
Osteoarthritis Initiative (OAI)

Design, subject characteristics,
data and images

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Primary objectives of OAI

- A shared clinical research resource to
 - Describe the structural and biochemical changes of early and progressive OA
 - Identify factors that influence OA onset and progression
 - Characterize imaging, biochemical and genetic biomarkers that predict and track the course of disease
 - Advance 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
- Evaluate biomarker level (and Δ) as predictors and correlates of patient outcomes



Achieving the OAI objectives

2. Public data resources

- Open access to the data, images and biospecimens has the potential to speed the generation of new knowledge about OA by enlisting the community of OA investigators worldwide in biomarker characterization and the investigation of natural history.
 - Downloadable clinical data archive on the web
 - Archived images distributed on request
 - Archived biospecimens available by application

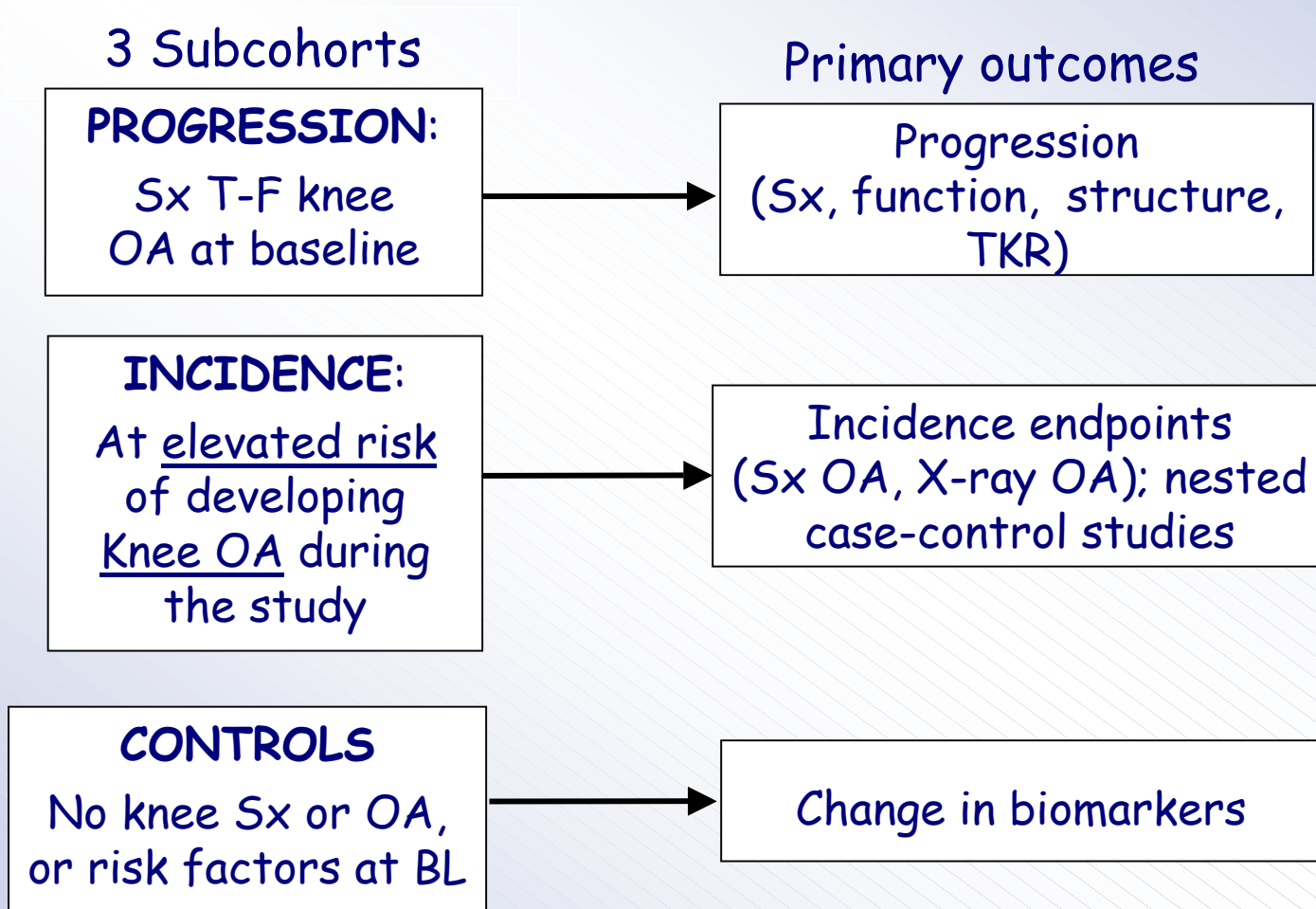


OAI study design resources

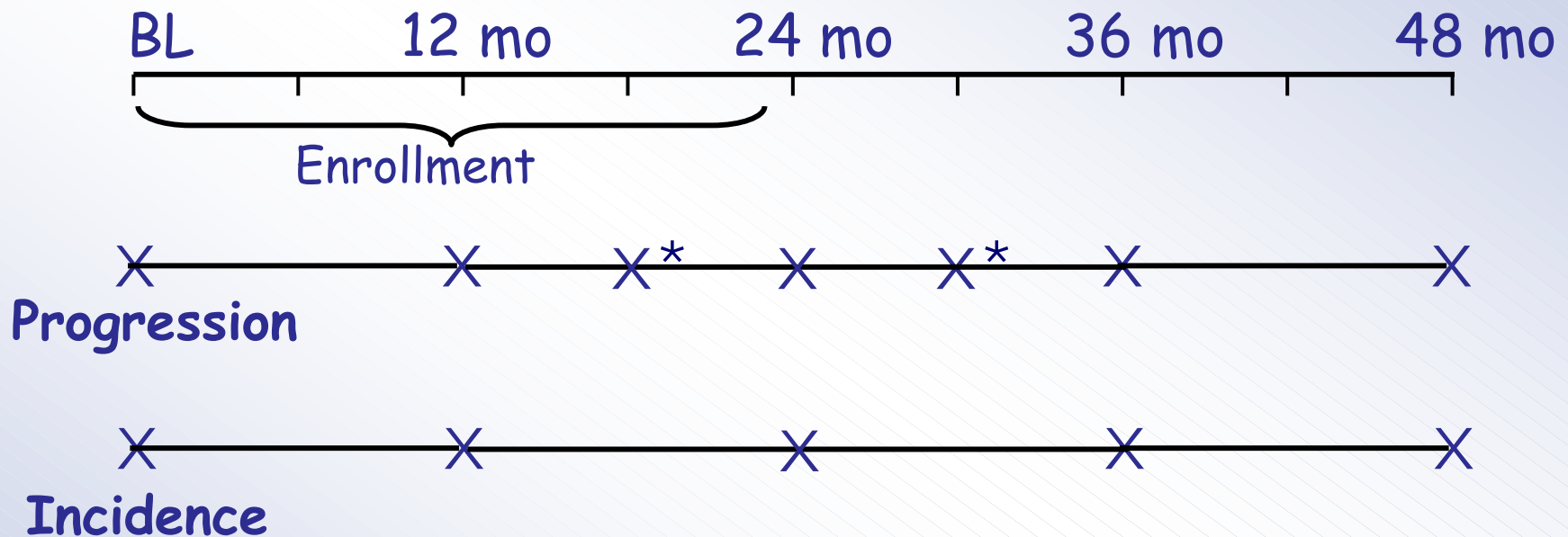
- OAI Online www.oai.ucsf.edu/datarelease/docs/about
 - Study protocol and measurements
www.oai.ucsf.edu/datarelease/docs/StudyDesignProtocol.pdf
www.oai.ucsf.edu/datarelease/operationsmanuals.asp
- Imaging protocol design mscpt - in review



OAI Design: Progression and Incidence cohorts



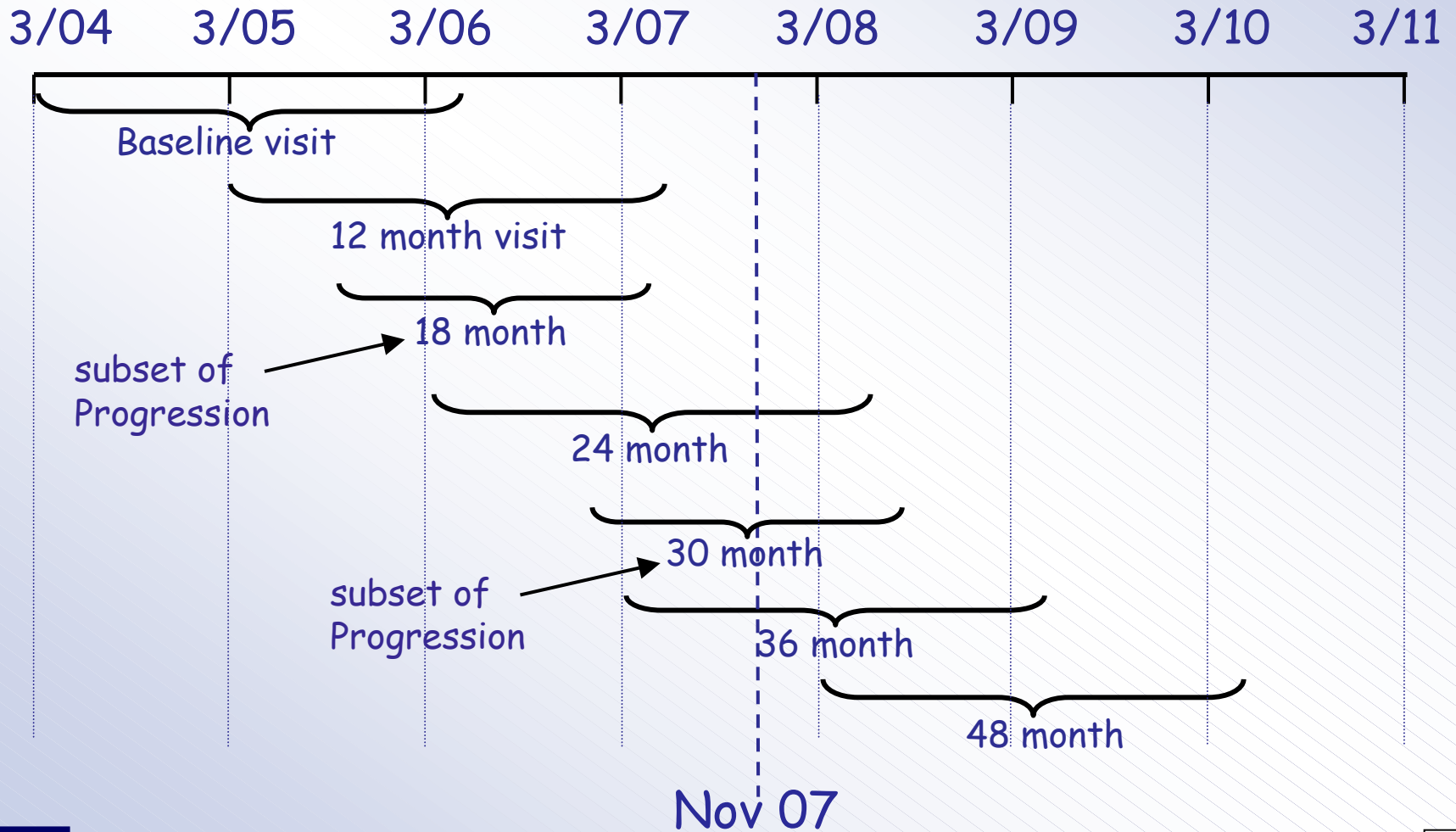
Schedule of clinic visits



All pts have knee MRIs and radiographs, clinical assessments and biospecimen collection at every visit

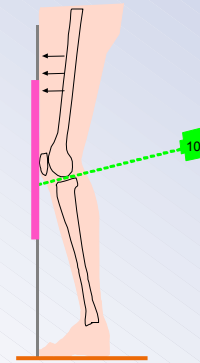
* Interim 6-mo visit in a subset of Progression pts for knee MRI, clinical outcomes and biospecimen collection: n = 300 at 18-mo visit, n = 500 at 30-mo visit.

Clinic visit timeline



Baseline and annual knee imaging

- Bilateral x-ray, PA fixed-flexion
- Bilateral knee MRI, 3T Siemens Trio
 - Extended protocol in right knee



MRI Scan	Right min	Left min
Localizer (3 plane)	0.5	0.5
SAG 3D DESS WE (Cor & Axial MPRs)	10.6	10.6
COR T1W 3D FLASH WE	8.6	--
SAG 2D MESE (T2 MAP)	10.6	--
COR IW 2D TSE	3.4	3.4
SAG IW 2D TSE FS	4.7	4.7
TOTAL	38.4	19.2

Other joint imaging

- Baseline and FU pelvis and hand x-ray
- Full limb x-ray for knee alignment
- Lateral knee x-ray in controls
- MRI of the thigh

Imaging schedule

www.oai.ucsf.edu/datarelease/docs/ExamMeasures.pdf



Who is enrolled in the OAI?



Overall inclusion and exclusion criteria

Inclusion

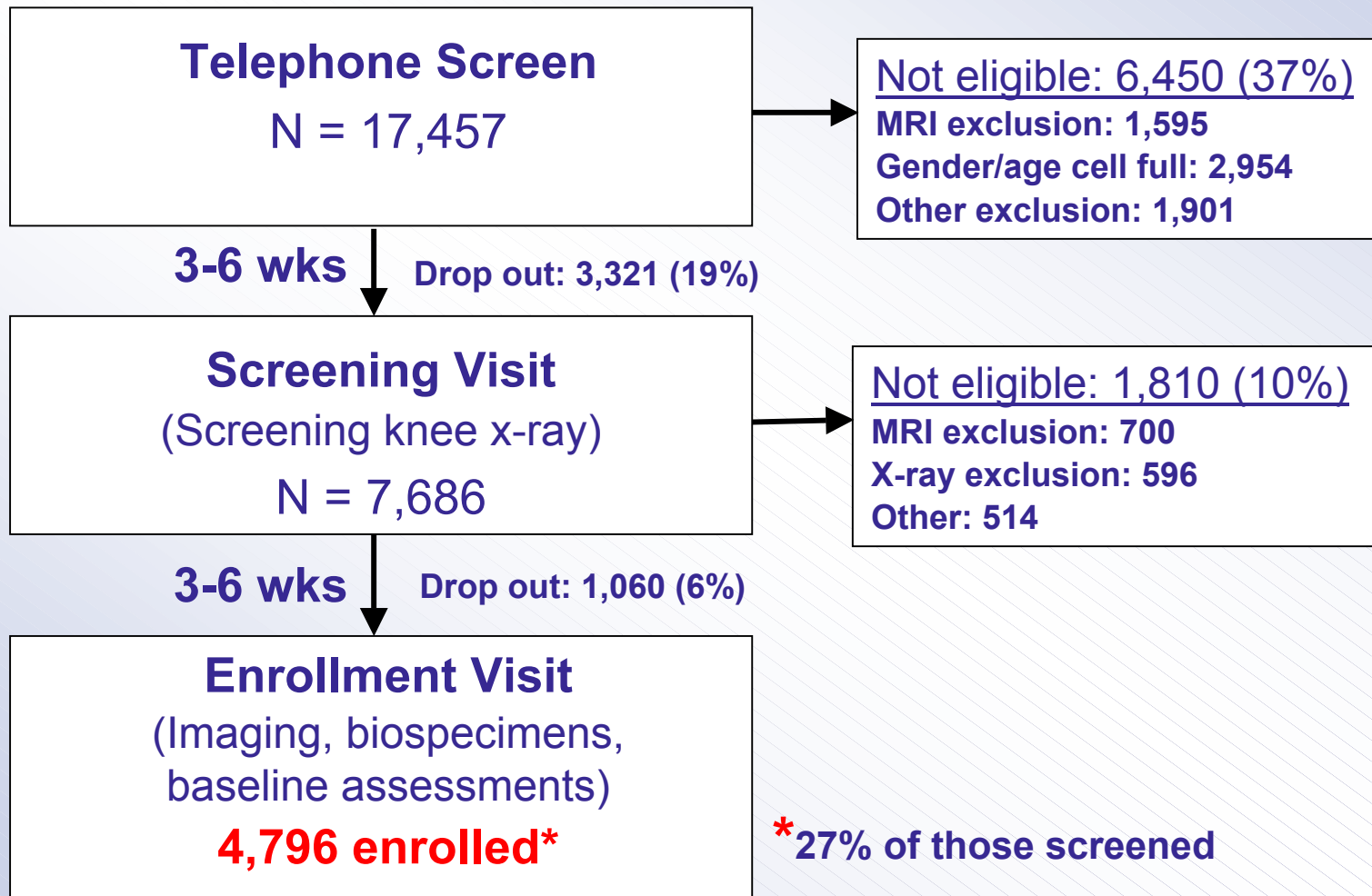
- Men and women ages 45 - 79
- With, or at risk for, symptomatic T-F knee OA
- All ethnic minorities (focus on African-Americans)

Major exclusions

- RA, inflammatory arthritis
- Bilateral end-stage knee OA
- Unable to walk without aids (single cane OK)
- 3-T MRI contraindication



Recruitment: March 04 - May 06



Excluded for MRI contraindication (n= 2,328, 13% of those screened)

<u>MRI contraindication</u>	<u>% of all MRI exclusions*</u>
Above study weight limits (M: 130kg; F: 114kg)	21
Surgically implanted stent, coil, device, etc	18
Knee/ppt too large for coil/bore	17
Eye injury with metal fragment	14
Non-ocular injury with metal fragment	9
Recent surgery (past 3 months)	7
Missing contraindication info	4
Unwilling to undergo MRI	2
Can't lie on back for 1.5 hrs	2
Other (claustrophobia, tremor, breathing problems, etc)	<1 each

* pts may have
>1 contraindication



Baseline clinic reading of screening knee x-ray for OA

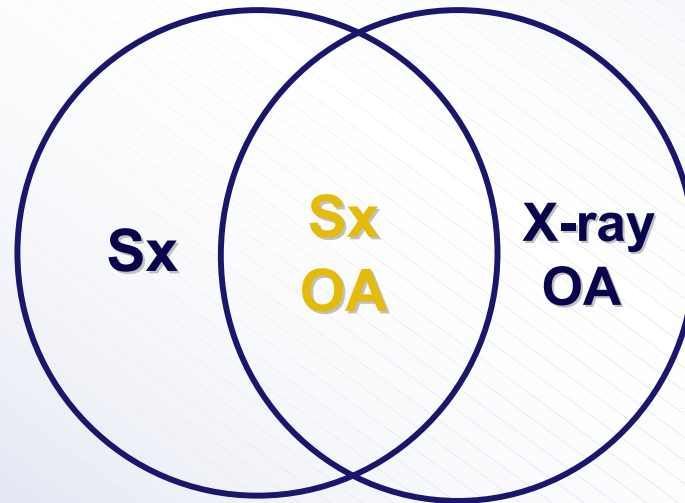
- PA fixed-flexion radiograph
 - Study definition of T-F X-ray OA: definite osteophytes (OARSI atlas grade ≥ 1)
 - JSN: OARSI gr 1-2 and gr 3 (bilat gr 3 excluded)
- Trained, certified readers at each of 5 clinics
 - A sample over-read at imaging QA center
- Central adjudicated longitudinal reading (n=320)
 - Central: Ost ≥ 1 \rightarrow Clinic Ost: Def=92%, Possible=8%



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

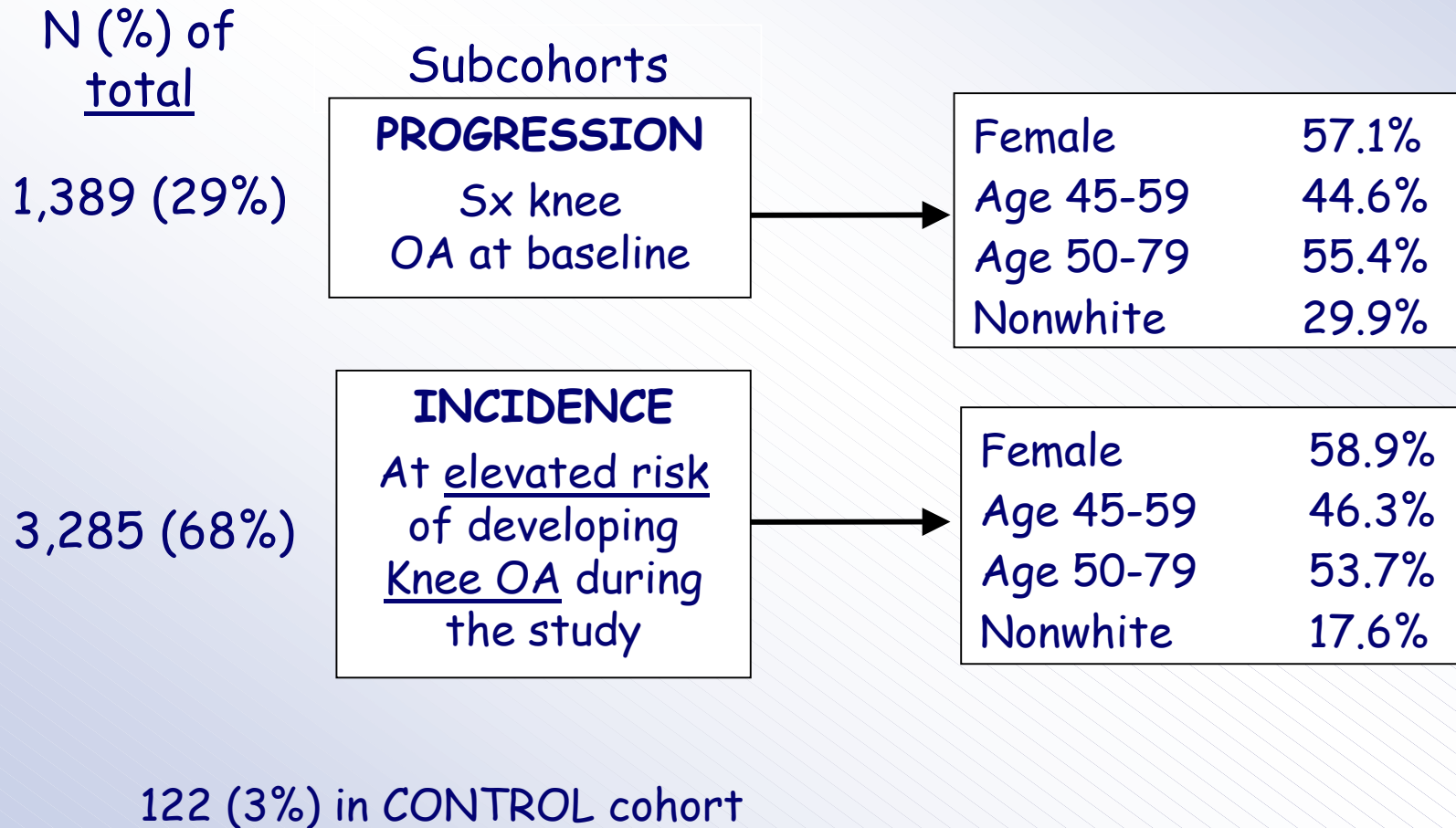
"Pain, aching or stiffness on most days of a month in past year"



Definite T-F osteophyte (OARSI atlas gr 1-3) from baseline clinic reading

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

Subcohorts at baseline



Progression subcohort (n=1,389)

Baseline characteristics



Progression subcohort

Body mass index

<u>Age</u>	<u>Men</u>		<u>Women</u>	
	<u>Mean BMI</u>	<u>% ≥30</u>	<u>Mean BMI</u>	<u>% ≥30</u>
45-69	30.0	46%	31.1	57%
70-79	29.2	36%	28.6	37%
All	29.8	44%	30.5	53%

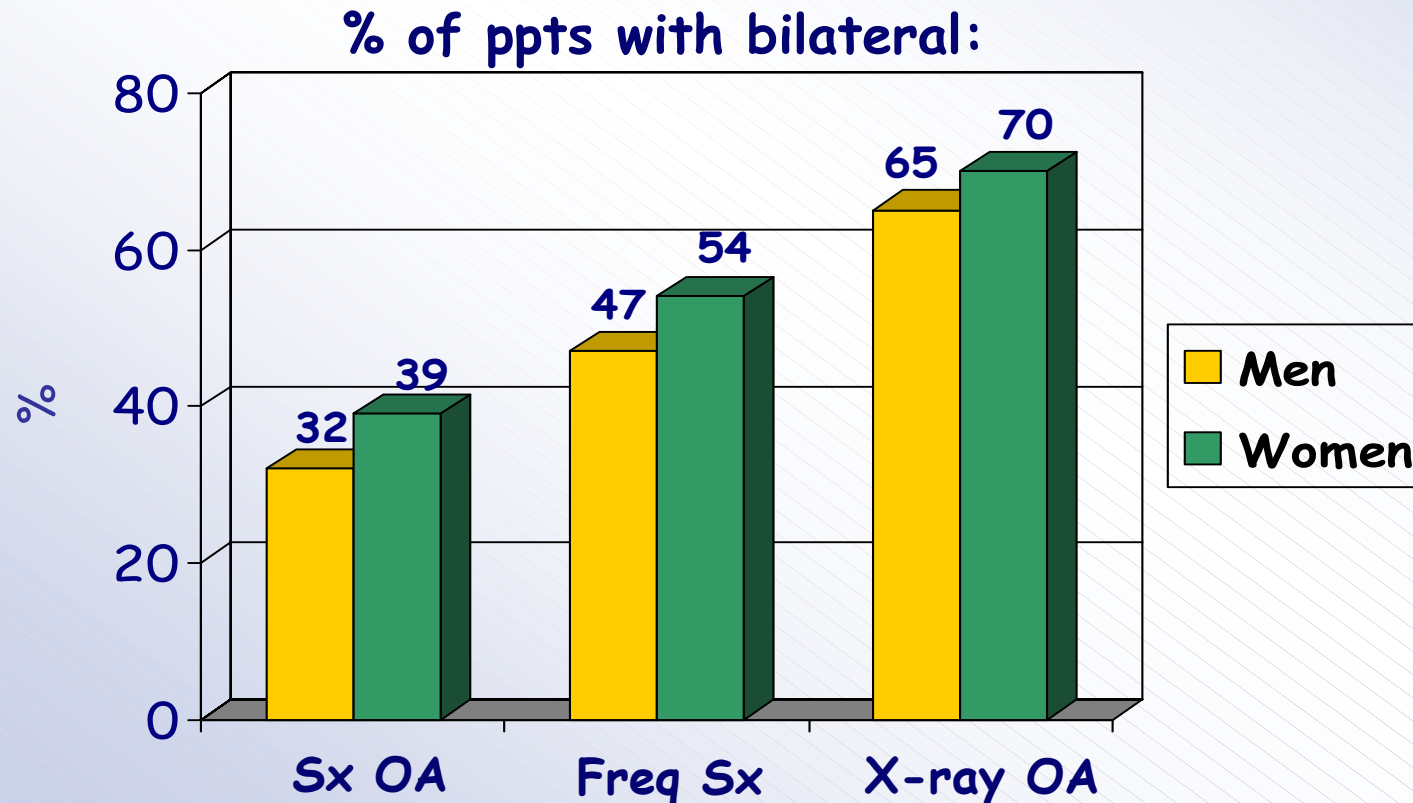
Other studies of Sx knee OA

- KOSTAR: M+F, mean age=60, **BMI=30.4** (Bingham, 2006)
- GAIT: M+F, mean age 58, **BMI=31.9** (Clegg, 2006)
- Clinic sample: M+F, mean age 63, **BMI=31.6** (Wolfe, 2002)

Progression subcohort

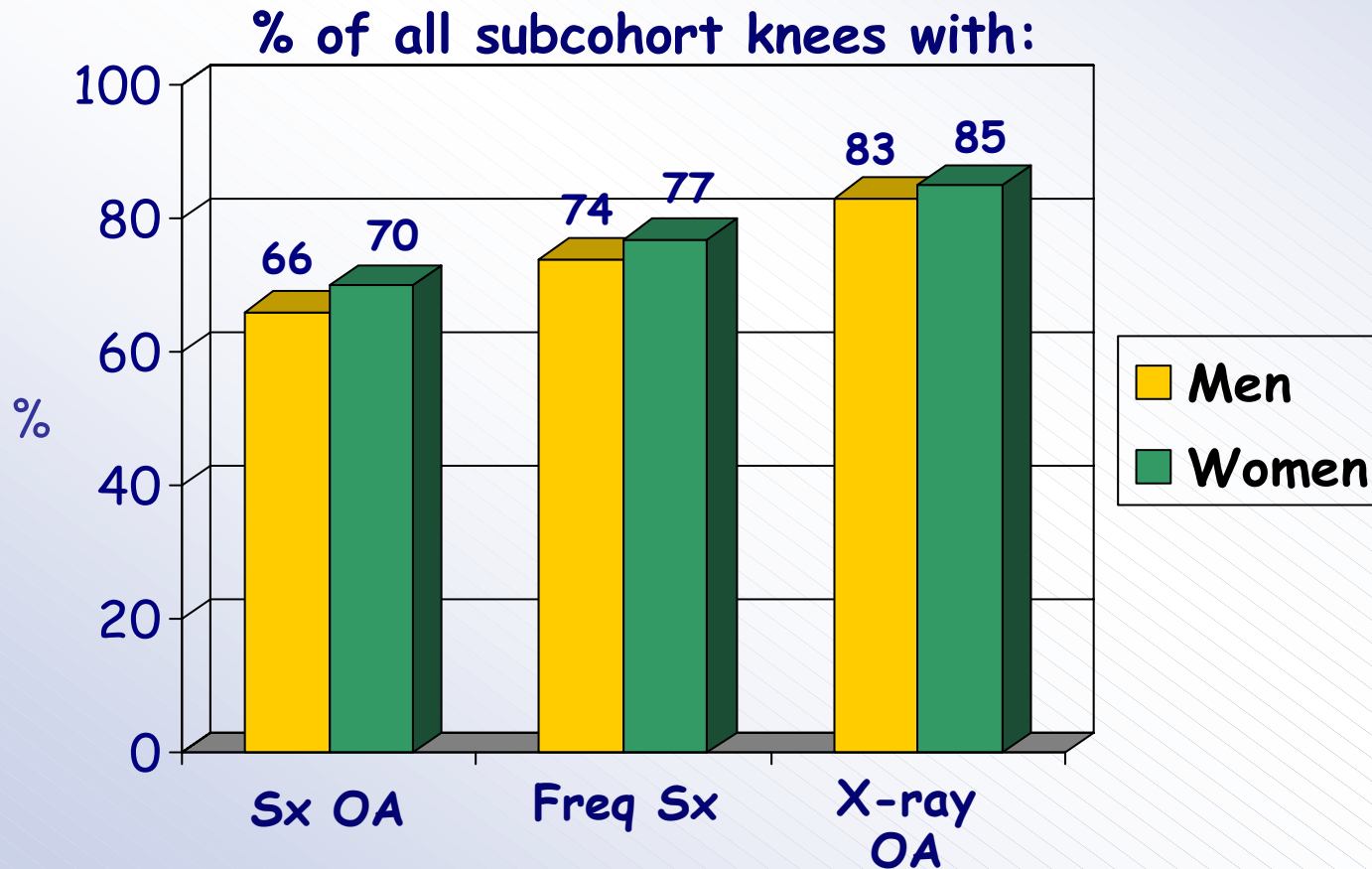
Baseline knee OA status of ppts

- All Progression ppts have Sx OA (frequent knee Sx and x-ray OA) in at least one knee



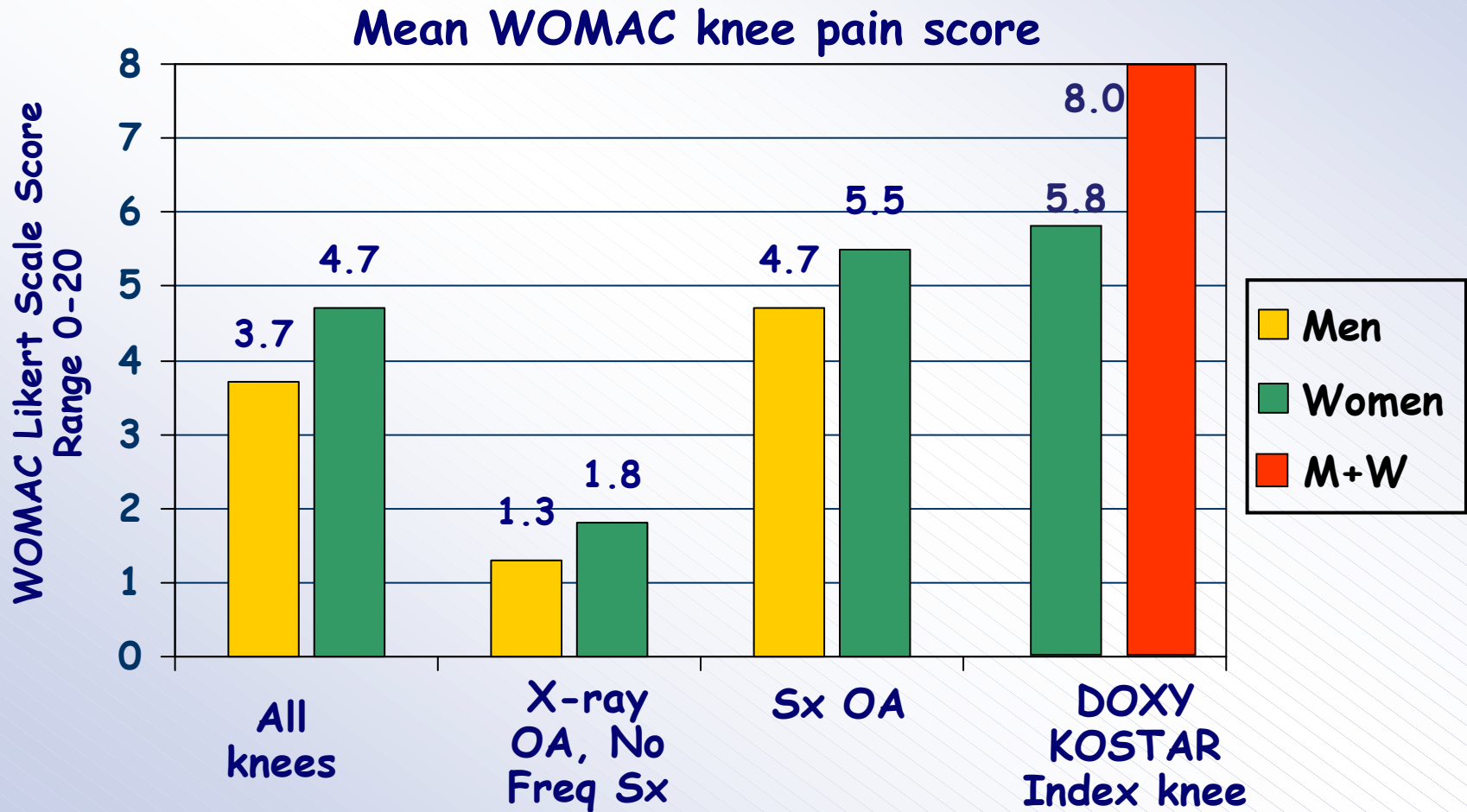
Progression subcohort: Baseline OA status of knees

- Both of the ppts knees are included in the subcohort



Progression subcohort

Baseline WOMAC Knee Pain scores



Progression subcohort

Changes observed during first 12 months of follow-up



Knees with BL Sx OA

Change in WOMAC pain and function

WOMAC scores normalized to 0-100

(negative value indicates improvement)

Study (mos of FU)	Δ Pain Mean (SD)	Δ Function Mean (SD)
OAI (12 mos)		
Women	-2.0 (15.1)	-2.5 (15.3)
Men	-3.0 (15.2)	-2.8 (13.5)
KOSTAR* (24 mos) (Bingham, 2006)	-8.4 (21.9)	-9.3 (21.8)
GAIT* (6 mos) (Clegg, 2006)	-17.2 (22.8)	-12.6 (20.1)

* Men and women

Joint space loss and cartilage loss

160 pts with BL Sx OA (O.B.2, 1.B.2)

Mean (SD) of change in OAI knees with Sx OA
(negative value indicates worsening)

	OAI BL - 12 mos	Other studies
Δ medial JSW (Duryea OARSI abst #29A, 332)	-0.26mm (.68)	DOXY -0.24mm (.54), 16m (Brandt, 2005) BRISK -0.12mm (.42), 12m (Spector, 2004)
Δ cart volume Medial cent femur Medial tibia (Hunter, 2006)	-2.5% (6.4%) -0.0% (7.5%)	Annual % loss* -7.4% -0.3% to -7.4% (Eckstein rev, 2006)

* Estimated from studies with ~24 mos of FU

Incidence subcohort (n=3,285)

Baseline characteristics



Incidence subcohort eligibility

Inclusion criteria

- Does not have Sx T-F knee OA
- Has an increased risk for knee OA

Increased risk defined as

- Frequent knee Sx without x-ray T-F OA*
- or
- Two or more eligibility risk factors

* A ppt can have x-ray T-F OA in one or both knees, but cannot have freq Sx in the same knee



Incidence subcohort Eligibility risk factors and BL prevalence

	<u>% of Men</u>	<u>% of Women</u>
Frequent knee Sx	36	37
Infrequent knee Sx	51	49
Overweight*	39	39
Hx of knee injury	48	34
Hx of knee surgery	27	12
Family Hx TKR	14	16
Hand OA (DIP nodes)	11	31

* Above age-specific cutpoint for NHIS self-report weight



Incidence subcohort

Body mass index

<u>Age</u>	<u>Men</u>		<u>Women</u>	
	<u>Mean BMI</u>	<u>% ≥ 30</u>	<u>Mean BMI</u>	<u>% ≥ 30</u>
45-69	28.7	37%	28.2	36%
70-79	27.9	25%	26.7	21%
All	28.5	34%	27.9	33%

BMI ≥ 30 in U.S., 2004 (NHANES)

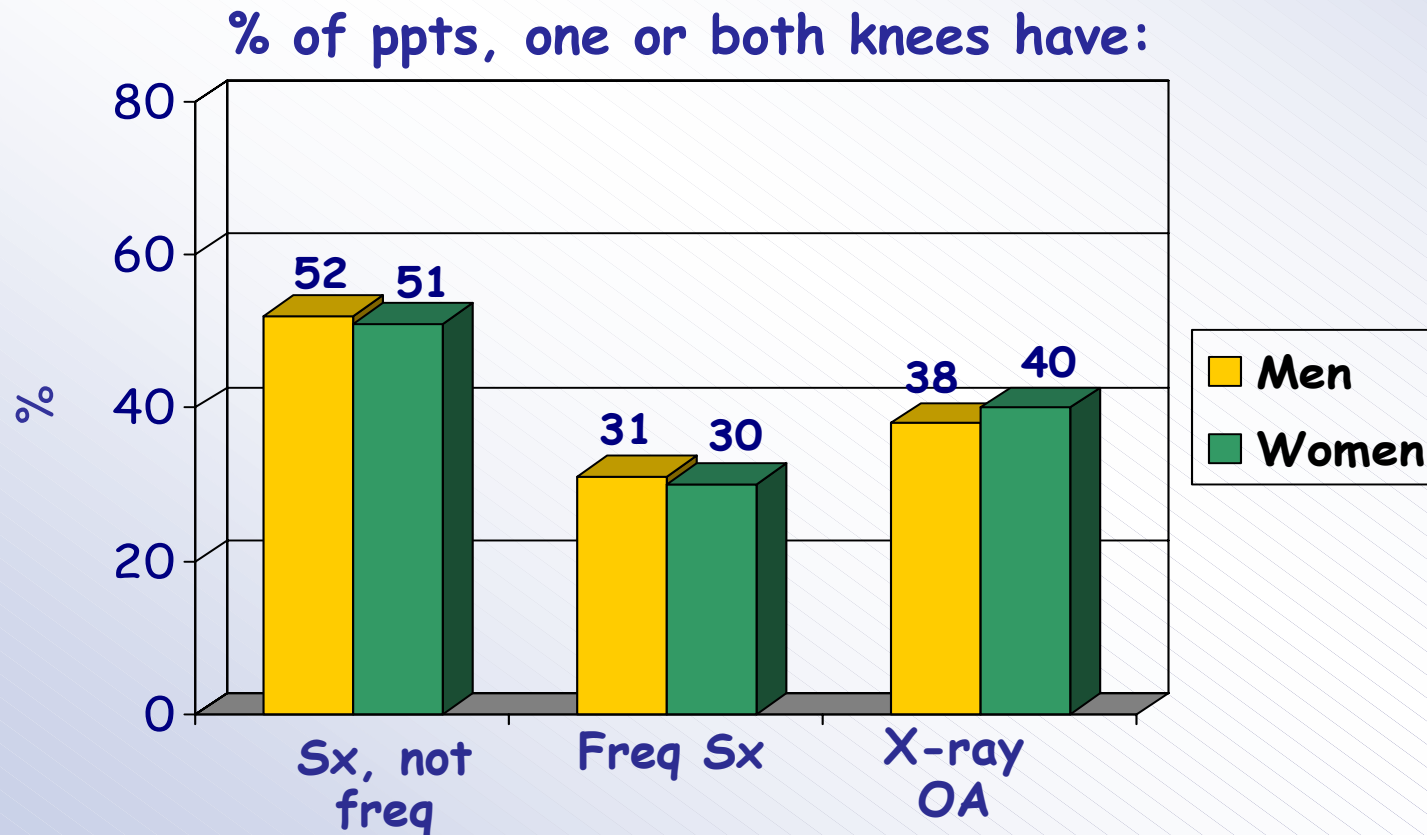
Men: age 40-59 = 35%; age ≥ 60 = 30%

Women: age 40-59 = 39%; age ≥ 60 = 32%

Incidence subcohort

Baseline knee Sx and OA status of ppts

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



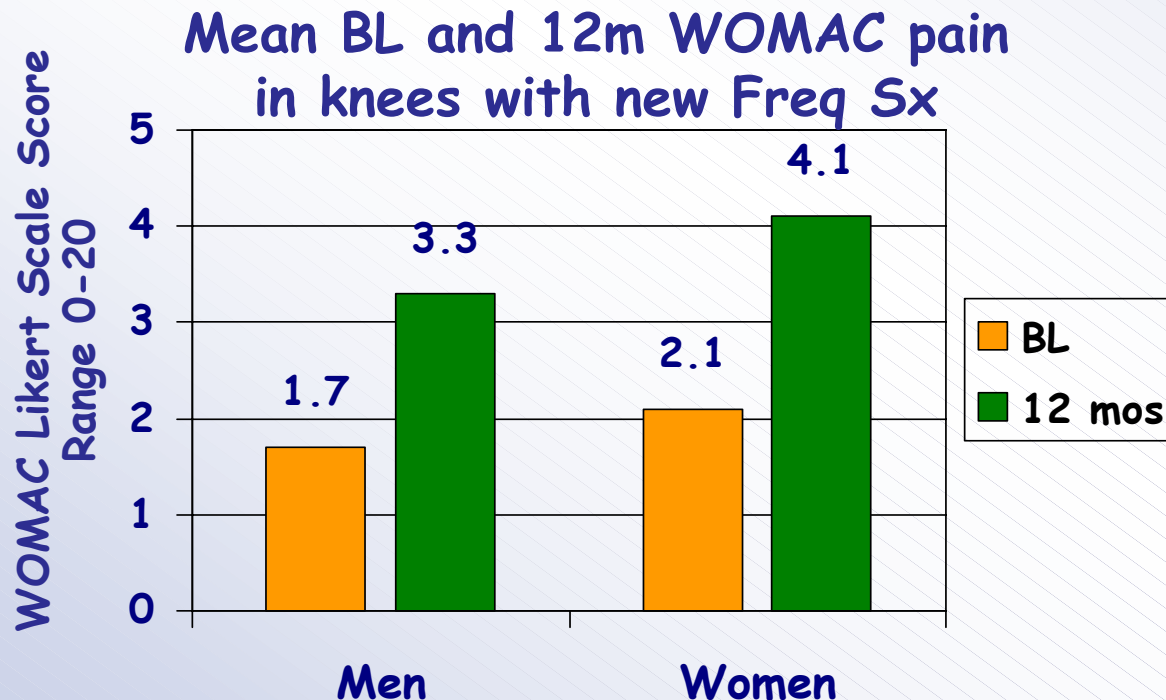
Onset of frequent knee Sx, BL to 12-mo

- Onset of frequent Sx at 12-mo* % of eligible knees

* No Freq knee Sx at BL,
Freq knee Sx in past 30 days
at 12-mo FU

Men 14.5%

Women 12.7%



Follow-up



12-mo follow-up visit status (11/07)

12-mo FU completion	N (%) of 4,796 enrolled
Clinic visit	4,293 (90%)
Telephone contact only	198 (4%)
No follow-up contact (deceased, withdrew, LFU)	302 (6%)

Follow-up imaging completion rates

- Ppts who have a 12-month clinic visit
 - ~1% refuse knee x-ray
 - ~2% refuse MRI
 - ~1.5% ineligible for MRI
 - ~1.0% due to new medical implants
- Of all ppts enrolled
 - ~87% 12-mo knee MRI
 - ~89% 12-mo knee x-ray

BL & 12-mo images available (Aug 07)

1st half pts*
n = 2,691

* The cohort is divided in two for data release

FU images acquired

Knee MRI: 2,340 (87%)
Knee x-ray: 2,394 (89%)
Both: 2,309 (86%)

BL-FU Images available for release

Knee MRI: 2,328 (86%)
Knee x-ray: 2,206 (84%)
Both: 2,111 (80%)

Outcomes/endpoints and central image assessments



Progression subcohort

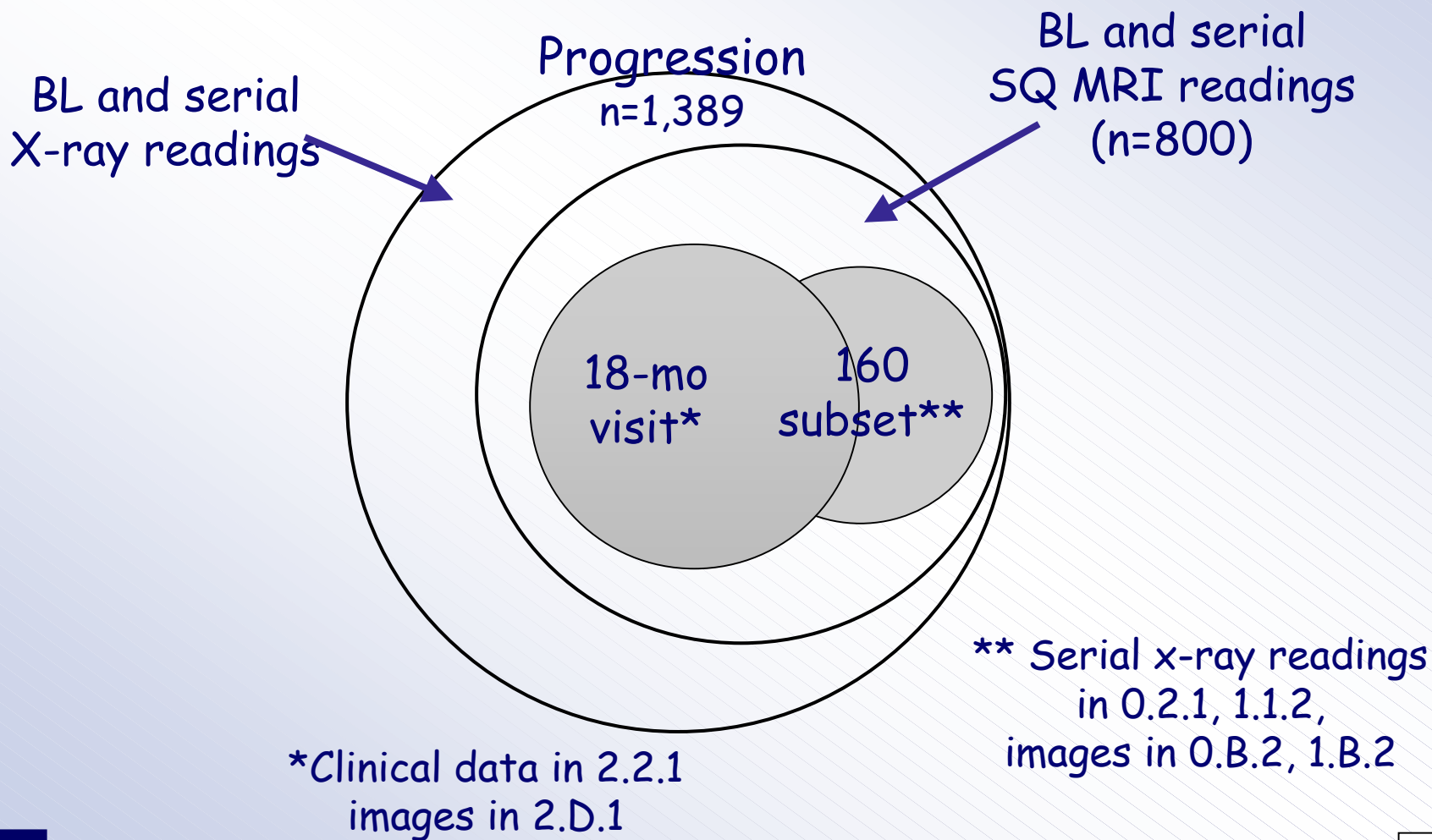
Outcomes and central image assessments

- Knee Sx, function, physical performance, TKR
- Planned central reading of knee radiographs (all)
 - BL IRFs, K-L grade
 - Longitudinal JSN, quantitative JSW
 - BL, 12-mo, 24-mo
- Planned central reading of MRIs
 - Core sample (~800 pts)
 - BL SQ whole organ assessment
 - Longitudinal SQ cartilage
 - BL, 12-mo, 18-mo, 24-mo



Progression subcohort

Central image assessments



Incidence subcohort

Outcomes and central image assessments

- Main incidence endpoints
 - X-ray OA, Sx OA, Freq Sx, TKR
- Planned central reading of knee radiographs (all)
 - First appearance of X-ray OA (definite Ost)
- Planned central reading of knee MRIs
 - Nested case-control studies
 - Read incident cases and random samples of controls
 - SQ whole organ assessment and/or quantitative morphology, TBD



Incidence subcohort

Estimated number of knee endpoints

Endpoint	N of knees by 4 yrs of FU
New X-ray OA (def Ost)	250 - 300
New Sx OA*	225 - 375
New Frequent Sx*	425 - 575

*Estimates vary by proposed definitions

Some limitations of OAI

- Observational study
 - Can't determine efficacy of treatments (e.g. supplements)
- Not a representative population sample
 - Can't estimate prevalence, incidence, etc.
- Progression vs. Incidence an artificial distinction based on study definitions
 - Some knees in incidence subcohort have OA at BL and changes may be either progression or incidence
- P-F OA not assessed by X-ray
 - Need to use MRI for P-F disease measures



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