Collaborating to Conquer Cancer: Lessons From Our Children

Michael P. Link

INTRODUCTION

Welcome to the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO). I invite you to share in the exciting findings that will be presented at this year’s meeting and to enjoy the opportunity to connect with current and former colleagues. It has been my great privilege to serve as ASCO president—one of the most exciting years of my professional career. This has been a year of challenges and change—both for those of us who provide cancer care and for the patients we serve. The pace of discovery remains exciting, but our capacity to deliver high-quality care is being challenged as never before. But I believe that we have the opportunity to lead the way forward.

Before I begin, I would like to thank my family, who have provided loving support and inspiration throughout my career and who remind me of the importance of family in all of our lives. ASCO is a complex organization that depends heavily on a cadre of enthusiastic volunteers. I have had the privilege to work with a fantastic group of individuals who represent the spectrum of subspecialists in our society as well as patient advocates and others. Their work is critically important to ASCO’s scientific, educational, and policy accomplishments. Special thanks go to Dr Hal Burstein, who chaired the Education Committee, and Dr Ron Levy, who chaired the Scientific Program Committee, and to all their track leaders and subchairs. They have devoted considerable energy to making this a wonderful meeting.

My sincere thanks to the ASCO staff. Led by our CEO and former ASCO President Allen Lichter, this is a productive, accomplished, and accommodating group of professionals. It has always been my pleasure to work with them, but in particular over the past year.

I dedicate this talk to patients and families I have cared for over the course of my career. As pediatric oncologists and parents know very well, there is nothing more motivating than a sick child, nothing to keep one honest and humble like the probing questions of an adolescent, and no greater pleasure than to have intervened in a child’s life—to have the gratification of seeing that child grow up, realize his or her dreams, and start a family. My patients have been my partners in a wonderful profession and collaborators in my own efforts to advance the field. I am grateful for how much they have enhanced my career and my life.

STATE OF ASCO AND THE STATE OF CANCER CARE

This has been a year of challenges, but it has also been one of accomplishments. With this year’s record number of new members, ASCO membership now includes more than 30,000 members in 122 countries.

In November, we celebrated the 40th anniversary of the National Cancer Act, which inspired the so-called war on cancer. We can be proud of what has been achieved in the four decades since it was enacted. In the United States, 5-year survival has increased dramatically, with the rate of deaths resulting from cancer dropping 18% since the early 1990s. Twelve million cancer survivors are alive in the United States today—up from just 3 million in the 1970s. Patients are living longer and with improved quality of life.

Looked at another way, more than one million US cancer deaths have been averted over the past 18 years.1 There is still work to be done, but members of ASCO deserve much credit for this progress, and the growing number of survivors is a testament to what has been accomplished.

Our challenges are many. The rising cost of medical care—and cancer care in particular—is not sustainable and must be addressed by the medical community. As one effort, ASCO joined the American Board of Internal Medicine Foundation’s Choosing Wisely campaign, first proposed in 2010 by Dr Howard Brody in his New England Journal of Medicine commentary.2 Dr Brody challenged medical specialties to take a critical look at their fields and to identify five costly practices that are commonly performed despite little or no evidence for their efficacy. Led by our Cost of Cancer Care Task Force, ASCO has formulated a top-five list of common,
costly procedures in oncology that should be questioned.\(^3\) Selections were based on a comprehensive review of published studies and current guidelines and on input from more than 200 oncologists, including ASCO’s Clinical Practice Committee, state oncology society leaders, disease experts, and patient advocates. Out of this extensive dialogue came agreement that we should question these five interventions before ordering them:

- Use of chemotherapy for patients with advanced cancer for whom a focus on palliative care and symptom management might be of greater benefit
- Use of advanced imaging for staging of early breast cancer
- Use of advanced imaging for staging of early prostate cancer
- Routine use of surveillance imaging to monitor asymptomatic women with breast cancer after therapy with curative intent
- Use of white cell–stimulating factors for patients at low risk of febrile neutropenia

To be clear, these are not five interventions that should never be performed. In selected situations, they may be indicated, but in most clinical situations, they are likely to contribute little to either prolonging survival or improving quality of life and therefore are likely to contribute only to the costs of care. We owe it to our patients and to society to question their use.

Another major issue has emerged over the past few years, and it is a growing threat to the well-being of our patients. Drug shortages—primarily of generic sterile injectable drugs—are having a major impact on cancer care. Multiple factors are responsible, and there is no obvious solution in sight. The number of drugs in shortage has escalated over the past 6 to 7 years. It involves multiple drug classes, many of which affect the care of our patients—including at least 23 chemotherapy agents that are in short supply during the past 2 years.\(^4,5\) Some of these drugs are key ingredients for curative therapy of several pediatric and adult cancers.

ASCO has brought national attention to this issue through participation in Congressional briefings and hearings; meetings with leadership of the Department of Health and Human Services, the National Cancer Institute, and the US Food and Drug Administration; and a concerted media outreach. We have provided extensive input into legislation, which has resulted in increased media outreach. We have provided extensive input into legislation, which has resulted in increased awareness of the issue and in the US Food and Drug Administration's responsiveness to this crisis. In the past, when shortages have threatened our patients, we have focused on Band-Aids to cover a lesion that is almost certain to recur. We need a better understanding of the root causes of shortages—and strategies that provide a durable solution.

First, high-quality care requires multidisciplinary collaboration. Second, what we learn from tumor tissue is critical, including its impact on risk stratification and therapy selection. Third, cancers are heterogeneous collections of diseases within traditional tumor types. Finally, we have a duty to the survivors: to understand the consequences of our therapies and to deliver treatments with these consequences in mind. So let me focus a bit on each of these lessons.

First, a bit of background. Cancer is not a trivial problem. Outside of the newborn period, it is the leading medical cause of US deaths in young people—exceeded only by accidents, homicides, and suicides. Nor is childhood cancer particularly rare. One in 300 children is diagnosed with cancer before the age of 20. There are approximately 12,500 new cases of cancer in children and adolescents younger than 20 each year in the United States, and more than 2,000 US children and adolescents died as a result of cancer in 2004. Taken together, childhood cancers represent the sixth most common cancer overall, exceeded only by the major adult cancers.

Progress in the management of children with cancer is one of the great success stories of modern medicine. There has been a dramatic improvement in outcome for almost every category of childhood malignancy. For childhood acute lymphoblastic leukemia (ALL)—the most common childhood cancer, which accounts for almost 30% of cases—the progress has been most gratifying. This is a disease that was virtually incurable in the 1960s. In the most recent trials, 5-year survival among children with ALL has approached 90%—truly spectacular progress over four to five decades. Even more amazing is the fact that very little of the progress in ALL—and for that matter in any of the childhood cancers—emerged from development of new agents. Virtually all drugs used today to cure childhood cancers were available when I started my residency many years ago. So how do we explain these results?

Perhaps there was an element of luck. Most pediatric cancers proved to be remarkably responsive to irradiation and to some of the earliest anticancer chemotherapeutic agents. Many patients with disseminated malignancies—including widely metastatic solid tumors—responded to single agents, and many achieved complete remission. Application of these agents in combination adjuvantly led to durable remissions and cures.

And perhaps the cancers of childhood are not terribly smart. In his remarkable ASCO presidential address last year,\(^6\) Dr George Sledge divided malignancies into stupid and smart cancers. The key distinguishing feature related to the number of mutational drivers and the number of total mutations in the tumor genome. As Dr Sledge presented so eloquently, stupid cancers are responsive, whereas smart cancers evade therapy through presentation with or development of resistance. The degree of stupidness can be quantified by the number of detectable mutations across the tumor genome. A study by Gaddy Getz et al at the Broad Institute showed that compared with stupid cancers with few mutations, smart carcinogen–induced cancers such as melanoma and lung cancer have a more than 100-fold increase in the number of mutations. A majority of childhood malignancies would qualify as stupid cancers in Dr Sledge’s classification and are remarkably responsive to treatment. That has been our good fortune.

Other factors worked in our favor as well. First, pediatric patients are capable of withstanding and recovering from the most-intensive therapies. They are mostly young people in prime physical condition, free of comorbidities—a situation that is regretfully changing rapidly.

Let me turn now to the theme of my presidential year—collaborating to conquer cancer and the lessons we have learned from experiences of pediatric oncology. Today, I will share my view that the remarkable successes in pediatric oncology would not have been possible without collaborations and that our collective goal to conquer cancer depends more than ever on partnering within and across specialties. I believe that pediatric oncology can serve as a model for the future, a future in which we achieve the goal of conquering cancer. In short, here are a few lessons we can learn from our children.
as more young people develop obesity. Second, we faced a less intrusive regulatory environment in the past, which undoubtedly facilitated the launch and conduct of our studies. And, of course, early successes reinforced the optimism that we were making progress. We cannot ignore the visionary leaders who were a major ingredient of early successes. It is no secret that some of the early innovators in oncology—including Sidney Farber, Tom Frei, Emil Freireich, Jim Holland, and others—cut their teeth on Childhood ALL. Perhaps because we deal with children, pediatric oncologists understand that prolonging a success. It is no secret that some of the early innovators in oncology—including Sidney Farber, Tom Frei, Emil Freireich, Jim Holland, and others—cut their teeth on Childhood ALL. Perhaps because we deal with children, pediatric oncologists understand that prolonging a child’s life by only a few years is insufficient. Durable remissions and curative therapies were an early goal of pioneers. Donald Pinkel, the first director of the St Jude Children’s Research Hospital and the ASCO Karnofsky lecturer in 1978,7 and later Joe Simone optimistically first director of the St Jude Children’s Research Hospital and the enormous contributions that have come from St Jude investigators.

But there is much more to the story of this enormous progress. Our history is really about collaborations among investigators from different specialties—a joining together that facilitated breakthrough findings and promoted early successes. Pediatric oncology pioneered the multidisciplinary approach to patients—something that is second nature to us today. There was early recognition of the need to collaborate beyond the confines of individual institutions. The rarity of individual childhood cancer types made it unlikely that any single institution could accrue sufficient numbers of patients to conduct meaningful clinical trials. In the interest of advancing clinical practice, pediatricians adopted a collaborative approach to clinical cancer research and were willing to participate in clinical protocols written by other investigators. Pediatric cooperative groups emerged as important engines for driving research. Clinical trials became the standard of care in pediatric oncology, with the majority of children with cancer in North America participating. Findings from clinical trials were rapidly incorporated into practice, largely because the best treatment emerging from one trial became the standard regimen of the successor trial.

The rapid fall in cancer mortality among children in North America closely paralleled the establishment and success of National Cancer Institute–sponsored clinical trial cooperative groups for children—a success that has continued with the merger of the four pediatric cooperative groups into the Children’s Oncology Group in 2000. Some cooperative group contributions to pediatric oncology are relatively straightforward. Protocols written by acknowledged experts assured physicians they were administering state-of-the-art therapy. Patients and their parents were similarly reassured. An infrastructure to support clinical trials was supplied even to small institutions, enabling their participation in cutting-edge research. The diagnosis of pediatric solid tumors is notoriously difficult. The cooperative group infrastructure provided central review by experienced pediatric pathologists. In this way, sophisticated technologies and scarce expertise became available to every institution and to every child. Similarly, the establishment of reference laboratories allowed application of the latest diagnostic tools to every case of childhood cancer long before individual institutions were able to offer such testing for routine use. On-treatment review by expert pediatric radiation oncologists assured that radiation oncologists with limited experience in managing rare childhood cancers could leverage the expertise of colleagues with specialized knowledge. The contribution of each of these elements is difficult to quantify, but the overall result is indisputable.

Collaboration With Laboratory Investigators

Among the most productive collaborations have been partnerships with laboratory investigators, which allowed rapid incorporation of biologic findings into the clinic for risk stratification and management. They advanced our understanding that pediatric cancers are heterogeneous collections of diseases within organ-specific or histomorphologic types. Such partnerships began with investigations of acute leukemia, facilitated by the ease of obtaining tumor tissue on repeated occasions from bone marrow and peripheral blood, the ease of making near-pure preparations of tumor tissue, and the relative ease of cryopreserving leukemias in tumor banks from which investigators could withdraw specimens of interest.

In addition to collaboration, our access to tumor tissue was critical to developing key insights into childhood cancers. Beginning in the 1970s, we began to understand the heterogeneity of ALL, both in terms of immunologic diversity and the division of ALL into T-cell, mature B-cell, and B-cell progenitor phenotypes with vastly different clinical presentations and responses to therapy. Subsequently, the molecular heterogeneity of each immunologic type was revealed, resulting in the division of the disease into multiple subsets with differing genetic mutations driving the leukemia, each with a different outcome on regimens then in use. Patients with B-cell progenitor leukemias that appeared identical morphologically could be reclassified based on molecular subtype into subgroups with markedly different prognosis. With contemporary therapy, leukemias characterized by specific trisomies or by TEL gene rearrangements fall into favorable-prognosis subsets of leukemia. By contrast, therapies in use until very recently were clearly inadequate for patients with leukemias with higher-risk features—those with translocations t(1;19), t(4;11), and t(9;22). Yet, empirical intensification of certain phases of treatment was successful in improving outcome even for patients with high-risk features. The result has been a steady, incremental improvement in outcome for all patients with ALL, study by study and era by era. Our most recent studies project that almost 90% of children with ALL will be cured.9

Of course, with improved understanding of the molecular drivers of leukemia, the hope was for the development of therapies directed specifically against the identified targets. The success of this approach is exemplified by recent results for the management of children with Philadelphia chromosome–positive ALL—the highest-risk form of ALL driven by the BCR-ABL tyrosine kinase. This relatively rare subset of children with Philadelphia chromosome–positive ALL had a dismal prognosis even with intensive therapies. Allogeneic stem-cell transplantation seemed to be the only intervention that was curative. However, recent studies have demonstrated the feasibility and efficacy of incorporating imatinib and second-generation inhibitors of BCR-ABL into intensive leukemia regimens for this subset of patients.10 If these results are confirmed, marrow transplantation will no longer be required to cure the majority of such patients.

The landscape of ALL has changed dramatically; we now recognize no fewer than 17 different diseases defined by immunologic and molecular subtype but all looking the same under the microscope.11 Each subtype has its own implications for clinical presentation and response to therapy and thus for risk stratification and choice of treatment. The numbers of patients diagnosed each year in each of these subcategories of ALL make meaningful, randomized clinical trials in the current trial paradigm infeasible.
Our understanding of the heterogeneity of cancers is relevant to virtually every tumor system. In neuroblastoma, the underlying biology is the major determinant of the behavior of the tumor and outcome and thus a key component in planning therapy. In particular, NMYC gene amplification is a key determinant of outcome among infants with advanced-stage neuroblastoma. For pediatricians, tumor sampling and molecular analysis of the tumor are a critical part of diagnostic studies for every newly diagnosed patient for appropriate treatment assignment. For example, proper risk stratification and treatment selection for children with neuroblastoma require detailed assessment of clinical data as well as molecular assessment of the tumor.

Recent data in childhood ALL suggest that things may be more complicated than we had hoped. Analysis of childhood ALL at relapse indicates that a minority of relapses emerge from a genetically distinct clone representing a true, unrelated leukemia. Forty-two percent of relapses emerge from the leukemic clone present at diagnosis with or without the acquisition of additional genetic lesions. But approximately one half of the relapses arise from clonal evolution of an ancestral clone that exists as a minor, unappreciated subclone at diagnosis. This subclone survives chemotherapy, and at relapse, some—but not all—of the molecular lesions found in the leukemic clone at diagnosis are retained. The implication should be no surprise; the tumor is more complex than is appreciated with current molecular studies, which may fail to detect a small population of tumor cells that nevertheless will be responsible for treatment failure. Childhood cancers are not so stupid after all.

A recent study suggests that the problem of tumor heterogeneity extends well beyond childhood leukemia and may significantly complicate the notion of developing a recipe that is personalized to an individual’s tumor. Specimens of metastatic renal cell carcinoma from different sites in the primary tumor and from different metastases proved to have heterogeneous somatic mutations, leading to diversity of tumor phenotype—including gene expression signatures of good and poor prognosis in different regions of the same tumor. Thus, molecular profiling from a single biopsy may severely underestimate the genetic alterations found in a single cancer and may be misleading when used to predict tumor behavior. How important this molecular heterogeneity will prove to be remains to be determined. Nevertheless, the message is clear: It’s complicated.

Survivorship

An important area of cancer care pioneered by pediatricians is the focus on survivorship. In part because we began early on to observe patients cured of their cancers, we were faced with the long-term consequences of our therapies. If one examines the average years of life lost to cancer among patients who are not cured, one can estimate the number of years of survival that can be expected for patients who are cured. For children, this represents nearly 70 years on average—70 years in which to develop and cope with adverse effects of therapy. For elderly adults with cancer who are cured, late effects of treatments with a long latency may never be seen. No such reprieve pertains to children and adolescents who live long enough to develop all of the manifestations of those health effects. Such late effects are not a trivial concern. More than one in 700 individuals now between the ages of 20 and 50 are survivors of childhood cancer. Nearly two thirds of those long-term survivors have at least one chronic condition, and more than one fourth of them have a severe or life-threatening condition.

Early lessons emerged from children treated with irradiation for Wilms tumor and Hodgkin lymphoma, where we learned the devastating effects of high-dose irradiation on bone and soft tissue growth when administered to rapidly growing young children. Late organ toxicities and the development of therapy-related second cancers are among the most distressing late effects observed. Two developments resulted from these experiences. The first was the establishment of further collaboration to study the late effects of therapy and quality of life for survivors. It was accomplished in a systematic fashion—a partnership with survivors of childhood cancer who willingly returned to the clinics where they had been treated years earlier for investigations into their health status. The result was a cataloging of late effects—some predicted and some unexpected—that plague survivors, interfere with their quality of life, and reduce their longevity.

More important was a renewed determination not only to strive for cure but to maximize the quality of life for survivors as well—a sentiment best articulated by one of our heroes, Giulio d’Angio, who believed “cure is not enough.” As a direct result of such studies, pediatric oncologists looked critically at their therapies to determine those components necessary for cure—and worked toward eliminating those components that contributed only to toxicity. This led to attempts to reduce the volume and dose of irradiation—and even to eliminate irradiation entirely in the setting of effective chemotherapy, where the safety of this modification could be demonstrated. An example is management of early-stage non-Hodgkin lymphoma, where we demonstrated that irradiation of primary sites contributed only toxicity, with no improvement in outcome. We no longer prescribe radiation for children with non-Hodgkin lymphoma, nor for most children with Wilms tumor. In the management of ALL, cranial irradiation, once a necessary component of therapy for all children, is now reserved for a small minority at particularly high risk of CNS relapse. Cumulative doses of alkylating agents have been reduced where possible to preserve fertility and reduce the risk of therapy-related leukemia. Cumulative doses of anthracyclines have been reduced and cardioprotective agents have been added to minimize the risk of cardiomyopathy—a complication to which children are particularly susceptible.

Future Challenges

Amid good news about progress in management of childhood cancers, there are some sobering reminders that we still have work to do. If we examine the mortality from childhood cancer as the rate plotted against year of diagnosis over time, the progress that has been made is clear. Also clear is that the curve has plateaued since 2000—and that further advancement is more difficult to demonstrate. It is evident that we have squeezed what we can from traditional chemotherapeutic agents; we have come close to optimizing the gains—including intensification of therapy up to the limits of patient tolerance. We need a new paradigm—one that will involve yet further collaboration if we are to make greater progress.

Optimism about the future is inspired by developments of the genomic era that hopefully stand as the new paradigm for progress. Pathways that drive malignancy have proven to be promiscuous—the number of relevant pathways is finite, and they are important in disparate tumors, so targeted therapies should find applications against multiple tumor types. The utility of imatinib and related drugs in tumors as different as chronic myelogenous leukemia and GI stromal tumor will, it is hoped, prove to be the rule rather than the
exception. The development of crizotinib—an ALK inhibitor—is an encouraging look at the future. ALK activation was discovered as the key molecular abnormality in anaplastic large-cell lymphoma from studies of this rare lymphoma conducted by a pediatric oncologist. That ALK is a key mutation driving a rare subset of adult lung cancers provided an incentive for commercial development of an ALK inhibitor, which has proven to be so promising. But this development proved to be fortuitous for pediatricians. In addition to its potential role in lung cancer, it is active against anaplastic large-cell lymphoma—a disease of young people. ALK mutations are also important in a subset of neuroblastoma. It seems to play a role in inflammatory myofibroblastic tumors and inflammatory breast cancer as well. It is almost certain that the tissue context of ALK will have a major influence on the effectiveness of agents that target it; results are certain to be different in lymphoma, lung cancer, and neuroblastoma. However, this represents a new paradigm for collaboration across widely diverse oncology specialties and tumor types. Medical oncologists with expertise in lung cancer, breast cancer, and sarcoma; experts in hematologic malignancies; and pediatric oncologists interested in solid tumors and lymphoma will share a new interest, collaborate with one another, and attend the same educational and scientific tracks at our ASCO annual meetings.

So what are the lessons that can be learned from our children and from the experience of pediatric oncology, and what are the implications for cancer care in general? First, caring for patients with cancer and restoring them to health require multidisciplinary expertise. Success depends on a wide-ranging collaboration of diagnosticians, therapists, and support services. It takes a village. Unfortunately, for most patients, care remains fragmented and uncoordinated. There is room for improvement.

The genomic era has brought stunning advances in our understanding of the biology of cancer. I hope that I have provided a convincing argument from the pediatric experience for the importance of collecting well-annotated tumor tissue from every patient. What we have achieved in ALL and neuroblastoma is already being demonstrated in breast cancer and lung cancer. Understanding tumors on a biologic basis is necessary to determine the most appropriate therapy. If childhood ALL has taught us anything, it is that we should be astonished that our crude, empirical therapies have been successful at all, especially in light of today’s understanding that we have been treating an assortment of diseases with distinct genetic profiles having little relation to one another. The lesson is that cancers are collections of orphan diseases.

Such considerations have enormous implications for the design of clinical trials. If what were once thought of as common cancers are more or less orphan diseases, how will we be able to accrue sufficient patients to provide levels of evidence that convince us of treatment efficacy and the evidence needed for regulatory approval of new agents? How will we keep the pharmaceutical industry engaged in the development of new treatments when we are pursuing specific targets of interest in increasingly narrow populations? As we have learned, wide-ranging and even international collaborations are required to overcome such challenges and to move our field forward. Nothing I have presented is unique to pediatric oncology, and all of the messages are well known to those of us who care for patients with cancer—that the paradigms adopted by pediatricians can serve as models of combining care delivery and clinical research, that we must leverage information from the laboratory, and that continuous learning from every patient is vital to achieving improved outcomes.

These lessons from our children that are recapitulated in caring for adults with cancer emphasize the challenges that face us. We do not yet understand which molecular pathways are most important, our current clinical trial designs are inadequate for the era of personalized medicine, and we are just beginning to realize the potential of health information technology. To address these challenges, ASCO released the Blueprint for Transforming Clinical and Translational Cancer Research this past year. Key elements of this blueprint include a discussion of new approaches to cancer drug development, trial designs with participants selected on the basis of the molecular features of their tumors, and a focus on what can be harnessed from health information technology. I urge you to explore the blueprint—a vision for the future—online at http://www.asco.org.

Our children have taught us that cure is not enough. We must understand the consequences of therapies we prescribe and continuously modify them to eliminate agents associated with the most important late effects. We must be attentive to the host genome and the clues it can provide about individual patient susceptibility to acute and long-term toxicities of treatment.

There is another lesson from our children—that an ounce of prevention is worth a pound of cure. This is a lesson not just from pediatric oncology but also from pediatrics in general. Prevention strategy through immunization has proven to be one of the greatest triumphs of pediatrics and of modern medicine. Rather than diagnosing and treating diphtheria, widespread immunization simply eliminated it as a health problem in North America. The near eradication of measles, polio, and serious infections from Haemophilus influenzae is a similar triumph. In the management of cancer, our best strategy would move us from the paradigm of diagnose and treat to one of predict and prevent. Here, too, pediatricians may hold the key—because the best opportunity to prevent cancers in adults is proper immunization and lifestyle counseling of children. Successful immunization against hepatitis B and human papillomavirus presents the prospect of preventing much of hepatocellular carcinoma and cervical cancer and perhaps a substantial portion of head and neck cancer as well. We can only hope for equally successful vaccines against Epstein-Barr virus, hepatitis C, and Helicobacter pylori. And pediatricians can also influence children and families to promote healthy lifestyles and to educate them about the dangers of smoking, obesity, and ultraviolet exposure—the major risk factors for preventable adult cancers.

What really underlies the success of pediatric oncology? It is the culture of collaboration and learning that permeates our specialty. It is the seamless integration of clinical research with medical practice, the collection of tissues for study as a key component of research, and a remarkable level of participation by physicians and patients in the clinical research process. It is the understanding by physicians, patients, and their families that clinical research is the key vehicle for progress. We accept the belief that research cures cancer. In fact, the secret to our success is that we have stepped beyond translating discoveries into practice; rather, we have integrated clinical research with medical practice. Recently, the model of pediatric oncology was promoted as the prototype for improving patient outcomes in other age groups and other conditions.

A critical component of our success is strong commitment to the belief that learning from every patient will lead to better outcomes and...
quality of life. Key to this has been the role of patients and their families as collaborators in our mission—and advocates for our cause. My mentor and colleague, Sharon Murphy, has promoted the collaborative model of pediatric oncology as the prototype for a rapid-learning health system. Well described by the Institute of Medicine, a rapid-learning system uses all available data—from clinical trials and from routine patient care experiences—to develop evidence that can move the field forward.23 Children with cancer have been treated in multi-institutional clinical trials with a central data repository, using protocols that guide therapy and standards of care. Patient-specific, diagnostic data, and tumor-specific biologic data are linked to each patient record and included in the database. And a majority of children with cancer in North America are part of this database. Analysis of the information aggregates individual patient data and ultimately defines a new standard of care. This learning is incorporated into new treatments that form the basis of the next-generation protocol. The rapid-learning loop is completed by assessing the degree of uptake of the new standard, whether the improved outcome is sustained when applied more widely, and the value of this new standard of care. The result has been successive, incremental improvements in outcomes for most childhood cancers.

What if this model permeated our entire specialty? Imagine if we could learn from every patient—not just the highly selected ones in clinical trials. The truth is that the treatment experience of the overwhelming majority of patients is confined to their medical records and unavailable to inform our understanding or decisions. Imagine if we could mine those data in real time, discovering answers to clinical problems that confront us every day. Imagine if we could have access to data on all of our patients and if retrieving these data could be automated through extraction from electronic medical records.

A rapid-learning system would collect and analyze data from electronic medical records of all patients, creating knowledge relevant to our daily practice. It would cause safety issues to surface; inspire the next generation of hypotheses; and provide insight about treatments, patient experiences, and ultimately outcomes. Instead of waiting years, our insight and progress would come in weeks or months. ASCO has embarked on a mission to create such a system. It is a vision for the future that will be realized in a major ongoing ASCO initiative: the Cancer Learning Intelligence Network or CancerLinq. Over the past year, ASCO leaders have begun the work of making this vision a reality. Guided by a group of seasoned leaders in the field, a new quality team has been laying the foundation for a system that will profoundly change cancer care and research. It will leverage the knowledge and experiences—like those I have described in pediatric oncology—and enrich them with unprecedented access to information about the millions of patient experiences happening in oncology every day. This is our vision, our passion, and our commitment to the future of oncology. We want you involved. You will be hearing much more about this exciting project at this meeting and as the component parts are assembled.

But all this newfound insight into these diseases and their treatment is only as good as our ability to deliver what we know. The current chemotherapy shortage is emblematic of the precarious nature of the path between the discovery and the delivery of our most exciting new findings. At our annual meeting, we rejoice in our growing understanding of cancer and its translation into better therapies in the clinic—the discovery phase. But we must also focus on our capacity to deliver.

Disparities in access to high-quality care are a grave concern. In this calendar year, almost 50 million Americans—or 16% of the population—had no health insurance, putting them at considerable risk for personal bankruptcy in the event of a serious illness.26 The rolls of the uninsured include one in four working adults and 10% of children. Thirty-five percent of children are insured through Medicaid, as are 25 million nonelderly adults. This harsh reality has an enormous impact on the delivery of cancer care.

It is clear that being uninsured is a risk factor for substantially worse outcome. And it seems that the outcome of patients covered by Medicaid is not much better than for uninsured patients.27 Obviously, a number of factors beyond insurance coverage contribute to this finding, but the data are compelling. And there are other distress signals that should give us pause. Oral targeted agents have revolutionized the treatment of many cancers, yet the high cost of these agents and the high insurance copays frequently make these drugs unaffordable even for patients with health insurance. Targeted therapies that are being added to our armamentarium against cancer are only worthwhile if patients take them, and that is only likely if our patients can afford them.

We have not begun to address the obstacles to delivery of what we know to the developing world. Eighty-five percent of the world’s population lives in low- and middle-income countries where aging populations will lead to an anticipated tsunami of cancer cases, overwhelming fragile health systems. For children with cancer in a resource-poor country, it is a matter of life and death. Although 80% of children with cancer in resource-rich countries will survive, in resource-poor countries, 80% of them will die. As an increasingly international professional society, ASCO—along with other organizations—must and does have a stake in this. There is an opportunity for collaboration here to leverage the expertise of our membership. At this year’s United Nations High-Level Meeting on Non-Communicable Diseases, world leaders made unprecedented commitments to accelerate global progress on cancer and other diseases. ASCO is engaged in this initiative and pursuing partnerships to improve quality of care throughout the world.

Finally, I would like to return to a focus on our patients—the reason we are here and, in my mind, the most important collaboration of all. It is, after all, the person who has the misfortune to harbor all those fascinating chromosomal rearrangements, mutations, amplifications, and deletions and who, without having desired it or consented to it, is transformed from person to patient. When we care for a patient with cancer, we establish a unique partnership with the individual and his or her family. Patients articulate their goals, the risks and toxicities that they are willing to endure, and the information they have obtained from variably reliable sources. It is our role to do our best to educate our patients and jointly arrive at a plan of action. Often, this entails enrollment onto a clinical trial. The patient then becomes a genuine collaborator in our research efforts, which in some cases offer little chance of benefit to them but may help future patients with cancer. It is this commitment to and partnership with our patients that defines what we do as oncologists. There are threats to this model, embedded in the great progress we have made in understanding cancer, in the sheer volume of data that must be digested to deliver precision medicine,25 and even in images of the future model of personalized oncology.

Some describe a future where newly diagnosed patients bring their tumor and germline genome to the oncologist on a thumb drive.

Michael P. Link
The oncologist dutifully plugs the information into an electronic medical record where complex data are uploaded, digested, and interpreted. A decision support application spits out a roadmap for therapy tailored to the patient’s tumor. A heady vision to be sure. Such visions got me thinking about what first attracted us to oncology and care of patients with cancer to begin with. Certainly there was excitement about the science and the prospect of translating scientific understanding into targeted treatments. And that continues to be an allure. But the real draw of our field is the privilege of participating in the most difficult sojourn our patients endure. They allow us into the most intimate spaces of their lives as they navigate a life-threatening and life-changing ordeal. We need to listen more and relish the opportunity to establish and enjoy these relationships, which are like no other. Ultimately, this is the most important of our collaborations and the one that makes this work doing. For me, this has meant taking a young woman through the rigors of a year of miserable chemotherapy, radical surgery, and irradiation—encouraging her at her lowest point to keep the faith and then to watch with satisfaction as she blossomed after completing therapy, restored (although not entirely the same) to the lovely, engaging young woman who might change our world. Or to have a former patient I cared for when he was 15 go to medical school, become a surgeon, and call to ask if he could run a case by me. I had become his colleague rather than his physician. Or of the young woman I cared for when she was 12 with a so-called high-risk ALL who now works in our clinic as a nurse practitioner—the very clinic where she was treated—understanding what patients are going through in a way that few of us on the other side can and contributing in her own special way to compassionate care of our patients. Or perhaps the story of a young woman who developed a rare leukemia at age 8 that was incurable during my residency—but a leukemia that we now cure with impunity. She participated in a clinical trial that was one of the incremental steps in improving the therapy of this leukemia. I watched her grow up and recently attended her wedding. I had the inestimable pleasure of watching the beaming smile on her father’s face when he danced with his daughter at the reception. Not all of the stories have happy endings, but many of the relationships with families have been enduring and a major source of professional satisfaction.

We have entered an era of medicine with growing emphasis on economics and quantitation: risk-benefit ratios, quality-adjusted life-years, numbers needed to treat, and more. And the increasingly mundane stuff that has intruded as a result of the “business-ification” of medicine as well: profit and loss; the economics of sustaining our practice, physicians, and patients as “providers” and “customers”; sustainable growth rate; and the ever more pervasive relative value unit. As difficult as it is these days, I admit that I am willing to abide by the advice provided by Albert Einstein, a very wise scientist indeed: “Not everything that can be counted counts.” The wonderful and unique relationship between oncologist and patient and what it provides to both patient and physician is valuable, even if that part of what we do is not always valued. Einstein’s wisdom again: “Not everything that counts can be counted.”

Eighty-five years ago, Francis Peabody, an astute physician, complained28 that “the most common criticism made … by older practitioners is that young graduates have been taught a great deal about the mechanism of disease, but very little about the practice of medicine—or to put it more bluntly, they are too scientific and do not know how to take care of patients.” Remarkably little has changed in 85 years. As Dr Peabody described, “the good physician knows his patients through and through. … Time, sympathy and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.”

It is a guiding principle well worth adhering to, because it has and will continue to serve us well. Thank you for attending the 2012 annual meeting, for the new ideas that you bring to our field, and for the caring and skill that you bring to our patients. Together, we can collaborate to conquer cancer.

**REFERENCES**


2013 ASCO Annual Meeting

Each year, ASCO organizes a wide array of high-quality meetings that provide educational and scientific programs to advance our understanding of cancer. At each of ASCO’s meetings, you can expect an engaging and interactive agenda featuring high-level scientific or clinical abstracts and educational sessions led by world-class faculty. Join us to earn CME credit, network with colleagues, and interact with cancer experts.

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