Prophylactic treatment for osteoporosis:
Student EBM Presentation

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Example patient

JS is a 67 year old lady who needs to start taking long-term corticosteroid treatment for chronic asthma - she asked her GP what the side effects of this might be.

Osteoporosis, and subsequent compression fracture, is a common and dangerous complication of corticosteroid therapy, partly due to decreased intestinal calcium absorption (and increasing urinary calcium loss). **Calcitriol (vitamin D)** acts to restore this absorption. **Calcitonin** may also help by inhibiting bone resorption - it has been shown to be useful in established corticosteroid osteoporosis, but has yet to be shown to be useful prophylactically. Since this problem is worst in the first 6-12 months of treatment, **a prophylactic approach could be very valuable.**

Do prophylactic vitamin D supplements prevent steroid-induced osteoporosis?

P - Patients receiving corticosteroids for any medical condition

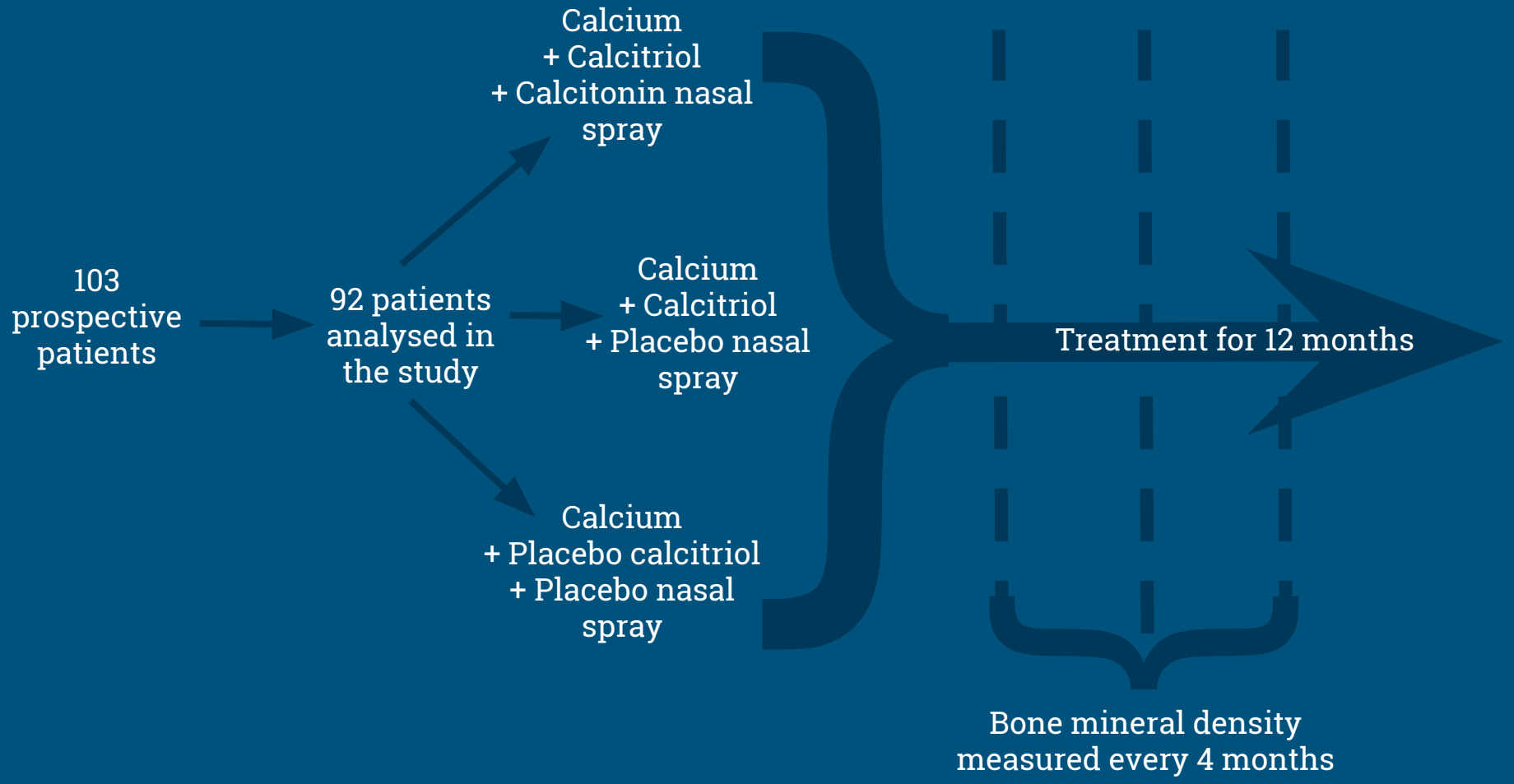
I - Calcitriol (vitamin D) supplement

C - Standard therapy (calcium supplements or equivalent) and placebos

O - Bone mineral density (as measured by dual-photon absorptiometry)

The search & search results

- PubMed database
- ((((((osteoporosis AND steroid induced) AND vitamin D) AND calcium supplement*) AND bone mineral density) AND lumbar spine OR femoral head) AND Clinical Trial[ptyp])
- 7 results retrieved
- Study selected for appraisal:
  - Sambrook, P., et al. “Prevention of corticosteroid bone loss.” *Osteoporosis International* 3.1 (1993): 141-143


103 prospective patients
92 patients analysed in the study
Calcium + Calcitriol + Calcitonin nasal spray
Calcium + Calcitriol + Placebo nasal spray
Calcium + Placebo calcitriol + Placebo nasal spray
Treatment for 12 months
Bone mineral density measured every 4 months

The study appraisal

- CONSORT 2010 Checklist - Key Points:
  - **Randomised, double-blinded, placebo-controlled study**
  - 103 patients on steroids, mean age 51, mean prednisone dose 13.5 mg/day
  - Only 92 included in analysis - **reasons for exclusion not given**
  - Assigned to groups based on age, gender, underlying disease, and initial corticosteroid dose, using an **adaptive assignment technique**
  - Age and prednisolone dose taken as covariates during analysis .: controlled for
  - No indication of how **double-blinding and randomisation** were achieved (e.g. computer-generated)
  - **Specific numbers** of patients in each group not specified
  - 'The **baseline data** for the patients were not different between groups' - no significant differences between groups for initial or cumulative dose
  - Nature and incidence of **side effects** well reported
  - **t-values not provided** in results, nor significance level
  - Data presented as absolute percentage change - **no ARR/RRR**
  - **Trial funding?** - no conflicts of interest declared
  - Didn't follow up by looking at **incidence of new fractures**

The Results

- **Calcium supplementation alone didn't prevent bone loss** at either site, but there was **no non-treatment group** to use as a comparison to set a baseline. Previous studies suggest this may have had an initial protective effect.
- **Calcitriol supplementation decreased bone loss in lumbar spine** (1.1 and 0.5%/yr in treatment groups cf. 5.5%/yr in control group) **but not at the femoral neck** (2.0 and 2.4%/yr in treatment groups and 3.7%/yr in control group, but not statistically significant). This may be linked to corticosteroids causing **differential bone loss** at different sites - it particularly targets trabecular bone such as lumbar spine.
- **Calcitonin co-supplementation had no effect on the efficacy of calcitriol supplementation**. The authors suggested this was due to **low bioavailability** as it was given nasally rather than intramuscularly. The effects of calcitonin without calcitriol was not investigated.
- The most frequent **adverse effects** included nasal irritation (36%), hypercalcaemia (17%), and gastrointestinal symptoms (16%). "Nasal irritation and GI symptoms weren't more common in the calcitonin treatment group", which suggests that hypercalcaemia may have been.

Related Cochrane review

“Calcium and vitamin D for corticosteroid-induced osteoporosis” (Homik, J. et al. 1997)

- Calcitriol + calcium, vs calcium alone or placebo, in the treatment of corticosteroid-induced osteoporosis
- 5 trials included (274 patients) and weighted according to quality.
- **Lumbar spine & radial bone mineral density significantly higher** in treatment vs controls, i.e. protective effect
- As with Sambrook et al. (1993), there was an observed but **non-significant decrease in bone loss at the femoral neck**
- Treatment had a large magnitude of effect in decreasing **fracture incidence**, but didn’t reach statistical significance.

Implications

- **Vitamin D (calcitriol) appears to have protective effect against trabecular bone loss in corticosteroid-induced osteoporosis**
- The efficacy is **modest**, but the drug combination is **relatively innocuous**, although blood calcium levels should be monitored for hypercalcaemia
- Other relevant **side effects** include GI effects such as constipation
- The effects on actual fracture incidence are not well-established due to **lack of follow-up** in relevant studies
- **Recommendation**: discuss preferences with patient, weighing up fracture risk vs over-medication and frequent monitoring required