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Is It Time to Rethink the Way We Assess the Burden of Work-Related Cancer?

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Abstract

Purpose of Review Population attributable fractions (PAFs) are increasingly used for setting cancer prevention priorities. Our review aims, first, to gather published estimates of the percentage of cancer attributed to causal agents in the workplace and, second, to analyze them from the perspective of their potential effects on population health inequities.

Recent Findings The estimates generally ranged from less than 2% to more than 8%, with an average of 4–5%. While most authors acknowledge that exposures concentrate in lower-socioeconomic status and more vulnerable workers, the literature has never considered the occupational group as a source of variation in the calculations. This knowledge gap is linked to the paucity of data describing the occupational patterning of exposures and cancer. More globally, the social gradient in cancer is often interpreted in the light of behavioral factors alone, a tendency linked by historians to the very foundations of modern epidemiology. Yet, there is accumulated evidence that work affects health and the risk of death through different pathways, which are also relevant to cancer.

Summary While the epidemiologic literature addressed conceptual and validity issues surrounding PAFs, it seldom questioned their potential impacts. There is in particular a lack of consideration of factors beyond individual behaviors and a paucity of attention to population health inequities. We hence propose to further the discipline's reflexivity by changing the focus, scope, and metrics in order to assess the burden of work-related cancer in a way that is more meaningful to the most disadvantaged workers.

Keywords Attributable fraction · Carcinoma · Occupational exposures · Health inequities · Undone science

Introduction

The concept of attributable fraction was promoted by epidemiologists in the early 1950s to quantify the proportion of people afflicted by lung cancer whose disease was attributable to cigarette smoking [1, 2]. It was further used as a surrogate to estimate potential health gains through reduction of exposures to causal agents, specifically by interpreting it as the proportion of adverse outcome that could be averted if the exposure were either eliminated or reduced to a minimum-risk level. Calculating a population attributable fraction (PAF) typically requires the combination of two dimensions that influence occurrences of new "cases" in populations: relative risk (RR) and prevalence of exposure. Since the Levin formula, multiple mathematical constructs have been proposed for this purpose [3••, 4••, 5••]. The attributable fraction also plays an important role in public debates on public health issues and has become one of the tools used to promote evidence-based policy-making [6••]. It is considered a critical driver of cancer prevention in general [7] and occupational cancer in particular [8]. In a still highly cited report by Doll and Peto, released in 1981 [9], the PAF for occupational exposures amounted to 4% of total US cancer deaths in 1978 among people aged 65 or less (uncertainty range 2–8%). Of particular interest is that those early estimates have been globally replicated over the

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past four decades [10] while trends in exposures have changed, different methods have been developed and new sources of data have emerged.

The aim of the present review is to gather recent estimates of total occupational cancer burden, to analyze whether and how they differ from the landmark figures and to describe how a focus on individual risk factors like smoking may have translated in an undercounting of cancers attributed to occupational exposures. Specifically, this article calls to attention the extent to which this tool has contributed to specifically defining occupational cancers, by focusing attention on some aspects such as their lesser importance compared with tobacco and diet issues, while ignoring or minimizing others such as their concentration among smaller groups (geographically or socially defined) that are very significantly affected. Finally, potential areas of improvement are identified in order to hopefully help us rethink how we assess the burden of work-related cancer.

Doll and Peto's Landmark Estimates: Do They Generally Hold True?

The latest review finds that the occupational PAF estimates published since Doll and Peto's report generally ranged from 2 to 8% in the USA, Great Britain, and Nordic countries [11••]. In that respect, the British figures published in 2012 by Lesley Rushton and her team may well constitute the landmark estimates of their day, with point estimates of 5.3% for cancer deaths and 4.0% for incident cancer [12]. PAFs were systematically higher among men (3 to 14%) than among women (1 to 2%). The major contributors to the burden of deaths were lung cancer, mesothelioma, and bladder cancer [13], with other tumors also being important for men (such as the larynx, nasal cavity, and kidney). Additional sites proved significant in terms of incidence, namely nonmelanoma skin cancer for both men and women, and breast cancer in women when shift work was considered [12].

In Table 1, we further the review of PAFs published since 2012 among populations of high income countries (HIC). The latest estimates focus increasingly on incidence and usually amount to 2 to 4%, except in Québec, where they reached 6% in the mid-2000s according to PAFs borrowed from Finland and Great Britain [18•]. Since those original UK estimates [12], only France has based its calculations on detailed national exposure data or the best available proxy [14••]. Indeed, the British update of 3.8% [15] is based on previous estimates [19], while the supposedly updated figures for the USA appear in a table with no reference to data sources or methods [17].

Looking back to the figures that have circulated in scientific reports and peer-reviewed publications since the unusually high figures proposed in the 1978 OSHA report [20] (which were quickly dismissed by the 4% report), we may group these estimates into three levels. The first group comprises very low figures of around or below 2%, which rather relate to incidence (2.3% in France [14••]; 2% in Nordic countries [21]), and women in general (from 0.4% [14••] to 2.7% [18•]). The second group comprises intermediate estimates of around 4–5% (incidence or mortality), which are in line with Doll and Peto's contribution [12, 15, 17]). The third group reports relatively higher estimates of around 8 to 10% and refers exclusively to deaths (7.6% in Québec [18•], 8.6% in Australia [16•]) and to men (8.2% in Great Britain [12], 13.8% in Finland [22]).

Sources of Variation: Occupational Class Missing

The above are examples of the influence of country, period, outcome, and sex. However, with respect to the gender gap, it remains uncertain the extent to which these PAFs actually reflect differences due to segregation of jobs and exposures or if they are grounded in gender bias resulting in a potential underestimation among women. There is actually a range of sex-related methodological biases (from the lesser inclusion of women in occupational health studies, to double standard issues in the assessment of their exposures) that may result in an underestimation of occupational risk factors [23–25]. Another important source of variation is the number of agent-tumor combinations that are included. This, in turn, depends on the available level of evidence, and the more or less conservative approaches used to assess causality. For example, the recent estimates for France ranged from 2.3% (3.9% in men, 0.4% in women) when considering Group 1 carcinogens alone (e.g., defined as "carcinogenic to humans" by the International Agency for Research on Cancer, Iarc) to 3.5% (5.7% in men, 1.0% in women) when further adding Iarc Group 2A carcinogens (e.g., those "probably carcinogenic to humans," meaning less conclusive epidemiological evidence). The actual inclusion of a given combination will then rely on the availability of relevant input data, which may often be lacking. The results are also highly influenced by the choice of RR, the metric used to define prevalence of exposure (latency, categories) and their concordance [4••]. As an illustration, Fig. 1 simulates variations in PAFs based on the respective values chosen for RR and prevalence of exposure.

Both components are also likely to vary by industry sector, as shown in the UK, where 2.0% of the attributed cancers were in agriculture, forestry, and fishing; 29.9% in manufacturing and mining; 41.0% in construction; and, interestingly, 30.2% in the service industries [26]. Although barely addressed, other sources of variability include outcome (premature mortality), age range, and geographic (subnational) area. Though data are scant, a French report estimated that

Table 1 Recent PAF estimates of cancer related to occupational exposures in high income countries

Reference	Country	Outcome	Year	All		Men		Women	
				PAF (%)	Range[1]	PAF (%)	Range	PAF (%)	Range
[14]	France	Incidence	2015	2.3		3.9		0.4	
		Incidence[2]	2015	3.5		5.7		1.0	
[15]	UK	Incidence	2015	3.8		5.0		2.5	
[16]	Australia[3]	Mortality	2015	8.6	(7.4–9.6)	13.1	(11.3–15.0)	2.4	(2.0–3.0)
[17]	USA	Mortality	2000–2010			4.0	(3.0–5.0)	≤ 1	
[18]	Québec[4]	Mortality	2002–2006	7.6	(6.9–10.9)	11.7	(11.0–17.3)	2.8	(2.1–3.6)
		Incidence	2002–2006	6.0	(5.0–8.4)	9.1	(8.3–13.2)	2.7	(1.6–3.3)
[12]	UK	Mortality	2005	5.3	(4.6–6.6)	8.2	(7.2–9.9)	2.3	(1.7–3.2)
		Incidence	2004	4.0	(2.7–5.9)	5.7	(4.0–8.4)	2.1	(1.4–3.2)

[1] Range, when provided by authors, usually refers to the uncertainty interval as estimated through either sensitivity analysis or comparison of low, plausible (or medium), and high scenarios, except in (12), where range represents 95% confidence intervals

[2] These estimates are based on a secondary analysis relaxing the causal criteria for a range of agent-tumor combinations (e.g., Iarc Group 1 and 2A carcinogens)

[3] These estimates were based on the Global Burden of Disease (GBD) 2015 study, which uses a distinct methodology

[4] These estimates are based on the selection of "plausible" attributable fractions published for different cancer sites, their translation into attributable cases in Québec, and further summing to derive an overall PAF for all cancer

PAFs for lung cancer and asbestos among men ranged from 5% in the 30–34-year age group to 16% in those aged 40 years and more, a gap explained by differences in lifetime prevalence of exposure [27]. In Italy, a review showed large variations in the fraction of lung cancer attributed to occupation depending on period and geographical prevalence of hazardous industries [28]; while a population-based case-control study conducted in a former highly industrialized area reported AF for lung cancer higher than 50% in French men aged 40–79 [29]. These observations indirectly mirror what most authors acknowledge when it comes to interpreting occupational PAFs, namely that "occupational cancer tends to be concentrated among relatively small groups of people among whom the risk of developing the disease may be quite large" [9]. Put in other words "if one considered the segments of the adult population in which exposures to occupational carcinogens almost exclusively occur (manual workers in mining, agriculture, and industry, broadly taken), the proportion of 4% in the overall population would increase substantially" [30]. When looking for estimates of attributable fractions among highly exposed (and sometimes to multiple hazards) sub-groups in the general population or even stratified

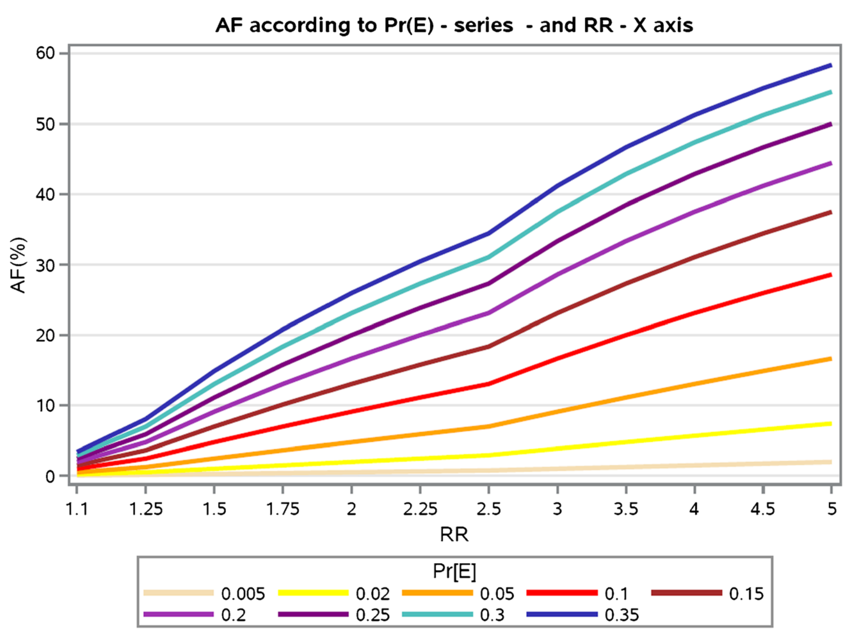

Fig. 1 Sensitivity analysis of Attributable Fraction (AF) estimates (*Y* axis) based on theoretical combinations of relative risk (RR, *X* axis) and prevalence of exposure (Pr(E), series)

by broad occupational categories (managers, manual workers), we were still unable to find any paper published to date.

A Case of Undone Science That Affects Lower-Status Workers

Recent trends in science studies have emphasized that knowledge does not develop uniformly but that various social factors explain the production of both knowledge and ignorance [31]. More specifically, some studies have highlighted the structural inequalities that can lead to the significant development of certain fields of knowledge and, on the contrary, to a lack of interest in other issues referring to it as "undone science" [32••]. From this perspective, this lack of interest in lower-status workers seems to us to fall into this category. This echoes concerns that were already expressed long ago by different authors [33–37] and reiterated recently [38••], though not specifically about PAFs and the occupational gradient of cancer.

This knowledge gap starts with the irregular and incomplete description of occupational exposures to carcinogens, and it is made even wider by the few data documenting their social patterning. Workplace exposure databases usually rely on monitoring systems of uncertain coverage and sustainability [39, 40]. Large initiatives such as the European CARcinogen EXposure database (CAREX) [41] and CAREX Canada [42] have provided nationwide estimates for the current number of workers exposed in different occupational groups. Other countries have instead conducted either one-time (Australia [43]) or repeated cross-sectional studies (France [44•]) to monitor the prevalence of hazardous exposures at work. The French SUMER surveys (SUrveillance Médicale des Expositions aux Risques professionnels) are among the few that allow quantifying exposure variations by occupational group (up to 28.5% exposed to CMRs in skilled BCW); function (up to 36.7% in installation, repair, and maintenance); and sex [44•]. Different trends are also observed for apprentices (e.g., increasing from 22.5 to 27.2% between 2003 and 2010) [45] and a lower level of control is observed in unskilled workers [46]. We nevertheless lack the global data on lifelong prevalence that is required in forming a clearer picture of the social stratification of work exposures in the general population over the life course. This is even more the case among the most disempowered workers (unskilled, temporary, non-unionized workers) that are most highly represented by women, people of color, and their intersection [47–49]. Moreover, occupational health studies (even more so labor statistics) typically do not include those who work in the informal sectors, "including very dangerous trades such as sex work, drug trafficking, personal and domestic services, nor the very dangerous exposures incurred during military service" [37]. The latter observations exemplify the "socially patterned gaps in knowledge about worker's health" [36]. Another gap in our knowledge concerns the common reliance on education rather than occupational group to capture the social gradient in cancer. Several HIC lack even the possibility of producing regular estimates of cause-specific death rates by occupation, as in France [50]; or they base their analyses on broad occupational categories, as observed in Belgium [51], Italy [52], and a recent 14-European country initiative focusing on middle-aged men [53••]. The problem is even greater for incidence data, although with certain notable exceptions such as the Nordic countries [54].

On the Relative Importance of Work and Way of Life

Interestingly, in the face of the accumulated evidence that socioeconomic disparities in health are still rising, notably in Europe [55], the interpretation of the gradient continues to question the relative importance of (social) causation and (health) selection (the healthy worker effect). Even when causation is thought to outweigh selection, as suggested recently in the transition from working to old age [56], the question raised by early studies on occupational health disparities remains: How much does the mortality (morbidity) of an occupational group reflect work environment and how much can be ascribed to way of life [57]? This echoes Alice Hamilton's early thoughts about the passionate debates opposing innate and socially constructed disparities in worker's health based on gender and race/ethnicity (Hamilton, 1925, cited by [36]). For cancer in particular, some authors have suggested that as much as 30% of the social disparities in mortality could be attributed to occupational exposures [58], while others instead conclude that "although cancer risk varies by occupation, only a smaller part of the variation can be attributed to occupational exposures in the strict sense." [59]. Many social and some occupational epidemiologists do argue that physical and chemical hazards in the workplace contribute minimally to the socioeconomic gradients in health and mortality, although Clougherty and her colleagues propose three presuppositions that may have contributed to this argument [37]. Firstly, those gradients were demonstrated among cohorts of white-collar workers, implying that such exposures are not a necessary component. Secondly, work-related physical and chemical hazards are said to have drastically declined in HIC over recent decades. Thirdly, the belief has long been held that most workers enrolled in hazardous occupations are compensated for the extra-risk through higher wages, which might mitigate the adverse health effects of hazardous exposures. Arguing against these three premises, the authors conclude that—at least for respiratory diseases and cancer—physical and chemical hazards in the work environment most likely play an important role in the higher rates of disease among lower-status workers. This public health and social justice issue has too often been overlooked when discussing priorities in cancer prevention.

Can We Take Late Lessons from Early Warnings?

If we simultaneously pay heed to the social stratification of occupational exposures, health and mortality, as well as to the socially patterned knowledge gaps in how such inequalities impact the population, then we cannot help but conclude that the time has come to rethink the way we assess the burden of work-related cancers. Yet, above all, it seems that the most necessary step to take is becoming more reflexive in regard to our own practices, not only in terms of scientific validity but also in terms of social liability.

Examining PAFs Through Science Studies

Indeed, as public policies are increasingly shaped by epidemiology, it is important not only to improve its tools scientifically but also to question them from a sociological and historical perspective. The development of PAFs may then be viewed as emblematic of the prominence of risk factor epidemiology over the last 30–40 years [60], an influence that has been achieved at the expense of other approaches that previously prevailed and that were more clinically grounded. This includes the epidemiology of occupational cancer developed by Wilhelm Hueper before World War II [61, 62]. By relying on much larger groups from a variety of socio-professional backgrounds, "modern epidemiology" [63] has sharpened its focus on some major public health risks threatening large populations, with the most representative of them being tobacco-related lung cancers [64]. However, the development of these approaches also made it more difficult to understand less massive risks and particularly when people experience multiple exposures. This issue is highly critical for occupational hazards, as work-related cancers tend to concentrate among small groups who potentially experience high disease risks; thus, providing an opportunity for reduction or even elimination. In the words of Doll and Peto: "The detection of occupational hazards should therefore have a higher priority in any programme of cancer prevention than their proportional importance might suggest" [9].

This latter point is illustrative of another dimension in the scientific works that compute PAFs. Situated at the boundary between the need to deepen knowledge and the willingness to guide public health interventions, such works are actually embedded in prevention policies [65, 66], which implies that researchers make choices regarding causes for which they think intervention is possible. Even categories such as "environmental" and "occupational" have not been consolidated within the field of epidemiology and they are subject to conflicting statements [67–70]. Today, the debates visibly shift from discussing "avoidable" to "preventable" burden of disease as concern grows about connecting PAFs to potential interventions through the quantification of an "attainable" risk reduction, e.g., through population preventable fractions (PPFs) [4••, 71]. Of course, defining what is and is not "attainable" is anything but scientific, nor is the selection of "modifiable" causes of cancers. Instead, such definitions and selections serve as very good examples of the type of socio-economic expertise that decision-makers increasingly use when seeking to promote evidence-based public policies [72, 73].

Coming back to the history of quantifying work-related cancers, the consequences of Doll and Peto's report in the social and political arenas were even more important than its scientific impact. This report was actually commissioned by the US Congress's Office of Technology Assessment (OTA) in order to end the controversy surrounding the evaluation of occupational and environmental causes of cancers. This controversy had been stirred by the publication of *The Politics of Cancer* [74] and the OSHA report [20], both of which had been widely circulated throughout US and UK trade union networks [75]. While Epstein generally warned about occupational and environmental carcinogens, the OSHA report estimated that 20 to 38% of cancer deaths were occupationally related, leading to numerous debates as to why cancers were on the rise and what policies were needed. In their report, Doll and Peto state that their "principal aim has been to explain matters to interested non-specialists" [9]. Therefore, it is difficult to classify their report as a scientific work, an expert report, or an exercise in popularization [76]. Despite this ambiguous status, the authors' scientific reputation helped lend this report great scientific and social legitimacy while contributing "to temper a growing anxiety at the time about a possible cancer epidemic resulting from occupational exposures" [10]. It also sustained the anti-regulatory policies that developed after President Reagan's election, as noted by the OTA administrator who hired the two scientists [75].

This brief foray into the recent past merely serves as a reminder that, despite common practice, scientific work should also be placed in a social and historical context and not considered to be a purely intellectual construct. When analyzing controversies in science studies, such as those that have developed around PAFs of occupational cancer, it is important to pay equal attention to the winners and losers in order to understand the precise rationale of both sides [77]. It is useful to look at the approaches that have been discarded and the moments when certain scientific choices have been made, as such an exercise may help explain the greater difficulty that epidemiology faces in trying to grasp some of the issues that have persisted until today. Our idea here is to make epidemiology less dependent on the previous ways that it faced some issues. Although we cannot propose definite solutions, we endeavor to share some avenues to be explored in future research, some of which have already proved either useful or promising. In our mind, there can be great value in rethinking at least three main areas for change: focus, scope, and metrics.

Change Focus? Towards a Perspective on Population Health Inequities

The Euro-GBD-SE consortium estimated that the share of deaths from cancer that might be avoided among men aged 30–59 if all occupational groups experienced the mortality of the upper non-manual workers varied between 7 and 46%, depending on country [53••]. As mentioned earlier, we so far have not found any such estimates relating specifically to occupational exposures and cancer. Based on a secondary analysis of a case-control study, one unique example made use of recent advances in mediation analysis to quantify the extent to which occupational exposures and smoking mediated the association between education and lung cancer incidence in men [78•]. Although we assume that the dearth of proper data—e.g., complete, multi-factorial, and stratified on relevant socioeconomic and occupational indicators—makes it a real challenge, we strongly encourage research and surveillance initiatives that could fill this gap by switching from a perspective on population health to one on population health inequities when trying to assess the burden of work-related cancer. In that respect, the choice of occupational classification scheme seems to be all the more important, as an increasing amount of empirical evidence indicates that the worksome—an extension of the exposome—encompasses far more than physical and chemical hazards [79••].

Change Scope? From Occupational Exposures to Work and Employment

A related issue concerns whether we should broaden our definition of "occupational cancer" to informal or less recognized work situations, for instance, those that affect female sex workers (exposure to HPV infection [80]), open-air workers (exposure to UV light [81]), and people working in bars and restaurants (alcohol intake, active smoking, and environmental tobacco smoke [12]). However, beyond those potentially new combinations of exposures and tumors that may each be important for the specific at-risk occupational groups, changing scope could also make it necessary to broaden the conceptual model by which we link work and health, cancer risk being no a priori exception. A thorough review of the literature did gather the best evidence of the different pathways through which work shapes the social gradient in health [37]. Apart from taking into account the most established hazardous exposures (physical and chemical) as well as job status (which overlaps particularly with one's socioeconomic position), it is also necessary to consider work stress, work organization, and precarious employment, with the latter receiving increasingly more attention over the last decade [82•]. The underlying conceptual model makes it clear that—beyond specific occupational exposures that are strictly defined—lower-status workers tend to accumulate various disadvantages across their working life. The model also questions the extent to which employment and working conditions broadly influence health behaviors through job strain and other adverse aspects, although we found very few studies that considered physical/chemical hazards together with psychosocial job stressors in relation to smoking, alcohol consumption, dietary habits, and physical activity [83–85]. Relevant information on the hidden components of the occupational gradient could be gained by documenting employment trajectories, hazardous working conditions, health behaviors, and outcomes among underserved populations, possibly through the follow-up of lower-income cohorts.

Change Metrics? From Relative to Absolute Measures

Although this review does not intend to provide insight into the many and well-studied validity issues that are particular to attribution and AF estimation (for a recent overview, see [4••] and, for a general presentation, see [5, 86]), we feel it is important to at least mention the more fundamental misconceptions and problems of interpretation that have been raised in the literature. Indeed, they occur equally among studies on work-related cancer and may well provide an opportunity for changing metrics or at least for combining different metrics, as each one may highlight a particular aspect that a single indicator would not fully capture. Two recent reviews have summarized the main pitfalls related to the conceptualization, interpretation, and application of AFs, and they most notably address terminological confusion, the invalid summing of PAFs and calculating the complement of PAFs to 100% [3], and underestimating the fraction of events in which exposure played a causal role (the etiologic fraction) [87•, 88•]. Alternative measures of public health impact have been proposed in order to overcome some of those limitations, such as average age at onset [89] or years of potential life lost [90], as well as broader calls to move from relative to absolute metrics [91]. Although such approaches are used far less and still debated [92], we do think more space should be given to scrutinizing the unintentional adverse effects of some of our long-held scientific *habitus*, including the claim that rate ratios are better than rate differences at capturing both strength of association and public health impact.

Conclusions

Going back to the question of the way in which PAFs shape the agendas of both research and public health policies, we should note that when even estimates of modest size (4–5%) are considered in isolation, they are often still accompanied by strong statements on "the value of prevention focused on the (relatively small) subpopulations that assume such risks" [93]. Other authors note that "care must be taken not to permit a disregard for a risk with a small PAF (e.g., occupation)" [94]. There are still many uncertainties surrounding the true magnitude of the occupational cancer burden [11••], specifically in regard to the continuing use of known agents and the introduction of potentially new carcinogens; a decrease in exposures to some well-characterized agents in HIC; a decrease in the industrial workforce; the transfer of remaining exposures to more precarious workers in HIC; and the fact that most hazardous industries are moving to lower and middle income countries. In contrast and in spite of those warnings, when using PAFs to compare "preventable causes of cancer," those related to occupational exposures almost invariably rank low. This relative downgrading may well contribute to shaping perceptions that occupational cancers are no longer a public health priority, if they ever were over the last 40 years. It is even more concerning that occupational factors were not included in the latest estimates of the fraction of cancer attributable to modifiable risk factors in the USA, Canada, and Australia, which is due to "lack of credible or useable prevalence data" [95] in some cases or they were excluded in others without explanation [96, 97]. Those different estimates thus focus essentially on modifiable behaviors. This same choice was made by the American Association for Cancer Research in its latest progress report, which, for the first time, did not include estimates of PAFs for occupational exposures [98].

As the demand grows for easy-to-use quantitative indicators for informing public decisions, the time has arrived for rethinking how we calculate PAFs by adopting a perspective on health equity [99••]. This is of particular relevance in the light of the effects of PAFs on health policies and on the public debates regarding how work contributes to inequities in cancer—although the effects are bound to extend far beyond this single health outcome. As environmental health issues increasingly become a priority, it may also be useful to remember that concerns about these issues originated historically with scientists such as hygienists, toxicologists, and physicians who were studying occupational hazards ranging from those in factories to environmental issues [100]. Perhaps now is also the time to ensure that environmental concerns do not lead to a neglect of occupational health issues.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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