Put Us Out of Business—Please!

It’s a well-guarded secret that I spent much of my early career in colon cancer prevention, evaluating numerous chemopreventive agents, sacrificing hundreds of mice with chemically induced colon cancer annually. Of course, I didn’t find the magic bullet. If I had, I guess it wouldn’t still be such a secret! But despite the fact that I was eventually seduced by the glory of clinical investigation, I’ve never lost my passion for prevention.

Working in cancer prevention is not easy. Although preventing cancer in mice might not be so hard, working this out in people is pretty complicated, especially when it’s not quite clear what the major risk factor is for a given disease. Tobacco control and colonic polyp control have had a striking impact on the incidence of lung and colorectal cancers, respectively. Those are common diseases, and we had a pretty good idea of where to start, but the payoff has been huge! We hope that increasing use of the human papillomavirus vaccines will have a similar impact in related cancers. That story is still unfolding.

But how do we tackle other common cancers, especially those increasing in incidence, like breast and prostate cancer, in which the etiologic factors or precursor lesions are less well defined? At least we have effective early diagnostic and therapeutic strategies for these patients, but wouldn’t it be better not to have to deploy them?

I find the clinical aspects of prevention science, especially chemoprevention, to be extremely daunting. Even with a promising candidate agent, there are so many issues to resolve in trial design. Age range within the cohort, length of treatment, and use of surrogate end points are just a few. And of course, the cohorts are large and you need a virtual army to recruit and retain subjects, not to mention ensure adherence. The price tag for such a trial is enormous.

Then consider the investigators, who seem to need the patience of Job. Data maturation can take years or even decades, not to mention the fact that, while doctors always get thanks for treating diseases, none ever gets thanked by someone who never got sick! So this field is definitely not full of immediate gratification.

Therefore, it’s not a surprise to me that cancer prevention has not been a priority in drug development. This reality was recently emphasized in an elegant article by Heidi Williams and colleagues from MIT. They applied economic models (I confess I didn’t understand the math), providing evidence that private firms underinvest in long-term research and, in fact, are discouraged from investing more. As a result, the value of life years at stake is very large. Williams et al provide some solutions for this: policy changes to accept surrogate end points, subsidies for research and development, and patent design, especially patent duration.

I would pose that another solution might involve our NCI Clinical Trials Network (NCTN). I have argued before that we need a publicly funded clinical trials network to do important work for which there is no sponsor. The infrastructure exists and has been used for prevention studies, although not many. Why not expand the capability there and shift the focus of the NCTN away from therapeutics and into prevention? This would give this important and difficult area of clinical science a real home and encourage more young investigators to apply their talents. And the NCTN can be a suitable partner with the private sector interested in developing these new drugs.

No matter how clever or effective we are at prevention, cancer will not disappear. But we need to think as a community, more than we do now, about developing strategies for prevention. It’s only through prevention that we can reduce the burden of cancer with the sequelae of cancer treatment—and the associated costs—on society. We can do this.

Reference