



LEIDEN UNIVERSITY MEDICAL CENTER

Molecular Epidemiology and OA biomarkers

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Molecular Epidemiology





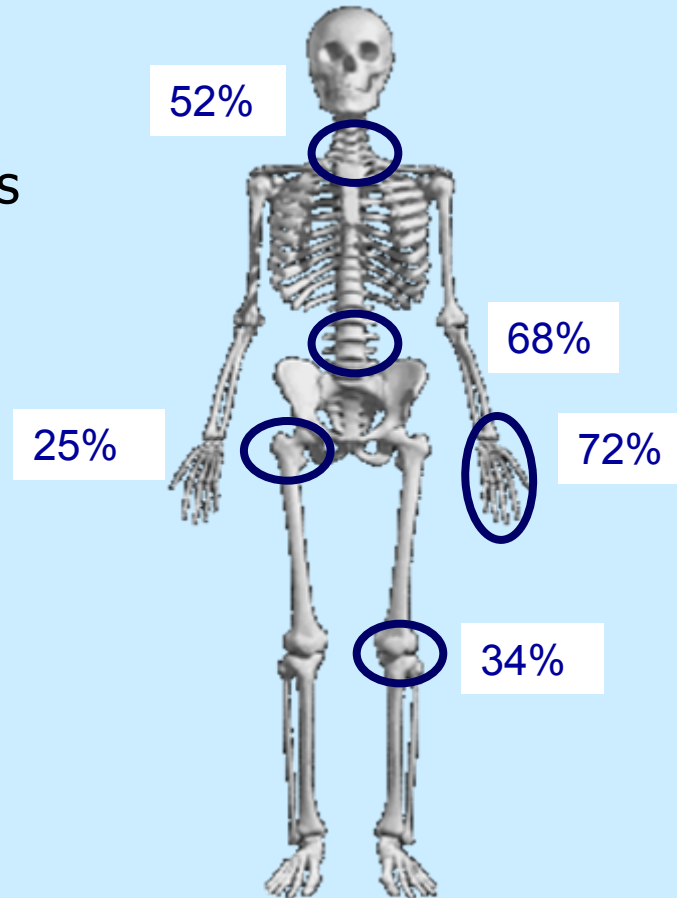
Genetics osteoARtritis and Progression

The GARP study, baseline

- 188 sibling pairs + 4 trios
- OA; ACR criteria and radiographs
- Age: 60 yrs (range 43-79)
- Female: 82%

Inclusion:

≥ 2 joints OA



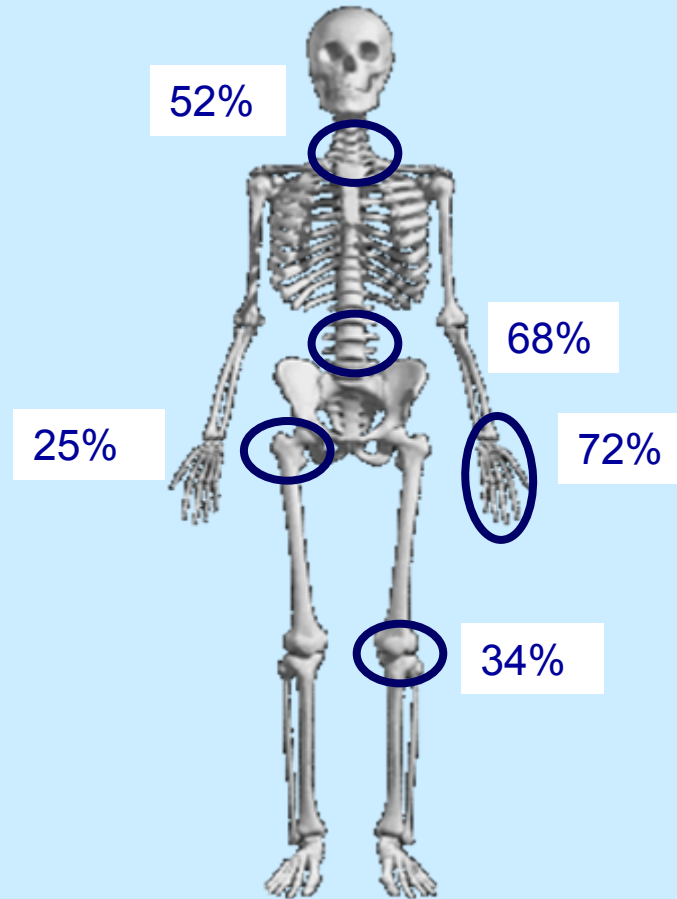
Familial background systemic factors

Progression:

6 mnths, 1 Y, 2 Y: 100 pairs

6 Y: 200 pairs

- ACR criteria and radiographs
- Questionnaires
- Urine / serum / blood RNA



- ➔ Familial background fast progression
- ➔ Course marker levels at timepoints
- ➔ Genetic predisposition



Biochemical markers

The Garp study

Blood

- Osteocalcin → bone formation
- HsCRP → inflammation
- COMP → cartilage metabolism / turnover
- PIIANP → collagen synthesis

Urine

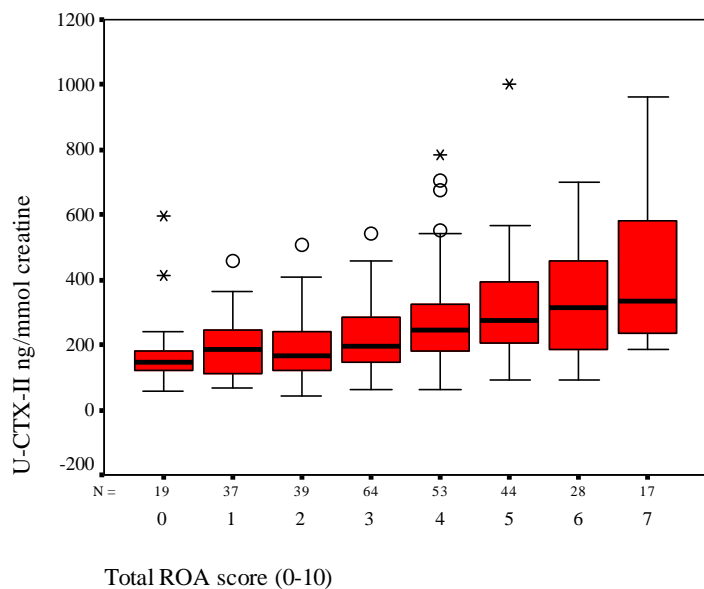
- u-CTXI → bone degradation
- u-CTXII → cartilage degradation
- TINE → cartilage degradation
- Glc-Gal-PYD → synovial tissue turnover



u-CTXII an OA biomarker ?

GARP study. Cross Sectional. I.Meulenbelt

- Associated independently to ROA in hip, hand , facet and knee and composite score
- No association to discus degeneration (DD) of spine.



u-CTXII levels reflect whole-body cartilage degradation.

What if you did not measure OA at different joints. Elderly.

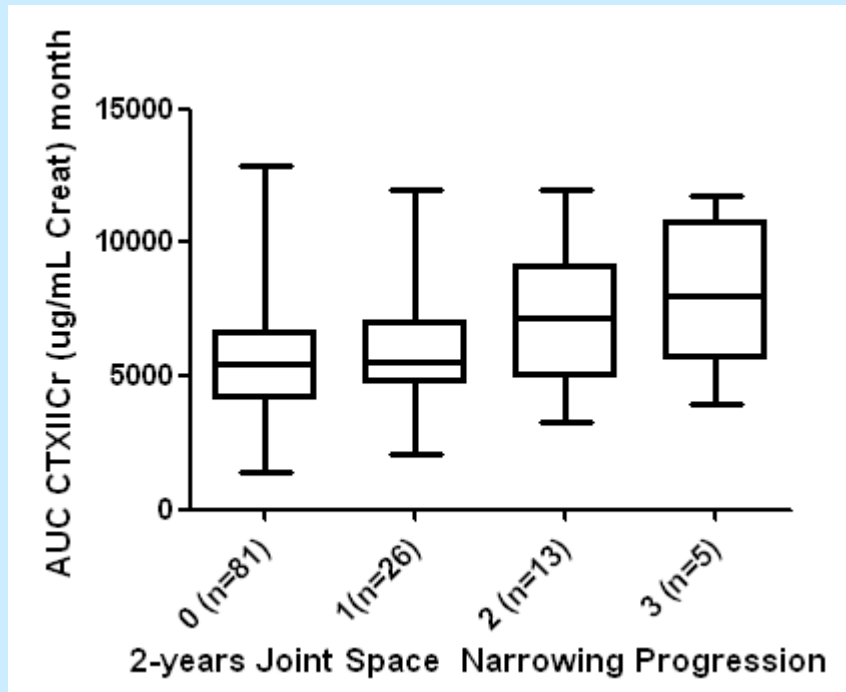
How specific is a marker for a joint
How realistic is such specificity



u-CTXII an OA biomarker ?

GARP study. Prospective. M. Kloppenburg, A. Yusuf

- Joint space narrowing (JSN) hip, hand, knee at 2Y
- Linear regression analysis JSN. Area Under the Curve



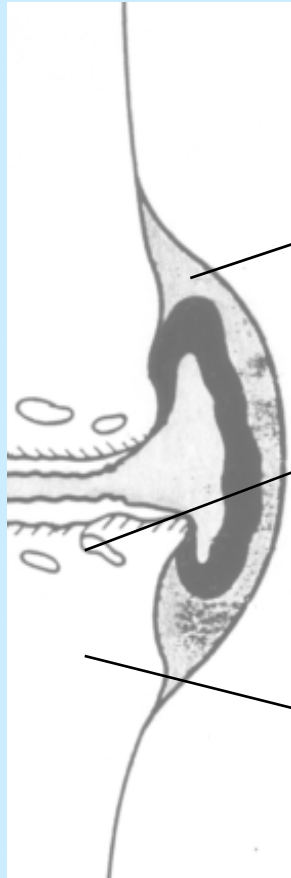
| AUC u-CTXII, corrected for age and sex | JSN 2 years | JSN 6 years |
|--|----------------------------|-------------|
| | OR | |
| Over 2 years | 1.1 (1.01 to 1.2), p=0.024 | p=0.92 |
| Over 1 year | 1.1 (0.96 to 1.2), p=0.077 | p=0.94 |
| Over 6 mnts | 0.98 (0.96 to 1.0), p=0.11 | p=0.91 |



u-CTXII weakly associates to short term progression in GARP
Adjust for age. What is the relation with calendar/biological age.

GARP study

Classification based on biomarker level;
PCA analyses I. Meulenbelt



Component

Inflammation →
Local/systemic

Cartilage/bone →
metabolism

Age related →
changes

Effect

HsCRP →
BMI

u-CTXI →
u-CTXII
Gly-Gal-Pyd
OC

COMP →
PIIANP

Joint

Knee

Hip

Hand/Facet
DD

Meulenbelt et al. (2007) Osteoarthritis and Cartilage 15:379-385

What is the relation with calendar/biological age.

Can genetics help The Garp study

Blood markers assessed

- Multiplex 17 cytokines / chemokines (Luminex)
- Thyroid levels
- Adipokines
- NMR spectra

Ex-vivo LPS stimulated cytokine levels (innate)

- IL-1 β , IL-1Ra, IL-10



- Meulenbelt et al. *Arthritis and Rheumatism*
- Bos et al. (2009) *Osteoarthritis and Cartilage* 17:621-6
- Bos et al. (2008) *Ann Rheum Diseases* 67:877-879

