



Revisiting time to translation: implementation of evidence-based practices (EBPs) in cancer control

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Abstract

Purpose Previous studies estimate translation of research evidence into practice takes 17 years. However, this estimate is not specific to cancer control evidence-based practices (EBPs), nor do these studies evaluate variation in the translational process. We examined the translational pathway of cancer control EBPs.

Methods We selected five cancer control EBPs where data on uptake were readily available. Years from landmark publication to clinical guideline issuance to implementation, defined as 50% uptake, were measured. The translational pathway for each EBP was mapped and an average total time across EBPs was calculated.

Results Five cancer control EBPs were included: mammography, clinicians' advice to quit smoking, colorectal cancer screening, HPV co-testing, and HPV vaccination. Time from publication to implementation ranged from 13 to 21 years, averaging 15 years. Time from publication to guideline issuance ranged from 3 to 17 years, and from guideline issuance to implementation, – 4 to 12 years. Clinician's advice to quit smoking, HPV co-testing, and HPV vaccination were most rapidly implemented; colorectal cancer screening and mammography were slowest to implement.

Conclusion The average time to implementation was 15 years for the five EBPs we evaluated, a marginal improvement from prior findings. Although newer EBPs such as HPV vaccination and HPV co-testing were faster to implement than other EBPs, continued efforts in implementation science to speed research to practice are needed.

Keywords Cancer control · Evidence-based practice · Translation · Implementation · Uptake

Introduction

The gap between research evidence and practice is a problem widely recognized by researchers, practitioners, policy-makers, and patients. In a highly cited review published in 2000 by Balas and Boren [1], the authors found that it takes an average of 17 years for research evidence to reach clinical practice. Subsequently, others [2, 3] also estimated an average of 17 years between research and practice. While these studies reviewed a broad range of health interventions, including flu vaccine, diabetic eye exam, mammography, and thrombolytic therapy as well as developments in other

areas of health such as cardiology and neonatal intensive care [1–3], evidence-based practices (EBPs) in cancer control have not been systematically examined.

Prior work by Balas and Boren [1] reviewed various clinical preventive care procedures that were established to be effective in clinical trials and calculated the time to implementation of evidence from published reviews, textbooks, and papers. The selection of procedures in their study was driven by the availability of evidence and data. Specifically, they selected procedures that were (a) supported by clinical trial evidence for their use and (b) had nationally available data on the use of the procedures. Using the landmark clinical trial publication for each clinical procedure, Balas and Boren measured the time it took from the publication to implementation, defined as a rate of use or uptake of 50% in clinical practice (it was assumed that the rate of use was zero at the time of landmark publication).

For this study, we examined the variation in translational pathways of evidence-based programs, practices, or interventions (herein referred to collectively as EBPs) across the

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cancer control continuum where there were data available on uptake, so we could track the time from landmark publication to implementation. Our main objective was to estimate the time to translation from publication to implementation in cancer control and to examine the implementation trajectories in the area of cancer control.

Methods

We examined EBPs in cancer prevention, screening, treatment, and survivorship. Selection of EBPs were dependent upon several factors: a published landmark study providing evidence for efficacy; published guidelines or recommendations from professional organizations or the United States Preventive Services Task Force (USPSTF) [4]; and availability of data on implementation or uptake of the EBP in practice.

Data sources on implementation

To find data on implementation, which we defined as 50% uptake to replicate Balas and Boren's work, we used the National Cancer Institute's (NCI) Cancer Trends Progress Report (CTPR) [5], which includes the most recent data from the NCI, the Centers for Disease Control and Prevention (CDC), other federal agencies, and professional organizations. NCI CTPR provided data on uptake over time for each EBP except HPV co-testing, for which no nationally representative data are available, so we used data from two recent publications reporting co-testing uptake [6, 7]. We also examined data from the Healthcare Effectiveness Data and Information Set (HEDIS) [8], which measures performance on the delivery of EBPs over time using data from private insurance companies, Medicaid, and Medicare. Additionally, we used State Cancer Profiles [9], which provides national data collected from public health surveillance systems, and CDC's Morbidity and Mortality Weekly Report (MMWR) [10] for HPV vaccine uptake.

Identifying a landmark study

The steps to identify the landmark publication which provided evidence for the efficacy of the EBP began with a review of the references listed in the published guideline or recommendation. The earliest publication of a clinical trial providing evidence for the efficacy for the EBP was selected and carefully reviewed to ensure no previous trial was referenced. The selection was confirmed by relevant scientific experts from the NCI and Food and Drug Administration (FDA) whose work focuses on the development of and/or adherence to guidelines for the EBP. Although we searched for a randomized clinical trial (RCT) for each of the EBPs,

in one case (e.g., for HPV co-testing), only an observational study provided evidence for approval of the co-test and it was confirmed with the FDA that it was the most influential study that led to the test approval.

Clinical guidelines and recommendations

To find clinical guidelines recommending the use of EBPs, we reviewed the United States Preventive Services Task Force (USPSTF) [4] and the Agency for Healthcare Research and Quality (AHRQ) guidelines and recommendations [11]. We also searched guidelines published by various professional organizations such as the American Cancer Society (ACS) [12]. For HPV vaccine recommendations, we used CDC's Morbidity and Mortality Weekly Report (MMWR) [10]. For each EBP, we comprehensively searched for and reviewed the first guideline published recommending use of the EBP and any subsequent changes to the guideline with careful attention to any new research evidence that was synthesized to formulate a revised recommendation.

Analysis

We calculated the number of years from the landmark study publication to initial guideline publication recommending the EBP, and from guideline publication to implementation in practice, defined as 50% uptake in the population for which that EBP was recommended. Additionally, we created timelines for each of the EBPs, highlighting critical events that influence implementation, such as regulatory approval and guideline issuance and updates.

Results

We identified five cancer control EBPs to include in our final analysis: mammography, clinicians' advice to quit smoking, colorectal cancer screening, HPV co-testing, and HPV vaccination. Data on uptake of EBPs in cancer treatment and survivorship were limited. Further, treatment guidelines changed too rapidly to track uptake as new evidence emerged for more efficacious ways to treat cancers. Thus, our final sample of EBPs included those in prevention and screening only.

Overall, the time from research publication to implementation ranged from 13 to 21 years and averaged 15 years. The time from landmark publication to guideline issuance ranged from 3 to 17 years, and the time from guideline issuance to implementation ranged from – 4 to 12 years (Fig. 1). For each EBP, we produced a timeline that depicts the pathway to translation beginning at the landmark clinical study publication to the most current rate of use that is available,

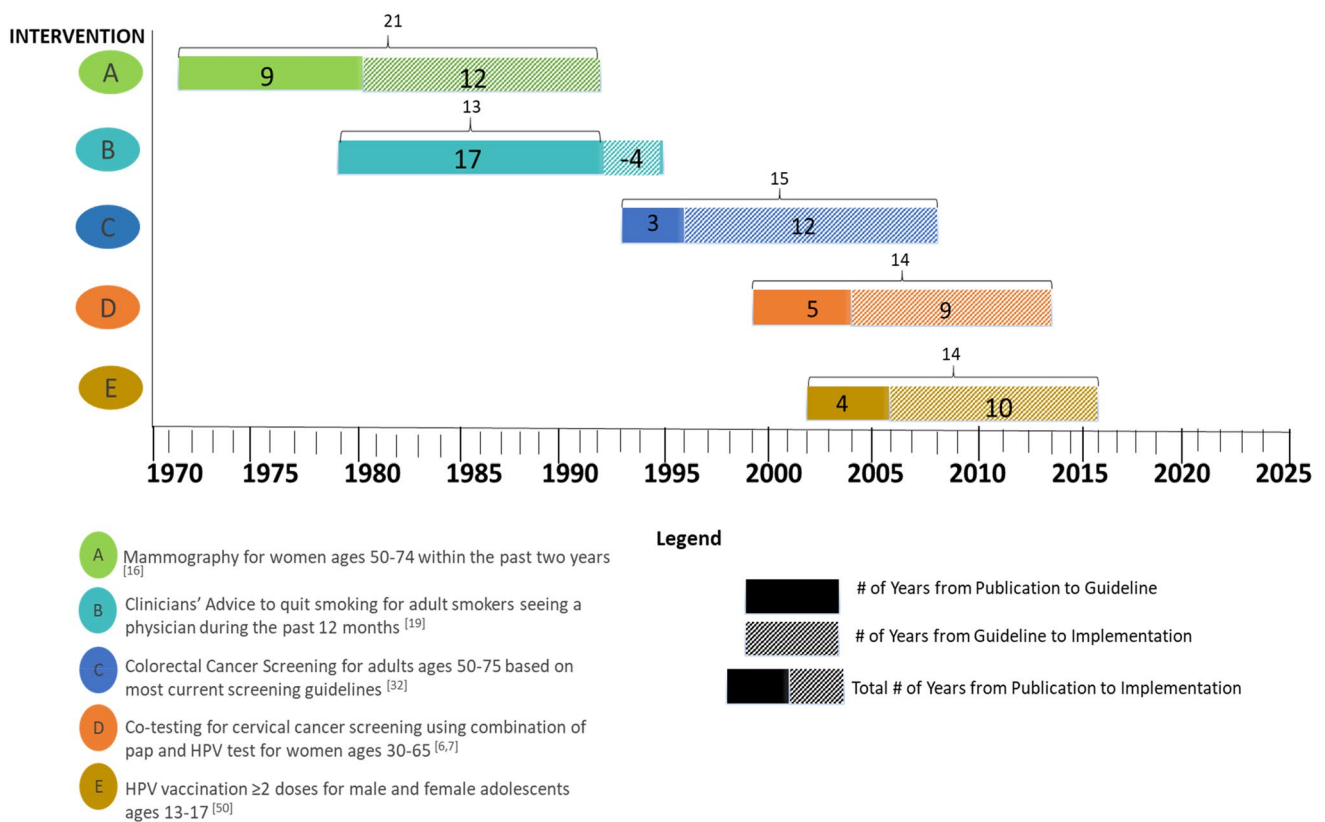


Fig. 1 Years from landmark publication to guideline to implementation

highlighting critical events along the way (Fig. 2). The following summarizes the findings for each EBP examined.

Mammography

While mammography has long been used as a modality of breast cancer screening, the understanding of how to optimize its use has shifted over time. The USPSTF gives the current mammography guidelines a B grade and recommends biennial screening mammography for women aged 50–74 years [13]. Mammography was the only EBP we reviewed with a grade B. HPV co-testing, colorectal cancer screening, and clinicians’ advice all received a grade A recommendation from USPSTF.

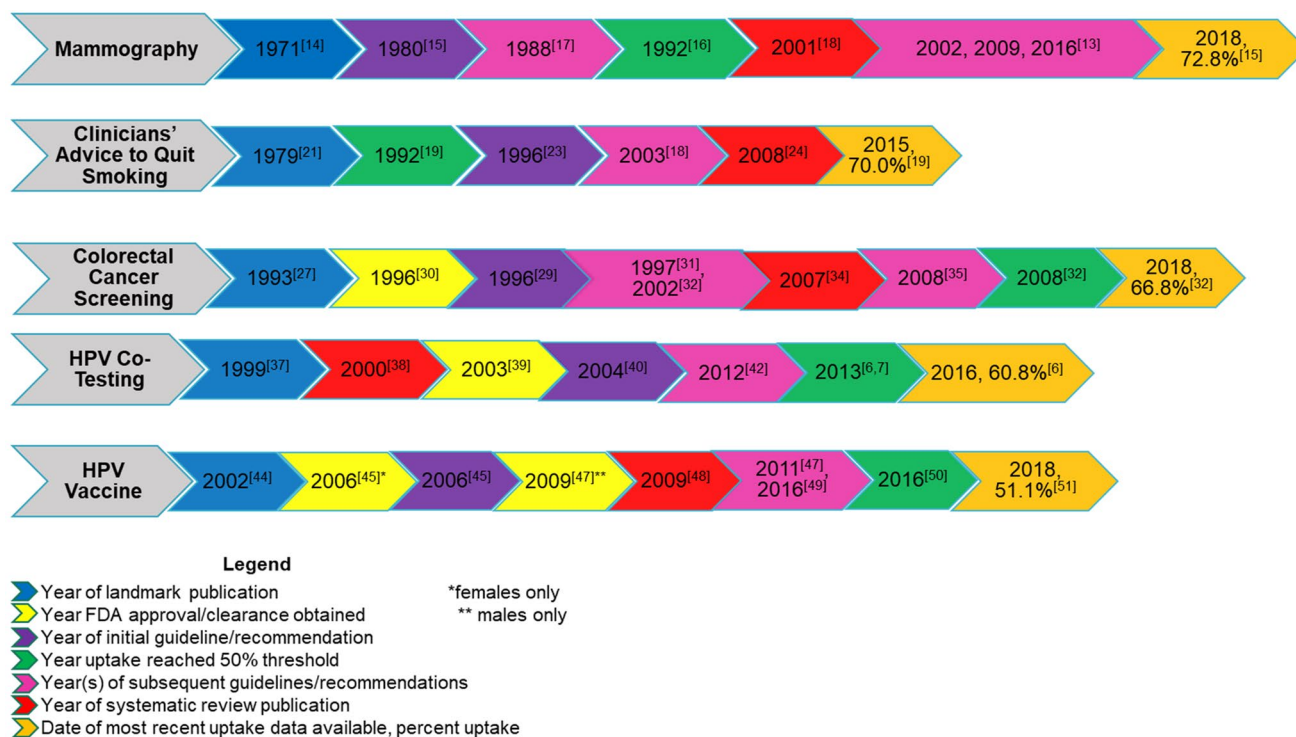
The Health Insurance Plan of Greater New York (HIP) trial published in 1971 was the first RCT in the United States that demonstrated mammography reduces breast cancer mortality (by 30%) [14]. In 1980, the ACS issued the first mammography guidelines recommending annual screening for women age 50+ [15]. In 1987, still only 30.2% of women aged 50–74 received mammography within the past 2 years [16]. In 1988, Joint Guidelines were issued by ACS, the American College of Radiology, and the NCI, endorsing

the 1980 recommendation for annual screening [17]. Uptake of mammography surpassed 50% in 1992, 21 years after the HIP trial was published, and continued to increase until plateauing in 1998 [16]. Implementation was achieved prior to the issuance of USPSTF guidelines on mammography, first issued in 2002 and later revised in 2009 and 2016 [13]. Uptake of mammography as of 2018 for women ages 50–74 within the past 2-years is reported as 72.8% [15].

Notably, a Cochrane review in 2001 concluded that the current evidence did not reliably demonstrate a survival benefit from mammography for breast cancer incidence and found inconclusive evidence for breast cancer mortality [18].

Clinicians’ advice to quit smoking

Clinicians’ advice to quit smoking is an effective smoking cessation intervention that increases the likelihood of quitting by 5–10% among smokers [19]. While the first USPSTF guideline recommending that clinicians ask all adults about tobacco use wasn’t published until 2003 [20], a 1979 landmark study of General Practitioners (GPs) that randomized 2,138 eligible smokers to one of four groups found that providing simple advice to quit smoking increased cessation



Note: References cited in the figure reflect data sources used to define each step of the translational pathway

Fig. 2 Timelines for pathway to translation

compared to no advice or completing a questionnaire. When clinicians' advice was combined with small media, the effect was enhanced in the short term but not the long term [21].

In the 1980s, additional trials of physician advice for smoking cessation had been published and reviewed [22]. However, data on uptake were not collected until much later. In 1992, CTPR reported that 51.2% of smokers age 18+ that had seen a physician in the past year were advised to quit smoking [19]. Notably, this uptake was substantial (i.e., > 50%) and achieved prior to any published guideline or recommendation.

A 1996 Joint Guideline issued by the Agency for Health Care Policy Research (AHCPR) (now AHRQ) was the first evidence-based guideline that recommended primary care clinicians identify and treat smokers with cessation or motivational intervention [23]. Guidelines continued to be revised after 1996, and subsequent ones were issued by USPSTF. By 2001, the percentage of smokers who reported receiving advice to quit smoking reached 61.9% [18]. Later, in 2003, the USPSTF issued its very first guideline recommending clinicians ask all adults about tobacco use and provide tobacco cessation interventions for those who use tobacco products, and uptake continued to increase, reaching 65.1% in 2006 [18]. In 2008, a Cochrane review pooled data from 17 trials of brief advice versus no advice and found that it increased quitting rates by 66% [24]. Thus, in 2009, the

USPSTF reaffirmed their recommendations [25]. In 2013, an updated review was conducted adding one additional trial and found that results did not change [26].

From the landmark publication (1979) to first guideline issuance (1996) took 17 years. However, substantial uptake (> 50%) occurred 4 years prior (in 1992) to the publication of the AHCPR guideline in 1996, suggesting that evidence had been disseminated through other channels and was quickly being adopted in clinical practice. The most recent data on uptake from 2015 report that 70.0% of adult smokers are being advised by a doctor to quit smoking [19].

Colorectal cancer (CRC) screening

Guidelines for colorectal cancer screening have broadened over time as new interventions are shown to be effective and added as additional modalities to clinical guidelines. Current CRC guidelines are multimodal, with no specific screening strategy considered to be most effective. To understand the translation of EBPs in colorectal cancer screening, we selected fecal occult blood test (FOBT) because it was the first intervention for CRC tested in a RCT citing evidence for its effectiveness. A landmark study published in 1993 provided the first conclusive evidence of the effectiveness of FOBT screening in reducing mortality from colorectal cancer [27].

While sigmoidoscopy in 1996 and colonoscopy in 2008 were later added to the guidelines, of note is that sigmoidoscopy was recommended by the USPSTF based on a single case–control study [28] and colonoscopy based primarily on extrapolation from sigmoidoscopy studies.

In 1996, the USPSTF issued a recommendation for FOBT or sigmoidoscopy for adults age 50+ [29]. Also, in 1996, FDA approval for FOBT was obtained [30]. In 1997, joint guidelines calling for universal screening of adults aged 50+ were issued by several professional organizations (e.g., ACS, American College of Gastroenterology, American Society of Colon and Rectal Surgeons, Oncology Nursing Society, and others) [31]. In 2000, 38.2% of adults ages 50–75 years were up-to-date with colorectal screening based on the most recent screening guidelines which now included a home FOBT in the last year, a sigmoidoscopy in the past 5 years, or a colonoscopy in the past 10 years [32].

The USPSTF guidelines were reissued in 2002, making a strong recommendation for screening men and women aged 50+, but noting insufficient evidence to prioritize among the different screening modalities or evaluate newer tests such as computed tomographic (CT) colonography [33].

In 2007, a Cochrane review confirmed that FOBT reduces colorectal cancer mortality [34]. Guidelines changed again in 2008 when the USPSTF reissued its recommendation for colorectal screening citing the use of fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults beginning at age 50 years and continuing until age 75 [35]. It was noted that there was convincing evidence that screening with any of the three recommended tests reduced CRC mortality. The uptake of screening reached 53.6% in 2008, 15 years after the landmark publication. USPSTF guidelines were updated in 2016, no longer emphasizing any screening procedure. The most recent data on uptake from 2018 report that 66.8% of adults ages 50–75 are up-to-date with CRC screening [32].

HPV co-testing

For women ages 30–65, screening tests such as the HPV test to find cervical changes that may lead to cancer are recommended by current guidelines. The Papanicolaou test (i.e., pap test), a cytology-based test used to detect potentially precancerous and cancerous abnormalities, is recommended in conjunction with the HPV test because it increases the sensitivity and specificity for cancer screening. This screening method for cervical cancer is referred to as co-testing [36].

A landmark case–control study published in 1999 [37] demonstrated that HPV infection, as measured by HPV DNA detection, greatly increases the risk of subsequent cervical squamous intraepithelial lesion (SIL). A systematic review subsequently concluded HPV testing was more sensitive than cytology [38]. In 2003, the FDA approved the HPV

DNA diagnostic test, Digene Hybrid Capture® 2 (HC2) High-Risk Test for women 30+ years to be used in conjunction with Pap testing to assess high-risk HPV types [39].

Joint guidelines were issued in 2004 by the American Cancer Society (ACS), American Society for Colposcopy and Cervical Pathology (ASCCP), and NCI, following FDA approval. This interim guidance recommended concurrent HPV and cytology testing (i.e., HPV co-testing) every 3 years for women age 30+ [40]. In 2006, uptake of co-testing reported by one study was < 10% [7]. This was similar to the data from the New Mexico HPV Pap Registry (NMHPVPR) reporting only 5.2% of women aged 30–65 receiving co-testing [41]. In 2012, the USPSTF issued comprehensive new screening guidelines recommending the option of co-testing at 5-year intervals for women aged 30–65 years [42].

There is currently limited population-based data on the use of HPV co-testing. In 2015, the National Health Interview Survey (NHIS) added a question asking women if they received an HPV co-test. While 81% of women aged 21–65 reported having a pap test within 3 years in accordance with recommendations, only 1/3 also reported a co-test with their most recent screening. There are several limitations to these data, as it was based on self-report, and 17% reported not knowing whether they had an HPV test [43]. More recently, data on co-testing uptake were reported from two separate studies conducted in Minnesota and Maryland [6, 7]. These studies provide the best estimate to date on the current uptake of co-testing in women ages 30–65 years, exceeding 50% in 2013 [6, 7], and reporting 60.8% in 2016 [6]. While these data are suggestive of expanded uptake of co-testing, we recognize that the true national rate may differ from what is reported here.

HPV vaccination

The Human papillomavirus (HPV) vaccine provides protection from the most common types of HPV infections that can cause various cancers in males and females. A landmark study published in 2002 found that HPV vaccine reduces the incidence of HPV-16 infection and HPV-related cervical intraepithelial neoplasia (CIN) [44]. In 2006, the FDA approved Gardasil, a recombinant vaccine indicated for the prevention of cervical cancer, cervical pre-cancer, vulvar pre-cancer, and vaginal pre-cancers caused by HPV type 16 and 18 for females age 9–26. Following FDA's approval, the CDC Advisory Council for Immunization Practices (ACIP) recommended routine vaccination of females age 9–26 years in 2006 [45]. Subsequently, uptake of the vaccine reached 16.6% in 2008 [46]. In 2009, the vaccine was approved for use in males ages 9–26 for prevention of genital warts, and in 2011, the CDC revised its recommendation to include routine HPV vaccination of males age 11–12 years [47]. Uptake for males has been slower, reaching only 6.9% in 2012 [46].

A systematic review of HPV vaccination showed HPV vaccination studies demonstrated high levels of efficacy [48]. In 2016, CDC issued a revised recommendation for 2+ doses rather than 3+ [49]. The uptake for all adolescents in 2016 reached 50.4% [50], 14 years after the landmark publication. The most recent data on uptake from 2018 report 51.1% uptake for adolescents [51].

HEDIS

Rates of uptake were compared between HEDIS and CTPR for all five EBP for the most recent available data (see Table 1 in Appendix). All but HPV co-testing was tracked by HEDIS. Rates did not vary substantially between HEDIS and CTPR except for HPV vaccination.

Discussion

Our objective was twofold: to review the translational pathway for a number of cancer control EBPs and to map out the translational timeline for each. We recognize the delays that exist in implementation but wanted to specifically examine this in cancer. Our study highlights the complex and iterative nature of the translational pathway from research publication to guideline to implementation, recognizing that these steps do not flow necessarily in a linear fashion. For example, clinicians' advice to quit smoking was implemented prior to guidelines recommending its use. In another example, colorectal cancer guidelines were published rapidly after the landmark study, but 50% uptake of screening took over a decade to achieve, resulting from other factors such as payment/insurance coverage, availability of tests/providers, and knowledge of varying screening schedules among different population of patients. We also noted differences in the speed of meeting the 50% implementation threshold by race/ethnicity across certain EBPs where data were available, such as clinicians' advice, mammography, and colorectal cancer screening. In colorectal cancer, Hispanics did not reach 50% uptake until 2018, and Blacks in 2008, while non-Hispanic Whites were the first to reach 50% uptake in 2005. These differences highlight the inequitable access and use of health care services that drive cancer health disparities for the Hispanic and African American communities.

The implementation science community has generally referenced the results from Balas and Boren's 2000 study, in which the lag from publication to implementation was

estimated at 17 years. In this study, we sought to determine whether this timeframe still held, or whether advances in understanding of implementation processes (and expanded efforts to improve uptake) might have narrowed the gap. Our study shows that the average time to implementation was slightly shorter for selected interventions in cancer control, averaging 15 years. Many of the practices we examined had timelines that preceded the newer focus on implementation science. And indeed, the newest of the cancer control EBPs, HPV vaccination, and HPV co-testing were one of the most rapidly implemented. It's worth noting that substantial investment has been made in recent years to improve HPV vaccination uptake, with its focus as a topic for a President's Cancer Panel report [52], NCI/CDC-supported activities to improve state level uptake, NCI-designated Cancer Center supplements fostering more understanding of community barriers to implementation, [53, 54] and other targeted initiatives. The marginal improvement in implementation from 17 to 15 years further support the need for implementation science to continue using relevant implementation science theories, models, and frameworks to identify barriers to implementation and develop and test strategies that would overcome those barriers, improving implementation, and speeding the timeline from evidence to practice.

Work done prior to our study also examined the time to implementation of mammography [1] and used data from HEDIS to report uptake. Our study examined mammography uptake using population-based data from NHIS, as reported in CTPR. Because HEDIS relies on data collected from health plans, it can be incomplete and have limited generalizability [55]. The advantage of NHIS is that it is a population-based, nationally representative survey design. These different data sources used for reporting 50% uptake may contribute to some variation in time to implementation among similar studies.

Delays in implementation that were observed for EBPs examined in this study remind us that implementation is complex, and producing an effective intervention is not sufficient for implementation. Barriers to implementation are multilevel and context dependent, and strategies to address those barriers should not only be informed by the extant literature where possible, but also informed by relevant theories and frameworks from the field of Dissemination and Implementation (D&I) research, of which there are many [56]. This can help us understand the characteristics of the innovation, the implementation processes, and the contexts in which they occur that may influence the speed of uptake.

We may expect to see reductions in this timeframe as newer interventions are ready for implementation, both from improvements in developing and testing implementation strategies [57] and from an increased attention to designing interventions to better fit the contexts in which they will be implemented. NCI, for example, has supported four cohorts of investigators in improved “design for dissemination” through a training program called SPRINT [58], which should help the next generation of cancer control interventions to be constructed and implemented with the target audience in mind.

We acknowledge several limitations to this work. Data on uptake were limited for cancer treatment, largely because the evidence changed so rapidly that we could not track uptake before the evidence and subsequent guidelines changed. Additionally, although we wanted to examine EBPs across the cancer control continuum, data on survivorship also were limited. The rigor of our selection process for EBPs was generally based on whether there was a current and existing USPSTF guideline and data available on uptake. Prostate cancer screening (i.e., PSA testing) was one example with a D rating that we did not include in our evaluation. We also did not include lung cancer screening which has a grade B rating, because guidelines were only recently released at the time of these analyses and data on uptake were limited and suggested less than 5% uptake.

Reliable nationally representative population-based data on uptake were unavailable on utilization of HPV co-testing. We reviewed several publications to understand any reported trends in co-testing uptake and used the most recent data reported from two regional cohorts on the use of co-testing for our estimate [6, 7]. Selecting a landmark study also posed challenges, in part, because study outcomes varied, making it difficult to consistently pick studies measuring the same endpoint (e.g., mortality vs incidence). To overcome this challenge, we consulted experts at NCI and FDA to get insights about the most influential research publications leading to the creation of guidelines and recommendations.

Lastly, we acknowledge the variability in the characteristics of the interventions and the critical role they play in influencing adoption, as explained by Rogers and others [59, 60]. Particularly, the perceived complexity, compatibility, and relative advantage of an intervention can influence implementation; we believe this variability is also reflected in our findings.

There are ways, however, to improve the precision of our study, as improvements in sources of data on uptake, the availability of a landmark study, and using a 50% threshold

as the indicator for implementation are all factors that may pose as limitations to our study.

Conclusion

In this study, we aimed to review EBPs in cancer control to understand the process and speed at which translation occurred. Using the methodology of a well-cited study which explored the question of time to translation in other clinical preventive procedures helped us reflect on the processes used to answer this question. The average time to implementation was 15 years across cancer control EBPs, indicating a marginally faster time to implementation compared to findings from Balas and Boren. Newer EBPs, such as HPV vaccination, for which substantial investment in implementation efforts were made, implemented more rapidly, helping to reduce the average time across all EBPs. While better sources of data on uptake are still needed, especially in areas like HPV co-testing where nationally representative data do not exist, researchers can reduce this lag through studies of strategies to hasten and improve implementation of EBPs using implementation science methods.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Appendix

See Table 1.

Table 1 comparing rate of uptake between HEDIS and CTPR

Evidence-based practice	2000 CTPR	2000 HEDIS rate of uptake (HMO)	2018 CTPR	2018 HEDIS rate of uptake (HMO)
Mammography	77.2%	74.5%	72.8%	73.5%
HPV co-testing	No data available	No data available	Co-testing data not available	No data available
Colorectal cancer screening	53.6% (2008)	58.6% (2008)	66.8%	64.1%
HPV vaccination	16.6% ^a (2008)	No data available in 2008	51.1% ^b	29.8% ^c
Clinicians' advice to quit smoking	61.9% (2001–2002)	66.3%	70.0% (2015)	77.8%

^aFemales only^bAdolescents, MMWR data [51]^cAdolescents

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