

# Accelerating the Pace of Cancer Prevention- Right Now

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## Abstract

As a nation, we underinvest in prevention and fail to implement strategies that ensure all population groups equitably share in the return on investment in prevention research and the benefits of prevention effectiveness. There is significant evidence indicating that by applying knowledge that we already have to reduce tobacco, inactivity, and obesity (known modifiable causes of cancer), we can prevent more than 50% of cancers. Vaccination against HPV, aspirin and selective estrogen receptor modulators, and screening programs further reduce risk. Evidence-based prevention strategies are inconsistently implemented across the United States. Substantial variation across States indicates that there is much room for improvement in implementation of

prevention. Implementation science applies innovative approaches to identifying, understanding, and developing strategies for overcoming barriers to the adoption, adaptation, integration, scale-up, and sustainability of evidence-based interventions, tools, policies, and guidelines that will prevent cancer through application of evidence-based interventions. When we get implementation of prevention programs right and at scale, we achieve substantial population benefits. Although many efforts are underway to maximize our knowledge about the causes and treatments of cancer, we can achieve reductions in the cancer burden right now by doing what we already know. The time to start is now. *Cancer Prev Res*; 1–11. ©2018 AACR.

More than half of cancers can be prevented by applying knowledge that we already have: Tobacco, inactivity, and obesity are modifiable causes of cancer (1–3). Vaccination against HPV, use of aspirin, and selective estrogen receptor modulators and screening programs further reduce risk of specific cancers (4, 5). Yet, as a nation, we continue to underinvest in prevention and fail to adopt strategies to ensure that all population groups equitably benefit from our knowledge of cancer prevention (6, 7). As a result, we continue to tolerate avoidable cancer morbidity and mortality (8). This is a significant paradox, especially in light of the significant focus on reducing the burden of cancer that the Cancer Moonshot initiative has created.

What is particularly distressing about the failure to invest in prevention is the resulting impact on cancer disparities. An analysis of medical advances and racial/ethnic disparities in cancer survival using SEER data estimated survival differences based on the degree to which a specific cancer is amenable to medical interventions (9). There are few racial/ethnic disparities in the nonamenable cancers (<40% relative survival rate). However, survival curves quickly widen as amenability level increases and are especially pronounced for cancers that can be detected early and treated successfully. This compelling study, and others that it confirms (10, 11), provides the background from which we

argue that research efforts must focus on increasing implementation of evidence-based strategies to ensure that all populations benefit from the cancer prevention and early detection knowledge that we currently have. In this article, to show the value of preventive interventions, equivalent to money left on the table if we do not act on this knowledge and implement programs, we summarize evidence for key cancer types, across intervention strategies, and identify additional opportunities for speeding cancer prevention through implementation science and through identifying additional levers to increase implementation of the evidence base. The goal of this article is to examine a wide range of opportunities to accelerate cancer prevention, including implementation science, as well as etiologic research focused on critical questions that would open new avenues for prevention.

## What We Know: The Evidence Base on Prevention of Lung, Breast, and Cervical Cancer

### We know: the current evidence base on cancer prevention

In Table 1, we summarize the benefits of implementing prevention strategies for 5 common cancers for which evidence-based strategies exist, and the potential magnitude of benefit. We examine approaches across medical, behavioral, social, and policy level interventions (12, 13), giving examples of the evidence base and the organizations that have summarized this evidence in practice or public health guidelines. Selected examples are discussed here.

For lung cancer, the evidence on the benefits of smoking cessation (14), effectiveness of clinical interventions for cessation (15), and the effectiveness of low-dose CT screening (16) combine to inform the USPSTF guideline (17) and CMS funding for screening services. Lung cancer screening achieves a 20% reduction in lung cancer mortality among smokers, and cessation during adolescence and at age 50 yields a 90% and 62% reduction

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**Table 1.** Combined benefits of evidence-based interventions for leading cancers

Cancer	Intervention (Ix)				Evidence	Magnitude of preventive benefit
	Medical	Behavioral	Social	Policy		
Lung	Serial CT			Long-term smokers	RCT (16)	20% reduction in mortality (16)
	Smoking cessation meds	Smoking cessation interventions		Adolescent & adults	USPSTF recommendation (17) Multiple cohort studies, case-control studies, and population data (14, 92, 93)	Cessation in adolescent 90+ % reduction mortality
				Smoke-free policies	Surgeon General Reports (SGR) 1990 (94, 95) Tobacco treatment guidelines (15) SGR (96)	Cessation at age 50 62% reduction mortality (14)
				Tobacco taxes	SGRv2014	Impact on lung cancer cannot be estimated based on present data 10 % increase in cigarette prices decreased smoking prevalence by 3.7% (98)
CRC	Screening			Graphic warning labels	WHO (97) Comparison of Canada to United States	Reduction in smoking rates by 2.9% to 4.68% (relative reduction of 12%–19%, ref. 99)
	Aspirin			Comprehensive advertising bans	Comprehensive bans in European Commission countries RCTs of screening methods + prospective observational studies (101–105) USPSTF (5) Randomized trials (106, 107)	Bans of advertising reduced smoking prevalence by 6% (100) 30% to 50% reduction in incidence and mortality (101–105)  30% reduction incidence and mortality (108)
	Smoking cessation meds	Smoking cessation Ix		Smoke-free policies	Systematic review meta-analysis (108) USPSTF in process 2016 Cohort studies (109)	Impact on CRC cannot be estimated based on present data
		Wt management/loss Ix PA Ixs	School/work Environment/clinical Urban design	Tobacco taxes Food & beverage	Surgeon General's Report, 2014 Tobacco treatment guidelines (15)  Epidemiologic evidence on burden due to obesity (110) RCT weight loss strategies  Sugar-sweetened beverages increase weight gain (111); processed/red meat increases risk (112)	11% CRC incidence attributable to overweight and obesity (110) 13% CRC incidence (110) Combined impact on CRC cannot be estimated based on present data

(Continued on the following page)



in lung cancer mortality, respectively (18). Environmental and policy strategies are particularly important in tobacco control (18–20).

There are a growing number of strategies that confer prevention benefits related to breast cancer. Screening among women over age 50 and those at high risk yields a 30% reduction in mortality (21, 22). Salpingo-oophorectomy in women with a BRCA1/2 genetic risk of breast and ovarian cancer may yield up to 50% reduction in breast cancer incidence (23, 24). Selective estrogen receptor modulators (SERM) reduce breast cancer incidence by 50% among high-risk women (25, 26).

Preventive and early detection strategies for cervical cancer are particularly effective. Screening results in greater than 95% reduction in mortality (27), and vaccine yields 100% reduction in mortality (28–30). Australia achieved quite rapid declines in cervical lesions after the widespread introduction of the HPV vaccine. High-grade cervical abnormalities decreased by 17% among women 25 to 29, in contrast with increasing incidence among older women (31). How benefits are presented, costs and access issues as well as framing of prevention messages, may modify willingness to begin or complete vaccination. Subsequent changes in screening with the implementation of HPV screening and an every 5-year schedule will dramatically change gynecologic practices (fewer pap smears, fewer biopsies, and so forth), and we must study how to reduce excess screening among women as the guidelines change.

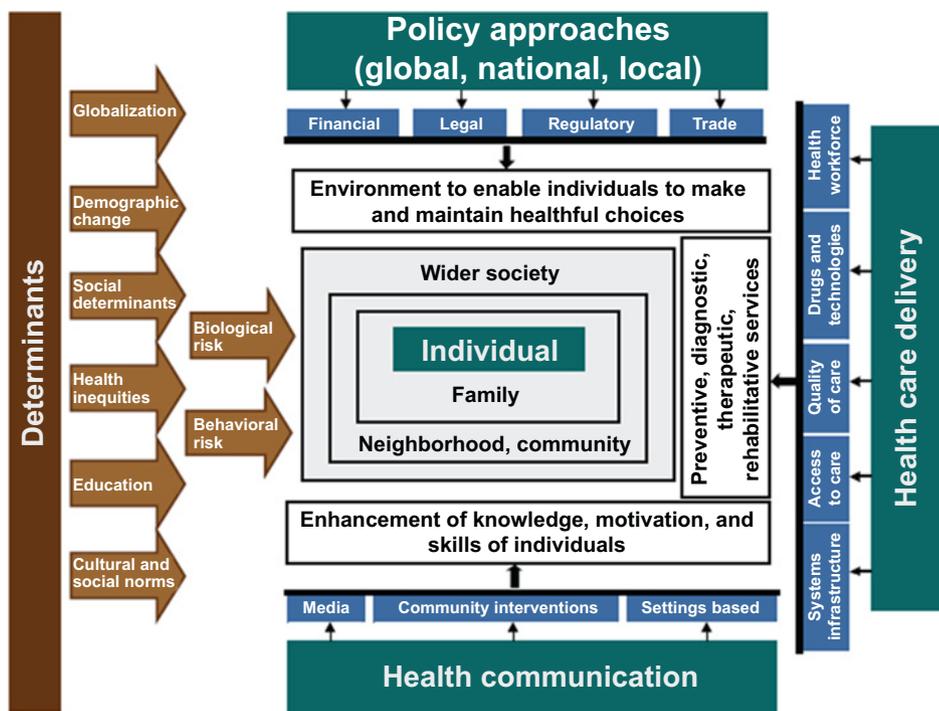
Obesity is a cause of cancer in numerous organs (32), yet weight loss is not well evaluated in the context of reducing incidence of cancer. The Diabetes Prevention Trial established that lifestyle interventions could prevent progression of pre-diabetes to diabetes and generated numerous subsequent trials moving to effectiveness of sustained weight loss approaches. Cohort studies of weight loss support reduction in breast (33) and endometrial cancer incidence (34), and sustained weight

loss after bariatric surgery has been related to lower incidence of postmenopausal breast cancer, endometrial, colon, and pancreatic cancers (35). On the other hand, public health and systems approaches to interventions focused on the physical activity environment, food and beverage environment, and schools and work environment are recommended by the IOM (36).

## What We Do: How Well Do We Implement Evidence?

Environmental and policy approaches are among the most effective ways to ensure that prevention strategies are available at the population level (37). However, there is variation in the implementation of these approaches, which reduces use of key drivers of change such as tobacco taxes, but can also lead to reduced revenue for prevention programs and subsequently higher prevalence of risk behaviors. An IOM report on cardiovascular disease (38) highlights the importance of four different policy approaches at the global, national, and local levels, including (i) financial; (ii) legal; (iii) regulatory; and (iv) trade (see Fig. 1). This framework is highly applicable to cancer prevention, as it highlights the critical need for integration in strategies that can lead to improved prevention at the individual, family, and community level.

Reviews of implementation of environmental and policy approaches highlight substantial variation. For example, in the United States, there is substantial variation in excise taxes, ranging from 17 cents in Missouri to a combined total of state and local taxes of \$6.16 in Chicago, IL, and \$5.85 per pack in New York City. (39) In contrast, Australia has shown a significant commitment to comprehensive tobacco control by increasing cigarette taxes by 12.5% each year over 4 years from 2016 to 2020, raising the cost of a pack from \$ AUS 25 (\$ US 18) to \$ AUS 40 (\$ US 29). Plain



**Figure 1.** Framework for prevention from Institute of Medicine, 2010 (32). A model developed for cardiovascular diseases but applicable to cancer prevention.

cigarette packaging was introduced in 2012, and it has very strong smoke-free workplace and public-place policies (40).

In the United States, there have been long-standing gaps in access to cessation treatment, which were addressed in the Affordable Care Act (15, 41). However, fewer than 20% of state health insurance marketplace plans provide smoking cessation treatment as a free essential health benefit, as required (42). This ACA requirement, if fully implemented, could bend the curve on smoking among those with the highest levels of prevalence (41). For breast and colorectal cancer screening in Medicare population where the ACA removed out of pocket expenses, comparison of screening rates before and after the ACA demonstrates increases in mammography but not colorectal cancer screening (43). Implementation research to understand the enforcement of this recommendation and the social barriers to accessing these preventive services for low income populations could add insights and speed progress to achieving cancer prevention.

Rates of colon cancer screening have increased to an average of 66.4% of adults (ages 50–75) being up-to-date in 2014 (44). However, this average masks substantial variability across states, ranging from 55.7% in Arkansas to 76.3% in Massachusetts (44). Furthermore, within-state variation is even more marked than the variation between states (45). The mortality hotspot for colorectal cancer in the Mississippi delta has evolved over 40 years from a region with low mortality to high mortality; as other regions have increased colorectal screening and decreased their mortality, the delta region has remained stable over this timeframe and now has the highest mortality (46). In 1990, state-based colorectal cancer mortality rates were 27.5/100,000 in Massachusetts and 21.1 in Mississippi, and by 2014, they were 12.5 in Massachusetts and 19.2 in Mississippi (47, 48). This shift from a relative excess in Massachusetts of 30% compared with Mississippi to a 35% lower mortality reflects the broader national trends to create the mortality hotspot (46).

The CDC provides funding to all states to promote screening for breast and cervical cancers, but at levels that served only 6.5% of eligible women for cervical cancer screening and 10.6% of those eligible for mammography screening in 2015 (49). In the United States overall, the average mammography screening rate in 2015 was 71.5% among women over age 40 (50). There is also considerable variability by state, with overall screening rates ranging from 62.5% for White women in Idaho to 82.1% in Massachusetts (2014 data). For non-Hispanic Black women, the mammography rates range from 65.4% in Arkansas to 87.5% in Maryland and 91.5% in California (51).

Despite current guidelines recommending use of SERMS to reduce breast cancer incidence for high-risk women (52), only 16% of eligible women use chemopreventive agents (53). Approximately 7.8 million U.S. women ages 50 to 69 who could reduce their breast cancer incidence from SERMS are not receiving this benefit (54). More research to understand decision making by women and their providers could help bridge the gap in use of this effective prevention strategy.

Variation in levels of implementation of HPV vaccination by region is substantial, ranging from 24.4% of adolescent girls in Mississippi to 68.0% in Rhode Island receiving 3 doses in 2015 (55); states with higher income and education levels had higher vaccination rates (56). In contrast, using a public health approach with mandatory school-based administration by nurses and provision of free vaccination in Australia has led to rapid uptake, with

3-dose vaccination of girls by 2014 at 74%; 81% of girls 14 to 15 had 2 doses. For boys, 75% of 14 to 15 year olds had one dose and 71% had 2 doses (57).

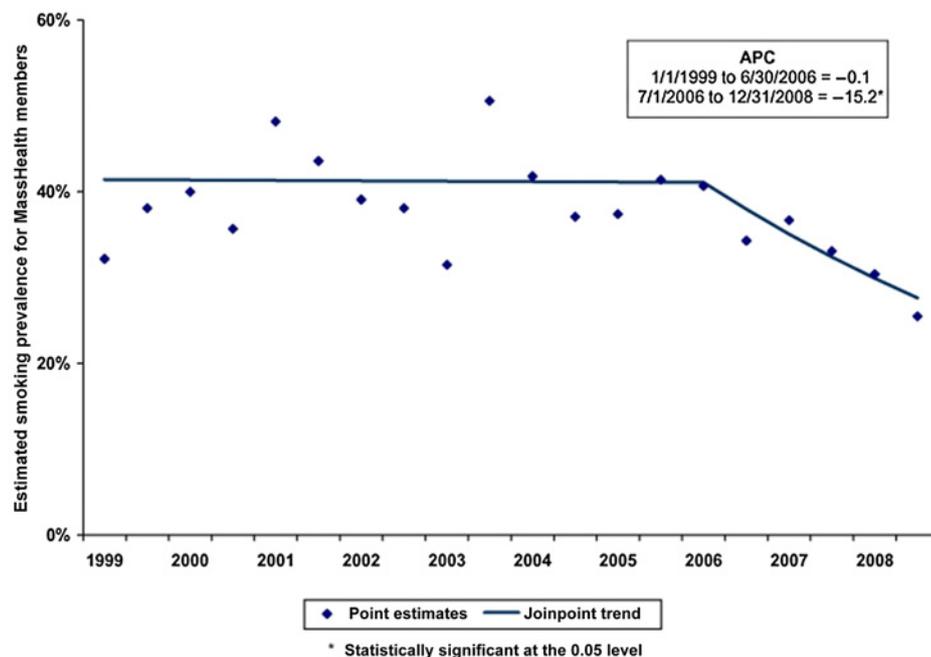
Cutting across most cancer prevention and cancer outcomes data are continued disparities that produce less screening and poorer morbidity and mortality outcomes among non-Whites and those from lower SES backgrounds. This is likely a combination of less and perhaps less effective implementation of evidence-based interventions, as well as systemic factors and social determinants that maintain these persistent disparities.

## What Would Happen if We Implemented What We Know?

Despite our overall poor performance at systematically implementing our cancer prevention knowledge, there are examples of substantial population benefits when we implement prevention programs right and at scale.

### Providing smoking cessation treatment to low income smokers

The Massachusetts Medicaid Program, MassHealth, began coverage for comprehensive smoking cessation treatment in 2006. Massachusetts has had a strong tobacco control program, since 1993, when it had a smoking prevalence of 24% (58). By 2005, the smoking prevalence in Massachusetts had dropped to 18%, while the national average was 20.5%. However, these benefits had not accrued uniformly to all population groups, and the rate of decline among those without a college degree was half of that among the more educated. Within 2 years of the MassHealth coverage of tobacco dependence treatment, including pharmacotherapy, 70,000 MassHealth subscribers had used the benefit, or 37% of all MA Medicaid smokers (59). Over this same period of time, the smoking prevalence among this group declined by 26%, in the very population that historically had a flat prevalence rate (see Fig. 2). The annual rate of admissions for heart attacks was reduced by 46%, and there was a 49% annualized decline in admissions for coronary atherosclerosis among MassHealth beneficiaries (60). Notably, \$3.12 in medical savings were realized for every dollar spent on the benefit. Comprehensive tobacco control yields tangible and important health outcomes, and significant cost savings for state governments that accrue within a relatively short period of time. And yet, this has not led to increased coverage of comprehensive tobacco control services by state Medicaid programs. A recent study estimated cost-savings associated with providing comprehensive tobacco dependence treatment to Medicaid-eligible populations in Alabama. Estimated net savings were \$157,000 annually per pregnant woman and her newborn, \$33,000 annually within four years for each child exposed to second-hand smoke at home, the estimates of annual net savings from smoking cessation treatment associated with short-term medical costs ranged and between \$11.5 million in the first year to \$5.2 million in the second year for the Alabama adult Medicaid population, depending on the choice of smoking attributable medical costs used (61). Comprehensive tobacco control yields tangible and important health outcomes, and significant cost savings for state governments that accrue within a relatively short period of time. And yet, we do not seem to know how to increase uptake of this life-saving evidence.

**Figure 2.**

Demographic-adjusted smoking prevalence of MassHealth members, Age 18–64, 1999 to 2008 (joinpoint trend). Reproduced from Land, et al, *plosone.org*, 2010 (50). The lines on the chart represent the smoking prevalence trends for the MassHealth population as estimated by the joinpoint analysis. The period between January 1, 1999, and June 30, 2006, showed no significant change ( $P = 0.93$ ). Beginning July 1, 2006, there was a significant downward trend ( $P = 0.05$ ).

### Integrating colon cancer screening and cancer treatment into care delivery

The organization of care delivery in ways that maximize population participation in colorectal cancer screening and link to treatment is highlighted by data from the California Cancer Registry (2001–2006; ref. 62). Patients who received care in a large integrated health system (Kaiser Permanente) had overall higher rates of adherence to treatment guidelines and the elimination of disparities in outcomes. The finding of improved mortality rates and elimination of disparities suggests that coordinating processes of care have significant potential for population health benefits and health equity. Research to develop and evaluate specific mechanisms to increase care coordination is critical if we are to more broadly achieve the impact on colorectal cancer mortality and disparities that is clearly possible.

These examples illustrate that when prevention programs are comprehensive and maximize the ability for all populations to participate, major changes in behaviors and morbidity and mortality are achieved in relatively short timeframes. Given the size and rigor of the evidence base, it is frustrating that there continues to be such variability in implementation of clearly beneficial programs.

### What Untapped Levers Could Maximize Use of Existing Evidence on Cancer Prevention?

Given the clear role that policy and environmental approaches play in ensuring population-level access to cancer prevention, increased research to illustrate how to more systematically increase implementation of these approaches is critical, although rarely funded. In the past 5 years, there has been an increasing emphasis on implementation science research, which is the study of methods to promote the integration of research findings and evidence into health care policy and practice (63). Implementation science seeks to understand the behavior of health care

professionals and other stakeholders as a key variable in the sustainable uptake, adoption, and implementation of evidence-based interventions. The field of implementation science offers innovative approaches to identify, understand, and develop strategies for overcoming barriers to the adoption, adaptation, integration, scale-up, and sustainability of evidence-based interventions, tools, policies, and guidelines. Expanding the focus of implementation science to include policy research could be very fruitful.

Brownson and colleagues (37) summarize lessons learned related to population-level prevention of chronic disease, including several that are relevant to implementation science in cancer prevention: (i) start with environmental and policy interventions as the key to initiating and sustaining systematic change; (ii) think across multiple levels of influence; (iii) make better use of existing tools for implementation; (iv) understand local context and politics; (v) build new and nontraditional partnerships; (vi) address health disparities; (vii) conduct more and better policy research. These lessons deserve particular attention in terms of identifying untapped levers for increasing implementation of the cancer prevention evidence base.

### Understand context and politics, think across multiple levels of influence, and build new and nontraditional partnerships

Federal funding agencies have a role in the attention paid to specific priority issues by our legislators and politicians, as the Cancer Moonshot illustrates. If funders better leveraged both this role and their relationships with grantees, several levers could increase implementation of evidence-based prevention programs. First, as a research institution, NIH (Bethesda, MD) has funded much of the existing cancer prevention evidence base. Although accelerating the pace of discovery may improve health, implementation of strategies that have already been demonstrated to be efficacious could also significantly improve population health. Targeted funding opportunities by both NIH and CDC could be used to increase our knowledge of strategies to enhance

implementation at the organization, community, and policy levels. Improved understanding of how organizational characteristics modify institutional behaviors related to implementation of evidence-based prevention strategies could significantly increase the speed of adoption. And in particular, funding specifically focused on policy implementation research could improve our understanding of how to maximize cancer prevention at the population level.

Second, NIH could also identify opportunities to increase uptake of evidence-based cancer prevention programs among institutions that it funds. For example, The NCI (Rockville, MD), which has funded extensive research that demonstrates the power of cancer prevention, spends over \$500 M/year on its 45 comprehensive cancer centers, but does not mandate that they provide cancer prevention services. Only about half provide tobacco use treatment (64), and a survey of medical oncologists reported that few provide cessation support (65). A cancer center that did not utilize evidence-based chemotherapy protocols would not likely be considered competitive for NCI cancer center funding. Applying the same expectation of evidence-based treatment of behavioral risk factors among people with cancer could accelerate reduction of risk among the 13 million cancer survivors in the United States and their families and caregivers. On the surface, this might seem like a largely symbolic recommendation. However, the 2014 Surgeon General's report concludes that there is a causal relationship between smoking and adverse health outcomes and mortality among people with cancer, and that the all-cause mortality could be lowered by 30% to 40% by quitting smoking at the time of cancer diagnosis (19). NCI has recently moved to address this gap in services through supplemental funding of Cancer Center Support grants in FY 17, which is an excellent start. NIH mandates that institutions receiving NIH funding protect research participants from harm. It is not a significant stretch to expect that institutions that receive federal research dollars also implement programs to protect their patients from known preventable harms.

#### Make better use of existing tools

As part of the Moonshot initiative, over 3,200 oncologists have enrolled in CMS' Oncology Care Model. Participating practices are incentivized to provide high value services, such as care coordination, navigation, and national treatment guidelines for care. Inclusion of evidence-based tobacco treatment services as an element of this program would provide these patients with access to a critical intervention that may improve cancer outcomes.

#### Start with environmental and policy initiatives

Settings that provide care to groups with higher prevalence of risk behaviors are critical settings in which to target environmental and policy strategies. People with mental health issues have a smoking prevalence 2 to 4 times greater than the general population; it is estimated that almost half of cigarettes sold in the United States are sold to smokers with mental illness or substance use disorders (66). Although in the last decade, there has been an uptick in the adoption of smoking bans in mental health and substance use (SU) treatment facilities, 20% of inpatient psychiatric facilities (67), and 10% of outpatient drug treatment facilities responding to a survey did not have a smoking ban. However, provision of comprehensive tobacco treatment in these settings is low; only about half of substance use treatment facilities provide any cessation counseling or medication (68), and psychiatrists

deliver cessation counseling to patients who smoke at only 12% of visits (69). The efficacy of smoking cessation treatment in the context of mental health care has been demonstrated, yet currently only 13 states require provision of cessation treatment in alcohol, drug rehabilitation, and/or mental health treatment centers (70). There is a significant opportunity to use accreditation and policy levers to increase uptake of comprehensive cessation treatment in mental health and substance abuse care.

#### Address health disparities

Social determinants contribute to cancer disparities, morbidity, and mortality. However, there is a dearth of evidence pointing the way toward solutions for the significant negative impact that social and economic factors have on health care costs and outcomes (71). There is growing recognition that nonprofit institutions can leverage their role as a stable community asset, or "anchor institution", to develop healthier communities and begin to address social determinants. An anchor institution strategy embeds the philosophy of community benefit throughout an organization's business practices, such as hiring, purchasing, and investing (72), harnessing the institution's economic power in ways that permeates its culture and changes how business is done. (73) This shifts the issue of community benefit from the margins to overall accountability, where virtually all of an institution's resources can be leveraged to benefit the communities in which it is located (73). There is a significant need for research that systematically evaluates the impact of an anchor institution strategy and community development efforts on social determinants and ultimately on cancer outcomes. There is also a need for health care and academic institutions that create scientific evidence to take responsibility for ensuring its implementation in ways that benefits all populations. Partnerships among health care systems and universities can help to harness new resources for population-level cancer prevention.

Low socioeconomic status is related to poor outcomes for cancer treatment even in countries with strong public funding and access to care (our Lancet editorial; ref. 71). Even broad social programs are not sufficient to buffer the effects of cost of care. Economic deprivation is related to increased risk of death from treatable cancers and is also related to access to and completion of screening for cancer. Further study is needed to identify strategies to support low income populations for whom time off work and foregone earnings may undermine participation in prevention programs, and time horizons may work against the promise of prevention.

#### Addressing the Gaps

If we are to benefit as a nation from our investment in cancer research, it is imperative that we focus our research efforts on strategies to reduce variation among states in implementation of effective cancer prevention programs, and within states that have higher uptake to determine how to sustain access and use of preventive services. For far too long, there has been both inertia and active political efforts to reduce the impact of prevention strategies on private industries and/or to use resources generated by cancer prevention strategies for other purposes. This situation is clearly evidenced by the continued underinvestment in tobacco control at the state level, with the highest level of investment being less than 50% of CDC-recommended levels. There is a significant need for research to

understand what social, political, and environmental factors can be used to increase implementation of evidence-based programs, and how to use evidence from successful implementations to increase uptake where it has been lacking.

The U.S. health care system's general approach to cancer screening is one target at a time. As a result, there is under-performance in terms of individuals receiving all recommended cancer screenings. For example, one study in a large community health system found that only about 43% of adults were current on all recommended screenings (74). For colorectal cancer alone, it is estimated that over 24 million adults ages 50–74 years need to be screened in the next 3 years to reach the goal of 80% population coverage by 2018 (75). The large majority of these adults are in the 50 to 64 age range and have less than a 4-year college degree.

Understanding how to scale up for cancer prevention with sufficient population coverage to improve population health metrics is also a research priority (76). An Institute of Medicine workshop identified the components of success: collaboration, community engagement, data, infrastructure and resources, and leadership and vision. Applying these to cancer prevention to reduce disparities and achieve reductions in cancer burden can begin now. Critically, if our efforts to reduce the cancer burden are to go beyond rhetoric, they simply must address implementation factors that influence cancer disparities and have the biggest impact on populations carrying the largest cancer burden. Research questions remain such as: How does scaling up differ from other implementation, if at all? Questions arise such as the strength of the evidence base, the ability to deliver the intervention at low cost, the approaches to monitoring consistency or integrity of the intervention delivery, and outcomes across levels of health system (provider or health department), and individuals. Will additional technical assistance be needed for broader implementation? How is this developed, delivered, and sustained? How flexible can and must the intervention be (77)? What are the measures of organizational success and of overall outcome?

## Deimplementation

The need for research on deimplementation is highlighted in the NCI PAR-16-238, which sees this as a means to move more quickly to effective and efficient delivery of evidence-based interventions. The PAR calls for "studies of the de-implementation of clinical and community practices that are not evidence-based, have been prematurely widely adopted, yield sub-optimal benefits for patients, or are harmful or wasteful." There have been efforts across health systems to focus on these types of practices. For example, The Choosing Wisely campaign launched in 2012 in the United States aims to encourage abandoning care that wastes resources or delivers no benefit in specific health areas, such as management of blood sugar and diabetes, and cancer screening. In Australia, the national cervical cancer screening program has incorporated evidence-based changes in practice, such as elimination of PAP smears and replacement with 5-year HPV testing. These types of programs offer opportunities to consider the perspectives, facilitators, and barriers to deimplementation from the patient, provider, testing laboratory, and insurance perspectives. Deimplementation will likely not be the inverse of implementation and dissemination uptakes (78). Furthermore, there are likely very different social factors at work in the

implementation versus deimplementation context. For example, women have been told for decades that they must have yearly mammograms and may have many friends who had breast cancer detected via routine mammography. Asking them now to have fewer mammograms, or at older ages to stop completely, may test their confidence in their provider and the health care system, and go against deeply rooted beliefs about taking care of themselves. Where to begin to remove inefficient or unnecessary practices remains an area of study to begin this process, as does identifying the characteristics of the people who will lead or resist deimplementation and how they may differ from those who lead implementation (79). The approach to studying deimplementation mechanisms examines variation among systems, providers, patients, and the actual implementation strategies that may modify the success of the program (80).

## Research on Etiology Still Needed

Although health behavior and medical components of effective prevention programs together demonstrate that more than 50% of cancer can be prevented, it is noteworthy that some of the common cancers still have few (e.g., lymphoma and multiple myeloma) or no (e.g., prostate, brain) identified major modifiable risk factors. Furthermore, several cancers, such as pancreas and breast cancer, have disparities in incidence that are not accounted for by established risk factors, or that leave subtypes disproportionately affecting non-Hispanic Blacks (81).

For pancreas cancer, incidence is higher in Blacks than Whites and mortality is significantly higher (82). On the basis of analysis of the prospective data from the American Cancer Society Cancer Prevention Study II, this excess burden is not accounted for by smoking and obesity (83).

Prostate cancer incidence rises with age, but even by age 45 to 49, excess incidence is observed among African American men in the United States. This, together with the known length of time needed to accumulate genetic changes to develop cancer in humans, points to early life factors that have been poorly evaluated in epidemiologic studies to date (84). Adiposity at ages 5 and 10 may be related to cancer risk across the life course, in part through modifying the tempo of growth and maturation (85, 86). This is evident for breast cancer in women, but data are less consistent for prostate cancer and extremely limited for lymphoma, although adiposity in adolescence and young adulthood is related to increased risk of non-Hodgkin lymphoma and myeloma (87), and pancreatic cancer (88).

For breast cancer, non-Hispanic Black women have historically had lower incidence but higher mortality. Recent evidence shows that incidence rates have converged with non-Hispanic White women and mortality is elevated, in part due to later stage at diagnosis and a higher proportion of triple-negative tumors (89).

Although fetal origins of adult health have been well accepted in cardiovascular disease and diabetes, in cancer, the study of *in utero* and early-life exposures has lagged. These exposures may importantly modify risk across the life course (90). Refined animal models may help reduce the elapsed time to gain insights to these life course pathways. Trajectories of weight change may also modify risk (91). How these markers vary or which markers may reflect pathways beyond measures of adiposity is actively being studied through large data banks and repositories. Integrating new markers to current lifestyle and genetic-based risk

prediction models will clearly challenge the ultimate usefulness of these markers for risk stratification and prevention. An essential question focuses on quantifying the added value of new markers above the measures of weight and height that are already available at much lower cost and with fewer office visits.

## Conclusion

When we implement evidence-based prevention programs correctly and at scale, we achieve substantial population benefits. Although many efforts are underway to maximize our knowledge about the causes and treatments of cancer, we can achieve reductions in cancer burden right now by doing what we already know.

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No potential conflicts of interest were disclosed.

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Conception and design: G.A. Colditz, K.M. Emmons

Development of methodology: G.A. Colditz

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): G.A. Colditz

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Writing, review, and/or revision of the manuscript: G.A. Colditz, K.M. Emmons

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