

# **Prevention Strategies**

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More study in the area of prevention is needed and we must be aware of false claims. First, vitamins, nutritional supplements, et cetera, is a multibillion dollar industry in the United States; there is a profit to be made in over-the-counter products. But natural products are not necessarily good; manufactured products are not necessarily good. Controlled clinical trials can determine whether an item is good.

As physicians, it is important to discover what products our patients are taking, and to discuss with them the uncertainty around whether or not these additional products help. These products may alter a person's metabolism, adversely affecting other products which we prescribe. The SELECT trial shows that selenium and vitamin E, either alone or in combination, did not prevent prostate cancer and may even be harmful; previous work had suggested that selenium and vitamin E alone or in combination might reduce the risk of prostate cancer.

Regarding diet, studies show that people who are obese or overweight are at increased risk for cancer, yet, no study has shown that weight reduction reduces this risk. Likewise, exercise has shown benefit in reduction of mortality and morbidity, yet regarding cancer, we do not know whether risk is reduced.

However, 5-alpha-reductase inhibitors (5ARIs) appear to be safe and effective, and are the only intervention which supports the results of a phase 3 controlled clinical trial in terms of reduction of cancer. The 5ARIs are the major player available for prevention of prostate cancer. These drugs have antiandrogenic activity and have already been demonstrated to be effective in BPH. The 5ARIs decrease the levels of available 5-alpha-reductase prior to testosterone binding to the enzyme, thus reducing the levels of dihydrotestosterone that derives from such a bond, and inhibit the enzyme that reduces excessive prostate growth.

In most men, BPH is a progressive disorder. Two of the 5ARIs have been approved by the FDA to treat BPH, both Proscar (finasteride) and Avodart (dutasteride). Their efficacy appears to be unrelated to symptoms but rather to prostate volume. Each agent has been examined in clinical trials to assess efficacy in preventing prostate cancer, as early data had suggested there was a lower rate in mean PSA; there was evidence of efficacy from 5ARIs in treating men who had biochemical recurrence of prostate cancer. Potential side effects of 5ARIs include increased erectile dysfunction, decreased ejaculate volume, decreased libido, and increased sexual dysfunction, all often reversible. Gynecomastia may not be reversible. Other side effects are decreased PSA and decreased male pattern baldness.

The Prostate Cancer Prevention Trial (PCPT) was a prevention study looking at the use of Proscar for seven years. Initial findings showed a decreased risk of prostate cancer, but there was early concern for increased risk of developing more aggressive tumors. Subsequent studies are clear that finasteride does not promote more aggressive tumors but actually reduces the risk of such tumors. Initial data from the large international clinical trial REDUCE indicate that dutasteride may help prevent prostate cancer in men who are at higher risk for prostate cancer. Men were found to be at no greater risk for developing aggressive prostate tumors. In summary, dutasteride and finasteride appear to be comparable to one another in reducing the occurrence of prostate cancer. It is unclear whether everyone with an elevated PSA should take 5ARIs. The data given thus far is incidence data; there is no mortality data.

The ARTS study was performed to assess the efficacy and safety of dutasteride in extending PSA doubling time in men who had been treated for clinically localized prostate cancer with a radical therapy with curative intent, but who experienced biochemical failure (PSA rise) afterwards without any signs or symptoms of metastases. Results have yet to be collected from this study.