Title: The need to invest more in cancer prevention

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Abstract: Global health often overemphasizes late-stage cancer treatments over early detection and prevention despite its potential to reduce cancer incidence and increase survivorship. A shift is needed: integrating cancer prevention strategies in primary care, developing robust research pipelines in translational science, and addressing socioeconomic barriers, thereby catalyzing a proactive stance against cancer's societal impact.

Overlooking Early Cancer Detection and Prevention

While the global emphasis on cancer research has been substantial, the allocation of these resources reveals a concerning trend. Despite heavy investment in combating cancer in its advanced stages, the crucial area of prevention and early detection—which holds the potential to significantly reduce cancer incidence— is often overshadowed by other research priorities. A recent study titled 'Global funding for cancer research between 2016 and 2020: a content analysis of public and philanthropic investments' published in The Lancet Oncology journal suggests that the vast majority of research investment is directed towards understanding tumor biology and treatments for cancers beyond their early stages, leaving only a fraction for early detection, diagnosis, and treatment [1]. Similarly, the private sector, a major contributor to the expansion of cancer clinical trials, is often reluctant to initiate cancer prevention projects. The National Cancer Institute (NCI) attributes this hesitancy to economic challenges, logistical complexities, regulatory requirements, and legal considerations[1]. Consequently, this lack of robust private sector involvement results in a dearth of clinical trials targeting cancer prevention, thereby hindering progress in this essential area. Adding to these concerns, the 2023 Journal Citation Reports™ (JCR) from Clarivate™ indicates that among the publications of the American Association for Cancer Research (AACR), the journal 'Cancer Prevention Research' ranks low in several critical impact metrics[2] [Figure 1]. It holds the least favorable position in both the standard two-year and extended five-year Impact Factor assessments, and its Eigenfactor score— which ranks journals based on how often they are cited by other influential journals— is relatively low[2]. However, an intriguing pattern emerges in its Immediacy Index. The journal exhibits

a relatively higher score in this metric, suggesting that its articles are timely and resonate with current scientific discussions.[2] [Figure 1] This dichotomy suggests two things: First, while the research in cancer prevention is immediately relevant and contributes to ongoing conversations in the scientific community, it may not be foundational for long-term studies nor frequently cited by the most influential publications. Second, the foundational research in cancer prevention is not having a sustained impact within the broader cancer research community. This discrepancy highlights the need for a strategic shift in focus towards building a robust, influential body of research in cancer prevention that is not only immediately relevant but also contributes significantly to the foundational knowledge in the field. Such a shift could catalyze more substantial, long-lasting scientific engagement and investment in cancer prevention strategies, echoing the urgent call for an open dialogue on this critical issue.

Early Detection is the Key to Cancer Survival

The statistics in cancer screening reveal that early detection significantly improves survival rates, yet the limitations of current methods clearly show the need for ongoing research and development in this area. A recent analysis published in the BMC Health Services Research journal used a mathematical model to estimate the impact of the US Preventive Services Task Force recommendations on cancer prevention and screening from 1996 to 2020 (2013 for lung cancers) [2]. Based on reported adherence to these screening recommendations, it's estimated that 12.2-16.2 million life years have been saved in the US, attributing this to the cumulative advantages of screening tests for breast, colorectal, cervical, and lung cancer [2]. Additionally, the American Cancer Society (NCI) in its Cancer Prevention and Early Detection Facts & Figures, 2023-2024 report, highlights that current screening approaches, such as mammography for breast cancer, colonoscopy for colorectal cancer, and HPV tests for cervical cancer, have been instrumental in identifying the malignancies at initial stages [3]. In the case of cervical cancer, for example, HPV tests, vaccination uptakes, and other preventive methods have led to a decrease in the incidence and mortality rates by more than 50% over the past three decades [3]. However, the same report also highlights that these tools have limitations and are not universally applicable to all types of cancer. For instance, the NCI points out that mammography may not detect all cancers, the ones it does detect might still be hard to treat leading to poor prognosis, and often it detects conditions like Ductal Carcinoma In Situ, a non-invasive breast condition that may not always progress to invasive cancer, leading to potential

overtreatment [3]. On top of this, the majority of lung cancers are still detected at advanced stages, presenting a dismal 5-year relative survival rate of only 6% [3]. Thus, emphasizing the necessity for extensive research to refine early detection techniques.

Integrating Cancer Prevention in Primary Care

Beyond well-known preventive tools such as mammography and colonoscopy, lifestyle modifications such as healthy eating, active living, and avoiding smoking tobacco have also demonstrated promise in reducing cancer risk [3]. However, simply implementing these preventive measures is insufficient to create a substantial impact in cancer prevention. Achieving this requires a cultural shift within public health. This shift involves not only educating patients about maintaining health but also seamlessly integrating cancer prevention strategies into primary care—a crucial step in emphasizing the importance of a preventive approach in healthcare settings. Primary care clinicians are the front-line defenders against cancer among physicians and other healthcare providers. The article ‘Can Cancer Prevention Be Better Integrated into Primary Care?’ published by the NCI resonates with this concept, offering firsthand perspectives from primary care clinicians like Dr. Adeola Fakolade and Dr. Marilyn Schapira[3]. Dr. Fakolade notes the difficulty in addressing cancer prevention in every single encounter she has with a patient, due to the high volume of patients she evaluates daily, many of whom present with other immediate medical concerns. The doctor also explains the challenges in obtaining patients’ cancer family history, as many patients struggle to recall family members who had cancer, while others can recall but don't know the specific type. Other clinicians, such as Dr. Marilyn Schapira, have pointed out the impracticality of cancer risk assessment tools, given the limited time available during patient evaluations.[3] Therefore, the constraints of limited time and high patient volume per day hinder the implementation of cancer prevention approaches in primary care. These are limitations that the health care system will have to address if we want to generate a real impact with novel prevention strategies. Parallelly, addressing these barriers could also boost participation in cancer prevention clinical trials, which currently face significant challenges due to low enrollment, as highlighted by the NCI in their article 'Transforming Cancer Clinical Trials for Better, Faster Results'[4].

Advances in Translational Science Around Cancer Prevention

In the scientific field, enabling translational science around cancer prevention is crucial, and fortunately, ongoing research and clinical trials are exploring novel avenues for this purpose. These include efforts towards the development of cancer biomarkers and the identification of microbial mechanisms involved in cancer initiation and progression. The study of the microbiome has gained increasing attention in the scientific community due to its significant potential for developing cancer diagnostics and therapeutics [4-5]. However, numerous questions in this area remain unanswered. Dr. Geniver El Takle and Dr. Wendy S. Garret from the Department of Immunology and Infectious Diseases at Harvard T. H. Chan School of Public Health highlight that despite substantial progress in this field, including the recognition of Dysbiosis of the gut microbiome as a hallmark of cancer, the identification of Helicobacter pylori as a contributor to tumorigenesis in conditions like gastric cancer and the improvements in gnotobiotic mouse models, it still lacks in-depth mechanistic studies on the underlying processes and interactions between the microbiome and cancer [5]. Additionally, there is also a need for improved detection methods for microbial entities and microbe-derived small molecules to gain accurate insights into the microbiome [5]. Thus, while this area of research holds promise for advancing cancer prevention, there remains a significant journey ahead.

Overcoming Cultural and Socioeconomic Barriers

As previously emphasized, healthy eating, active living, and avoiding tobacco smoking could significantly decrease cancer rates and thus support cancer prevention strategies [3]. However, for many, accessing and maintaining a healthy lifestyle is unfortunately a luxury. The NCI 2023-2024 report highlights that persistent poverty and inadequate access to healthcare are substantial barriers to adopting preventive measures and surveillance [3]. For instance, tobacco smoking is responsible for 30% of all cancer deaths in the US and is prevalent in specific subpopulations such as those with low socioeconomic status, historically marginalized racial and ethnic groups, and individuals with mental illness. Similarly, individuals lacking insurance, often from the aforementioned subpopulations, have less access to cancer prevention screenings. [3] Therefore, there is an urgent need for culturally appropriate and equitable support for these groups, as they have restricted opportunities to adopt a healthy lifestyle and access preventive cancer screenings, both of which are essential for enhancing well-being and reducing cancer risk.

Concluding remarks and future perspectives

Ultimately, these challenges demonstrate the complexity and interconnectedness of multiple issues within the cancer prevention landscape, illustrating the urgent need for enhanced investment across various spheres—clinical, translational, and socioeconomic. While the points addressed here are crucial, they represent only a fraction of the many factors contributing to the challenges of establishing and implementing a robust cancer prevention strategy. [Figure 2] Current clinical trials for cancer prevention, as reflected by the AACR and the National Cancer Society clinical trials database, predominantly concentrate on uncovering methods to circumvent or manage known carcinogenic factors, pioneering strategies for earlier detection of precancerous conditions, and exploring chemoprevention as a proactive defense against the onset of cancer[5-6]. These endeavors are crucial steps forward; however, the emphasis should not only be on refining and developing advanced preventive measures but also on ensuring equitable access to these interventions, thereby bridging the existing disparities. Moving forward, it's crucial to introduce streamlined protocols and tools, leveraging technology like electronic health records (EHRs), to facilitate the integration of cancer prevention into primary care consultations. It's also important to develop robust pipelines, such as cancer genomics, to interrogate data and identify patterns that reveal critical cellular pathways for cancer prevention, particularly in emerging areas like the microbiome. Additionally, establishing collaborations with community leaders and organizations is essential for tailoring interventions to specific populations. By doing so, we can harness collective knowledge to innovate and implement effective strategies that substantially reduce the global cancer burden.

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Resources List

[1] https://www.cancer.gov/research/areas/prevention

[2]https://aacrjournals.org/pages/impact-factor

[3]https://www.cancer.gov/news-events/cancer-currents-blog/2023/integrating-cancer-prevention-primary-care

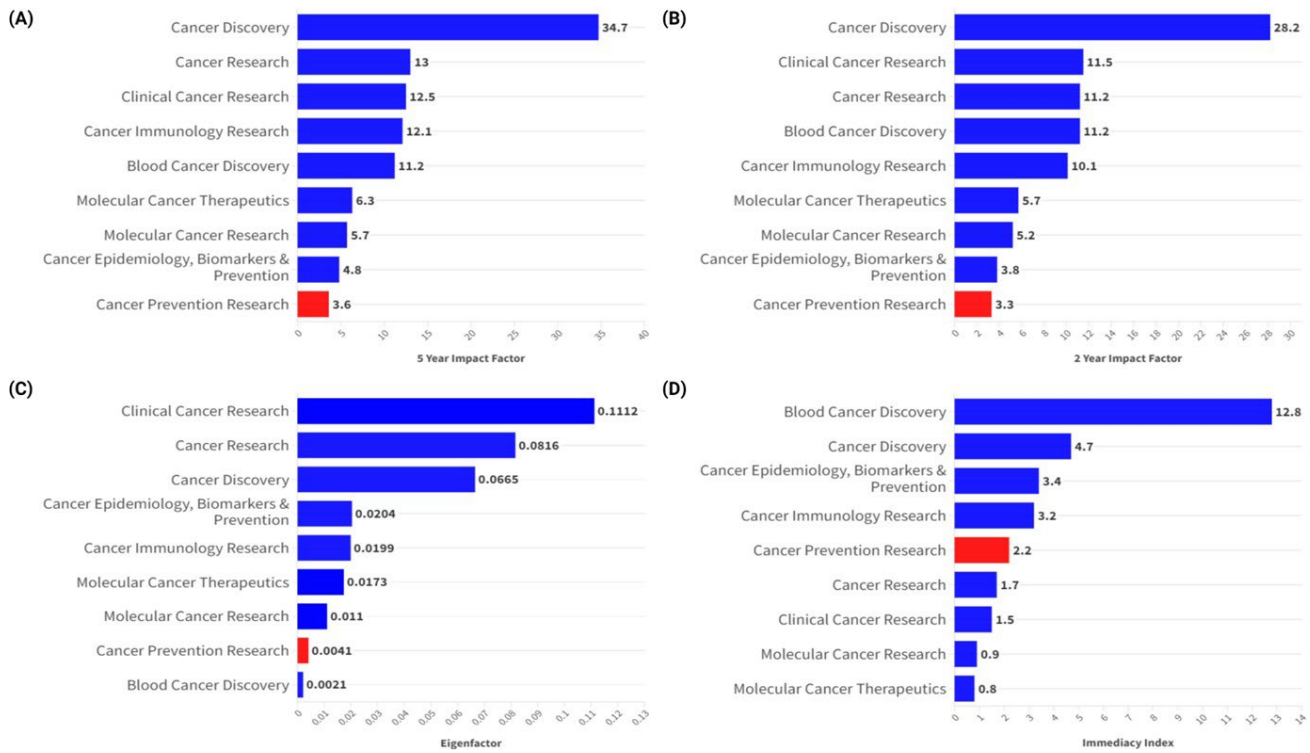
[4]https://www.cancer.gov/news-events/cancer-currents-blog/2023/transforming-nci-cancer-clinical-trials

[5] https://prevention.cancer.gov/clinical-trials/clinical-trials-search

[6]https://www.aacr.org/patients-caregivers/about-cancer/cancer-prevention/

Figures

Figure 1



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Comparative Analysis of Impact Metrics for AACR Journals

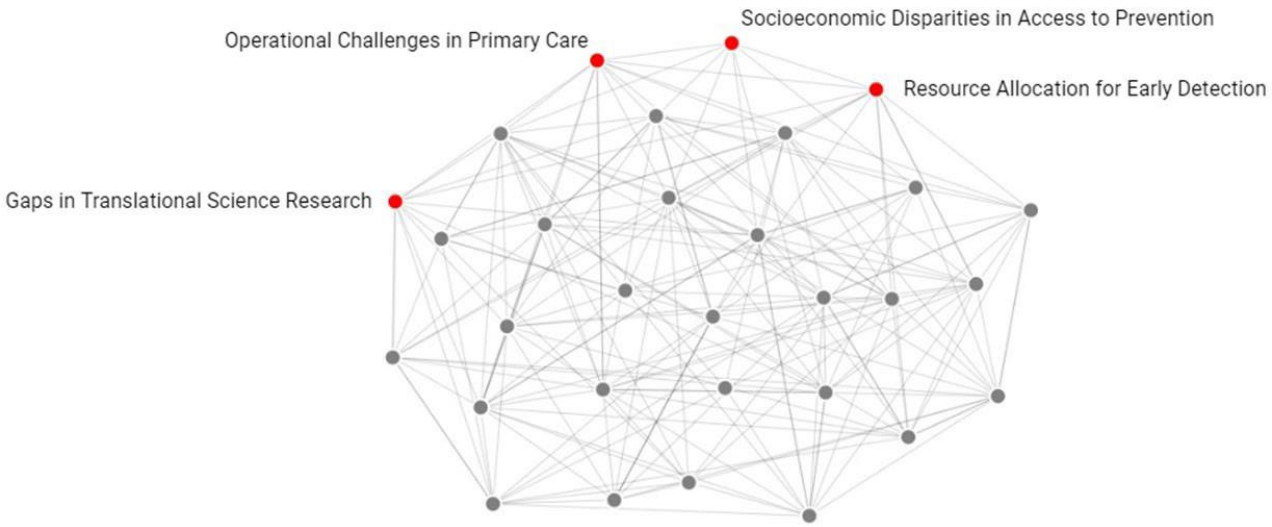
A graphical representation of various impact metrics for journals under the American Association for Cancer Research (AACR) banner. (A) and (B) depict the 2-year and 5-year impact factors, respectively. (C) presents the Eigenfactor scores, which measure the journal's total importance to

the scientific community. (D) represents the immediacy index for each journal. Data sourced from the AACR Journals website (https://aacrjournals.org/pages/impact-factor).

Figure created with FlourishStudio.

This map is also available as an interactive figure.

Figure 2



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Cancer Prevention Neural Network

This network map illustrates the intricate web of challenges in establishing a comprehensive cancer prevention approach, with interconnected nodes representing diverse issues that require attention. The highlighted red nodes signify the critical areas addressed in this study, highlighting the urgency of these dialogues. While the grey nodes represent the broader array of challenges yet to be extensively discussed, they are essential for understanding the full scope and depth of effective cancer prevention strategies. The emphasis on the selected challenges exemplifies the need for a comprehensive, multi-faceted dialogue in the scientific community to navigate this intricate landscape.

Figure created with FlourishStudio.

This map is also available as an interactive figure