Patient Registries and Biorepositories in Myositis: MYOVISION Myositis Patient Registry

The Myositis Association International Annual Patient Conference

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Clinical Data Registry

- Organized database of healthcare information on certain diseases. Can be patient registry, physician-collected data, or collection of information from government and other organizations (Medicare, Social Security Death Index, US census data, or exposures based on geographic location).
  - May have patient data with a condition and healthy controls, or only patient data
- **Purposes:**
  - Evaluate patient features and outcomes
  - Understand how patients with different characteristics respond to different therapies
  - Examine exposures and effects on health outcomes
  - Population level health status

Biorepository

- Catalogued collections of biological specimens, often linked to clinical data. Collects, processes, stores and distributes biospecimens to support future scientific investigations.
- Can be human (patient) or animal specimens
- Often contain blood specimens – serum, plasma, DNA, RNA (nucleic acids, white blood cells, and tissues
- Often linked to clinical/patient data

Purposes of Registries and Biorepositories

- Major impact in understanding epidemiology, clinical features, outcomes and prognosis of various disorders, especially rare diseases
- Potentially helpful in treatment studies
  - May serve as a control arm in a clinical trial (if FDA approved in a trial)
  - May be used to learn about adverse events associated with some medications
- Especially helpful for rare diseases like myositis – more rapidly collect large enough sample with variations to see new patterns, make new discoveries

Major Research Advances Through Myositis Registries and Repositories

- Careful phenotyping of disease features – define clinical and serologic subgroups
- Defined natural history, risk factors for complications, long-term prognoses
- Defined myositis autoantibody groups
- Development of new classification criteria for myositis
- Defined genetic and environmental risk factors
- Understanding pathogenesis (disease mechanisms/ process) – including muscle, skin and other tissues, developed biomarkers (new blood tests) that can guide treatment decisions
- Developed validated, standardized outcome measures and new response criteria for myositis therapeutic trials

Rider et al., Curr. Opin. Rheum., 2014; Lundberg and Vencovsky, Curr. Opin. Rheum., 2017

Myositis Registries/Repositories Around the Globe Available for Research Collaborations

- More than 75 myositis registries available for research collaborations
  - 50 international, 26 national or regional registries
    - **North America** (US, Canada), **Europe** (Italy, UK, Sweden, Spain, France, Hungary, Moldova, Poland, Belgium, Denmark, Norway), **Asia** (India, Japan, Hong Kong, Saudi Arabia, Turkey), **Australia, South/Central America** (Brazil, Mexico, Argentina, Chile, Guatemala)
  - 27 all forms myositis, 32 adult DM, PM, IBM, IMNM, 17 JDM, JPM
  - 53 with biorepositories: serum, plasma, DNA most frequent; muscle & other tissues, RNA, cells, urine- less common
  - More than 26,000 patients enrolled
  - Individual registry size: 10 – 5000 IIM patients each (average size ~400)

Rider et al., Curr. Opin. Rheum., 2014; IMACS Database of Myositis Databases (unpublished)

Myositis Registries/Repositories are Growing in Size and Sophistication: Recent Examples

- **MYONET:** More than 4,000 patients from > 20 centers worldwide
  - Core demographic and clinical data, longitudinal core set measure evaluations
  - Research on spectrum myositis, prognosis, outcomes, autoantibodies, genetics
  - Assist with clinical decision making
    Lundberg and Vencovksy, Curr Opin. Rheum., 2017
- **Univ. Pittsburgh Myositis Center** (Oddis/Aggarwal): > 1100 patients, 4000+ encounters, core set data, > 37,000 sera, 1100 DNA, 350 cells, 100 RNA samples; Research Data Management System
- **UK JDM Cohort and Biomarker Study (JDCBS)** (Wedderburn): 17 centers, > 543 patients, longitudinal data/samples, 48 projects
- New inception cohorts – Canada, Brazil

Myositis Registries/Repositories – Varying Objectives

- Frequent objectives of 46 registries include:
  - Phenotypes – defining (clinical, myositis autoantibodies): 18
  - Outcomes: 16
  - Epidemiology: 12
  - Clinical features: 12
  - Disease assessment: 12
  - Treatment responses: 12
  - Pathogenesis/disease mechanisms (including 2 DM skin disease): 12
  - Genetic and/or Environmental Factors: 6-8
  - Other: Biomarkers, Classification criteria, Research repositories, Patient reported outcomes, Quality care

Rider et al., Curr. Opin. Rheum., 2014

Challenges for Myositis Registries and Repositories – I

- Inconsistency in myositis classification criteria used
  - **Advance:** EULAR-ACR International Myositis Classification Criteria
    Lundberg et al., Ann. Rheum. Dis., Arthr. Rheum., 2017
- Lack of standardized terms, collection of varying data elements, variations in data collection platforms
  - **Advance:** Carefully define variables, standardize data collection
    - Optimum dataset for JDM
      McCann et al, Ann Rheum Dis, 2017
    - IMACS Outcomes Repository, new IMACS project on Common Data Elements

    https://www.niehs.nih.gov/research/resources/imacs/researchguidelines/index.cfm
- Variations in disease assessment
  - **Advance:** IMACS and PRINTO core set disease measures with publicly available training materials

    https://www.niehs.nih.gov/research/resources/imacs/diseaseactivity/index.cfm

Challenges for Myositis Registries and Repositories – II

- Variations in assays for myositis autoantibodies, other biomarkers
  - **Advance:** IMACS Myositis Autoantibody Scientific Interest Group addressing autoantibody testing platforms
- Variations in samples collected, processing procedures, and storage
  - **Advance:** CARRA standardization in sample collection procedures, biospecimen storage, assay methodologies
    Yeung et al., Nature Reviews Rheum., 2016
- Varying rules for ethics approval, data sharing
- Increased number of registries → redundancy: consolidate
  - Needed support for maintenance, expansion and integration

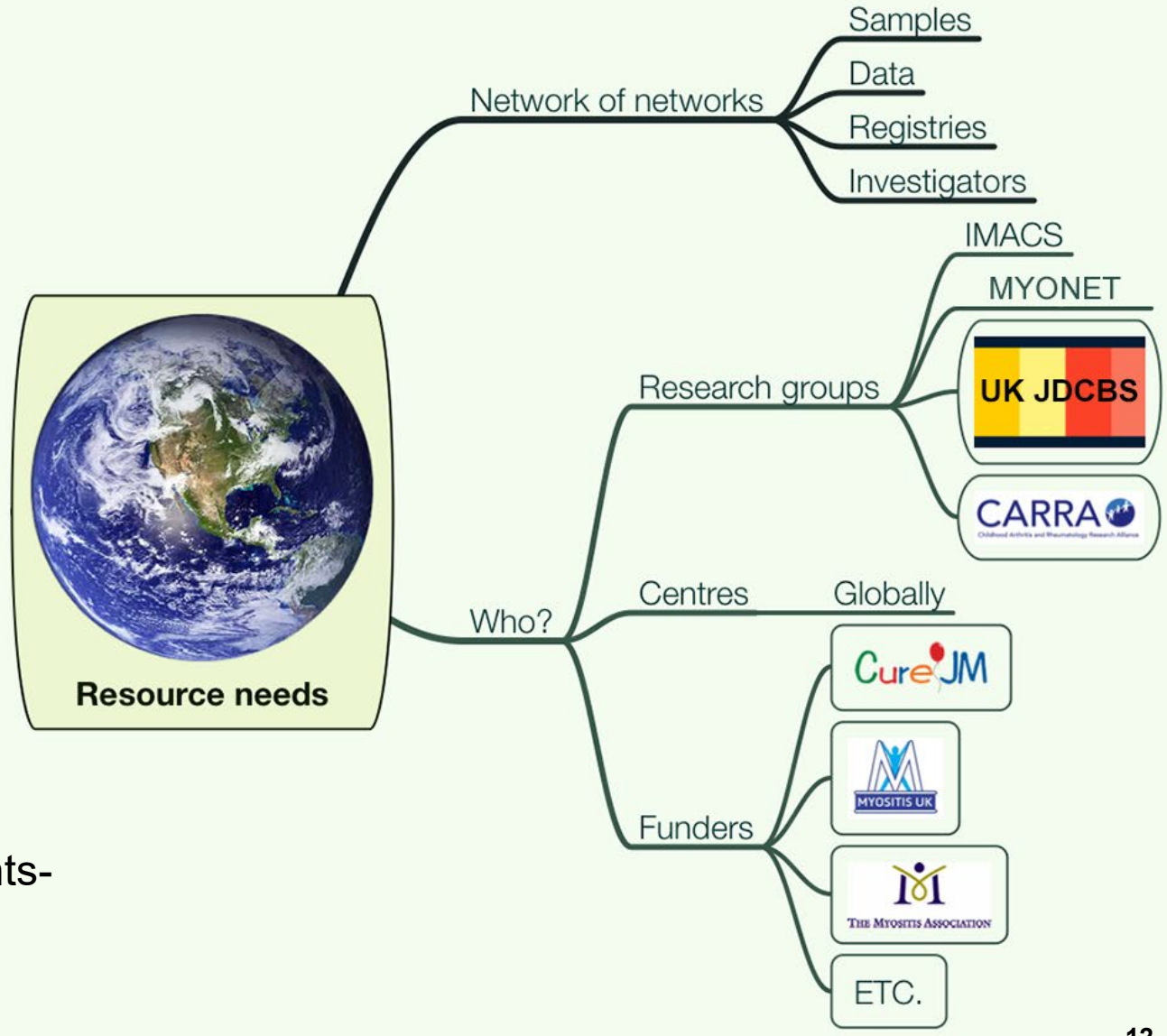
Challenges for Myositis Registries and Repositories – III

- Registries focus on selected research questions, potentially unprepared for future research in new directions;
  Needs to examine longitudinally and through the lifespan
  - **Advance:** Informed consent provision to allow future research not covered under current protocol (opt-in provision)

- Registry closures: stewardship to enable future use of data and samples
  - **Advance:** Transfer to existing ethics review board approved registry study to enable ongoing use of data/samples and new collaborations

Network of Myositis Registries

Bring together multiple researchers, who have separate registries and repositories, to work together on specific research questions



New IMACS project: To create common data elements- to be able to share these myositis databases

Courtesy of Dr. Brian Feldman

Myositis Registries and Repositories – Summary

- A number of myositis registries and repositories exist as opportunities for substantial research and collaborations
  - Understanding myositis subgroups, risk factors, outcomes/prognosis, disease mechanisms, and disease assessment has rapidly and vastly expanded as a result
- Possibility for patients to join and researchers to collaborate with large myositis registries and networks
  - MYONET: large network, worldwide data collection/database (multiple sugroups)
  - CARRA, UK JDCBS: national registries with multiple collaborators, projects (JDM)
  - IMACS: consortium of myositis researchers with number of projects, databases
- Further progress in myositis will require overcoming current challenges, securing support for these registries and repositories for future, and ensuring their effective integration (network of myositis networks)

MYOVISION National Myositis Patient Registry

- A national patient registry of patients diagnosed with adult and juvenile DM, PM, IBM and rarer forms of myositis
- Patients residing in the United States or Canada at diagnosis
- Joint collaboration between The Myositis Association, Cincinnati Children's Hospital Medical Center, and Environmental Autoimmunity Group, NIEHS, NIH; TMA received CDC funding
- Data collected through paper and online questionnaires (1605 paper, and 351 online surveys)

CDC
Centers for Disease Control and Prevention

The Myositis Association

Cincinnati Children's® Hospital Medical Center

NIH National Institute of Environmental Health Sciences

MYOVISION Goals

1. Establish a myositis patient registry to investigate:
   - Demographics
   - Manifestations of illness
   - Medications received and responses
   - Types of physicians involved in care
2. Investigate potential environmental exposures related to onset of disease
3. Evaluate impact of disease on quality of life
4. Examine additional exploratory research questions related to environmental risk factors
5. Create a population that can be re-contacted for future studies

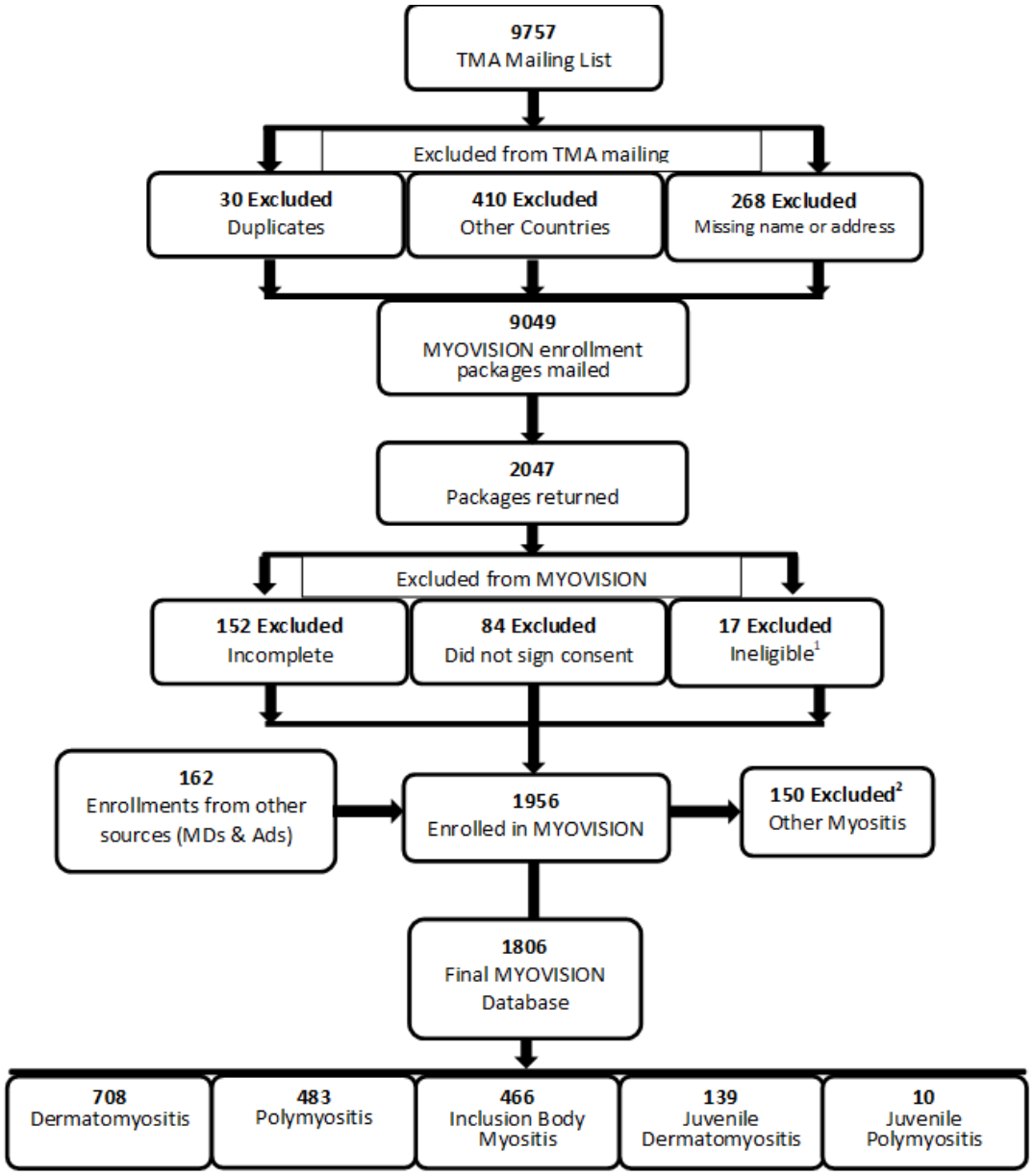
MYOVISION Questionnaire

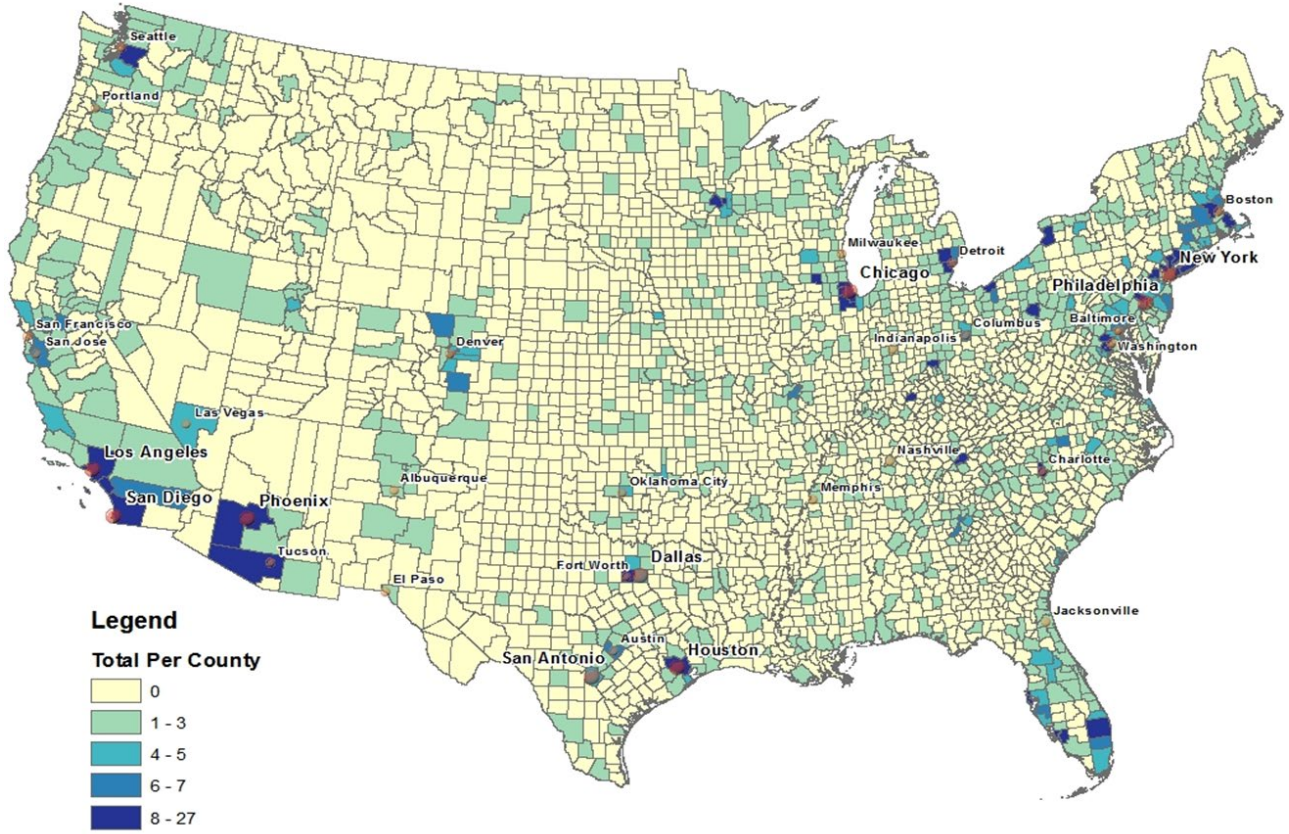
- 38 pages, 83 questions, including:
  - Demographic information
  - Illness features
  - Quality of life measure (SF12, SF10)
  - Geographic locations
  - Environmental exposures:
    - Pollutants and exposures by geographic location
    - Smoking
    - Occupational and hobby exposures
    - Infections
    - Medications
    - UV exposure





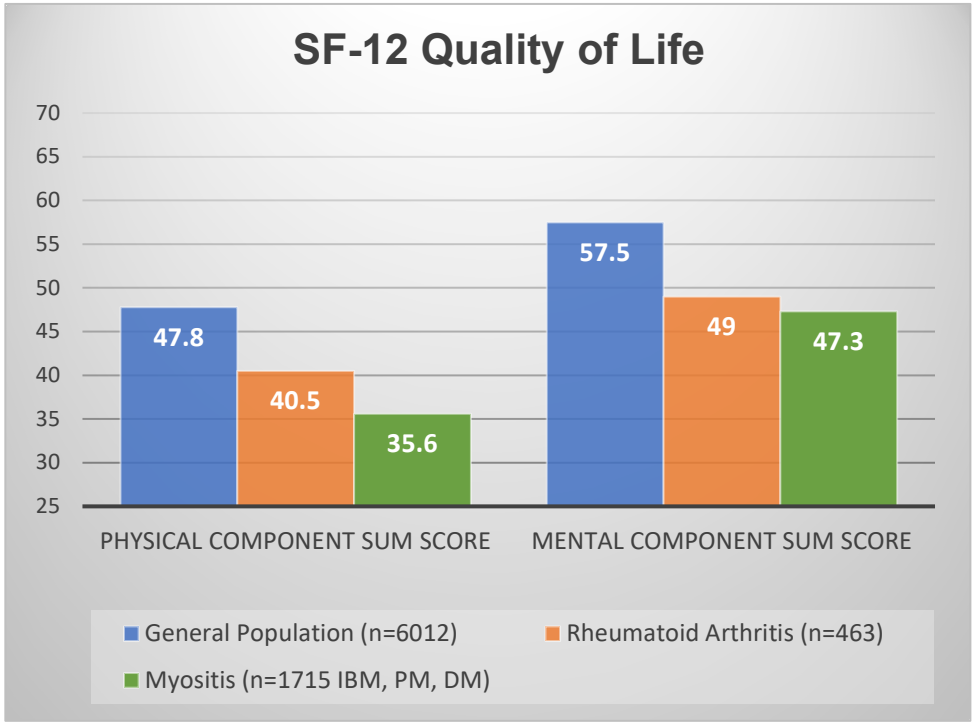

MYOVISION Patients and Geographic Distribution





HRQoL Reduced in Myositis Patients Compared to Rheumatoid Arthritis and General Population

- Quality of life (HR-QoL), by SF-12, was lower in myositis patients than general population sample or patients with rheumatoid arthritis
  - Physical component scores lowest in IBM, intermediate in PM, higher in DM
  - Mental component scores did not different between subgroups
- Impairments in all domains in myositis vs. general population:
  - Physical and social function, pain, general health, vitality, emotional, mental health
  - Compared to patients with RA, lower QoL in all domains, except comparable bodily pain



Feldon et al., Arthritis Care Res., 2017

- Associations with lower physical component of HR-QoL: older age, negative effect of myositis on work performance, autoimmune disease overlap, lung disease, arthritis, use of multiple medications
- Lower mental component scores associated with negative effect on work, arthritis

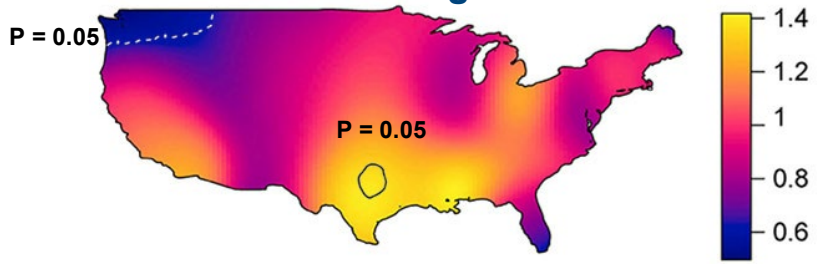
Geospatial Distribution of Myositis in the United States from MYOVISION Patient Registry Suggests Clustering by Phenotype

- Used spatial modeling to examine spatial characteristics and possible risk factors (484 DM, 358 PM, 318 IBM)
- More myositis cases in East/Northeast, including DM and IBM; PM ↑ in South
  - Clustering of cases with differences by subgroup (IBM vs. DM/PM)
- Relative prevalence of DM vs. PM – ↑ West, ↓ NW
- Relative prevalence of lung disease vs. no lung disease – ↑ SW, ↓ NW
- Trend of higher prevalence of IIM, esp. IBM, living within 50 m of major roadway

Spatial Distribution and Clustering of IIM in MYOVISION

Relative Prevalence of DM vs. PM

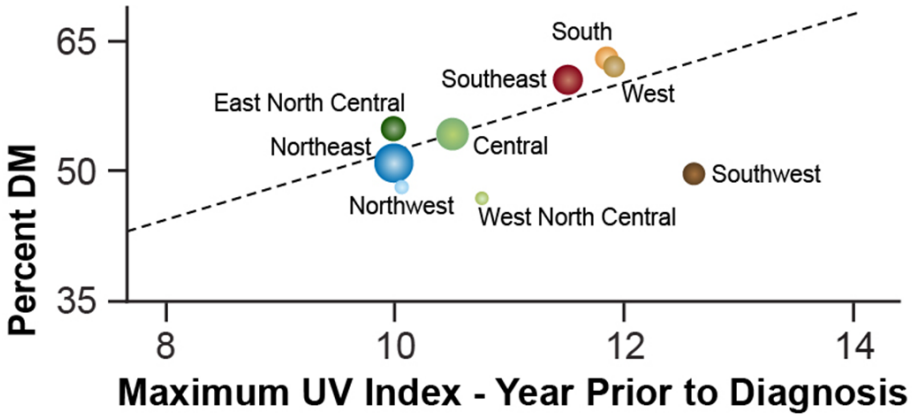
Relative Prevalence of Lung Disease vs. No Lung Disease

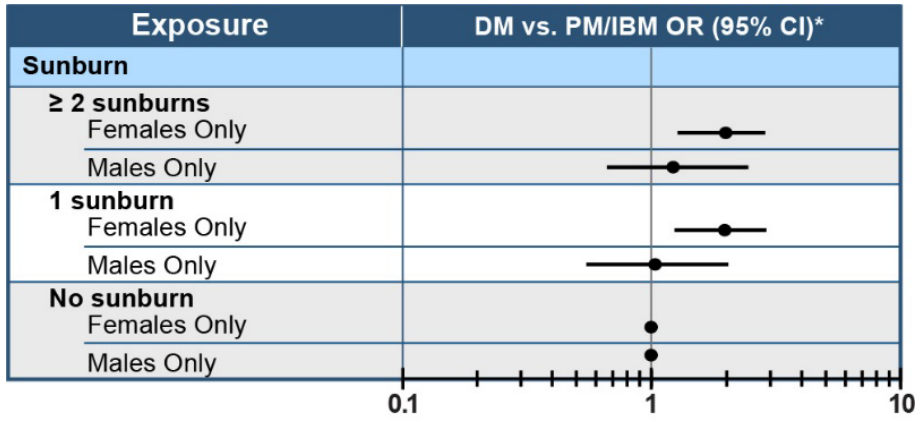


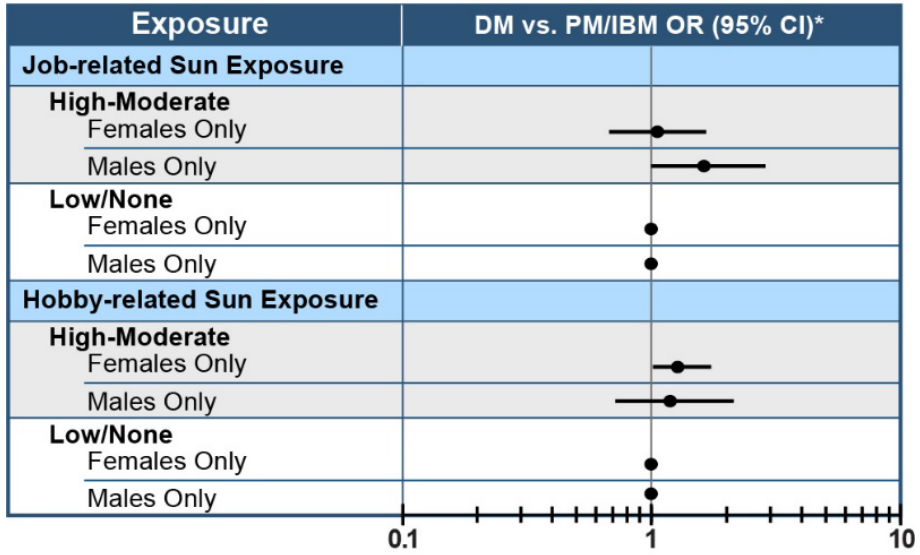
Hossain…Rider 2022 Frontiers Medicine

MYOVISION National Myositis Patient Registry: Personal Sun Exposure Associated with DM

- Sunburn in year before diagnosis associated with DM, not PM/IBM
  - Frequency sunburns in women increased compared to healthy population (31% vs. 24%)
- Sun exposure related to jobs in men, hobbies in women with DM
- Residential UVB exposure in year prior to diagnosis associated with DM in women



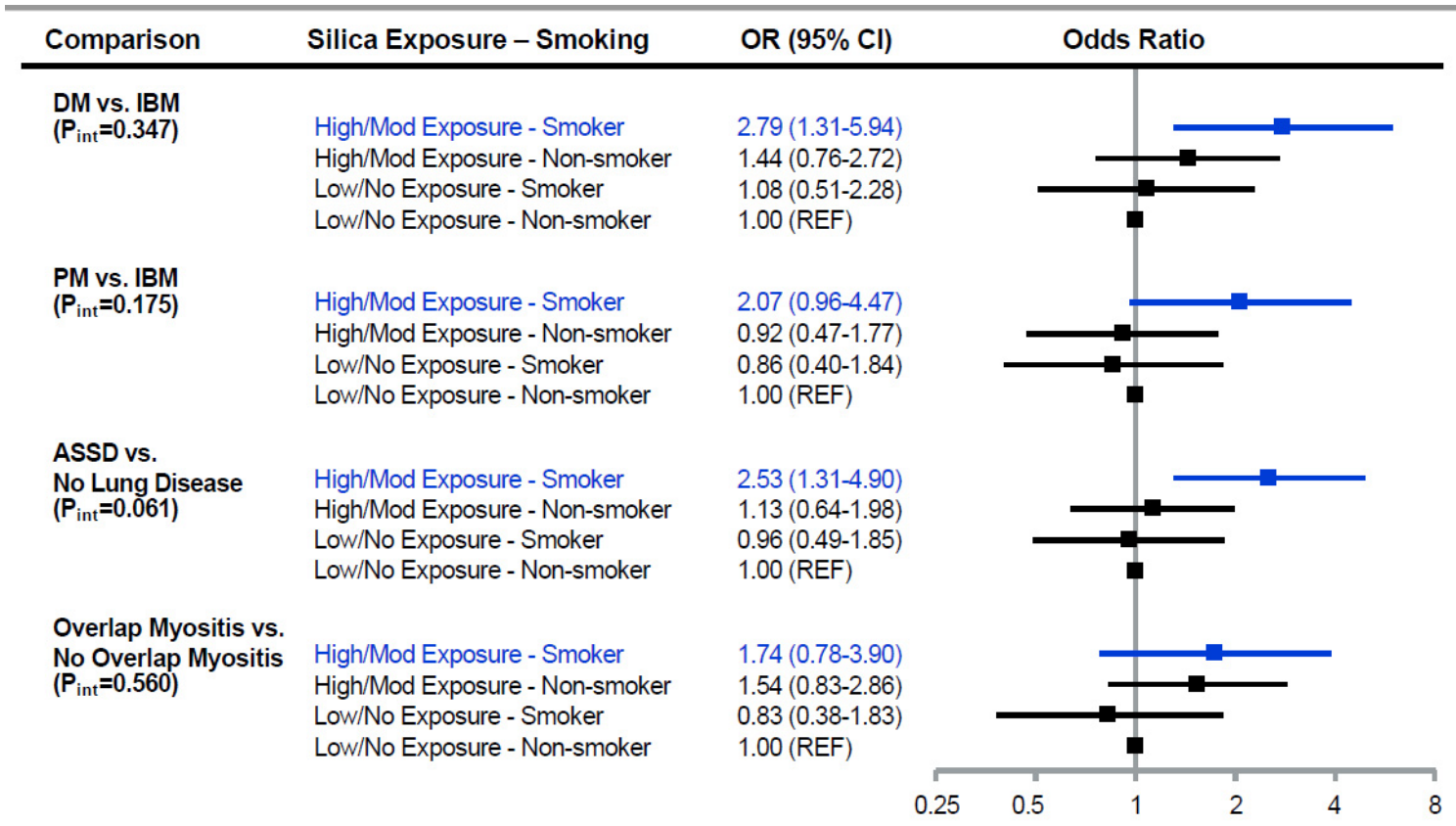




Parks…. Rider et al. 2020 Arthritis Care Res.

Occupational/Hobby Exposure to Silica, Heavy Metals, Solvents Associated with Myositis Subgroups

- Occupation/hobby exposures evaluated by occupation coding, epidemiologists assessed level of exposure and certainty
- High silica dust exposure associated with DM compared to IBM, with ASynS (ASSD) and overlap myositis
- Moderate to high heavy metals and solvents also associated with ASynS (ASSD) and overlap myositis
- Odds highest among smokers with these exposures



Parks…. Rider et al., 2023, Arthritis Rheum (ACR Convergence), MS under review

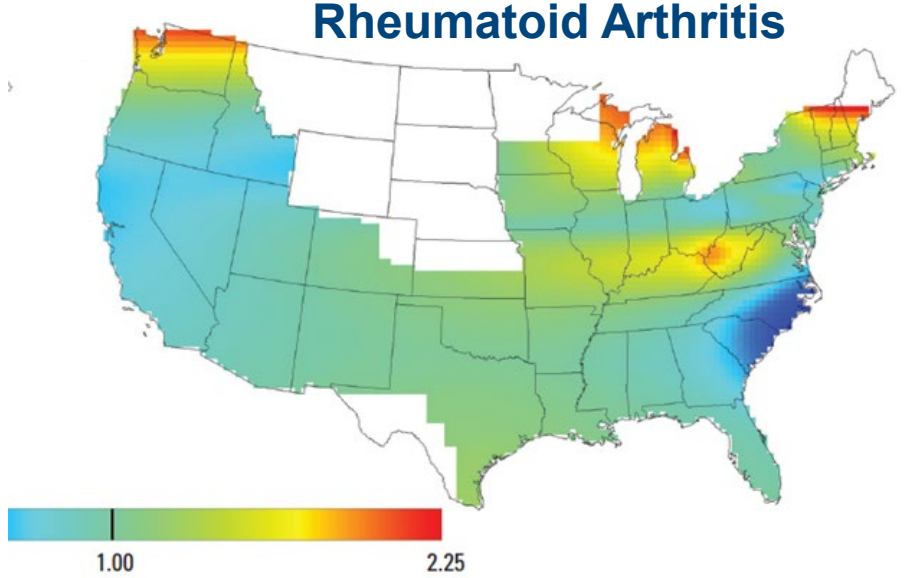
MYOVSION – Future Work

- Complete basic epidemiologic analysis: clinical features, co-existing cancer and autoimmune diseases, and treatment data among myositis subgroups (*Iazsmin Bauer-Ventura, Univ Chicago*)

- Evaluation of infections and medications as risk factors

- Evaluation of exposures as risk factors based on residential location at diagnosis: pollutants, pesticides, social vulnerability, others
  (Shan Shan Zhao, NIEHS; Monir Hossain, Cincinnati Children's)

Northern Latitude Associated with Rheumatoid Arthritis



Veira, 2010, EHP

MYOVISION – Summary

- First large national myositis patient registry, with various myositis subgroups, established, as collaboration between TMA, Cincinnati Children's, and NIEHS
- HR-QoL is impaired in myositis patients, more than rheumatoid arthritis and general population, in all areas
- Ultraviolet radiation and sunburn in year prior to diagnosis, is a risk factor for DM, especially in females and is from personal sun exposure
- Occupational and hobby exposures, including silica dust, solvents, heavy metals, appear to increase risk of certain myositis subgroups (lung disease – ASynS-like, overlap myositis, others), especially with heavier exposure and in smokers
- Clustering of patients with differences among subgroups in U.S.
  - Examination of exposures based on geographic location at diagnosis are ongoing

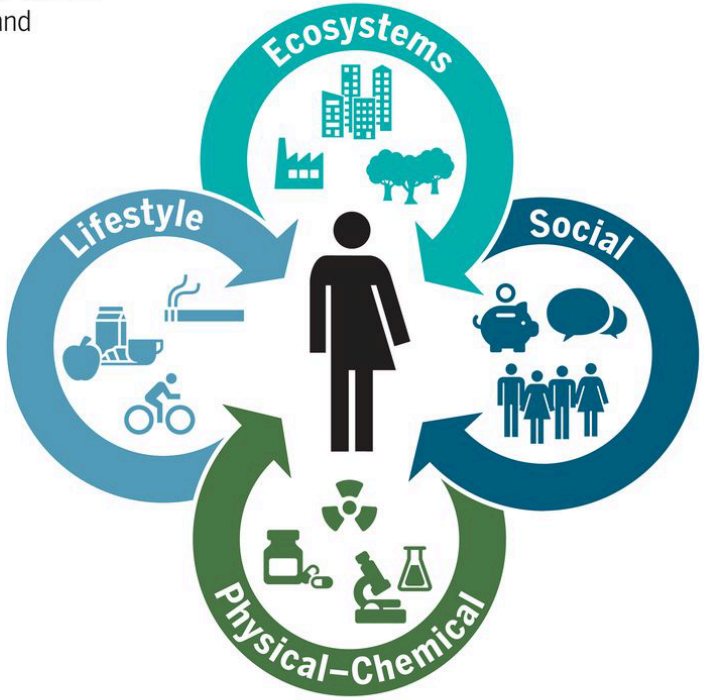
The Exposome Over the Life Course

Exposome – A new paradigm to assess how a lifetime of exposures, from conception through the lifespan, affects the risk of developing chronic diseases

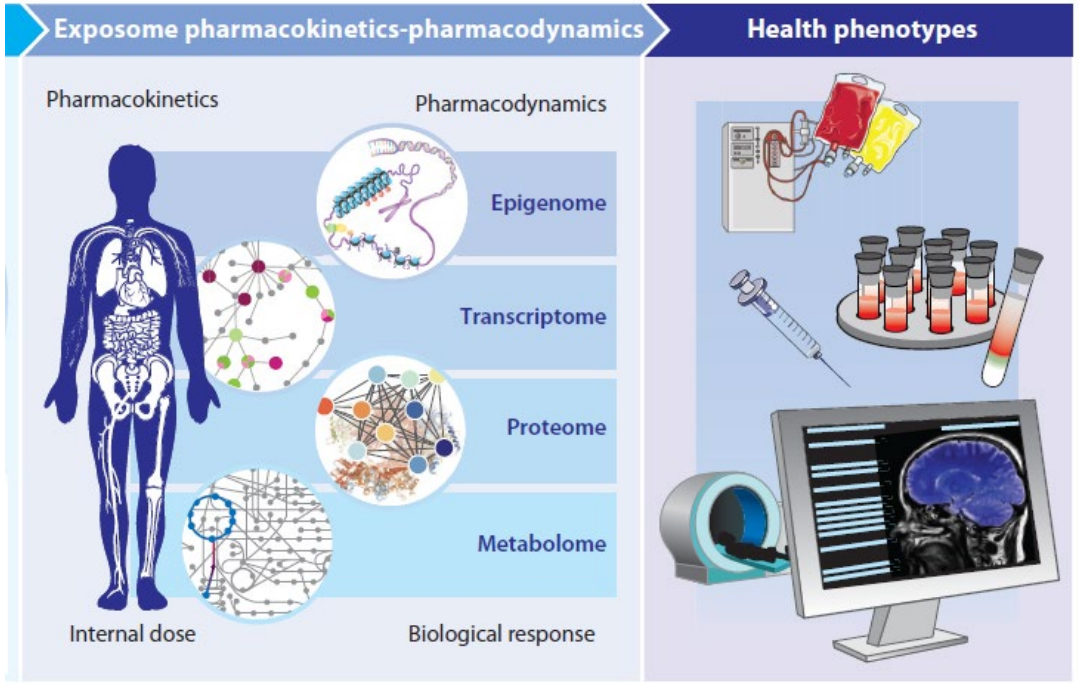
Ecosystems
Food outlets, alcohol outlets
Built environment and urban land uses
Population density
Walkability
Green/blue space

Lifestyle
Physical activity
Sleep behavior
Diet
Drug use
Smoking
Alcohol use

Social
Household income
Inequality
Social capital
Social networks
Cultural norms
Cultural capital
Psychological and mental stress



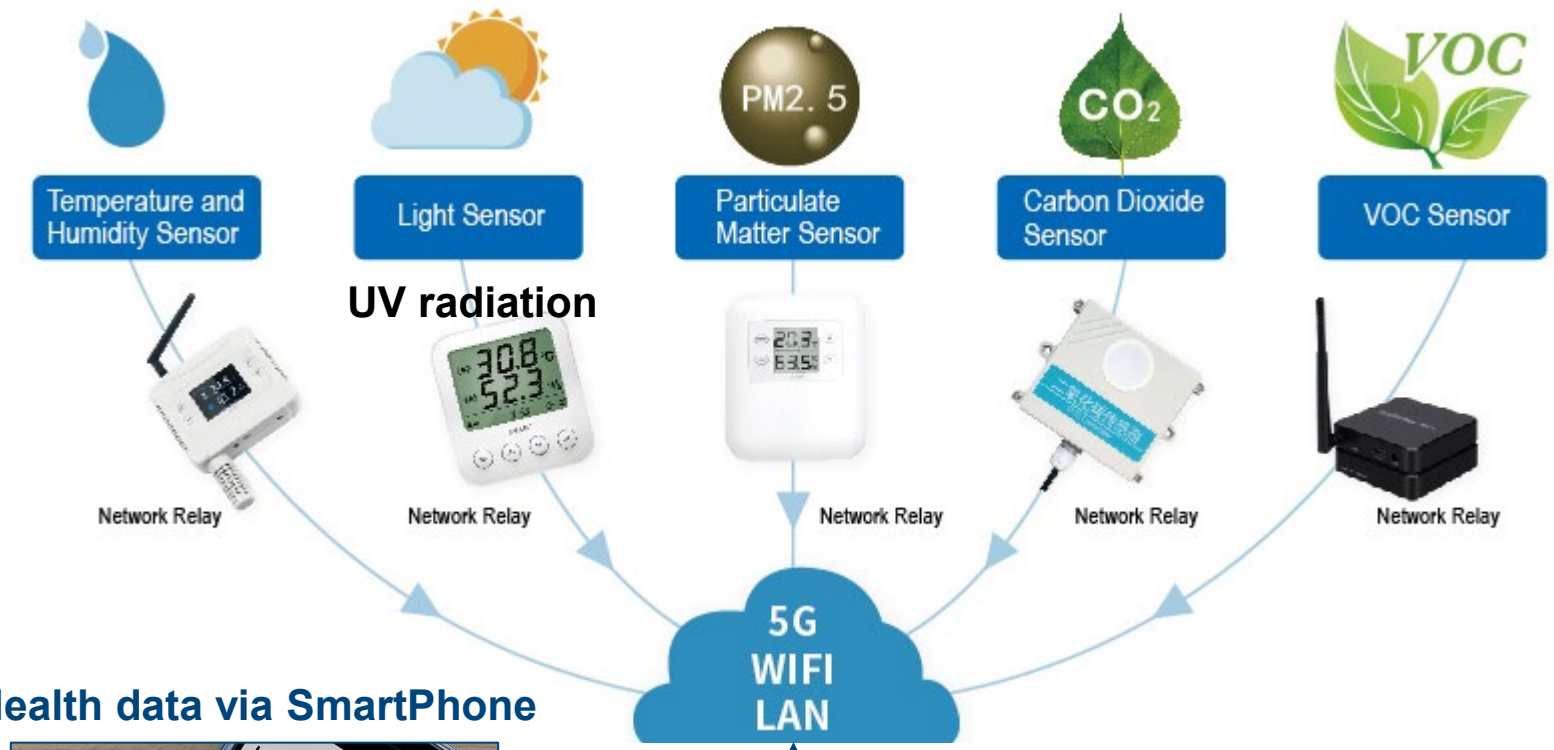
Physical–Chemical
Temperature/humidity
Electromagnetic fields
Ambient light
Odor and noise
Point, line sources, e.g. factories, ports
Outdoor and indoor air pollution
Agricultural activities, livestock
Pollen/mold/fungus
Pesticides
Fragrance products
Flame retardants (PBDEs)
Persistent organic pollutants
Plastic and plasticizers
Food contaminants
Soil contaminants
Drinking water contamination
Groundwater contamination
Surface water contamination
Occupational exposures



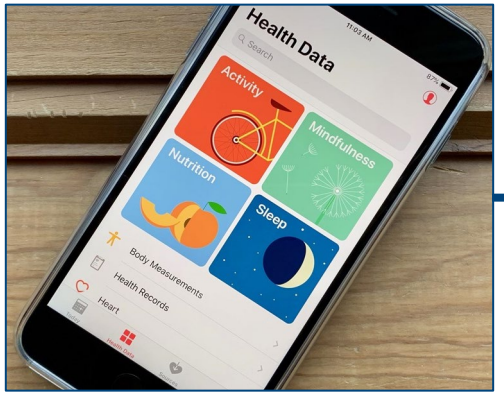
Childhood Adolescence Adulthood

Vermeulen et al. 2020 Science; Esher et al. 2017 Environ International

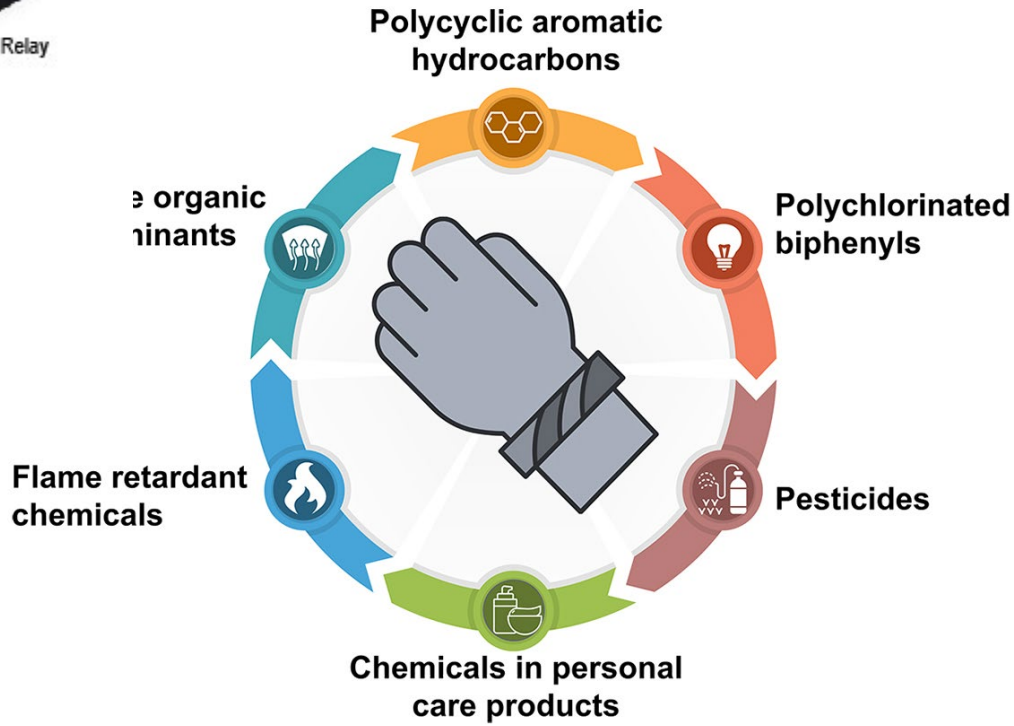
Wearable Real Time Environmental Sensors



Health data via SmartPhone



Silicone Wrist Bands



Chen et al. 2012 Atmos Environ; O'Connell et al., 204 Environ Sci Technol

MINT
Myositis ILD Nintedanib Trial

Rohit Aggarwal, UPMC

Study Flow

Recruitment

Local sites

Decentralised site

Screening, consent and enrolment

In clinic and/or telemedicine

Telemedicine

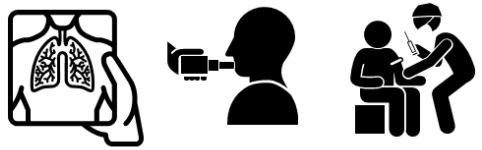
Local physician partner

Home Drug Delivery

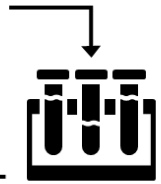
Remote data collection

Patient-reported outcomes | Physical activity monitors | Pulse oximetry | Blood pressure and heart rate monitors | Home spirometry | Telemedicine | Medical records

Other data collection



HRCT at local site* or other centre near patient's home | Clinic PFTs at local site* or other centre near patient's home | Blood collection during nurse home visits, or at local site* or other centre near patient's home



Specimen storage

Bluetooth

Spirometry

Oxygen Saturation

Blood Pressure

Secure server

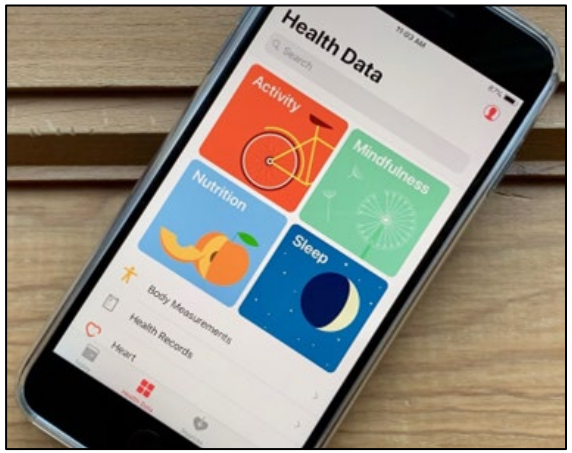
*Only for patients recruited at local sites.

Website: https://mint.pitt.edu
ClinicalTrial.gov: NCT05799755

Registries – Critical Research Resource

- Registries are a critical tool to make progress in rare disease research, such as myositis
- Patient participation is essential to the success of myositis registries!

The Myositis Association



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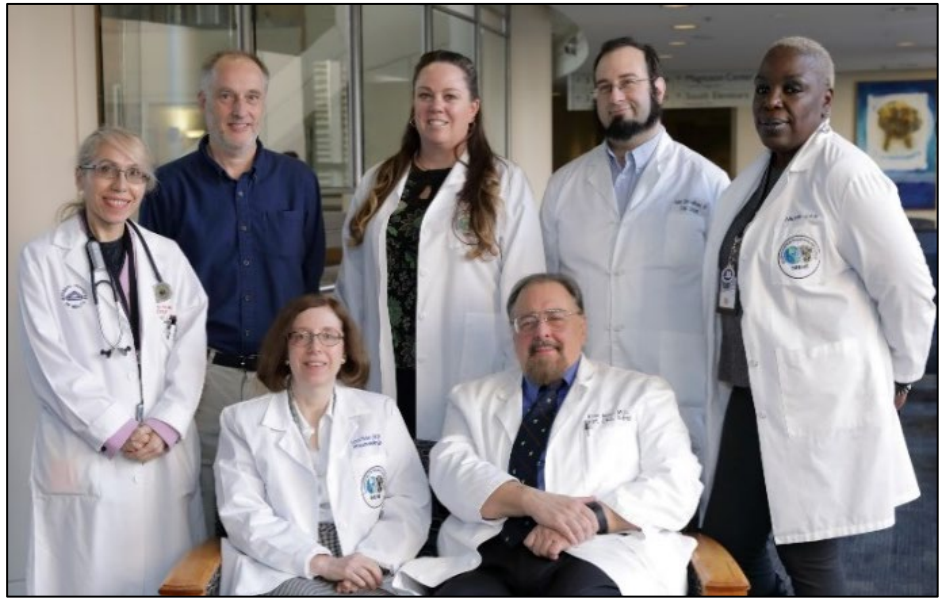
- **Collaborators**
  - NIEHS and others: Christine Parks, Jesse Wilkerson, Clare Weinberg, Min Shi, Shanshan Zhao,
  - Rohit Aggarwal, Nicola Ruperto, IMACS Investigators
  - MYOVISION: Hermine Brunner, Ed Giannini, Lukasz Itert, Michal Feldon, students, Iazsmin Bauer-Ventura, Bob Goldberg, TMA
- Our patients and their families



NIH National Institute of Environmental Health Sciences

THE MYOSITIS ASSOCIATION

IMACS

Cincinnati Children's Hospital Medical Center

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION

INTERNATIONAL ANNUAL PATIENT CONFERENCE

HILTON BALTIMORE INNER HARBOR

SEPTEMBER 6-8, 2024

CELEBRATING OUR CONNECTION

THE MYOSITIS ASSOCIATION®

Thank you!