

Medications for Corticosteroid Associated Osteoporosis: Guidelines and Evidence

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disclosures

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drug information question

When prescribed to people taking prednisone, do bisphosphonates "work better" than when prescribed for postmenopausal osteoporosis?

therapeutics letter
September - October 2017

83

33 trials
25,735
postmenopausal women

<https://www.ti.ubc.ca/therapeutics-letter/>

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CMAJ

2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

Alexandra Papaioannou MD MSc, Suzanne Morin MD MSc, Anaela M. Cheung MD PhD, Steph Anth Kerr Oste

age > 50

≥ 7.5 mg prednisone or equivalent per day ≥ 3 months cumulative in preceding year

should initiate a bisphosphonate continue for at least the duration of glucocorticoid therapy

PAPAIOANNOU CMAJ 2010;182:1864-73

Cochrane 2016 Systematic Review

27 randomized controlled trials
3075 participants

men, pre + post menopausal women

various indications for corticosteroid
rheumatologic, respiratory,
dermatologic, nephrologic,
gastrointestinal, hematologic, neurologic

variable corticosteroid exposures
dose & duration

few trials > 12 months

ALLEN Cochrane Database Syst Rev 2016, Issue 10. Art. No.: CD001347

Cochrane 2016 Systematic Review

27 randomized controlled trials
3075 participants

trials were more likely to report bone mineral density (BMD) than clinically relevant fracture as an efficacy outcome

↓

"correlation between BMD and fracture has not been established in corticosteroid-induced osteoporosis"

ALLEN Cochrane Database Syst Rev 2016, Issue 10. Art. No.: CD001347

US FDA Drug Approval

postmenopausal osteoporosis

- fracture is the only clinically meaningful outcome
- there is no valid surrogate (eg, BMD) that has been adequately shown to predict fractures

glucocorticoid osteoporosis

- expansion of the indication of a drug for this indication involves demonstrating BMD changes similar to those in postmenopausal osteoporosis

https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208743Orig1s000MedR.pdf; SAAG Lancet Diabetes Endocrinol 2018;6:445-454

Cochrane 2016
bisphosphonates for corticosteroid osteoporosis

hip fracture
unable to examine separately
non vertebral fracture

RR 0.79 (95%CI 0.47, 1.33)
55 per 1000 → 42 per 1000

ALLEN Cochrane Database Syst Rev 2016, Issue 10. Art. No.: CD001347

Cochrane 2016
bisphosphonates for corticosteroid osteoporosis

vertebral compression
RR 0.57 (95%CI 0.35, 0.91)
77 per 1000 → 44 per 1000

absolute risk reduction 3.3%

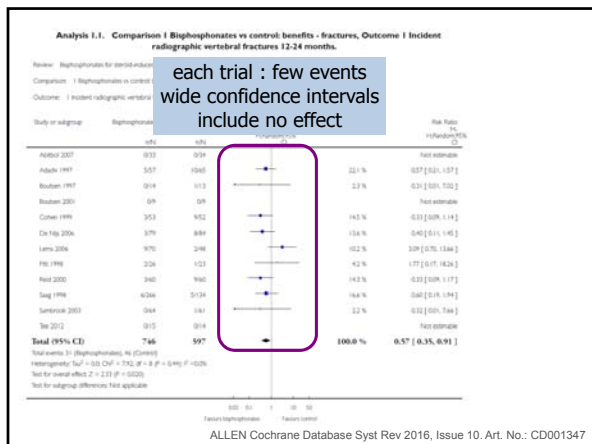
NNT 31 (95%CI 20 to 145)
(12-24 months)

ALLEN Cochrane Database Syst Rev 2016, Issue 10. Art. No.: CD001347

what counts as a vertebral fracture in osteoporosis trials?

- radiograph at baseline and then serially (eg, annually)
- participants are assessed for new vertebral compressions whether or not there are symptoms suggestive of vertebral fracture
- few data on symptomatic fractures
- no consensus definition
- trials vary in their definition
 - ≥ 20% ↓ vertebral height
 - ≥ 15% ↓ vertebral height
- US FDA = surrogate outcome¹

https://www.fda.gov/downloads/drugs/newsevents/ucm470577.pdf; JARVINEN BMJ 2015;350:h2088



drug information question

When prescribed to people taking prednisone, do bisphosphonates “work better” than when prescribed for postmenopausal osteoporosis?

There has been such little credible attention to clinically relevant outcomes that we cannot with confidence conclude that a bisphosphonate will add substantially to how a person ‘feels, functions or survives’