

# **Aspirin and bone health: Is there any connection?**

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# Use of Aspirin

- Analgesic & antipyretic
- Primary prevention: atherosclerotic cardiovascular disease (ASCVD)
- Acute Coronary Syndrome
- Ischemic Stroke & Transient Ischemic Attack
- Anti-Inflammatory
- Colorectal Cancer Prophylaxis (Off-label)



Cyclooxygenase (COX) inhibitor

# Aspirin and bone health: does it help?

- The use of low-dose aspirin in older adults is increasing as is the prevalence of osteoporosis
- Aspirin has been shown in numerous studies to affect bone metabolism
- However, there is no clear link between low-dose aspirin use and bone mineral density (BMD)

# Aspirin and bone health: does it help?

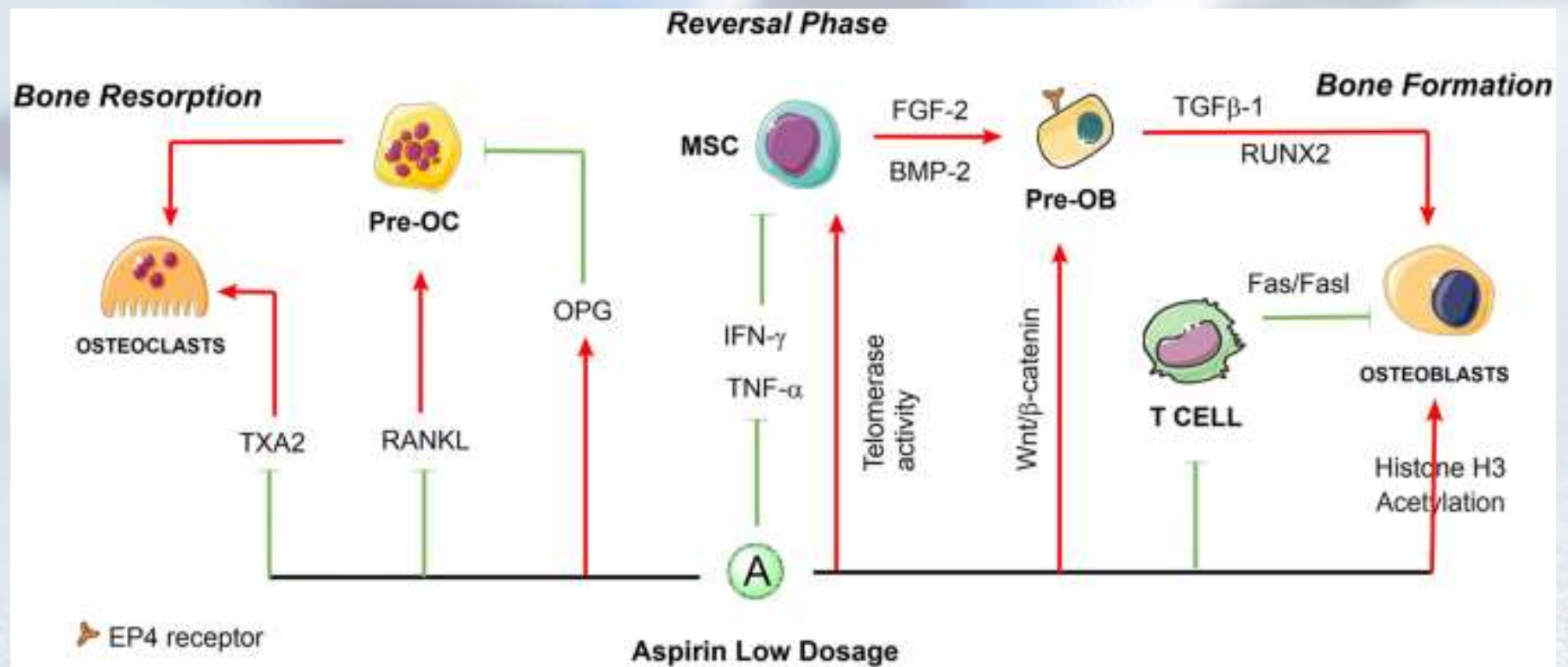
- Growing interest particularly in prevention of age-related conditions like
  - Osteoporosis-low bone mineral density (BMD)
  - Structural deterioration of bone leading to increased risk of fractures

# Role of Aspirin in bone remodeling

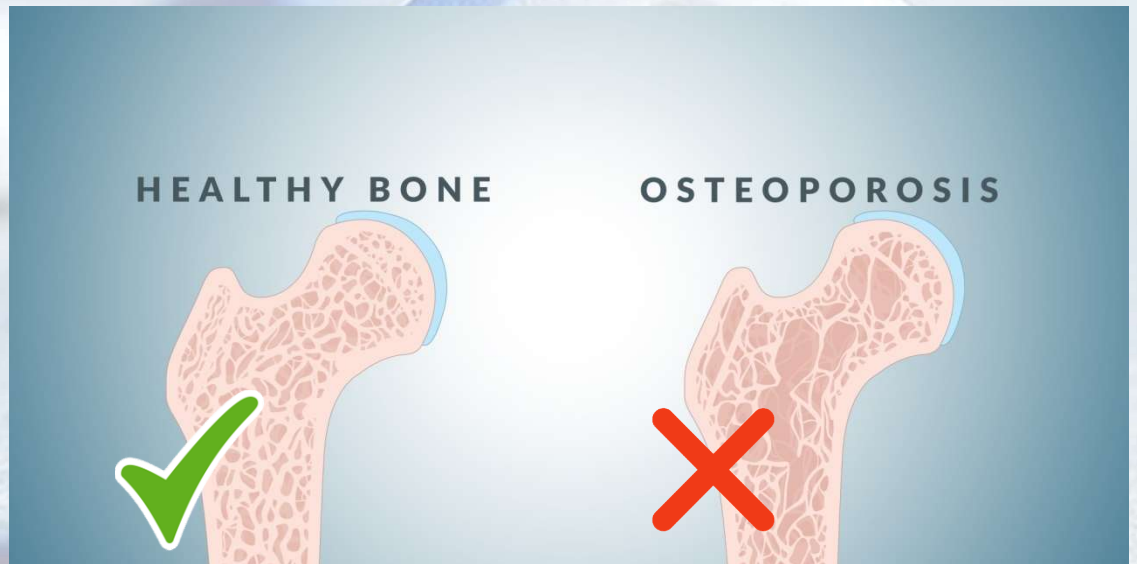
- Promotes the survival of osteoblast precursor stem cells and differentiation of preosteoblast
- Suppress the differentiation of osteoclast by
  - Inhibition of the nuclear factor kappa-B (NF $\kappa$ B) pathway
  - Reduction of the expression of receptor activator of NF $\kappa$ B ligand (RANKL)
  - Increasing osteoprotegerin (OPG)



# Role of Aspirin in bone remodeling



**Thus, aspirin may increase bone mineral density and reduce the risk of fractures**



# A systematic review of 12 observational studies in 2020 showed aspirin use reduced fracture risk by 17%

Open access

Original research

## BMJ Open Aspirin and fracture risk: a systematic review and exploratory meta-analysis of observational studies

A L Barker,<sup>1,2</sup> Sze-Ee Soh,<sup>1,3</sup> Kerrie M Sanders,<sup>4,5</sup> Julie Pasco,<sup>6</sup> Sundeep Khosla,<sup>7</sup> Peter R Ebeling,<sup>8</sup> Stephanie A Ward,<sup>1</sup> Geeske Peeters,<sup>9</sup> Jason Talevski,<sup>4,5</sup> Robert G Cumming,<sup>10</sup> Ego Seeman,<sup>11,12</sup> John J McNeil<sup>1</sup>

**To cite:** Barker AL, Soh S-E, Sanders KM, *et al.* Aspirin and fracture risk: a systematic review and exploratory meta-analysis of observational studies. *BMJ Open* 2020;**10**:e026876. doi:10.1136/

### ABSTRACT

**Objectives** This review provides insights into the potential for aspirin to preserve bone mineral density (BMD) and reduce fracture risk, building knowledge of the risk-benefit profile of aspirin.

**Methods** We conducted a systematic review and

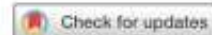
### Strengths and limitations of this study

- ▶ This systematic review extends prior observational studies by providing new evidence that suggests aspirin may be associated with reduced fracture risk and potentially higher bone mineral density



# A cross-sectional study published in September 2022

## scientific reports

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### Low dose aspirin associated with greater bone mineral density in older adults

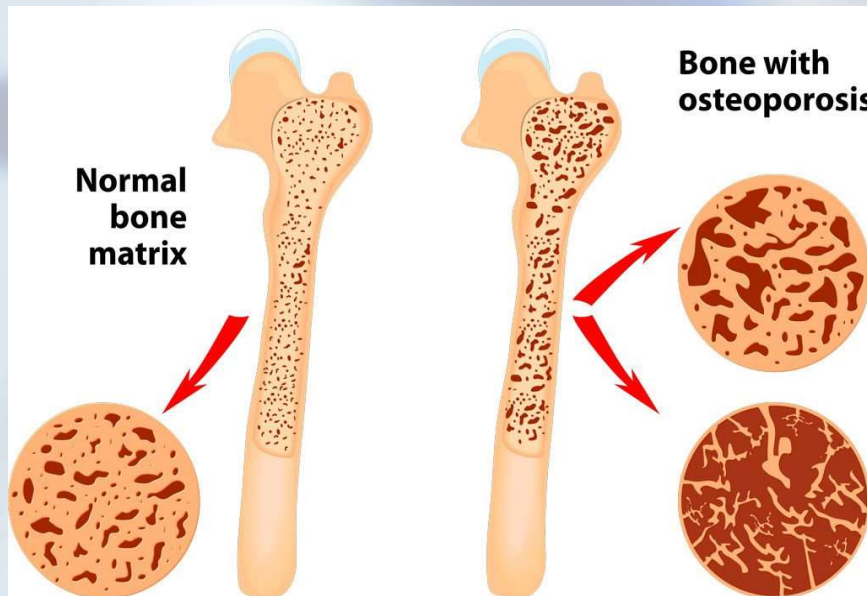
Hongzhan Liu<sup>1</sup>, Xungang Xiao<sup>2</sup>, Qiaojing Shi<sup>3</sup>, Xianzhe Tang<sup>2</sup> & Yun Tian<sup>2</sup>

The use of low-dose aspirin in older adults is increasing as is the prevalence of osteoporosis. Aspirin has been shown in numerous studies to affect bone metabolism. However, there is no clear link between low-dose aspirin use and bone mineral density (BMD). This study examined differences in bone mineral density between low-dose aspirin users and non-aspirin users in adults aged 50–80 years. We conducted a cross-sectional study of 15,560 participants who participated in the National Health and Nutrition Examination Survey (NHANES) 2017–March 2020. We used a multivariate logistic regression model to evaluate the relationship between low-dose aspirin and femoral neck BMD, femoral total BMD, intertrochanteric BMD, and the first lumbar vertebra BMD (L1 BMD) in patients aged 50 to 80 years. A total of 1208 (Group 1: femoral neck BMD, total femur BMD, and intertrochanter BMD) and 1228 (Group 2: L1 BMD) adults were included in this study. In both group 1 and group 2, BMD was higher in the low-dose aspirin group than in the non-aspirin group. (Total femur

## Low dose aspirin and bone mineral density in older adults


- Examined differences in bone mineral density between low-dose aspirin users and non-aspirin users in adults aged 50–80 years
- Regular low-dose aspirin may be associated with a higher BMD in older adults

# Aspirin and bone health: does it help?



# The first randomized double blind, placebo controlled trial (The ASPREE-FRACTURE sub study) published in November, 2022

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## Original Investigation

November 7, 2022

# Daily Low-Dose Aspirin and Risk of Serious Falls and Fractures in Healthy Older People

## A Substudy of the ASPREE Randomized Clinical Trial

Anna L. Barker, PhD<sup>1,2</sup>; Renata Morello, PhD<sup>1</sup>; Le Thi Phuong Thao, PhD<sup>1</sup>; [et al](#)

[» Author Affiliations](#)

*JAMA Intern Med.* 2022;182(12):1289-1297. doi:10.1001/jamainternmed.2022.5028



## **Daily Low-Dose Aspirin and Risk of Serious Falls and Fractures in Healthy Older People**

- Nearly 17,000 older adults were randomly assigned to take a low-dose aspirin (100 mg) or an identical placebo daily
- They were then monitored for fractures or serious falls over a period of almost five years



## Daily Low-Dose Aspirin and Risk of Serious Falls and Fractures in Healthy Older People

- There was no difference in the risk of fracture between the aspirin and placebo groups
- Aspirin users had a significantly higher rate of serious falls, may be due to aspirin's blood thinning effect
- The study finally concluded that low-dose aspirin failed to reduce the risk of fractures while increasing the risk of serious falls

# NHANES cross sectional study of aspirin and fractures in the elderly published in February, 2023

**scientific** reports

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## OPEN NHANES cross sectional study of aspirin and fractures in the elderly

Sarya Swed<sup>1</sup>, Amro A. El-Sakka<sup>2</sup>, Yasmeeen Abouainain<sup>3</sup>, Ka Yiu Lee<sup>4</sup>, Bisher Sawaf<sup>5</sup>, Mhd Kutaiba Albuni<sup>5</sup>, Elias Battikh<sup>5</sup>, Eman Mohammed sharif Ahmad<sup>6</sup>, Nashaat Kamal Hamdy Elkalagi<sup>7</sup>, Kirellos Said Abbas<sup>8</sup>, Wael Hafez<sup>9,10,12</sup> & Amine Rakab<sup>11,12</sup>

Bone fractures are a global public health concern, yet no thorough investigation of low-dose aspirin usage to prevent fractures in the elderly has been conducted. Many interventional human and animal studies have tried to detect the correct role of low-dose aspirin on fractures in elderly persons. The literature doesn't consist of a retrospective observational study that includes a large number of older individuals and evaluates the accurate effect of aspirin on the fractures post falling from low heights. This cross-sectional includes 7132 elderly persons and aimed to detect if there was a link between taking low-dose aspirin to prevent fractures in the elderly. Data was extracted from the National Health and Nutrition Examination Survey (NHANES) database for 2017–2020 and 2013–2014. Demographic and examination data were collected during in-home interviews and study visits to a

# Aspirin and fractures in the elderly: from National Health and Nutrition Examination Survey (NHANES) data

Taking low-dose aspirin to prevent fractures in the elderly is statistically insignificant



## Take home messages

- Initial observational studies found aspirin beneficial in reducing fracture risk
- But it failed to show the same effect on randomized controlled trial (RCT) later on while increasing the risk of serious falls
- Impressive results from observational studies may be unreliable, and may not hold up in the wake of more powerful studies



**THANK YOU**

