# Clinical, translational and epidemiological musculoskeletal research

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UNIVERSITY OF EASTERN FINLAND

KMRU
Kuopio Musculoskeletal Research Unit
University of Eastern Finland
Kuopio campus

KUOPIO UNIVERSITY HOSPITAL

# The most multidisciplinary university in Finland

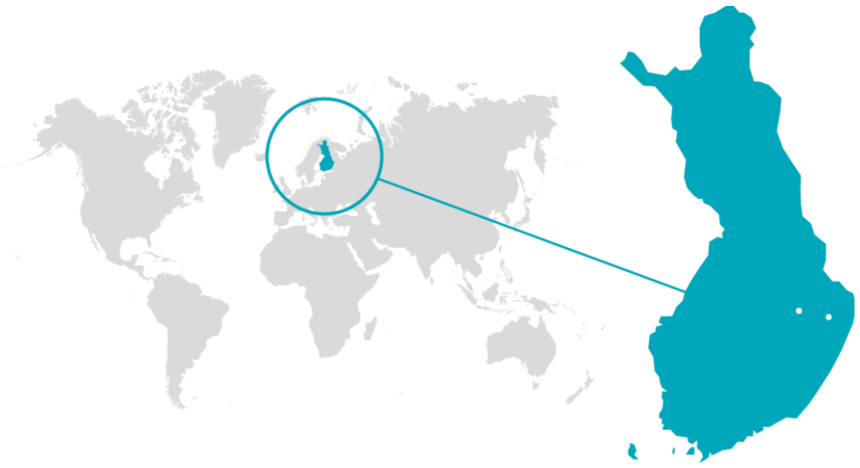
**13**

**FIELDS OF STUDY**

- widest selection in Finland

**We are in the middle of knowhere**

**UEF**

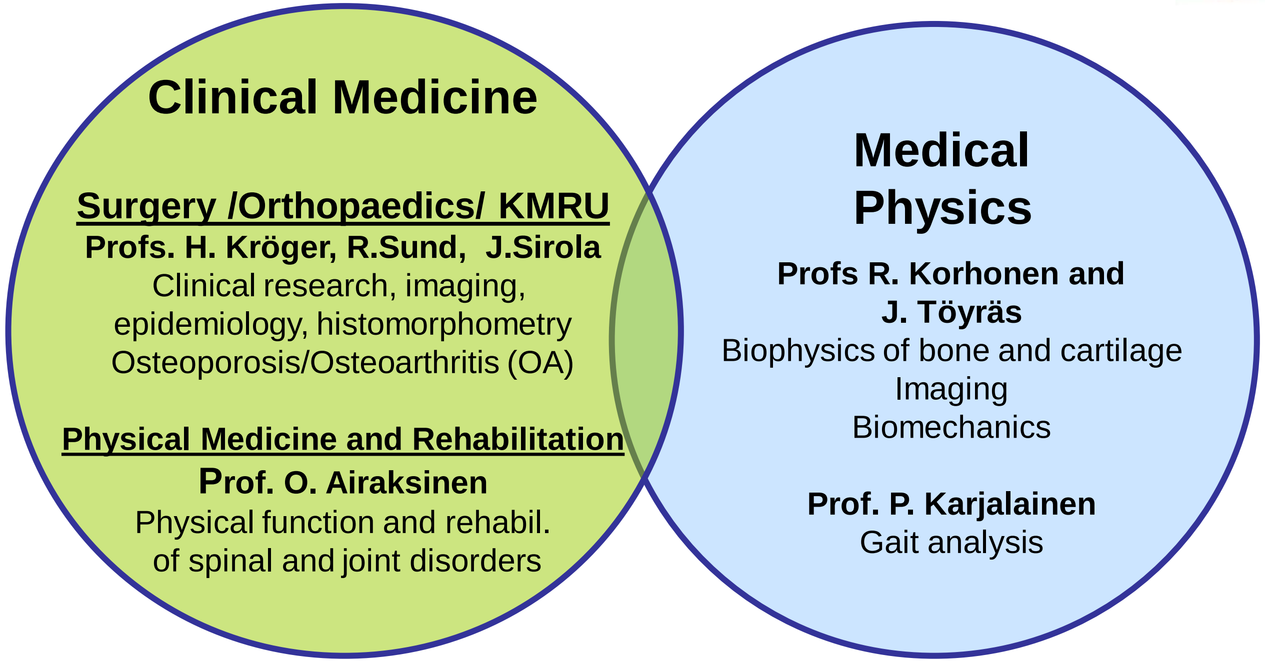


- Pharmacy
- Dentistry
- Humanities
- Education
- Economics and business administration
- Natural sciences
- Medicine
- Forest sciences
- Law
- Psychology
- Theology
- Health sciences
- Social sciences

# Kuopio Musculoskeletal Research

**Research Continuum Bone and Cartilage**

- Basic Research
- Applied Research
- Instrumentation
- Clinical Research
- Epidemiology




*”Musculoskeletal Diseases - research community (RC) covering two faculties”*

*Musculoskeletal Research is one of the <u>UEF strong research areas</u>*

## Principal investigators

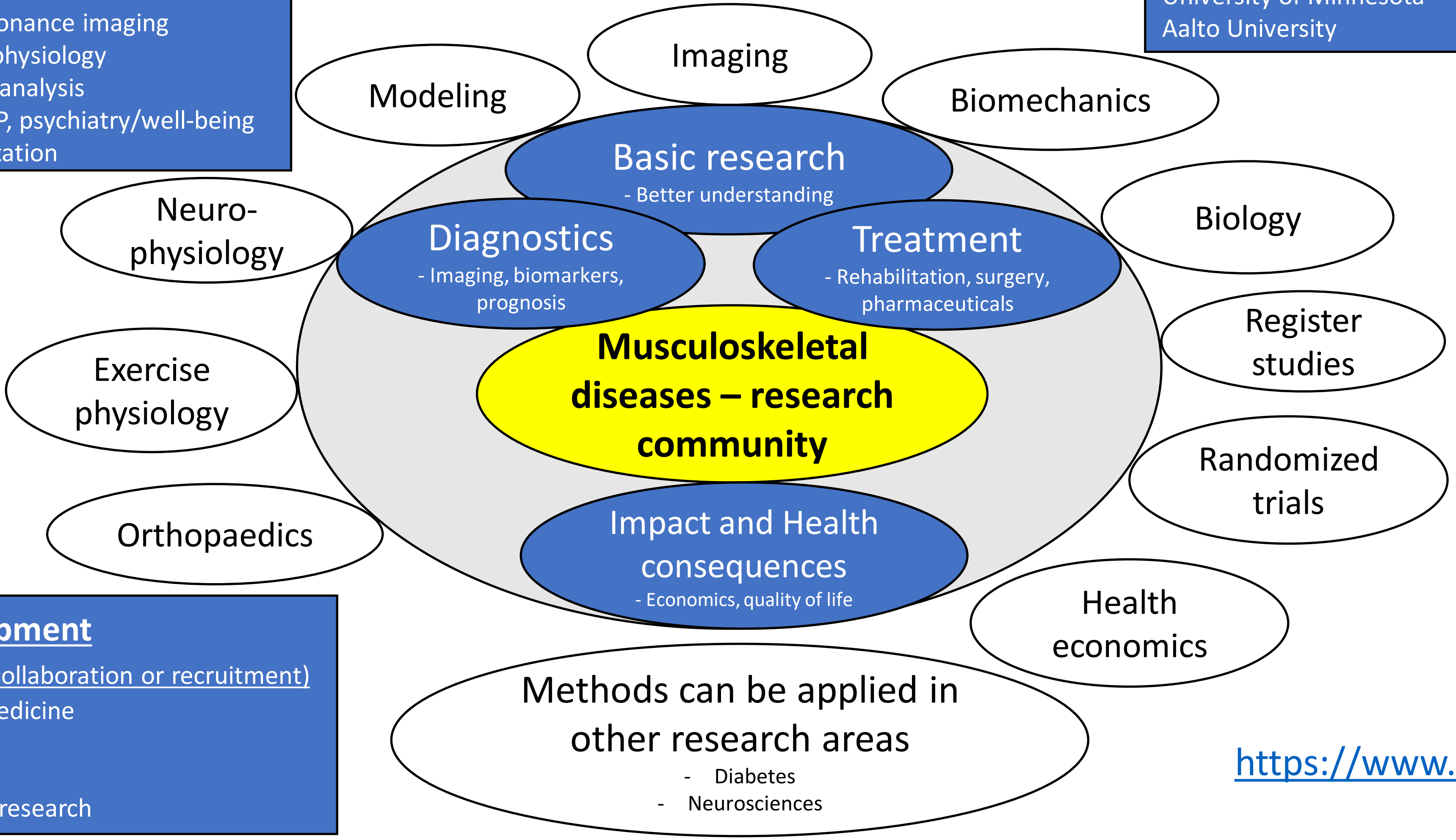
Kröger H, orthopaedics, bone research
Korhonen R, biomechanics and modeling
Töyräs J, imaging
Julkunen P, neurophysiology
Nieminen P, cell and molecular biology
Sund R, register studies, epidemiology
Martikainen J, health economics
Sirola J, orthopaedics
Nissi M, magnetic resonance imaging
Tikkanen H, exercise physiology
Karjalainen P, motion analysis
Koivumaa-Honkanen P, psychiatry/well-being
Airaksinen O, rehabilitation

- **Clinicians**
- **Physicists/engineers**
- **Biologists and physiologists**
- **Epidemiologists**
- **Health economists**

**>3 M€ annually**

## Relevant collaborators

University of Queensland
Massachusetts Institute of Technology
Utrecht University
University of Calgary
University of Oulu
University of California San Francisco
University of Cambridge
University of Minnesota
Aalto University




## Areas of development

(within UEF, through collaboration or recruitment)

- Excercise/sports medicine
- Drug therapy
- Tissue engineering
- Translational bone research

https://www.uef.fi/en/research

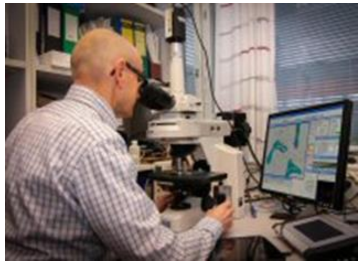
KMRU
Kuopio
Musculoskeletal
Research Unit
University of Eastern Finland
Kuopio campus

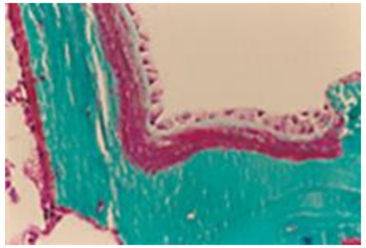
# Kuopio Musculoskeletal Research Unit (KMRU)

Mediteknia

Epidemiological studies
(OSTPRE – study)

Bone histomorphometry laboratory





Bone Densitometry laboratory
(DXA, pQCT, QUS)

Randomised controlled trials
RCT (KFPS, Phase II-III drug trials)

Kuopio University Hospital

# Department of Orthopaedics, Traumatology and Handsurgery

Clinical RCTs

Recruitment and follow-up of clinical patient materials

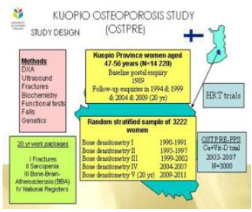
Testing of novel instruments, implants

Bone/cartilage samples

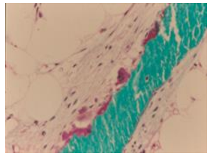
Excellent radiological facilities in the hospital

# Kuopio Musculoskeletal Research Unit (KMRU)- Main Research Lines

I OSTPRE –study  - population based 30 yr follow up osteoporosis study (n=14 400) with fall prevention, sarcopenia and national registers substudies



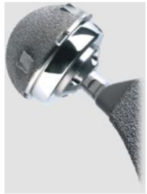

II Bone Quality – characterization of bone specimens using sophisticated techniques



III Improved Diagnostics –development of new techniques for diagnostics of OP and OA, eg. intra-artic. ultrasound, cone-beam CT, spin-off companies…


IV Physical function, gait and rehabilitation in OA – RCTs in knee and hip  OA, Spinal stenosis - project

V RCTs in clinical orthopaedics – local and multicenter RCT trials

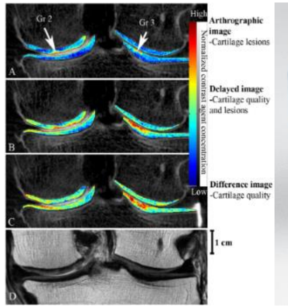


VI National health care registry - studies

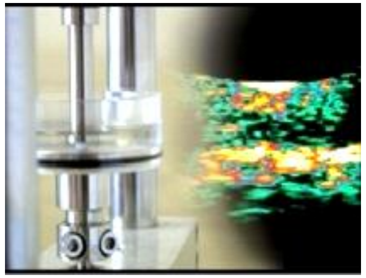
*more than 500 publications since 1991…*

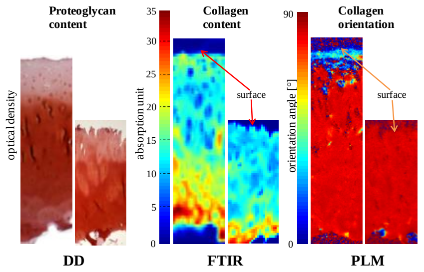
# Biophysics of Bone and Cartilage Group (BBC) – Main Research Lines

I Development of novel diagnostic methods (US, MRI, CT, optical, mechanical) for osteoarthritis and osteoporosis



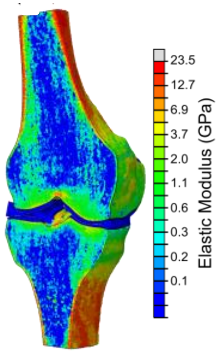

II Development of microscopic and spectroscopic techniques for evaluation of cartilage and bone

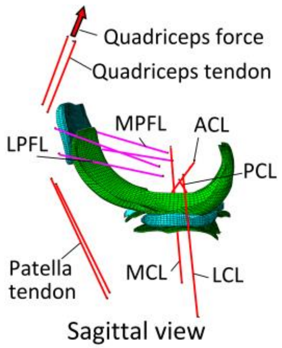





III Biomechanics of soft tissues, hard tissues and cells

IV Computational modeling of knee OA, functional imaging



**MD Nadia Afrin**
Health-related predictors and outcomes of falls in postmenopausal women (2021)

**MD Timo Nyyssönen**
Achilles tendon rupture (2020)

**MD Toni Tapaninen**
Bone mineral density changes and histomorphometric findings after hip arthroplastic surgery (2019)

**Dsc Noora Airaksinen**
Accidents among cyclists, moped drivers and motorcyclists - factors related to injuries and accident statistics (2018)

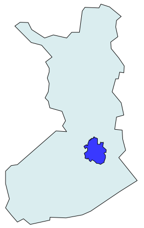
**MD Antti Jaroma**
Assessment of bone after total knee arthroplasty (2018)

**MD Miettinen Simo**
Results and complications of large diameter head cementless metal-on-metal total hip arthroplasty and hip resurfacing arthroplasty (2018)

**MD Xiaoyu Tong**
Cortical bone histomorphometry – microarchitectural heterogeneity across anatomical sites in healthy males (2017)

**MD Jaakko Järvenpää**
Patient and operation related factors influencing the outcome of knee arthroplasty (2016)

# KUOPIO OSTEOPOROSIS STUDY (OSTPRE)



## ADDITIONAL DATA AQUIRED

**_SUBGROUP MEASUREMENTS_**

- ✓ Neuropsych. tests
- ✓ Carotid Artery & Bone Ultrasound
- ✓ Blood samples; *Biochemistry, Genetics, Metabolomics*

**NATIONAL REGISTRIES**

- ✓ Hospital discharge
- ✓ Hip fractures
- ✓ Causes of death
- ✓ Work disability
- ✓ Medications
- ✓ Cancers
- ✓ Implants

## MAIN STUDY FLOW

**Kuopio Province in Eastern Finland**
**All women aged 47-56 years (N=14 220)**
Baseline <u>postal enquiry</u> in1989
Follow-up enquiries at 5-year intervals;
1994 & 1999 & 2004 & 2009 & 2014 & 2019

↓

**Random stratified sample of 3222 women**
DXA scans and functional tests
at 5-year intervals1989-2021

↓

**Women´s Healthy Aging** OSTPRE
WP1 Functional Capacity
WP2 Subjective Wellbeing
*Methods: DXA, body composition, functional tests, psychosocial scales, questionnaires registries (N=3 222-14 220, 2016-2022)*

## STUDIES

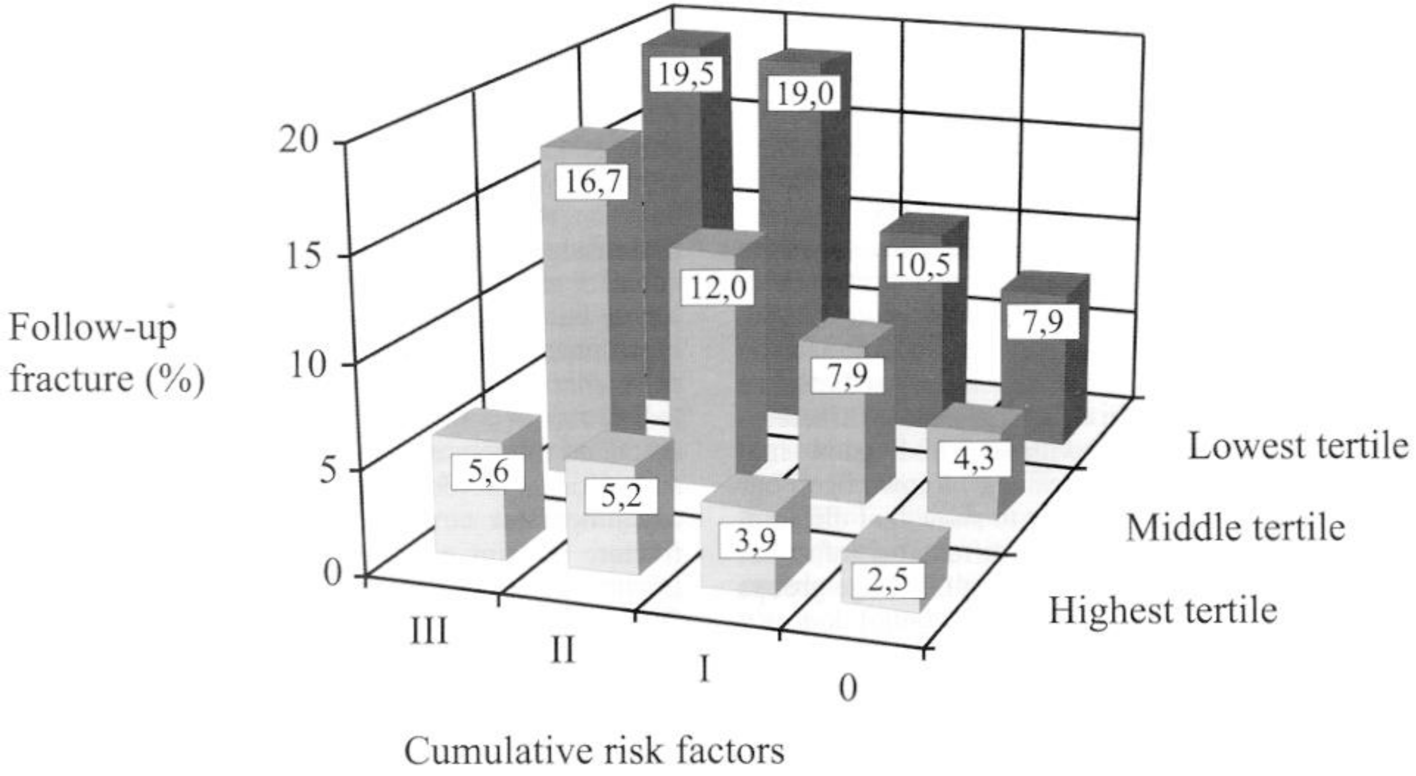
**<u>OSTPRE-FPS</u>**
*"Fracture Prevention Study"*
Ca+Vit-D supplementation RCT
2003-2007
N=3000

**<u>WORK PACKAGES</u>**
I Fractures
II Sarcopenia
III Bone-Brain-Atherosclerosis (BBA)
IV National Registers
2009-2019
N=14 222

**<u>OSTPRE-KFPS</u>**
*"Kuopio Fall Prevention Study"*
Exercise intervention with municipality
2016-2019
N=1078

# Bone Density and Cumulative Risk Factors Predict Fractures in Early Menopausal Women

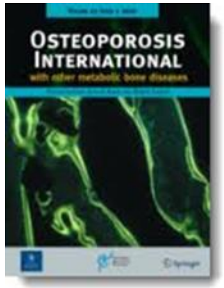
## - Kuopio Osteoporosis Study (OSTPRE)




*Huopio et al. Osteopor Int 2000*

# Long-term effects of functional impairment on fracture risk and mortality in postmenopausal women

T. Rikkonen[1] · K. Poole[2] · J. Sirola[3] · R. Sund[1] · R. Honkanen[1] · H. Kröger[1,3]




2018

**Table 2** Functional impairments with their respective prevalence ($n$, %) and hazard ratios (95% CIs) for mortality and fractures in comparison to the referent ($n = 1600$). Crude and adjusted HRs are shown. Non-significant $p$ values ($p > 0.05$) are indicated with ns. All other $p$ values are significant ($p < 0.01$) for crude models and ($p < 0.05$) for adjusted models

| | Prevalence | Mortality | Mortality[a] | Hip fracture | Hip fracture[b] | Any fracture | Any fracture[b] |
|---|---|---|---|---|---|---|---|
| Single impairment | | | | | | | |
| 1. Unable to squat and touch the floor | 759 (27.0%) | 1.6 (1.3–2.0) | 1.3 (1.1–1.7) | 3.1 (2.0–5.0) | 2.3 (1.4–3.7) | 1.2 (1.0–1.5) | 1.2 (1.0–1.5) [ns] |
| 2. Unable to stand on one foot 10 s | 200 (7.1%) | 2.5 (1.9–3.4) | 1.4 (1.5–2.6) | 4.3 (2.3–8.0) | 2.5 (1.2–5.2) | 1.6 (1.2–2.2) | 1.6 (1.2–2.2) |
| 3. Lowest grip strength tertile (kPa) | 688 (24.4%) | 1.7 (1.4–2.1) | 1.5 (1.2–1.9) | 2.0 (1.2–3.4) | 1.3 (0.8–2.3) [ns] | 1.3 (1.0–1.5) | 1.1 (0.9–1.4) [ns] |
| 4. Any of the three | 1215 (43.2%) | 1.5 (1.3–1.8) | 1.4 (1.1–1.6) | 2.4 (1.5–3.4) | 1.7 (1.0–2.6) | 1.3 (1.1–1.5) | 1.2 (1.0–1.4) |
| Combination of impairments | | | | | | | |
| 5. Squat + one foot stand | 145 (5.2%) | 3.2 (2.4–4.3) | 2.3 (1.7–3.3) | 5.9 (3.1–11.2) | 3.2 (1.5–7.0) | 1.6 (1.1–2.2) | 1.5 (1.0–2.1) |
| 6. Squat + low grip strength | 269 (9.6%) | 2.2 (1.7–2.9) | 1.9 (1.4–2.4) | 3.5 (1.9–6.4) | 2.0 (1.0–3.9) | 1.2 (0.9–1.5) [ns] | 1.0 (0.8–1.4) [ns] |
| 7. One foot stand + low grip strength | 97 (3.4%) | 2.8 (2.0–4.1) | 2.1 (1.5–3.2) | 4.6 (2.0–10.4) | 1.9 (0.7–5.0) [ns] | 1.6 (1.0–2.4) | 1.4 (0.9–2.2) [ns] |
| 8. All three | 79 (2.8%) | 3.4 (2.3–4.9) | 2.6 (1.7–3.8) | 5.9 (2.6–13.5) | 2.4 (0.9–6.5) [ns] | 1.5 (1.0–2.4) [ns] | 1.4 (0.8–2.2) [ns] |

[a] Adjusted for age, BMI, and baseline smoking status (y/n)

[b] Adjusted for age, BMI, and BMD (T-score)

[ns] Non-significant ($p > 0.05$)

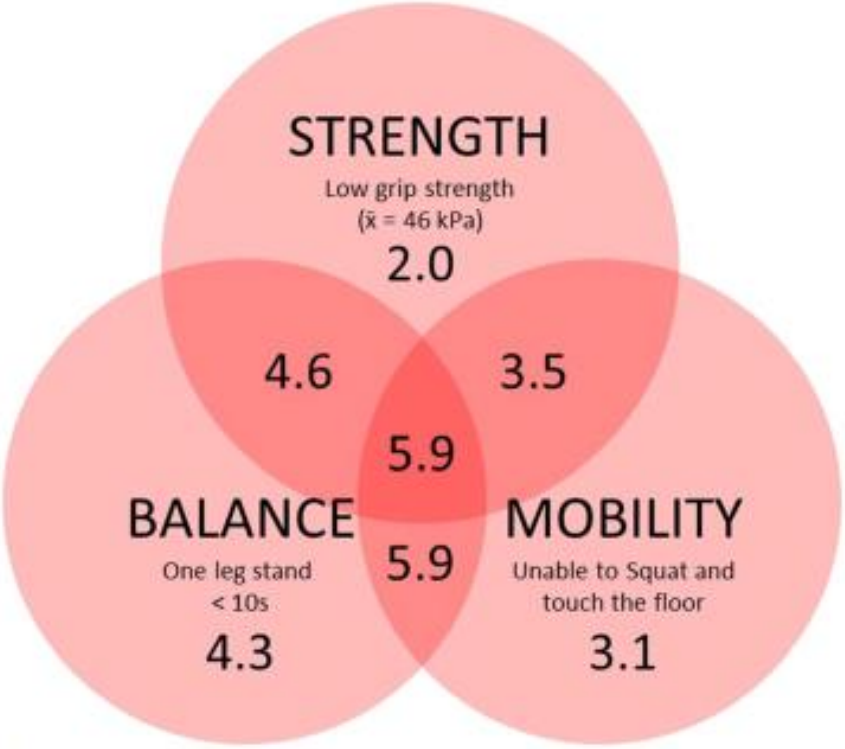
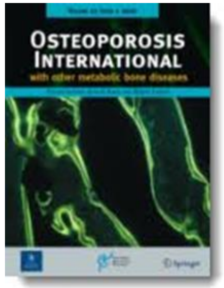



**Fig. 4** Cumulative effect of different functional impairments on hip fracture risk (adopted from Table 2.). For complete set of hazard ratios with functional impairment combinations and outcomes of interest, see Table 2

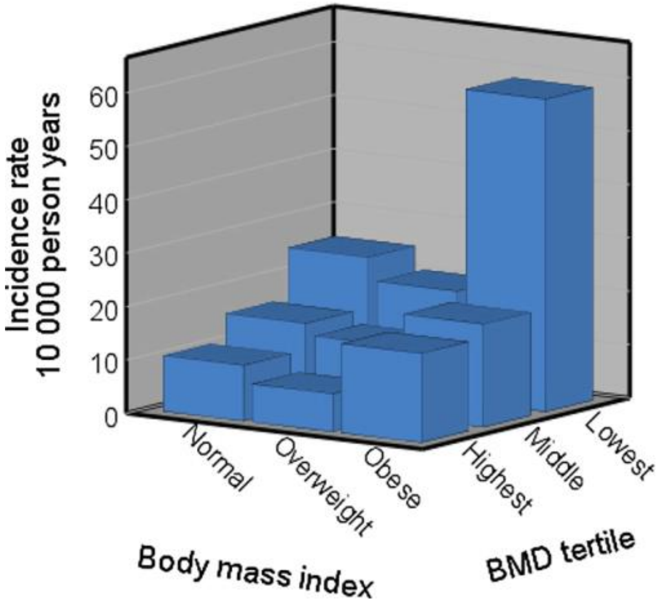
# Obesity is associated with early hip fracture risk in postmenopausal women: a 25-year follow-up

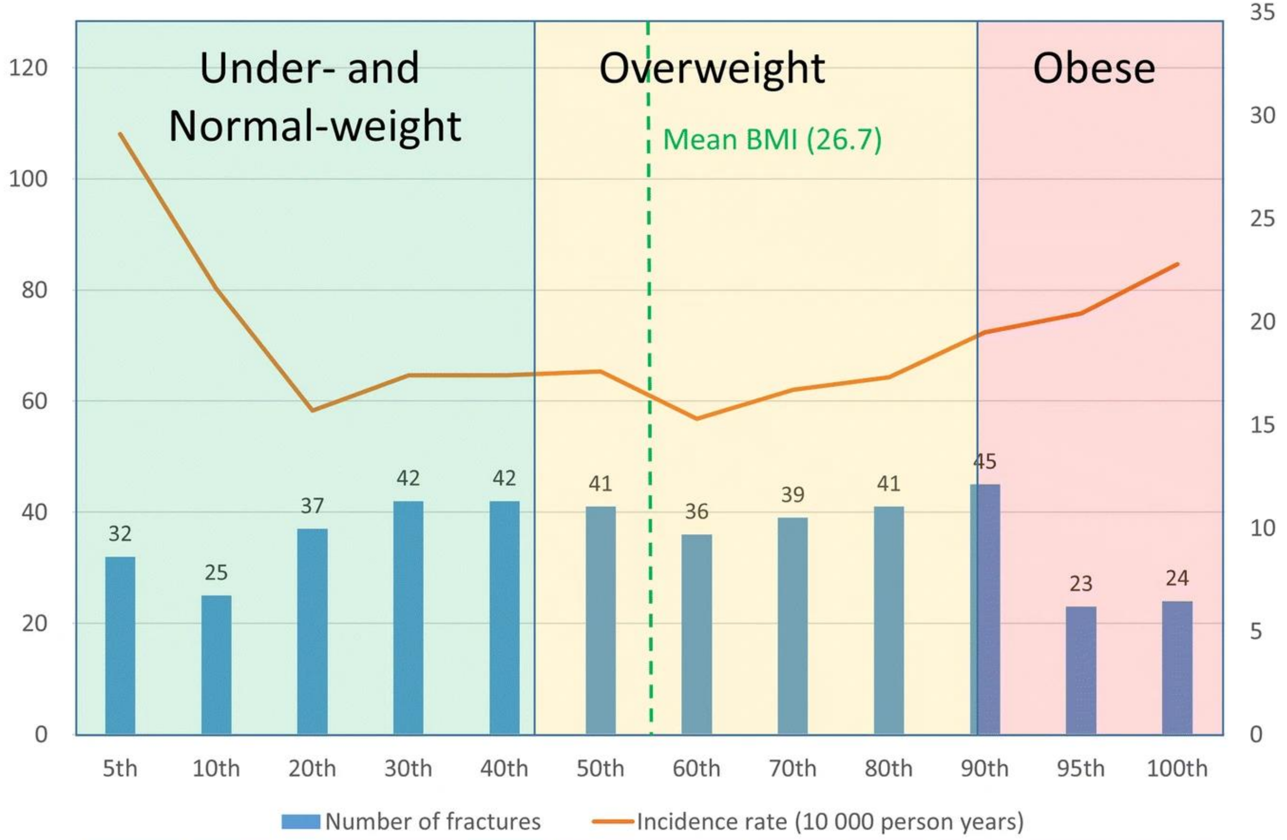
T. Rikkonen[1] · R. Sund[1] · J. Sirola[1,2] · R. Honkanen[1,3] · K.E.S. Poole[4] · H. Kröger[1,2]




*2020*

**Fig. 3** Cumulative number and incidence rate of hip fractures (per 10,000 person years) in 25 years according to baseline BMI percentile. The highest and lowest deciles are presented in groups of 5%



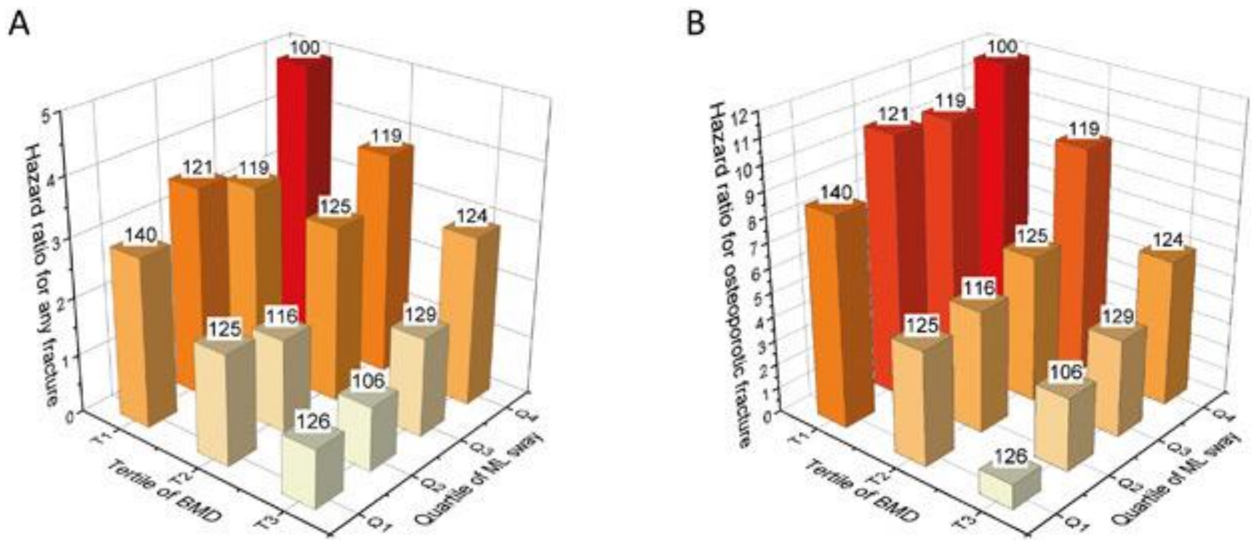

| Percentile | 5th | 10th | 20th | 30th | 40th | 50th | 60th | 70th | 80th | 90th | 95th | 100th |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BMI cutoff | <20.8 | <21.8 | <23.1 | <24.0 | <25.0 | <26.0 | <27.1 | <28.3 | <30.0 | <32.5 | <35.9 | <68.6 |
| Incidence rate | 29.1 | 21.6 | 15.7 | 17.4 | 17.4 | 17.6 | 15.3 | 16.7 | 17.3 | 19.5 | 20.4 | 22.8 |

# High Postural Sway Is an Independent Risk Factor for Osteoporotic Fractures but Not for Mortality in Elderly Women

JBMR®

Sarang Latif Qazi,[1] Joonas Sirola,[1,2] Heikki Kröger,[1,2] Risto Honkanen,[1] Masoud Isanejad,[1] Olavi Airaksinen,[3] and Toni Rikkonen[1]


**Fig. 2.** Kaplan-Meier hazard curves for any fracture according to quartiles of mediolateral sway (Log rank, $p < 0.001$).




Postural sway predicts fracture risk in postmenopausal women. A combination of low bone density and high ML sway poses an even higher risk than either factor alone. High postural sway also appears to associate with all-cause mortality, although not independently.

N=1450

Multimorbidity predicts falls differentially according to the type of fall in postmenopausal women

Nadia Afrin[a,*], Risto Honkanen[a], Heli Koivumaa-Honkanen[b,c], Pyry Lukkala[d], Toni Rikkonen[a], Joonas Sirola[a,e], Lana J. Williams[f], Heikki Kröger[a,e]

Role of musculoskeletal disorders in falls of postmenopausal women

N. Afrin[1] · R. Honkanen[2] · H. Koivumaa-Honkanen[2,3,4,5] · R. Sund[2,6] · T. Rikkonen[2] · L. Williams[7] · H. Kröger[2,8]

***Table 7. Adjusted risk of frequent falls (≥2 falls/12months) related to multimorbidity by type of fall***

| Morbidity | Slip fall<br>OR (95 % CI) | Nonslip fall<br>OR (95 % CI) |
|---|---|---|
| Healthy | 1.0 | 1.0 |
| 1–2 diseases | 1.34 (1.13–1.60) | 1.89 (1.51–2.37) |
| 3+ diseases | 1.45 (1.12–1.87) | 2.64 (1.95–3.58) |

*Adjusted for age, 3-category number of medications and smoking (No/Yes).

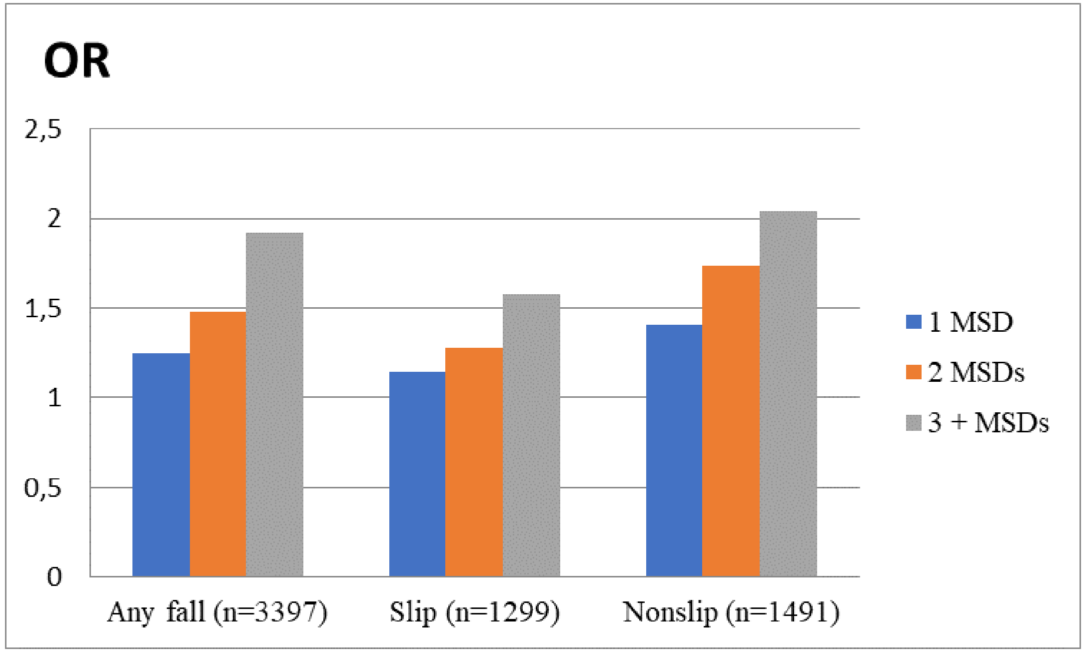
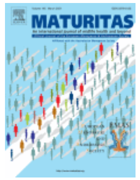
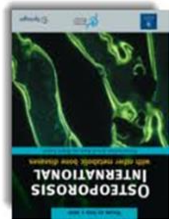


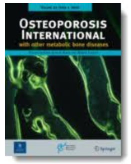

**Fig.4 Fall risks (OR, 95 % CI) related to number of musculoskeletal disorders (MSDs)**



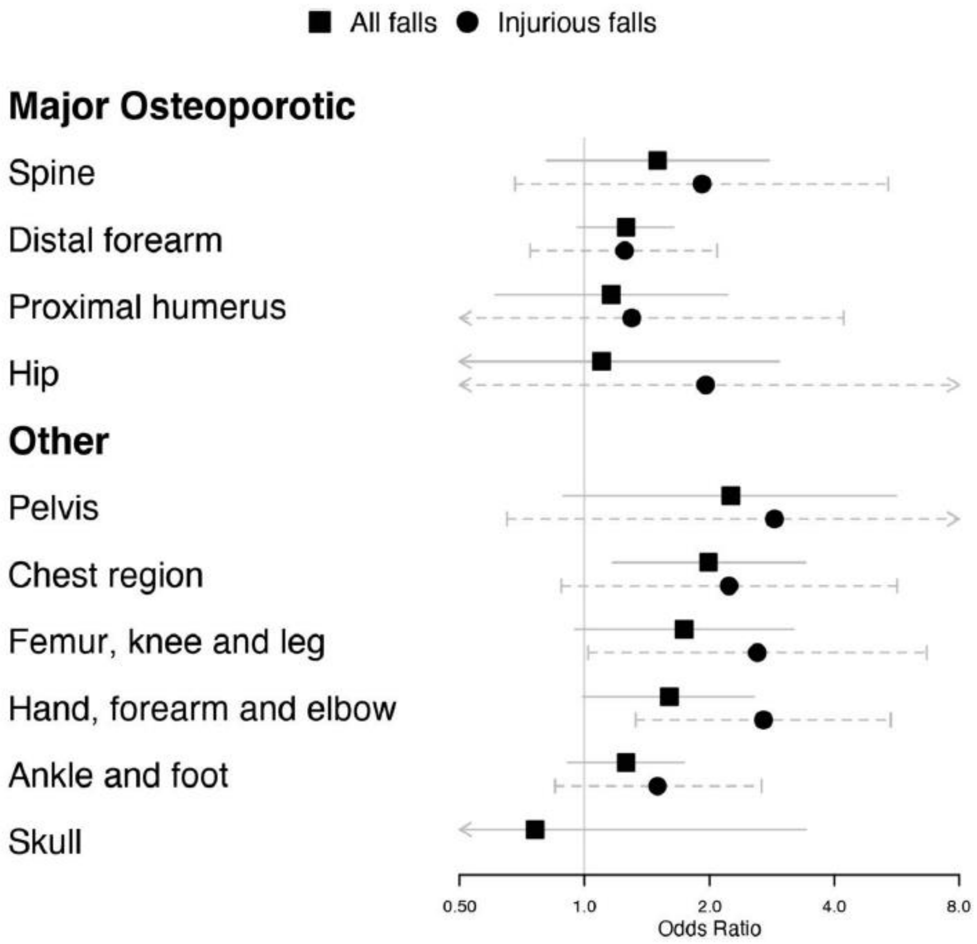

MSDs are common and an important risk factor for falls and especially nonslip falls among postmenopausal women. The number of excess falls due to MSDs in this population group is greater than that due to any other disease class.



# A fall in the previous 12 months predicts fracture in the subsequent 5 years in postmenopausal women




N. Afrin[1] · R. Sund[1] · R. Honkanen[1,2] · H. Koivumaa-Honkanen[1,2,3,4,5,6,7] · T. Rikkonen[1] · L. Williams[8] · H. Kröger[1,9]




History of falls (especially injurious falls) predicts subsequent fractures (mainly other than major osteoporotic fractures)

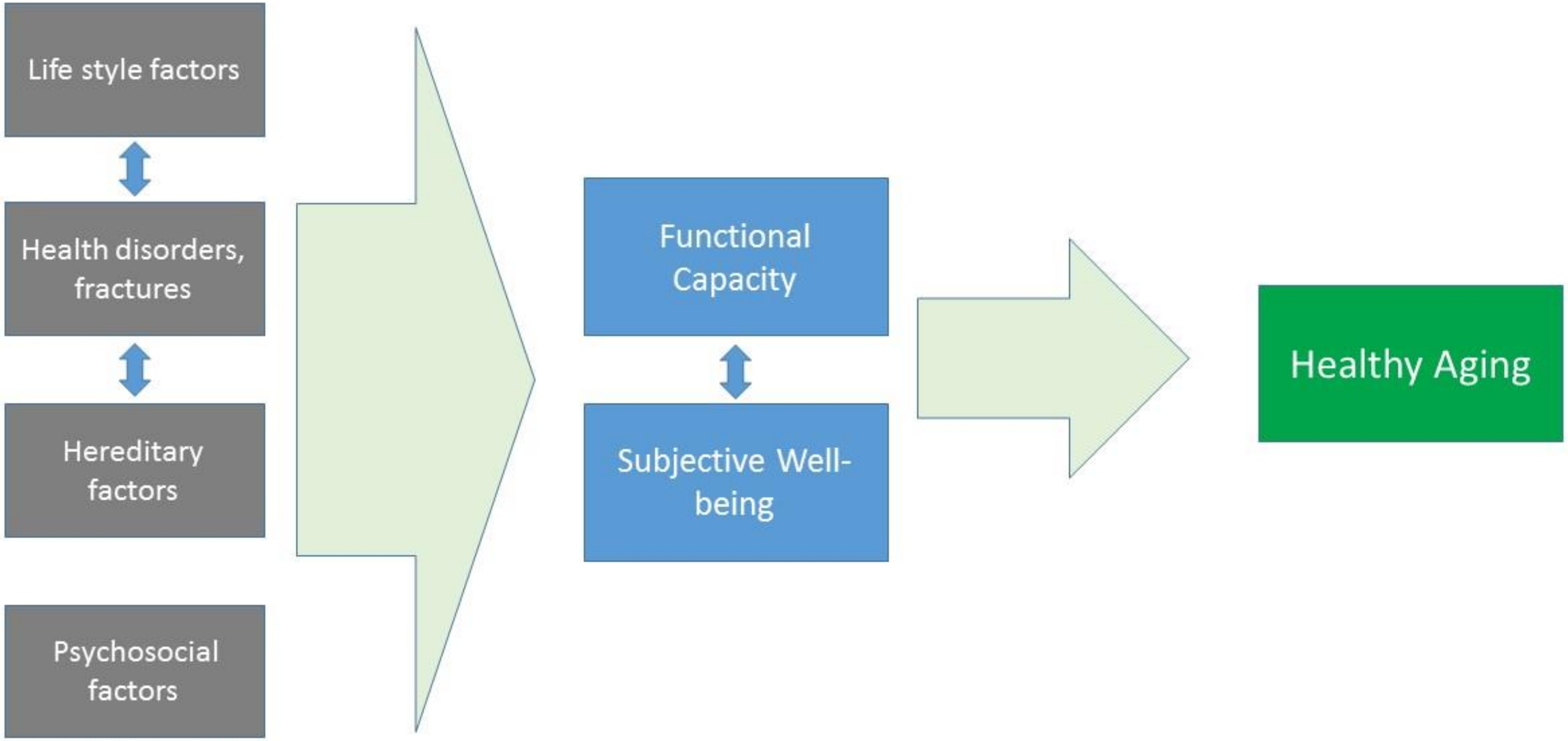
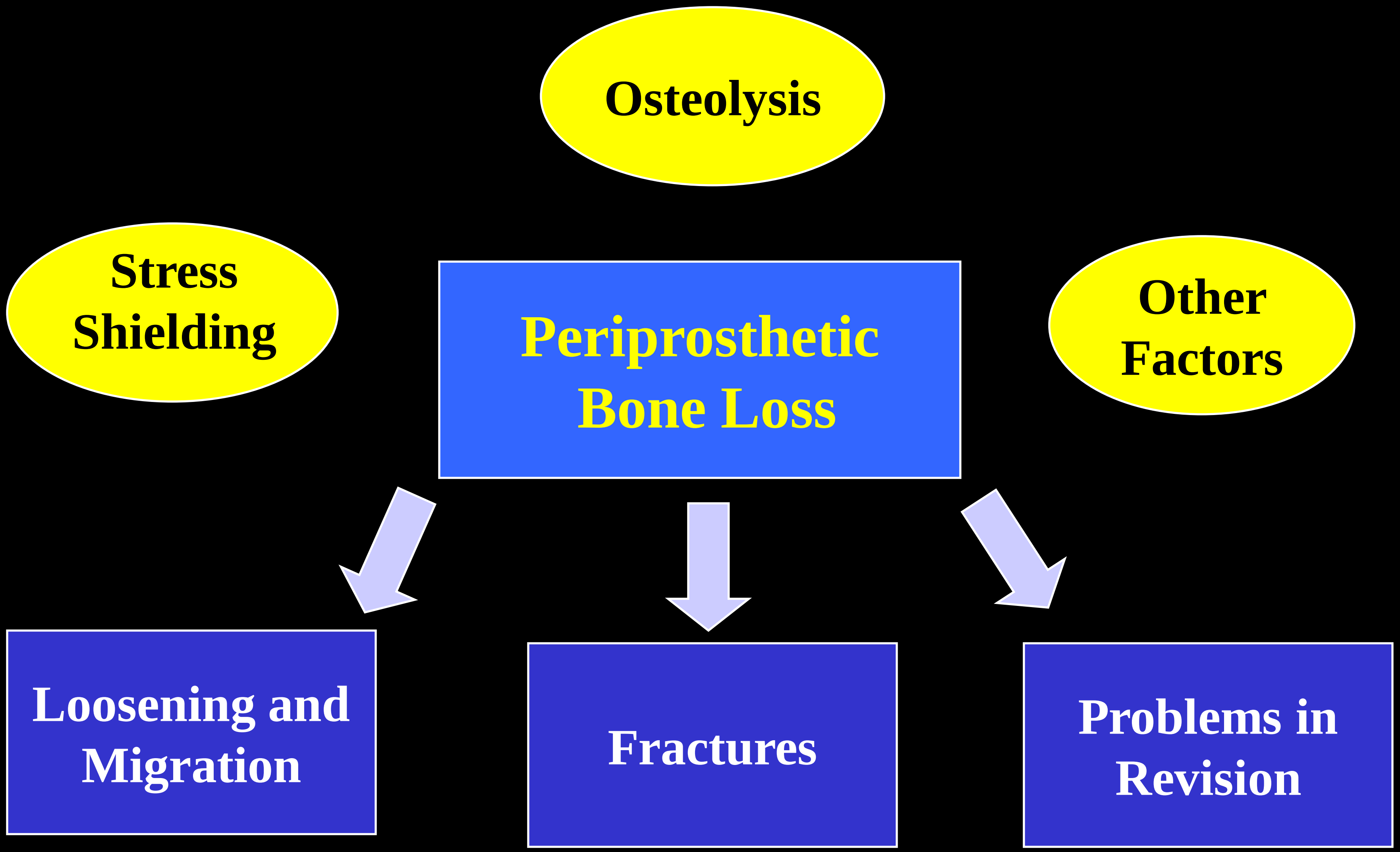


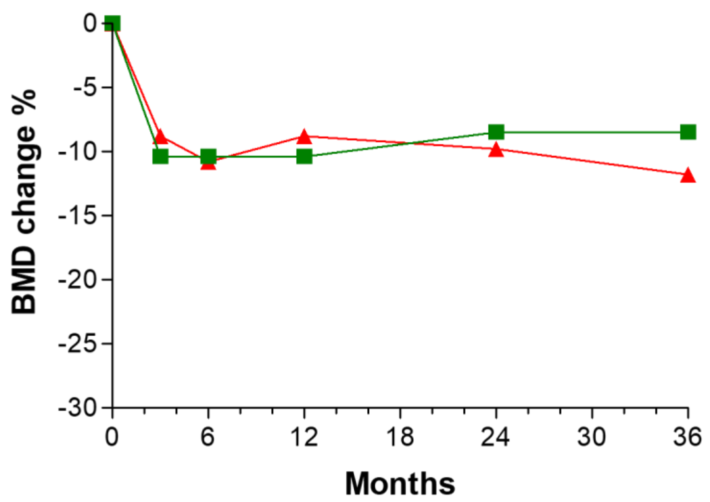

Figure 1. Determinants of Healthy Aging

# Periprosthetic Bone Loss after Arthroplasty

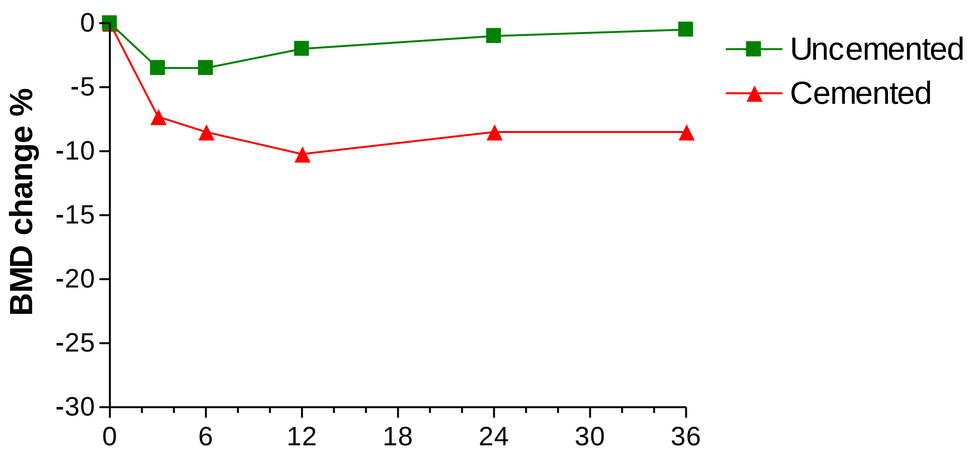


# Periprosthetic BMD Change during 3 Years Follow-up

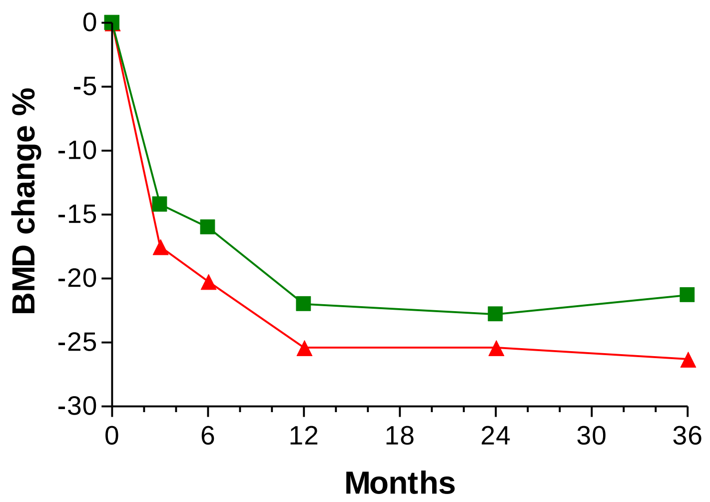
Gruen Zone 1

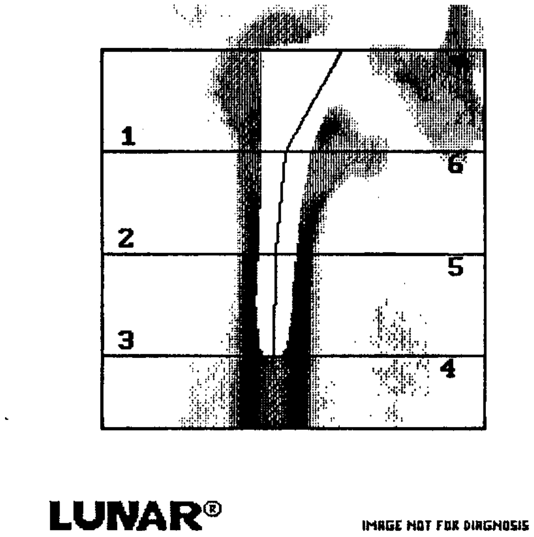



Gruen Zone 3




Gruen Zone 7



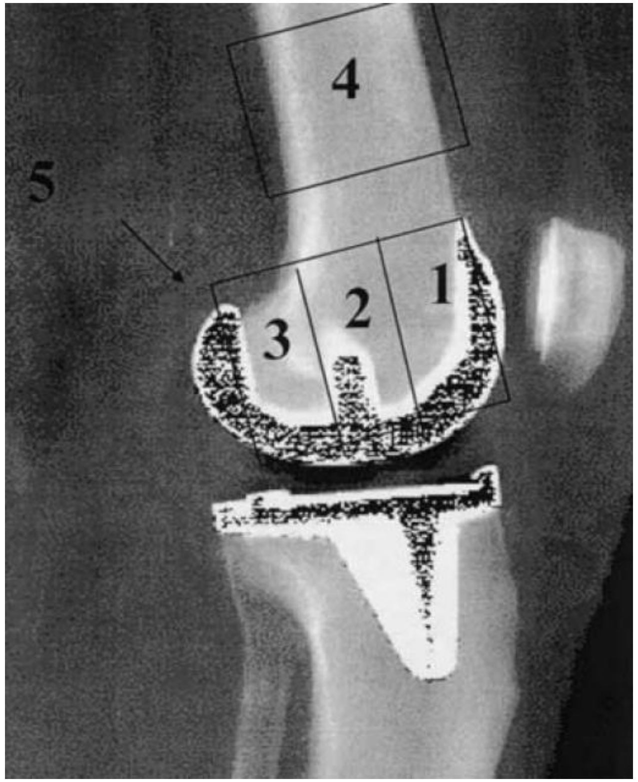

*Venesmaa et al. JBMR 2001 & Venesmaa et el. Acta Orthop 2003*

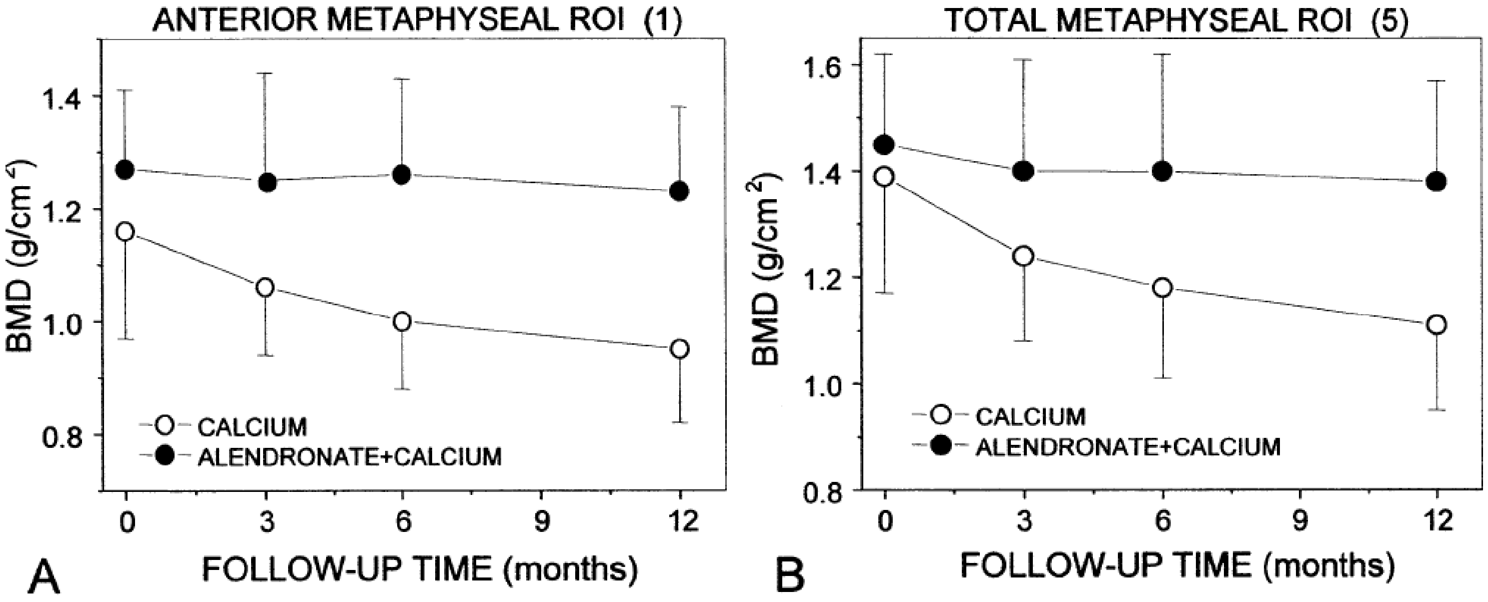
# Effect of Alendronate on Periprosthetic Bone Loss After Total Knee Arthroplasty: A One-Year, Randomized, Controlled Trial of 19 Patients

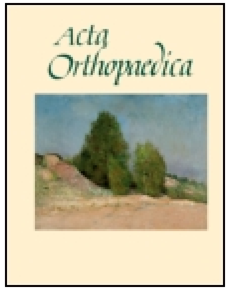
Calcified Tissue International



T. A. Soininvaara,[1,3] J. S. Jurvelin,[2] H. J. A. Miettinen,[3] O. T. Suomalainen,[3] E. M. Alhava,[3] P. J. Kröger[3]

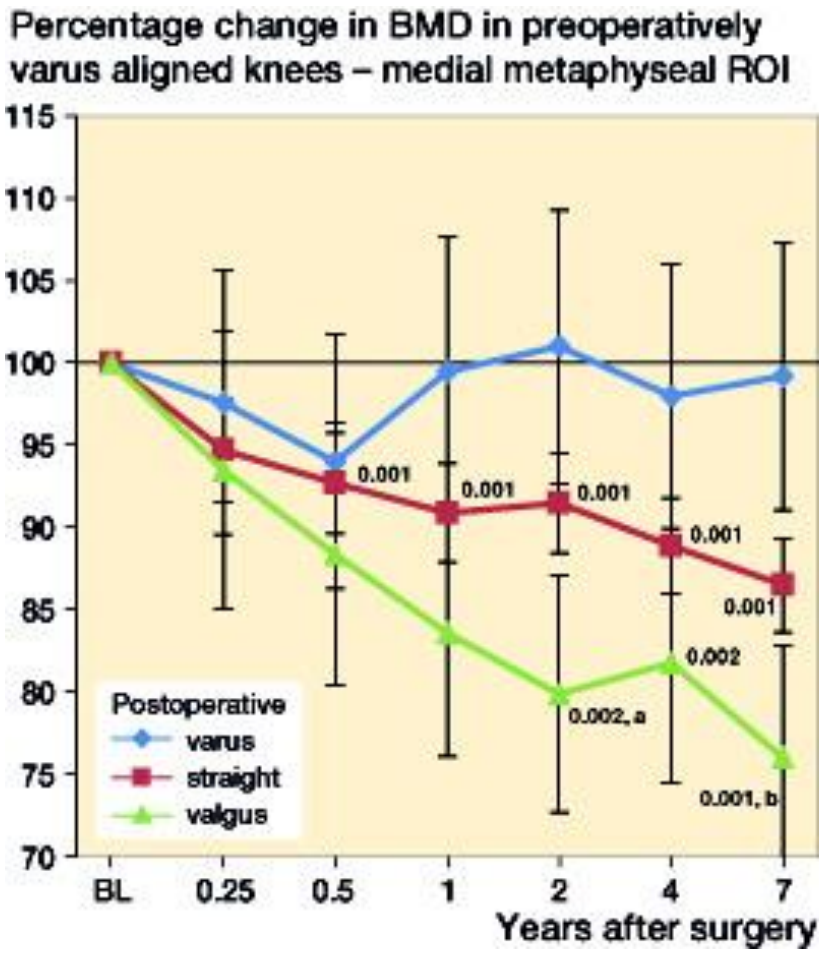


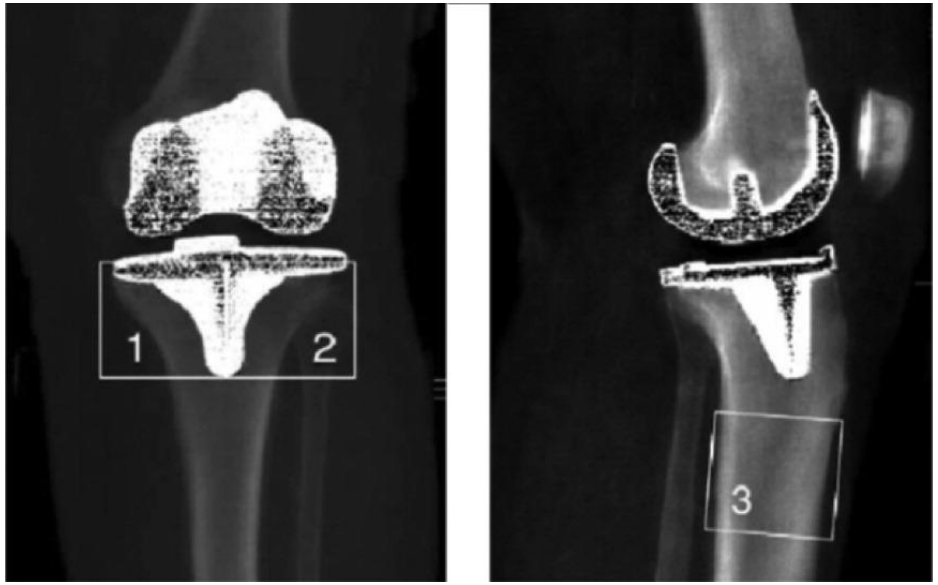



# Periprosthetic tibial bone mineral density changes after total knee arthroplasty
## A 7-year follow-up of 86 patients

Jaroma A, Soininvaara T, Kröger H Acta Orthopaedica. 2016

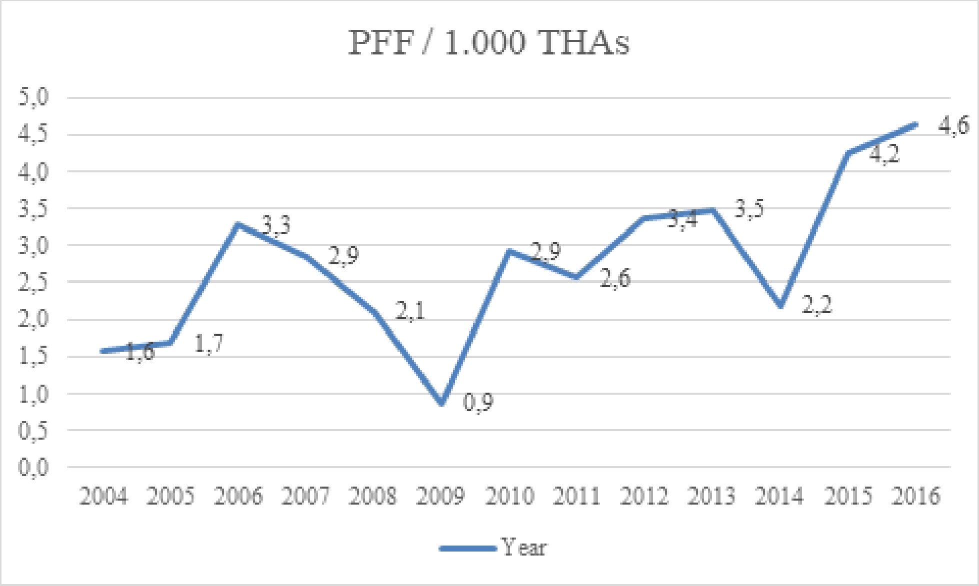


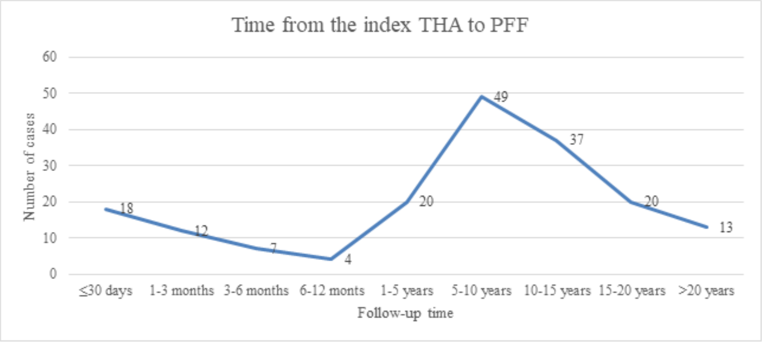

The baseline BMD of the medial tibial metaphyseal region of interest (ROI) was higher in the varus aligned knees (25%; $p < 0.001$). Tibial metaphyseal periprosthetic bone is remodeled after TKA due to mechanical axis correction, resulting in more balanced bone stock below the tibial tray.



# Retrospective population-based cohort study of incidence, complications and survival of 202 operatively treated periprosthetic femoral fractures

*Miettinen S et al. J Arthroplasty  (submitted)*





This country-specific study showed a threefold increasing trend in the incidence of operatively treated PFFs from 2004 to 2016 per 1000 THAs. The Vancouver type B1 fracture was the most common type. A high number of complications was associated with PFFs, 10.9 % were re-revised and 7.4% of the patients had died within 1 year after PFF surgery.

The Bone & Joint Journal
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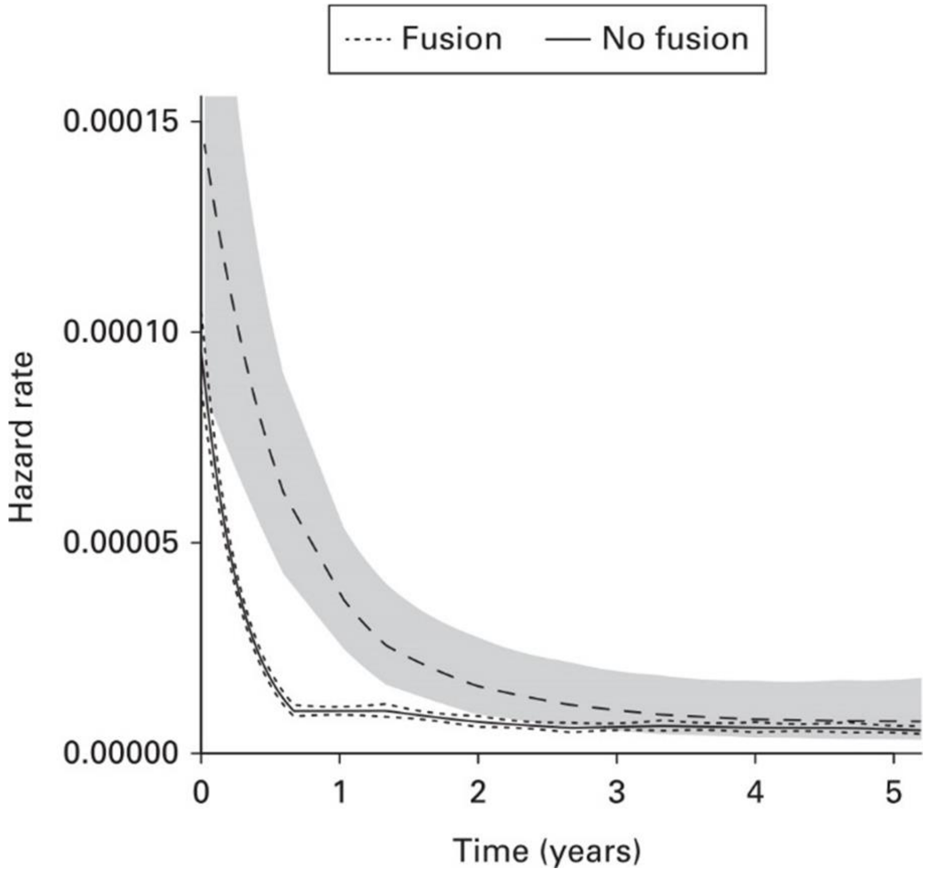
# Following total hip arthroplasty: femoral head component diameter of 32 mm or larger is associated with lower risk of dislocation in patients with a prior lumbar fusion
# a retrospective cohort study of 101, 443 total hip arthroplasties

Bone Joint J 2020;102-B(8):1003–1009.

Mononen H, Sund R, Halme J, Kröger H, Sirola J




Lumbar fusion surgery was associated with higher rate of hip prosthesis dislocation and higher risk of revision surgery. Femoral head component of 32 mm (or larger) associates with lower risk of dislocation in patients with previous lumbar fusion.

Data used in this study were compiled from several Finnish national health registers, including the Finnish Arthroplasty Register (FAR) which was the primary source for prosthesis-related data. Other registers used in this study included the Finnish Health Care Register (HILMO), the Social Insurance Institutions (SII) registers, and Statistics Finland

# OBESITY HAS A NEGATIVE IMPACT ON CLINICAL OUTCOME AFTER TOTAL KNEE ARTHROPLASTY

J. Järvenpää[1], J. Kettunen[2], T. Soininvaara[2], H. Miettinen[2], H. Kröger[1,2]

Scandinavian Journal of Surgery 101: 198–203, 2012

TABLE 3

*The postoperative functional, radiological and subjective results at the follow-up examination in April 2009 per knee, expressed as mean (SD).*

| | Group 1 (n = 27) (BMI < 30) | Group 2 (n = 25) (BMI ≥ 30) | p–value |
|---|---|---|---|
| Knee score | 88.9 (16.3) | 83.6 (13.0) | 0.01 |
| Function score | 76.3 (31.5) | 63.6 (30.1) | 0.051 |
| ROM | 109.6 (8.1) | 104.6 (9.2) | 0.016 |
| WOMAC pain (VAS 0-100) | 11.6 (17.9) | 20.7 (24.7) | 0.021 |
| WOMAC stiffness | 13.4 (21.2) | 26.9 (24.3) | 0.006 |
| WOMAC physical function | 14.4 (22.4) | 26.5 (10.7) | 0.003 |
| Walking distance (m) | 2935 (2303) | 1894 (1852) | 0.072 |
| Up and Go-test (s) | 12.1 (6.3) | 12.7 (4.9) | 0.25 |
| Deviation from straight mech.axis | 3.3 (3.3) | 3.3 (2.4) | 0.69 |

Results have been calculated based on control BMI at the last follow-up

*Number of complications and technical errors were also increased in BMI ≥ 30 Group*

# Risk factors for early readmission due to surgical complications after treatment of proximal femoral fractures – A Finnish National Database study of 68,800 patients

Tero T. Yli-Kyyny[a,*], Reijo Sund[b,c], Mikko Heinänen[d], Antti Malmivaara[e,f], Heikki Kröger[a]

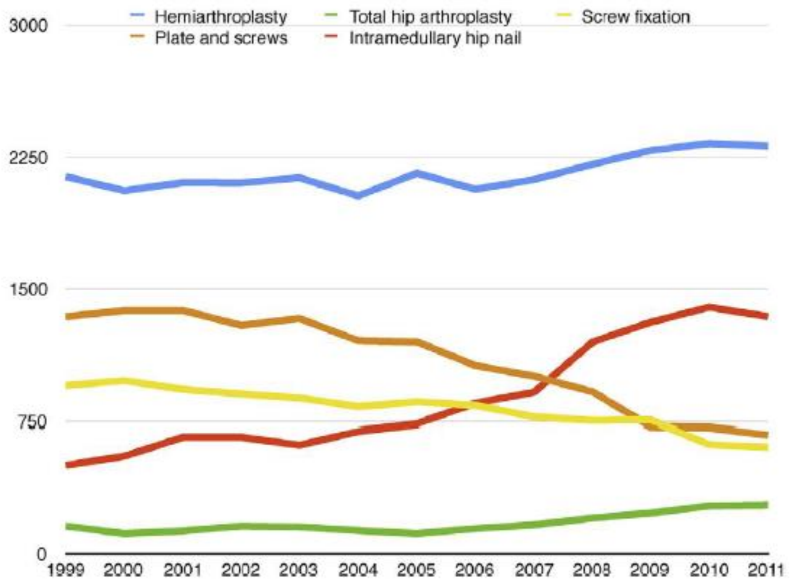




**Fig. 2.** The annual use of different surgical methods in the treatment of hip fractures in Finland 1999–2011 (first hip fractures in over 50-year-old patients.

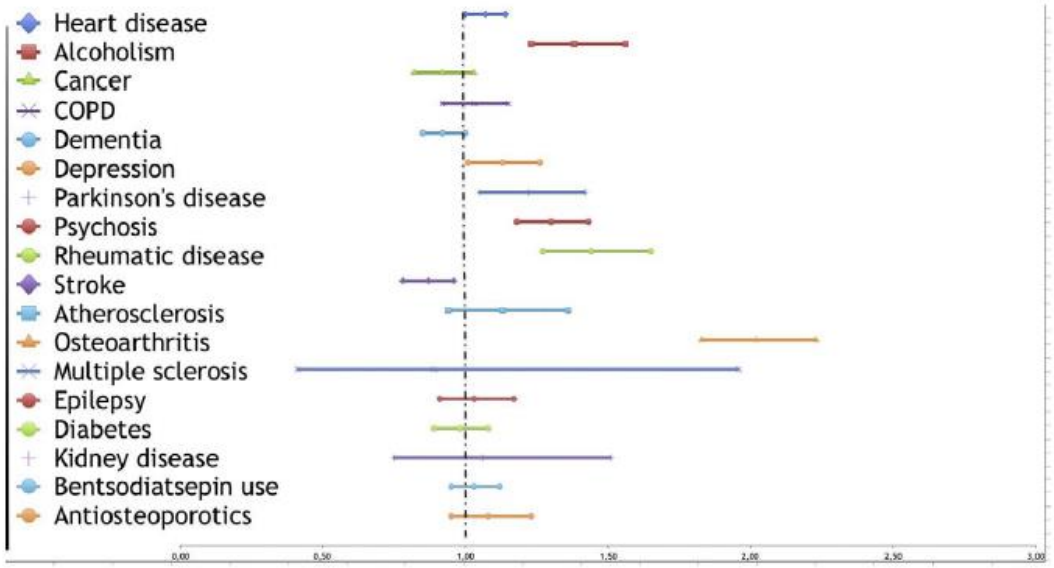
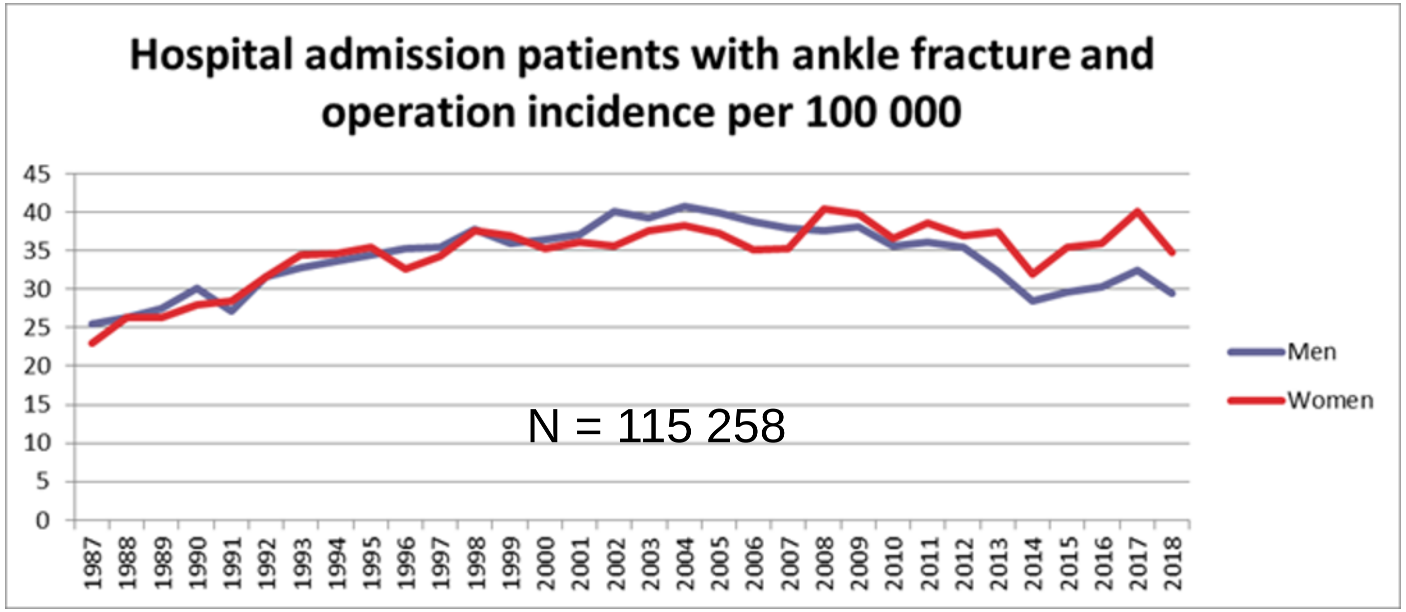
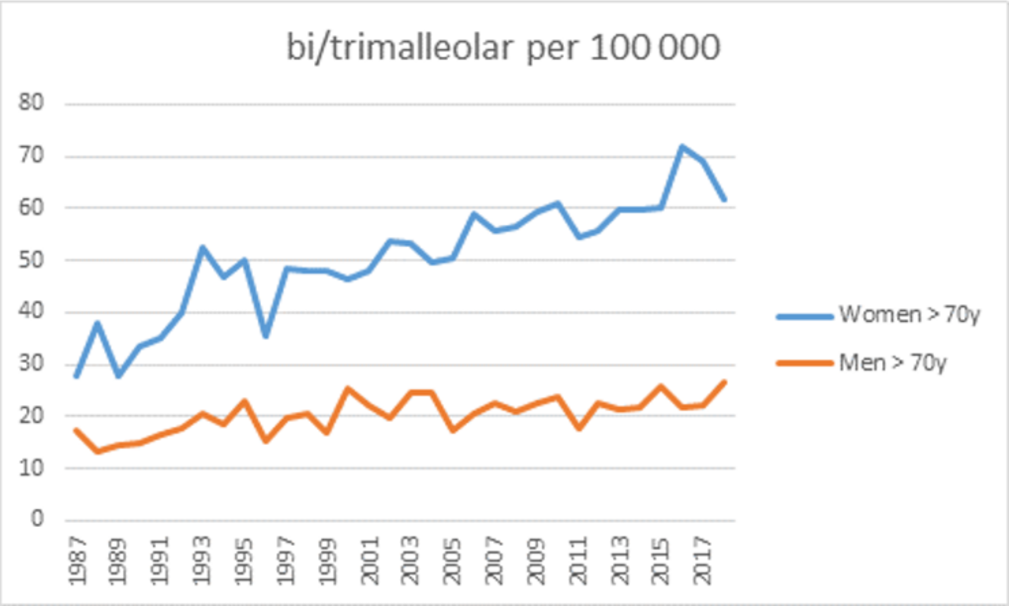



**Fig. 5.** Relative risks for an early readmission due to a surgical complication in patients with above-mentioned, pre-existing comorbidities.

# Operatively treated ankle fractures in Finland 1987-2018

Happonen V, Kröger H, Sund R (unpublished data)




Data extracted from the National Hospital Discharge Register (HILMO)

Bi- and trimalleolar ankle fractures seem to increase especially in older women (>70 yr)

SCANDINAVIAN JOURNAL OF
MEDICINE & SCIENCE IN SPORTS

# Drug treatments associated with Achilles tendon rupture. A case-control study involving 1118 Achilles tendon ruptures (2018)

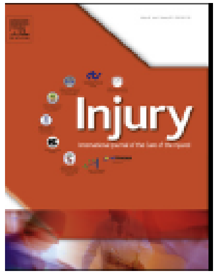
Nyyssönen T, Lantto I, Luthje P, Selander T, Kröger H

Table 1. Drug groups that had a statistically significant association with AT rupture according to the medical data for 1118 case-control pairs.

| Drug group | ATC code | Cases | Controls | OR | p-value |
|---|---|---|---|---|---|
| Renin-angiotensin system agents | C09 | 95 | 60 | 1.64 | 0.039 |
| Sex hormones | G03 | 102 | 61 | 1.74 | 0.013 |
| Systemic corticosteroids | H02 | 87 | 24 | 3.85 | 0.000 |
| Systemic antibacterials | J01 | 407 | 317 | 1.45 | 0.001 |
| Anti-inflammatory agents | M01 | 411 | 252 | 2.00 | 0.000 |
| Topical pain relievers | M02 | 150 | 45 | 3.69 | 0.000 |
| Analgesics | N02 | 48 | 23 | 2.14 | 0.037 |
| Drugs for obstructive airway disease | R03 | 101 | 59 | 1.78 | 0.010 |

The increased risk for AT rupture in patients using antihypertensive ACE-2 antagonists is a new and interesting finding.

The increasing AT rupture incidence, especially in middle aged and elderly patients, might partially be a consequence of increased use of certain drug treatments.




# Cycling injuries and alcohol

Noora K. Airaksinen[a,*], Ilona S. Nurmi-Lüthje[b], J. Matti Kataja[c], Heikki P.J. Kröger[d], Peter M.J. Lüthje[e]

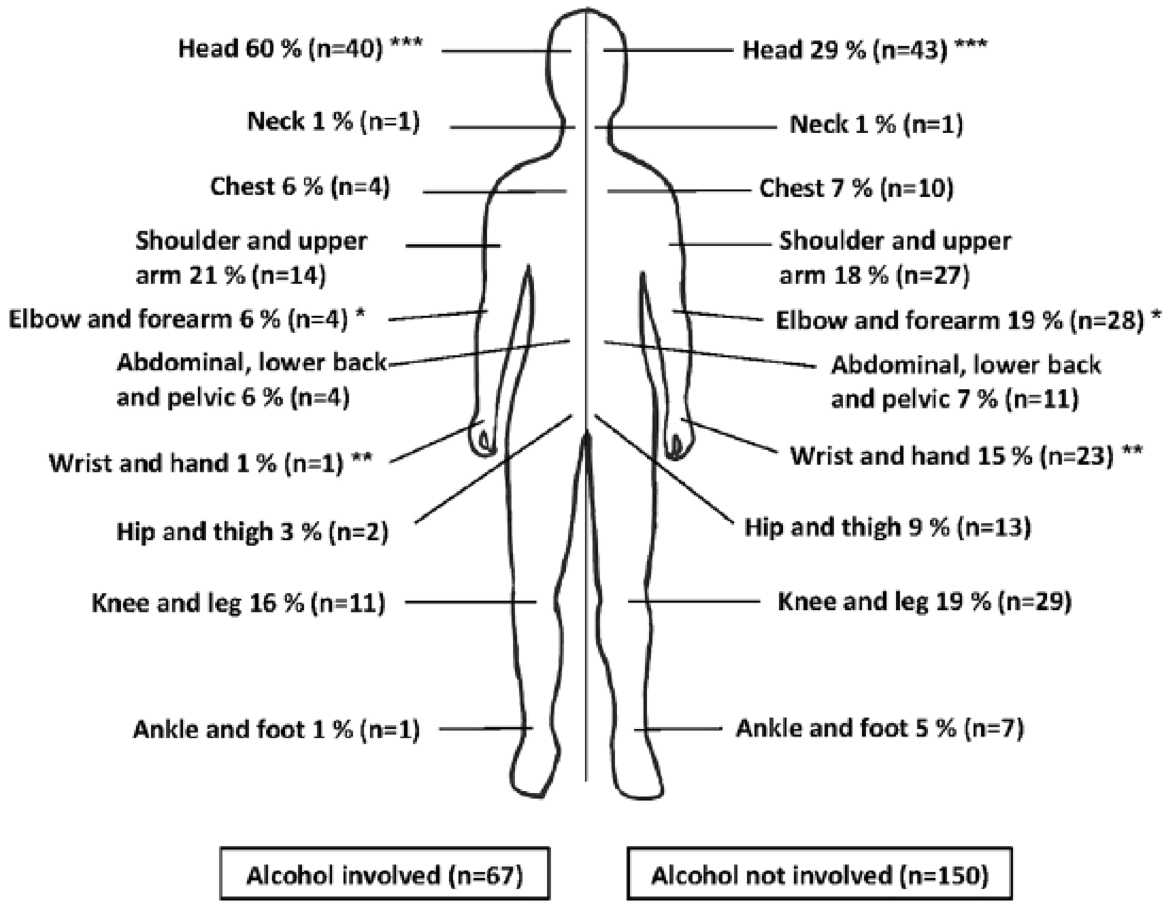
Injury 2018

Table 2
Use of bicycle helmet among cyclists according to involvement in alcohol.

| | Alcohol involved (n = 67) | | Alcohol not involved (n = 150) | | Total (n = 217) | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Yes | 0 | 0 | 30 | 20 | 30 | 14 |
| No | 44 | 66 | 76 | 51 | 120 | 55 |
| Unknown | 23 | 34 | 44 | 29 | 67 | 31 |
| Total | 67 | 100 | 150 | 100 | 217 | 100 |

$\chi^2 = 15.66$, d.f. = 2, $p < 0.001$.

Bicycle helmet in use: 0 % !



# Preoperative Predictors of Better Long-term Functional Ability and Decreased Pain Following LSS Surgery

SPINE Volume 45, Number 11, pp 776–783

*A Prospective Observational Study with a 10-year Follow-up Period*

Iina Tuomainen, MD,[a,b] Janne Pesonen, MD,[a,b] Marinko Rade, MD,[a,c,d] Maarit Pakarinen, PhD,[e]
Ville Leinonen, PhD,[f,g] Heikki Kröger, PhD,[h] Olavi Airaksinen, PhD,[a,b] and Timo Aalto, PhD[i]

**TABLE 5. Multivariate Linear Mixed Models for Longitudinal ODI- and VAS Scores in the 10-year Follow-up Period**

| | ODI | | | VAS | | |
|---|---|---|---|---|---|---|
| **Preoperative Variable** | **Estimate (SD)** | ***P*** | **95% CI** | **Estimate (SD)** | ***P*** | **95% CI** |
| Non-smoking | −8.9 (3.2) | 0.006 | −15.2 to −2.6 | −8.5 (3.7) | 0.026 | −15.9 to −1.0 |
| Body mass index, ≤30 kg/m$^2$ | 3.2 (2.3) | 0.176 | −1.5 to 7.9 | 2.6 (2.8) | 0.366 | −3.1 to 8.2 |
| No previous lumbar surgery | −8.7 (3.3) | 0.011 | −15.3 to −2.1 | −12.4 (4.0) | 0.003 | −20.3 to −4.5 |
| Better self-rated health | −10.9 (2.6) | 0.000 | −16.1 to −5.6 | −10.8 (3.2) | 0.001 | −17.2 to −4.4 |
| Regular use of painkillers for <3 mo* | −13.9 (3.1) | 0.000 | −20.0 to −7.7 | −11.8 (3.6) | 0.002 | −19.0 to −4.5 |
| Regular use of painkillers 3–12 mo* | −11.1 (3.1) | 0.001 | −17.3 to −4.8 | −13.1 (3.8) | 0.001 | −20.6 to −4.7 |

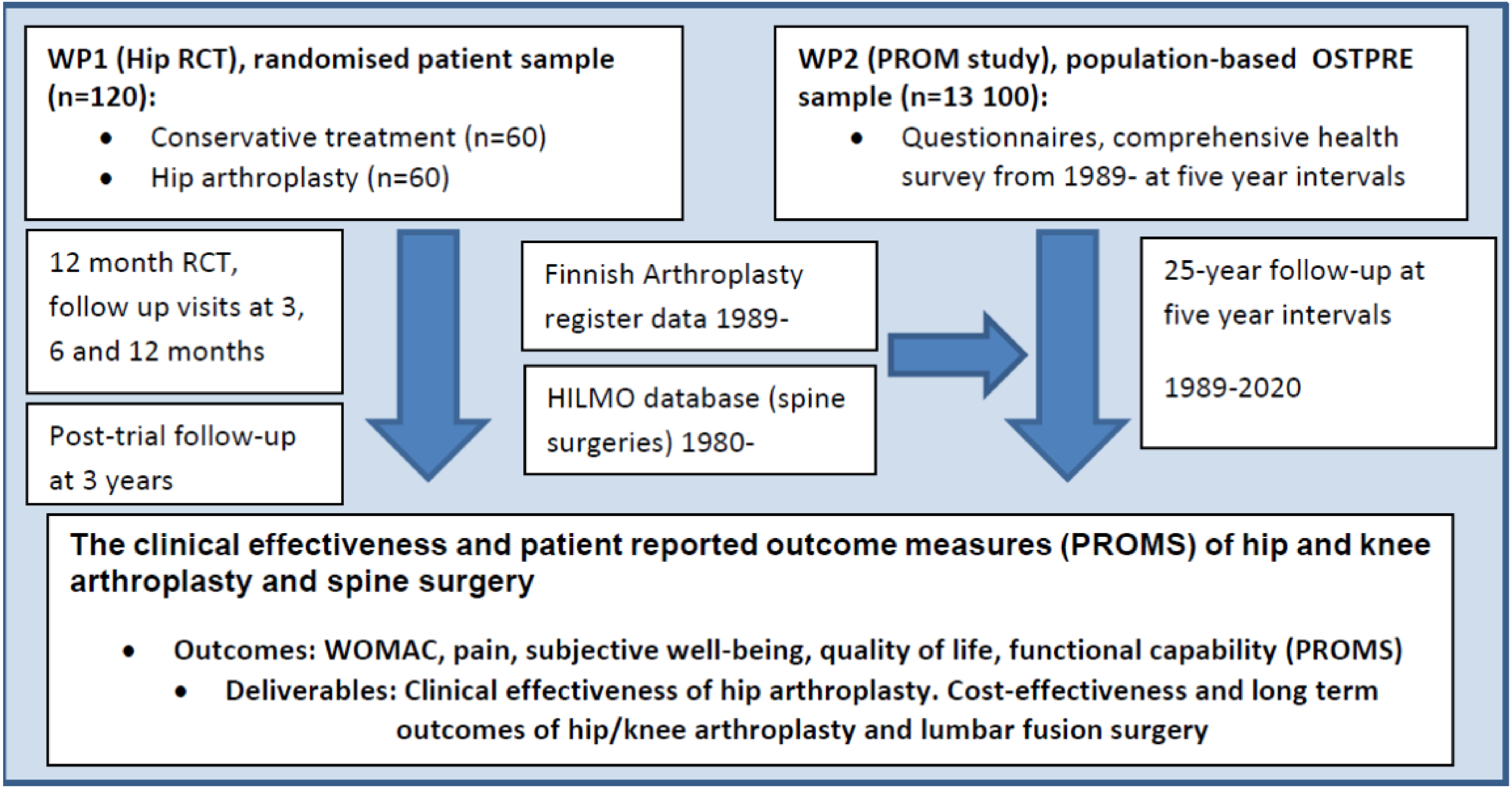
*95% CI, 95% confidence interval; ODI, Oswestry Disability Index; SD, standard deviation; VAS, Visual Analog Scale.*

**Regular use of painkillers for >12 months was set as a reference.*

Patients who smoked preoperatively or had previous lumbar surgery experienced more pain and disability at the 10-year follow-up.

N=102 → 72

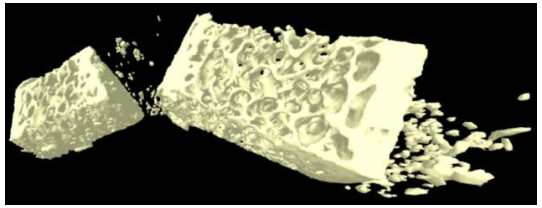
**Figure 1. Work packages and outline of the present study.**

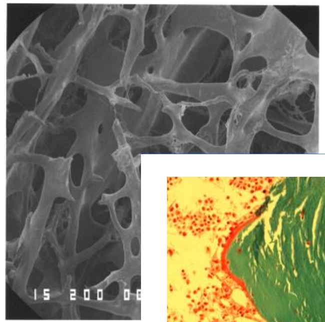


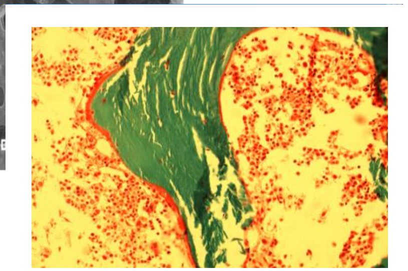
# Bone Quality -project

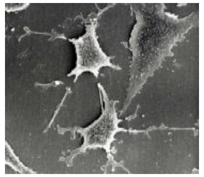
*Bone strength depends not only on bone mass but also:*

- Microarchitecture
- Mineralization
- Bone material properties
  - Collagen, mineral
- Bone turnover
- Microcracks

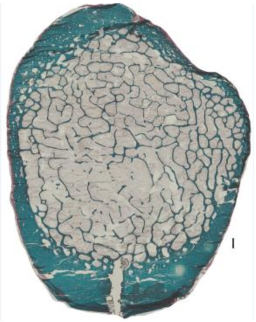


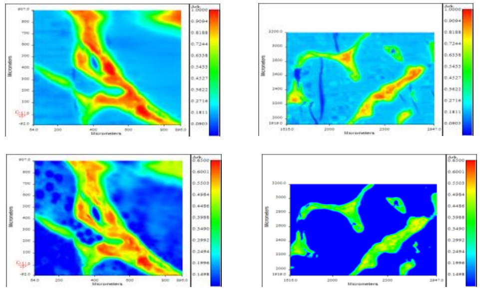






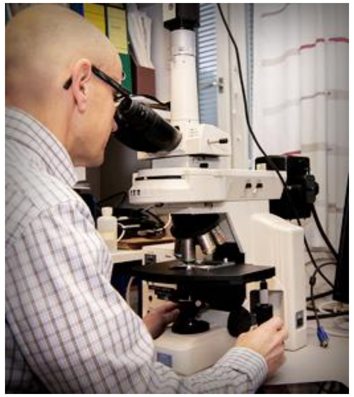
Human bone samples (hip, calcaneus, patella, tibia, iliac crest ) n = 100 (18-80+yr)

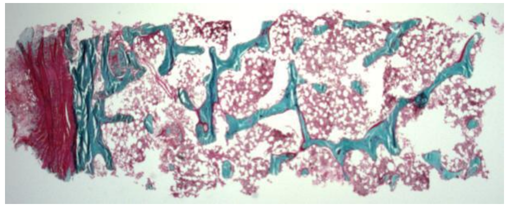


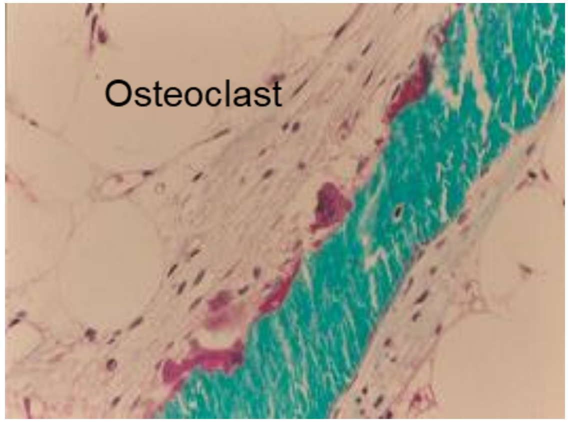


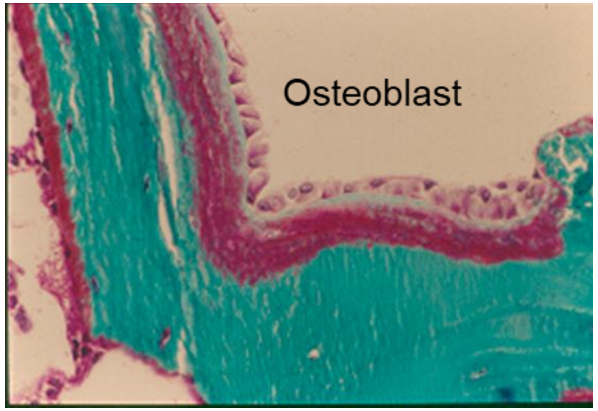
Bone material characteristics are assessed by histomorphometry, micro-ct, acoustic microscope, nanointendation and IR/Raman spectroscopy

# Iliac crest bone biopsy and quantitative bone histomorphometry

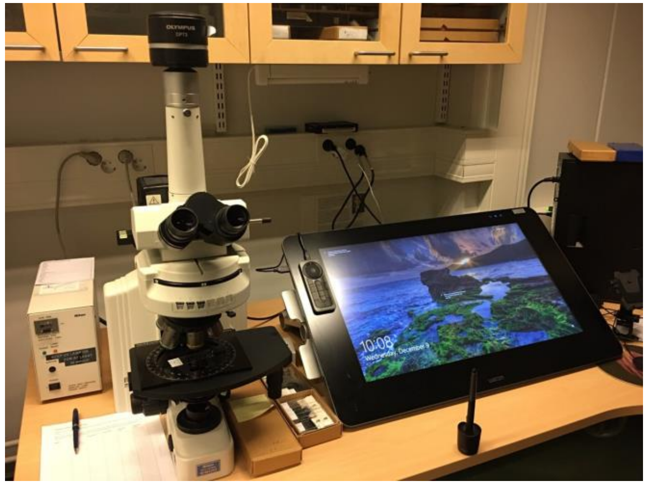


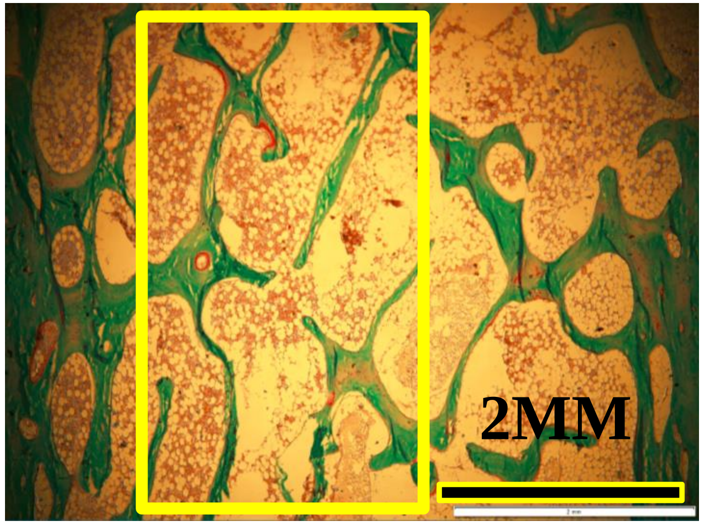


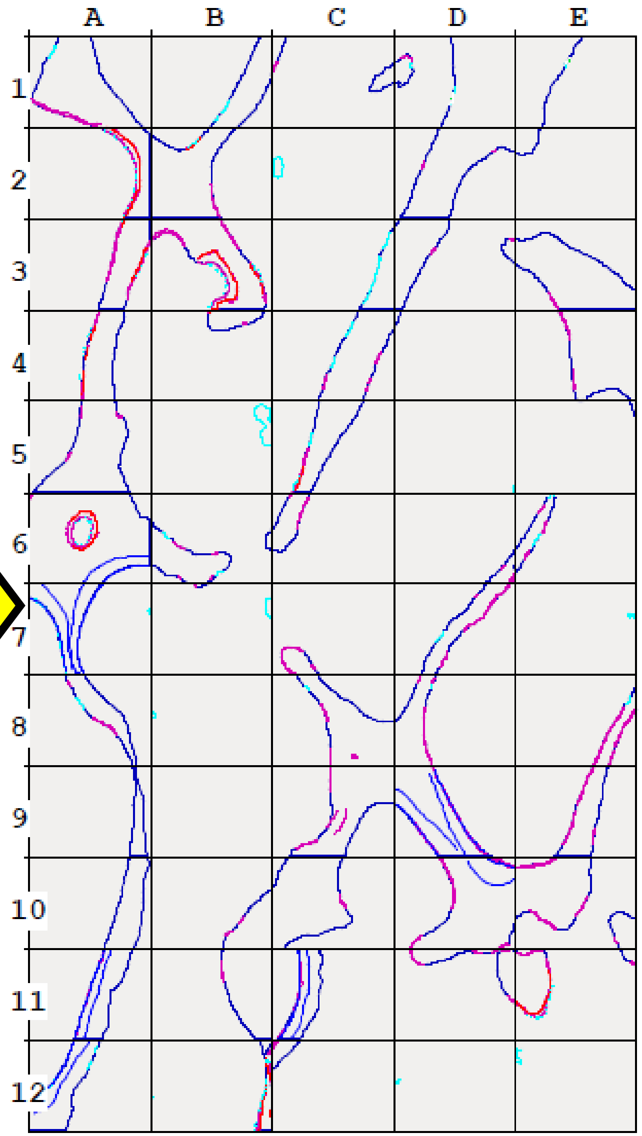


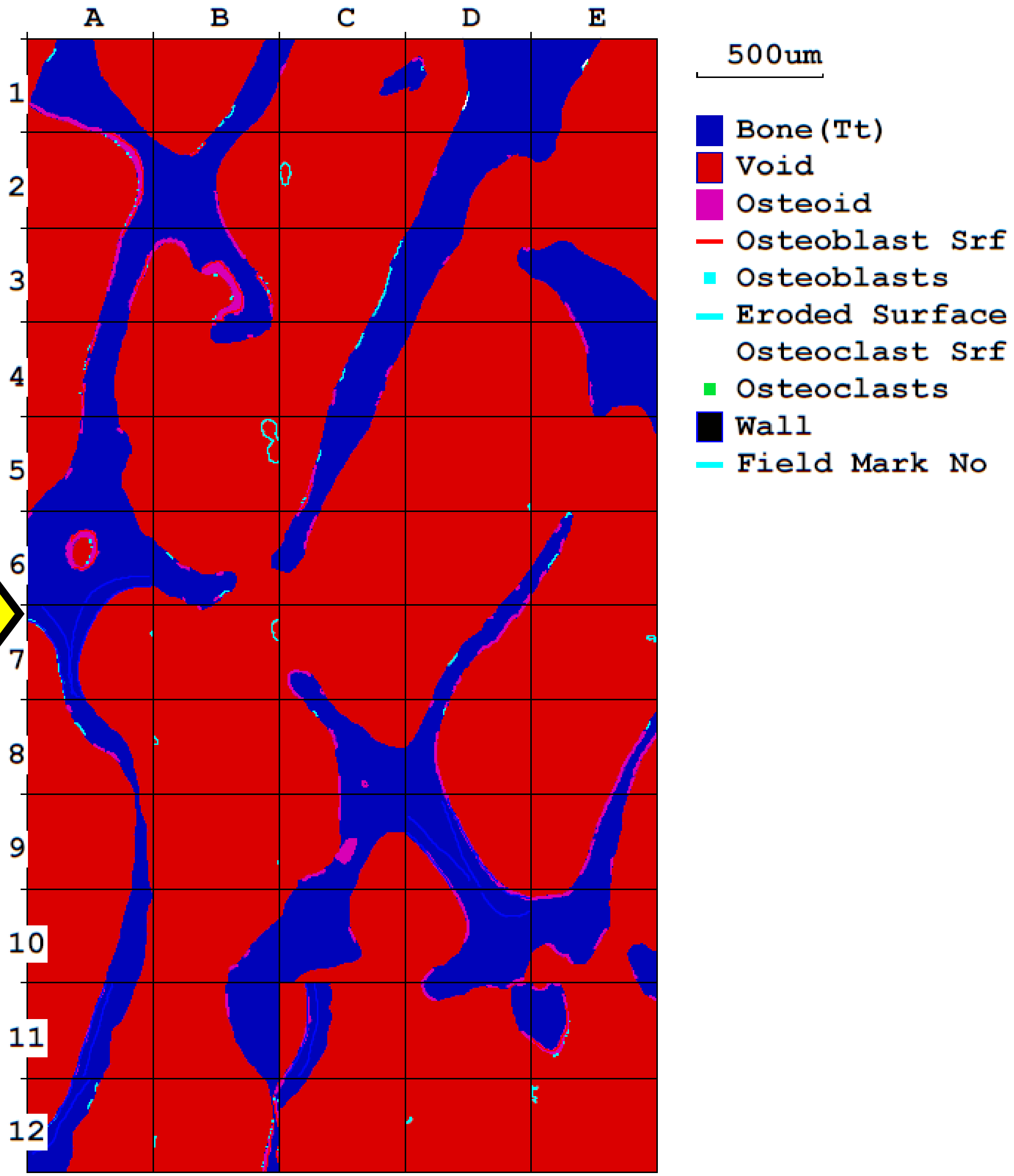




# OsteoMeasure Digital Video System



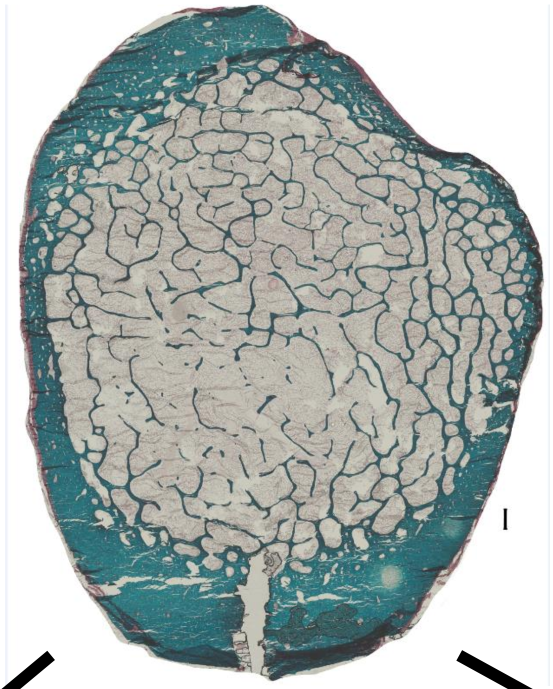


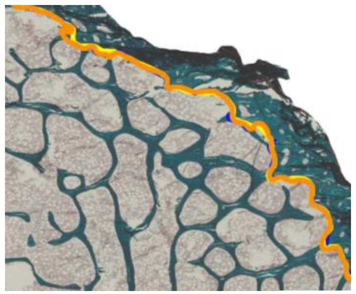



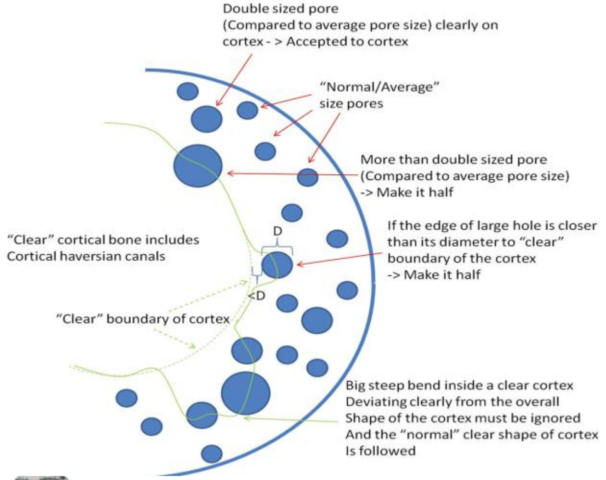



# Development of new criteria for cortical bone histomorphometry in femoral neck

*Tong et al. JBMM 2015, Calcified Tissue Int 2015*





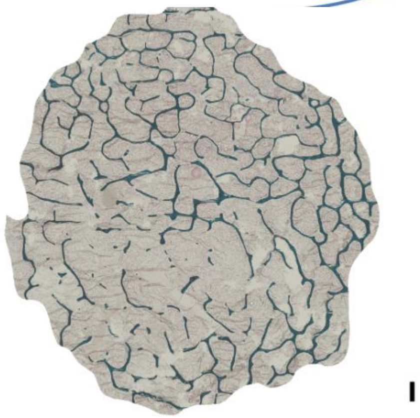



**ZONE 1**

**ABSOLUTE CORTEX AREA**

**ZONE 2**

**ENDOCORTICAL BONE AREA**



**ZONE 3**

**CANCELLOUS BONE AREA**

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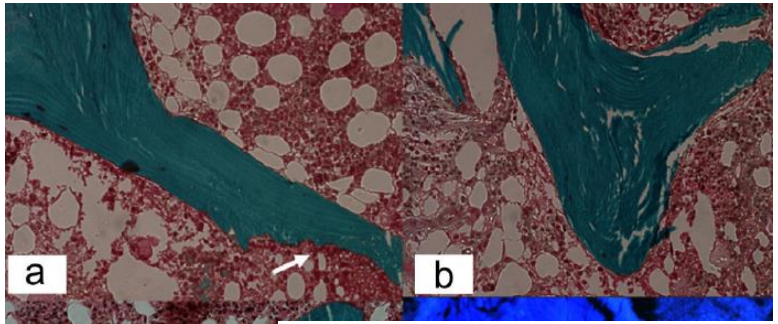


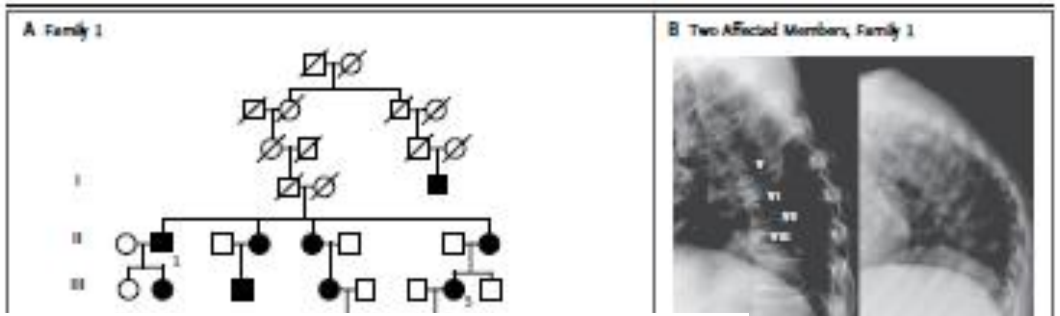




Figure S1. Histomorphometry of t

(a) Histomorphometry of a 36-year-
shows no osteoid seams. The bone r
A 44-year-old man (III-3) has no ren
sample from a 14-year-old boy (IV-2
Fluorescent microscopy of an unstai
tetracycline double labels (arrow) bu
defective bone mineralization. A mo
200 X magnification in all images.

The NEW ENGLAND JOURNAL of MEDICINE

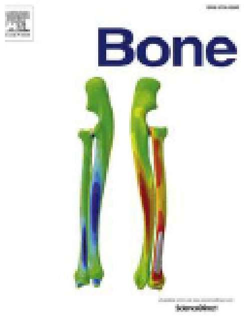
BRIEF REPORT

# *WNT1* Mutations in Early-Onset Osteoporosis and Osteogenesis Imperfecta

Christine M. Laine, M.D., Ph.D., Kyu Sang Joeng, Ph.D., Philippe M. Campeau, M.D., Riku Kiviranta, M.D., Ph.D., Kati Tarkkonen, Ph.D., Monica Grover, M.D., James T. Lu, B.S., Minna Pekkinen, Ph.D., Maija Wessman, Ph.D., Terhi J. Heino, Ph.D., Vappu Nieminen-Pihala, M.Sc., Mira Aronen, Tero Laine, M.D., Ph.D., Heikki Kröger, M.D., Ph.D., William G. Cole, M.D., Ph.D., Anna-Elina Lehesjoki, M.D., Ph.D., Lisette Nevarez, B.S., Deborah Krakow, M.D., Cynthia J.R. Curry, M.D., Daniel H. Cohn, Ph.D., Richard A. Gibbs, Ph.D., Brendan H. Lee, M.D., Ph.D., and Outi Mäkitie, M.D., Ph.D.

younger affected sibling at 20 months of age, in Panel E, reveal severe left cerebellar hypoplasia (arrows). Panel F shows the structure of WNT1 (introns not drawn to scale), along with the positions of the mutations and the sites of palmitoylation (Palm), glycosylation (Glycos), and phosphorylation (Phospho).

# Correlation between $^{18}$F-Sodium Fluoride positron emission tomography and bone histomorphometry in dialysis patients




Louise Aaltonen[a,*], Niina Koivuviita[a], Marko Seppänen[b], Xiaoyu Tong[c], Heikki Kröger[c,d], Eliisa Löyttyniemi[e], Kaj Metsärinne[a]

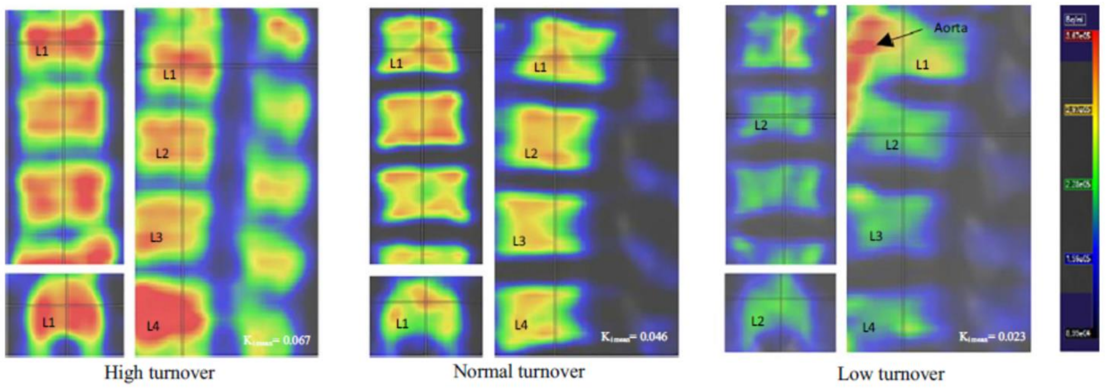
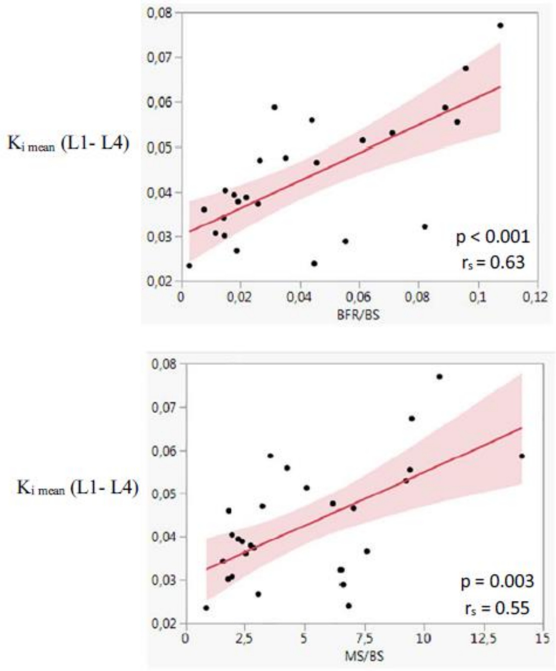
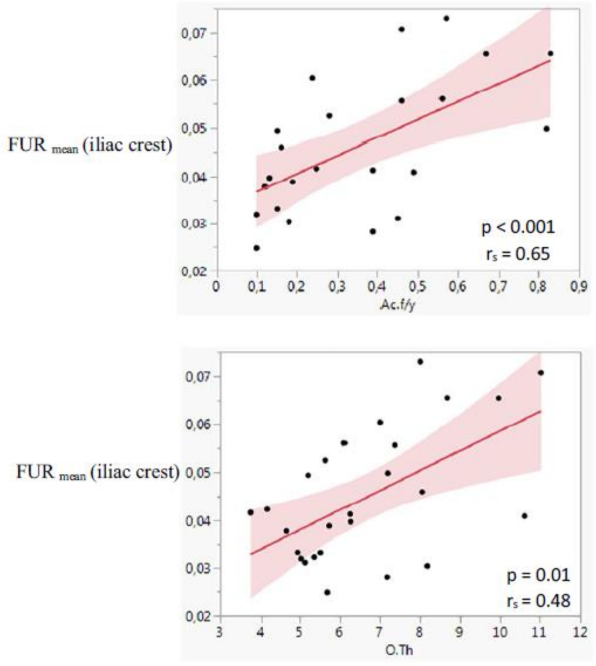



Fig. 4. Images of patients with high, normal and low turnover bone disease in the dynamic $^{18}$F-NaF PET scan of the lumbar spine.



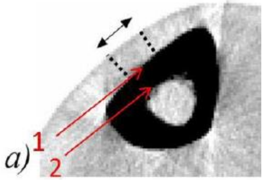



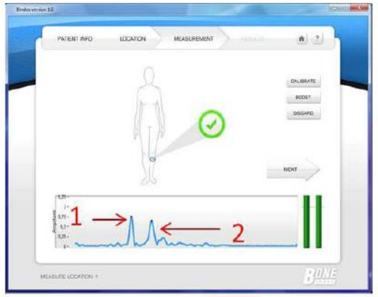

N=26

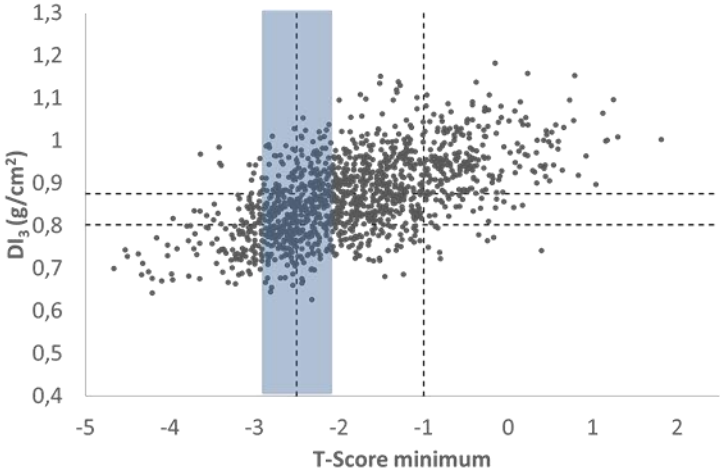
Bone 2020

# Bindex®

- Measures cortical bone thickness at the tibial and radius shaft and gives an estimate from proximal femur BMD (Density Index, DI)


Based on 9 study sites from Finland and USA including 1830 subjects, only 30 % of the cases needed referral to axial DXA in osteoporosis diagnostics (sensitivity and specificity 82-87 %)

*Karjalainen et al. Osteoporos Int 2012*
*Karjalainen et al. Osteoporosis Int 2016*
*Karjalainen et al. Osteoporosis Int 2018*

# Diagnosis of Knee Osteochondral Lesions With Ultrasound Imaging

Pekko Penttilä, M.D., Jukka Liukkonen, M.Sc., Antti Joukainen, M.D., Ph.D., Tuomas Virén, M.Sc., Ph.D., Jukka S. Jurvelin, Ph.D., Juha Töyräs, Ph.D., and Heikki Kröger, M.D., Ph.D.

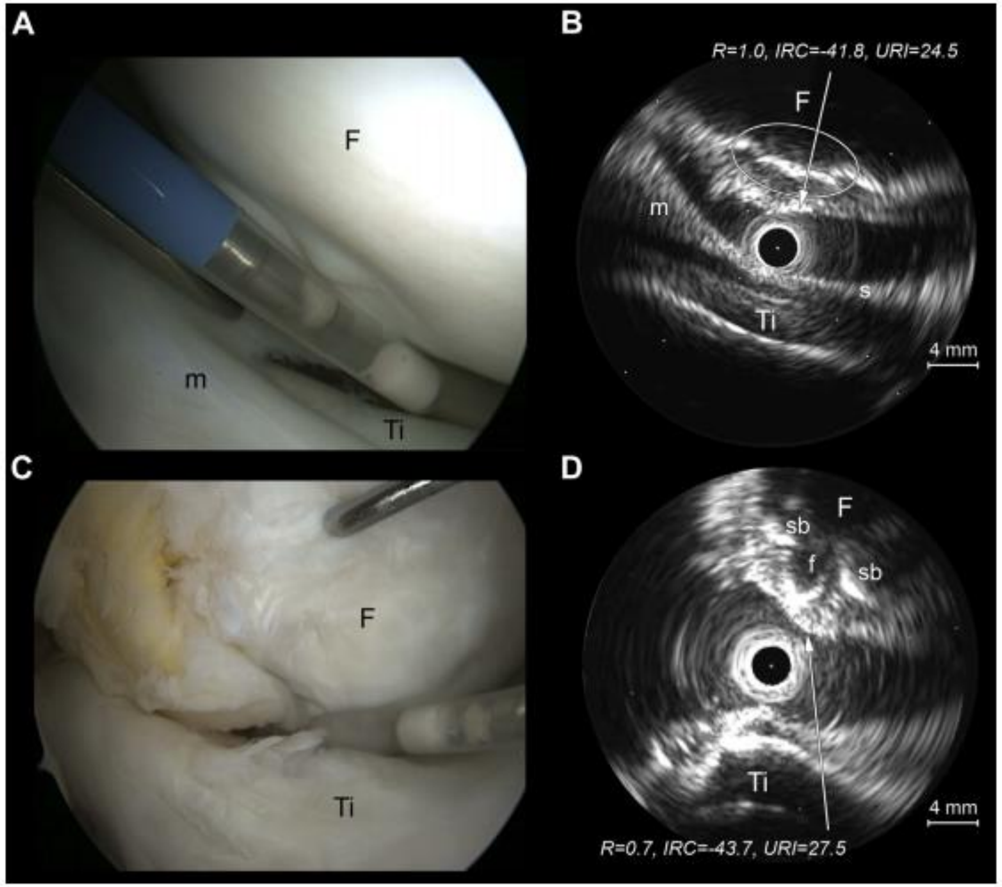



**Fig 1.** (A, B) The characteristic subchondral separation (oval) encountered in osteochondritis dissecans lesions can be visualized with ultrasound arthroscopy as gaps of otherwise intact subchondral bone signal. (C, D) Furthermore, if ultrasound arthroscopy shows fluid beneath the cartilage surface, an unstable osteochondritis dissecans can be suspected. (f, fluid; F, femur; IRC, integrated reflection coefficient [decibels]; m, meniscus; R, ultrasound reflection coefficient [percent]; s, arthroscope artifact; sb, subchondral bone; Ti, tibia; URI, ultrasound roughness index [micrometers]).

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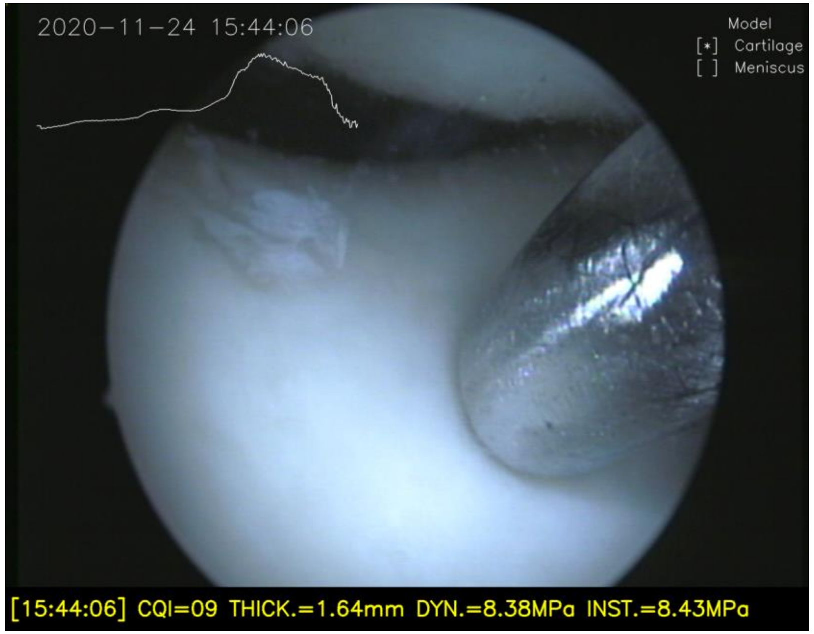
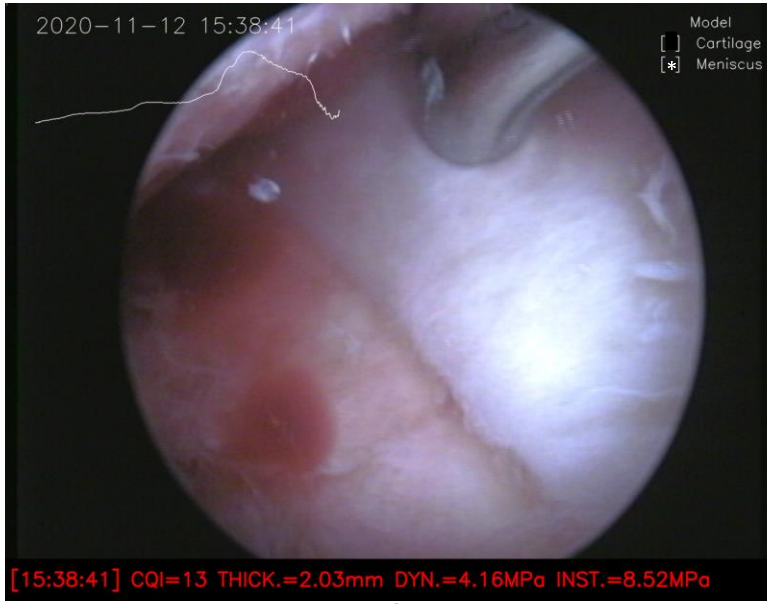
# *NIR arthroscopy*

## *Ex vivo* and *in vivo* measurements

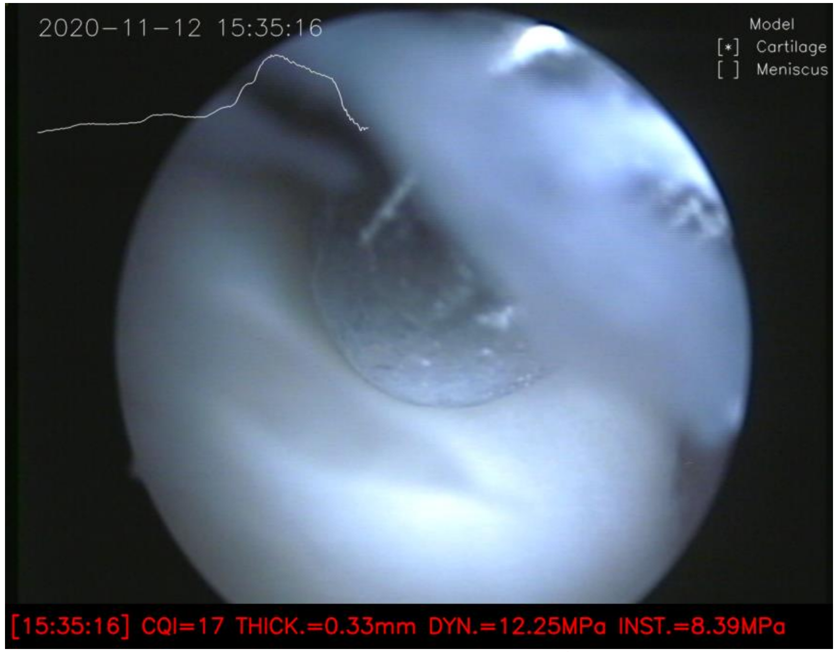



***Healthy cartilage***




***Diseased meniscus***

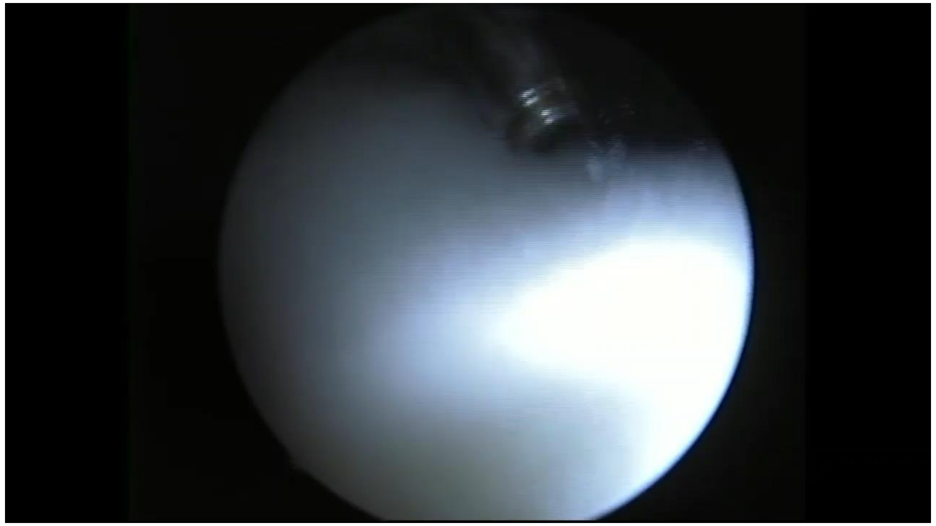
*Ex vivo*




***Diseased cartilage***

*In vivo*

Arthroscopy



# MIRACLE

Mid-infrared arthroscopy innovative imaging system for real-time clinical in depth examination and diagnosis of degenerative joint diseases

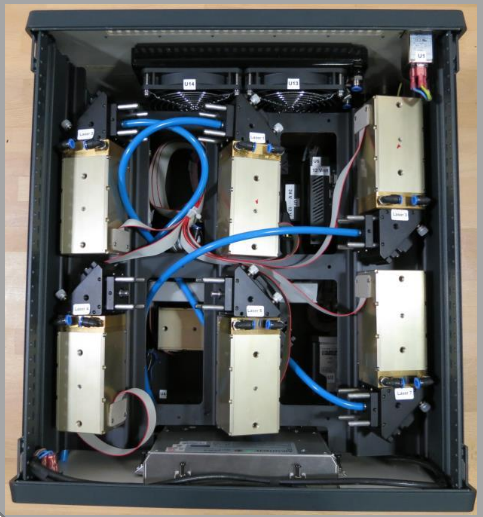
## *MIR arthroscopy*

### *Device*

MIRACLE will enable the *in vivo* accurate evaluation of the biochemical status and composition of articular cartilage

Prototype of the MIR-ATR based arthroscopic system


Quantum cascade lasers (QSLs)



MIR-ATR arthroscopy probe

Department of Orhopaedics, Traumatology and Hand Surgery

KMRU staff

https://sites.uef.fi/kmru/

# Kuopio Musculoskeletal Research Unit – KMRU

UNIVERSITY OF EASTERN FINLAND



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HOME

## Musculoskeletal Disorders Research Area

KMRU
Kuopio Musculoskeletal Research Unit

Musculoskeletal diseases are the leading causes of pain and disability, having an enormous impact on individuals, societies and economies. The number of patients with osteoporosis (OP) and osteoarthritis (OA) will increase sharply due to aging of the population. Urgent scientific development in diagnostics and treatment of these diseases is needed to manage successfully the future health challenge.