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OAI Data Users  
ACR Study Group

ACR Annual Meeting  
Oct 27, 2008



# Outline of session

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- **Objectives:** introduce prospective and new users to the OAI, describe how to access the public data, images and biospecimens, suggest analytical strategies for OAI data
- Overview of study design and data *M Nevitt*
- 'OAI On-line', access to data, images and biospecimens *S. Rubin*
- Using OAI images *J. Lynch*
- Analysis methods and issues *C. McCulloch*
- *Open discussion*



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# OAI design, subject characteristics, data and images

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OAI Coordinating Center



# Primary objectives of OAI

- A shared clinical research resource to
  - Describe the structural and biochemical changes of early and progressive knee OA
    - Understand natural history
  - Identify factors that influence knee OA onset and progression
  - Characterize imaging, biochemical and genetic biomarkers that predict and track the course and outcome of disease
    - Biomarker qualification



# Achieving the OAI objectives:

## 1. Longitudinal cohort study of knee OA

- Well-defined and characterized community sample assessed longitudinally
  - Imaging, molecular, genetic and risk markers
  - Symptoms, function, disability, surgery
- Multiple stages in the spectrum of knee OA

At risk → Early/preclinical → Established → Endstage
- Evaluate biomarker level (and  $\Delta$ ) as predictors and correlates of disease and patient outcomes



# Achieving the OAI objectives

## 2. Public data resources

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- Open access to the data, images and biospecimens to speed the generation of new knowledge about OA, enlist the community of OA investigators worldwide in understanding natural history and biomarkers
  - Downloadable clinical data archive on the web
  - Archived images on demand
  - Archived biospecimens by application



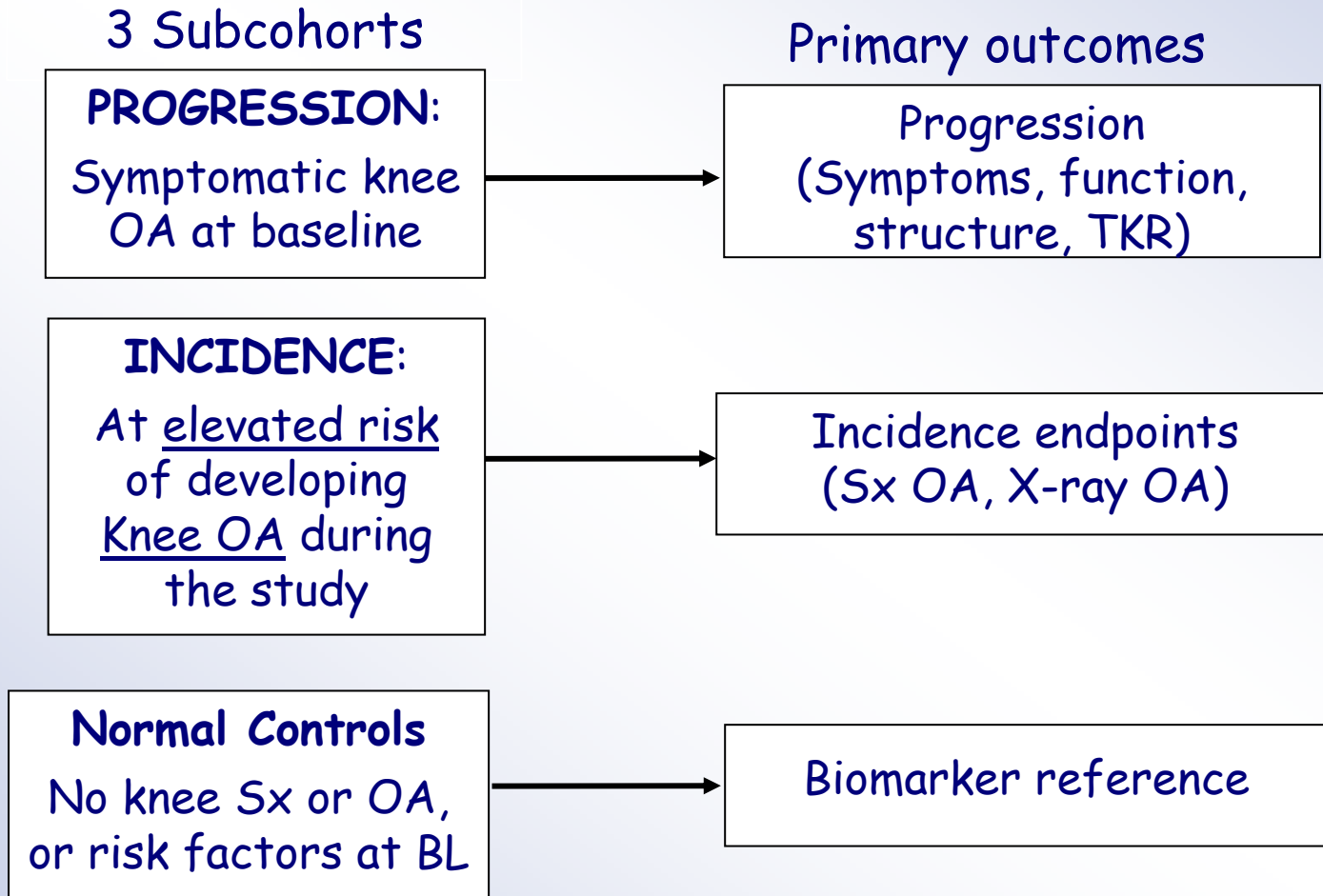
# OAI study design resources

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- **OAI Online** [www.oai.ucsf.edu/datarelease/docs/about](http://www.oai.ucsf.edu/datarelease/docs/about)
  - **Study protocol and measurements**  
[www.oai.ucsf.edu/datarelease/docs/StudyDesignProtocol.pdf](http://www.oai.ucsf.edu/datarelease/docs/StudyDesignProtocol.pdf)  
[www.oai.ucsf.edu/datarelease/operationsmanuals.asp](http://www.oai.ucsf.edu/datarelease/operationsmanuals.asp)

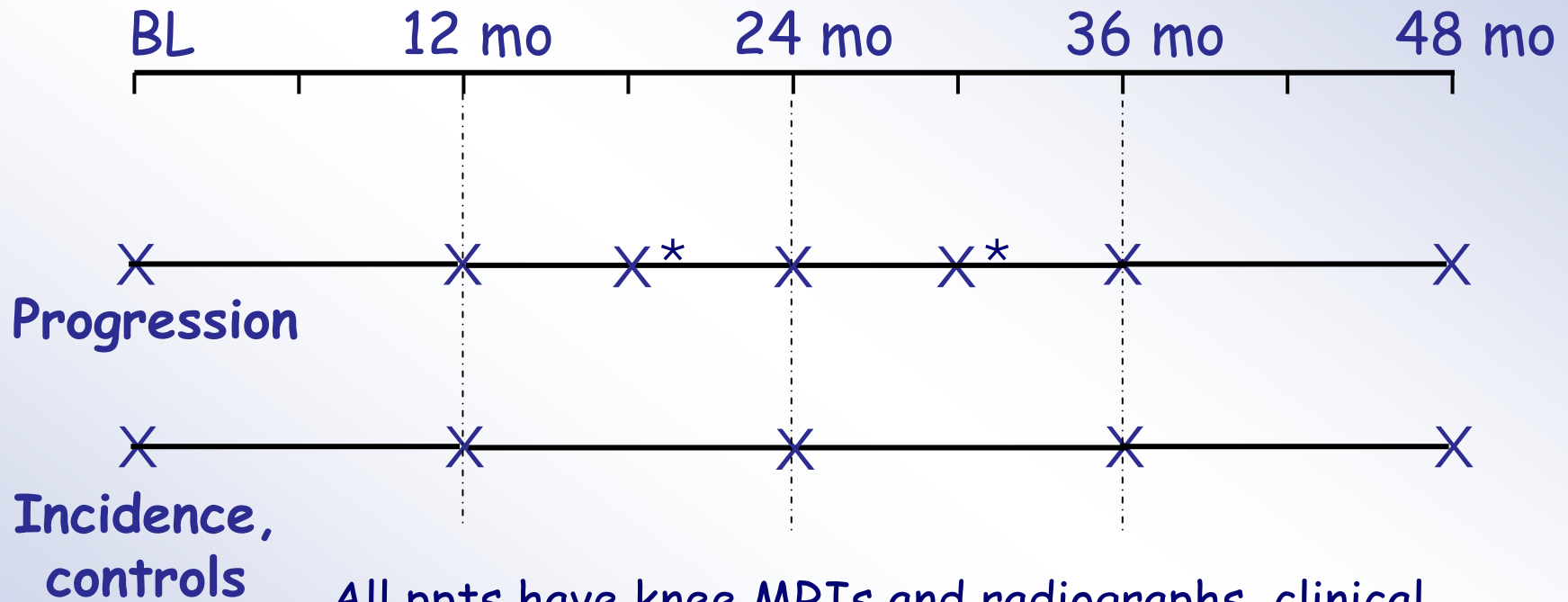


# OAI Design: Subcohorts





# Schedule of clinic visits



All pts have knee MRIs and radiographs, clinical assessments and biospecimen collection at all visits

\* Interim 6-mo visit in a subset of Progression pts for knee MRI, clinical outcomes and biospecimen collection

# Imaging

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## Baseline and annual knee imaging

- Bilateral x-ray, PA fixed-flexion
- Bilateral knee MRI, 3T Siemens Trio

## Other joint imaging

- BL and FU hip/pelvis, hand x-rays
- Full limb for knee alignment
- MRI of the thigh

Imaging schedule and protocols

[www.oai.ucsf.edu/datarelease/docs/DataImaging.asp](http://www.oai.ucsf.edu/datarelease/docs/DataImaging.asp)



# Clinical data and biospecimens

- Knee symptoms and function
- Hip and other joint symptoms
- General function, QOL
- Physical performance
- Knee examination
- Risk factors, health behaviors, psychosocial measures
- Medications, supplements
- Blood, urine, DNA, lymphocytes (archived)

Measurement schedule

[www.oai.ucsf.edu/datarelease/docs/ExamMeasures.pdf](http://www.oai.ucsf.edu/datarelease/docs/ExamMeasures.pdf)

[www.oai.ucsf.edu/datarelease/docs/Questionnaires.pdf](http://www.oai.ucsf.edu/datarelease/docs/Questionnaires.pdf)



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# Characteristics of OAI participants



# Overall inclusion and exclusion criteria

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## Inclusion

- Men and women ages 45 - 79
- With, or at risk for, symptomatic T-F knee OA
- All ethnic minorities (focus on African-Americans)

## Major exclusions

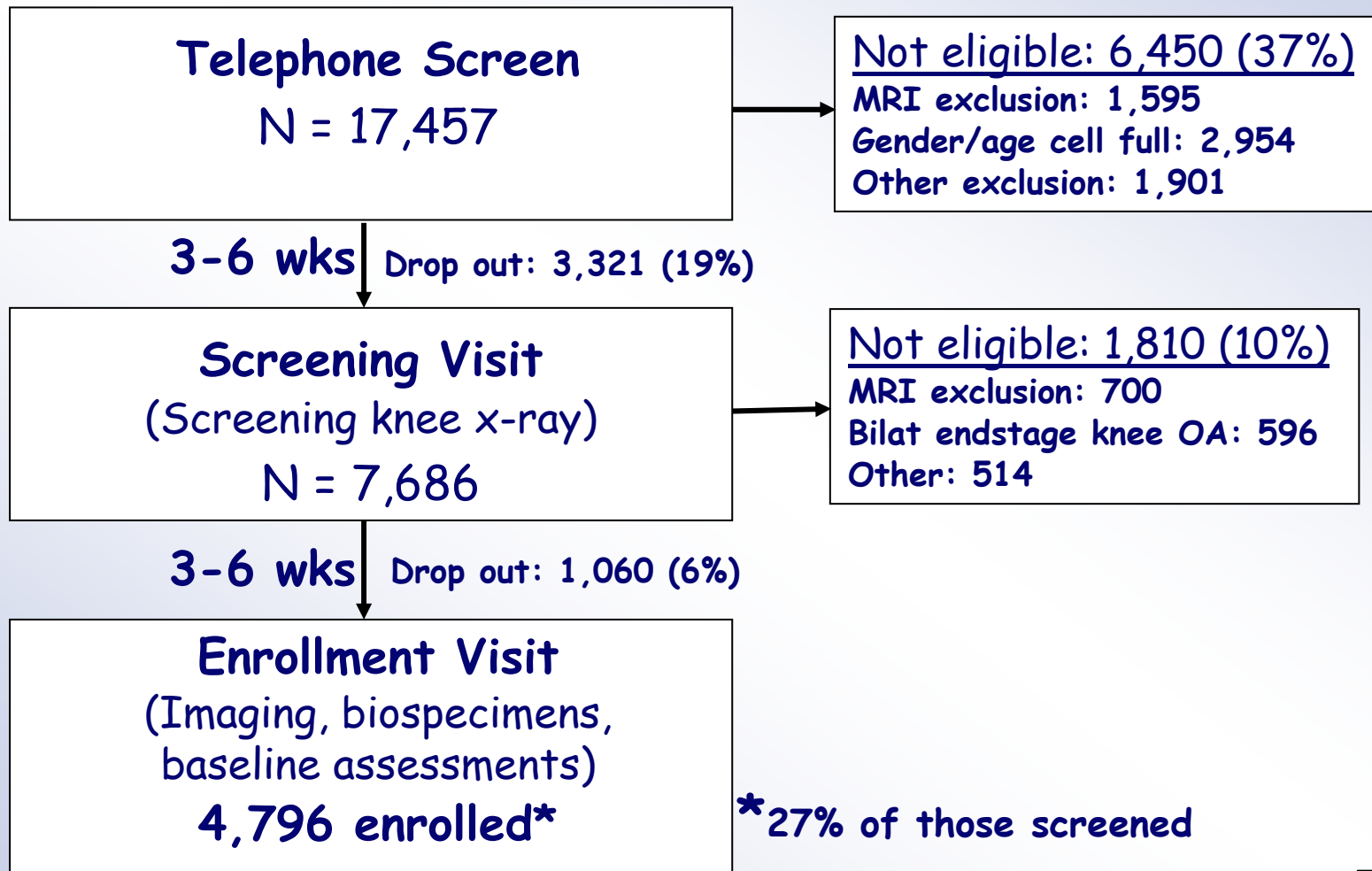
- Inflammatory arthritis (RA)
- 3-T MRI contraindication
- Bilateral end-stage knee OA



# Recruitment: March 04 - May 06

- 17,457 phone screen → 4,796 (27%) enrolled
  - Targeted mailing lists
- Main reasons not eligible
  - Gender age/cell full (n=2,954)
  - MRI contraindication (n=2,295)
  - Bilateral end-stage knee OA (n=514)
  - Not interested/dropped out (n=4,381)

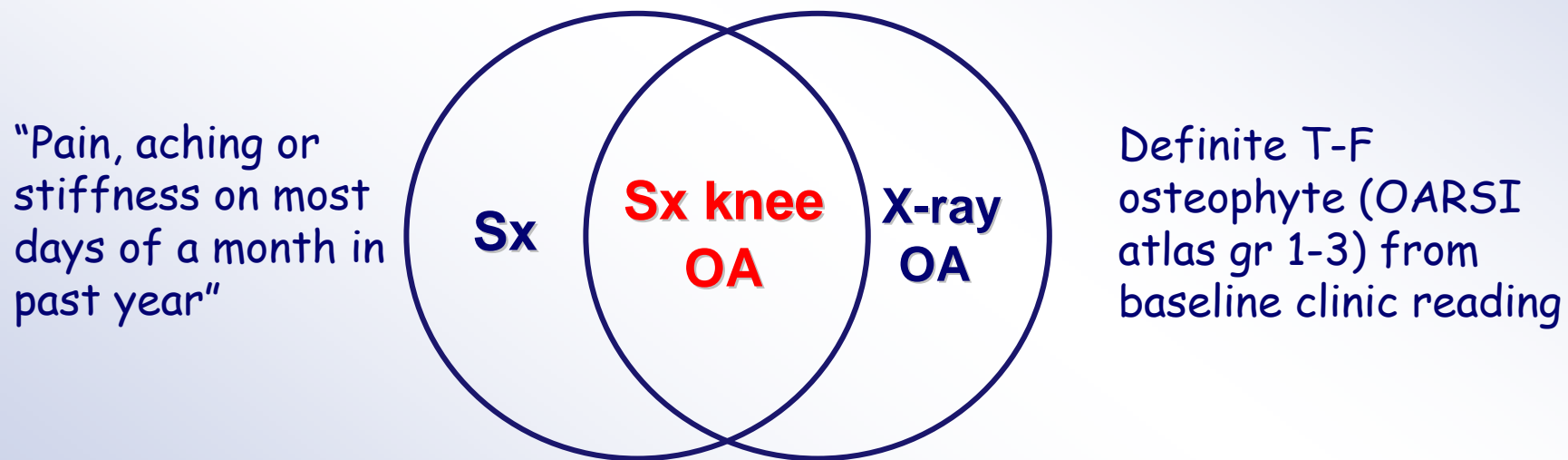
# Recruitment: March 04 - May 06



# Progression subcohort eligibility

## Baseline Symptomatic T-F Knee OA (Sx OA)

- Co-occurrence of knee Sx and structural pathology in one or in both knees
  - cause of disability, public health impact



- Population studies
  - ~ 50% overlap between knee Sx and x-ray OA



# Progression subcohort at baseline

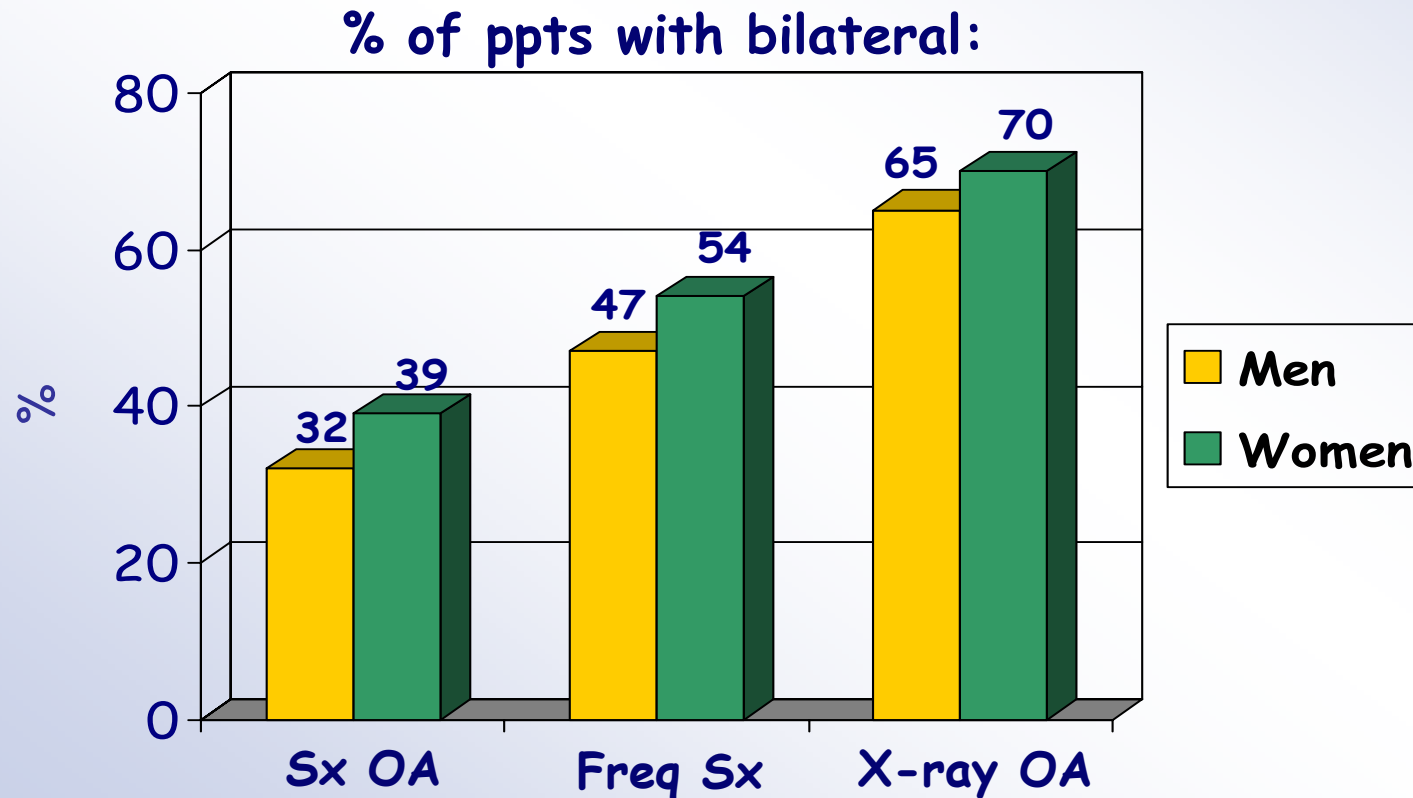


	<u>Men</u>	<u>Women</u>
• BMI $\geq$ 30.0	44%	53%
• Hx knee injury/surgery	35%	18%
• Hand OA-DIP nodes	38%	48%

# Progression subcohort

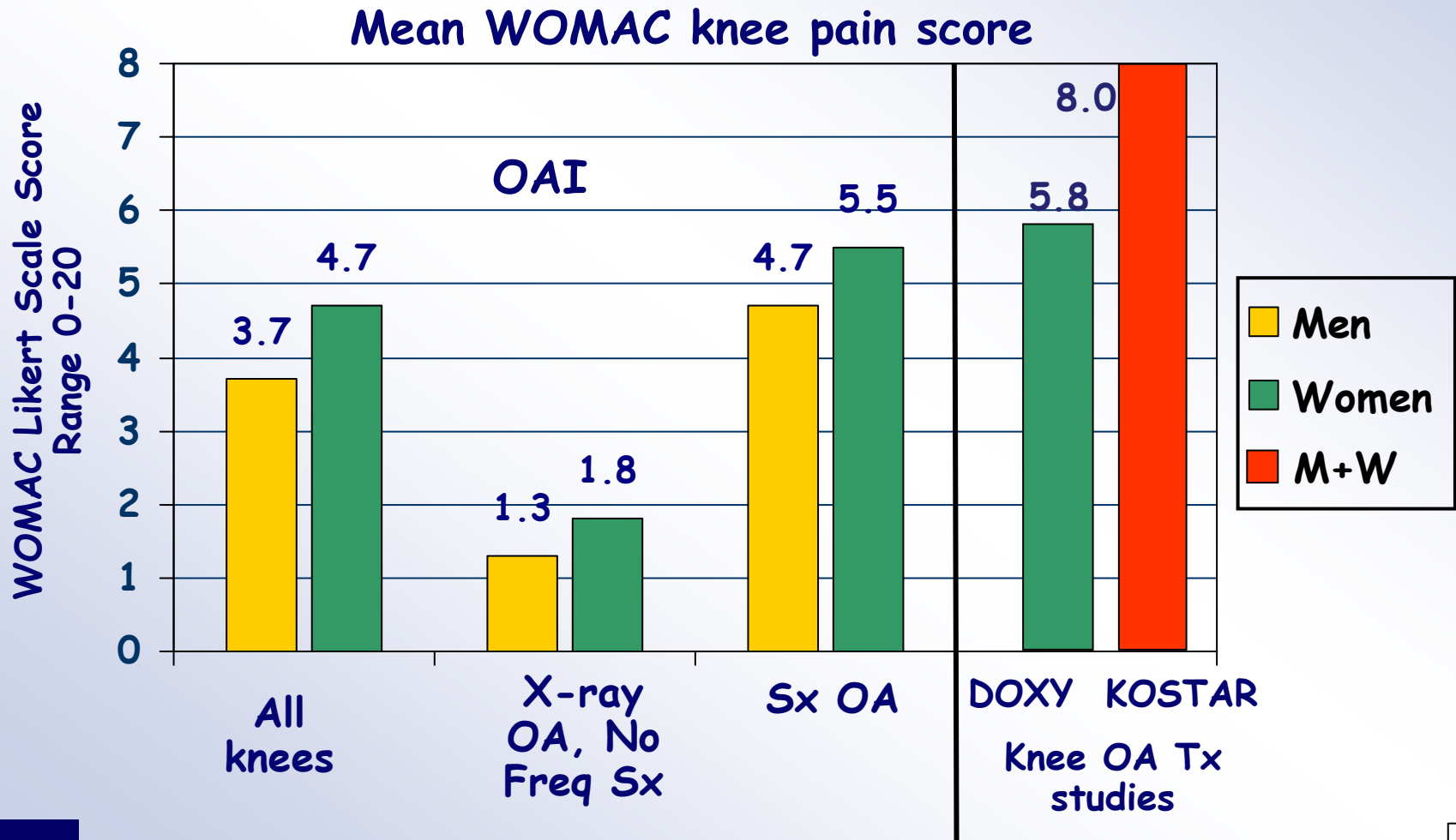
## Baseline knee OA status

- All Progression pts have Sx OA (frequent knee Sx and definite osteophyte) in at least one knee



# Progression subcohort

## Baseline WOMAC Knee Pain scores



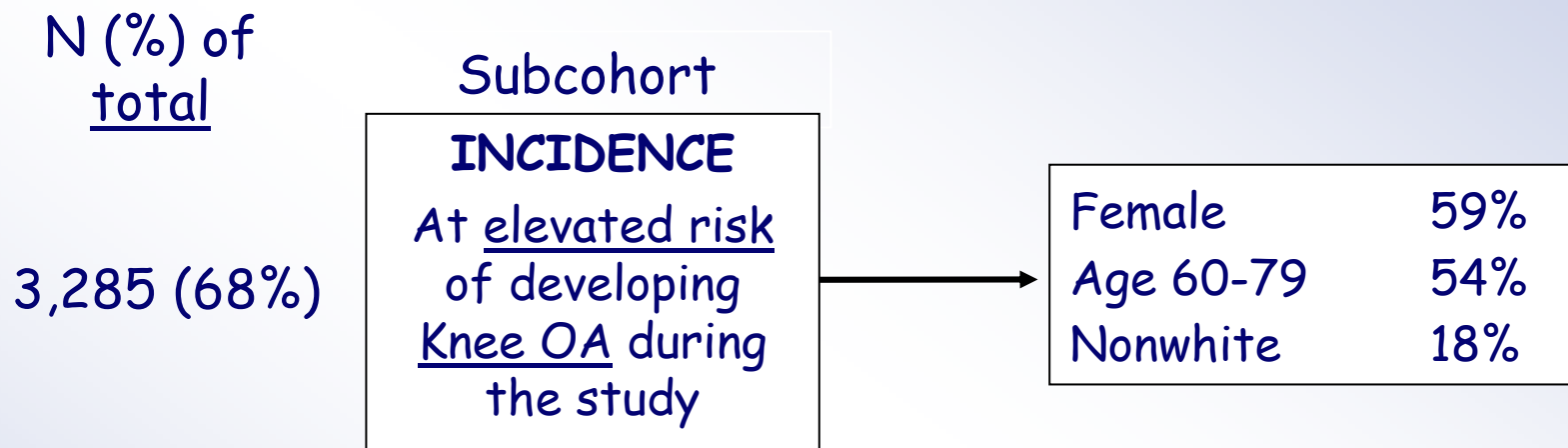
# Incidence subcohort eligibility

## Inclusion criteria

- Does not have Sx T-F knee OA either knee
- Has an increased risk for knee OA in  $\geq 1$  knee
  - Frequent knee Sx without x-ray T-F OA\*
  - Two or more eligibility risk factors

\* A ppt may have x-ray T-F OA (osteophytes) in one or both knees, but did not have freq Sx in the same knee

# Incidence subcohort at baseline

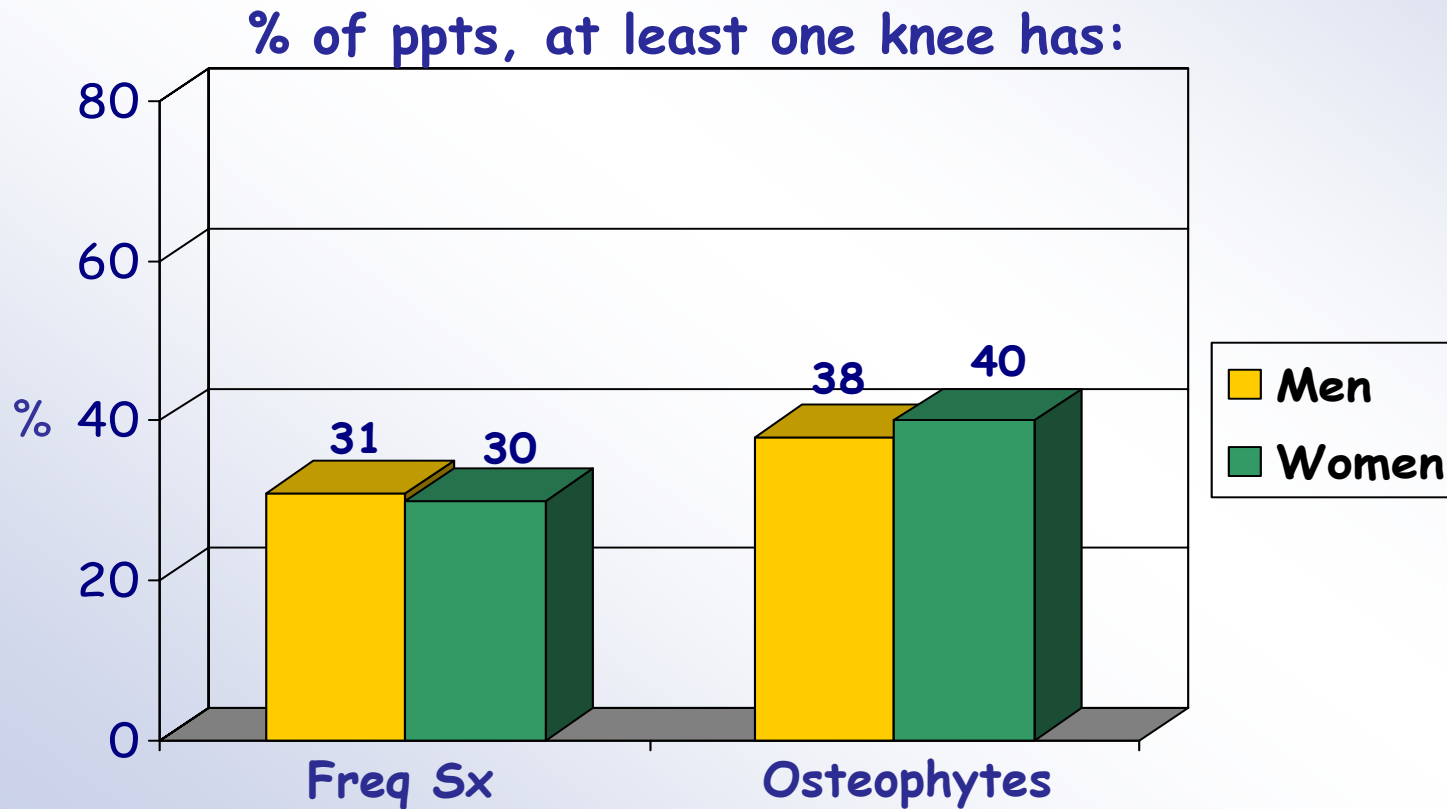


	<u>Men</u>	<u>Women</u>
• BMI $\geq$ 30.0	34%	33%
• Hx knee injury/surgery	20%	9%
• Family Hx of TKR	14%	16%
• Hand OA/DIP nodes	37%	53%

# Incidence subcohort

## Baseline knee OA status

- No pts have Freq Sx and X-ray OA in the same knee



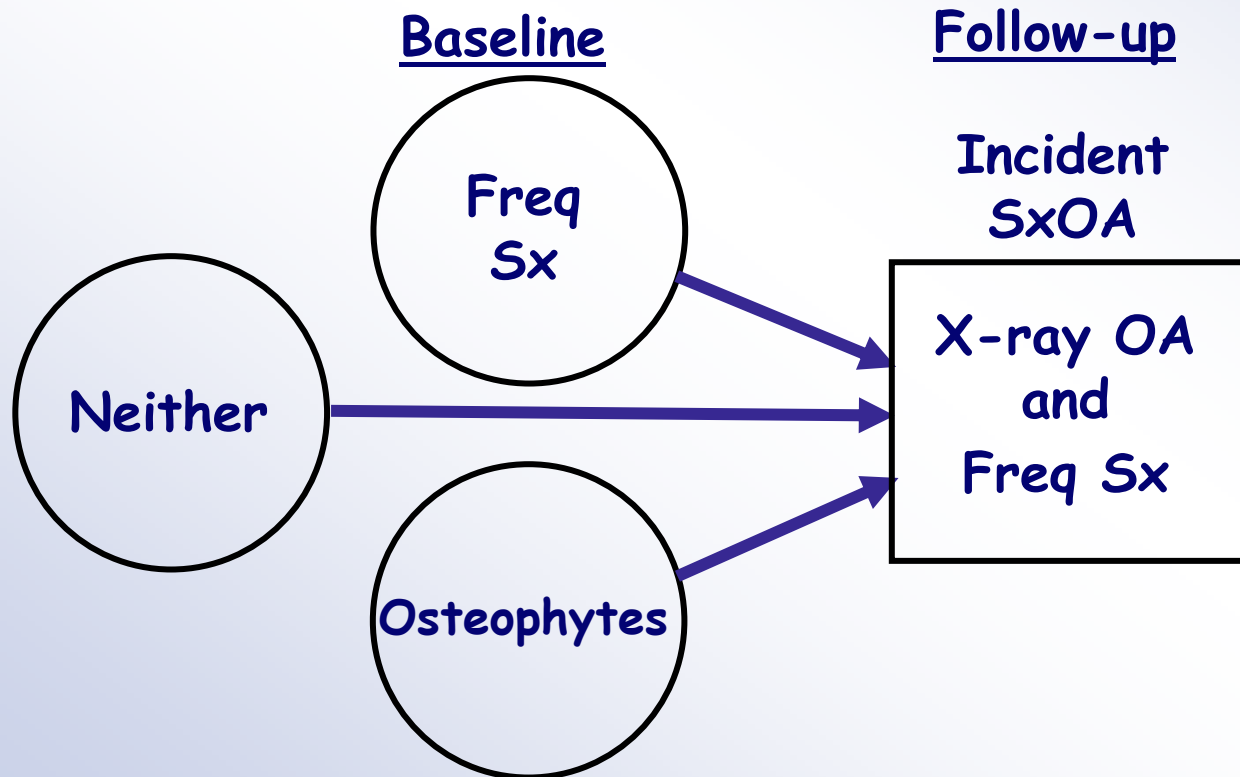
# Things to keep in mind about the subcohorts

- Definition of Sx OA based on measures that change
  - Frequent knee Sxs come and go
  - X-ray OA defined by definite Osteophyte from clinic reading
    - Osteophyte  $\neq$  K-L grade 2
    - Readers often disagree
- Incidence cohort includes some knees with symptoms, some with radiographic findings

At risk  $\rightarrow$  Early/preclinical  $\rightarrow$  Established  $\rightarrow$  Endstage
- Many analyses will use knees from both subcohorts

# Why are there ppts in the "incidence" subcohort who already have Sx or x-ray OA?

- Key endpoint: incident Sx OA (freq Sx and x-ray OA in same knee)





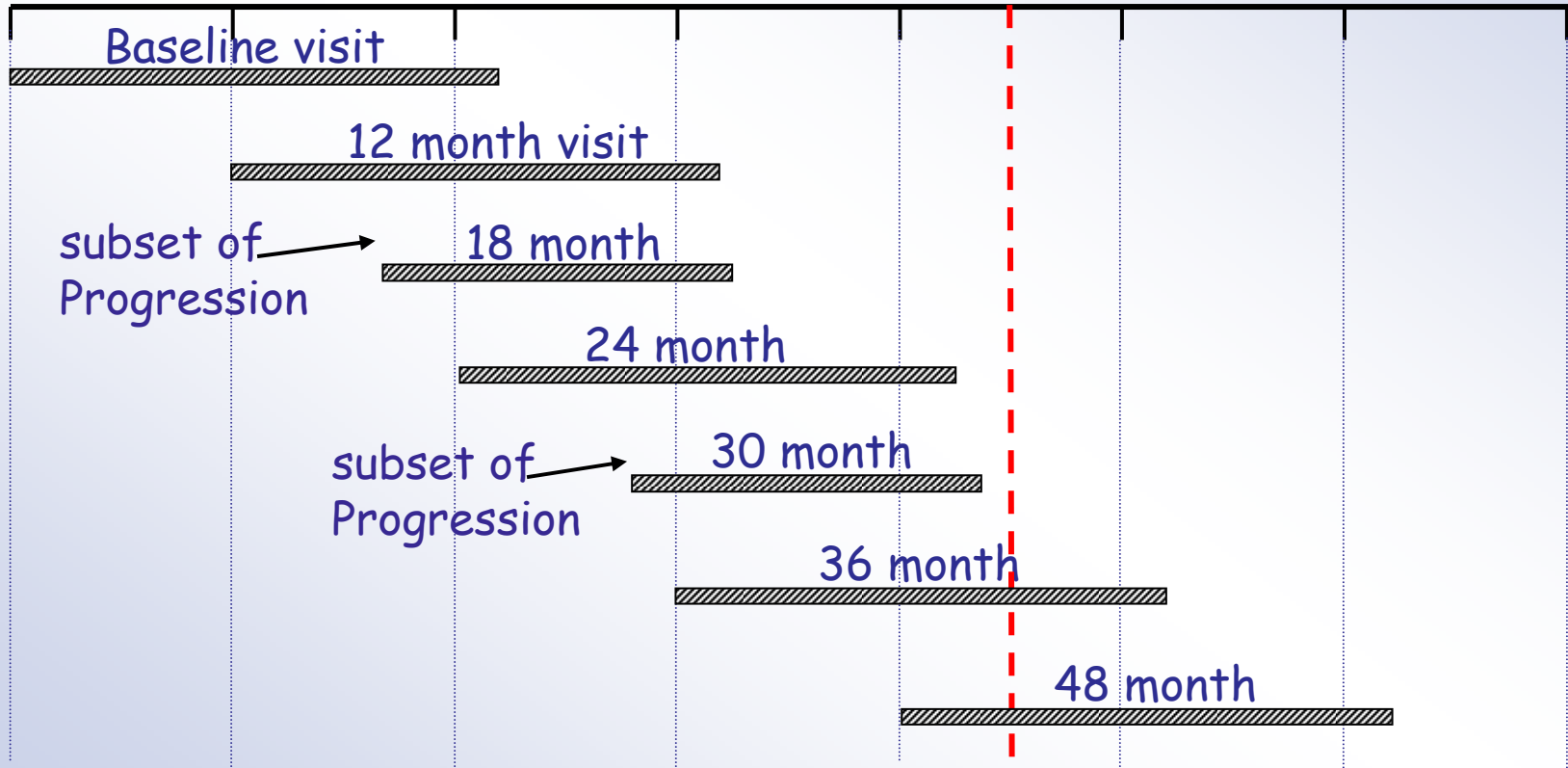
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# Follow-up and retention of the cohort



# Clinic visit timeline

3/04 3/05 3/06 3/07 3/08 3/09 3/10 3/11



Oct 08



# Follow-up status (10/08)

Status	Follow-up Visit (N entered follow-up window)	
	12-mo (4,796)	24-mo (4,755)
Clinic visit	4,294 (90%)	3,888 (85%)
Telephone contact only	198 (4%)	258 (5%)
Deceased, withdrew, LFU	304 (6%)	472 (10%)

# Completion rates for biomarker measures in subjects with a follow-up clinic visit (10/08)

Measurement	% with a clinic visit who had the measurement	
	12-mo	24-mo
Knee x-ray	<b>98%</b>	<b>97%</b>
Knee MRI	<b>97%</b>	<b>94%</b>
Blood and urine	<b>&gt;99%</b>	<b>&gt;99%</b>

# Completeness of longitudinal knee imaging (10/08)

Percent of all subjects with:  
both baseline and 24-mo images

	Knee MRI	Knee X-ray	MRI and Xray
Images available at both timepoints	82%	85%	81%

both baseline and 36-mo images

	Knee MRI	Knee X-ray	MRI and Xray
Images available at both timepoints	77%	80%	76%

# Central image assessment

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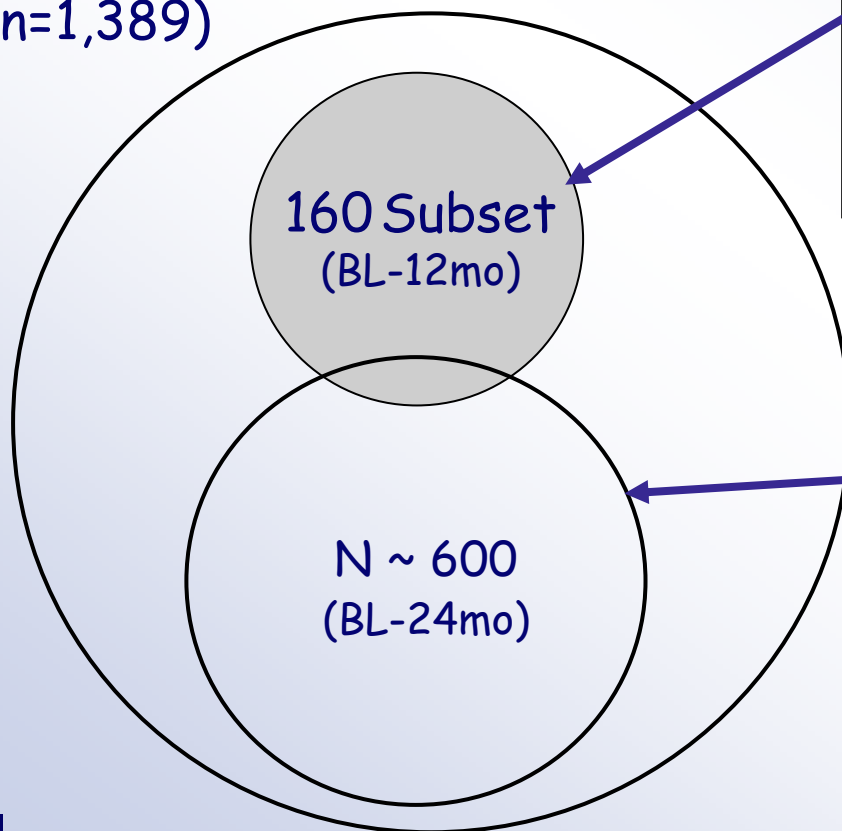
- What is it?
  - Standardized measurement/interpretation of selected samples of images using validated methods
  - Sponsored by OAI (for public release) and/or by users (eventual public release)
- Structural progression and incidence endpoints for public users
- Ongoing



# Central image assessments

## Progression subcohort

Progression  
subcohort  
(n=1,389)



### BL-12mo X-rays (completed)

- K-L grade, osteophytes, JSN
- Joint space width (JSW)\*

### BL-12mo MRIs (completed)

- quantitative cartilage\*

\* funded by OAI Pharma partners

### BL-12-24mo X-rays (ongoing)

- BL K-L grade, Ost, JSN
- Longitudinal K-L, JSN, JSW

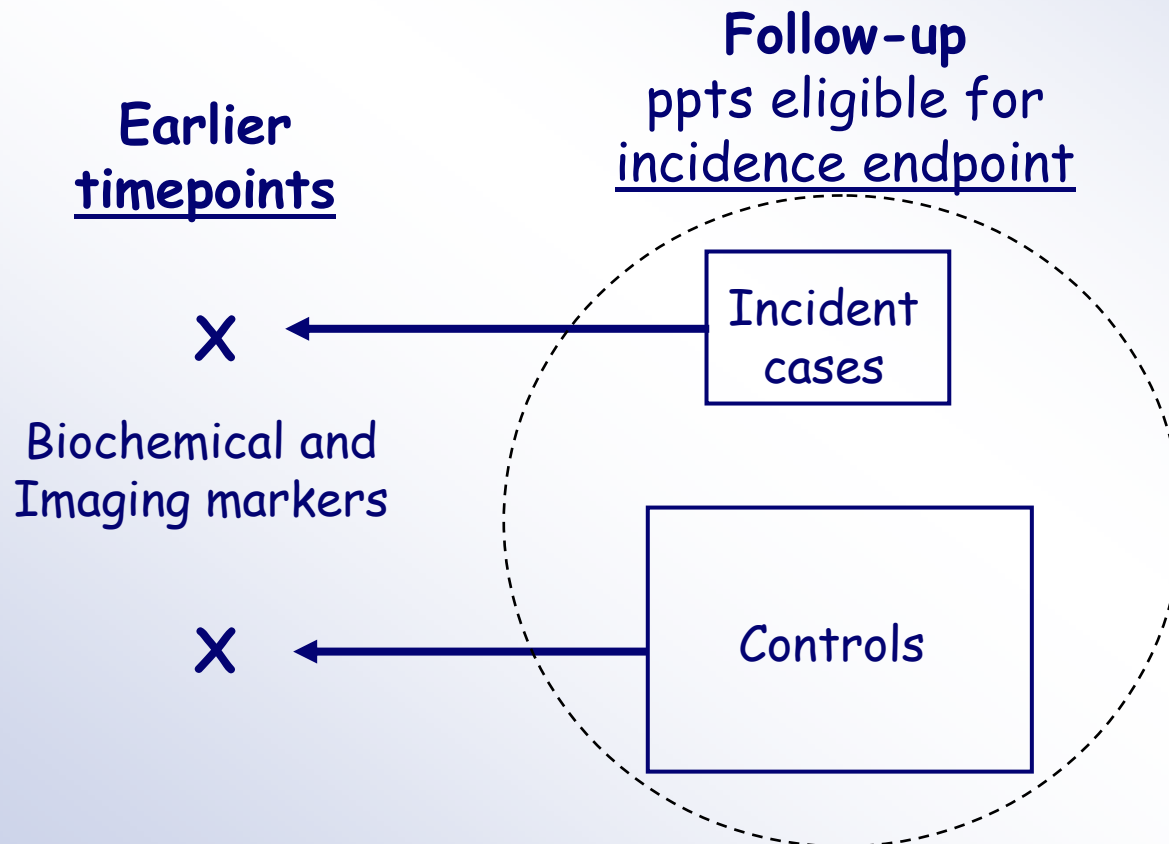
### BL-12-24mo MRIs (ongoing)

- BL Whole organ score
- Long. quantitative cartilage
- Long. semiquantitative cartilage

# Central image assessments

## Incidence subcohort

- Primary goal: Identify incident knee OA for nested case-control studies of biomarkers





# Acknowledgements

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  - John's Hopkins University
  - Brown University
  - University of Pittsburgh
  - University of California, San Francisco
  - Synarc, Inc
  - Boston University



# *OAI Coordinating Center - UCSF*

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Laura Bettencourt

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Jean Hietpas

Eve Benton

Jason Maeda

Michael Nevitt

And the great team at Synarc!



# OAI Collaborators (partial list)

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