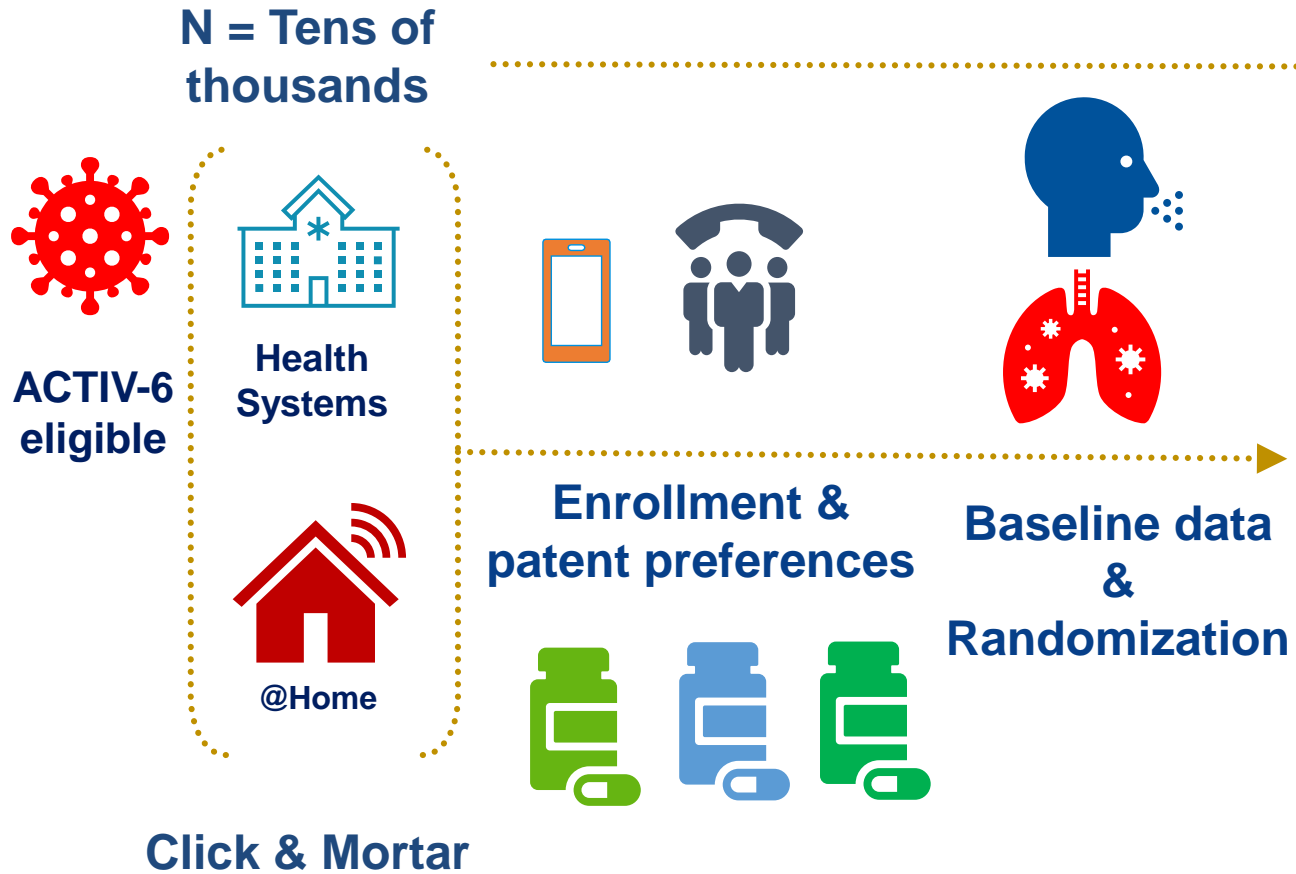


Enrollment &
patient preferences

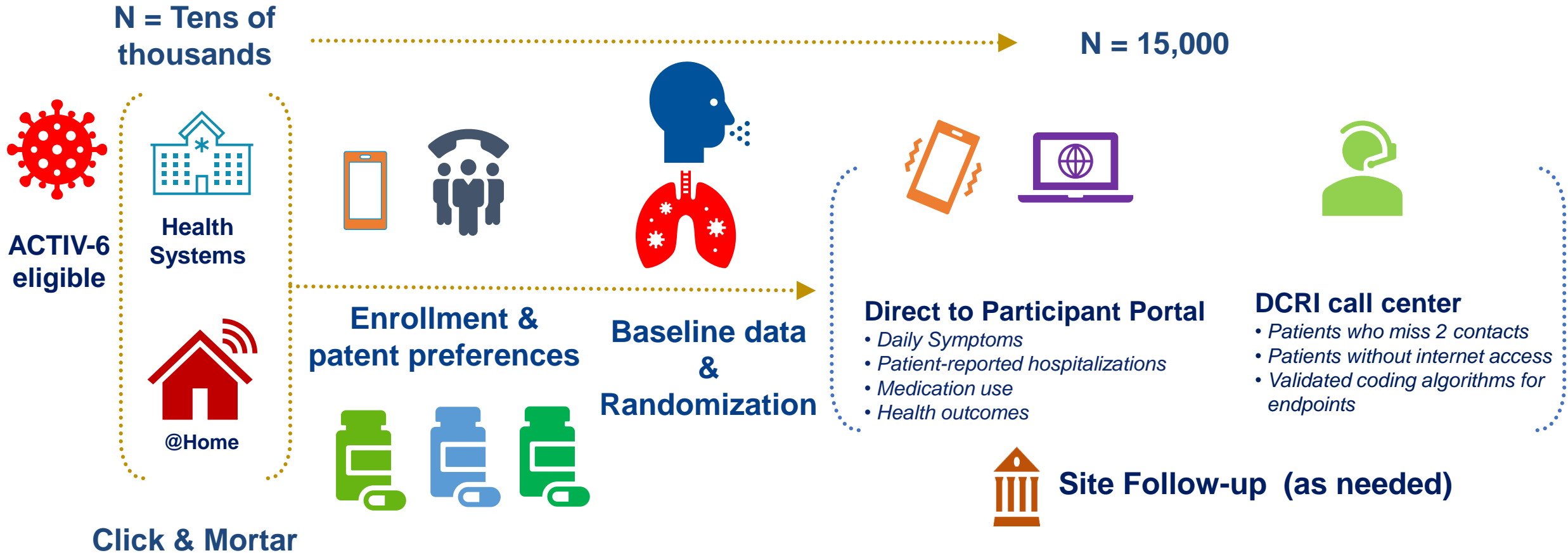


Click & Mortar

ACTIV-6 Hybrid Approach: Engagement, Recruitment and Follow-up

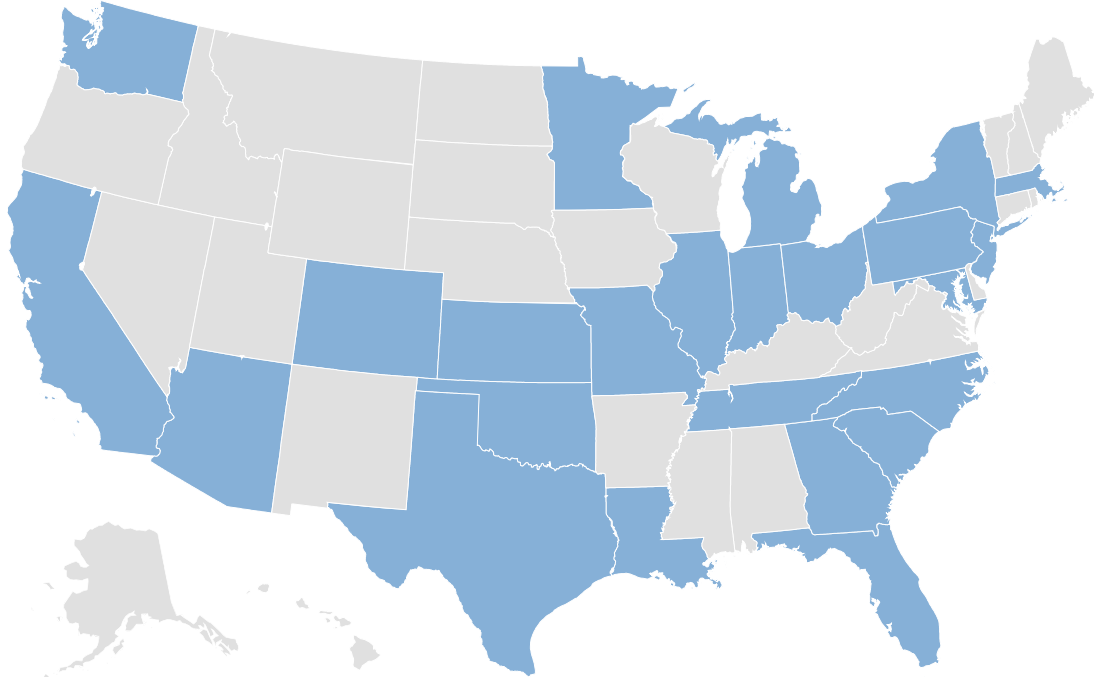


ACTIV-6 Hybrid Approach: Engagement, Recruitment and Follow-up



ACTIV-6: Enrollment by Location

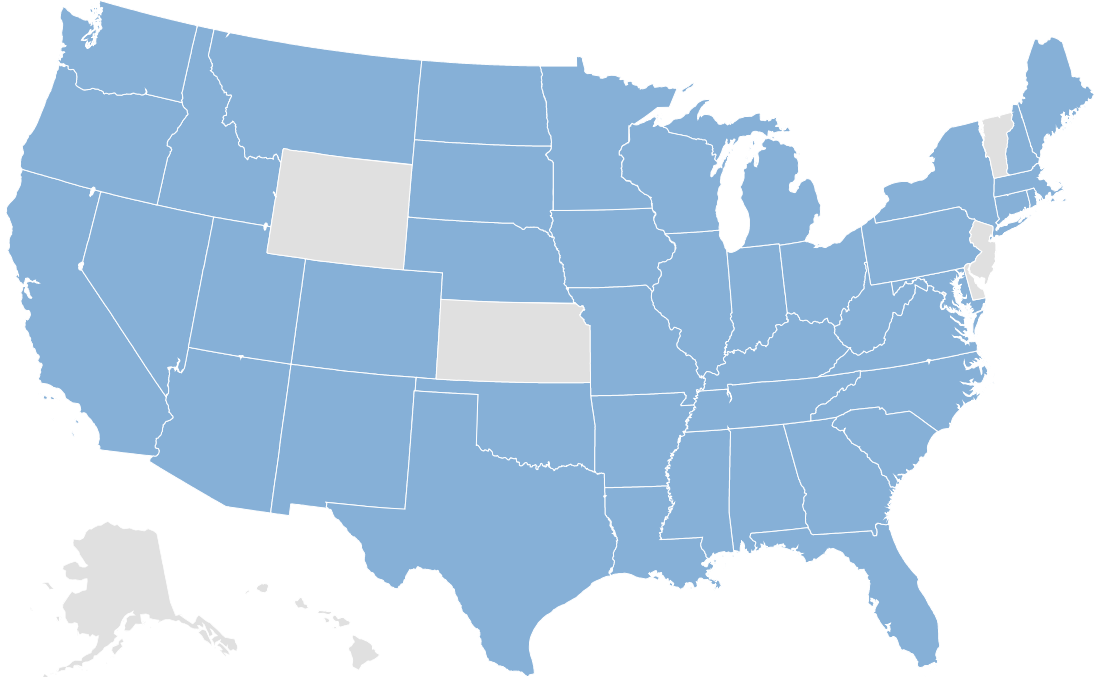
Enrollment by Local Sites



25 states

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Enrollment by DCRI PRO Center



43 states

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Agenda

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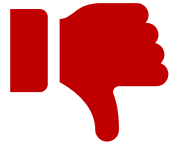
Naughty or Nice?

Now what?



Now a little game

Is this a good trial?
Vote in Chat or Reactions



Informed Consent

- Following scenarios are purely hypothetical.
- They may or may not represent real research questions, populations or drugs or devices.
- Your answer will not be disclosed outside of this session.
- Your answer is from you as an individual and does not represent your institution, organization or any sports affiliation.



Scenario 1: OmegaMiracleTrial

- You just left your doctor's office in Port Arthur, Texas with a new diagnosis of a rare disease called omega (Ω). They inform you they have nothing they can offer and no other major center in Texas has any clinical trials.
- Google search:
 - Incidence = 1/1Million. 5-year survival rate= 10%
 - Discover world's leading research center in San Francisco with a new drug, omegawondershot, in pivotal phase 3 trial.
- Omegawondershot is 1 shot regimen given every year. Given the ease of use and safety profile in development, the research center is offering on site and siteless trial.
- You have no gas money or travel money.
- You decide to enroll into the trial online.

Is this a good trial?
Vote in Chat or Reactions



Scenario 2: OmegaCURETrial

- You are the world's expert in a rare disease, omega (Ω) and have invented a cure, Omegawondershot!
- Given how rare the disease is you realize it will take 30 years to complete the pivotal trial if you only rely on your site or colleagues who see this population.
- You launch a siteless trial and purchase access to global electronic record vendor to identify potential candidates for the trial. Somehow, you are able to contact candidates through the vendor to offer the trial.
- You also set-up social media ads including with "cure" tags for any searches for omega disease.

Is this a good trial?
Vote in Chat or Reactions



Scenario 3: Pi Prevention of Death Trial

- You just left your doctor's office in Port Arthur, Texas with a new diagnosis of a common disease called pi (π) that ultimately leads to heart attacks, strokes and cardiovascular death.
- However, your doctor tells you there isn't a gold-standard treatment yet.
- As you start searching google, you notice a lot of different options to treat pi including snake oil, gummy bears, candied apples and stem cells.
- You're intrigued with the idea of stem cells and stumble on a site that is offering a remote clinical trial of a therapy called reincarnationstemcells.
- Given your busy day job and limited time to go to trial site, you decide to enroll into this siteless trial testing reincarnationstemcells.

Is this a good trial?
Vote in Chat or Reactions



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As decentralized trials become more popular...

What are the differences of decentralized trials compared to other types?

- Right people?
- Right interventions or exposure?
- Right outcomes?
- Right safety outcomes?
- Retention? (especially > long-term trials)
- Right processes?
 - Are there any ethical or regulatory boundaries or uncertainties?
- Right engagement with patients, clinicians?



A Check List: Decentralized Trials

Trial Characteristic	Naughty	Nice
Engagement Patient Clinician		
Eligibility criteria confirmation		
Representative cohort		
Consent Comprehensive Format		
Data Collection		
Quality assurance (Source documents)		
Endpoint adjudication		



Conclusions:

- Carpe Diem: Leverage learnings from COVID-19 for decentralized methods
- Integrating decentralized methods offers potential
 - Filling in clinical trial deserts
 - Meeting people where they are
 - Closing the research and evidence gaps
- But let's create the research on research & policies
 - Benefits vs. risks of decentralized trials
 - Promote *honesty over hype*
 - Ensuring ethical and informed methods

