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An Ounce of Prevention: Deaths Averted From Primary Prevention Interventions

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Abstract

Introduction—The U.S. lags in the nationwide implementation of primary prevention interventions that have been shown to be efficacious. However, the potential population health benefit of widespread implementation of these primary prevention interventions remains unclear.

Methods—Authors reviewed the meta-analytic literature from October 2013 to March 2014 of primary prevention interventions published between January 2000 and March 2014. Authors then estimated the number of deaths that could have been averted in the U.S. in 2010 if all rigorously studied, efficacious primary prevention interventions for which population attributable risk proportions could be estimated were implemented nationwide.

Results—A total of 372,054 (15.1%) of all U.S. deaths in 2010 would have been averted if all rigorously studied, efficacious primary prevention interventions were implemented. Two in three averted deaths would have been from cardiovascular disease or malignancy.

Conclusions—A substantial proportion of deaths in the U.S. in 2010 could have been averted if efficacious primary prevention interventions were implemented nationwide. Further investment in the implementation of efficacious interventions is warranted to maximize population health in the U.S.

INTRODUCTION

In 2010, the U.S. ranked 24th of the 30 member countries in the Organization for Economic Cooperation and Development with respect to life expectancy.¹ This poor ranking is driven by higher burdens of preventable diseases, including diabetes and cardiovascular disease, as

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compared with similar countries.¹ Americans also spend far more on health care than any other country. Between 2009 and 2013, a total of 17.9% of U.S. gross domestic product was spent on health care.² Per capita healthcare spending over the same period was \$8,895, nearly twice the average of high-income countries and nearly \$3,000 more than the next-highest spender.² Healthcare costs have grown faster in the U.S. than in any other country over the past 40 years. Although U.S. health outcomes and spending per capita were similar to those in other Organization for Economic Cooperation and Development countries in 1975, costs have increased while survival advantage has decreased comparatively.³

One potential explanation for the discrepancy in health outcomes relative to health spending is the proportion of health expenditures allocated to primary prevention—activities, often occurring outside of clinical settings, intended to prevent morbidity and mortality prior to disease occurrence. In 2012, the U.S. spent \$74.9 billion on government-related public health activities, comprising 2.7% of total health expenditures.⁴ During this same time, the U.S. spent \$1.1 trillion on hospital care and prescription drugs.⁴

Although there are several reasons for this relative underinvestment in primary prevention, including prolonged time horizon for returns and the size and value of the curative healthcare industry, one central challenge is lack of quality data about the efficacy of primary prevention.⁵ Disease prevention is often equated with clinical, or secondary, preventive services.^{6–8} These services are provided in the clinical setting, and tend to be costly and sometimes ineffective. For example, prostate-specific antigen screening may not only be expensive (costing \$214,00 per year of life saved), but may produce more harm than good.⁹ Other clinical preventive services, including counseling adults in primary care settings to increase physical activity, have similarly inconclusive support.¹⁰ Even so, current estimates suggest that adopting a package of 20 of the U.S. Preventive Services Task Force–recommended secondary prevention interventions would result in 7,233,195 life years saved per annum.^{7,8}

The systematic exclusion of primary prevention interventions in extant analyses raises the question: How many deaths could be averted if the U.S. adopted efficacious primary prevention interventions nationwide? To answer this question, authors: (1) systematically reviewed the current primary prevention literature identifying efficacious interventions; and (2) estimated the number of deaths that could have been averted in the U.S. in 2010 if those interventions were implemented nationwide.

METHODS

Data Sample

First, authors reviewed the ICD-10 of 358 causes of death in the U.S. to determine causes of death that could be prevented by primary prevention interventions,¹¹ as defined by Centers for Disease Control and Prevention (CDC).¹² Two public health physicians (SG, PM) independently categorized causes of death into preventable and non-preventable classes. In the case of categorization discrepancy, a third physician made the final determination (AME). Causes of death for which there was no categorization consensus were included as preventable. Second, the number of age-specified deaths in the U.S. in 2010 were obtained

from CDC's Underlying Cause of Death database.¹² Causes of death for which <1,000 people died were removed, as elimination of these deaths would have relatively little public health consequence, leaving a final list of 124 preventable causes of death in the U.S. Third, authors identified preventable risk factors for the preventable causes of death identified through a review of UpToDate, a database of medical information for clinicians,¹³ and if not available, searched content-specific websites or databases (e.g., National Cancer Institute) or PubMed with the search terms *cause of death* AND *risk factors*.

Study Selection and Data Collection

Authors appraised the primary prevention literature for the U.S. to identify intervention meta-analyses that prevented the identified causes of death and known proximal risk factors through a systematic review performed from October 2013 to March 2014. First, the Cochrane Library¹⁴ was searched; if the search returned no meta-analyses, then PubMed was searched following the same process. Studies were eligible for review if: they were meta-analyses, the intervention was primary prevention, the review was published between 2000 and March 2014, results were in English, article full text was available, and the intervention was generalizable in the U.S. The following search terms were queried: *prevention* and *intervention*, with the cause of death or risk factor. Two authors (SH, SK) performed all of the searches to determine article inclusion by reviewing article titles and abstracts. Second, the following information was extracted from articles: citation, publication year, study population, intervention, outcome, number of articles in meta-analysis, summary effect estimate, CIs, and heterogeneity and bias assessment. Third, effect estimate applicability was determined based on the generalizability of the intervention to populations at risk of developing the disease. For example, interventions from low- and middle-income countries may not be suitable to the U.S. context. Fourth, authors assessed summary effect estimate statistical significance. Fifth, for each summary effect estimate, its rigor was evaluated related to statistical heterogeneity, which assesses consistency of effects across studies, and bias risk. Primary prevention protocols, defined as any applicable summary effect estimate for an intervention in a meta-analysis, were considered rigorous, informed by the Cochrane Collaboration,¹⁵ if: (1) the I^2 heterogeneity score was <75% and χ^2 for heterogeneity $p>0.10$; and (2) the bias risk was low to medium. Sixth, to identify the most rigorous and efficacious primary prevention protocol, if there were overlapping interventions addressing the same population for the same cause of death, mortality-specific interventions were prioritized, over risk factor-specific outcomes, followed by those with longer lag periods between intervention and outcome. If overlap still remained, the most efficacious intervention protocol was applied in the calculation of preventable deaths. Although multiple primary prevention protocols could theoretically be applied to the same population, to avoid overestimating the number of averted deaths, one protocol was applied to each underlying mortality population. Authors removed summary effect measures where the population attributable risk (PAR) could not be calculated (absolute effect measures). Figure 1 shows an overview of selection and inclusion process.

Statistical Analysis

To maximize rigor, the analysis was restricted to primary prevention protocols where an attributable risk estimate could be obtained (e.g., ratio estimates).¹⁶ For example, no

estimate of the impact of removing cigarette smoke exposure from the U.S. population was calculated, but rather the application of smoking prevention programs to the U.S. population. The number of preventable deaths from chosen interventions was calculated by applying the PAR formula to 2010 data from CDC's Underlying Cause of Death database:¹²

$$p\left(\frac{RR - 1}{RR}\right), \quad \text{Equation 1}$$

where p is the proportion of those that died who had the intervention-targeted risk factor or behavior and RR is the relative risk (protocol efficacy).¹⁷ If this information was unavailable, the PAR was applied to the underlying risk factor distributions among those diagnosed with the disease or illness, or the risk factor distributions among the U.S. population as a proxy (e.g., 2010 data from CDC's Behavioral Risk Factor Surveillance System),¹⁸ ensuring calculated potentially averted deaths were restricted to only that subpopulation that could have benefited from the intervention. For consistency, all relative estimates were reported as >1 ; if original documentation presented relative estimates <1 , they were inverted ($1/RR$) and the interpretation was similarly adjusted.¹⁶ The same formula was applied for ORs and RRs under the rare disease assumption.¹⁹ Appendix Figure 1 provides an example of review process and PAR calculation for one cause of death.

RESULTS

Out of 808 identified primary prevention protocols, 25 met evidence quality criteria for inclusion into the analysis (Figure 1). Applying these 25 rigorously studied, efficacious prevention protocols for which PAR could be calculated could have prevented 372,054 deaths (15.1%) in the U.S. in 2010.

The proportion of preventable deaths varied by cause of death and intervention (Table 1). The 25 discrete efficacious protocols ranged in efficacy from $RR=0.15$ (6.67 inverted, human papillomavirus [HPV] vaccine, type 16)²⁰ to $RR=0.88$ (1.14 inverted, home fall prevention environment/assistive technology interventions, Table 1).²¹ When applied to specific risk populations, efficacious protocols could have averted between 68.4% (HPV vaccine type 18 averting vulva/vagina malignant neoplasms)²⁰ to 0.2% (school-based obesity prevention averting pulmonary embolism)²² of potentially preventable cause-specific mortality. Implementing a smoking prevention protocol could have averted the highest number of deaths (219,825, 8.9% of all-cause mortality).

Table 2 shows mortality by cause of death, potentially preventable mortality, and averted deaths, had rigorously studied, efficacious primary prevention protocols been implemented. Cardiovascular diseases (784,422 deaths, 31.8% of all-cause mortality) and malignancy (589,655 deaths, 23.9% of all-cause mortality) accounted for $>55.7\%$ of U.S. mortality in 2010, and 67.7% of deaths potentially averted.

Figure 2 maps causes of death (Panel A), risk factors (Panel B), and efficacious protocols (Panel C). The area of each circle is proportional to the absolute number of deaths that would have been averted in 2010. Chronic ischemic heart disease and trachea, bronchus, and

lung malignant neoplasms accounted for the highest number of averted deaths. Smoking and alcohol abuse were the two risk factors with the highest associated avertable mortality. Smoking prevention programs and statin use for cardiovascular disease prevention were the two protocols accounting for the greatest proportion of avertable deaths. Panel D shows linkages across categories. Hand washing, motorcycle helmets, fire/hazardous material home safety, and HIV prevention interventions were responsible for averting several causes of death for which no other efficacious prevention protocol existed.

DISCUSSION

Nationwide implementation of rigorously studied, efficacious primary prevention protocols could have averted at least 15.1% (372,054) of all 2010 deaths. This is the first study that has systematically reviewed and considered the population health consequences of the implementation of evidence-based primary prevention interventions. This work builds on and contrasts with a large body of research about efficacy and effectiveness of primary prevention.^{7,8,23,24}

This analysis differs from previous work in three important ways. First, this study considered implementation of primary prevention protocols that extended beyond clinical interventions to pre-clinical interventions.⁸ Second, this analysis only admitted evidence-based interventions, rather than relying on expert opinion.^{25,26} Third, the interest was in providing data about the number of deaths that would be averted by applying the most efficacious primary prevention protocols evaluated to date.

The approach was conservative, as it excluded potentially efficacious prevention protocols that have not been evaluated or for which PAR could not be calculated. This may explain why these estimates of averted deaths are lower than those derived from other approaches, including theoretic maximal risk factor removal, which usually implies theoretic statistical reduction or removal of risk factors, independent of interventions to achieve such reductions.^{26,27} It is not implausible that the widespread implementation of other primary prevention efforts could avert more deaths than those documented; however, the deaths averted here present a theoretic minimum given the state of the evidence base. As other interventions are shown to be efficacious, and are successfully implemented, deaths that can be averted through prevention will increase.

Three primary prevention protocols with most impact accounted for 76.1% (283,279 deaths) of total averted deaths. Although the smoking prevention protocol applied here was not one of the most efficacious, it was among the most effective given the primacy of smoking as a determinant of many downstream causes of death. This is consistent with current interventions to address distal, universal factors that increase mortality, such as those preventing violent victimization,²⁸ transportation fatalities,²⁹ and lung and pancreatic cancer.³⁰ Although there is good reason to suspect that distal interventions would be effective at reducing mortality, data on these interventions are sparse and suggest a need for research to fill the gap around potentially important distal interventions.

Limitations

The reader should be aware of several limitations. First, the analysis relied on national death records, which may be imprecise in recording exact causes of death.³¹ However, it is unlikely that this would have systematically biased the evaluation of the potential of primary prevention interventions as it is an inherent limitation in all national, surveillance system-based analyses. Second, the analysis did not encompass the full universe of efficacious primary prevention protocols. Some were excluded because they could not be statistically manipulated and some may have been excluded in the search strategy. Importantly, there were no causes of death against which only studies with absolute measures were available; the exclusion of these studies did not exclude potentially efficacious prevention against full causes of death. Moreover, this exclusion results in an underestimate of the true death-averting capacity of evidence-based primary prevention, suggesting that the findings should be interpreted as a minimum proportion of averted deaths. Third, as the substance of the review was meta-analyses, it is plausible that structural (e.g., cigarette taxes) or newer interventions that have not been subject to meta-analysis or where meta-analytic approaches are inappropriate were excluded. One major omission is early life education programs, which have been tested in experimental studies but for which mortality reductions are poorly documented.³² However without meta-analytic evaluation, authors were unable to evaluate the evidence, echoing the need for more research. As with other limitations, this omission likely results in an underestimate of averted deaths. Fourth, although the approach used involved the theoretic implementation of evidence-based interventions rather than risk factor removal, potential challenges posed by competing risks were inadequately addressable. For example, if an intervention successfully prevents smoking among those who would have died of smoking-related lung cancer, those factors that predicted their likelihood of smoking may have exposed them to other risk factors, which might have led to early death even without smoking.³³ This was a major motivation for exploring deaths averted in a single calendar year within which other causes of death are less likely, making it a metric less susceptible to this limitation. Fifth, consistent with other intervention application analyses,^{7,25,34} the population estimates used to calculate PAR could have been different from the actual populations at risk because of differences between populations used to derive those estimates and the U.S. population overall. Sixth, at times precise population estimates of risk factor burdens among individuals who died from a cause of death were unavailable, thus population estimates based on disease burden, not mortality, were applied. It is well documented that those who die from a cause of death might have a different distribution of risk factors than those diagnosed.³⁵ Thus, interventions might have greatest efficacy at the extremities of disease severity, with counterbalancing implications for estimate validity.^{5,31} Seventh, it is possible that those who died had some level of exposure to the proposed interventions that addressed the associated risk factors, overestimating averted deaths. Data are limited as to the proportion of people who were exposed to a primary prevention intervention that addressed a risk factor for a disease and subsequently died from that disease. As the interventions included in this analysis have not been fully scaled, it is assumed that this would not change the results considerably. Eighth, the analysis uncovered efficacious, not effective interventions, assuming effectiveness would follow. Exploring barriers to scale-up, adherence, and potential decreases in efficacy over time and the life course are beyond the scope of this analysis; data about implementation barriers for

effectiveness assessments are limited.²⁷ Ninth, though the review aimed to include interventions considered primary prevention, the distinction between primary and secondary prevention is not always clear.³⁶ For example, statins as primary prevention among people without prior cardiac events and who were naive to statin use were included. The goal was to include interventions for which data suggested efficacious prevention of disease ahead of pathologic development, consistent with most definitions of primary prevention,³⁶ while recognizing that other definitions are possible.

This systematic review of the prevention literature highlights two important challenges to prevention science. First, a small proportion of primary prevention interventions for which research has been conducted were rigorously studied and efficacious. Of 808 primary prevention protocols, only 25 met stringent quality criteria for inclusion into the analysis. Several interventions that are often considered by the public health community to be efficacious, such as mass media campaigns for the prevention of drug use and omega-3 fatty acid supplements for cognitive function, were not statistically significant.^{37,38} There were 11 potentially preventable causes of death with no known cause-specific or risk factor-specific intervention and four clusters of causes of death and associated risk factors for which only one efficacious primary prevention protocol existed. These data suggest the need for more prevention research.

Second, there is a dearth of evidence for primary prevention interventions that are efficacious against the most prevalent causes of mortality. For example, ischemic heart disease was the most common cause of death in 2010, killing 379,543 (15.4%) Americans.¹² By contrast, the most efficacious primary prevention intervention was the HPV vaccine, targeting HPV and cervical cancer, which killed 3,939 Americans in 2010.¹² This may be a function of the etiologic complexity of prevalent diseases. Although complexity may decrease the efficacy of any one intervention, it also opens several more avenues for intervention; the analysis did not find higher prevalence diseases generally had a higher number of efficacious interventions to counterbalance the relative inefficacy of those documented. There still remains substantial room for investment in creating and testing primary prevention interventions that target the most common causes of mortality in America.

CONCLUSIONS

Based on the dearth of rigorous intervention studies identified here, more research regarding the efficacy of primary prevention interventions is needed. Another extension of this work would be to consider the cost effectiveness of implementing primary prevention interventions. These findings suggest that investments in primary prevention interventions have the potential to avert substantial mortality in the U.S. This implies that the 2.7% of health funding currently allocated to prevention may be inadequate and deeper investments are needed, considering that 15% of mortality could potentially be prevented through current interventions. In particular, interventions against high burden risk factors, even if minimally efficacious, can lead to substantial public health gains. Early investments in primary prevention should target highly burdensome risk factors to maximize the potential public health influence of primary prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Woolf, SH., Aron, L. U.S. Health in International Perspective: Shorter Lives, Poorer Health. Washington, DC: National Academies Press; 2013.
2. The World Bank. [Accessed November 14, 2014] Health expenditure, total (% of GDP). 2014. <http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS>
3. Muennig PA, Glied SA. What changes in survival rates tell us about U.S. health care. *Health Aff (Millwood)*. 2010; 29(11):2105–2113. <https://doi.org/10.1377/hlthaff.2010.0073>. [PubMed: 20930036]
4. Martin AB, Hartman M, Whittle L, Catlin A. National Health Expenditure Accounts Team. National health spending in 2012: rate of health spending growth remained low for the fourth consecutive year. *Health Aff (Millwood)*. 2014; 33(1):67–77. <https://doi.org/10.1377/hlthaff.2013.1254>. [PubMed: 24395937]
5. Yach D, Calitz C. New opportunities in the changing landscape of prevention. *JAMA*. 2014; 312(8): 791–792. <https://doi.org/10.1001/jama.2014.8900>. [PubMed: 25032720]
6. Woolf SH. The power of prevention and what it requires. *JAMA*. 2008; 299(20):2437–2439. <https://doi.org/10.1001/jama.299.20.2437>. [PubMed: 18505953]
7. Maciosek MV, Coffield AB, Edwards NM, Flottemesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services: results of a systematic review and analysis. *Am J Prev Med*. 2006; 31(1):52–61. <https://doi.org/10.1016/j.amepre.2006.03.012>. [PubMed: 16777543]
8. Maciosek MV, Coffield AB, Flottemesch TJ, Edwards NM, Solberg LI. Greater use of preventive services in U.S. health care could save lives at little or no cost. *Health Aff (Millwood)*. 2010; 29(9): 1656–1660. <https://doi.org/10.1377/hlthaff.2008.0701>. [PubMed: 20820022]
9. Albertsen PC. Screening for prostate cancer is neither appropriate nor cost-effective. *Urol Clin North Am*. 1996; 23(4):521–530. [https://doi.org/10.1016/S0094-0143\(05\)70332-3](https://doi.org/10.1016/S0094-0143(05)70332-3). [PubMed: 8948407]
10. Eden KB, Orleans CT, Mulrow CD, Pender NJ, Teutsch SM. Does counseling by clinicians improve physical activity? A summary of the evidence for the US Preventive Services Task Force. *Ann Intern Med*. 2002; 137(3):208–215. <https://doi.org/10.7326/0003-4819-137-3-200208060-00015>. [PubMed: 12160371]
11. WHO. International Classification of Diseases, Tenth Revision. 2010. www.who.int/classifications/icd/en/
12. CDC. [Accessed September 15, 2013] CDC Wonder: Underlying Cause of Death. 2010. <http://wonder.cdc.gov>
13. UpToDate. UpToDate website. <http://www.uptodate.com>
14. The Cochrane Collaboration. The Cochrane Library. <http://www.thecochranelibrary.com>
15. Higgins, JPT., Green, S. Cochrane Handbook for Systematic Review of Interventions. Version 5.1.0. Updated March 2011. The Cochrane Collaboration. 2011. <http://handbook.cochrane.org>

16. Greenland S. Bias in methods for deriving standardized morbidity ratio and attributable fraction estimates. *Stat Med*. 1984; 3(2):131–141. <https://doi.org/10.1002/sim.4780030206>. [PubMed: 6463450]
17. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. *Am J Public Health*. 1998; 88(1):15–19. <https://doi.org/10.2105/AJPH.88.1.15>. [PubMed: 9584027]
18. CDC. Behavioral Risk Factor Surveillance System. <http://www.cdc.gov/brfss/>
19. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998; 280(19):1690–1691. <https://doi.org/10.1001/jama.280.19.1690>. [PubMed: 9832001]
20. Lu B, Kumar A, Castellsague X, Giuliano AR. Efficacy and safety of prophylactic vaccines against cervical HPV infection and diseases among women: a systematic review & meta-analysis. *BMC Infect Dis*. 2011; 11:13. <https://doi.org/10.1186/1471-2334-11-13>. [PubMed: 21226933]
21. Gillespie, LD., Robertson, MC., Gillespie, WJ., et al. Interventions for preventing falls in older people living in the community; Cochrane Database Syst Rev. 2012. p. CD007146 <https://doi.org/10.1002/14651858.cd007146.pub3>
22. Gonzalez-Suarez C, Worley A, Grimmer-Somers K, Dones V. School-based interventions on childhood obesity: a meta-analysis. *Am J Prev Med*. 2009; 37(5):418–427. <https://doi.org/10.1016/j.amepre.2009.07.012>. [PubMed: 19840696]
23. Vitality Institute. Investing in Prevention: A National Imperative; Key Findings and Recommendations of the Vitality Institute Commission on Health Promotion and the Prevention of Chronic Disease in Working-Age Americans. New York: Vitality Institute; 2014. http://thevitalityinstitute.org/site/wp-content/uploads/2014/06/Vitality_Recommendations2014.pdf
24. McGinnis JM, Williams-Russo P, Knickman JR. The case for more active policy attention to health promotion. *Health Aff (Millwood)*. 2002; 21(2):78–93. <https://doi.org/10.1377/hlthaff.21.2.78>.
25. World Economic Forum. From Burden to "Best Buys": Reducing the Economic Impact of Non-Communicable Diseases in Low- and Middle-Income Countries. Geneva, Switzerland: World Economic Forum; 2011. http://www3.weforum.org/docs/WEF_WHO_HE_ReducingNonCommunicableDiseases_2011.pdf [Accessed November 22, 2014]
26. Hutubessy R, Chisholm D, Edejer TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. *Cost Eff Resour Alloc*. 2003; 1(1):8. <https://doi.org/10.1186/1478-7547-1-8>. [PubMed: 14687420]
27. Yoon PW, Bastian B, Anderson RN, et al. Potentially preventable deaths from the five leading causes of death--United States, 2008–2010. *MMWR. Morb Mortal Wkly Rep*. 2014; 63(17):369–374. [PubMed: 24785982]
28. Cerda M, Tracy M, Ahern J, Galea S. Addressing population health and health inequalities: the role of fundamental causes. *Am J Public Health*. 2014; 104(Suppl 4):S609–619. <https://doi.org/10.2105/AJPH.2014.302055>. [PubMed: 25100428]
29. Fuller D, Morency P. A population approach to transportation planning: reducing exposure to motor-vehicles. *J Environ Public Health*. 2013; 2013:916460. <https://doi.org/10.1155/2013/916460>. [PubMed: 23840236]
30. Rubin MS, Clouston S, Link BG. A fundamental cause approach to the study of disparities in lung cancer and pancreatic cancer mortality in the United States. *Soc Sci Med*. 2014; 100:54–61. <https://doi.org/10.1016/j.socscimed.2013.10.026>. [PubMed: 24444839]
31. German RR, Fink AK, Heron M, et al. The accuracy of cancer mortality statistics based on death certificates in the United States. *Cancer Epidemiol*. 2011; 35(2):126–131. <https://doi.org/10.1016/j.canep.2010.09.005>. [PubMed: 20952269]
32. Muennig P. Can universal pre-kindergarten programs improve population health and longevity? Mechanisms, evidence, and policy implications. *Soc Sci Med*. 2015; 127:116–123. <https://doi.org/10.1016/j.socscimed.2014.08.033>. [PubMed: 25174771]
33. Rothman KJ. Causes. *Am J Epidemiol*. 1976; 104(6):587–592. [PubMed: 998606]
34. Kelly M, Morgan A, Ellis S, Younger T, Huntley J, Swann C. Evidence based public health: A review of the experience of the National Institute of Health and Clinical Excellence (NICE) of developing public health guidance in England. *Soc Sci Med*. 2010; 71(6):1056–1062. <https://doi.org/10.1016/j.socscimed.2010.06.032>. [PubMed: 20678836]

35. Murphy DG, Ahlering T, Catalona WJ, et al. The Melbourne Consensus Statement on the early detection of prostate cancer. *BJU Int.* 2014; 113(2):186–188. <https://doi.org/10.1111/bju.12556>. [PubMed: 24206066]
36. Gordon RS Jr. An operational classification of disease prevention. *Public Health Rep.* 1983; 98(2): 107–109. [PubMed: 6856733]
37. Ferri, M., Allara, E., Bo, A., Gasparrini, A., Faggiano, F. Media campaigns for the prevention of illicit drug use in young people; *Cochrane Database Syst Rev.* 2013. p. CD009287<https://doi.org/10.1002/14651858.cd009287.pub2>
38. Sydenham, E., Dangour, AD., Lim, WS. Omega 3 fatty acid for the prevention of cognitive decline and dementia; *Cochrane Database Syst Rev.* 2012. p. CD005379<https://doi.org/10.1590/s1516-31802012000600013>

Figure 1.
Systematic meta-analyses literature search and primary prevention intervention protocol selection process.

Figure 2.

Density maps of potentially preventable deaths from published primary prevention interventions, 2010.

Notes: The area of each circle indicates the relative importance of each factor with respect to potential averted mortality in 2010, while connections map the ways in which published prevention interventions map to potentially preventable deaths. Figures are displayed to facilitate interpretation; apparent geo-clustering is not analytically relevant. The largest two categories, by potentially preventable deaths, in each map are highlighted (1, malignant neoplasms of the trachea, bronchus, and lung; 2, chronic ischemic heart disease; 3, smoking; 4, alcohol abuse; 5, smoking prevention programs; 6, statins for cardiovascular disease prevention). Light gray, cause of death; dark gray, risk factor; black, intervention.

Deaths Potentially Averted by Published Primary Prevention Intervention Protocol, 2010

Table 1

Primary prevention protocol	Cause(s) of death (Risk factor)	Effect estimates (95% CI)	Cause-specific deaths N	Absolute cause-specific deaths averted N (95% CI)	Cause-specific deaths averted N (95% CI)
All interventions				372,054 (145,738, 513,314)	15.1 (5.9, 20.8)
Smoking prevention programs	Conditions from perinatal period; diseases of the circulatory system; digestive system; respiratory system; mental and behavioral disorders; musculoskeletal system and connective tissue; osteopathies, chondropathies and other disorders of musculoskeletal system and connective tissue; neoplasms; sudden infant death syndrome (Smoking)	2.04 (1.15, 3.57)	1,144,741	219,825 (56,034, 310,342)	19.2 (4.9, 27.1)
Statins for prevention of cardiovascular disease events	Diseases of the circulatory system (Cardiovascular disease)	1.37 (1.25, 1.49)	419,663	37,959 (28,117, 46,394)	9.0 (6.7, 11.1)
Mentoring to prevent alcohol use	Diseases of the circulatory system; digestive system; genitourinary system; respiratory system; endocrine, nutritional and metabolic diseases; external causes of mortality - accidents; mental and behavioral disorders; musculoskeletal system and connective tissue; neoplasms (Alcohol abuse)	1.41 (1.11, 1.75)	1,012,728	25,859 (9,533, 40,992)	2.6 (0.9, 4.0)
Statins for prevention of circulatory system related diseases ^a	Diseases of the circulatory system	1.28 (1.12, 1.47)	136,796	24,268 (12,134, 35,298)	17.7 (8.9, 25.8)
School-based obesity prevention	Diseases of the circulatory system; digestive system; respiratory system; endocrine, nutritional and metabolic diseases; neoplasms (Obesity)	1.23 (1.03, 1.47)	346,935	16,169 (2,784, 27,103)	4.7 (0.8, 7.8)
Hazardous materials home safety interventions	External causes of mortality - accidents	1.53 (1.27, 1.84)	35,460	12,284 (7,539, 16,188)	34.6 (21.3, 45.7)
Adjusted-dose warfarin for prevention of general stroke ^b	Diseases of the circulatory system (Atrial fibrillation)	1.47 (1.18, 1.85)	122,965	5,902 (2,767, 8,485)	4.8 (2.3, 6.9)
Compression stockings	Diseases of the circulatory system (Deep venous thrombosis)	6.25 (2.94, 14.29)	20,314	5,119 (4,022, 5,668)	25.2 (19.8, 27.9)
Hand washing	Infectious and parasitic diseases	1.64 (1.09, 2.50)	10,347	4,035 (828, 6,208)	39.0 (8.07, 60.0)
HPV vaccine, type 18	Neoplasms (HPV)	4.17 (2.38, 7.14)	20,034	3,316 (2,530, 3,752)	16.6 (12.6, 18.7)
Skills-based interventions to prevent hard drug use	Diseases of the circulatory system; endocrine, nutritional and metabolic diseases; external causes of mortality - intentional; mental and behavioral disorders (Drug abuse)	2.22 (1.18, 4.17)	93,358	2,996 (817, 4,140)	3.2 (0.9, 4.4)
Influenza vaccine	Bacterial and viral pneumonia (Influenza)	2.56 (1.92, 3.33)	2,985	1,735 (1,365, 1,991)	58.1 (45.7, 66.7)
Antiretroviral therapy as prophylaxis	Infectious and parasitic diseases - HIV	3.03 (1.82, 5.00)	8,369	1,501 (1,008, 1,792)	17.9 (12.0, 21.4)

Primary prevention protocol	Cause(s) of death (Risk factor)	Effect estimates (95% CI)	Cause-specific deaths N	Absolute cause-specific deaths averted N (95% CI)	Cause-specific deaths averted N (95% CI)
HPV vaccine, type 16	Neoplasms (HPV)	6.67 (4.35, 10.00)	16,104	1,998 (1,810, 2,116)	12.4 (11.2, 13.1)
Motorcycle helmets	External causes of mortality – accidents	1.72 (1.47, 2.00)	4,288	1,801 (1,372, 2,144)	42.0 (32.0, 50.0)
Home environment or assistive technology interventions	External causes of mortality – accidental falls	1.14 (1.04, 1.25)	14,780	1,774 (591, 2,956)	12.0 (4.0, 20.0)
Fire prevention home safety interventions	External causes of mortality – accidents	2.01 (1.45, 2.77)	2,781	1,188 (734, 1,510)	42.7 (26.4, 54.3)
Prenatal iron multiple- micronutrient supplements	Conditions from perinatal period (Preterm birth and low birth weight)	1.23 (1.03, 1.47)	20,894	874 (138, 1,473)	4.2 (0.7, 7.0)
Safer-sex behavioral interventions ^c	Diseases of the respiratory system; infectious and parasitic diseases – HIV	1.37 (1.18, 1.59)	8,369	867 (482, 1,188)	10.4 (5.8, 14.2)
Healthy diet interventions	Conditions from perinatal period; diseases of the respiratory system; sudden infant death syndrome (Preterm birth and low birth weight)	1.47 (1.04, 2.08)	10,288	670 (84, 1,089)	6.5 (0.8, 10.6)
Sexual health interactive computer based interventions ^d	Diseases of the respiratory system; infectious and parasitic diseases – HIV	1.75 (1.18, 2.59)	8,369	581 (207, 832)	6.9 (9.9, 2.5)
Male circumcision	Bacterial and viral pneumonia (Influenza)	2.17 (1.61, 2.94)	8,369	460 (324, 563)	5.5 (3.9, 6.7)
Adjusted-dose warfarin for prevention of ischemic stroke	Diseases of the circulatory system (Atrial fibrillation)	1.89 (1.47, 2.44)	6,509	459 (312, 576)	7.1 (4.8, 8.9)
Neuraxial blockade, individuals undergoing surgery	Diseases of the respiratory system	2.22 (1.27, 3.85)	46,610	385 (147, 517)	0.8 (0.3, 1.1)
Vitamin D and calcium	Osteoporosis	1.19 (1.04, 1.37)	1,089	29 (7, 49)	2.7 (0.6, 4.5)

Notes: Efficacy of intervention protocol was originally published as either ORs or RRs. Efficacy estimates that were originally reported as protective (less than 1.0) have been inverted to be greater than 1.0 for comparison purposes in this analysis. For example, vaccines targeting HPV type 16 were published with a summary effect estimate of 0.15 interpreted as the decreased risk of death after vaccination. Once inverted, 1/RR, the summary effect estimate becomes 6.67 interpreted as the increased risk of life or death averted after vaccination. 95% CIs and cause-specific causes of death based on primary protocol publication.

^aNot specific to CVD.

^bDoes not include ischemic stroke.

^cSpecific to men who have sex with men populations.

^dDoes not include men who have sex with men population. HPV, human papillomavirus; CVD, cardiovascular disease

Table 2

Causes of Death and Percent of Deaths Prevented by Published Primary Public Health Interventions, 2010

	Deaths 2010	Potentially preventable deaths	Deaths averted
Cause of death category	(n=2,468,260)	(n=1,902,529)	(n=372,054)
	N	N	N (%)
Circulatory system diseases	784,422	706,353	140,229 (17.88)
Rheumatic heart diseases	2,987	n/a	n/a
Hypertensive diseases	63,111	63,111	2,260 (3.58)
Ischemic heart diseases	379,543	379,543	85,228 (22.46)
Other heart diseases	178,654	103,572	12,535 (7.02)
Cerebrovascular diseases	129,474	129,474	30,573 (23.61)
Arteries, arterioles and capillaries diseases	26,413	26,413	8,039 (30.44)
Other circulatory system disorders	4,240	4,240	1,593 (37.57)
Malignant neoplasms	589,655	492,080	111,666 (18.94)
Respiratory system diseases	237,427	204,680	62,376 (26.27)
External causes of mortality	183,258	164,641	24,071 (13.14)
Accidents	120,843	106,943	19,111 (15.81)
Intentional self-harm (suicide)	38,357	38,357	3,588 (9.35)
Assault (homicide)	16,242	16,242	298 (1.83)
External causes of mortality – undetermined intent	4,905	3,099	1,074 (21.90)
Legal intervention/war	421	n/a	n/a
Misadventures of drugs and medical procedures	2,490	n/a	n/a
Diseases of the nervous system	141,105	n/a	n/a
Mental and behavioral disorders	120,819	117,143	13,945 (11.54)
Endocrine, nutritional and metabolic diseases	98,890	31,696	4,134 (4.18)
Digestive system diseases	91,310	54,964	5,934 (6.50)
Infectious and parasitic diseases	67,532	60,442	7,445 (11.02)
Genitourinary system diseases	65,675	55,261	643 (0.98)
Symptoms, signs and abnormal clinical and laboratory findings	38,333	2,063	300 (0.78)
Musculoskeletal system and connective tissue diseases	13,323	2,786	140 (1.05)
Certain conditions originating in the perinatal period	12,127	8,408	1,171 (9.66)
Blood and blood-forming organ diseases	9,773	n/a	n/a
Congenital malformations, deformations, and chromosomal abnormalities	9,673	n/a	n/a
Skin and subcutaneous tissue diseases	3,995	2,012	0 (0)
Pregnancy, childbirth, and the puerperium	825	n/a	n/a
Ear and mastoid process diseases	65	n/a	n/a
Eye and adnexa diseases	53	n/a	n/a

Notes: n/a indicates that cause of death accounted for less than 1,000 deaths in 2010 or was not deemed preventable by study team. Numbers in the sub-categories may not exactly add to total number in the higher category due to rounding.