



## Commentary

## Population attributable fraction of gas cooking and childhood asthma: What was missed?

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The population attributable fraction (PAF) is a measure of public health impact that is commonly defined as the proportion of cases of an adverse health outcome in the population that can be attributed to an adverse exposure and, therefore, could have been eliminated had the adverse exposure been removed from the population [12,21]. In order for a PAF estimate to be valid, multiple assumptions need to be met, primarily including (1) the adverse exposure is a cause of the adverse health outcome, (2) upon removal of the adverse exposure, the risk of the adverse health outcome among those formerly exposed is immediately reverted to the risk among those never exposed, and (3) the removal of the adverse exposure does not affect other risk factors of the adverse health outcome [1,12,15,22]. Since its first introduction in the 1950s, multiple formulas for the PAF have been developed for different scenarios (e.g., polytomous vs. binary exposure, with vs. without confounding) and a variety of terms have been used, sometimes improperly, to refer to it [1,21,22].

Miscalculations and misinterpretations of PAFs in the epidemiology literature have long been recognized, but they continue to appear in new publications, often times misleading the general public and even public health professionals. For example, nearly 20 years ago, a controversy over PAF estimates for obesity as a cause of mortality triggered much discussion among scientists, extensive coverage in the news media, and confusion in the general public [16,20]. More recently, in early 2023, Gruenwald *et al.* [7] published PAF estimates for indoor gas stove use for cooking and current childhood asthma in the US and nine specific states, which also garnered a considerable amount of attention. Relying on summary results from three North American studies (meta-odds ratio [OR] = 1.36, 95% confidence interval [CI]: 0.76–2.43) and seven European studies (meta-OR = 1.34, 95% CI: 1.13–1.60) reported in a meta-

analysis by Lin *et al.* [18] of epidemiology studies published between 1977 and 2013, Gruenwald *et al.* [7] reported that “12.7% (95% CI = 6.3–19.3%) of current childhood asthma in the US is attributable to gas stove use.” However, in Gruenwald *et al.* [7], a series of common mistakes were made in calculating and interpreting this PAF, some, but not all, of which have been pointed out previously [2,13,17]. Below, we discuss these common mistakes and their impacts.

### Disregarding the lack of an established causal relationship

As noted above, one of the key assumptions underlying a valid PAF estimation is that there exists an established causal relationship between the exposure and health outcome of interest. In the case of gas cooking exposure and childhood asthma, a causal relationship is not supported by the epidemiology literature [2,13,17]. The requirement of an established causal relationship was not addressed in Gruenwald *et al.* [7]. In fact, one of the authors acknowledged after the publication that their analysis “does not assume or estimate a causal relationship” [4], contradicting the fundamentals of PAF estimation. A PAF has no real public health implication if the fundamental assumption of causation is not met.

### Overlooking biases in the underlying risk estimate

A PAF estimate in the epidemiology literature is most commonly derived from two measurements – the risk estimate (here and throughout, referring to measure of association such as risk ratio [RR]) for the exposure-outcome relationship of interest and the prevalence of the exposure [1]. Virtually all epidemiology risk estimates are subject to

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biases, and any biases in risk estimates are carried over to the subsequent PAF estimates. For example, the effects of exposure and outcome misclassifications on PAF estimates have long been recognized [8,9]. The biases in risk estimates and their impacts on the subsequently estimated PAFs should be at least acknowledged and ideally assessed in terms of direction and magnitude using quantitative bias analysis [14]. This can inform the extent to which a PAF calculated from observational data (e.g., an RR) should be interpreted as causal vs. non-causal. In the case of gas cooking exposure and childhood asthma, the meta-OR that the PAF was calculated from was subject to not only publication bias but also biases that were common among the contributing individual studies, primarily due to exposure measurement error, reverse causation, confounding, and selection bias [17]. While Gruenwald *et al.* [7] calculated 95% CIs of their PAF estimates to account for random variation, they did not address the potential biases in their PAF estimates that were carried over from the meta-risk estimates extracted from Lin *et al.* [18].

### Neglecting the transportability of the underlying risk estimate

PAFs are often calculated from a risk estimate (e.g., RR) that is generated from a study population and a prevalence of exposure that is estimated from a target population (i.e., a population for which the PAF estimate is intended) that differs from the study population. The importance of the transportability of the risk estimate from the study population to the target population has been pointed out repeatedly. That is, primarily, the exposure definition and distribution underlying the risk estimate should be the same or sufficiently similar as those underlying the estimated prevalence of exposure, as well as the intended PAF estimate; the health outcome definition underlying the risk estimate should be the same or sufficiently similar as that underlying the intended PAF estimate; and the population characteristics should be sufficiently similar between the study population and the target population [1,3,6,23]. In the case of gas cooking exposure and childhood asthma, Gruenwald *et al.* [7] extracted North American- and European-specific meta-risk estimates from Lin *et al.* [18] and further combined them “given the similarities in housing characteristics and gas-stove usage patterns across these geographies.” However, as shown in Li *et al.* [17], the exposure definition (e.g., primarily use gas for cooking vs. ever use gas for cooking vs. presence of gas stove) and distribution (e.g., prevalence being 5.1% vs. 86.5%), health outcome definition (e.g., doctor-diagnosed asthma vs. study-diagnosed asthma vs. had asthma symptoms in the last 12 months), and population characteristics (e.g., aged 0–7 years with family history vs. aged 9–16 years in the general population) all varied substantially across the individual North American and European studies, obscuring the transportability of the combined meta-risk estimate to the target US population. In addition, no detail was provided in terms of how Gruenwald *et al.* [7] defined gas cooking exposure in estimating its prevalence in the US and specific states, further obscuring the transportability of the meta-risk estimate to the target US population.

### Using confounding-adjusted risk estimates in unadjusted PAF formulas

Among the various formulas that have been developed to date to calculate PAFs, the first introduced and probably also the most widely used is Levin's 1953 formula, which is an unadjusted PAF formula that combines an unadjusted risk estimate with the prevalence of exposure in the target population [1,12,22]. When a confounding-adjusted risk estimate is used to calculate a PAF, Miettinen's 1974 formula, an adjusted PAF formula, should be used instead; though, this formula also requires an estimate of the prevalence of exposure among cases, which is not always readily available [1,5,10–12,19]. Using a confounding-adjusted risk estimate instead of an unadjusted one in Levin's 1953 formula produces a biased PAF estimate [1,3,24]. This has long been identified

as a common error in PAF estimation in the epidemiology literature, and recent studies are paving the way for assessing the direction and magnitude of the associated bias [3,5,22,24]. In the case of gas cooking exposure and childhood asthma, Gruenwald *et al.* [7] used Levin's 1953 formula and applied it to meta-risk estimates that were generated from confounding-adjusted risk estimates from individual studies. The potential bias in their calculated PAFs as a result of this mistake was not discussed or quantified.

### Overinterpreting the public health implications of PAFs

It has long been recognized that even a correctly-calculated PAF has limited, hypothetical meaning, due especially to the underlying assumptions often not being met (e.g., a causal relationship has not been established) and the fact that it is not linked to any well-defined, realistic intervention [15,16,22]. Still, PAFs are often overinterpreted in the literature by epidemiologists as having real-world public health implications [16]. In the case of gas cooking exposure and childhood asthma, Gruenwald *et al.* [7] acknowledged two key assumptions underlying PAF estimation, including “(1) exposure to gas cooking among children is orthogonal to other risk factors such as exposure to tobacco smoke and (2) that we can conceive of a broad-based public health intervention to reduce the disease risk in children exposed to gas cooking to that of the unexposed, while holding all other risk factors equal.” However, they did not discuss whether or the extent to which each assumption was met and its implications on the validity of their estimated PAFs. Gruenwald *et al.* [7] also put forward two interventions and asserted in their conclusions that their analysis “demonstrates that known mitigation strategies will lessen childhood asthma burden from gas stoves,” when in fact their PAF estimates were not linked to any “mitigation strategies” or to any data on causal impacts of interventions [2].

Gas stoves are commonly used for cooking purposes, and their potential health and climate impacts have become an area of particular interest in recent policy making. However, the PAFs reported by Gruenwald *et al.* [7] have largely been taken at face value by the news media, policy makers, general public, and even some public health professionals, without fully recognizing the common mistakes in their calculation and interpretation or the associated impact on their validity and public health implications. Due to the mistakes discussed above, the PAFs reported by Gruenwald *et al.* [7], like those reported in a large proportion of other analyses in the epidemiology literature, are likely to be biased; these biases have not been quantified. As a result, the reported conclusions do not have any known real-world public health implications. We caution against taking miscalculated or misinterpreted PAFs at face value when informing public health interventions, as this could lead to wasted precious public health resources with no or little public health benefit in return.

### CRediT authorship contribution statement

**Wenchao Li:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Julie E. Goodman:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Christopher Long:** Writing – review & editing.

### Declaration of competing interest

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science. None were involved with the conception or drafting of this commentary.

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