Assessing Cancer Prevention Technology
Assessing Cancer Prevention Technology

E. R. Greenberg MD
Professor, Dartmouth Medical School
Fred Hutchinson Cancer Research Center
Sr. Epidemiologist: Cancer Research and Biostatistics
Assessing Cancer Prevention Technology

1. Principal prevention strategies.
2. Key assessment questions.
3. Evaluating efficacy, the need for RCTs: Beta-carotene example.
4. Issues of feasibility, cost/effectiveness, etc. [Later]
Principal Prevention Strategies

• Screening
• Chemoprevention
• Behavioral Change
• Public Policy
Screening

• Focus is on the individual with occult cancer.

• Goal is to identify patients.

• Reflects a surgical mindset:
  “If you find it early enough, I can cure it.”

• Evaluation usually is based on an RCT with cancer mortality as the endpoint.
Chemoprevention

- Focus is on the individual with pre-cancer.

- Goal is to prevent progression of precancer.

- Reflects an oncologists viewpoint:
  “Drugs kill pre-cancer even better than cancer.”

- Evaluation is usually by RCT with invasive cancer incidence as the endpoint.
Behavioral Change

• Focus is on the well individual.

• Goal is to prevent risky behaviors.

• Reflects a health educator’s mindset:
  “If you don’t change your foolish habits, you will get cancer or some other bad disease.”

• Evaluation usually based on RCT with behavior or physical measurement as the endpoint.
Public Policy

- Focus is on **populations**, not individuals.

- Goal is to change aspects of the political, social, and physical environment that contribute to cancer.

- Reflects an **epidemiologist’s** mindset:
  
  “To effectively lower disease rates one must intervene at the population level.”

- Evaluation usually is by **analyses** of historical patterns of risk factor prevalence or **mortality rates**.
Two Key Questions For Evaluating a Cancer Prevention Strategy

1. Does it work?
   “Is the strategy effective in reducing cancer occurrence or death?”

2. Is it worth doing?
   “Do the beneficial effect of the strategy merit the side-effects and costs?”
Answering “Does it work?”

1. Requires a valid test of the hypothesis, usually by an RCT.

2. A decrease in cancer mortality will be more convincing than a decrease in incidence.

3. Effects on intermediate markers are less convincing.
Answering “Is it worth doing?”

1. Focus is **estimation**, not testing hypotheses.

2. **Precision** of estimates is important.

3. Relevant measures are: preventive efficacy, adverse effects, costs, and acceptance by target group.

4. Usually measured by large-scale observational studies.
The Need for Randomized Trials:
The example of Beta carotene 1981-1996
Beta carotene structure

“Human cancer risks are inversely correlated with (a) blood retinol and (b) dietary beta-carotene. If dietary beta-carotene is truly protective--which could be tested by controlled trials---”

“The results of both case-control and cohort studies show a remarkable consistency for the association of increased lung cancer risk with low amounts of dietary beta-carotene or low plasma beta-carotene concentrations.”

CONCLUSIONS. “In persons with a previous nonmelanoma skin cancer, treatment with beta carotene does not reduce the occurrence of new skin cancers over a five-year period of treatment and observation.”

“Unexpectedly, we observed a higher incidence of lung cancer among the men who received beta carotene than among those who did not (change in incidence, 18 percent; 95 percent confidence interval, 3 to 36 percent).”
ATBC Investigators (1994).

The graph shows the incidence of lung cancer over years for two groups: Beta carotene and No beta carotene. The graph indicates a higher incidence in the No beta carotene group compared to the Beta carotene group. The p-value is 0.01 by the log-rank test.

Conclusions: “…. beta carotene and vitamin A …may have had an adverse effect on the risk of death from lung cancer, cardiovascular disease, and any cause in smokers and workers exposed to asbestos.”
Caret Investigators (1996)

Conclusions: “In this trial among healthy men, 12 years of supplementation with beta carotene produced neither benefit nor harm in terms of the incidence of malignant neoplasms, cardiovascular disease, or death from all causes.”
Physicians’ Health Study (1996)

**Conclusions:** “Treatment with beta carotene, vitamin A, and vitamin E may increase mortality.”
WHY DID WE GO WRONG?

• Misinterpretation of dietary associations.

• Over-reliance on epidemiological and laboratory data without an RCT.

• Adherence to an unproven theory of benefits of dietary anti-oxidants.
CONCLUSIONS

• Beta carotene and other “anti-oxidant” vitamin supplements do not lower risk of cancer, cardiovascular disease or all-cause mortality and might increase risk.

• The billions of dollars that are still spent on these supplements are wasted, and perhaps will cause harm.