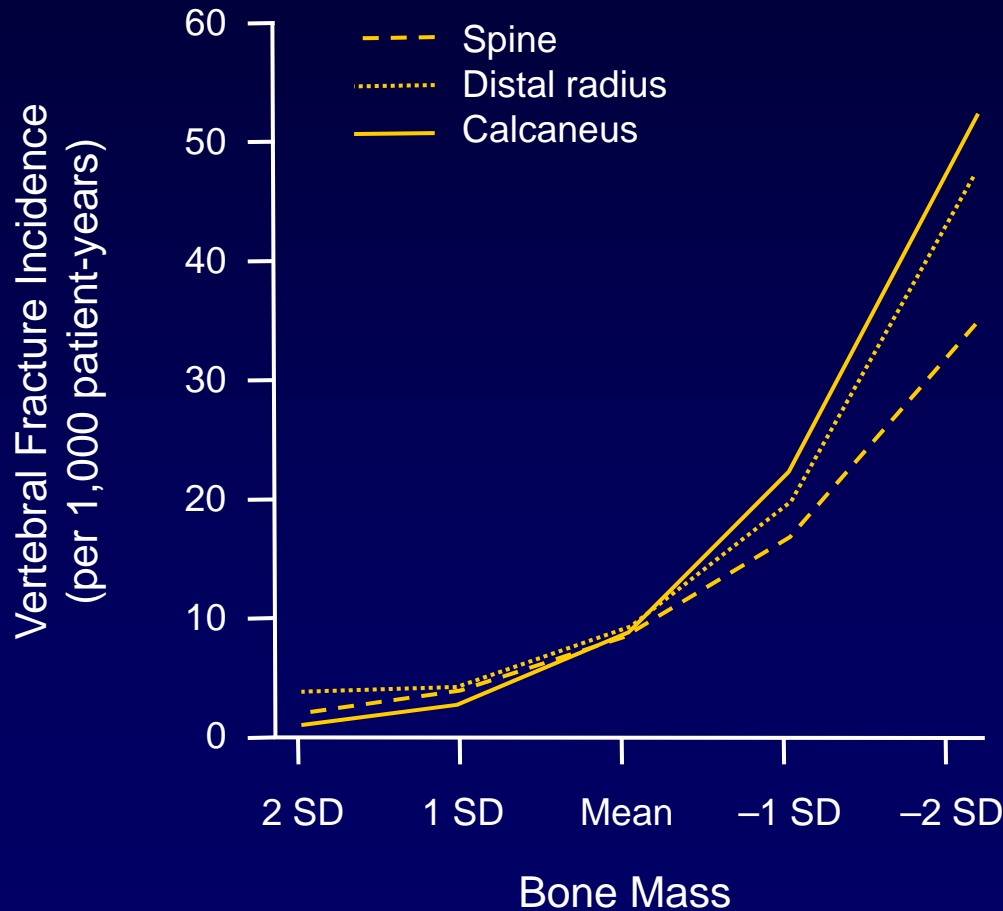
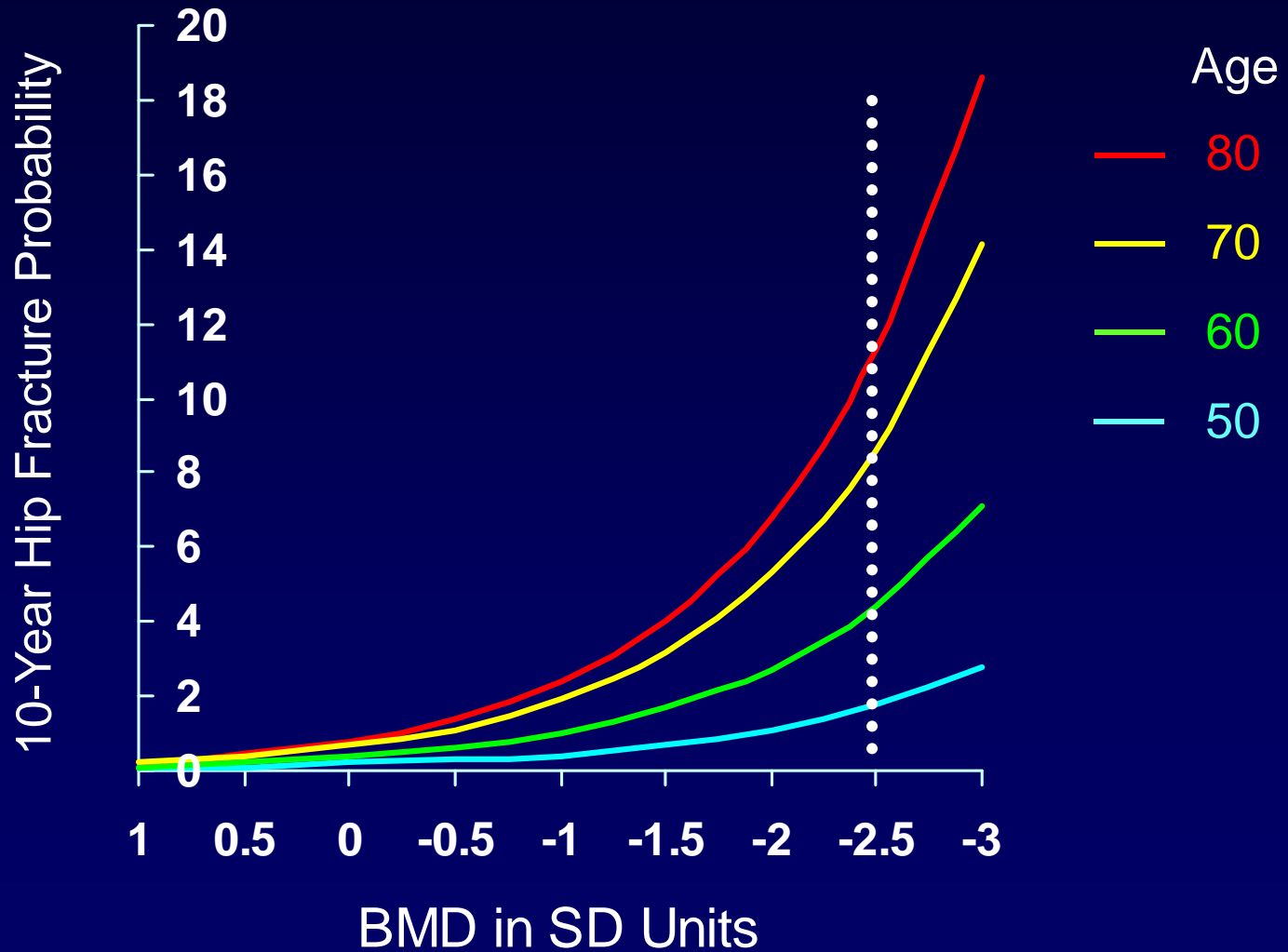


The Relationship Between Declining BMD and Increasing Vertebral Fracture Risk



Wasnich RD et al. *J Nucl Med* 1989;30:1166–1171.

Bone Density and Fracture Risk by Age

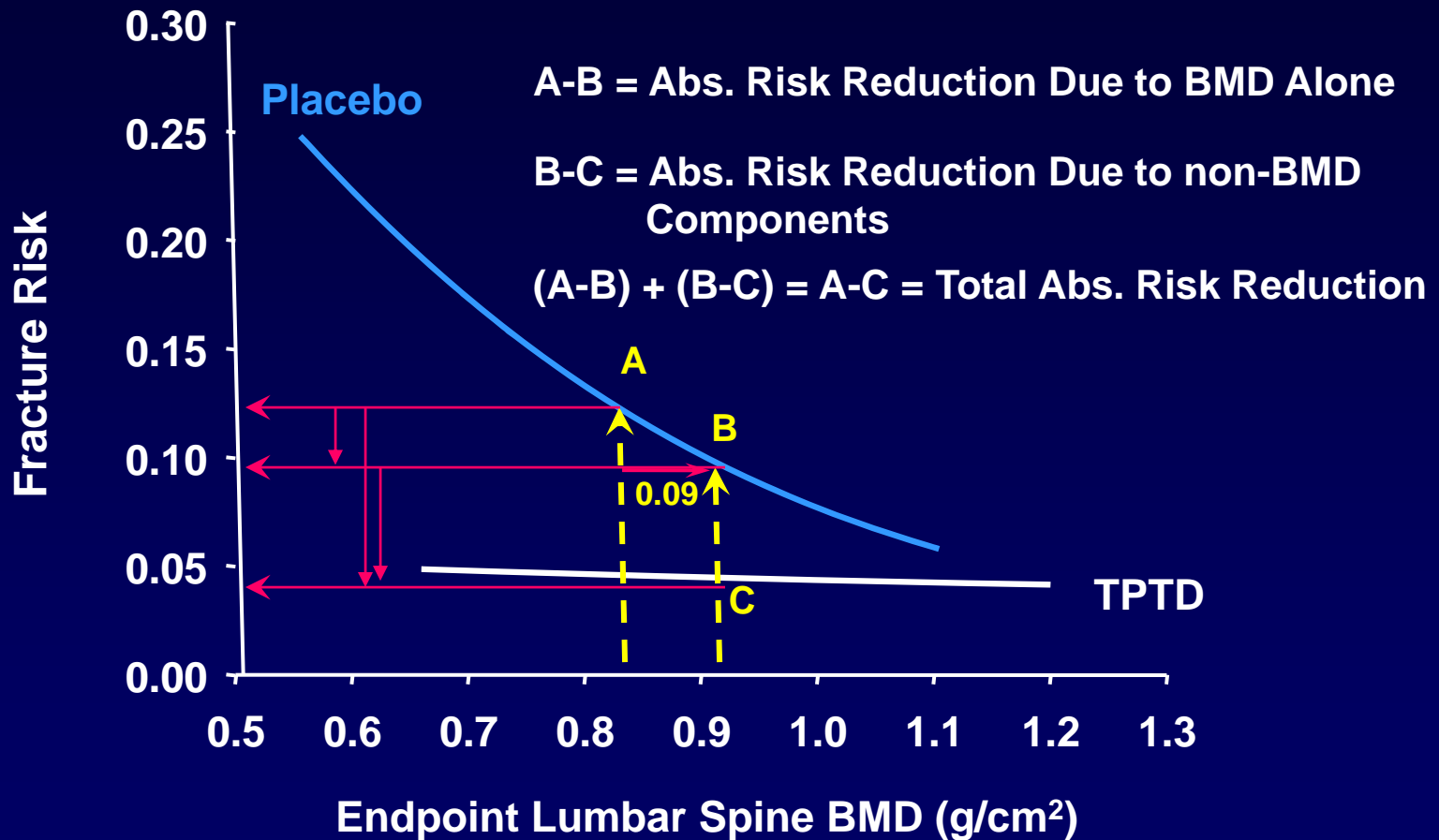


| | $\Delta\%$ Spine BMD v PBO | Spine Fx Risk Reduction | Publication Date |
|--------|-------------------------------|----------------------------|---------------------|
| FIT I | 6.2% | 47% | 1996 |
| FIT II | 6.8% | 44% | 1998 |
| MORE | 2.1% | 30% | 1999 |
| RVN | 4.3% | 41% | 1999 |
| RVE | 5.9% | 49% | 2000 |
| PROOF | ~0.6% | 36% | 2000 |

Black DM, et al. *Lancet* 1996;348:1535-1541.
 Ettinger B, et al. *JAMA* 1999;282:637-645.
 Reginster JY, et al. *Osteoporos Int* 2000;11:83-91.

Cummings SR, et al. *JAMA* 1998;280:2077-2082.
 Harris ST, et al. *JAMA* 1999;282:1344-1352.
 Chesnut CH, et al. *Am J Med* 2000;109:267-276.

Relationship Between Endpoint Lumbar Spine BMD and Vertebral Fracture Risk After 18-Months of TPTD Treatment



To Find Your Short-Term Precision

Scan...

✓ 10 people 4 times each

✓ 15 people 3 times each

✓ 30 people 2 times each

Complete the scans in 2 weeks
to 1 month

The Root-Mean-Square Standard Deviation

$$SD_{RMS} = \sqrt{\sum_{j=1}^m \frac{SD^2}{m}}$$

where “m” is the number of subjects

3 Things Required to Determine the LSC

1. Your Precision (Pr) as the RMS-SD or RMS-CV
2. The number of measurements at each time point (n_1 and n_2)
3. The Z' value for the desired level of confidence & approach

$$Z'(\text{Pr}) \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$$

1 x 1 Least Significant Change
-2 Sided

$$Z' \sqrt{2} (\text{Pr})$$

- $1 \times 1 \text{LSC}^{95-2}$ $1.96 \times 1.414 (\text{Pr}) = 2.77 (\text{Pr})$
- $1 \times 1 \text{LSC}^{80-2}$ $1.28 \times 1.414 (\text{Pr}) = 1.81 (\text{Pr})$

But Do I Care?

- There *is* a statistically significant relationship between increasing BMD vs. placebo and decreasing fracture risk.
 - The *magnitude* of this relationship is the subject of debate but not the existence of the relationship itself.
 - The majority of fracture risk reduction appears to be due to non-density related factors, but the increase in BMD, as a single quantifiable factor, does indeed account for a sizable proportion of the reduction in spine fracture risk.
- Although no change in BMD vs placebo in patients on therapy still appears to confer a reduction in fracture risk, greater reductions in spine fracture risk are seen in patients on therapy who gain BMD than in those on therapy who lose it.
- There is no evidence that fracture risk reduction is achieved on therapy if a significant loss in BMD is seen.
- A significant loss of BMD may indicate lack of therapeutic responsiveness, a previously undetected secondary cause of bone loss requiring treatment or non-compliance.
- At present, when it comes to objectively assessing therapeutic efficacy, there is nothing better than the measurement of BMD.