Digital, Decentralized, and Democratized: New Approaches to (Long COVID) Research

The PaxLC Trial Team

October 27, 2023

Yale SCHOOL OF MEDICINE

The PAX LC Trial

US IND Number: *164417*

ClinicalTrials.gov ID: *NCT05668091*

Principal Investigator

Dr. Harlan Krumholz

Study Design

A decentralized Phase 2, 1:1 randomized, double-blind, superiority, placebo-controlled study on non-hospitalized highly symptomatic adult participants with Long COVID.

Aim

To determine the efficacy, safety, and tolerability of 15 days of nirmatrelvir/ritonavir compared with placebo/ritonavir.

Rationale

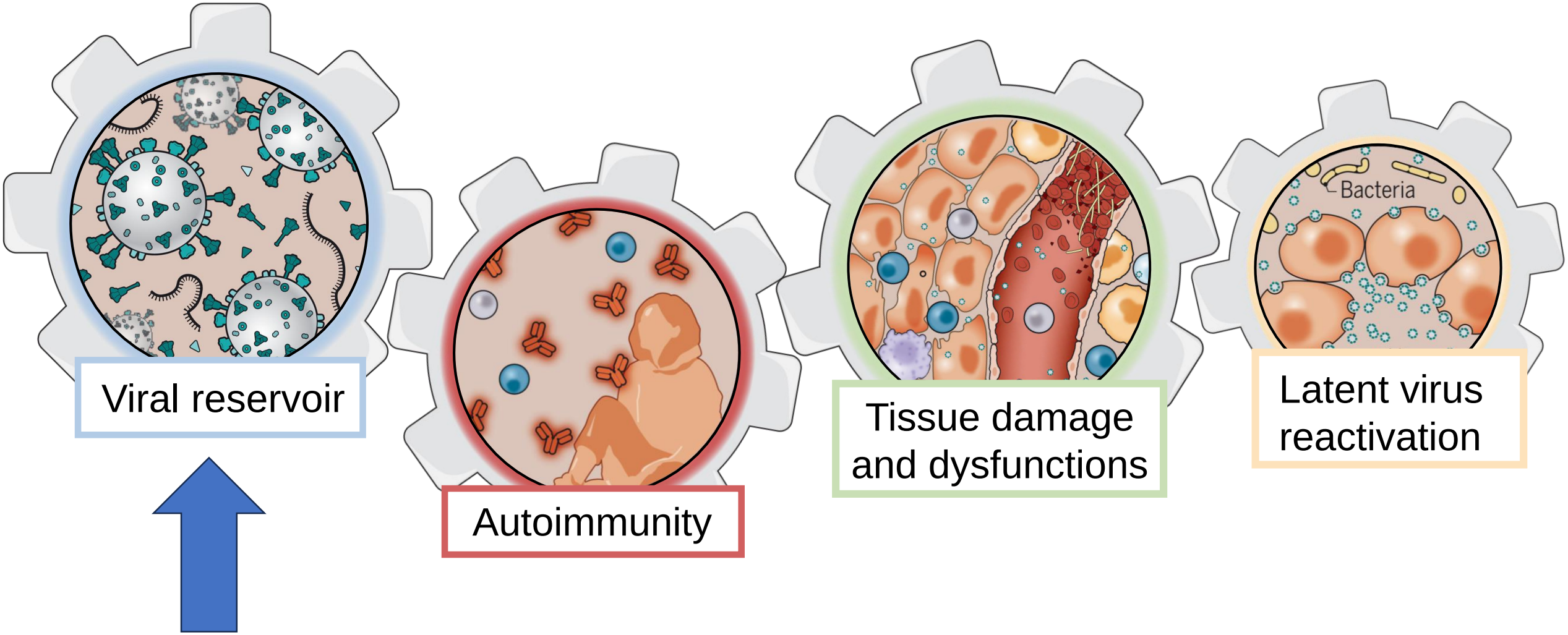
A plausible mechanism for PASC is viral persistence. PAXLOVID, which includes nirmatrelvir (PF-07321332), an antiviral agent that targets the SARS CoV-2 3- chymotrypsin–like cysteine protease (Mpro: also referred to as 3CLpro or nsp5 protease), and ritonavir, a human immunodeficiency virus (HIV)-1 protease inhibitor and CYP3A inhibitor.

Outcomes

- Primary outcome is the PROMIS-29 Physical Health Summary Score at Day 28 (2 weeks after the end of the trial drug treatment).
- Secondary outcomes will include other health status measures.
- Exploratory outcomes: immunophenotyping to explore the effects of treatment on immune signatures and immune markers of response.

Number of Participants: 100

Four possible root causes of long COVID



Decentralized study design

Non-hospitalized symptomatic adult participants with PASC (WHO definition)

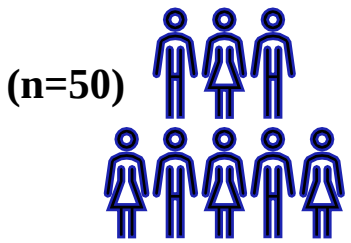
Preliminary consent

HIV, renal, liver function, TSH (thyroid), CBC counts, pregnancy tests (CLIA approved tests)

Screened PASC participants (*n= 100*)

Randomization

No history of clinically significant hypersensitivity to the product
No known/suspected debilitating chronic conditions
HIV negative
Liver function normal
Renal function normal
TSH levels normal
Not Pregnant
Not breastfeeding
No neutropenia



(n=50)

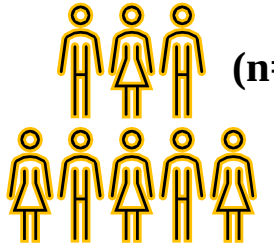
Placebo /Ritonavir

Day1-Day 15

15 days
2doses/ day

Nirmatrelvir/Ritonavir

Day1-Day 15



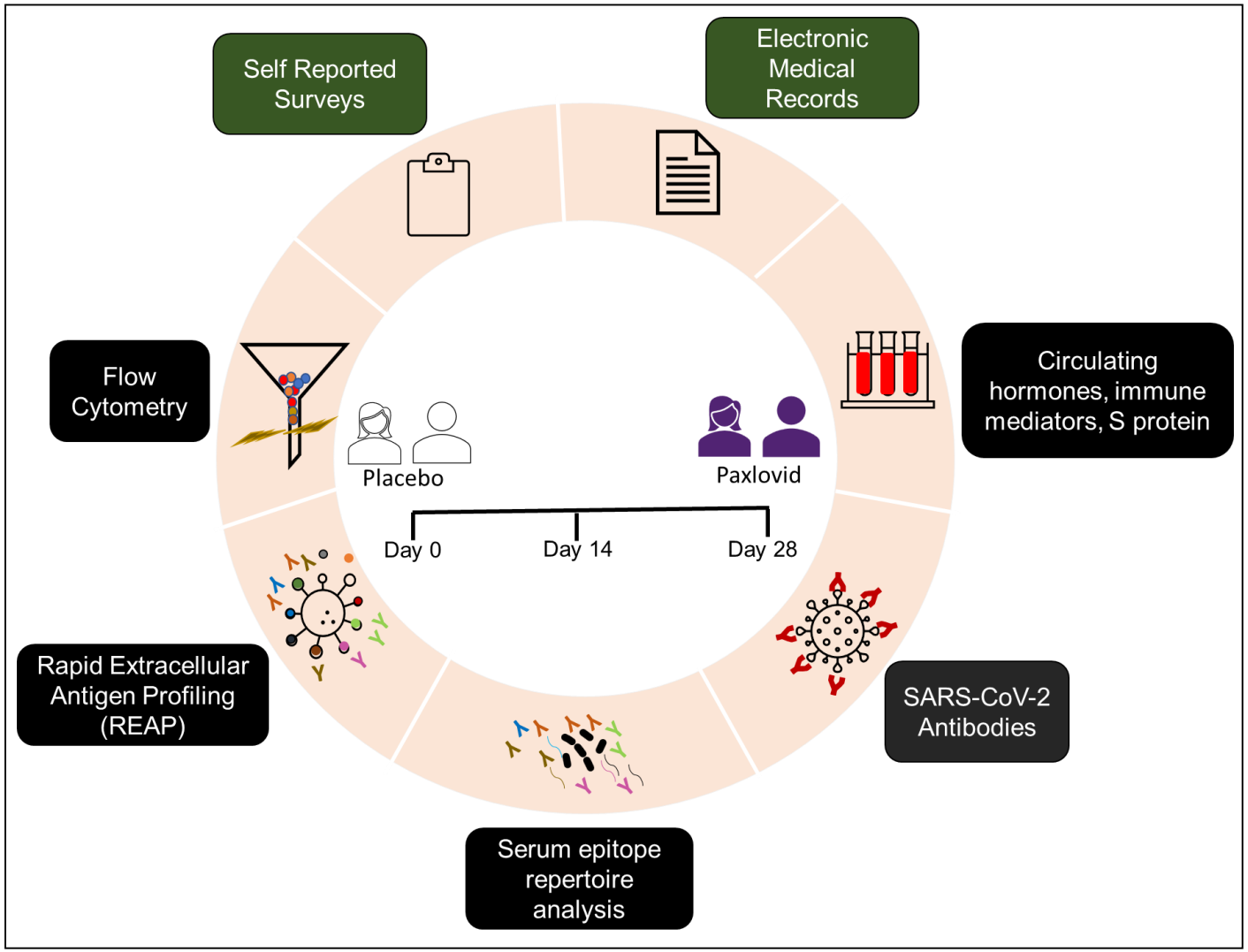
(n=50)

Biospecimen Collection

Day 0 — Day 14 — Day 28

Pharmacokinetics analyses

Deep immune phenotyping



Disclosure

Harlan Krumholz is a co-founder of Hugo Health, a digital health company that enables people to gain agency over their health data and provide permissions for sharing. Hugo Health is being used in the PaxLC study.

Yale Center for Clinical Investigation

Center for Infection & Immunity

Yale SCHOOL OF MEDICINE


NORGE

This talk describes our strategies to implement **digital, decentralized, and democratized** approaches to multidisciplinary research.

Our approach seeks to address the deficiencies of traditional research studies, which can tend to be **hierarchical, siloed, slow, expensive, and inconvenient.**

We believe that research can improve by simultaneously leveraging **advances in technology and culture.**

Our studies must be **convenient, meaningful, respectful, efficient, rapid, and fair**.

The research optimization requires **partnership with participants**, including involvement in study design and workflow, data collection and analysis, and data and results sharing.

Participants should have access to investigators and the results of the studies.

So, we have developed an approach that is **digital, decentralized, and democratized.**

PaxLC Trial Goals

Meet or exceed the standards of traditional trials

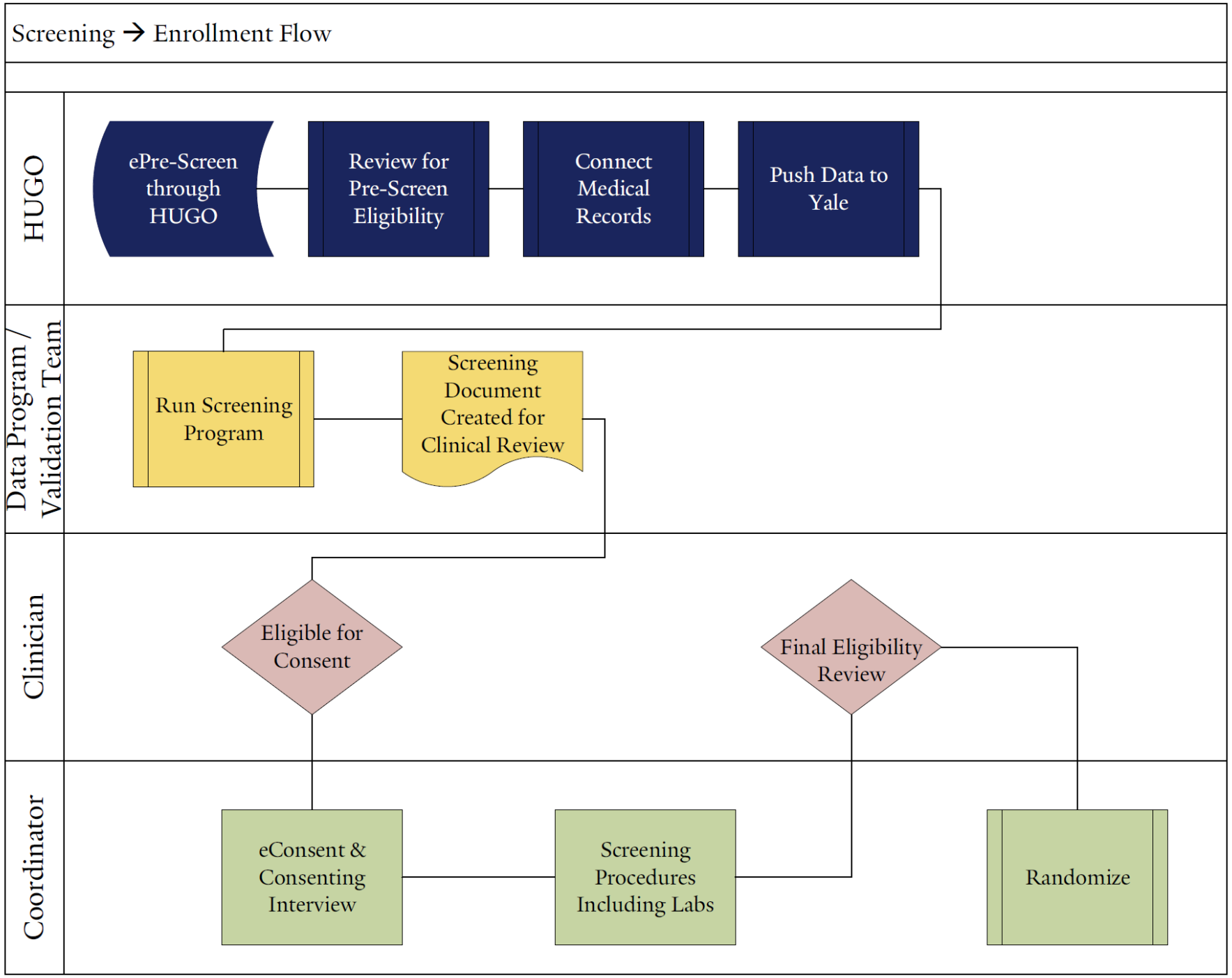
Optimize rigor, access, convenience, efficiency, and speed

Support meaningful participant partnership

PaxLC brings together many innovations.

- Online screening
- Digital medical record review
- e-Consent
- Home-delivery of medications
- Local clinical blood draws
- Home-based biospecimen collection
- Online diaries and surveys
- Digital medical record outcomes
- Participant-centricity, and return of results


WASHINGTON
OREGON
CALIFORNIA
IDAHO
NEVADA
MONTANA
WYOMING
UTAH
ARIZONA
COLORADO
NEW MEXICO
NORTH DAKOTA
SOUTH DAKOTA
NEBRASKA
KANSAS
OKLAHOMA
TEXAS
MINNESOTA
IOWA
MISSOURI
ARKANSAS
LOUISIANA
WISCONSIN
ILLINOIS
MICHIGAN
INDIANA
OHIO
KENTUCKY
TENNESSEE
MISSISSIPPI
ALABAMA
GEORGIA
FLORIDA
SOUTH CAROLINA
NORTH CAROLINA
VIRGINIA
WEST VIRGINIA
PENNSYLVANIA
NEW YORK
MARYLAND
DELAWARE
NEW JERSEY
DC
VERMONT
NEW HAMPSHIRE
MAINE
MASSACHUSETTS
CONNECTICUT
RHODE ISLAND


Screening → Enrollment Flow
HUGO
ePre-Screen through HUGO
Review for Pre-Screen Eligibility
Connect Medical Records
Push Data to Yale
Data Program / Validation Team
Run Screening Program
Screening Document Created for Clinical Review
Clinician
Eligible for Consent
Final Eligibility Review
Coordinator
eConsent & Consenting Interview
Screening Procedures Including Labs
Randomize

Thank you.

harlan.krumholz@yale.edu