



# Grand challenges in cancer epidemiology and prevention

Farhad Islami<sup>1,2</sup>, Farin Kamangar<sup>2,3</sup> and Paolo Boffetta<sup>4,5\*</sup>

<sup>1</sup> International Agency for Research on Cancer, Lyon, France

<sup>2</sup> Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Public Health Analysis, School of Community Health and Policy, Morgan State University, Baltimore, MD, USA

<sup>4</sup> The Tisch Cancer Institute and Institute for Transitional Epidemiology, Mount Sinai School of Medicine, New York, NY, USA

<sup>5</sup> International Prevention Research Institute, Lyon, France

\*Correspondence: paolo.boffetta@mssm.edu

Cancer is the second cause of overall mortality in the world (Abegunde et al., 2007), with approximately 12.5 million new cases and 7.5 million deaths each year (Ferlay et al., 2010; Jemal et al., 2011). Many cancers are preventable, and cancer control represents a global challenge which will be significantly aided by increasing our knowledge of distribution, causes, and methods for prevention of cancer. This journal, *Frontiers in Cancer Epidemiology and Prevention*, is dedicated to publishing papers on the distribution, etiology, and prevention of cancer. In this article, we present our vision for the *Journal*. We discuss what has been discovered, what lies ahead, and what papers we hope to receive from authors. The overall scope of the *Journal* is summarized in **Figure 1**.

In the past few decades, cancer registries have produced data on incidence, prevalence, and mortality of cancers in many regions of the world, and shown variations by sex, race, geographic region, and other demographic determinants. Examples include the Surveillance Epidemiology and End Results (SEER) program in the United States (Hayat et al., 2007) and the compilation of cancer registry data within the volumes of Cancer Incidence in Five Continents (Parkin et al., 2010). We now have a reasonably good idea of distribution of cancers in many areas of the world, overall and within specific subgroups of the population. This is a unique and fortunate characteristic of the descriptive epidemiology of cancer, compared to other chronic diseases. However, cancer incidence and mortality rates change; hospitals and cancer registries prepare new reports; and new registries are established. We welcome reports on the incidence, prevalence, and mortality from cancers from all over the world and manuscripts based on original analyses of descriptive data.

Whereas by 1950 little was established about etiology of cancer, epidemiologic studies in the past 60 years have helped us know about some major causes of many cancers. One can cite many examples. Groundbreaking case-control studies by Doll and Hill (1950), Wynder and Graham (1950), and Levin et al. (1950) in the early 1950s established smoking as a cause of cancer. In the past two decades, a large number of case-control, cohort, and nested case-control studies showed the strong association between certain types of human papillomavirus (HPV) and cervical cancer, and later cancers of the vulva, vagina, penis, anus, oral cavity, and oropharynx and tonsil (Munoz et al., 2003; Bouvard et al., 2009). The causal role of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection in hepatocellular carcinoma (Bouvard et al., 2009) and of several occupational exposures in a variety of cancers (Baan et al., 2009) are other important examples. Likewise, since 2006, genome-wide association studies have shown over 100 associations between common genetic polymorphisms and risk of various cancers (Stadler et al., 2010). Notwithstanding these discoveries, there remains much to be understood in relation to the etiology of cancer. Association of physical activity (Prentice et al., 2004; Reeves et al., 2007), shift-working (Straif et al., 2007; Stevens et al., 2011), and exposure to many chemical agents and mixtures (Ritz and Rull, 2008; Olsson et al., 2011) with cancer are a few examples. Studying environmental risk factors of cancer, from childhood, in repeated measures, with considering potential modifying effect of other factors such as microbiome, and in the light of development and teratogenesis, may increase our understanding of cancer risk factors (Wild, 2005, 2011; Hanash, 2011; Perera, 2011; Potter, 2011; Rappaport, 2011; Spitz, 2011). The continuing decline

in cost of sequencing will make it possible to identify rare polymorphisms that strongly increase risk of cancer. The *Journal* welcomes reports on new factors associated with risk of cancer that may have a possible etiologic role, as well as null results from high-quality studies.

Epidemiologic studies can use new instruments or refine modeling to provide better understanding of the causes of cancer. For example, it has been suggested that, compared to food frequency questionnaires, using multiple 24-h recalls may increase our ability to measure diet more accurately and hence reduce measurement error (Schatzkin et al., 2009b). During the past few decades, a wide range of biomarkers has also been applied to cancer epidemiology (Boffetta, 2010; Hartman et al., 2010). A classic example of successful application of biomarkers in cancer epidemiology is the study between aflatoxins and risk of hepatocellular carcinoma (Ross et al., 1992). However, intra-individual variability (e.g., diurnal variation in hormonal level) and measurement error (e.g., sampling and laboratory variation) do also occur with biomarkers, and most biomarker studies rely on a single biological sample, which may not represent long-term exposures. Many investigations are being conducted to identify new biomarkers and improve the validity and precision of existing biomarkers. Cancer results from a complex interplay of environmental, genetic, and epigenetic factors (Spitz and Bondy, 2010). New modeling strategies have increased our ability to more accurately study well-established associations such as the association between smoking and lung cancer (Lubin et al., 2008), as well as the association of diet (Ferrari et al., 2008; Schatzkin et al., 2009a) or genetic factors (Pashayan et al., 2011; Wakefield et al., 2010) with cancer, and to better control the effects of confounding factors (de Vocht et al.,



**FIGURE 1 | Cancer research areas that are within the scope of *Frontiers in Cancer Epidemiology and Prevention*\*.**

\*Null results from high-quality studies are also welcome.

<sup>a</sup>Including environmental, genetic, and epigenetic factors and their interactions.

<sup>b</sup>Including advances in data collection methods and biomarkers, as well as translational studies.

2009). The *Journal* accepts papers on new instruments or biomarkers, improved statistical models, and also stronger studies of previously known associations.

Study subjects in epidemiological studies generally have heterogeneous environmental exposures and genetic background, which interact with each other and may influence the association between risk factors and health outcomes. In order to study such interactions, epidemiologic studies require large sample sizes, and therefore epidemiology falls into the category of “big science” (Kreeger, 2003). Large cohort studies, pooling and consortia of several studies, networks, and “networks of networks” have been helpful in achieving large sample sizes and to study interactions

(Brennan et al., 2004; Allen et al., 2009; Hashibe et al., 2009; Cook et al., 2010; Gallicchio et al., 2010; Zheng et al., 2011). Requirements and considerations for successful execution of large studies and making fruitful collaborations between multiple groups have been discussed elsewhere (Boffetta et al., 2011). We invite papers from such consortia and large-scale studies.

Cancer prevention, using the knowledge from epidemiology and molecular biology, has achieved many successes. Recognition of smoking as an important cause of lung cancer has resulted in smoking control policies in Europe, the United States, and some other countries (Chaloupka et al., 2011) that have in turn reduced exposure to tobacco smoke

(Callinan et al., 2010) and are expected to reduce the burden of tobacco-related cancers in those populations (Alberg et al., 2007; Sturgis and Cinciripini, 2007). Discovery of HPV as a cause of cervical cancer has successfully led to the development of effective vaccines against potent carcinogenic types of HPV (Monsonogo et al., 2010). Global vaccination of newborns against HBV is another example of success that has reduced the rate of hepatocellular carcinoma in Taiwan (Chang et al., 2009) and would likely lead to serious declines in the worldwide rates in the coming decades (Yang and Roberts, 2010). Rapid reduction of the cost of genetic information has made it possible to screen and take actions when cancer risk

is very high, such as in individuals with certain BRCA1 mutations (Balmana et al., 2010). On the other hand, cancer prevention science has also faced many failures. A number of initially promising agents were later shown to have either no effect or even cause harm. Well-known examples include the failure of alpha-tocopherol and beta-carotene in preventing lung cancer (The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group, 1994) and failure of selenium in preventing prostate cancer (Lippman et al., 2009). The *Journal* invites papers on new findings and methods on cancer prevention research. We are interested in receiving papers on both successes and failures of agents that are hypothesized to prevent cancer, including chemopreventive agents, vaccines, or lifestyle modification. We especially encourage submission of randomized clinical trials.

The *Journal* also accepts papers on screening and secondary prevention of cancer. It has now been well established that early screening for cervical, colorectal, and breast cancers through various methods can save lives (Sankaranarayanan et al., 2009; Schiffman and Solomon, 2009; US Preventive Services Task Force, 2009; Cunningham et al., 2010). New screening methods are being continuously devised; criteria are revised by age and sex; and revisions are made due to changes in effectiveness of treatments and invasiveness and cost of procedures. Screening studies are subject to a number of potential biases (Croswell et al., 2010), and new studies often refine previous studies and correct for biases. Publications of high-quality screening studies are within the scope of this *Journal*.

With rising availability of early detection facilities and more efficient treatments, survival of cancer patients has increased overall (Jemal et al., 2010). Survival has been shown to be related to a number of factors, including cancer site (e.g., breast versus pancreatic cancer), stage, age, other demographic, lifestyle, and genetic factors, as well as availability of facilities for early diagnosis or treatment of cancers. Consequently, cancer survival can vary across individuals and populations (Kamangar et al., 2006b; Jemal et al., 2010; Slatore et al., 2010; Coleman et al., 2011). However, many prognostic factors are not yet known. For example, low-cost sequencing may enable us to

predict survival much more accurately. Some prognostic factors are modifiable and active secondary prevention activities can be undertaken to prolong survival. For example, improving awareness of effective screening methods and enhancing health services to offer such screening could lead to downstaging of cancers. We welcome reports on survival of cancer patients and its prognostic factors, and also research on methods leading clinical downstaging of cancers.

In addition to original research papers, we encourage authors to submit review articles, systematic reviews, and meta-analyses. These articles help establish or exclude associations (Kellen et al., 2007; Islami and Kamangar, 2008; Renehan et al., 2008; Lee et al., 2009; Turati et al., 2010; Gandini et al., 2011), revise estimates of initially inflated associations that may happen due to publication bias (Kamangar et al., 2006a), suggest associations or interactions relevant to cancer research (Minelli et al., 2011), or identify gaps in a research field (Islami et al., 2009).

Whereas the *Journal* is mainly dedicated to human studies, we also invite papers on animal or laboratory studies that have a direct relevance to cancer prevention in humans (Kern et al., 1991; Kim et al., 1991; Jokelainen et al., 1994; Watanabe et al., 1998; Wang et al., 2010). For example, papers that show high amounts of mutagenic or carcinogenic substances in certain foods and beverages (Zhang et al., 1983; Kamangar et al., 2008; Perello et al., 2008) will fall in the repertoire of this *Journal*.

In summary, while we have learned much about the distribution, etiology, primary and secondary prevention of cancer in one century of systematic research, many things remain to be learned. Development of large-scale trials and cohort studies, consortia of analytical epidemiology studies, new statistical methods, novel measurement methods, ever-increasing ability to sequence genome, among other factors, are giving us the opportunity to delve more deeply into research questions. We believe that *Frontiers in Cancer Epidemiology and Prevention* will play an important role in disseminating new knowledge in this field and can increase communication among basic scientists, epidemiologists, clinicians, and public health professionals in the field of oncology.

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