ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

IDeA States Pediatric Clinical Trials Network

SCT
SOCIETY FOR CLINICAL TRIALS

Overview of the IDeA States Pediatric Clinical Trials Network Sites and DCOC

Song Ounpraseuth, PhD
ISPCTN Data Coordinating and Operations Center
University of Arkansas for Medical Sciences
STOunpraseuth@uams.edu
501-686-7233

Disclosures

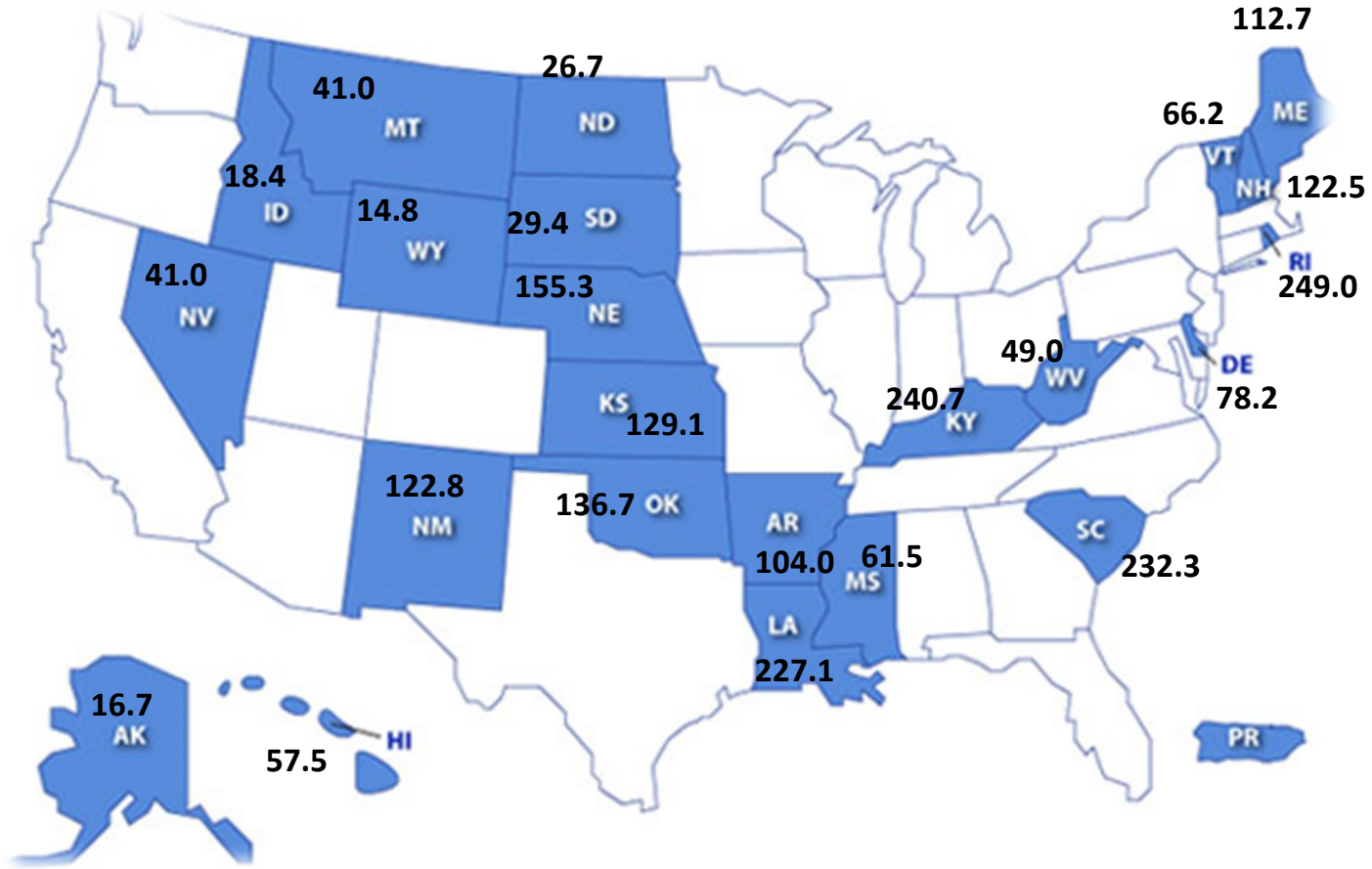
- No Relevant Disclosures
- No Conflict of Interest
- Research reported in this presentation was supported by the Office of the Director of the National Institutes of Health under award numbers UG1OD024955; UG1OD024948; UG1OD024943; UG1OD024946; UG1OD024942; U24OD024957; UG1OD024959; UG1OD024950; UG1OD024951; UG1OD024958; UG1OD024944; UG1OD024952; UG1OD024956; UG1OD024945; UG1OD024954; UG1OD024947; UG1OD024949; UG1OD024953.

Outline

- Overview Network
  - Criteria for sites
  - ECHO Focus Areas
  - Network Goals
- Overview of DCOC
- Network Studies
- Cross Group Studies with Other Networks

Criteria for IDeA State

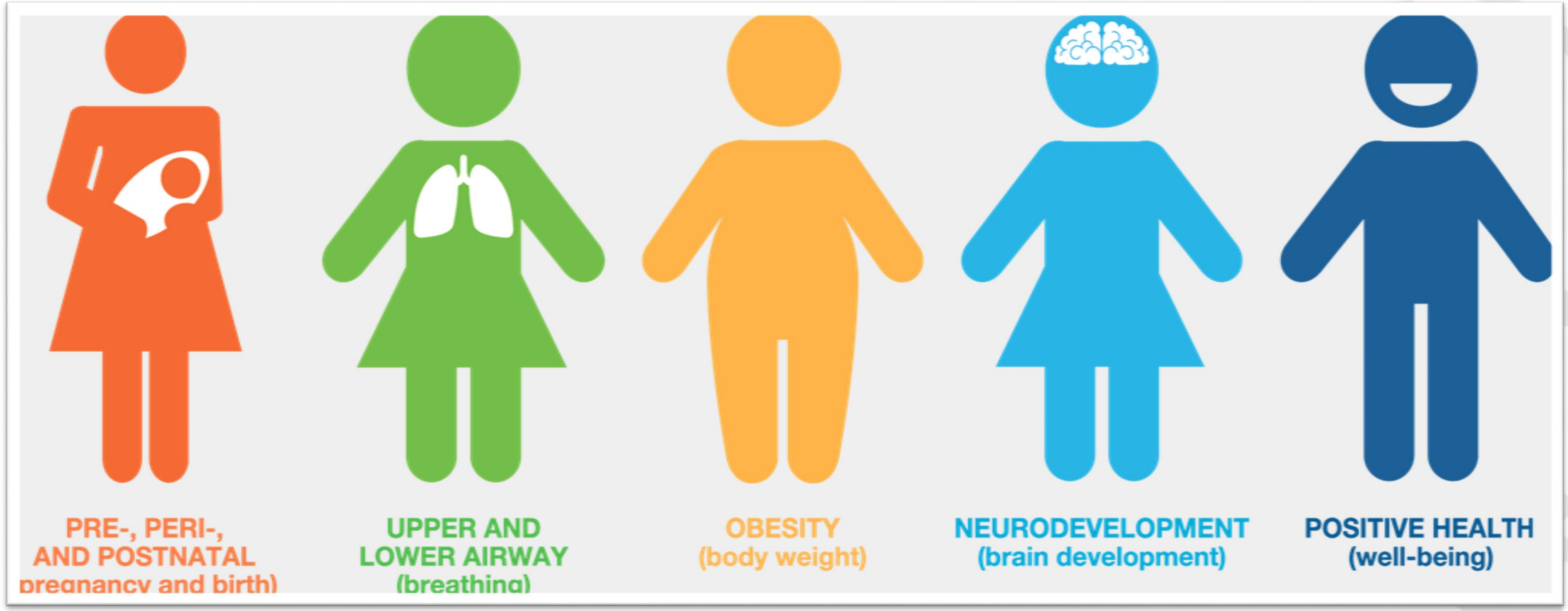
- The Institutional Development Awards (IDeA) Program (23 states and Commonwealth of Puerto Rico)
  - Authorized by Congress in 1993
  - Goal of broadening the geographic distribution of NIH funding for biomedical & behavioral research to states with historically low success rate



NIH Research FY2022 ($M)

- 50 states plus DC ($36,683)
- 23 IDeA states ($2,332)
- 18 ISPCTN states ($2,119)

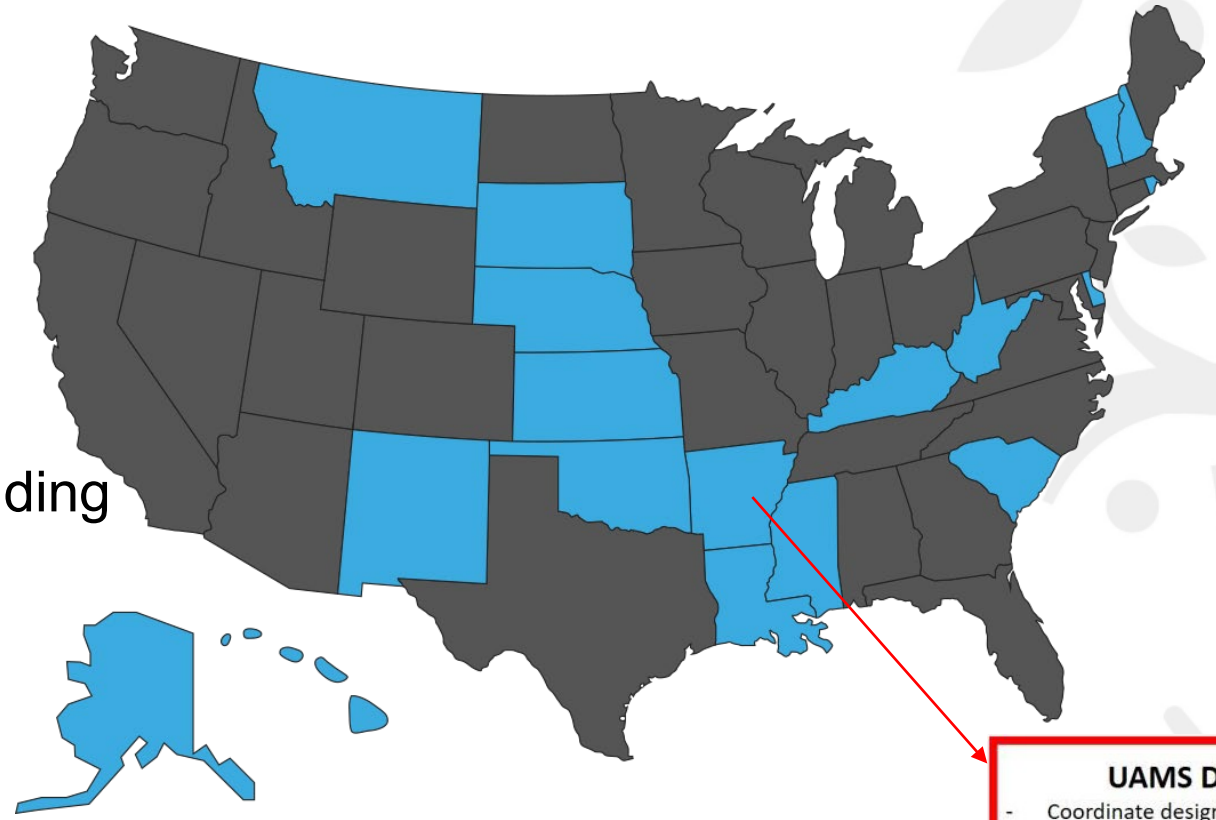
ECHO Program Focus Areas



https://echochildren.org/

ISPCTN Composition

- Initiated in September 2016
- Current Composition:
  - 18 awardee sites (blue states)
    - Support site level capacity building
    - Perform clinical trials
  - 1 Data Coordinating and Operations Center

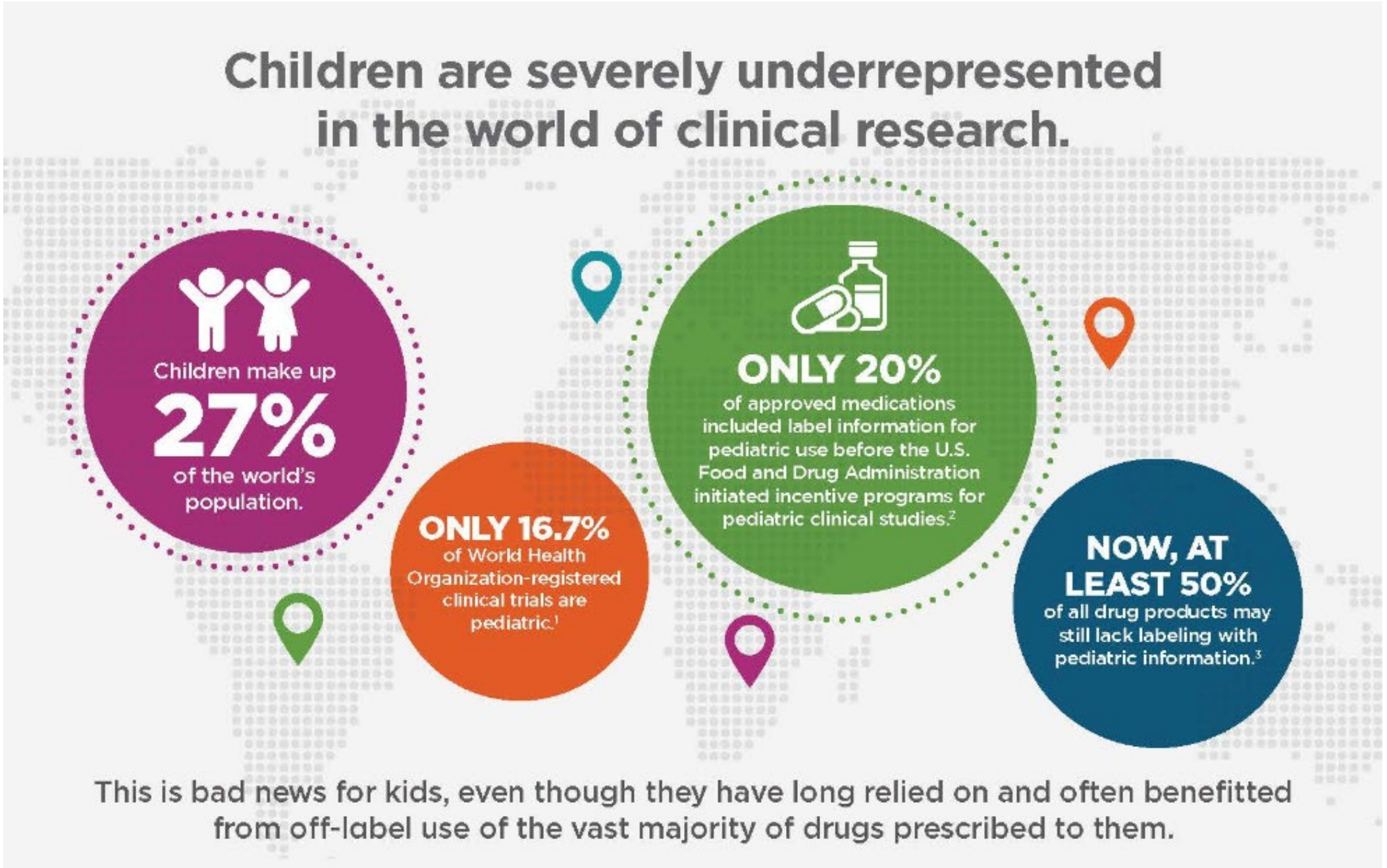


UAMS DCOC

- Coordinate design, implementation, data management, and analysis of multisite clinical trials
- Coordinate Network programmatic functions
- Lead multisite professional development

IDeA States Pediatric Clinical Trials Network (ISPCTN) Goals

- Enhance the health of our rural or underserved pediatric populations through clinical trials research
- Build pediatric clinical trial capacity in IDeA States
  - Foster clinical site capacity to conduct clinical trials
- Promote community engagement in ISPCTN clinical trials with rural or underserved children
  - Build relationships with community to support clinical trials



https://www.worldwide.com/resources/infographics/overcoming-the-challenges-of-pediatric-research/

Gaps in Pediatric Clinical Research

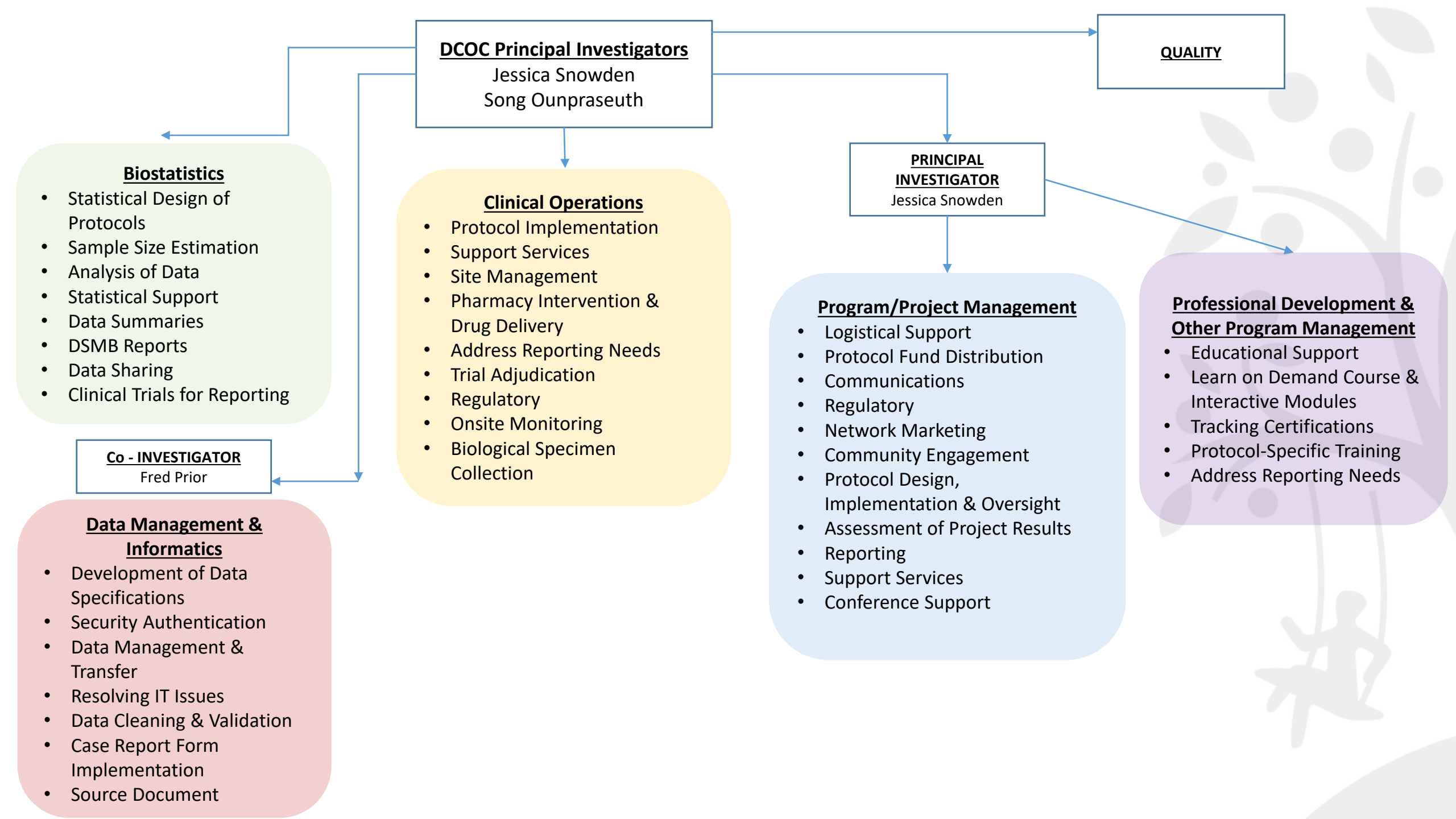
- Certain groups of children are particularly underrepresented in clinical trials (consistent with goals of ISPCTN)
  - Rural
  - Lower socioeconomic status
  - Racial and ethnic minorities
- Mismatch between disease prevalence & sites of pediatric research
- Limits generalizability of data and access to cutting edge care offered through clinical trials

Rural Health Disparities

- Increased risk
  - 40% more likely suffer from coronary artery disease
  - 8.6% more likely to suffer from diabetes
  - Rural youth are twice as likely to commit suicide
  - More likely to smoke cigarettes (26.6% rural youths over 12 v 19%)
  - Accidental death
    - More than 50% of vehicle crash-related fatalities occur in rural areas
    - 22% more likely to have injury-related death
    - Increased risk of opioid overdose deaths

Data Coordinating and Operations Center

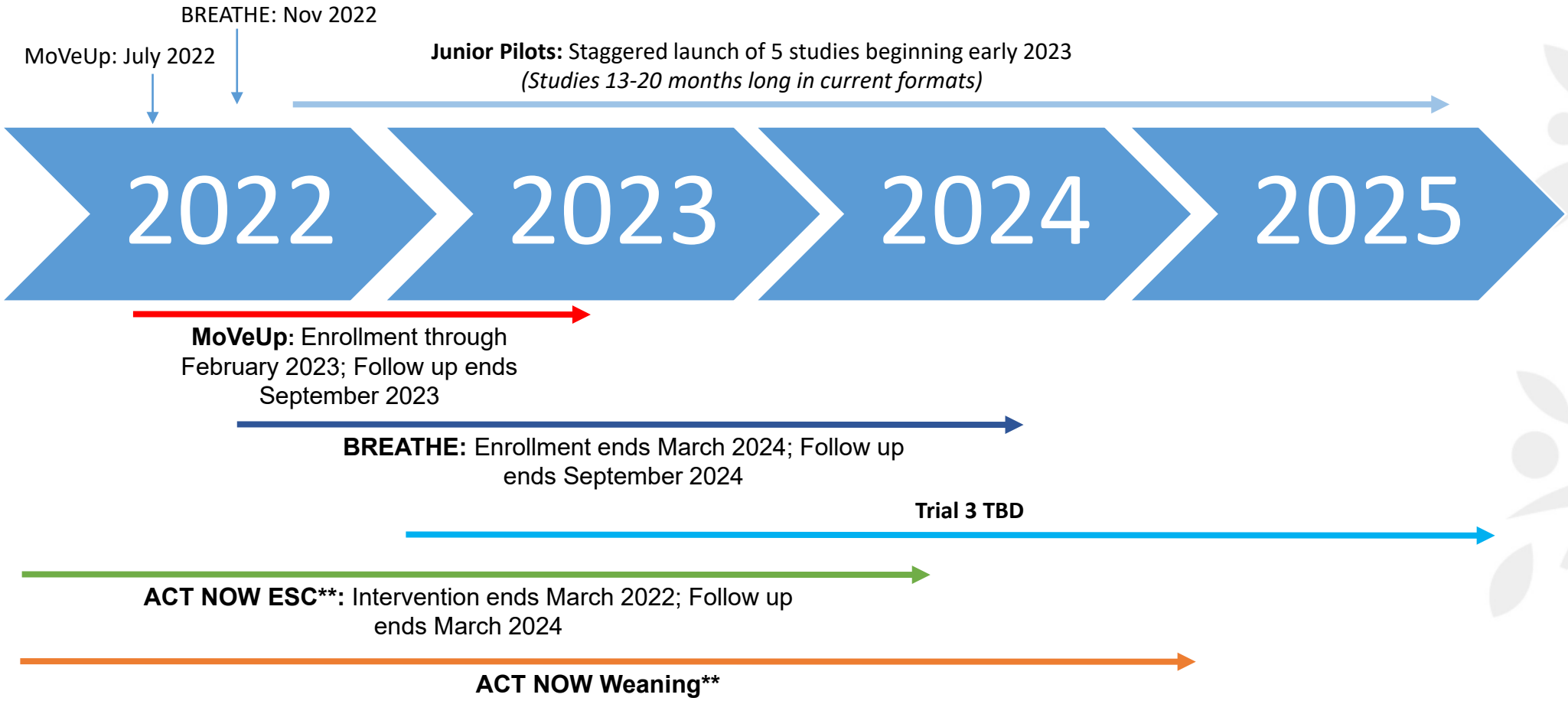
- DCOC manages the following activities for the ECHO ISPCTN:
  - Data coordination
  - Technical instruction
  - Data standards
  - Quality control and assurance
  - Operational coordination for ECHO ISPCTN clinical trials


DCOC Principal Investigators
Jessica Snowden
Song Ounpraseuth
QUALITY
Biostatistics
• Statistical Design of Protocols
• Sample Size Estimation
• Analysis of Data
• Statistical Support
• Data Summaries
• DSMB Reports
• Data Sharing
• Clinical Trials for Reporting
Clinical Operations
• Protocol Implementation
• Support Services
• Site Management
• Pharmacy Intervention & Drug Delivery
• Address Reporting Needs
• Trial Adjudication
• Regulatory
• Onsite Monitoring
• Biological Specimen Collection
PRINCIPAL INVESTIGATOR
Jessica Snowden
Co - INVESTIGATOR
Fred Prior
Program/Project Management
• Logistical Support
• Protocol Fund Distribution
• Communications
• Regulatory
• Network Marketing
• Community Engagement
• Protocol Design, Implementation & Oversight
• Assessment of Project Results
• Reporting
• Support Services
• Conference Support
Professional Development & Other Program Management
• Educational Support
• Learn on Demand Course & Interactive Modules
• Tracking Certifications
• Protocol-Specific Training
• Address Reporting Needs
Data Management & Informatics
• Development of Data Specifications
• Security Authentication
• Data Management & Transfer
• Resolving IT Issues
• Data Cleaning & Validation
• Case Report Form Implementation
• Source Document

Examples of Network Studies

- Improving pediatric COVID-19 vaccine uptake using mHealth tool: a randomized, controlled trial (MoVeUp)
  - Phone App for parents/caregivers to enhance COVID-19 vaccine uptake in children
  - Multi-site, parallel, randomized, controlled trial involving 29 clinics in 15 ISPCTN states
- The BREATHE Study: Bronchiolitis Recovery and the Use of High Efficiency Particle Air (HEPA) Filters
  - Indoor air filtration units to improve indoor air quality in homes of infants (under 1 year old) with bronchiolitis
  - Multi-center, parallel, double-blind, randomized controlled trial in 17 ISPCTN states

Cycle 2 ECHO ISPCTN Activities



**HEAL funding outside of DCOC funds

Cross Group Studies

- NIH initiative “Helping to End Addiction Long-term” (HEAL)
  - Partnership with other networks: Pediatric Trial Network (PTN) and Neonatal Research Network (NRN)
- Eating, Sleeping, Consoling for Neonatal Opioid Withdrawal (ESC-NOW): a Function-Based Assessment and Management Approach
  - Compare length of time until infants are medically ready for discharge (ESC vs. Usual Institutional Care)
  - Stepped-wedge cluster randomized controlled trial with transition period
- Pragmatic, Randomized, Blinded Trial to Shorten Pharmacologic Treatment of Newborns with Neonatal Opioid Withdrawal Syndrome
  - Limit exposure to opioids & keep mother-infant dyad together through to use of a rapid weaning protocol

Thank you to the ISPCTN Site Principal Investigators

James Keck, MD; Paul Darden, MD; Tamara Perry, MD; Judith Ross, MD; Venkataraman Balaraman, MD; Ann David, PhD; Lori Devlin, MD; Sara Watson, MD, MS; Daniel Hsia, MD; J. Marc Majure, MD; Paul Smith, DO, FAAP, FACOP; Russell McCulloh, MD; Paul Palumbo, MD; Hengameh Raissy, PharmD; Alberta Kong, MD, MPH; Amanda Bogie, MD; Jeannie Tryggestad, MD; Thomas Chun, MD, MPH; Abbott Laptook, MD; Lisa Knight, MD; Andrew Atz, MD; Amy Elliott, PhD; Kathy Wang, MD; Kelly Cowan, MD; Leslie Young, MD; Lesley Cottrell, PhD; Lee Pyles, MD, MS

ECHO

Environmental influences on Child Health Outcomes

A program supported by the NIH

IDeA States Pediatric Network

Contact us for more information:
AskDCOC@uams.edu
stounpraseuth@uams.edu
jsnowden@uams.edu

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

IDeA States Pediatric Network

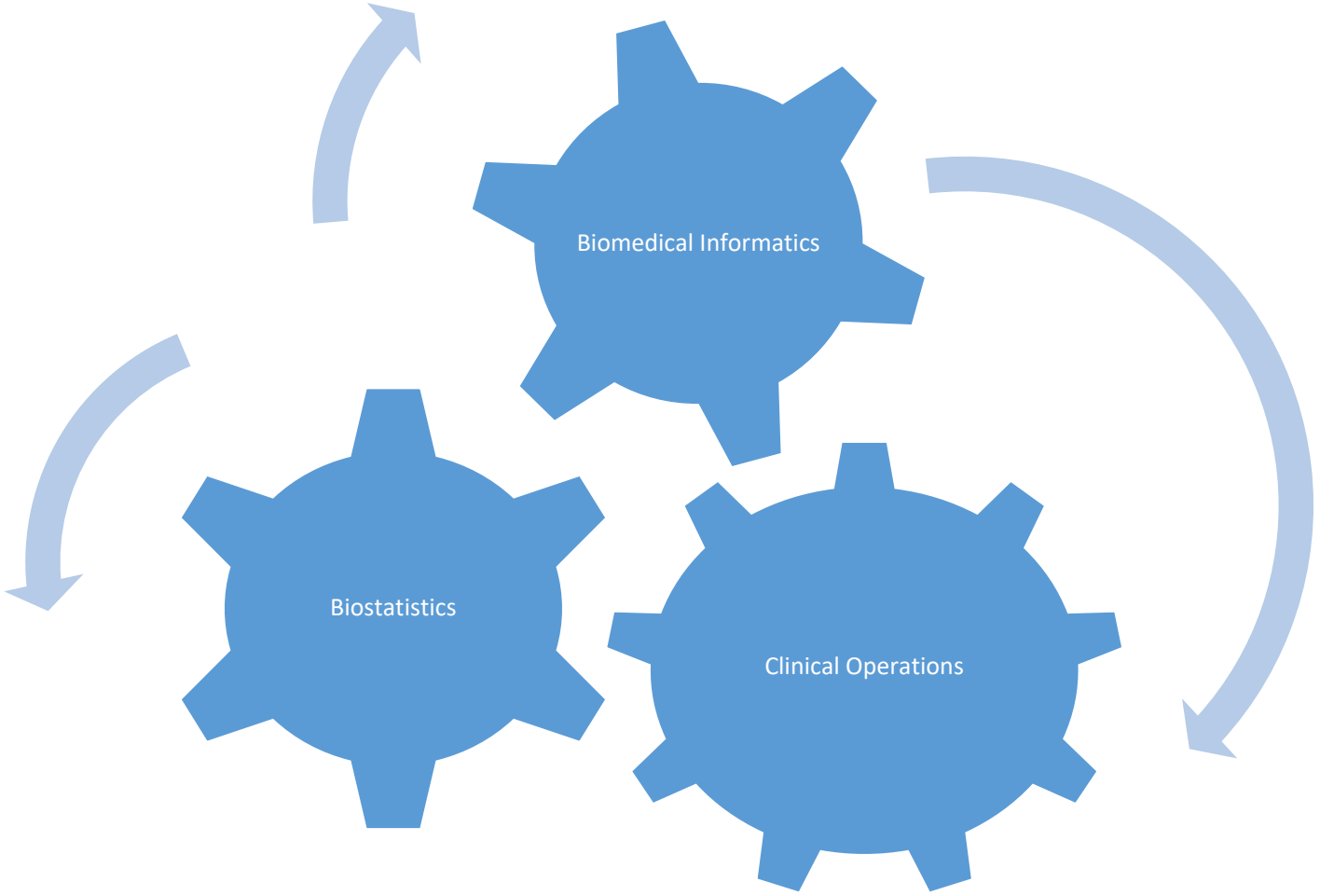
Clinical Operations: Reaching Children in Rural and Underserved Populations

Amy Doville, MBA, CCRP
Director of Research
ISPCTN Data Coordinating and Operations Center
adoville@uams.edu

Disclosures

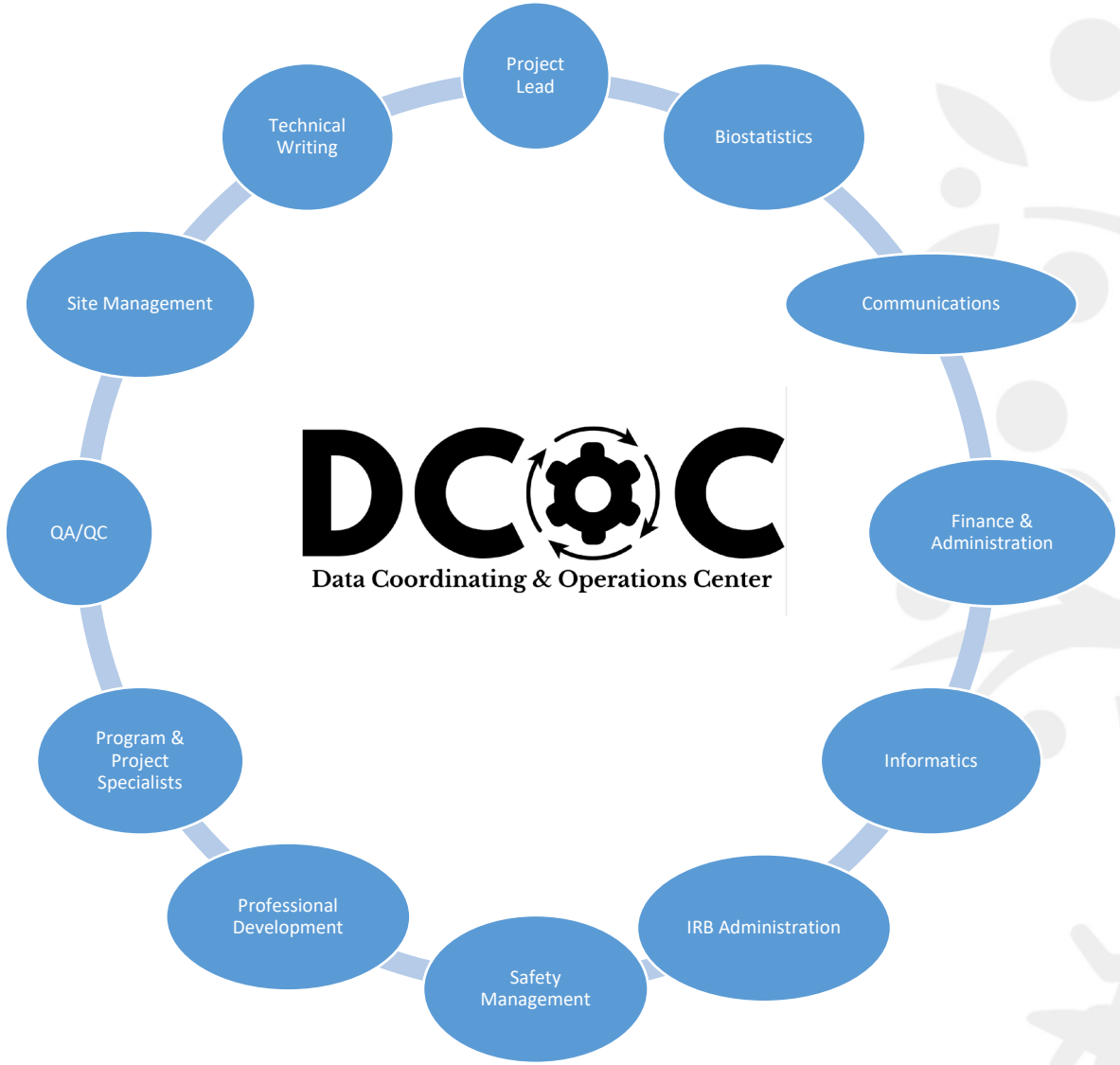
- No relevant disclosures

Data Coordinating and Operations Center

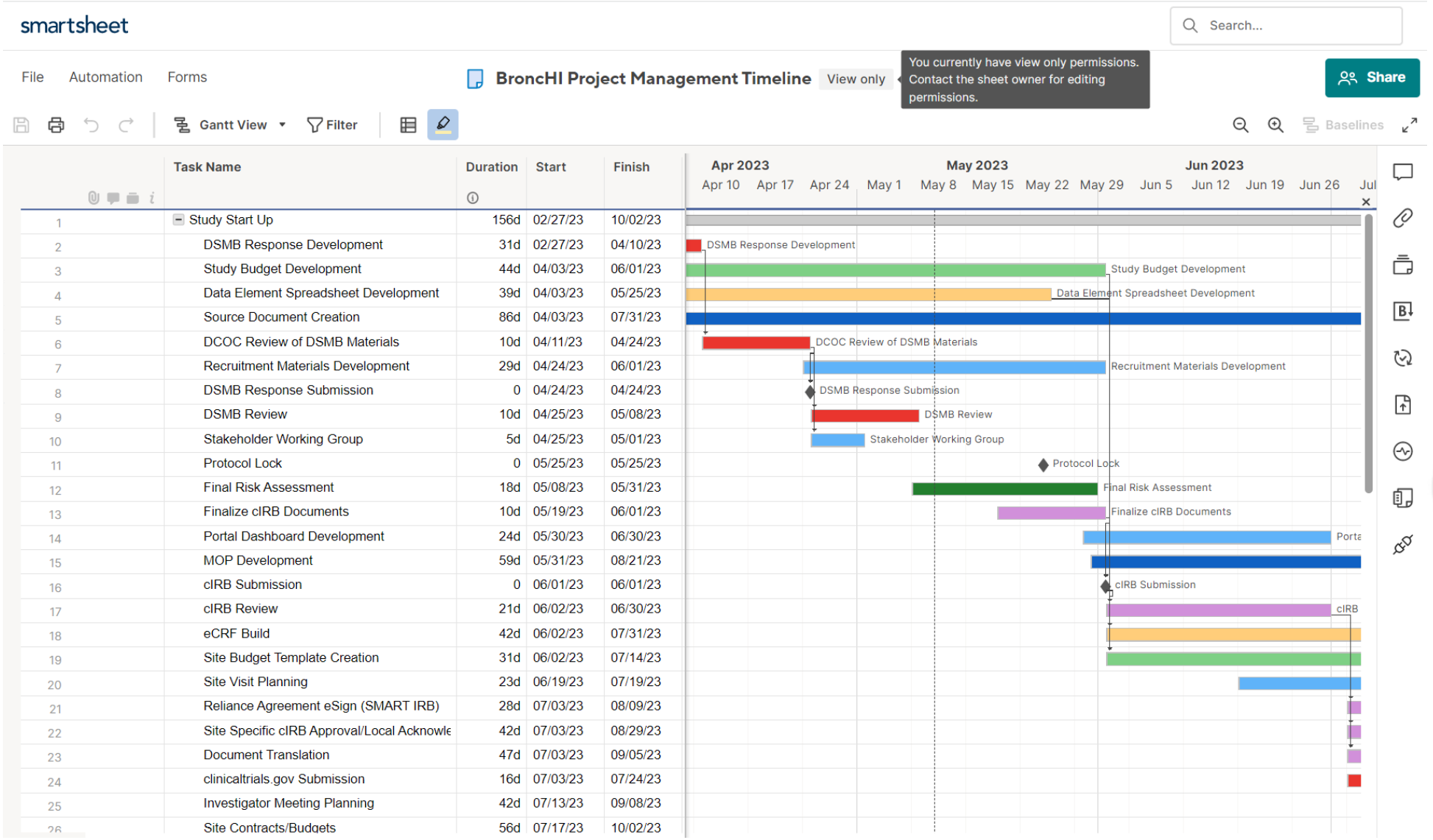


Clinical Operations

- Project Leadership
- Site Management
- IRB Administration
- Finance & Administration
- Quality Management
- Participant Safety
- Program & Project Specialists
- Technical Writing
- Professional Development
- Communications



Project Leaders/Site Management



Quality Management System

- SOPs
- Individualized study monitoring plan
- Internal monitoring of study data
- Working with external vendors (pharmacy, CRO, labs)

Safety Management

- Dedicated Safety Officer
- Medical Monitor for each study
- Safety Plan for each study, taking into consideration the target research participant population's needs, as appropriate
- Regular safety meetings
- Monitoring and maintenance of safety events
- Reporting to the Data Safety Monitoring Board

cIRB and Regulatory

- UAMS is the central IRB for the ISPCTN Network
- Work with individual sites on each protocol for overall cIRB communication and site-specific context
- IRB Administrators serve as cIRB contacts for network sites
- Approximately 80 IRB submissions ongoing
- Collects and monitors regulatory documents for each site

Administration

- Study and site team meetings
- Overall grant budget management
- Study budget development and negotiation
- Contract preparation (obtaining docs to prep for contracts)
- Publications and presentations

Professional Development

- Tasked with ensuring that our sites, many of whom had limited research experience, develop a strong research background.
  - Site investigators
  - Research coordinators
  - Finance and administration
  - cIRB
- Monthly professional development offerings
- Topic-specific offerings (ex: clinicaltrials.gov)
- Professional development opportunities from other sources

Rural and underserved populations

Considering “rural and underserved”

- ISPCTN, by definition, is an 18-state network with rural and underserved populations and site that have not traditionally had robust research infrastructure
- The network has often discussed what “rural and underserved” means
  - Rural
  - Race and ethnicity
  - Socio-economic status
  - Medically underserved
- Protocol teams discuss their focus during protocol development
- Team determines whether the grantee site, community clinics, or local hospitals should be used for recruitment and/or study procedures
- Who is engaged and not engaged in the research?
- Recruitment methods are determined
- Organize study-specific Investigator Training meetings in partnership with the study PIs and study team

How do we engage rural/underserved study participants?

- Helps facilitate interaction with Community Advisory Boards
- Develops study-specific communication plans
  - Professional and lay presentations and talking points
  - Recruitment and retention materials
    - Touchpoint reminders
    - Study-branded materials for participants
  - Videos for coordinators and/or participants

Hello from the BREATHE Team!

Staying in touch is so important!

We know life is busy right now!

Thank you again for your continued participation in the BREATHE study.

Here is what's most important each week for the BREATHE study to be successful:

- Keep your study equipment running.
- Keep returning the completed surveys.

Please let us know if you have a change in the following:

- Mailing address
- Email address
- Contact phone number

You and your baby are making a difference in children's health research, and your help is greatly appreciated.

<Study Coordinator/Contact>
<Site Location>
<Study Coordinator/Contact Email>
<Contact Phone>

Available Recruitment Materials for the BREATHE Study:

12. **BREATHE Study Info Flyer V-01 (2022-05-31)**
*After choosing the quantity, the photo options will generate.
- 24
- 36
- 48
- Other

13. **BREATHE Two-fold Brochure V-01 (2022-05-31)**
*After choosing the quantity, the photo options will generate.
- 24
- 36
- 48
- Other

14. **BREATHE Study Thank You Card V-01 (2022-05-31)**
*After choosing the quantity, the photo options will generate.
- 24
- 36
- 48
- Other

14. **BREATHE Study Symptom Recall Tool (not custom) - English only (stock item):**
Must order a minimum of 6

BREATHE Recruitment Flip Chart (not custom) - English only (stock item) Not meant for participants to keep:
Must order a minimum of 6. Maximum order of 10.

BREATHE Presentation Folder (stock item):
- 12
- 24
- 36

reset

Must order a minimum of 6

BREATHE Equipment Instructions Laminated (not custom) - English only (stock item):
- 6

*Each set of instructions has 3 individual pages.

ECHO

Environmental influences
on Child Health Outcomes

A program supported by the NIH

IDeA States Pediatric
Clinical Trials Network

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

IDeA States Pediatric Clinical Trials Network

Protocol Development and Implementation: the MoVeUP Experience

Russell McCulloh, MD
University of Nebraska Medical Center

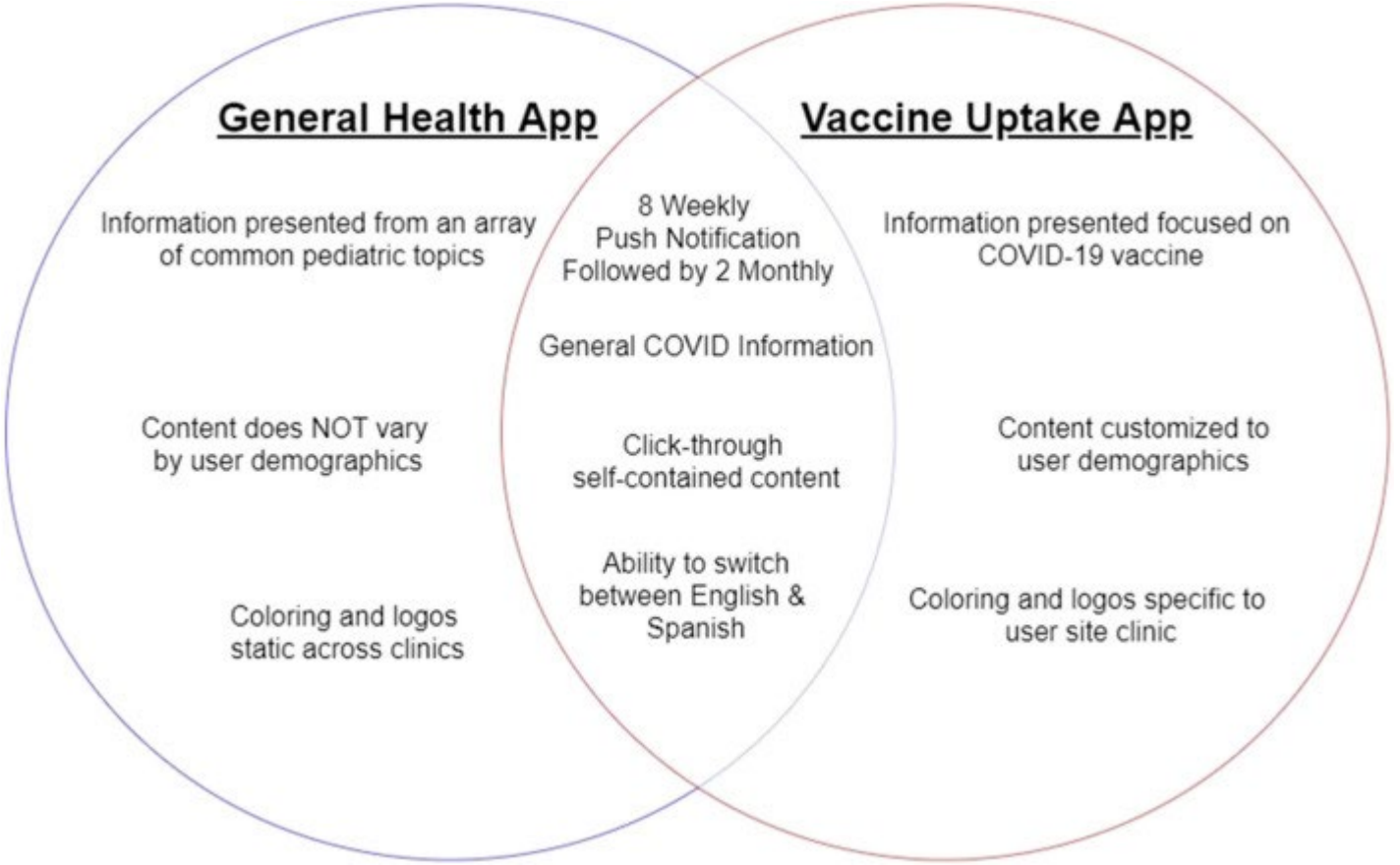
MoVeUP

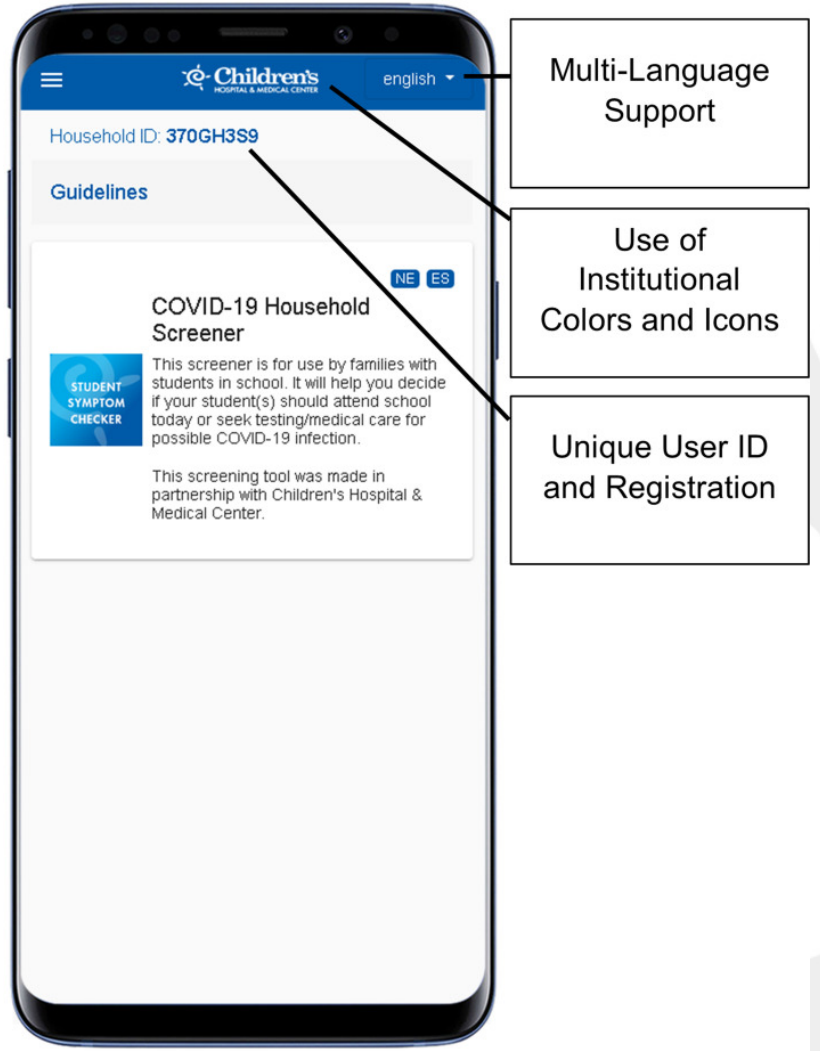
Disclosures

- Receive support from the Merck Investigator Studies Program for vaccine communication research
- Author on software used for clinical research (including MoVeUP)

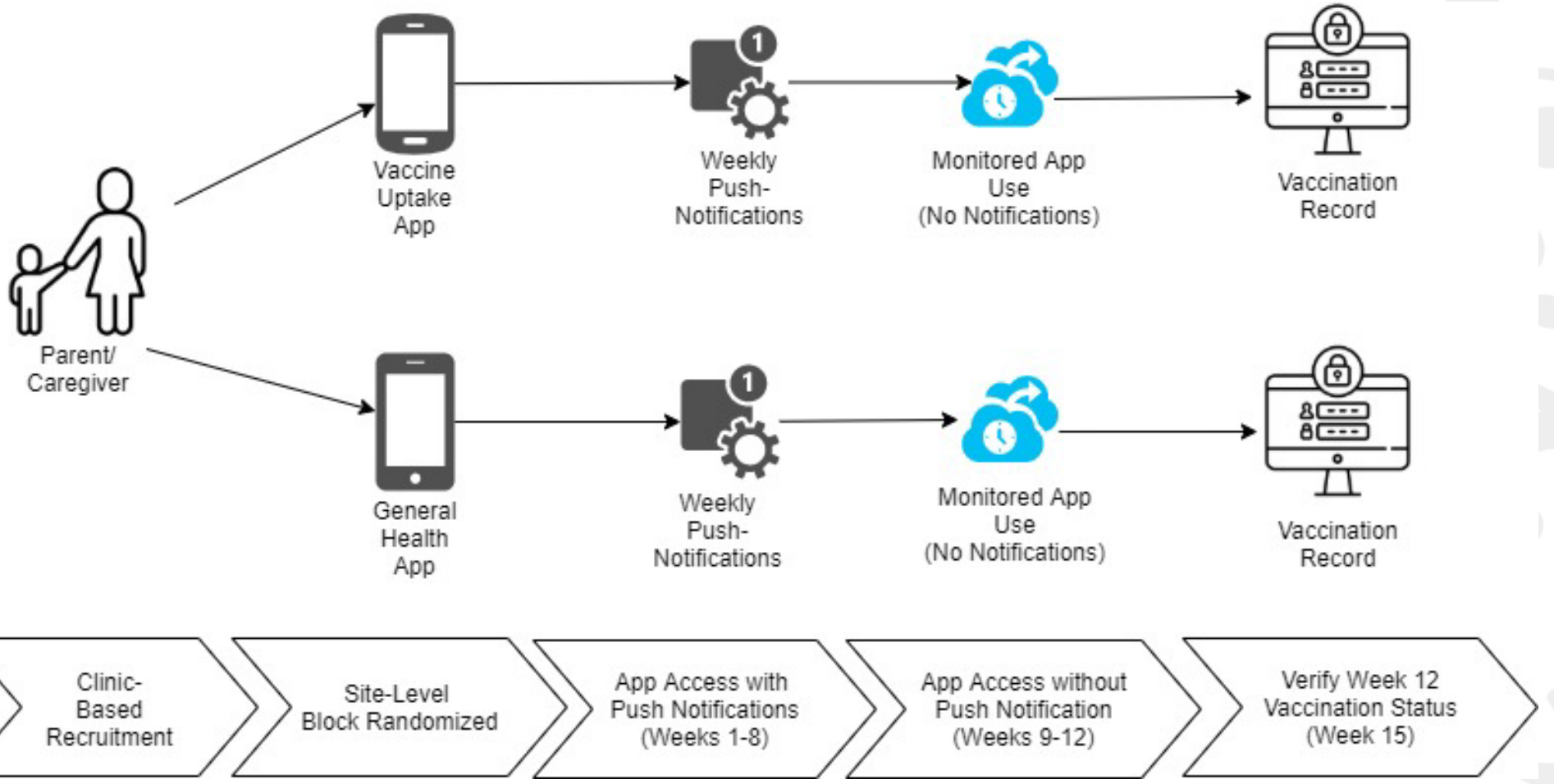
MoVeUP Overview

- Study motivated by higher COVID-19 vaccine hesitancy in rural populations





RCT

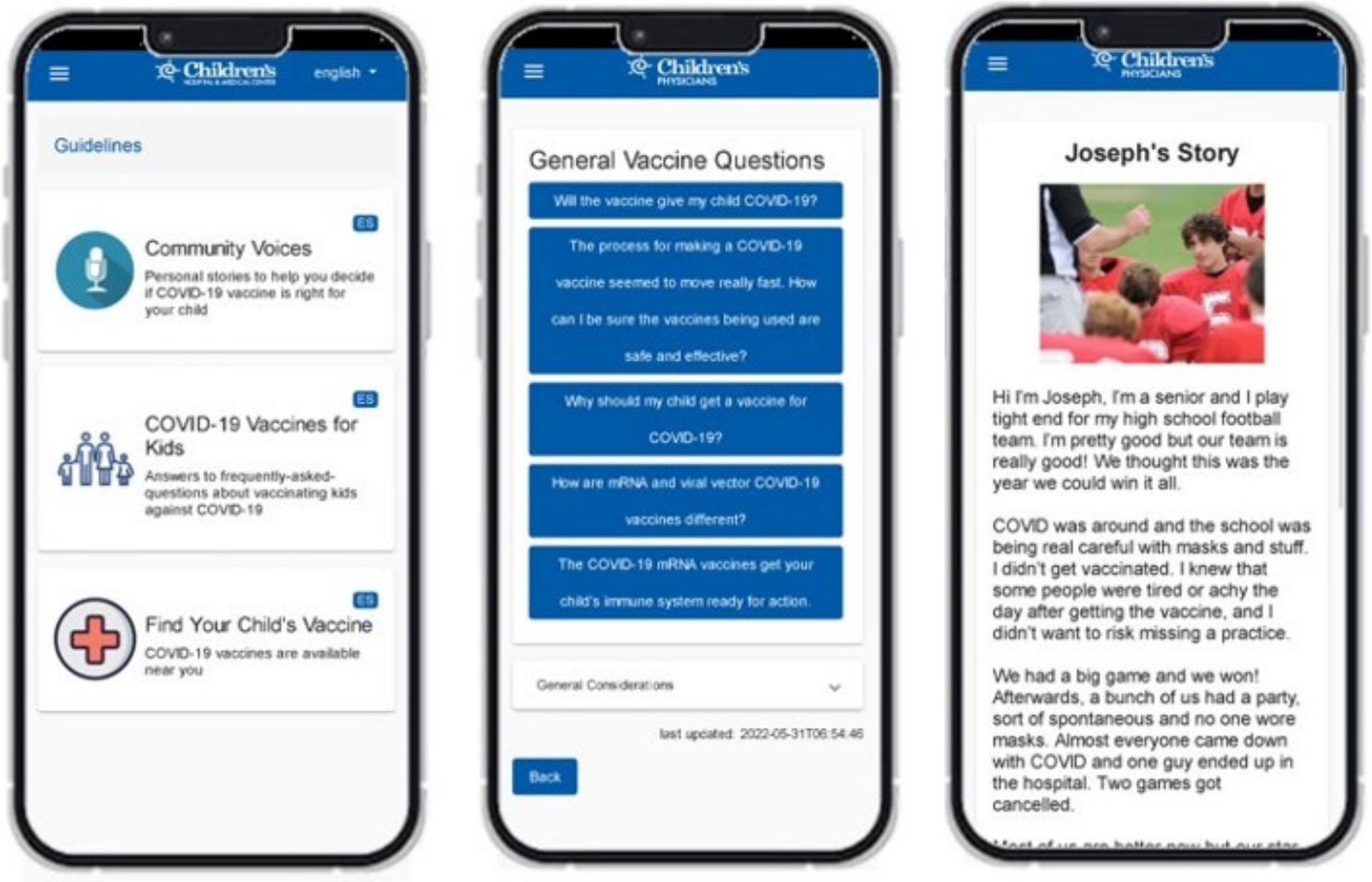

Parent/
Caregiver
Vaccine
Uptake
App
Weekly
Push-
Notifications
Monitored App
Use
(No Notifications)
Vaccination
Record
General
Health
App
Weekly
Push-
Notifications
Monitored App
Use
(No Notifications)
Vaccination
Record
Clinic-
Based
Recruitment
Site-Level
Block Randomized
App Access with
Push Notifications
(Weeks 1-8)
App Access without
Push Notification
(Weeks 9-12)
Verify Week 12
Vaccination Status
(Week 15)

Challenge: Protocol Development

- Two study protocols:
  - Qualitative → informed content of intervention app for RCT
  - Quantitative → 15-state, 29 clinic RCT
- Different study team compositions, expertise, and team dynamics
- Protocol leadership overlapped
- Qualitative protocol focused on demographics facing vaccination disparities

Awardee sites: Challenges to implementation

- Site PI
  - Identifying staff for each protocol
  - Working with staff to implement studies
  - Identifying appropriate clinics for recruiting participants
  - Obtaining local context for app customizations
  - Often first CT that a site has performed

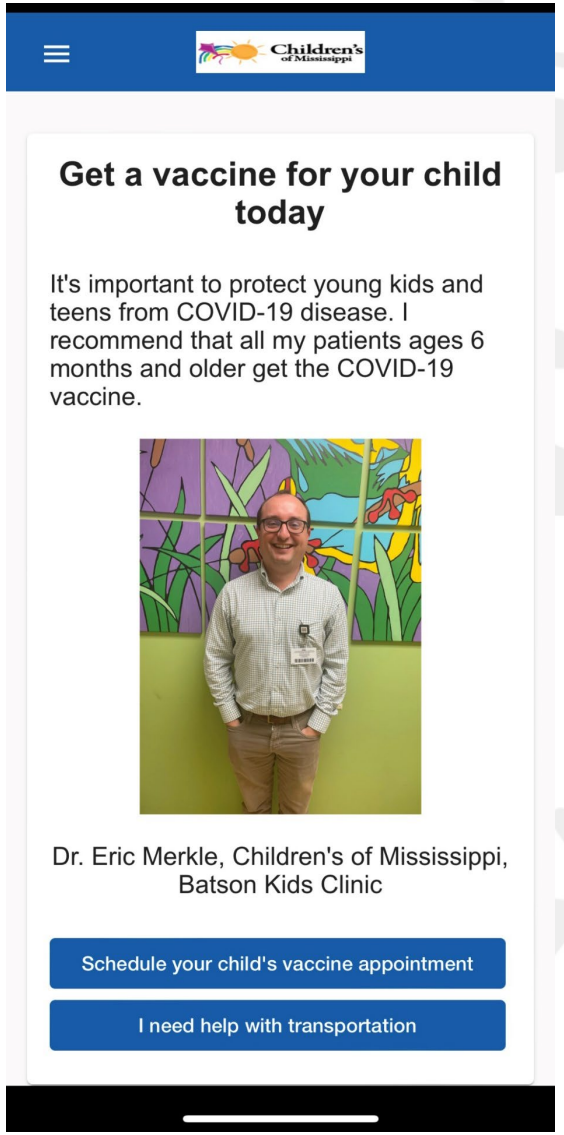


Qualitative protocol: challenges to recruitment/study conduct

- Populations of interest reticent to participate
  - Particularly rural NHW
- Interviews done via teleconference
  - Video created barriers
  - Discomfort with sharing opinions while on video
  - Important context missing from analysis (non-verbal cues)

Getting local providers to use their likeness

- Local logos and contact information readily submitted
- Some clinics did not want to use local provider names or likenesses
- Substituted providers from other clinic in same state or a generic picture and screen made in-house



Recruitment challenges

- Emotions can run high during contact with potential participants
- “I have to buy a lot of coffee and pizza parties to support my staff.”
- “Some people just hang up on you as soon as you call. Others just cuss you out by phone.”
- **Intensity of engagement greater than expected for local coordinators**

Adherence challenges

- RCT powered assuming most patients will download and use the app at least once (measure of adherence)
- App studies generally list 50% adherence as typically expected
- Power calculation originally assumed 80%
- Adjusted to 60% based on observed adherence (adjustments to onboarding)
- Current rate: 63%

Retention challenges

- Longitudinal survey completion approx. 70%
- Final study surveys→currently awaiting participants to finish on-study period
- Critically important to define completion of vaccine survey in way that is clear, concise, repeatable, and works for those who vaccinate AND for those who do not!

ECHO

Environmental influences
on Child Health Outcomes

A program supported by the NIH

IDeA States Pediatric
Clinical Trials Network

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

IDeA States Pediatric Clinical Trials Network

Clinical Trial Study Implementation: Research Coordinator Perspective

Sara McClure Cox RN-C, BSN, MPH, CCRP
Montana Pediatric Clinical Trials Site
U of MT School of Public Health- ISPCTN ECHO NIH

Disclosures:

- No relevant disclosures

Building Capacity to Make Research Happen

- Vast difference in research capacity among sites
- 18 very unique sites, 1 national network
- Team approach essential

Working It Out, Working It Through

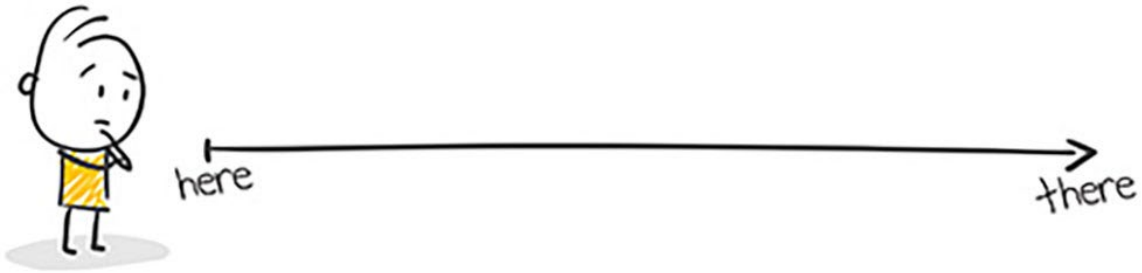
- Identifying ways to recruit in our communities
  - Geographic distances
  - In-Person Recruiting vs Phone/Text Recruiting
  - Shipping Costs
  - Participant access barriers (lack of internet, cell)
- EMR access/IRB ceding/contracting
  - Much administrative resources required

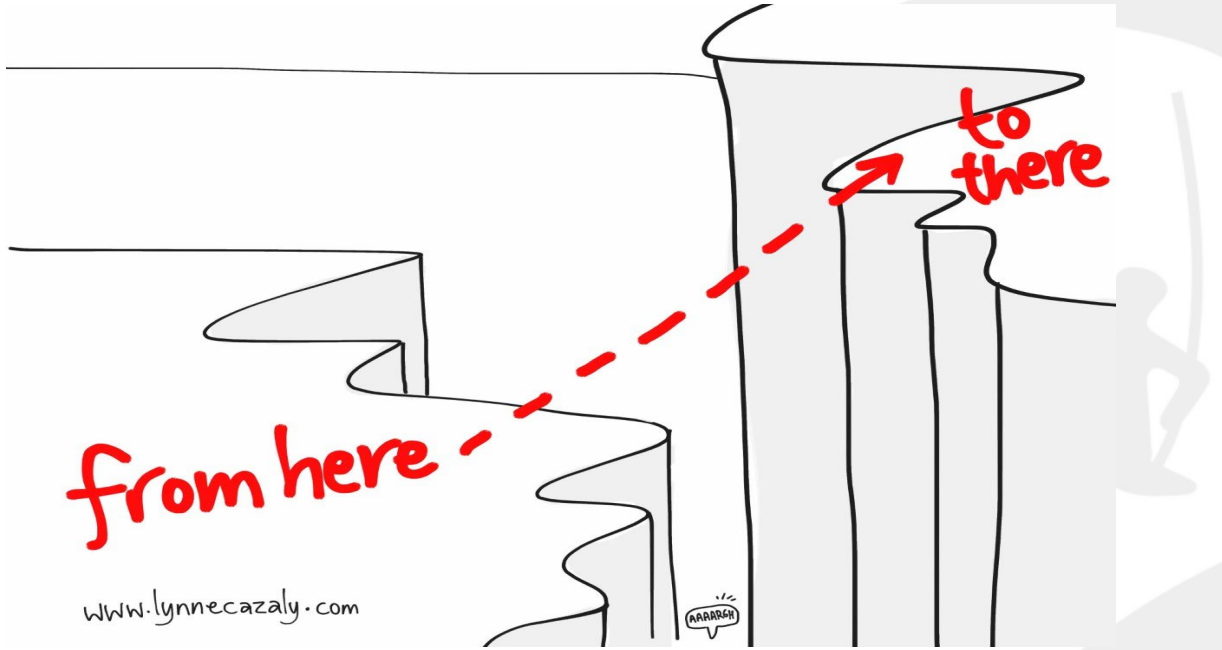
Integrating Leadership and Input Early

- RCs on every protocol writing team
- RCs are authors within MOP writing group
  - RCs DCOC/Informatics Collaboration
    - Project management
    - Trainings
    - EDC end user testing

Working Together While Apart

- Sticking to deadlines
- Communication and prompt action
- RC as advocate for RC (strong trainings/support)





BREATHE Clinical Study

- N =218 infants 12 months or younger
- First hospitalization for bronchiolitis
- “Will the the use of HEPA units in the home decrease respiratory burden in these infants?”
  - Will it change doctors visits? Re-admissions?
  - How will it impact quality of life?
  - How will it impact PM 2.5 levels in the home?

BREATHE Clinical Trial

- 2 PurpleAir air quality monitoring units (w/WiFi hotspot)
- 2 air units either active or control
- Weekly symptom surveys
- Approximately 6 months on intervention
- Blinded study (staff and participant families)
  - Unblinded site team at University of Montana (blinded team at UM as well)
  - “all things equipment intervention”

Show Time!

- Recruitment/retention in service of rural/underserved
  - Truly thinking about what we mean by ‘informed consent’
  - Study Advocate/Participant Advocate
    - Knowledge/Retention/Relationship
      - Do they feel welcome?
      - Do they feel overwhelmed?

Back to Informatics/DCOC/RC Collaboration

- Where the testing and planning pays off
  - –EDC systems that work
  - –Weekly meetings that deliver important information as change inevitable
  - –BREATHE Equipment ‘plug and play’ ‘SD card’

End.

ECHO

Environmental influences on Child Health Outcomes

A program supported by the NIH

IDeA States Pediatric Network

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

IDeA States Pediatric Clinical Trials Network

Data Management and Informatics in the ISPCTN

Jaime Baldner, BS, CCDM
ISPCTN Data Coordinating and Operations Center
University of Arkansas for Medical Sciences
jbaldner@uams.edu
501-686-8513

Disclosures

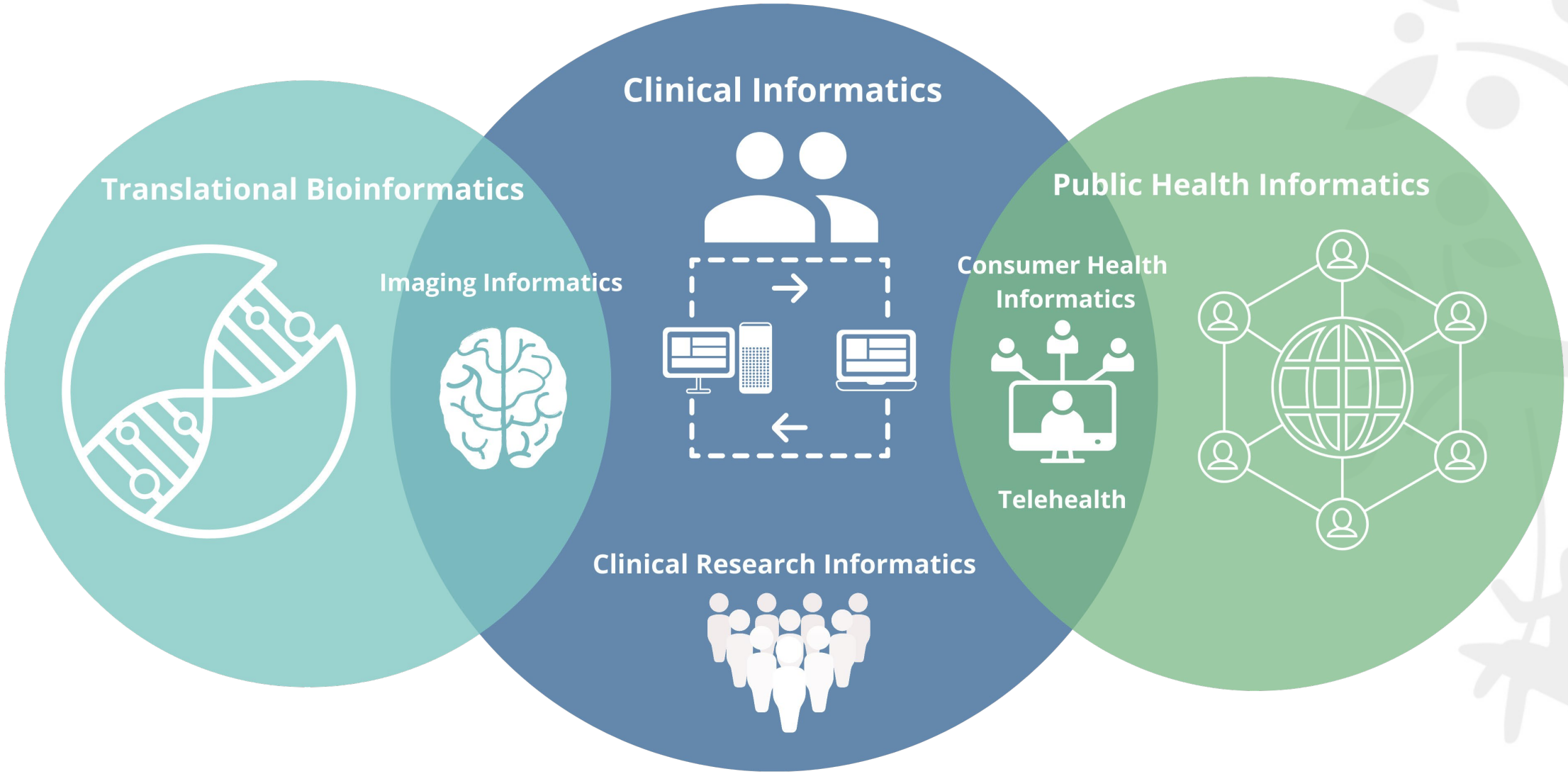
- No Relevant Disclosures
- No Conflicts of Interest

What is Data Management?

DATA MANAGEMENT

- PROTOCOL DEVELOPMENT
- CROSS-COLLABORATION
- EDC & SYSTEMS DEVELOPMENT
- DATA INTEGRATION
- DATA ARCHITECTURE
- DATA GOVERNANCE
- DATA QUALITY
- INFRASTRUCTURE & ARCHITECTURE
- METADATA MANAGEMENT
- DATA WAREHOUSING
- OPERATIONAL SUPPORT
- IDENTIFY DATA SOURCES
- DATA SHARING
- DATA SECURITY
- DATA STANDARDS
- BUSINESS INTELLIGENCE

What is Biomedical Informatics?

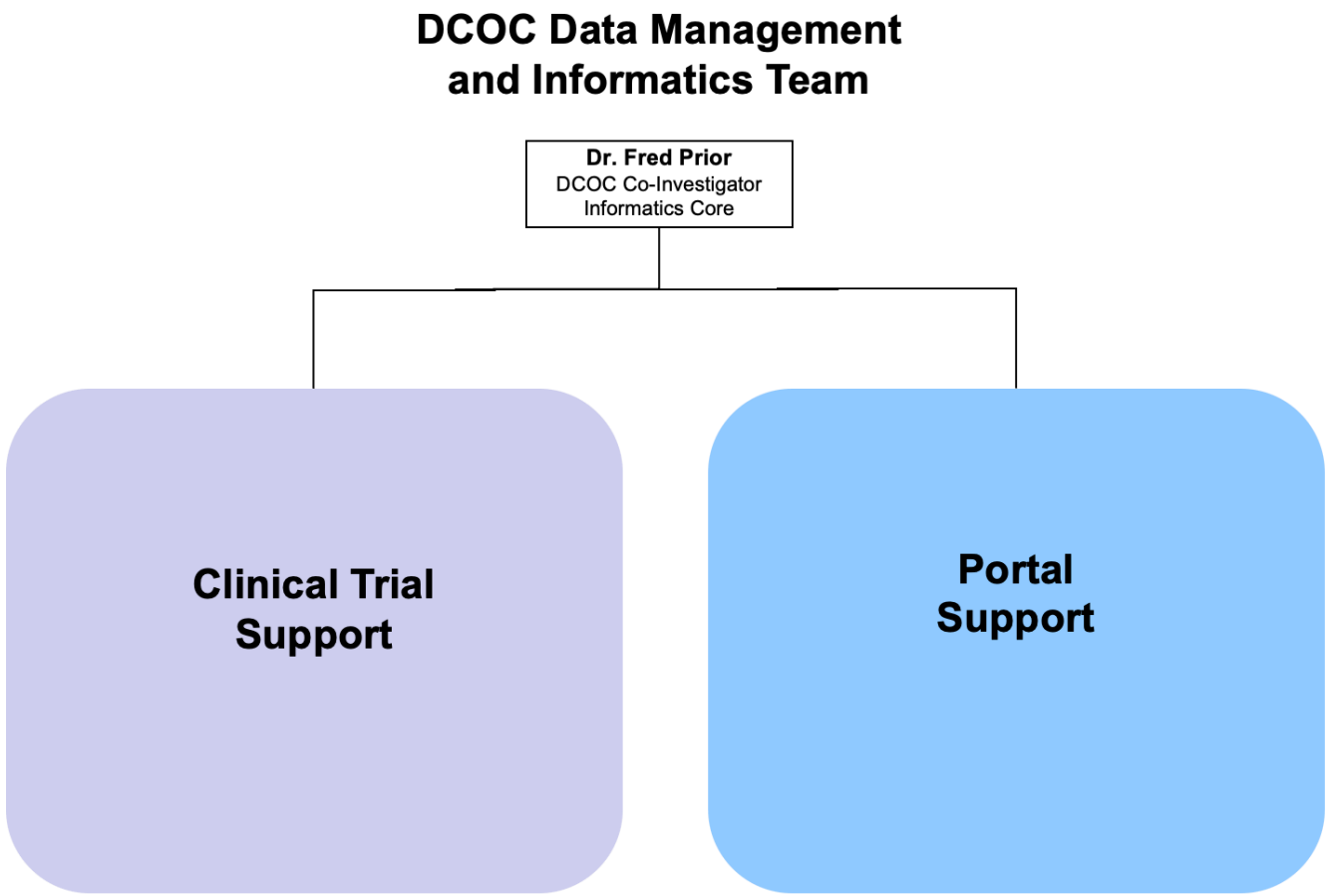


Molecular Level **Individual Level** **Population Level**

Meet the Team!

Data Management & Informatics (DM+I)

- DM+I have roles in front of and behind the scenes
- Organizational structure highlights team members with whom the ISPCTN is most likely to interact
  - Most of the ISPCTN have Portal accounts and use the Portal on some frequency
  - Some of the ISPCTN directly work on clinical trials



Quality Management System – SD Focus

Software Development Lifecycle (SDLC)

- Building or selecting software
- Installing software
- Validating the installation
- Maintaining the software
- Backing up / restoring the software
- Changing the software in a controlled manner
- Retiring the software
- Managing user identities in Network systems

Quality Management System – DM Focus

Data Management (DM)

- Data management planning
- Creating data capture strategies
- Developing case report forms (CRFs)
- Building databases
- User testing
- Acquiring, processing, reporting, extracting, sharing, and archiving data
- Managing user access to data systems

Data Management & Informatics

Long Term

- Contributing to DM&I Components of DCOC QMS
- Reviewing concept proposals & contributing to scientific & DM components of protocols
- Assessing data system needs for CRF & non-CRF data; collaborating with external data providers
- Creating data flow diagrams
- Creating data element spreadsheets
- Representing Informatics on study meetings

- Developing & maintaining ISPCTN Portal
- Processing CRF & vendor data
- Extracting data for analysis
- Writing papers & manuscripts
- Publishing data to DASH

Strategic

Tactical

- Creating user testing plans for EDC systems
- Creating CRF & EDC training materials
- Creating data management plans
- Designing data entry forms
- Designing the reporting suite
- Managing change control projects for Portal & EDC
- Contributing to writing teams

- Processing user access requests (UARs)
- User Testing of EDC systems
- Contributing to DSMP & MOP
- Creating alerts to facilitate operations & data flow
- Running study reports & posting them to Box
- Storing & archiving study data

Short Term

Data Collection Strategy - 1

- Case Report Forms (CRFs) serve as the bridge between the experimental design laid out in the protocol and the analytical conclusions drawn from the results of the experiment
  - CRFs are required documents in the Trial Master File (TMF)
- Data quality measures should be focused on endpoint measurements and determined in advance of the study going into the field

Data Collection Strategy - 2

- Non-CRF data, if applicable, must have a defined plan for acquisition and processing
- Recognition and separation of clinical data needed for analysis from operational data needed to facilitate workflow at the sites and/or by the study team
- DM+I Team’s primary focus is on clinical data, but we will assist, as possible within project constraints, with operational data solutions

Mapping Out the Data Ecosystem

Possible Data Sources

- Electronic health record
- Observed assessments / procedures performed by study personnel, e.g., height / weight collection for BMI calculation
- Clinical Outcomes Assessments (COA)
  - Patient Report Outcomes (PRO), e.g., QoL surveys
- External data providers / sources, e.g., central laboratory

Start with the End in Mind

- DCOC obliged to provide regular updates to DSMB for ongoing studies
- DCOC obliged to return data once two criteria are met:
  1. End of study
  2. Primary manuscript is accepted for publication
- ISPCTN publicly shares data from completed clinical trials via NICHD DASH
  - First completed study in the Network conducted 2018-2019 and uploaded to DASH in 2020

DM+I Team in Action - 1

- Data Quality Assurance in the MoVeUP App study
  - Endpoint data managed by the DCOC who also facilitated the quality assurance efforts to confirm vaccination status for the following by identifying participants to verify, notifying sites of the need to act, and tracking completion status of vaccination confirmation activities:
    - Participants who had not provided the vaccination status of their children
    - Participants who had provided incomplete vaccination information
  - In contrast, mobile app (active and control intervention) managed by the App Team with oversight by the DCOC

DM+I Team in Action - 2

- Operational support of the Unblinded Central Site in the BREATHE study
  - Endpoint data ($PM_{2.5}$) managed by the Unblinded team with DCOC oversight
  - In contrast, inventory and distribution of air units (active/placebo intervention) managed by the Unblinded team with active support by the DCOC in the form of formatted inventory log and data entry forms to track shipping dates and details

Thank you to the DCOC Data Management and Informatics Team

Faculty

Dr. Fred Prior (DCOC Co-I)
Dr. Maryam Garza
Dr. Melody Greer
Dr. Lawrence Tarbox

Staff

Robert Brown
Gonghe (Marlow) Dai
April Davis
Julie Frund
Jeremy (Quasar) Jarosz
Sunitha Kenchey
John Klinger
Ye (Wilson) Luo
Keith Powell
Emel Seker
Jeff Tobler

ECHO

Environmental influences on Child Health Outcomes

A program supported by the NIH

IDeA States Pediatric Network

Contact us for more information:
AskDCOC@uams.edu
stounpraseuth@uams.edu
jsnowden@uams.edu