Of the 56 million deaths that occurred worldwide in 2012, 38 million were caused by noncommunicable diseases. The majority (82 percent) of these deaths were caused by just four noncommunicable diseases: cardiovascular disease, cancer, chronic respiratory diseases, and diabetes. The number of deaths from noncommunicable diseases has been rising in every part of the world for more than a decade, and it is predicted that globally, there will be 52 million deaths from these diseases in 2030 including 13 million deaths from cancer.
Precision medicine, sometimes referred to as personalized medicine, molecular medicine, or tailored therapy, is broadly defined as treating patients based on characteristics that distinguish them from other patients with the same disease. Factors such as a person's genome, the genome of his or her cancer, disease presentation, gender, exposures, lifestyle, microbiome, and other yet-to-be-discovered features (indicated by the question mark) are considered in precision medicine. Precision prevention is a conceptual framework that aims to tailor cancer prevention to the individual patient by accounting for the various factors that may play a role in developing a particular cancer; it is analogous to the manner in which precision medicine treats patients. The following factors could be considered in the implementation of precision prevention: a person's genome; age; gender; family history, including genetic predisposition to developing cancer; lifestyle factors including tobacco and alcohol use, being overweight or obese, and levels of exercise; reproductive and medical factors; exposures to known carcinogens like viruses; socioeconomic status; and geography, as well as yet-to-be-identified factors (indicated by the question mark). The order in which the factors appear in the images is not meant to imply that one factor is more important than another.
Research has identified numerous factors that increase an individual's risk for developing cancer. By modifying behavior, individuals can eliminate or reduce many of these risks and thereby reduce their risk of cancer. Developing and implementing additional public education and policy initiatives could help further reduce the burden of cancers related to preventable cancer risk factors.
Smoking tobacco increases an individual's risk of developing not only lung cancer, but also 17 other types of cancer. No level of exposure to tobacco smoke is safe, including exposure to secondhand smoke, which is estimated to have resulted in more than 260,000 of the 5 million lung cancer deaths in the United States attributable to smoking from 1965 to 2014.

American Association for Cancer Research (AACR) Cancer Progress Report 2016
There are laws legalizing some form of marijuana use in 25 U.S. states and the District of Columbia. In most states, marijuana is legalized only for medical purposes, but it is legalized for both medical and recreational purposes in Alaska, Colorado, Oregon, Washington, and the District of Columbia. With more and more states legalizing some form of marijuana use, it is imperative that we conduct more research to fully understand the health consequences of marijuana use, including how it affects cancer risk.

Data are current as of July 31, 2016
Fourteen types of cancer—the adenocarcinoma subtype of esophageal cancer, advanced prostate cancer, meningioma, multiple myeloma, and colorectal, endometrial, gallbladder, kidney, liver, ovarian, pancreatic, stomach, thyroid, and postmenopausal breast cancers—have all been directly linked to being overweight or obese.
The percentage of adolescent girls in the United States to have received the recommended three doses of the human papillomavirus (HPV) vaccine is very low compared with the percentages vaccinated in other high-income countries, such as Australia and the United Kingdom. Rwanda, a low-income country, has implemented a national, multisector, collaborative, school-based HPV vaccination program. A trial of a school-based HPV vaccination program in Molepole, a traditional village in Botswana with a population of more than 60,000, was recently reported to have led to 79 percent of eligible girls receiving three doses of the HPV vaccine and to a nationwide rollout of the program in 2015.
Many cancers are progressive in nature. In the example depicted here, an initial genetic mutation can lead to normal cells taking on precancerous characteristics. As these cells multiply and acquire more genetic mutations, the precancerous lesion becomes increasingly dysplastic, or abnormal. Over time, as additional genetic mutations accumulate, the dysplastic precancerous lesion may evolve into a cancerous lesion, then spread to nearby lymph nodes and, as it becomes more advanced, ultimately metastasize. Screening tests—such as the Pap test and colonoscopy—can be used to prevent cancer because they can find precancerous lesions, which can then be removed before they develop into cancerous lesions either through surgery or with the use of certain therapeutics. Use of other screening tests, such as mammography, aims to find cancer at an early stage, when it is more likely that the patient can be treated successfully. The treatment a patient receives depends on numerous factors, including the type of cancer and the stage of disease at which diagnosis occurred, but it can include surgery, radiotherapy, chemotherapy (both cytotoxic and molecularly targeted), and/or immunotherapy. Treating a precancerous lesion or early stage cancer detected by screening is sometimes called cancer interception.

American Association for Cancer Research (AACR) Cancer Progress Report 2016
Results from any type of research can fuel biomedical research by providing observations relevant to the practice of medicine, which lead to questions, or hypotheses, that are tested in experiments during the discovery phase of research. During the discovery phase, traits unique to a disease may be uncovered, leading to the development of a potential therapeutic. Before entering clinical testing, potential therapeutics are subjected to preclinical testing to identify any toxicities and help determine initial dosing. Clinical testing is a multiphase process aimed at demonstrating the safety and efficacy of a potential therapeutic. If a therapeutic is safe and effective and is approved for use by the U.S. Food and Drug Administration (FDA), it will enter into clinical practice, where it can improve the lives of patients. Importantly, observations made during the routine use of a new therapeutic can feed back into the biomedical research cycle and further enhance the use of that therapeutic or the development of others like it. If, however, a therapeutic is not safe or effective and fails to gain FDA approval, the observations from the clinical testing still feed back into the biomedical research cycle to spur future research efforts. Because the cycle is iterative, it is constantly building on prior knowledge, and research undertaken during any part of the cycle continually powers new observations.
FIGURE 10  
GENOMICALLY INFORMED CLINICAL TRIALS

One of the major uses of genomics in clinical research is in the design and execution of novel clinical trials. Two such types of trials are basket and umbrella trials. In the basket trial depicted here, one drug is being tested against a particular genetic mutation (green dots) across liver, lung, bone, colon, and stomach cancers. In the umbrella trial illustrated here, three different drugs are being tested against multiple genetic mutations (yellow, green, blue, and red dots) in lung cancer.

American Association for Cancer Research (AACR) Cancer Progress Report 2016
Data of any kind are measured in bytes. A byte is a unit of computer storage equal to eight binary digits (01000000) and is recognized by a computer as a single character. One thousand bytes make up a kilobyte (kB); the average Word document (five pages) is tens to hundreds of kB. The average compact disc can hold 700,000 kB, which is 700 megabytes (MB), of data (gold disc). A thousand MB are contained within a gigabyte (GB), illustrated by the thumb drive, and the average digital video disc (DVD) holds nearly 5 GB of data (gold DVD). It would take more than 60 DVDs to store the data from sequencing an individual's entire genome (the Human Genome Project), which is approximately 4 GB. A 2011 McKissock/MGI report estimated that all of the world's recorded music up to that year could be stored in 6 terabytes (TB; music note); it would take 6,000 1-GB thumb drives to store all of these data. As of April 25, 2012, the Library of Congress's digital holdings collection contained 3 petabytes (PB; stack of books) of data, which is 3,000 TB or 3 million 1-GB thumb drives. Researchers at the Lawrence Berkeley National Laboratory estimate that within the next few years, it will generate more than an exabyte (EB; cloud) of data modeling the weather. It would take more than 1 billion 1-GB thumb drives to store these data. It is estimated that in 2012, the world collectively created more than 1.2 zettabytes (ZB; globe) of data. Big data sets are unique in that they are too large to be stored and analyzed using traditional relational methodologies. The complexity of cancer and its treatment is creating big data sets, and the field and the patients it serves will benefit greatly from research into big data systems, methodologies, and solutions.
Physicians often refer to the “pillars” of cancer treatment. For thousands of years, there was only one treatment pillar: surgery. In 1896, a second pillar, radiotherapy, was added. The foundations for the third treatment pillar, cytotoxic chemotherapy, were laid in the early 1940s when a derivative of nitrogen mustard was explored as a treatment for lymphoma. These three pillars—surgery, radiotherapy, and cytotoxic chemotherapy—continue to be the mainstays of cancer care. However, in the late 1990s, the first precision therapeutics were introduced, leading to the fourth pillar, precision therapy, which continues to grow. Likewise, the late 1990s laid the groundwork for the fifth treatment pillar, immunotherapy. The number of anticancer therapeutics that form the most recent pillars of cancer care has increased dramatically in the past 5 years.
Lung cancer is the leading cause of cancer-related death in the United States. In the 12 months covered by the report, from Aug. 1, 2015, to July 31, 2016, the U.S. Food and Drug Administration (FDA) made eight decisions that have provided new hope for many patients diagnosed with lung cancer. In October 2015, the FDA approved two immunotherapeutics that work by releasing the PD-1 brake on immune cells called T cells for treating certain patients with non–small cell lung cancer (NSCLC). The first was pembrolizumab (Keytruda), which was approved for treating advanced NSCLC that has progressed after other treatments and tests positive for the protein PD-L1 using the PD-L1 IHC 22C3 pharmDx test—a companion diagnostic that was approved alongside the immunotherapeutic. The second was nivolumab (Opdivo), which was approved for treating patients with advanced NSCLC that has progressed after treatment with a platinum-based traditional chemotherapeutic. In November 2015, the FDA approved the molecularly targeted therapeutic osimertinib (Tagrisso) for treating advanced NSCLC that tests positive for EGFR mutations using the cobas EGFR Mutation Test v2 and that has become resistant to other EGFR-targeted therapeutics. The FDA also approved necitumumab (Portrazza) for treating advanced squamous NSCLC. Alectinib (Alcraensa) is a molecularly targeted therapeutic that was approved by the FDA for treating advanced NSCLC fueled by ALK mutations that have become resistant to the ALK-targeted therapeutic crizotinib (Xalkori) in December 2015. In March 2016, the approved uses of crizotinib were expanded to include the treatment of advanced NSCLC fueled by ROS1 mutations. Another treatment for advanced squamous NSCLC, the molecularly targeted therapeutic aflatinib (Gilotrif), was approved in April 2016. The cobas EGFR Mutation Test v2 was approved by the FDA for testing plasma, the colorless liquid component of blood, for the presence of EGFR mutations in June 2016.
Venetoclax (Venclexta) is a molecularly targeted therapeutic that works by blocking the protein BCL2, which promotes cell survival by preventing cells from undergoing a natural self-destruct process called apoptosis. It is currently the only anticancer therapeutic of its kind to be approved by the U.S. Food and Drug Administration (FDA). Many years of basic, translational, and clinical research underpinned the development of venetoclax. The term apoptosis was first coined in 1975. A decade later, researchers discovered BCL2 and then went on to show that its function was to prevent apoptosis. The development of the first BCL2-targeted therapeutic to enter clinical trials, navitoclax, was hampered by the fact that it causes platelet death, which limits the dose that can be given. Venetoclax was approved for treating patients with chronic lymphocytic leukemia (CLL) shown to have a 17p deletion with the Vysis CLL FISH Probe Kit companion diagnostic in April 2016.
The DNA synthesis inhibitor hydroxyurea was the first therapeutic for the systemic treatment of metastatic melanoma approved by the U.S. Food and Drug Administration (FDA). Its approval in 1968 was followed by the approval of the DNA-damaging agent dacarbazine (DTIC) in 1975. Twenty-three years passed before another systemic therapeutic, the immune system stimulator recombinant interleukin-2 (aldesleukin; Proleukin), was approved for the treatment of melanoma. In 2011, ipilimumab (Yervoy) became the first immune-checkpoint inhibitor approved by the FDA and the first new systemic treatment for melanoma in 23 years. That year also saw the approval of vemurafenib (Zelboraf), a therapeutic that selectively inactivates the mutant form of the protein BRAF that occurs in approximately 50 percent of melanomas. In 2013, the FDA approved a second mutant BRAF–targeted agent, dabrafenib (Tafinlar), as well as trametinib (Mekinist), a therapeutic that targets other proteins in the BRAF signaling pathway, MEK1 and MEK2. The combination of dabrafenib and trametinib was FDA approved in 2014, as were two new immune-checkpoint inhibitors, nivolumab (Opdivo) and pembrolizumab (Keytruda). In 2015, the FDA approved the use of ipilimumab and nivolumab in combination, as well as a new MEK-targeted therapeutic, cobimetinib (Cotellic), for use in combination with vemurafenib for the treatment of BRAF-mutant metastatic melanoma. Note: this timeline focuses on systemic, primary treatments for regional and metastatic melanoma; other therapeutics have been approved for the prevention of disease recurrence or the treatment of localized lesions.
Cancer immunotherapeutics are anticancer therapeutics that work by unleashing the power of a patient’s immune system to fight cancer the way it fights pathogens like the virus that causes flu and the bacterium that causes strep throat. One class of cancer immunotherapeutics works by releasing the brakes on the natural cancer-fighting power of immune cells called T cells. These revolutionary anticancer agents are called checkpoint inhibitors. They have yielded remarkable and durable responses for some patients with an increasingly broad array of cancer types. As of July 31, 2016, the FDA has approved four checkpoint inhibitors: atezolizumab (Tecentriq), ipilimumab (Yervoy), nivolumab (Opdivo), and pembrolizumab (Keytruda). The cancers for which these immunotherapeutics have been approved or have been granted FDA breakthrough designation are highlighted in the figure.
The biomedical research and development price index (BRDPI) reflects the rising cost of personnel, supplies, and equipment needed to conduct biomedical research. From 2004 to 2015, the National Institutes of Health (NIH) budget did not keep pace with BRDPI. However, the gap is closing as a funding increase of $2 billion in fiscal year (FY) 2016 provided real growth in excess of inflation. Additional increases proposed for FY 2017 are helping us continue to turn the corner after the decade of stagnant investment (see blue bars).