

# Cross-sectional and predictive associations of systemic biochemical markers with early-stage radiographic osteoarthritis

Erwin (W.E.) van Spil  
MSc, MD  
Rheumatology & Clinical Immunology



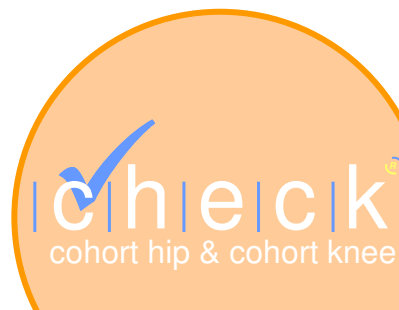
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## Cohort Hip & Cohort Knee

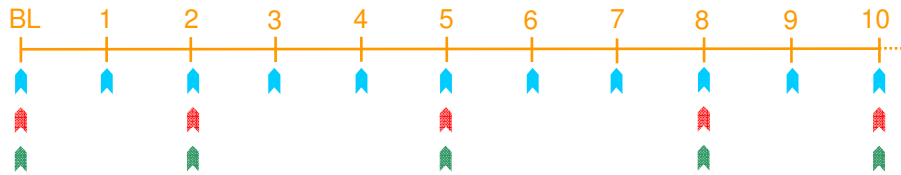
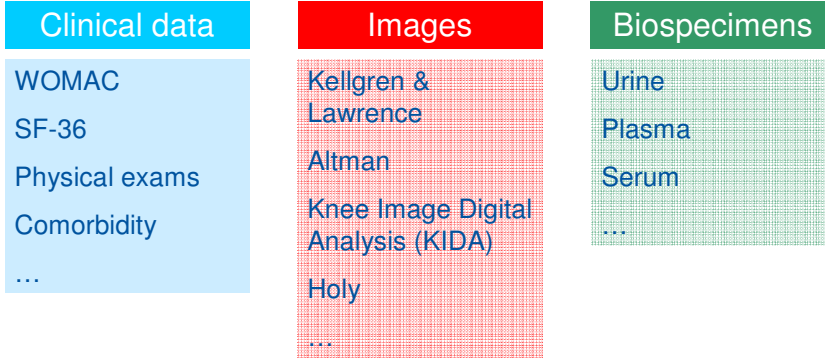


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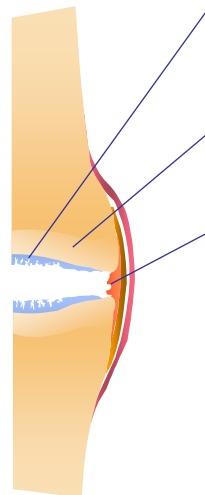
- 1002 Subjects
- Inclusion criteria:
  - Pain and/or stiffness of knee(s) and/or hip(s)
  - Never or no longer than 6 months ago visited a general physician because of these complaints
  - Age 45-65 years



# Extensive characterization



# Biochemical markers



**Cartilage**  
 Degradation uCTX-II, sCOMP  
 Synthesis sPIINP, sCS846

**(Subchondral) bone**  
 Degradation uCTX-I, uNTX-I  
 Synthesis sPINP, sOC

**Synovial membrane**  
 Degradation sHA  
 Synthesis sPIINP

**Inflammation**  
 hsCRP, ESR

**Adipokines**  
 pLeptin, pAdiponectin, pResistin

## Current goal

To investigate to what extent biochemical markers of joint metabolism...

- ...reflect current radiographic knee and hip OA
- ...predict future knee and hip OA
  - incidence
  - progression

## Index joints

- Each subject one index knee and one index hip
- One painful joint -> index joint
- Two painful joints -> index joint randomly selected
- No painful joint -> index joint randomly selected
- Presence OA: K&L grade =1
- Incidence OA: K&L grade increase  $\geq 1$  in baseline K&L =0
- Progression OA: K&L grade increase  $\geq 1$  in baseline K&L =1

## Statistics



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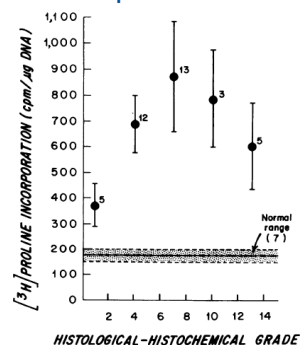
- Binary logistic regression
  - Present vs no present radiographic OA
  - Incidence vs no incidence of radiographic OA
  - Progression vs no progression of radiographic OA
- Odds ratio per standard deviation change of biochemical marker level
- Interaction with pain index joint: separate analysis painful and not painful joints when  $P < 0.200$

## Results cartilage markers



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- Cartilage markers showed many associations with both radiographic knee and hip OA
- Some showed interaction with pain
- Both cartilage degradation and synthesis markers showed positive associations



Lippiello *et al*, J Clin Inv, 1977

## Results cartilage markers



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- Unexpectedly negative associations with incident knee OA
- Increased levels of cartilage degradation ever beneficial?
- Confounded by other mechanisms?
- Coincidental finding?

## Results bone markers



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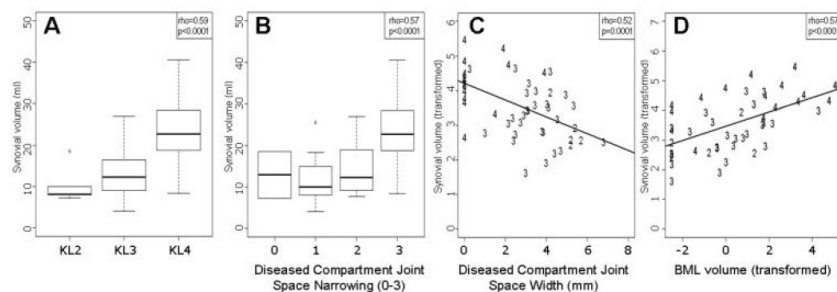
- Increased bone marker levels, more bone turnover, less mineralized bone
- Bone markers showed **positive** associations with presence of radiographic knee OA
- In accordance with rationale for testing calcitonin, biphosphonates, and risedronate in knee OA
- But **negative** associations with progression of radiographic hip OA
- In support of hypothesized inverse association between osteoporosis and OA

## Results bone markers

- Bone markers showed positive associations with knee OA, but negative associations with hip OA
- Contradictory literature data
  - Both increased and decreased bone marker levels observed in OA
  - Different effects of bone mineral density
    - Between joints  
(Hochberg *et al.*, Osteoarthr Cart, 2004)
    - Between OA incidence and progression  
(Zhang *et al.*, J Rheum, 2000)

## Results synovial markers

- Synovial markers showed positive associations with radiographic knee and hip OA
- Once more underscores relevance of synovitis



## General conclusions

- Cartilage and synovial markers are the most promising (Van Spil, Osteoarthr & Cart, 2010)
- Bone metabolism may have different effects between joints
- Associations of biochemical markers with continuous measures of individual OA features would be of additive value

Rheumatology & Clin. Immunology,  
Images Sciences Institute, UMC Utrecht

FPJG Lafeber  
JWJ Bijlsma  
J Wesseling

[www.check-research.com](http://www.check-research.com)

w.e.vanspil@umcutrecht.nl

f.lafeber@umcutrecht.nl

  
cohort hip & cohort knee

  
Dutch Arthritis Association