Vision Statement

*Relieve the burdens of **osteoarthritis patients** through **science**.*

Arthritis Foundation®

Mission Statement

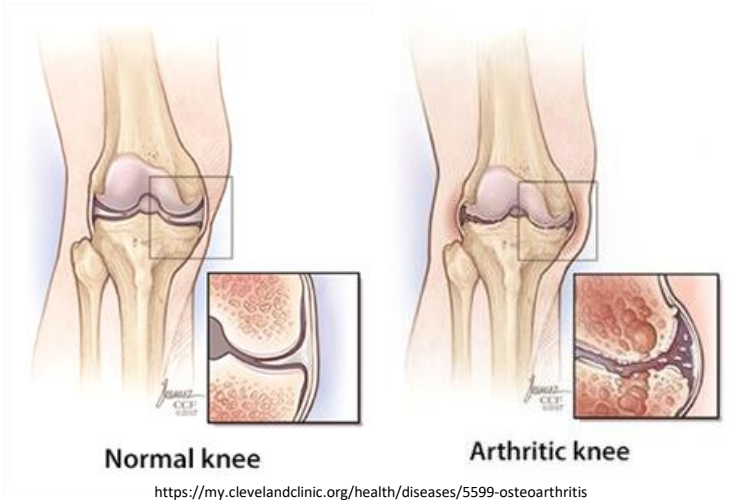
Maximize the number of promising therapies ready for clinical trials that can effectively intervene in the progression of osteoarthritis through convening of diverse expertise and directed research programs.

Introduction

- **Osteoarthritis (OA)** is a degenerative disease of the entire joint: bones, cartilage, tendons, ligaments, etc.
- OA is the **most common** form of arthritis
- Over **32.5 million Americans** diagnosed with OA

10%

of the US population



https://my.clevelandclinic.org/health/diseases/5599-osteoarthritis

- **Who** is affected by OA?
  - 88% of people with OA are **45 years or older**
  - 62% are **women**
  - 78% are white*
- **Increased risk** of developing OA in people who are **obese,** and/or who have had a **joint injury**
- **Economic Burden**
  - Estimated at **$136.8 BILLION** annually in the US, expected to continue to rise
  - Approx.1 million knee and hip replacements needed due to OA

The Need

There is no disease-modifying cure available for OA

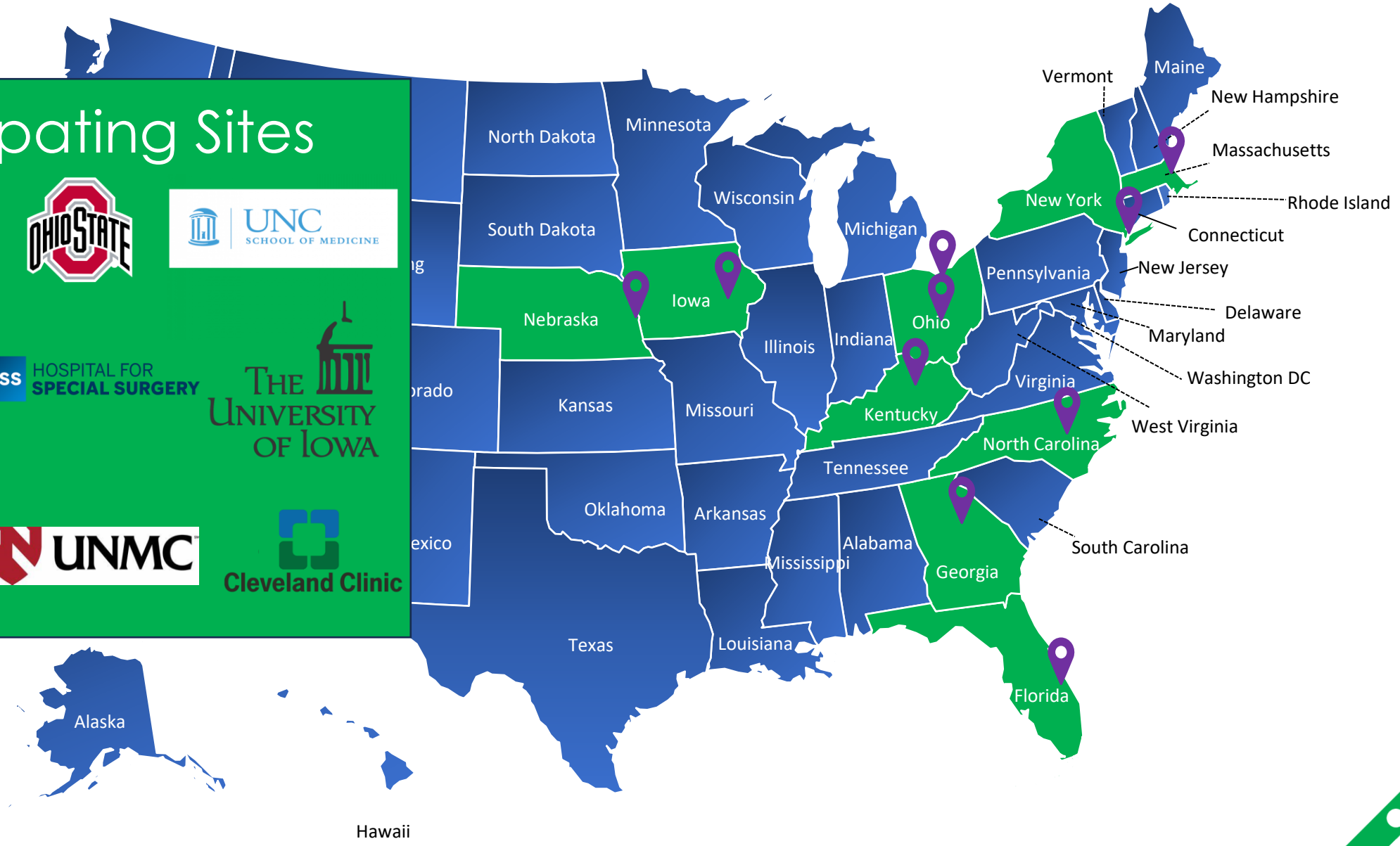
Current treatment recommendations focused on symptom management, and load and activity modification

****physical activity is ENCOURAGED****

Enter OACTN: Osteoarthritis Clinical Trials Network

Participating Sites

- Mass General Brigham
- Ohio State
- UNC School of Medicine
- UK HealthCare
- HSS Hospital for Special Surgery
- The University of Iowa
- Emory University
- UNMC
- Cleveland Clinic



Champions of Yes

PIKASO

PREVENTING INJURED KNEES FROM OSTEOARTHRITIS: SEVERITY OUTCOMES

A Multi-Site Phase II Randomized Clinical Trial to Test the Metformin Drug Intervention in Patients at High-Risk for Post-traumatic Knee Osteoarthritis

Champions of Yes

The Arthritis Foundation's Biggest Idea Yet.

9 of the Best Institutions.
50+ World-Class Scientists.
Hundreds of Patients at High-Risk of OA.
Testing an Exciting, Low-Cost, Off-Patent Drug.
First-of-Its-Kind PTOA Prevention Trial after Joint Injury.

The PIKASO PROJECT

PIKASO
PREVENTING INJURED KNEES FROM OSTEOARTHRITIS: SEVERITY OUTCOMES

- Can Metformin prevent the development of knee OA after injury?

- Why Metformin?
  - A safe, affordable, off-patent drug
  - May decrease inflammation and pain
  - May preserve cartilage and slow degradation

- Who?
  - People who have had an ACL tear, scheduled for surgery

- First of its kind prevention trial following joint injury

PIKAS

PREVENTING INJURED KNEES FROM OSTEOARTHRITIS: SEVERITY OUTCOMES

A randomized, double-blind, placebo-controlled clinical trial to study the effect of metformin in patients receiving anterior cruciate reconstruction (ACLR).

Subjects will receive one of two treatments through a random process:

- 3x500 mg metformin pills each day for a year and reimbursement for physical therapy co-pays.
- 3x500 mg placebo pills each day for a year and reimbursement for physical therapy co-pays.

Timeline	Baseline	Surgery	3 months	6 months	9 months	12 months	18 months	24 months	0-12 Months	0-9 Months
Format	In-person visit, 2 hours	Surgery	Email	Email	Email	In-person visit, 3 hours	Email	In-person visit, 3 hours	Daily medication	Physical therapy
Research Components	✓ Survey ✓ MRI ✓ X-Ray ✓ Blood and urine sample	✓ Samples of knee joint fluid and tissue	✓ Survey	✓ Survey	✓ Survey	✓ Physical assessment ✓ Survey ✓ MRI ✓ X-Ray ✓ Blood and urine sample	✓ Survey	✓ Physical assessment ✓ Survey ✓ MRI ✓ X-Ray ✓ Blood and urine sample	✓ Up to 3 pills daily (metformin or placebo), taken with food ✓ Bluetooth pillbox to track adherence ✓ Text reminders	✓ Financial incentive to attend physical therapy of choice
Payment	$150	N/A	$25	$25	$25	$200	$25	$200	$50 every 3 months, up to $200	$30 per PT visit, up to 27 total visits

Champions of Yes

Pathway to the Rest of OA

Successful PTOA studies may help to:

- Allow surgeons to prescribe Metformin right away to slow or prevent early OA
- Develop more sensitive diagnostics → earlier opportunity to intervene
- Guides alternative approaches/areas of work in the effort to find treatments for OA
  - Establish the standard for future clinical trials
    - Advanced Imaging
    - Movement assessments


Yes

Secondary Outcomes: Project Cores

Biomarkers Core
Core Lead: Virginia Byers Kraus, MD, PhD
Secondary Outcomes:
- Urine biomarkers (CTXII, NTXI)
- Blood biomarkers [serum, plasma, whole blood (PAXgene), buffy coat (DNA)]
- Synovial fluid biomarkers (CTXII, COMP, sGAG, MCP-1, IL1β, IL-6, IL-8, TNFα, MMP-3)
- Synovial tissue (RNAsequencing)

Biomechanics Core (BFUNC)
Core Lead: Brian Pietrosimone, PhD
Secondary Outcomes:
- Knee ROM
- 3D gait biomechanics
- Isokinetic knee flexion/extension
- 1m/10m habitual walking speed
- Single Leg Hop Test

Primary Outcomes:
- KOOS Pain
- Modified MOAKS Cartilage

Imaging Core (OIC)
Core Leads: Xiaojuan Li, PhD and Carl Winalski, MD
Secondary Outcomes:
- Knee structure changes on XR/MRI
- Changes in T1rho, T2 on compositional MRI
- Synovitis on contrast MRI

Brigham Coordinating Center (BriCC)
Core Lead: Elena Losina, PhD
Secondary Outcomes:
- Medication adherence
- PROMs [KOOS, MARX Activity Rating Scale, Work Productivity and Activity Impairment (WPAI), EuroQoL, Tampa Scale of Kinesiophobia, MHI-5, Pain Catastrophizing Scale, demographics, comorbidities]
- Adverse events