Vitamin E and the Risk of Prostate Cancer. The Selenium and Vitamin E Cancer
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Background:
Lifetime risk of prostate cancer in the US is 16%. Most cases found at early, curable
stages, but tx is costly and has urinary, sexual and other adverse effects. Predclinical
evidence existed that selenium and Vitamin E could prevent prostate CA.

SELECT trial started on Aug 2001 – randomized men into 4 groups
(selenium/placebo, Vit E/ placebo, selenium/Vit E, placebo). In Sept 08 study
discontinued early b/c of lack of efficacy. At that time w/ median f/u of 5.5 yrs,
more prostate CA found in Vit E/placebo group, but was not statistically significant
(p=.06). Follow-up continued. In May 2011 trial data re-examined.

Methods:
Healthy men at average risk of prostate CA were selected. (Figure 1) PSA </- 4 and
normal DRE. Age 50 for black men, 55 yrs for others. Doses: Selenium 200
micrograms/d, Vitamin E 400 IU/d. Monitored q6 mo w/ physical exam. Screened
w/ PSA, DRE, prostate bx based on standard of care in community. Patients mostly
in 55-64 y/o age group, majority white, most common PSA .1-1. (Table 1)

Prostate CA status determined by self-report at each 6 mo study visit. Med records,
path report, Gleason, diagnostic method examined. Supplements were d/ced in
2008 and f/u continued unblinded.

Statistical Analysis:
RCT - data analysis for primary endpoint of prostate CA incidence resulting from
“routine community care.” Cancers not centrally confirmed w/ path (17%) were
included in analysis. 2-sided p values reported. Proportional hazard model used to
compare prostate CA incidence between study groups. Chi squared test used to test
RR DM.

Results:
Study added 54,464 additional person-years of f/u (23% increase). 521 additional
prostate cancers diagnosed since the initial report (113 in placebo, 147 in vit E, 143
in selenium, 118 in combo). Statistically significant increase in Vit E group (HR 1.17,
P .008). Vitamin E and selenium group not significant (P .02) (Table 3).

Difference in rates of prostate CA between Vit E and placebo became apparent
during 3rd year in the trial – HR 1.10 at that point and increased slightly each year
thereafter to 1.17 (Figure 2). Absolute increase in risk was 1.6 per 1000 in vitamin
Risk of Gleason 7 or greater disease higher in all groups, but not statistically significant. Most common grade was Gleason 6, in more aggressive dz Gleason 7 (Table 4).

No significant risk of DM in selenium group. No increase in other cancers, deaths or grade 4 CV events (Table 5).

Discussion:
Prevention of prostate CA is important public health goal because of high rate of cure- but significant adverse events of tx. The risk of prostate CA at 7 years of f/u was increased by 17% in men taking Vitamin E – a finding that occurred 3 yrs after randomization. Confidence intervals have narrowed over the duration of the study, and results now statistically significant.

Selenium may have a protective effect- no statistically sig difference in cancer in the selenium/placebo or selenium/Vit E group.

Results differ from ATBC trial – reported 35% RR in men taking 50 IU/d Vit E for 6.1 yrs. In the PHS II, 400 IU Vitamin E every other day for 8 yrs had no effect on incidence of prostate CA.

More than 50 % of those over 60 take supplements w/ Vit E – and 23 % are taking at least 400 IU q day. Recommended daily dietary allowance 22.4 IU

Limitations:
Not discussed extensively in manuscript
“Standards of the community” over or under screening??
Dose was 8x what had previously been shown to decrease prostate CA rates (50 IU) in ATBC trial ( though on internet search 100-1000 IU found, most in 400 IU range for purchase)
Incidence of prostate CA not the primary feature of the studies upon which the SELECT trial was based upon (ATBC it was a secondary endpoint)
Analysis of Vit E and Selenium in tissue/blood pending- adherence?
Were confounders measured and controlled for (ie FHx)?
Difference in dietary Vit E and chemically derived Vit E?

Bottom line:
There may be an increased prostate CA risk with 400 IU of Vitamin E supplementation. Results between trials are inconsistent. I may recommend a balanced MVI – but not extra supplementation.