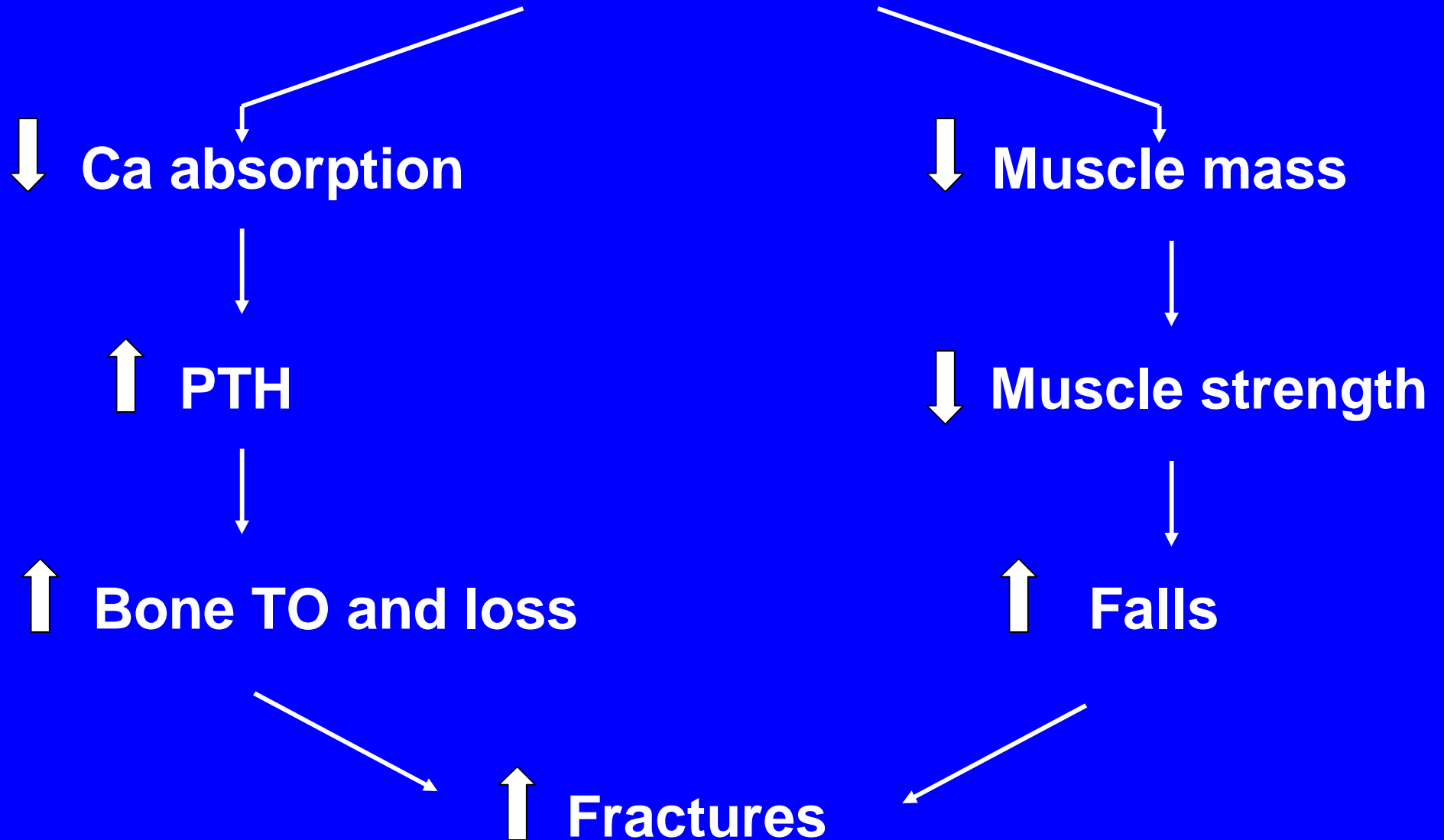
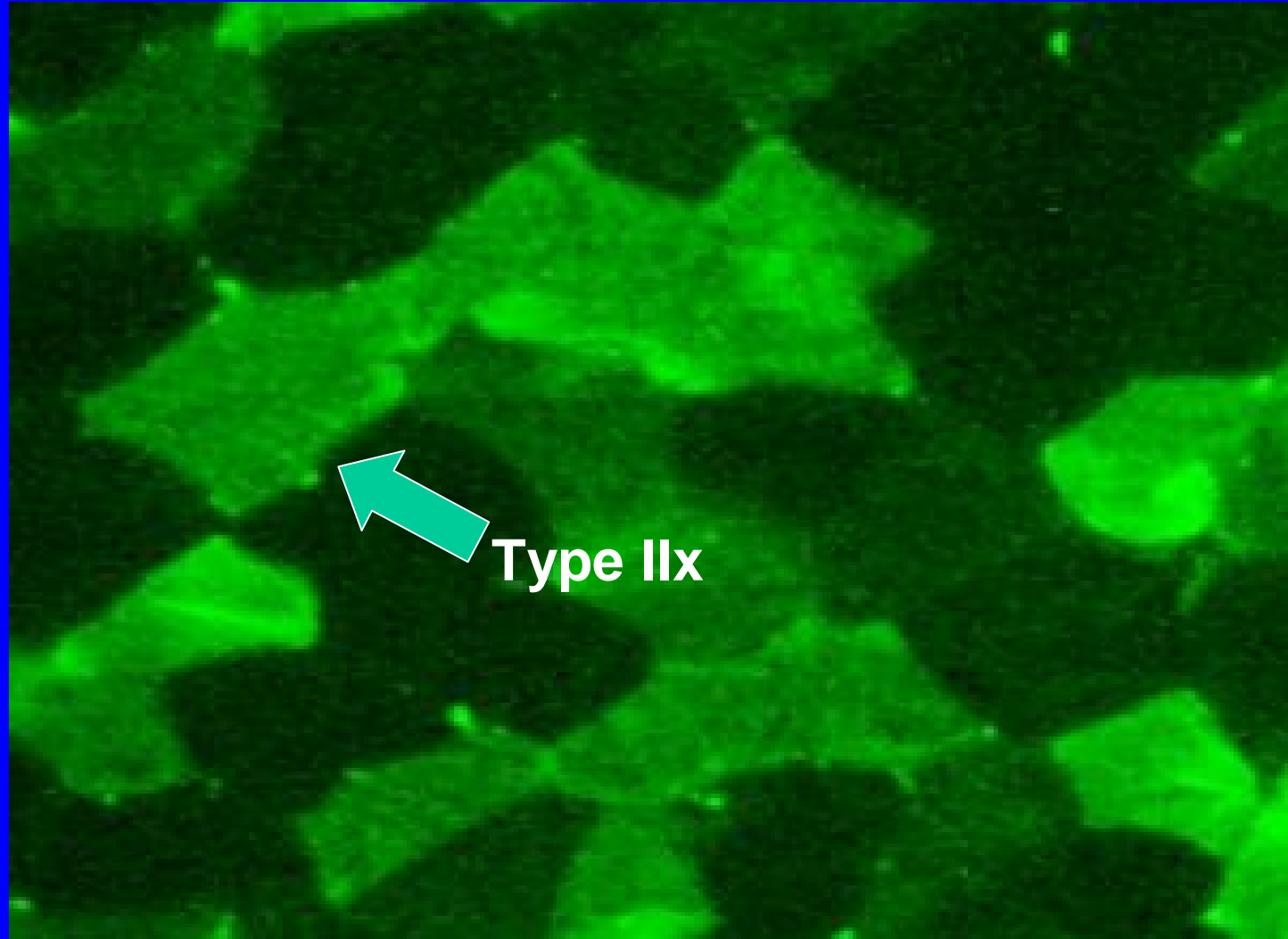


Vitamin D – Falls and Fractures in Men and Women Aged 65 Years and Older

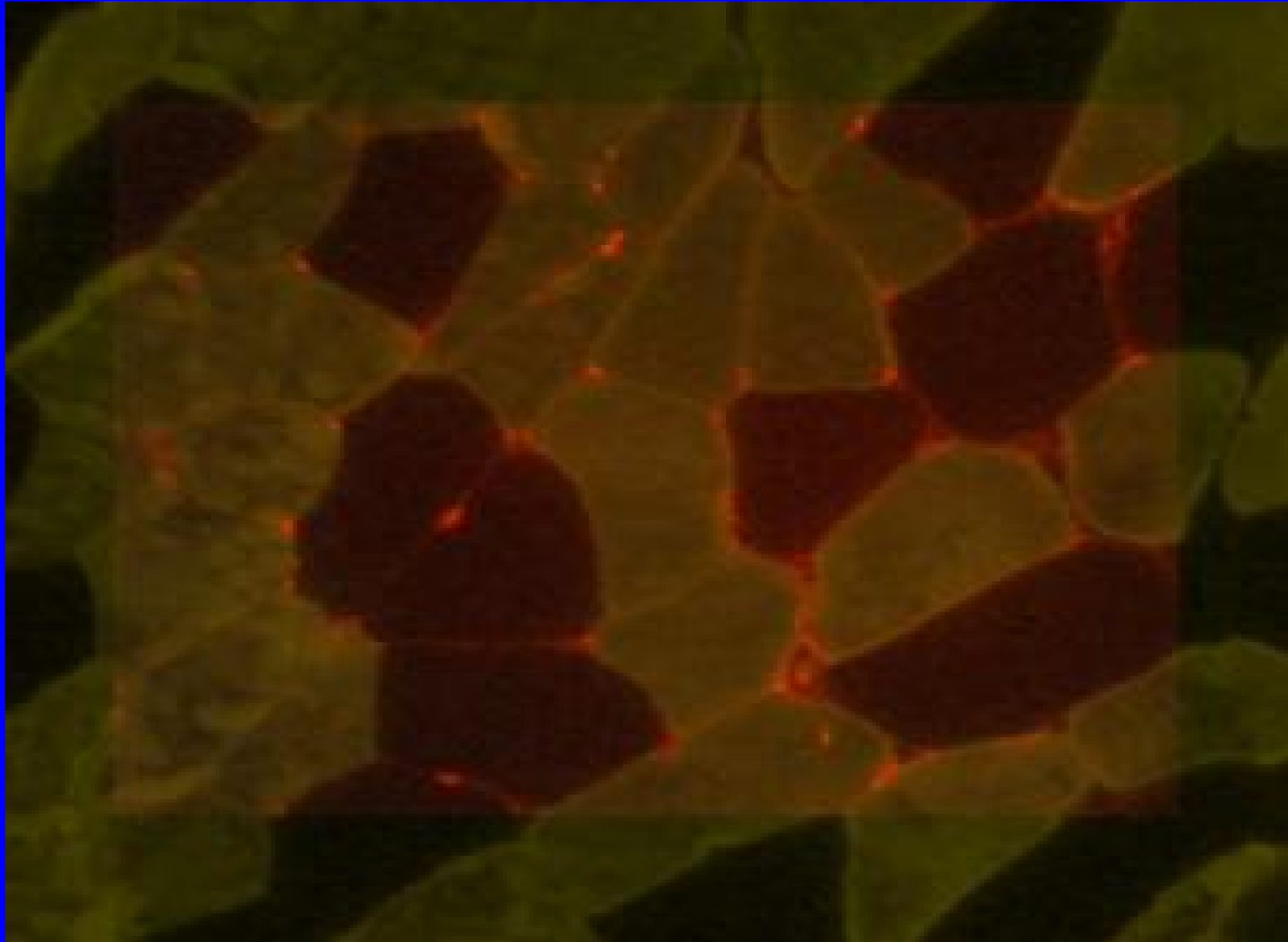
Vitamin D Insufficiency



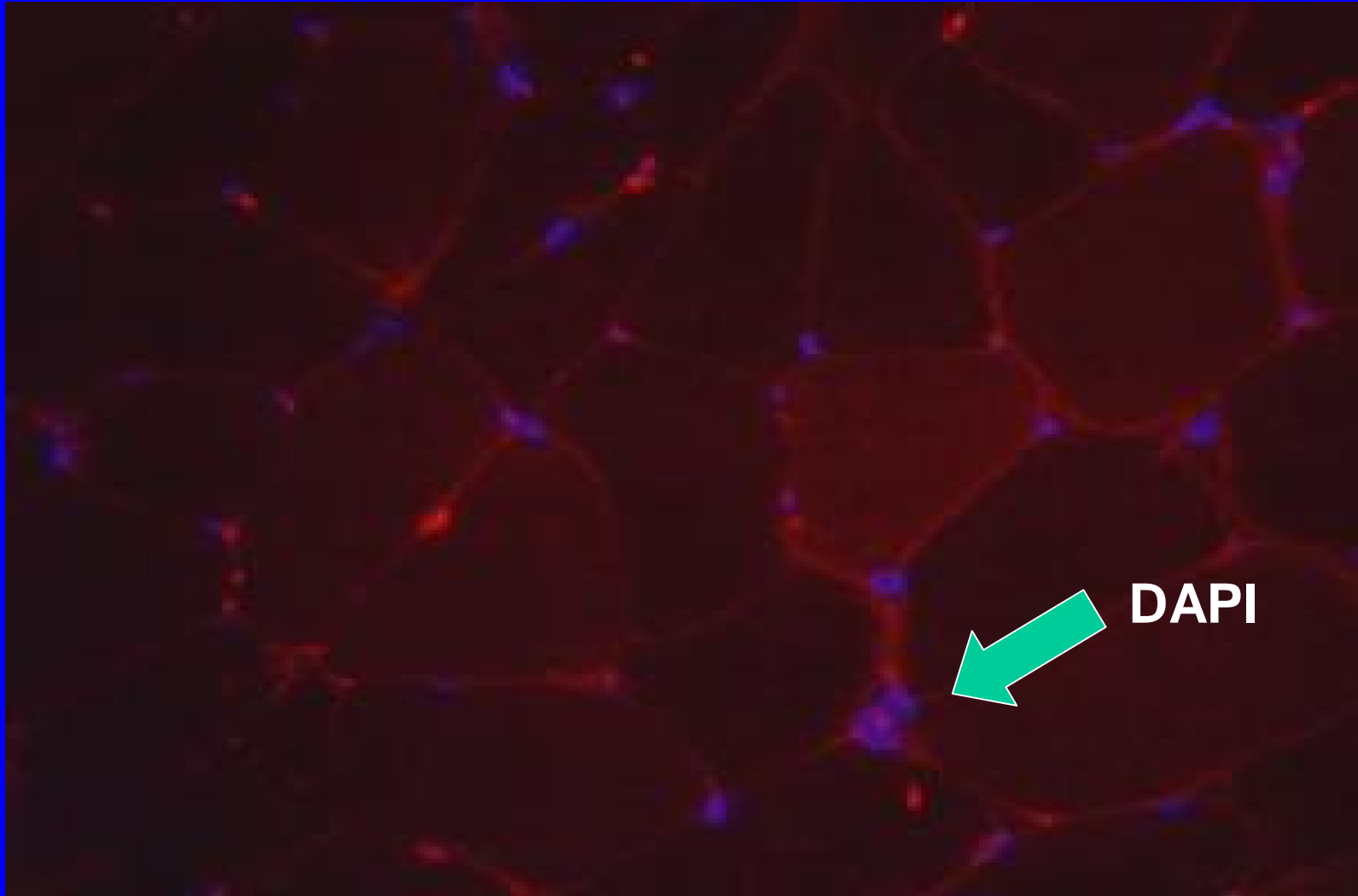
Fiber Type IIx



Type IIa – VDR Overlay

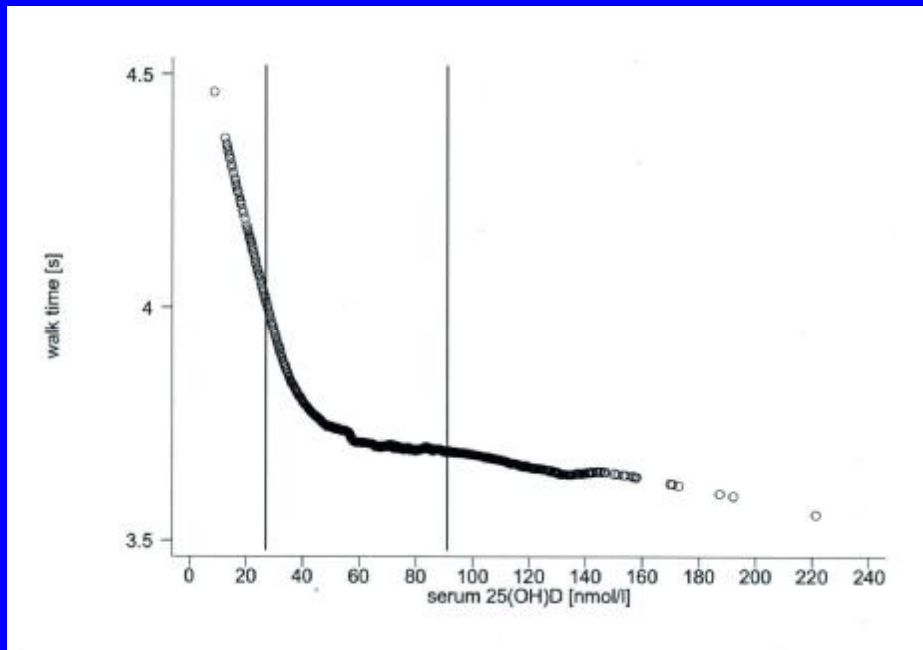


VDR – DAPI Overlay

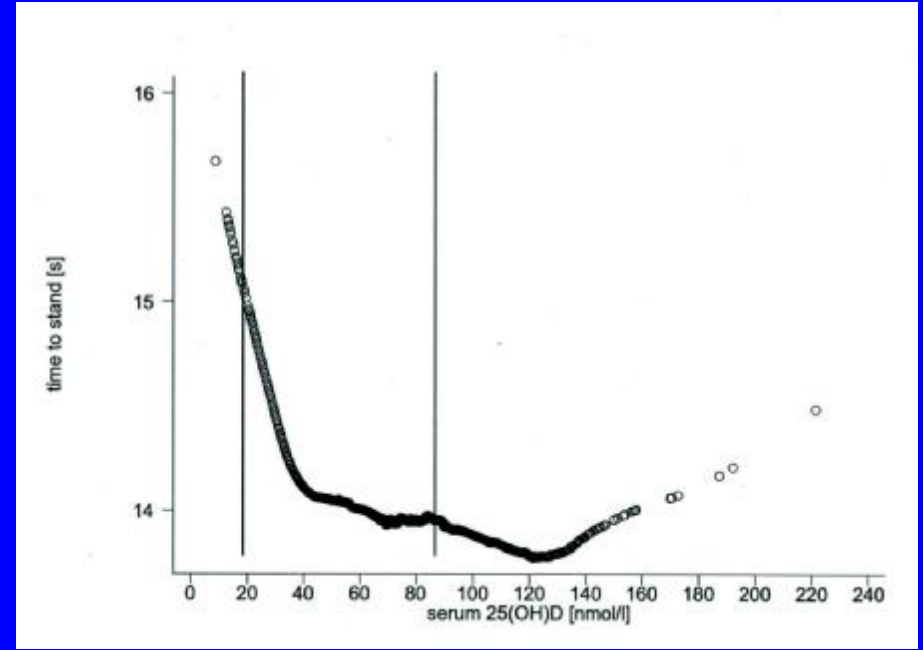


NHANES III – Serum 25(OH)D and Performance

Walk time

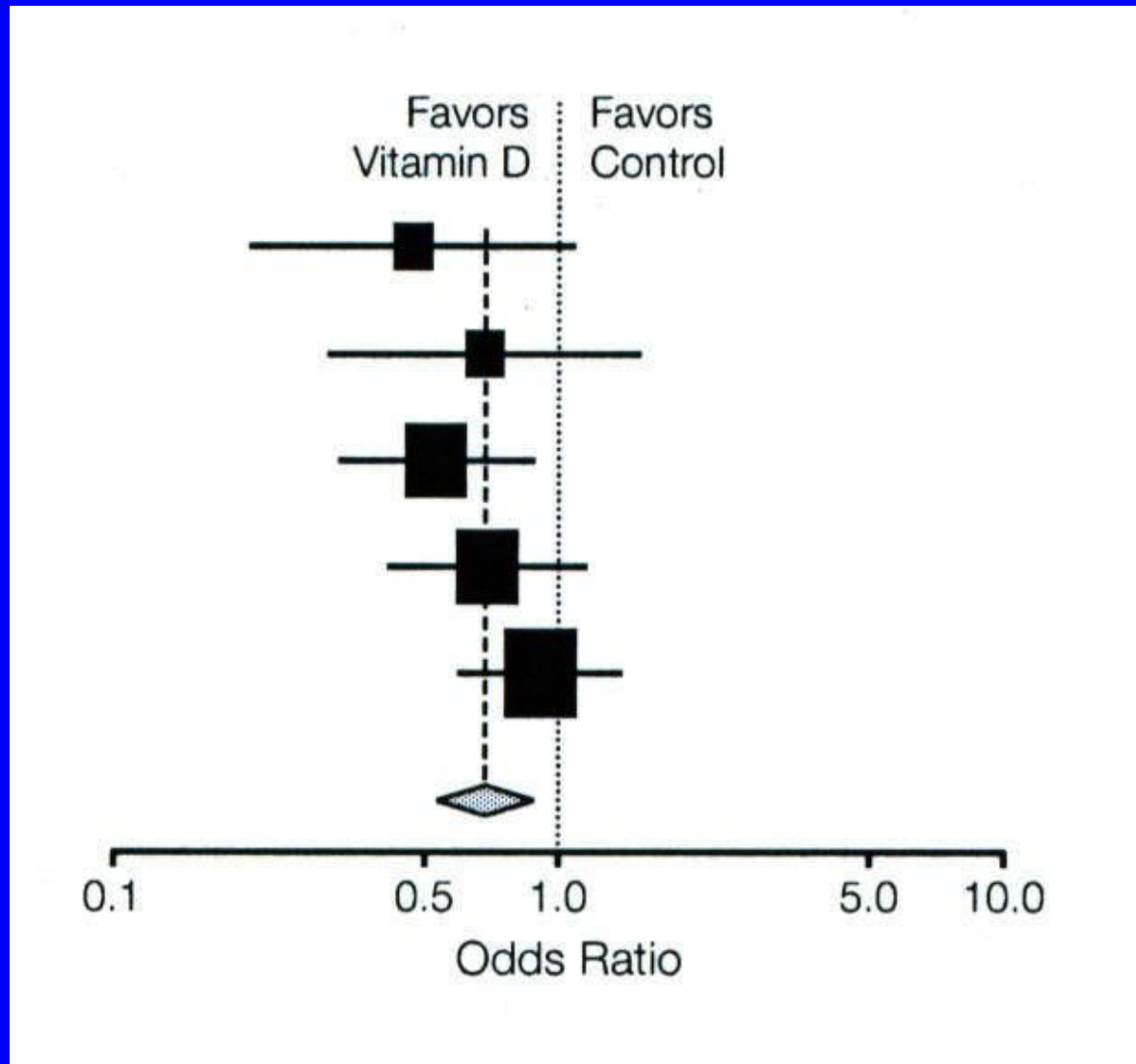


Sit-to-stand



Bischoff-Ferrari HA. Am J Clin Nutr 2004;80:752-8.

Meta-Analysis of Vitamin D and Falls



Bischoff-Ferrari HA. JAMA 2004; 291: 1999-2006.

Updated Meta-Analysis of Vitamin D and Falls 2009

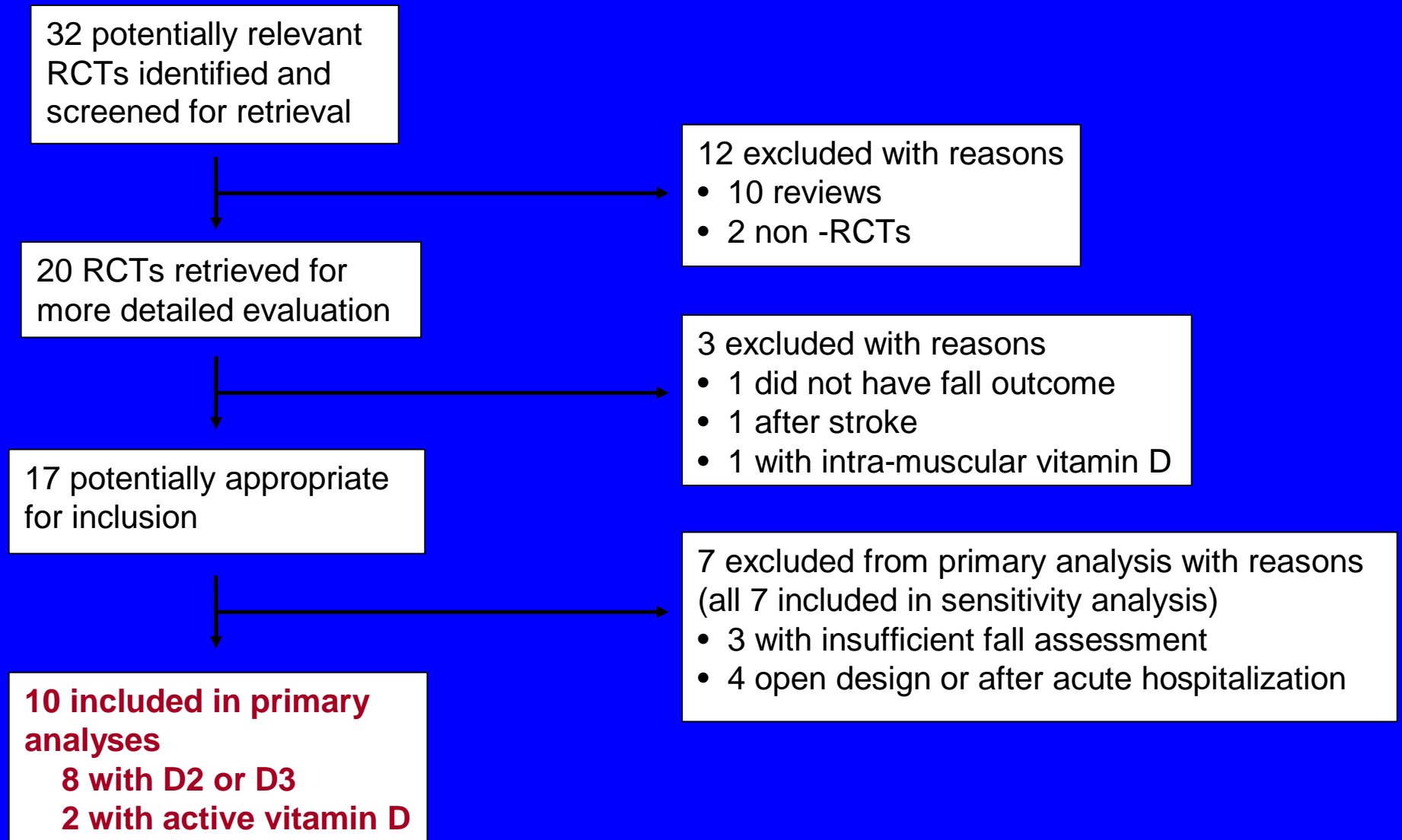
Aims of Meta-analysis

- We performed a meta-analysis on the efficacy of supplemental vitamin D with or without calcium in preventing falls among older individuals.
- Only double-blind RCTs among older individuals (mean age 65+) with sufficient fall assessment were included in the primary analysis

Sufficient fall assessment:

- 1) falls as a primary or secondary endpoint defined at the onset of the trial
- 2) definition of falls and how they were assessed
- 3) assessment of falls for the entire trial period

Disposition of 164 Articles Found

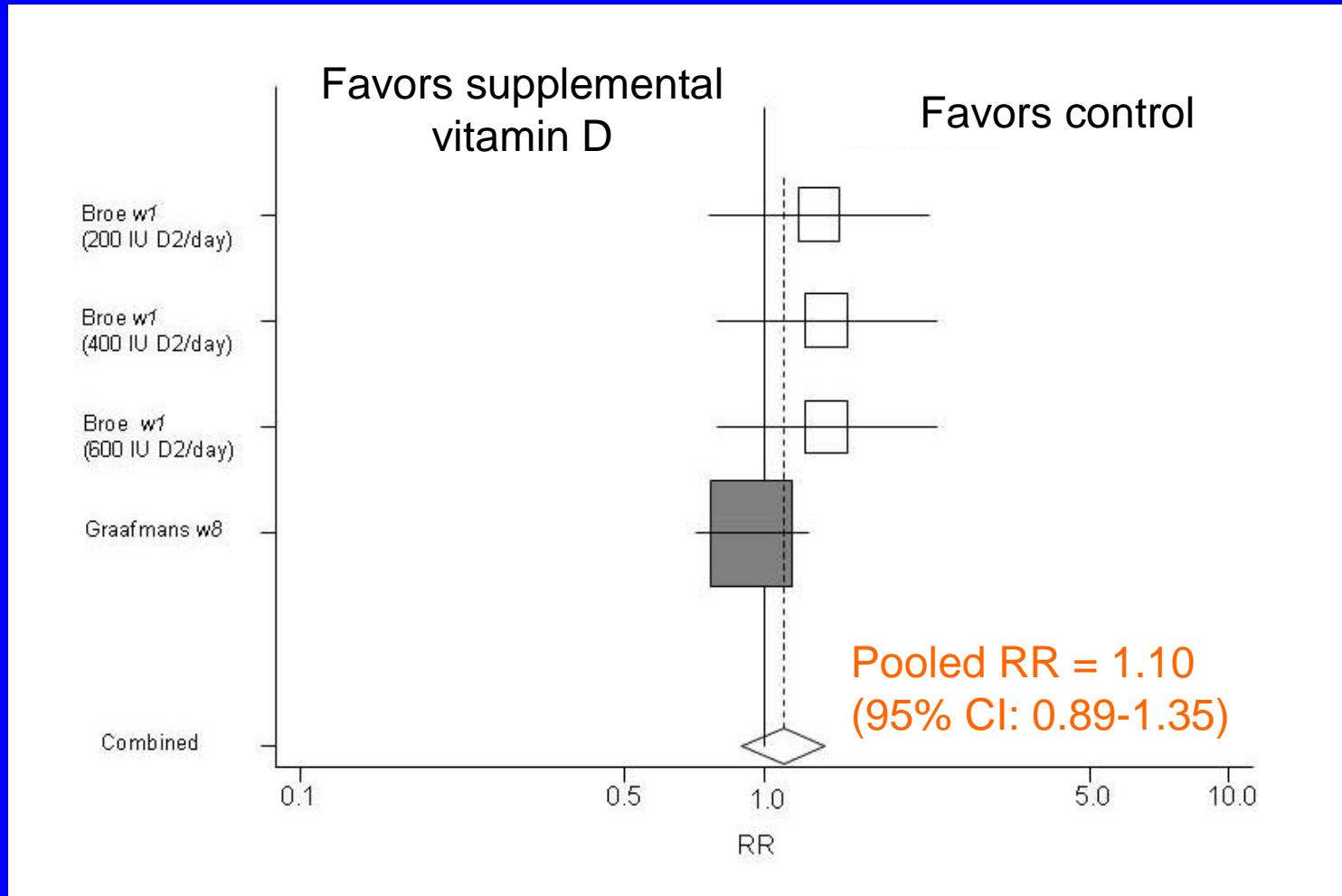


Meta-analysis – Vitamin D and Fall Prevention

- **8 double-blind RCTs were included in the primary analysis (n = 2376 individuals)**
- **In the 8 RCTs, the pooled RR for any dose of vitamin D preventing a fall was 0.87 (95% CI, 0.77-0.99).**
- **However, heterogeneity in results was seen among studies (Q-test: p = 0.05).**

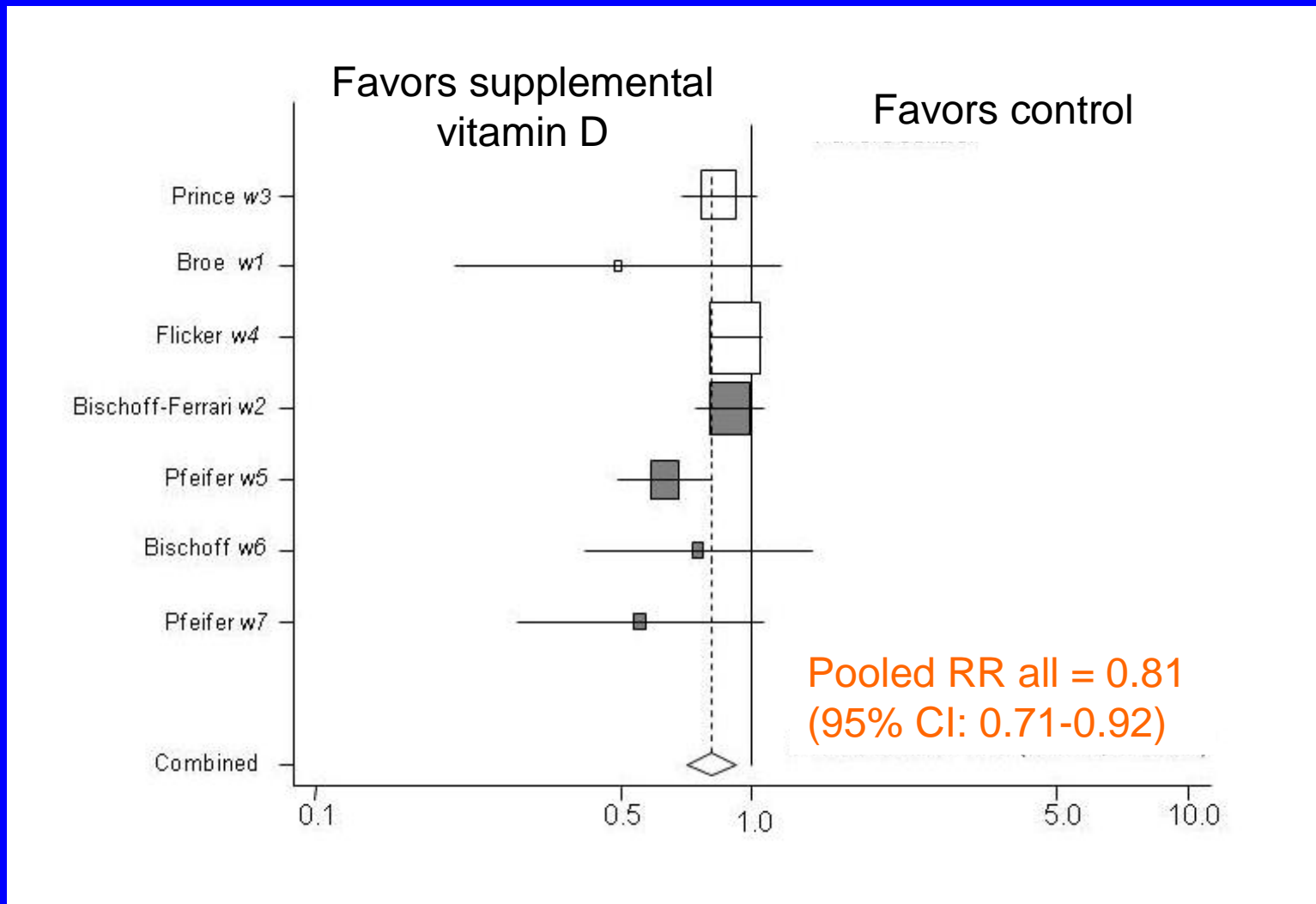
Bischoff-Ferrari, Dawson-Hughes, et al. BMJ 2009; in press.

Fall Prevention with Lower Dose Vitamin D (200-600 IU/d)



Bischoff-Ferrari, Dawson-Hughes et al. BMJ 2009: in press.

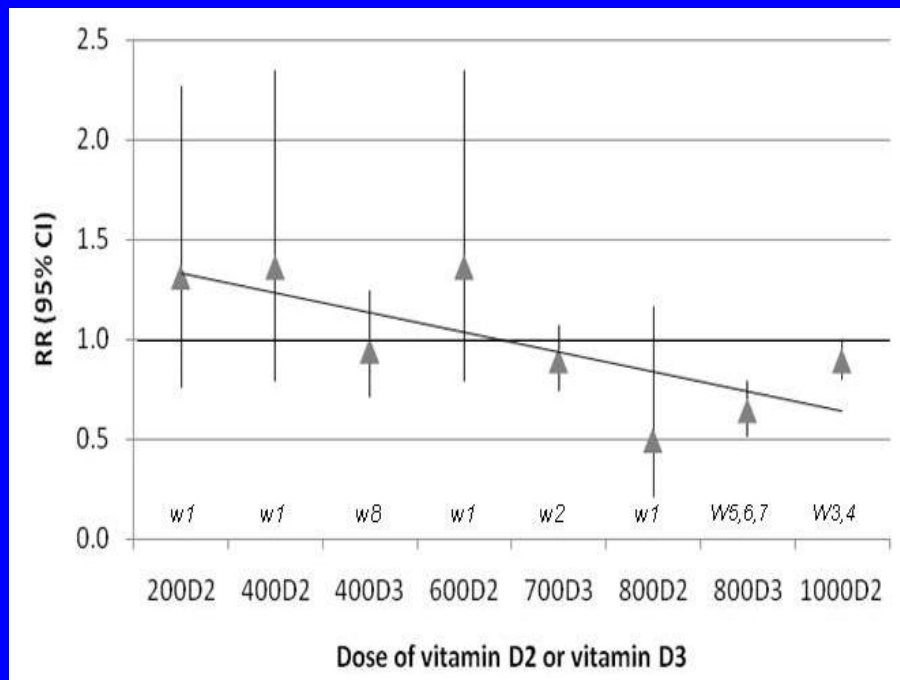
Fall Prevention with Higher Dose Vitamin D (700-1000 IU/d)



Bischoff-Ferrari, Dawson-Hughes et al. BMJ 2009: in press.

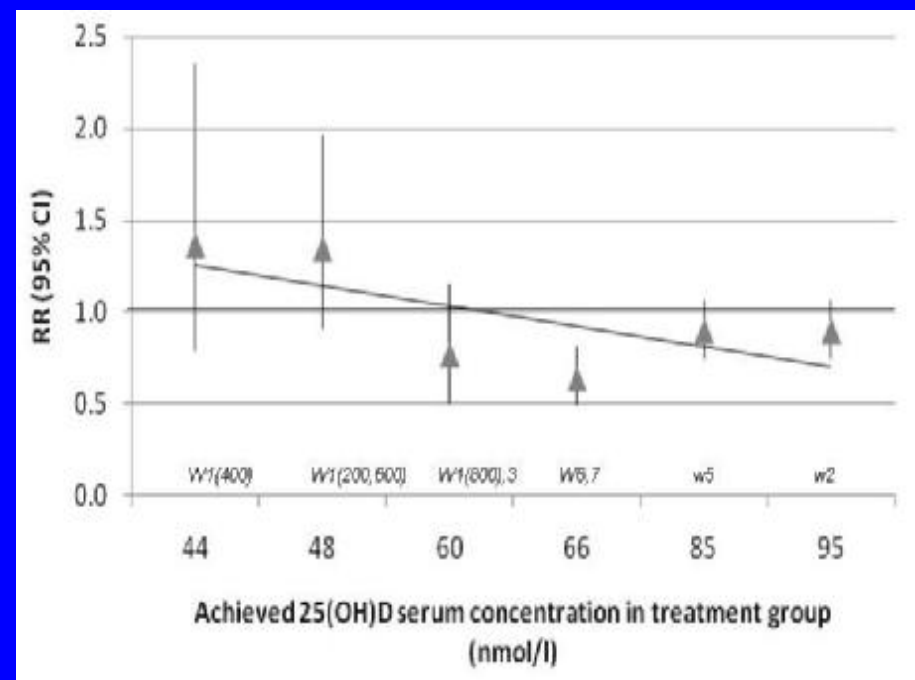
Fall Prevention by Vitamin D Dose and 25OHD Level

Dose



P = 0.02

25OHD level



P = 0.005

Bischoff-Ferrari, Dawson-Hughes et al. BMJ 2009; in press.

Vitamin D and Fractures

Meta-analysis: Vitamin D – Anti-fracture Efficacy

- **Men and women age 65+**
- **Double-blind RCTs**
- **Sub-analyses**
 - **received dose (dose X compliance)**
 - **25(OH)D level achieved**
 - **institutionalized vs free-living**
 - **vitamin D3 versus D2**
 - **combination with calcium**

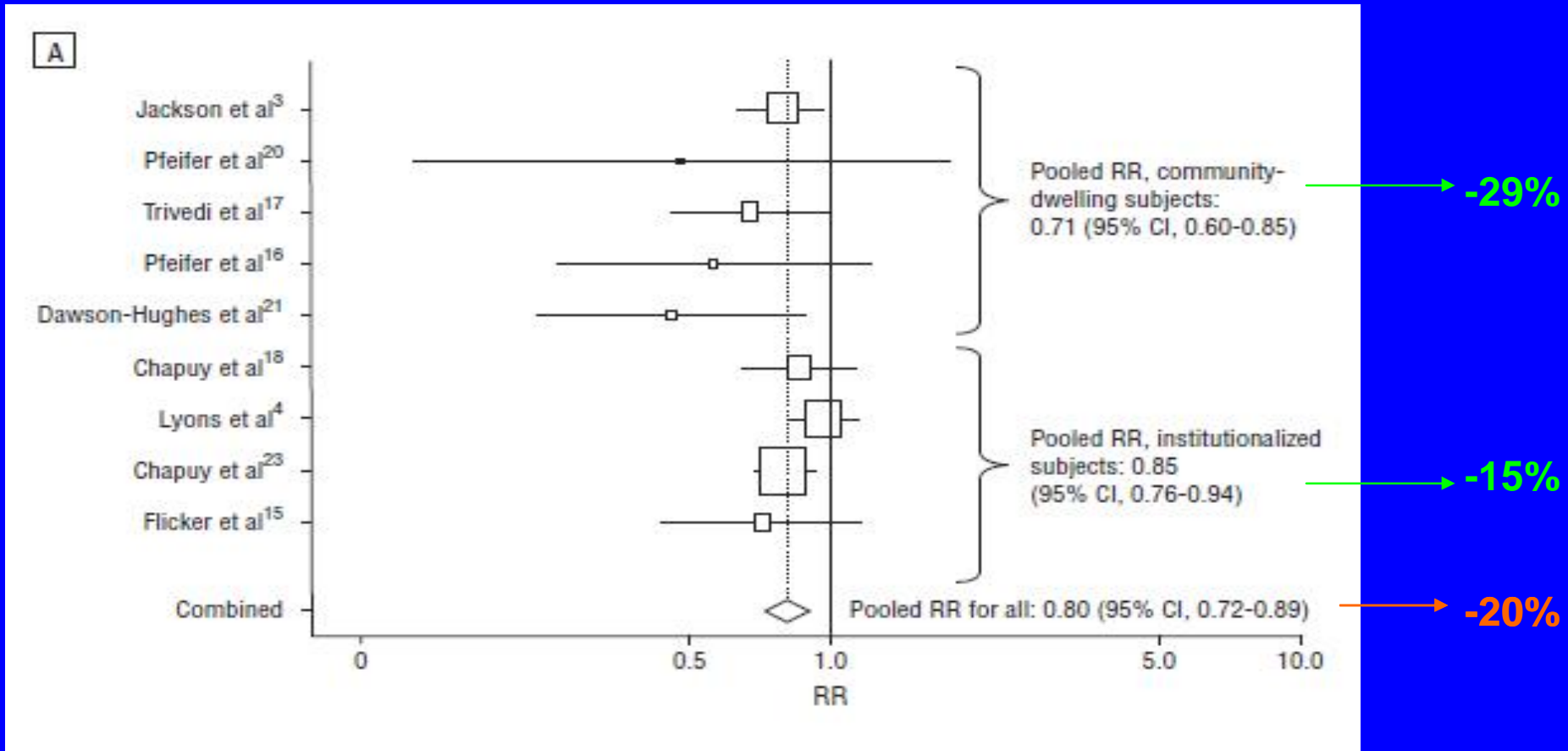
Summary of Results

- **Non-vertebral fractures**
12 RCTs (n = 42,279)
RR: 0.86 (95% CI, 0.77-0.96)
- **Hip fracture**
8 RCTs (n = 40,886)
RR: 0.91 (95% CI, 0.78-1.05)
- **There was significant heterogeneity for non-vertebral and hip fractures – related to dose**

Lower Dose Vitamin D Trials: RR of Fracture (340-380 IU/d; n = 9,014 from 3 trials)

- Non-vertebral fracture
pooled RR = 1.02 (95% CI; 0.92-1.15)
- Hip fracture
pooled RR = 1.09 (95% CI; 0.90-1.32)

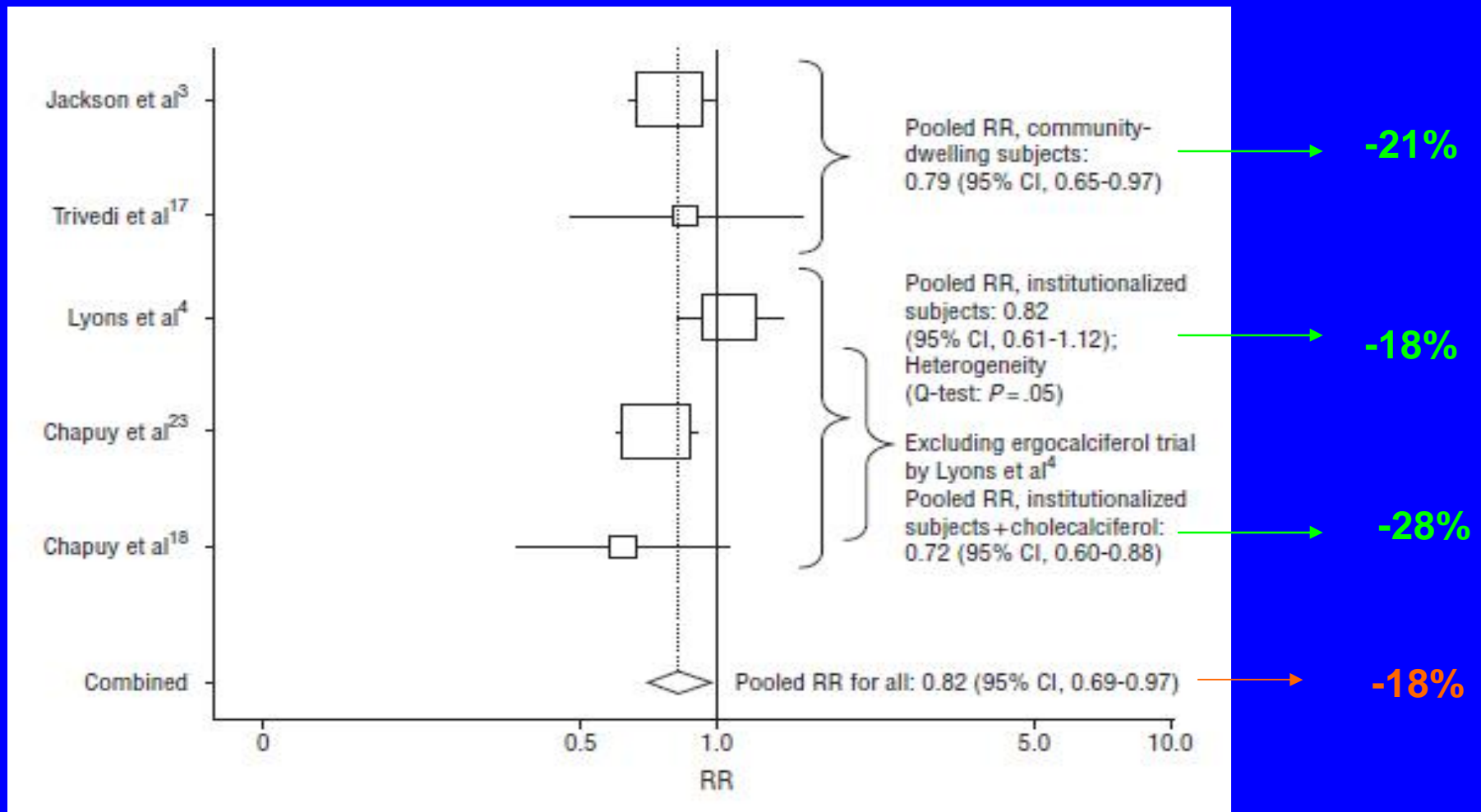
Higher Dose Vitamin D Trials: RR of Non-vertebral Fractures (Range: 482 - 770 IU/d; n = 33,265 from 9 trials)



Bischoff-Ferrari HA. Arch Int Med 2009;169:551-61.

Higher Dose Vitamin D Trials: RR of Hip Fracture

(Range: 482 - 770 IU/d; n = 31,872 from 5 trials)

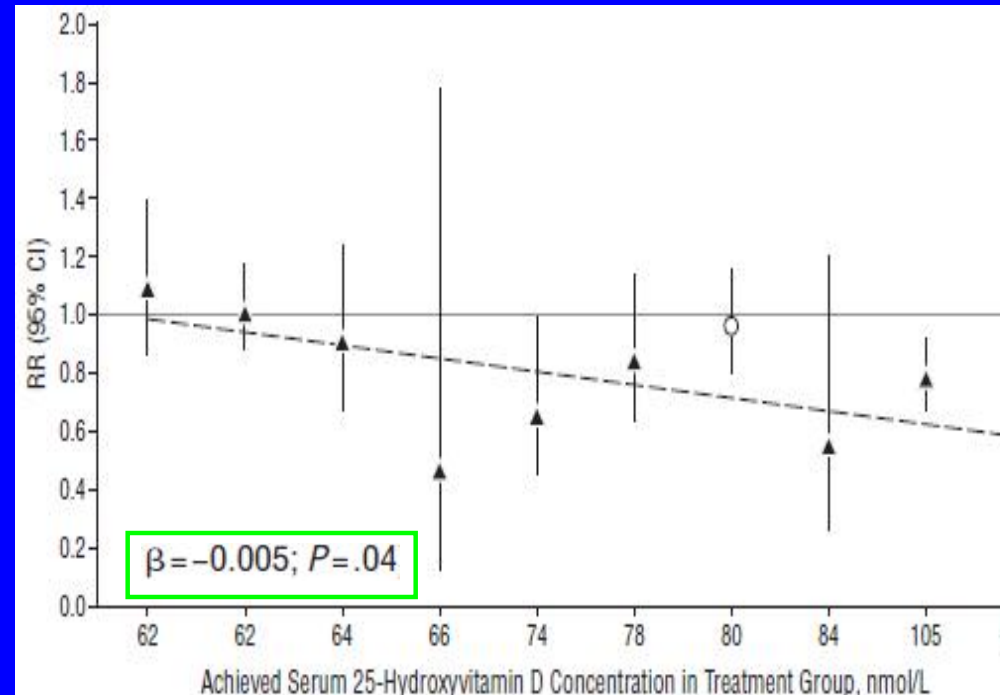
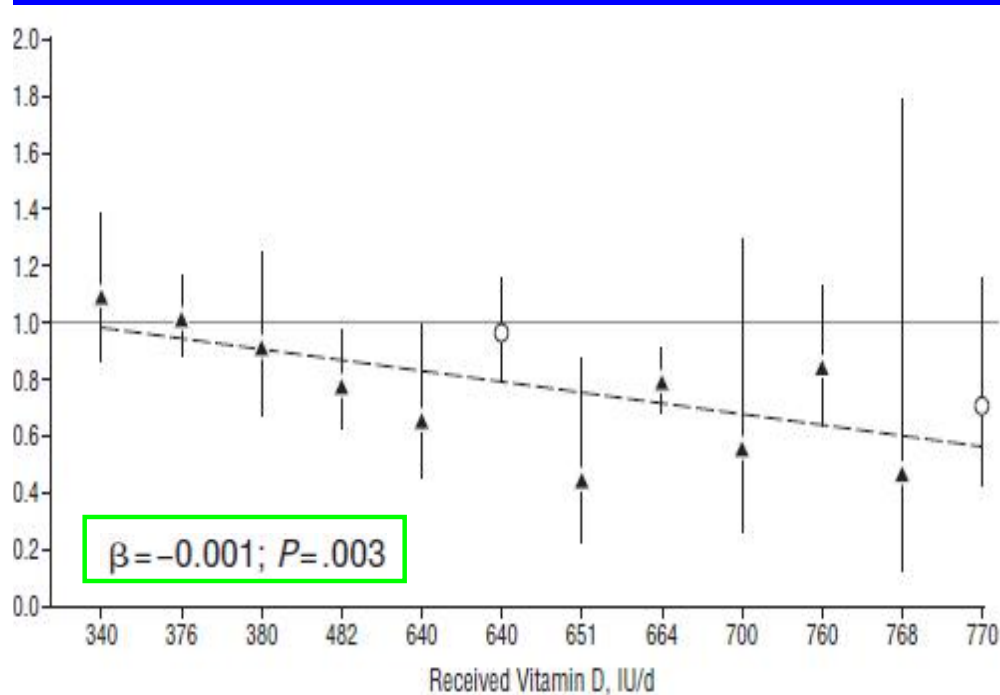


Bischoff-Ferrari HA. Arch Int Med 2009;169:551-61.

Higher Received Dose Vitamin D and Non-vertebral Fracture Risk— subgroup analysis

Primary analysis of higher dose RCTs	- 20%*
Subgroup analysis of higher dose	
D3 only	- 23%*
D2 only	- 10%
Age 65-74	- 33%*
Age 75+	- 17%*
Vitamin D	- 21%*
Vitamin D + calcium	- 21%*
	*p<0.05

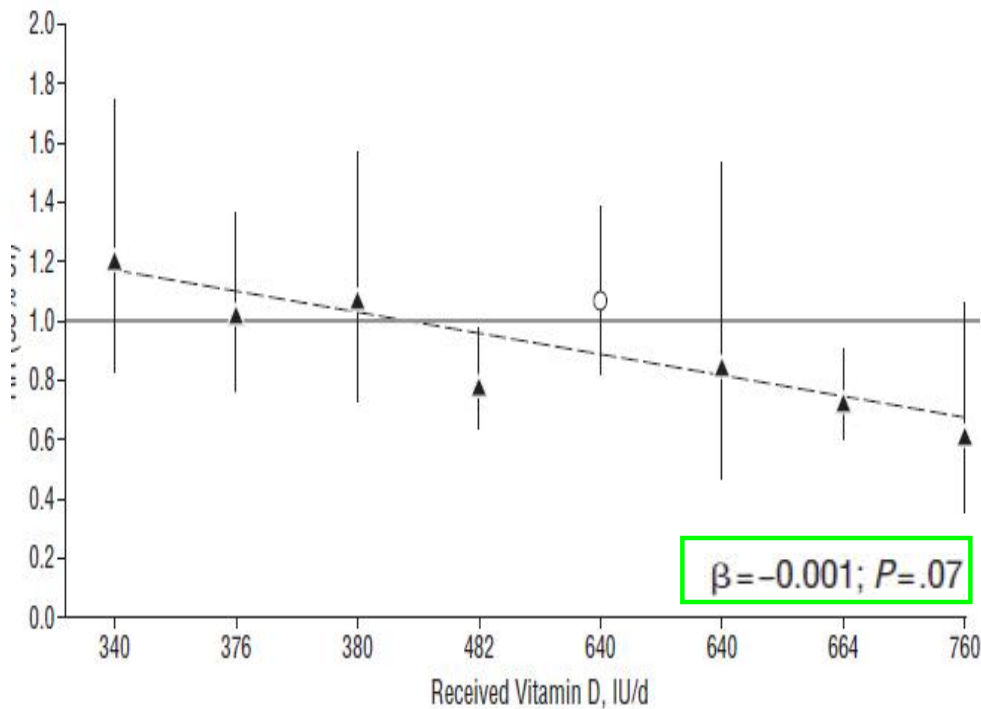
All Trials: Variation of Non-vertebral Fracture Prevention by Received Dose and Achieved 25(OH)D



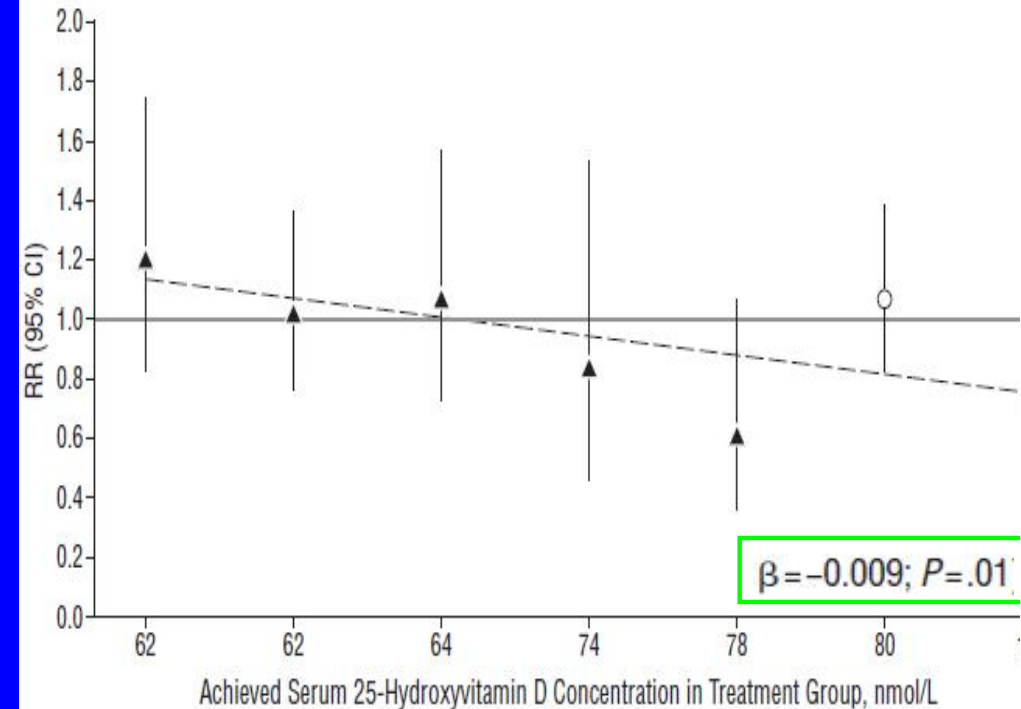
(Range: 340 - 770 IU/d;
n = 42,279 from 12 trials)

(Range: 62 - 112 nmol/L;
from 10 trials)

Variation of Hip Fracture Prevention by Received Dose and Achieved 25(OH)D



(Range: 340 - 760 IU/d;
n = 40,886 from 8 trials)



(Range: 62 - 105 nmol/L;
from 7 trials)

Impact of Adding Open Trials to the Analyses

- For any received dose,
 - 12 RCTs: pooled RR = 0.86 (95% CI; CI 0.77-0.96)
 - 12 trials + 4 open trials: pooled RR = 0.88 (95% CI; CI 0.80-0.97)
- For higher dose trials,
 - 9 RCTs: pooled RR = 0.72 (95% CI 0.72,-0.89)
 - 9 trials + 3 open trials: pooled RR = 0.83 (95% CI; CI 0.74-0.95)

Conclusions

- These results support use of higher dose vitamin D to prevent falls and fractures in men and women age 65 years and older.
- Fall risk begins to ↓ at a mean administered dose of 700 IU/d, with further improvement thereafter.
- Non-vertebral fracture risk begins to ↓ at a mean received dose of 482 IU/d, with further improvement thereafter.
- The magnitude of the risk reduction in the higher dose trials averaged about 20% for both falls and fractures.
- The benefit appears to be independent of dwelling, age, and calcium intake.