

1. Osteoarthritis

# OSTEOARTHRITIS

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2005

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2. William Heberden (1710 - 1801) on *Digitum Nodi*

## William Heberden (1710 - 1801) on *Digitum Nodi*

"What are these little hard knobs, about the size of a small pea, which are frequently seen upon the fingers, particularly a little below the top, near the joint? ...more unsightly than inconvenient."

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3. Symptoms and Signs of OA

## Symptoms & Signs of OA

- Pain
- Stiffness
- Mechanical
- Tenderness
- Crepitus
- Bony swelling
- Soft tissue swelling
- Deformity
- Malalignment

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4. OA Societal Impact

## OA Societal Impact

- *symptomatic* knee OA incidence 240/100K PY
- 2-10% of all adults
- Among the most frequent causes of impairment in lower limb tasks
- 68 million work loss days per year
- > 5% of the annual retirement rate
- most frequent reason for joint replacement = \$billions of dollars/yr

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### Normal Cartilage

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### Osteoarthritic Cartilage

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- Proteoglycan loss
- Collagen II degradation
- Edema

Hypercellularity  
Hyperplastic chondrocytes

- cytokines
- metallo-proteinases
- C-reactive protein

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7. OA Risk Factors

## OA Risk Factors

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8. Occupations and Osteoarthritis

## Occupations and Osteoarthritis

<b>Occupation</b>	<b>Joint(s) involved</b>
Cotton Workers	Fingers
Miners	Knees, spine
Jackhammer Operators	Elbows, wrists, MCP's
Farmers	Hips (?)
Shipyard and Dockyard Workers	Knees, fingers

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## History of Major Knee Injury and the Prevalence of Radiographic Knee OA-Framingham

	Adjusted OR of Knee OA (95% CI)	
	<u>Men</u>	<u>Women</u>
No history of knee injury	1 (ref)	1 (ref)
History of major knee injury	5.5 (2.8, 10.9)	3.4 (2.0, 6.0)

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## What Percentage of OA is Inherited?

	<u>Female English Twins</u>	<u>Framingham Subjects (Men &amp; Women)</u>	<u>Framingham Women</u>
Hand	48-59%	25-50%	42-56%
DIP		36-44%	
PIP		20-58%	
MCP		20-64%	
Thumb base		22-54%	
Knee	34-39%	21-31%*	

\*Discordant knees excluded

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**Estrogens and OA:  
Pertinent Clinical Observations**

- Cecil and Archer (1925) described menopausal arthritis -- development of painful knee OA 2 - 5 years after menopause
- Kellgren and Moore (1952) described generalized OA (hands, spine, knees) in perimenopausal women.
- Ehrlich (1972) described abrupt onset erosive inflammatory OA in women with mean age of onset 51 years

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Mechanical Factors

## Mechanical Factors

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## Knee Joint Alignment

# Knee Joint Alignment

Mechanical axis Adduction moment

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## Alignment and Joint Space Loss

### **Alignment & Joint Space Loss Over 18 Months\***

- 240 subjects with knee OA
- Varus associated with OR=3.6 ( $p<.001$ ) for medial progression
- Valgus associated with OR=3.8 ( $p<.001$ ) for lateral progression

\* Sharma et al, ACR,2000

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Mechanical factors

Mechanical factors predicting radiographic progression of knee OA over 4-years (N=74)

	<b>P Value</b>	<b>OR</b>	<b>95%CI</b>
Body mass index	0.2	1.2	0.91 - 1.61
Mechanical axis (°)	0.5	0.9	0.66 - 1.23
Joint space width (mm)	0.6	0.7	0.25 - 2.19
Adduction moment	0.0002	6.5	2.40 - 17.45

Miyazaki T. et al. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann Rheum Dis* 2002; 61: 617-22.

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Role of Bone

## Role of Bone

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## Knee OA Scintigraphy

# Knee OA Scintigraphy

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## Femoral Neck BMD

# Femoral neck BMD and risk of *progressive* radiographic knee OA

	Number of Knees	Progressive OA %	Multivariate Adjusted OR* (95% CI)
<b>Age-specific BMD</b>			
1 quartile (low)	32	34.4	1.0
2 quartile	41	22.0	0.3 (0.1- 0.9)
3 quartile	59	20.3	0.2 (0.1- 0.6)
4 quartile (high)	74	18.9	0.1 (0.03 - 0.3)

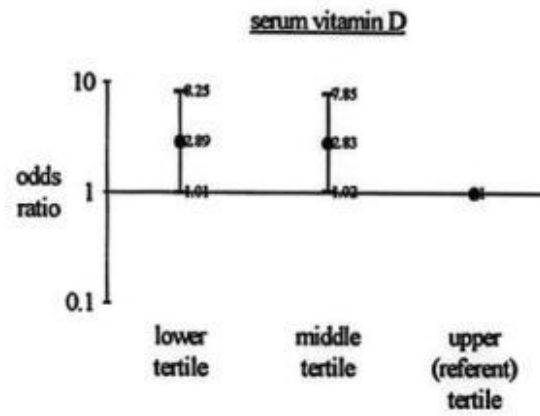
\* Adjusted for age, BMI, weight change, estrogen use, smoking status, physical activity level, knee injury history, and baseline Kellgren-Lawrence grade.

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**Progressive radiographic knee OA in Framingham elders and vitamin D status**



odds ratios adjusted for age, gender, BMI, weight change, PAI, knee injury, health status.

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Nutrition

# Nutrition

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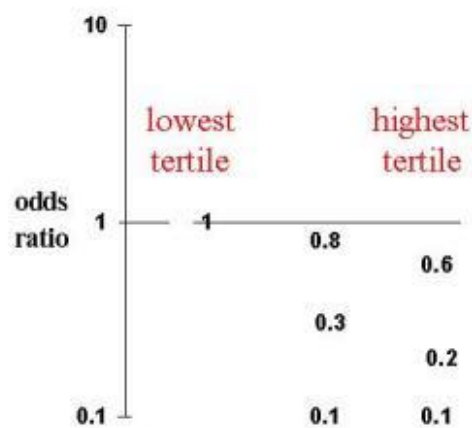
## Hypothesis: Role of Cumulative Oxidative Damage as a Cause of OA

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Vitamin C Intake

## Vitamin C intake & risk of progression of knee OA in the Framingham cohort



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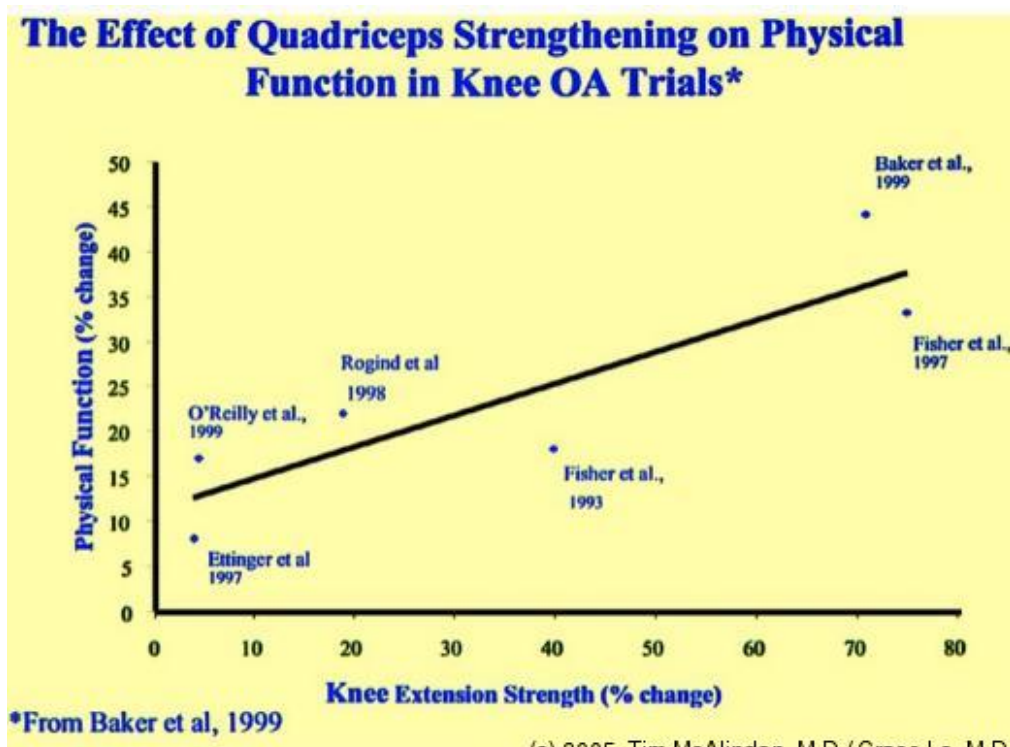
Treatment

## Treatment

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25.

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### Placebo Controlled Trials of Intra-articular Corticosteroids in OA

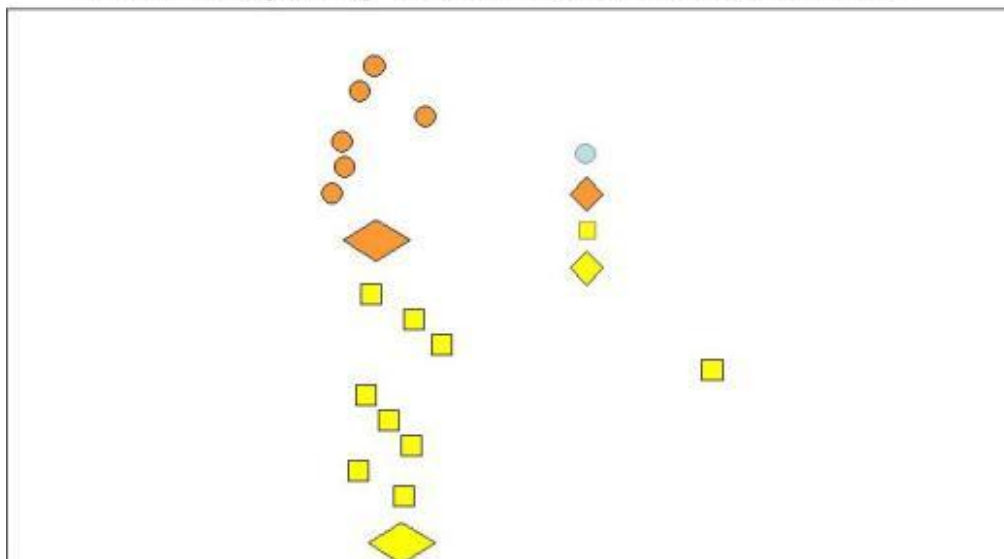
Author	Intervention	Number of subjects	Duration (weeks)	Efficacy
Cederlof 1966	Prednisolone 25 mg v placebo	44	8	Equal
Friedman 1980	TH 20 mg v placebo	34	8	TH > placebo at 1 week only
Dieppe 1980	TH 20 mg v placebo	12+16	6 + 2	TH > placebo at 2 weeks only
Gaffney 1995	TH 20 mg v placebo	84	6	TH > placebo at 1 week only
Jones 1996	MP 40 mg v placebo	59	8	MP > placebo at 3 weeks only

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### *Meta-analysis of Glucosamine & Chondroitin*



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### *Glucosamine: Disease modification studies*

Reginster et al, Lancet 2001

	Intent-to-treat analysis			p
	Placebo (n=106)	Glucosamine sulphate (n=106)	Difference (95% CI)	
Mean JSN (mm)	-0.31 (-0.48 to - 0.13)	-0.06 (-0.22 to 0.09)	0.24 (0.01 to 0.48)	0.043
Minimum JSN (mn)	-0.40 (-0.56 to - 0.24)	-0.07 (-0.22 to 0.07)	0.33 (0.12 to 0.54)	0.003
WOMAC change	9.8% (-6.2 to 25.8%)	-11.7% (20.3 to -3.2%)	21.6% (3.5 to 39.6%)	0.020

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Treatment of OA – ACR Guidelines

## Treatment of OA – ACR Guidelines

- Exercise
- Non-pharmacologic approaches (education, orthotics)
- Acetaminophen (safe and inexpensive)
- Non-steroidal anti-inflammatory agents (can cause side effects, especially in older persons)
- Joint aspiration & injection of corticosteroids (particularly for inflammation)

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29. Treatment of OA – ACR Guidelines

## Treatment of OA – ACR Guidelines

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- Arthroplasty, other surgery
- Other therapeutic approaches widely used *that require further evaluation*, include visco-supplementation, glucosamine/chondroitin, diacerhein
- Alternative therapies like acupuncture, transcutaneous nerve stimulation, and pulsed electromagnetic field therapy “are possible treatments”.

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30. OA as Organ Failure: Future Treatments

## OA as Organ Failure: Future Treatments

- **Cartilage**
  - Metalloproteinase inhibitors
  - Growth factors
  - bioengineering
- **Bone**
  - Vitamin D
  - Antiresorptive agents
- **Mechanical**
  - Orthotics
  - Braces
- **Inflammation**
  - Cytokine inhibitors

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