5th Conference on Clinical Research for Rare Diseases

Rare Diseases Clinical Research Network
Initiative of the National Center for Advancing Translational Sciences (NCATS)

“Challenges and solutions to conducting clinical research in rare diseases”

Peter A. Merkel, MD, MPH
Professor of Medicine and Epidemiology
University of Pennsylvania
Principal Investigator
Vasculitis Clinical Research Consortium

Penn
University of Pennsylvania

NIH National Center for Advancing Translational Sciences

Office of Rare Diseases Research
National Center for Advancing Translational Sciences – NIH

Peter A. Merkel, M.D., M.P.H.
Financial Disclosures

Dr. Merkel has current or has had recent financial support for research, consultation, and/or educational activities from the following sources:

Consulting:
- Actelion
- Boston Pharm.
- Bristol-Myers Squibb
- ChemoCentryx
- Genzyme/Sanofi
- GlaxoSmithKline
- Genentech/Roche
- InflaRx
- Insmed

Royalties:
- UpToDate

Research Support:
- Actelion
- Bristol-Myers Squibb
- CaridianBCT
- Celgene
- ChemoCentryx
- Genentech/Roche
- GlaxoSmithKline
- Kypha
- MedImmune/AZ

Research Support:
- American College of Rheumatology
- European League Against Rheumatism
- National Institutes of Health (NHLBI • NIAMS • NIAID • NCATS • ORDR)
- US Food and Drug Administration
- The Patient-Centered Outcomes Research Institute
- The Vasculitis Foundation

Off-label use of various medications will be discussed in this presentation

Rare Diseases

- What is a rare disease?
  - A disease with a prevalence of <200,000 persons in USA
    - Estimated to be ~7000 rare diseases
    - US estimate: 25-30 million people with a rare disease (8-12% of US population)
- Increasing awareness of rare diseases by public via media, internet, advocacy/support groups
- Many major scientific breakthroughs have arisen stemming from investigation of rare diseases that often have impact on common disorders
- Rare disorders have fascinated physicians and non-physicians for centuries

Why do we do rare diseases research?

- When you or a loved one are the patient with a rare disease, the disease is no longer rare
- When you have a patient with a rare disease, your ignorance will not help: become expert or refer
- People are drawn to rare disease research for the some of the same reasons others choose a research focus
  - Fascination with subject
  - Opportunity
  - Inspiration by patient/teacher

Some Joys & *Challenges* of Rare Disease Care and Research

- Nice to be an expert about things most people don’t know about
- *Nobody really knows what on earth you study or see clinically*

- There are HUGE unanswered questions for rare diseases
- *There are HUGE unanswered questions for rare diseases*

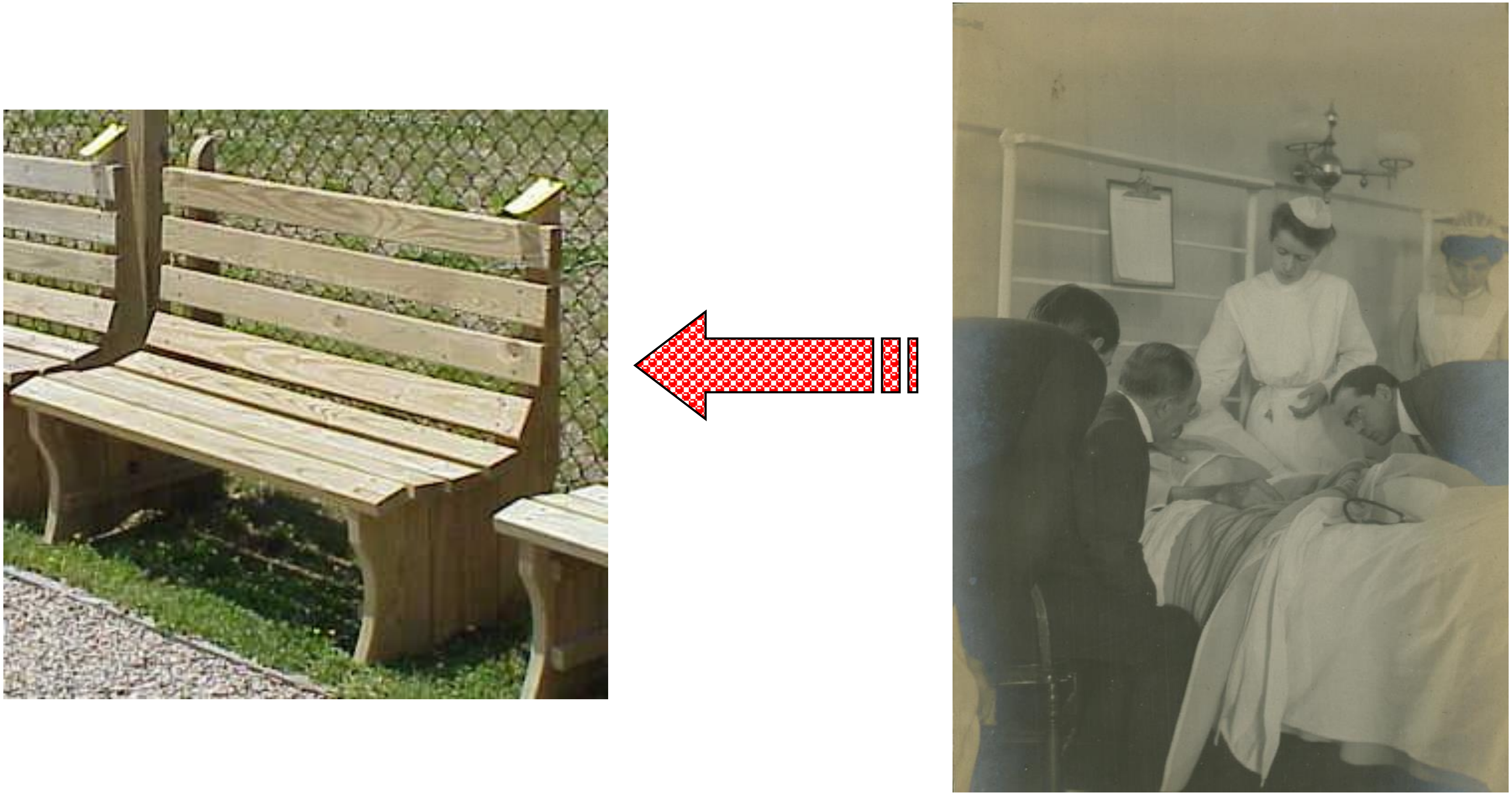
- You can carve out your own niche when studying a rare disease
- *You must carve out your own niche when studying a rare disease*

- Often work in collaborative, multi-center research groups
- *Markedly increased complexities with multi-center studies*

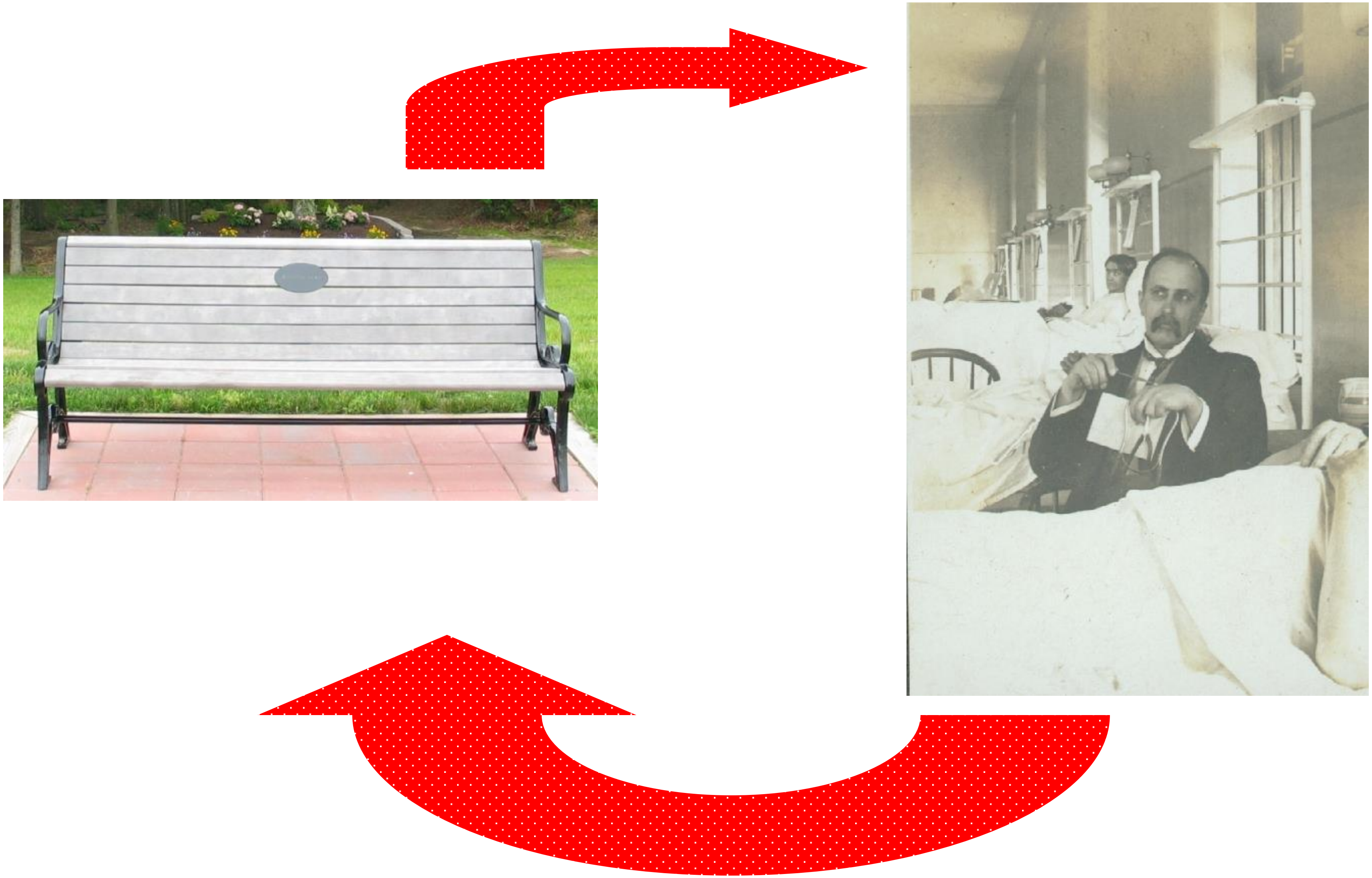
- Face interesting and unique issues in dealing with rare diseases
- *Still face the same challenges as studying common disorders*

Bench to Bedside is a nice model…

Bedside to Bench is likely more productive and common (esp. for rare disease)



Bedside ⟷ Bench is really a bidirectional process, especially for rare diseases



Rare Disease Research: Opportunities

- HUGE unanswered questions for rare diseases
- Potential to make a major impact on a clinically and scientifically underserved population
- The internet is now a key resource for rare disease research
  - Referrals/Recruitment
  - Networking
  - Conduct of research
- Increasing recognition in the scientific community and among funding agencies regarding the importance and benefits of research in rare diseases
- You can carve out your own niche when studying a rare disease

Rare Disease Research: Challenges

- **Sample sizes and recruitment:**
  - these *are* rare diseases!
- **IRB/HIPPA:**
  - must protect privacy
- **Funding:**
  - these markets are, by definition, small
- **Career development**
  - mentors/models are harder to find
  - obtain protected time while still a clinical expert
- **Still have all the usual challenges of a career in academic medicine...**

Solutions: Clinical Piece

- Don’t forget the patient
  - Listen to your patients-they will teach you
- Master the disease
  - Become a student of the disease
- Join/engage with patient advocacy groups
  - Become a citizen of the disease
- Promote your expertise (if it is real)
- Protect your time and focus (well, try)

Solutions: Science Piece

- Do good science
  - There is a limit to compromising due to small sample sizes
  - “Pilot” does not mean “less than good”
  - Be realistic

- Look to “borrow” ideas and approaches from other fields
  - Research approaches for related common diseases may be well-developed and adaptable

- Work collaboratively—Network, including internationally
  - Face the challenges to sharing credit among many people

Solutions: Funding Piece

- Don't believe the hype
  - There IS funding for research (in US)
  - The NIH budget doubled in the past 25 years
    - Shift to more collaborative and multi-specialty approaches
    - Need to work with the new funding realities
  - Take advantage of opportunities and Grants:
    - Federal: NIH, FDA, PCORI, VA, DOD, Other
    - Non-federal funding: Industry, Patient Groups, Institutional, Others
  - Leverage resources (not just $)
    - Clinical Trials
    - Existing Datasets/Repositories/Cohorts
    - Collaborations
    - Core Resources: Institutional, National/International
  - Expand the focus of your inquiry
    - E.g.: Not just vasculitis but vascular inflammation in general
  - Keep your eyes open

NIH Numerology, Alphabet Soup, and Nomenclature

- K08
- K12
- K23
- K24
- K30
- T32
- NRSA (F32)
- Other

- R01
- R13
- R21
- R01
- U01
- U34
- U54
- Other

- Grants
- Contracts
- Cooperative agreements
- Networks
- SBIRs
- ISTs
- RFAs
- RFPs
- Other

Solutions: Career Piece

- Find a good mentor or at least a supporter
- Don’t be afraid of learning new research skills
- Create the right environment for research
  - Ask for the resources you need
- Contribute and receive benefit from collaborations
  - Be a team player but don’t just be a follower

Successful Rare Disease Research is *Clearly* Possible!

- The posters at this meeting testify to this fact
- As with any type of research, challenges exist but solutions are available

This is an excellent time to engage in clinical research in rare diseases

Multi-center research collaborations are extremely helpful for conducting high-quality, high-impact clinical research in rare diseases

Research Networks for Rare Diseases

- ***Pros:***
  - ➢ **Reduce start-up time/costs-leverage resources**
    - **Centers, personnel, systems already in place**
    - **Forms/data entry/CRFs, training, communications**
  - ➢ **Established cohorts and recruitment streams**
  - ➢ **Share workload & credit → *trust***
  - ➢ **Combine expertise**
  - ➢ **Recycle experience**
  - ➢ **Look good to funding agencies/sponsors**

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- ***Cons:***
  - **Must maintain infrastructure**
  - **Need to avoid stagnation → add flexibility**
  - **Require work to maintain cohesiveness**
  - **Takes a long time until productive**
  - **Many, many authors share credit-problem for jr. faculty**

Rare Diseases Clinical Research Network
National Institutes of Health

The Rare Diseases Clinical Research Network (RDCRN)

Office of Rare Diseases Research
National Institutes of Health

Rare Diseases Clinical Research Network
Initiative of the National Center for Advancing Translational Sciences (NCATS)

Goals of the RDCRN

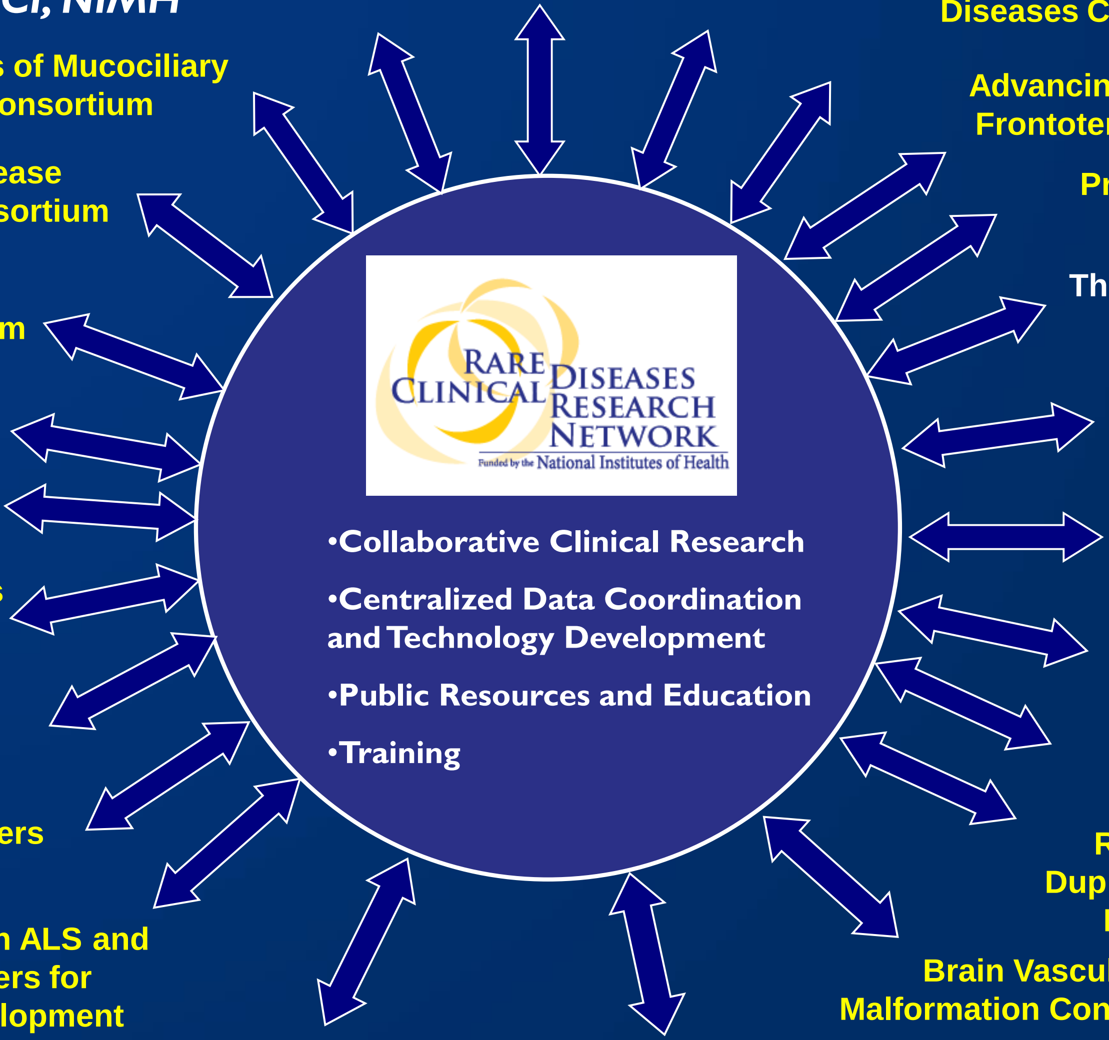
- Facilitate clinical research by:
  - Creation of Consortia focused on related diseases
  - Cost-sharing research infrastructures
  - Establishing uniform protocols for data collection
  - Making meaningful large-scale studies possible
    - Longitudinal cohorts, pilot projects, and randomized trials
- Directly engage patients and their advocates
- Train new investigators in rare diseases research

History of the RDCRN

- Established by the Office of Rare Diseases Research
- Started in 2003--currently in 3rd 5 year cycle
  - 1st cycle (10 Consortia) supported by ORDR, NCRR, NINDS, NIAMS, NICHD, NHLBI, NIDDK
  - 2nd cycle (19 Consortia) supported by ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIAID, NIDCR, NCI
  - 3rd cycle (22 Consortia) supported by ORDR, NCATS, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIAID, NIDCR, NCI, NIMH, ODS
- Currently involves 267 institutions world-wide
- Collectively studying >200 diseases
- 46,760 patients enrolled in studies (during all 3 grant cycles)

DHHS-NIH

ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI, NIMH



Rare Diseases Clinical Research Network

Funded by the National Institutes of Health

- **Collaborative Clinical Research**
- **Centralized Data Coordination and Technology Development**
- **Public Resources and Education**
- **Training**

Dystonia Coalition

Coalition of Patient Advocacy Groups (CPAG)

Consortium of Eosinophilic Gastrointestinal Disease Researchers

North America Mitochondrial Diseases Consortium

Advancing Research & Treatment for Frontotemporal Lobar Degeneration

Primary Immune Deficiency Treatment Consortium

The Data Management and Coordinating Center

Rare Kidney Stone Consortium

Nephrotic Syndrome Rare Disease Clinical Research Network

Chronic Graft Versus Host Disease Consortium

Rare Lung Disease Consortium

Rett Syndrome, MECP2 Duplications, and Rett-related Disorders Consortium

Brain Vascular Malformation Consortium

Autonomic Rare Diseases Clinical Research Consortium

Sterol and Isoprenoid Diseases Consortium

Clinical Research in ALS and Related Disorders for Therapeutic Development

Urea Cycle Disorders Consortium

Development Synaptopathies Consortium

Inherited Neuropathies Consortium

Brittle Bone Disease Consortium

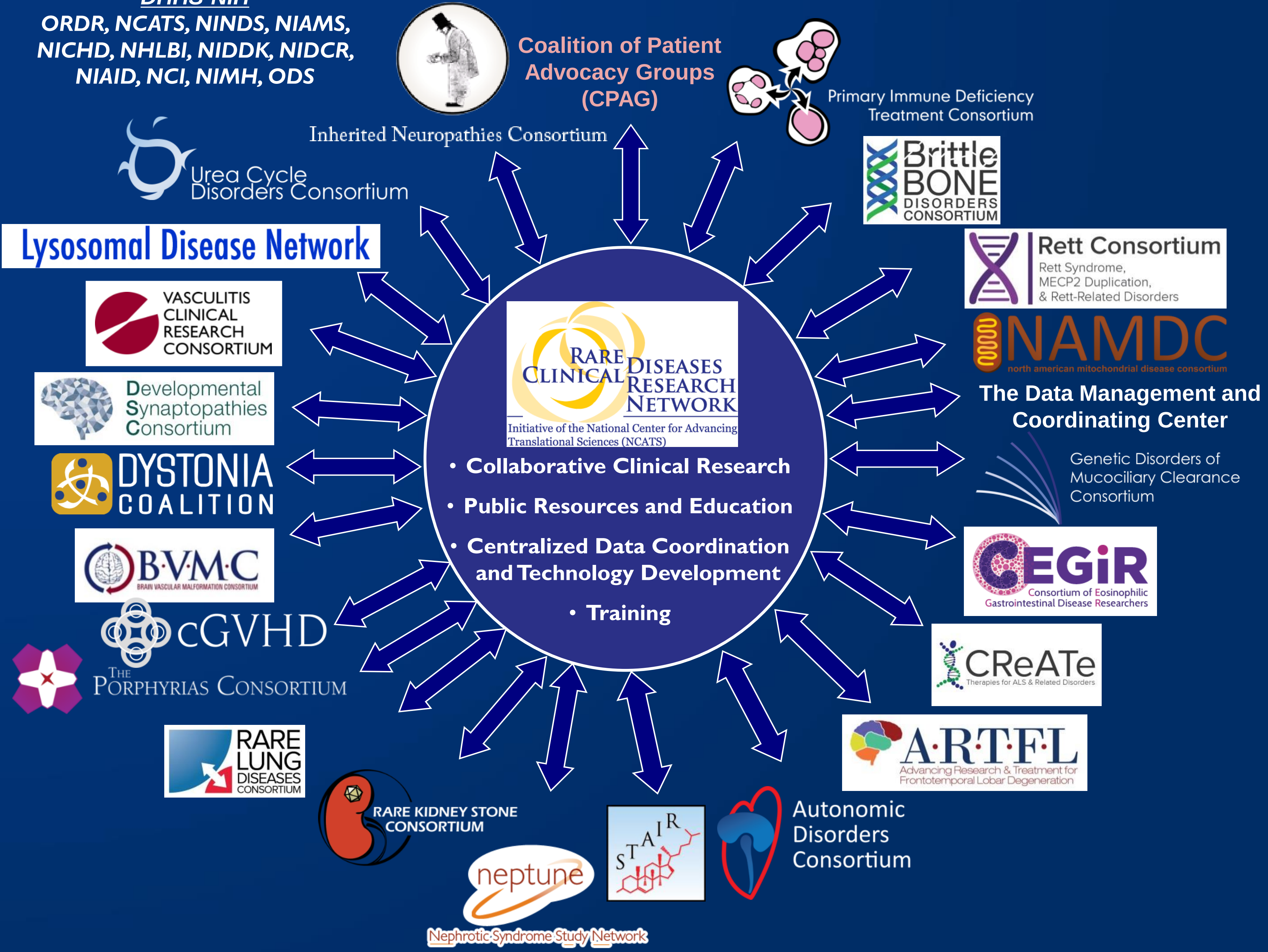
Lysosomal Disease Network

Vasculitis Clinical Research Consortium

Porphyria Rare Disease Clinical Research Consortium

Genetic Disorders of Mucociliary Clearance Consortium

DHHS-NIH
ORDR, NCATS, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI, NIMH, ODS



RARE DISEASES CLINICAL RESEARCH NETWORK
Initiative of the National Center for Advancing Translational Sciences (NCATS)

- **Collaborative Clinical Research**
- **Public Resources and Education**
- **Centralized Data Coordination and Technology Development**
- **Training**

Coalition of Patient Advocacy Groups (CPAG)

The Data Management and Coordinating Center

Inherited Neuropathies Consortium

Primary Immune Deficiency Treatment Consortium

Urea Cycle Disorders Consortium

Brittle BONE DISORDERS CONSORTIUM

Lysosomal Disease Network

Rett Consortium
Rett Syndrome, MECP2 Duplication, & Rett-Related Disorders

VASCULITIS CLINICAL RESEARCH CONSORTIUM

NAMDC
north american mitochondrial disease consortium

Developmental Synaptopathies Consortium

DYSTONIA COALITION

Genetic Disorders of Mucociliary Clearance Consortium

BVMC
BRAIN VASCULAR MALFORMATION CONSORTIUM

CEGIR
Consortium of Eosinophilic Gastrointestinal Disease Researchers

cGVHD

THE PORPHYRIAS CONSORTIUM

CReATe
Therapies for ALS & Related Disorders

RARE LUNG DISEASES CONSORTIUM

A·R·T·F·L
Advancing Research & Treatment for Frontotemporal Lobar Degeneration

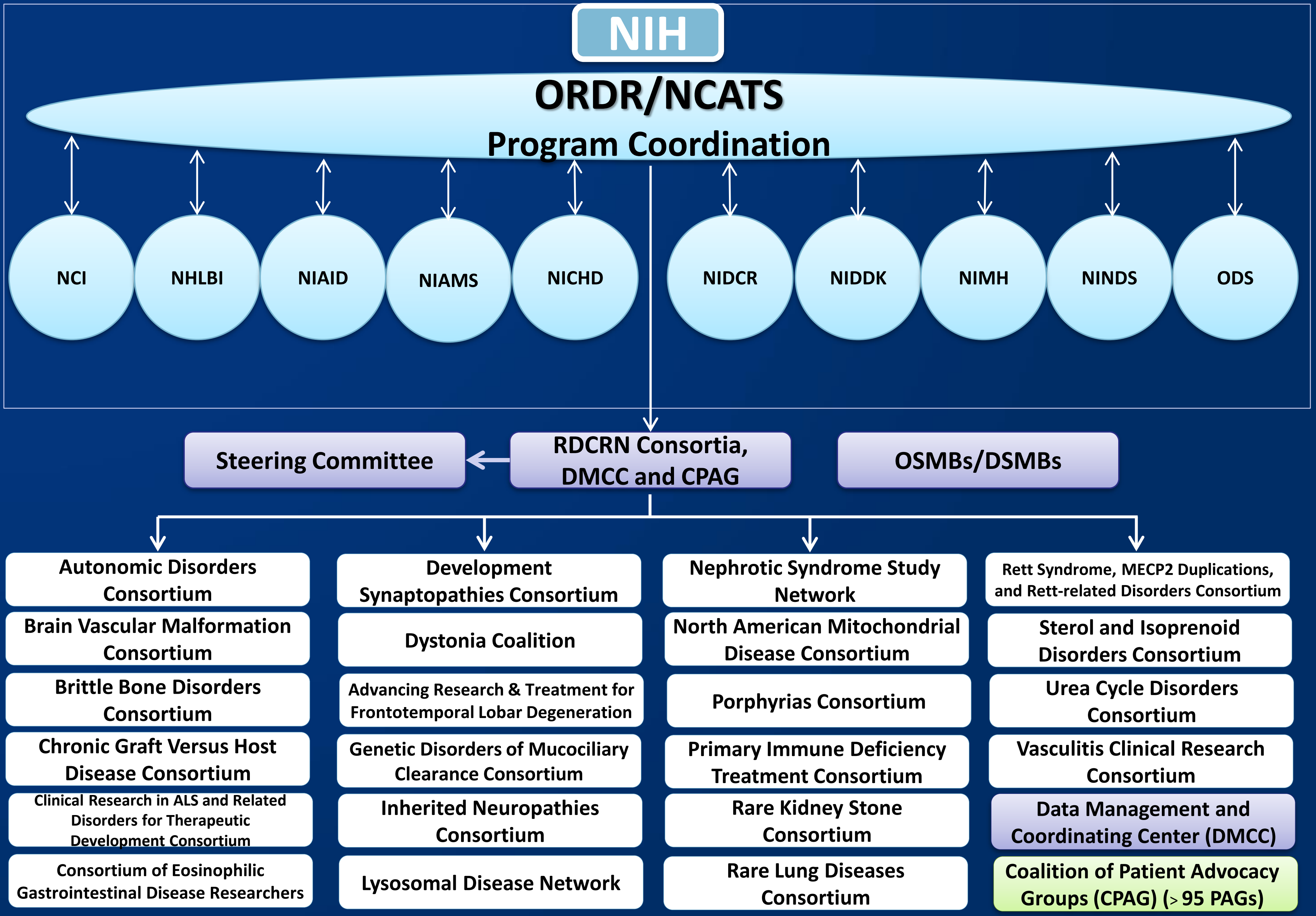
RARE KIDNEY STONE CONSORTIUM

STAIR

Autonomic Disorders Consortium

neptune
Nephrotic Syndrome Study Network

Rare Diseases Clinical Research Network (RDCRN)



NIH

ORDR/NCATS

Program Coordination

NCI
NHLBI
NIAID
NIAMS
NICHD
NIDCR
NIDDK
NIMH
NINDS
ODS

Steering Committee

RDCRN Consortia, DMCC and CPAG

OSMBs/DSMBs

- Autonomic Disorders Consortium
- Brain Vascular Malformation Consortium
- Brittle Bone Disorders Consortium
- Chronic Graft Versus Host Disease Consortium
- Clinical Research in ALS and Related Disorders for Therapeutic Development Consortium
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- Sterol and Isoprenoid Disorders Consortium
- Urea Cycle Disorders Consortium
- Vasculitis Clinical Research Consortium
- Data Management and Coordinating Center (DMCC)
- Coalition of Patient Advocacy Groups (CPAG) (> 95 PAGs)

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IT CAN BE DONE!