The Promise of a Cancer-Free World: Where Are We?
The Presidential Address from the 35th Annual Meeting
of the American Society of Preventive Oncology (ASPO)

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Over the past several decades, there have been many individuals who have in some way contributed to where we are in terms of conquering cancer and have paved the way for us to conduct our research today. Some of these individuals did not even know that they had a profound impact on the war on cancer. Take for example, Henrietta Lacks. She did not know or even comprehend that her cervical cancer cells were taken and used by Dr. George Gey to create the HeLa cell line (1), the first cells grown successfully in culture, which contributed to many, many discoveries, for example, the Human Papillomavirus (HPV) vaccine (2), that many of us have used to discover ways to end cancer. In examining the promise of a cancer-free world, I am going to focus on 4 numbers, as a good epidemiologist would. At this meeting, we celebrate: 40 years since the signing of the National Cancer Act, the 35th anniversary of the founding of ASPO, the 20th anniversary of the start of the journal, Cancer, Epidemiology, Biomarkers and Prevention (CEBP), and 1—the impact one person has on ending cancer. The main message of my talk is “You Are the Answer to Cancer” (Fig. 1).

35: ASPO’s 35th Anniversary

In 1976, ASPO was started with a Board of Directors of 9 men plus the Founding President, Daniel Miller, with David Schottenfeld as the first Secretary/Treasurer. The areas of focus for ASPO members are aligned along the Cancer Control Continuum of prevention, early detection, diagnosis, and survival (3). ASPO was the first professional society to solely focus on cancer prevention and control.

Cancer prevention and control, as an area of scientific inquiry, has a rich history, beginning in 1913 with the precursor to the American Cancer Society (ACS; ref. 4, 5). More recently, there have been several frameworks and foundations that have helped to shape and define the field. In 1982, Greenwald and Cullen defined cancer control as "the reduction of cancer incidence, morbidity, and mortality through an orderly sequence from research on interventions and their impact in defined populations to the broad, systematic application of the research results” (6). The Division of Cancer Prevention and Control was formed that year at the National Cancer Institute (NCI), with Peter Greenwald as the director (3). In 1994, the National Cancer Institute of Canada followed with their framework for Cancer Prevention and Control (3). In 1997, The Division of Cancer Control and Population Sciences was formed at the NCI, with the first director being Barbara Rimer (3). Rimer and Hiatt provided a modernization of the current cancer control strategy of NCI to include: the concept of trans-disciplinary research teams, a shared conceptual framework, a link between basic biology and population science, and funding for programmatic trans-disciplinary science initiatives (5).

20: The 20th Anniversary of CEBP

In 1991, cancer prevention and control scientists felt that they needed their own journal to report their results. CEBP, a journal in the AACR family of publications, became the official journal of ASPO with Peleyo Correa as the first editor-in-chief (7). To date, there have been 4,494 articles and reviews published in CEBP through November 2010 (7). More than 43% of those articles have been cited more than 200 times. Several important findings have been published in CEBP, including results on HPV infection and cervical cancer risk, genetic susceptibility and cancer, nutrition and energy balance, cancer survivorship, biomarker discovery and characterization, and behavioral interventions (7).

40: The 40th Anniversary of the National Cancer Act

In this section, I am going to focus on the history of the National Cancer Act of 1971, the progress that has been made in cancer prevention and control since 1971, future areas that are ripe to explore, the challenges researchers face in moving these areas and others forward, and my suggestions for what it will take to end cancer.

History of the National Cancer Act of 1971

The burden of cancer was evident to many in the first decades of the 1900s. In 1937, the National Cancer
Institute Act, crafted by Senator Magnuson, was signed by President Franklin D. Roosevelt to establish the NCI in the Public Health System with a starting budget of $700,000 per year (8). In 1944, the NCI was incorporated as a division of the NIH, and the cap on appropriations to the NCI was removed. During the 1950s and 1960s, Congress increased funding to the NIH, with the NCI getting a large share of those funds (8).

In the late 1960s, however, NCI funding leveled off, which actually resulted in existing programs being reduced by 10% to 15% (8). For example, in 1969, only $200 million per year was allocated to cancer research (9). Enter Mary Lasker, a wealthy, influential, connected woman who was outraged at the fear and death cancer was causing, concerned about the reduction in funding for cancer research, and, like many other lay persons, had the perception that the NIH and scientists only cared about research and not human suffering (10). Mrs. Lasker and her fellow influential colleagues on the Panel of Consultants worked their influence and publicity to have Senators Yarborough, Javits, and Kennedy introduce legislation for the National Cancer Act in 1971 (8).

From their successful business experience, this group knew how to get things done. One strategy that Mrs. Lasker and her Panel used was publicity—an Ann Landers column and strategic planning—an analogy with the then successful space program. In 1971, the annual expenditures to land a man on the moon in the United States were $19 per person (equivalent to $100 in 2009) compared with $0.89 per person (equivalent to $5 in 2009) for cancer research (8). Mrs. Lasker and her group knew what it took to get a man on the moon: (i) a commitment from the highest office in the nation; (ii) dedicated funding and a plan; (iii) brilliant people from different disciplines working together toward a common goal; (iv) risk taking with successes and failures that served as lessons learned; and (v) thinking out of the box. This is exactly the strategy they used to address the cancer problem.

With this work by the Panel of Consultants and support in Congress, the stage was set for President Richard Nixon to sign the National Cancer Act in December of 1971. In signing the legislation and announcing “the war on cancer,” President Nixon stated, “As this year comes to an end, cancer remains one of mankind’s deadliest and elusive enemies” (9). In approving the National Cancer Act of 1971, Congress stated that this act would “end cancer by 1976—our nation’s bicentennial.” The act did increase funding to the NCI (from $181 million in 1971 to $580 million in 1974; ref. 8), and the amendment in 1974 also expanded the authority of the NCI director, established cancer centers, programs, the National Cancer Advisory Board, and cancer control, among other initiatives (11).

Progress in cancer prevention and control

Overall, we have seen many successes in the war on cancer—many malignancies are now curable; we have better treatments for many cancers including chemotherapy, surgery, radiation therapy, etc.; and we have addressed symptoms and quality of life for cancer patients. Five-year cancer survival rates document our progress. In 1975 to 1977, 50% of adults and 58% of children survived for 5 years after a cancer diagnosis; in the period of 1999 to 2005, 68% of adults and 80% of children survived for 5 years after a cancer diagnosis (12). Along the way, many important scientific discoveries were made by dedicated researchers focused on ending cancer, each “one” contributing to a cancer-free world.

Before 1971, several researchers each reported significant discoveries that laid the foundation for research to come in later years. For example, in 1775, Percival Potts discovered the link between cancer of the scrotum and soot in chimney sweeps (13). His warnings to change the practices of these workers went unheeded in England—where rates of this cancer continued to be elevated in chimney sweeps for several years—but were heeded in Holland where rates decreased in chimney sweeps (14). Ciufo discovered the HPV in 1907 (2), Doll and Hill identified the link between smoking and lung cancer in 1950 (15), George Gey took cervical cancer cells from Henrietta Lacks in 1951 (1), and in 1964, the first Surgeon General’s Report on Smoking was released (16). Cancer screening tests were developed before 1971—the Pap test by George Papanicolaou in 1928 (17), the first equipment dedicated to breast imaging in 1956 by Leborgne (18), and screening for colorectal cancer (CRC) using sigmoidoscopy by Cameron in the 1960s (19).

In the 1970s, researchers began moving from observation to linking cause and effect in an orderly sequence. For example, the cohorts of the Harvard group, led by Willett, Colditz, and Stampfer, such as the Nurses Health Studies, the Professionals Follow-up Study, and the
Physicians’ Health Studies were launched, to subsequently publish findings related to cancer etiology, incidence rates, and survivorship (20–22). Antismoking regulations were instituted in the 1970s (15) which facilitated the development of research into how to best enforce these regulations and assess their impact on cancer and smoking rates. Michael Sporn coined the term “chemoprevention” in 1976 (23). Jordan found that tamoxifen prevented mammary tumors in rats in 1974 (24), building on his earlier discovery of the estrogen receptor in breast cancer (25). HPV was linked to cervical cancer by zur Hausen in 1974 as well (26). Jimmie Holland founded the discipline of “psycho-oncology” in 1977 (27).

The 1980s saw researchers developing new tools and paradigms to address cancer prevention and control. For example, Gritz published a seminal paper on the health consequences of smoking in women (28). The field of molecular epidemiology was established in 1982 by leaders such as Perera, Spitz, and Shields (29, 30). The precursor to the Women’s Health Initiative (WHI), called the Women’s Health Trial (focused on diet and breast cancer) was launched by Henderson and Prentice in the 1980s (31). The widespread use of mammography was promoted in the 1980s by leaders such as Meissner, Smith, and Rimer (32). In 1988, the Bethesda System was introduced for classifying Pap tests (33), and Vogelstein published the multistep model of carcinogenesis (34).

Genetics and survivorship burst on the scene in the 1990s. BRCA1 was discovered in 1990 by King (35) and the discovery of BRCA2 followed by Wooster in 1994 (36). Ganz started research in the area of survivorship care in 1990 (37). An association between lung cancer and genetic malformations and environmental tobacco smoke was reported by Hecht in 1993 (38). The association of COX-2 in pulmonary in adenomas and colorectal cancer was reported by DuBois in 1994 (39). Rowland became the first full-time Director of the Office of Cancer Survivorship at the NCI in 1996 (40). The results of the P-1 trial—known as the Breast Cancer Prevention Trial—were released by Fisher in 1998 and showed that tamoxifen reduced breast cancer risk by 50% in women at risk for the disease (41). Vernon published a seminal article on CRC screening promotion research in 1997 (42). Gillison first reported an association between HPV and oral cancer in 1999 (43).

The first decade of the 21st century was the decade of patient-reported outcomes (PRO) and chemoprevention trials. Health outcomes research and PROs, which include health-related quality of life and other patient-reported symptoms like physical functioning, pain, nausea, etc., were introduced by researchers including Weeks, Lipscomb, and Cella in 2000 (44–46). In the area of chemoprevention, the WHI trial results were published which indicated that estrogen plus progesterin (HRT) increased the risk for breast cancer (47); that a low-fat diet had no effect on breast cancer incidence (48); and that the reduction in the use of HRT that came nationally as a result of trial results, coincided with a decrease in breast cancer incidence in the United States (49). Other chemoprevention trials reported results also: the Prostate Cancer Prevention Trial (PCPT) found that finasteride prevented prostate cancer (50); several aspirin trials found that aspirin (both 80 mg/d and 325 mg/d) reduced the risk of developing adenomas (51–53); and the study of tamoxifen and raloxifene (STAR) concluded that raloxifene also prevents breast cancer, with a better safety profile in some women than tamoxifen (54). Other important findings of the decade included demonstration of the value of prophylactic surgery by Rebbeck (55), the differential effects of tobacco addiction on underserved populations in 2005 by Wetter (56), the ability of the HPV vaccine to prevent HPV 16 infection and cervical intraepithelial neoplasia (CIN) by Koutsy in 2006, and in 2007, named “the year of the GWAS”—many Genome Wide Association Studies were reported (58).

Future areas to explore in cancer prevention and control

I would like to suggest areas that are ripe to explore in this decade and beyond, areas that each of us can ask what am I/can I do to contribute to a cancer-free world.

1. **Etiology:** We need to explore the multilevel causes of disease, including spatial factors. We also need to further explore the role of biomarkers on measuring “risk,” and, who is in the “at risk” population.

2. **Disparities:** The widening gap in cancer rates between racial, ethnic, education or income-level groups, and the continued effects of the economy on health need to be examined, especially as some people put health second to food, shelter, and employment concerns.

3. **Environment:** Gene-environment interactions across the lifespan need to be explored in detail. The role that biomarkers play in perhaps identifying these interactions early, therefore, prompting prevention and/or early detection strategies needs to be explored.

4. **Personalized medicine:** This is one of the “buzz” words today, but can we provide a personalized prescription for cancer prevention and control that includes genetic markers, behavioral profiles, environmental factors, social influences, and policy factors? That is tailored to individual demographics, reading level, language? Delivered by a clinician or a lay navigator? What is the prescription—behavioral, medical, and/or social change?

5. **Prevention:** Several areas are high priority for prevention including: (a) the Obesity epidemic—what is the role of biologic mechanisms and behavioral factors? What can we learn from using animal models along with human studies? (b) Sun exposure vs. Vitamin D: can genetics help determine who benefits from sun exposure? (c) What about innovative chemoprevention agents such as those drugs used to treat other illnesses, like metformin,
or food products, such as freeze dried raspberries which are being tested by Stoner and colleagues Ohio State University (59), and (d) when considering where to go next in chemoprevention trials, the A, B, C’s of chemoprevention need to be addressed: Agents, Biomarkers, Cohorts, Design, and Endpoints.

6. **Adherence:** Why won’t people do what we know prevents cancer? For example, tamoxifen and raloxifien both have been shown to prevent breast cancer and are approved by the Food and Drug Administration for this indication; yet, uptake is only about 30% among women at risk (60). Aromatase inhibitors are now approved as adjuvant therapy for women with hormone receptor positive breast cancer. Hershman and colleagues found that 31% of women prescribed these agents discontinued use and 28% of those still using them had adherence problems, and among these women, survival rates were lower (60). In the area of smoking cessation—can we understand addiction better—especially among those with cancer who continue to smoke, as evidence is mounting that tobacco smoking may stimulate angiogenesis in smokers (61). The last example is the HPV vaccine—the vaccine has been proven to prevent cervical cancer but yet the prevalence of those at-risk females getting the first shot is only 40% and the prevalence of those receiving all 3 shots is 30% in the United States (62).

7. **Early detection:** Recent reports from the Institute of Medicine on screening for breast cancer and cervical cancer have created chaos and confusion about who, when and how to screen among both providers and women (63). Smith and colleagues estimate that only 54% of eligible women are adherent for regular mammography (62). Informed decision-making for prostate cancer screening needs to be disseminated to clinical practice. Screening for CRC continues to be underserved in the adult population compared to other screening tests (64). Quality and access issues still are widespread, even with the Centers for Disease Control and Prevention (CDC)-sponsored Breast and Cervical Cancer Early Detection Program (BCCEDP; ref. 65). It is not clear what role the Patient Protection and Affordable Care Act (62) will have on access for underserved populations. Newer tests are being explored to screen for common cancers, but is newer better and/or more cost-effective? For example, FOBT has been proven effective in reducing mortality from CRC (62), but are newer devices, for example, the “pill cam,” (66) better? What about fatal cancers where we do not have any valid screening tests? We need to continue exploring ways to detect, for example, ovarian and pancreatic cancer, earlier.

8. **Survivorship:** There are almost 12 million survivors in the United States (12) who have unique problems and side effects from treatment such as lymphedema, congestive heart failure, fatigue, depression, and pain (67). Can we develop new assessments of toxicity and extend these assessments into clinical practice? What about assuring quality and appropriate treatment for those diagnosed with cancer? Alderman and colleagues found that only 81% of elderly women received radiation therapy after breast conserving treatment (68). New areas to explore include the etiology of recurrence and new primaries and ways to prevent these outcomes as well as detect them early in survivors (69). Will the realignment of the cooperative group structure (70) provide new opportunities for cancer prevention and control research in this population?

9. **Comparative effectiveness research (CER):** There are multiple definitions of CER, but this area includes the use of large observational and clinical databases and results from interventional trials to “inform clinical and health policy decisions” (71). Can we use what is learned to change practice and impact cancer incidence, morbidity, and mortality?

**Challenges to researchers**

To explore these areas, I have described above, there are several challenges that must be addressed. Each one of us can be the answer to these challenges with innovative solutions, for example, as Harold Freeman did using patient navigation in New York City (72) to address high rates of breast cancer mortality among African-American women.

The major challenge we face is the magnitude of the problem: 1,529,560 new cancer cases were diagnosed in 2010 (12). 569,490 Americans are expected to die this year from cancer (12); that is more than 1,500 people per day, equal to 5 jumbo 747’s crashing every day for 1 year (73). Approximately, 11.4 million Americans with a history of cancer are alive (12). The NIH estimates that the overall cost of cancer in 2010 at $263.8 billion (12). The number of Americans who die from cancer each year is more than all those who have died in all US wars combined (73).

This challenge was conveyed to me by individuals in several of my research studies. The first woman I interviewed for my dissertation was a young African-American woman who had an abnormal Pap test, but would not return for treatment, saying, “I don’t want to have my womb removed because I will stop being a woman to my man” (74). In our work in Appalachia, we soon learned from community members that “we don’t talk about cancer” (75). In North Carolina, several African-American men told us in focus groups that “If they can put a man on the moon, they can cure cancer” (76).

**Disparities**

Even though this was mentioned as an opportunity, it is also a major challenge that this country faces. Is patient navigation one solution? Freeman’s navigation program showed a dramatic increase in 5-year breast cancer
survival rates in Harlem Hospital after implementation (72). However, to address disparities in cancer risk factors, incidence, and mortality, will we need to also address nonhealth issues such as poverty and education? While we are developing newer technologies to disseminate health-related interventions, will these technologies reach underserved populations, or should we work within the confines, for example, of the digital divide, and use old-fashioned ways to educate communities such as billboards? Can we eliminate barriers to appropriate services at medical institutions such as not using self-reported race/ethnicity or failure to routinely provide translation services routinely?

**Access**

Appropriate access includes exposure and acceptability of the services to be delivered. Can we improve the dissemination and uptake of efficacious interventions to all populations? For example, less than half of the states in the United States have access to the National CRC Control Program (77). Clinical services need to be available and affordable—will health care reform solve this problem? Trust in and ability to communicate with health care providers is also important. Hispanics, for example, are more likely to report problems communicating with their physician compared with whites (33% vs. 16%, respectively; ref. 78). Acceptability is related to: knowledge (source and literacy level), beliefs (self and others), and barriers (personal, interpersonal, or system).

**Partnerships**

Cancer centers include basic, clinical and population science researchers. Forging partnerships with basic and clinical researchers can often be challenging. Trans-disciplinary teams, however, are needed to address complex problems related to cancer prevention and control, but are we prepared to work in teams? Another buzz word is "translational research" (3). T1 (bench) to T2 (bedside) research is discussed a lot but where does cancer prevention and control fit? T3 research—translation to the "sidewalk" or the community—is not as well explored.

**Funding**

The current NIH payline is the lowest that it has been in several decades. Fewer grants are being funded, and changes in peer-review are taking place in terms of application formats, the scoring system, and review panels (79). There is a greater focus on timelines and deliverables, with carryover of funds from 1 year to the next becoming a thing of the past. This is now the age of fiscal responsibility, even though, as stated by Kufe "...we have invested at a level of approximately 1/10 of 1% in the research required to cure and prevent a disease that will take the lives of 25% of our population" (80). It is feared that the impact of this lack of funds will be the greatest on junior investigators. "Success" may, therefore, need a new metric, or alternative sources of funding must be sought and accepted. With the increased burden of the uninsured in clinical care, the burden of uncompensated care is also increasing. What will happen next to unfunded mandates that we all participate in, such as outreach activities, as clinical services need more of any revenue generated for this uncompensated care? Lastly, administrative and regulatory burdens are increasing. Institutional Review Boards, Health Insurance Portability and Accountability Act regulations and internal review groups are all demanding more time and work from researchers.

**Surveillance of cancer incidence, mortality, and survivorship**

Can we obtain more representative coverage of these rates in the United States by increasing the role of state registries, completeness in data items abstracted, and follow-up of cancer patients, including the documentation of all treatments received? Other types of registries should be developed, for example, registries for families with hereditary cancers (81). Treatment summaries are needed to capture treatment information on patients—these would be helpful especially in population-based cohorts where treatment information is lacking, or not reliable from self-reports.

**New paradigms for research inquiries**

Community-based participatory research (82) needs to be better defined and used to implement successful programs for sustainability. Multilevel interventions (83) are promising new strategies, but do we have the tools needed (definitions, analytic methods, designs, peer review committees, and journals to publish results) to move forward in this area? Innovative approaches are needed to solve many tough questions—we need to find ways to include new disciplines in our teams and "systems" models (83). Cross-institution work is also becoming more important to address hard questions, but we need a mechanism for rewards in our institutions, a process for getting credit for this type of work, and ways to define oversight.

**Reporting results**

Ways to disseminate and diffuse efficacious interventions to clinical care are needed, for example NCI just launched a new website, "Research to Reality," to help disseminate research practices to communities (84). Can we disseminate both evidence-based and evidence-informed interventions? In terms of reporting our findings, we have a responsibility to convey accurate results, that is, do not call a nonsignificant effect, "significant," and not to confuse the public with our conclusions.

**How do we end cancer?**

If we go back to the space race analogy, after we sent a man to the moon, another challenge arose. Astronauts could not use pens to write in space because of zero gravity and pencils were not safe because the lead could break off and the wood was flammable (85). This problem
was solved by a private investor, Paul Fisher, with a good idea, the Gravity Pen (85). To end cancer, I propose 4 P’s.

1. **Policy:** This includes expanding smoke-free laws, nutritional information on restaurant menus, mandating completeness in cancer registry coverage, patient navigation reimbursed as part of care, treatment summaries for all cancer patients as part of health care reform, and increased funding and coverage for the NBCCEDP—to meet their goal of increasing the percentage of eligible women who use this service from 15% to 70% (65).

2. **Publicity or the power of the media:** This is similar to what Mary Lasker did in 1971. How powerful is it on Sunday National Football League games to see the teams running up and down the field with pink shoes, socks, sweat bands, and hats? What about the live coverage of Katy Couric’s colonoscopies—how does that impact CRC screening? Or Lance Armstrong and his LIVESTRONG Foundation (86) and the publicity around the WHI Hormone Replacement Trial results (47–49)?

3. **Partnerships:** We need to establish partnerships to create a cancer-free world—these partnerships should include federal agencies, public/private ventures, be across institutions, across countries, and include organizations and societies. For example, all 4 childhood cancer cooperative groups merged in 2000 to form one large cooperative group—the Children’s Oncology group (87). Almost all children with cancer are treated at a children’s hospital with access to cooperative group protocols, resulting in a remarkable decline in cancer mortality rates among children with cancer (88).

4. **People:** “You are the ‘one.’” My challenge to you is to find what you can do to be the answer to cancer and contribute to a cancer-free world.

In summary, this quote by John T. Kalberer, Jr. in March 1975 still rings true today: “. . . money alone will not solve the cancer problem. In order to progress in the fight against cancer, the talents of individual investigators is essential. There are more opportunities in cancer research and more promising areas for accelerated exploration than ever before” (8).

Perhaps each of us needs to be as Mary Lasker was and organize our influential group of friends to change policy, use the power of the media, and form partnerships to realize a cancer-free world.

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