Editorial Commentary

On the use of the "*Population Attributable Fraction*": application in cost estimation

Alberto Martini[1,2]^

[1]Unit of Urology, University Vita-Salute, San Raffaele Scientific Institute, Milan, Italy; [2]Division of Experimental Oncology, URI, Urological Research Institute, IRCCS San Raffaele Scientific Institute, Milan, Italy

Correspondence to: Alberto Martini, MD. Department of Urology, IRCCS San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milan, Italy. Email: a.martini.md@gmail.com; martini.alberto@hsr.it.

Submitted Aug 01, 2020. Accepted for publication Nov 25, 2020.
doi: 10.21037/tau-20-1146
View this article at: http://dx.doi.org/10.21037/tau-20-1146

The population attributable fraction (AF) represents how much of an outcome can be ascribed to a certain factor (1) and it represents an important statistical tool in epidemiology for estimating "how much" a certain exposure influences an outcome. The AF is useful in situations where patient randomization would be virtually impossible or extremely unethical.

The first description of what today represents the AF was published in 1951 by Doll, who tried to estimate how much of the incidence of lung cancer could have been attributed to smoking habits (2). Two years later, Levin proposed a formula (3) that set the ground for the various estimates of AF that are available today. These estimates span from AF formulas that can be applied from different study designs to the "adjusted" AF (4,5). In fact, like in all measures of associations, bias of the estimate might occur if confounding factors are present. Presently, we have the ability to obtain a more or less accurate estimation of the AF when deriving it from an adjusted regression model.

Assuming that we want to predict how much the cost of a certain treatment can be attributed to the presence of a defined factor, we would have to fit an appropriate regression model predicting the treatment administration and account for potential confounders. Next, we would obtain the adjusted attributable fraction (aAF) and associated 95% confidence interval (95% CI). Herein, we now know how much of a certain treatment can be ascribed to the presence of the defined variable. The financial impact of this variable could be extrapolated by multiplying the aAF and the associated 95% CI for the cost of the treatment. A concrete example follows.

During the surgical treatment of tumors, a positive surgical margin (PSM) can occur if the surgeon cuts through the tumor leaving a piece of malignant tissue behind. This occurrence is not uncommon in prostate cancer (PCa), since the prostate lies very close to the nerves that control erectile function and urinary continence. To ensure the optimal functional outcome, in terms of continence and erectile function, surgeons have to perform a "conservative" dissection. Whilst this might sound like an oxymoron, it represents what we, urologists, try to achieve, if oncologically safe (6,7). During prostatectomy, two main kinds of PSM might occur: (I) when resecting through tumorous tissue that has extended *per continuitatem* beyond the prostatic capsule (II) when breaching the capsule with instruments, in an effort to maintain the periprostatic structures *in toto*. The administration of adjuvant treatments such as radiation therapy should be evaluated under these two circumstances and/or in case of other adverse pathologic features. Without diving too much into details, an expectant management followed by RT in case of recurrence could also be considered, especially in absence of PSMs (8,9).

Given the aforementioned considerations, we have recently tried to estimate how much the presence of a PSM influences aRT administration, with the ultimate goal of achieving an estimate for the cost of a PSM (10). To do so, we fit a logistic regression predicting the administration

^ ORCID: 0000-0003-1272-7154.

of aRT adjusting for multiple factors. After the regression, we obtained the aAF and associated 95% CI. We then multiplied this and associated 95% CI for the estimated cost of aRT, according to the formula:

$$C_{PSM} = aAF \ x \ C_{aRT} \quad [1]$$

To the best of our knowledge, this represents the first case where the aAF has been used for cost estimation. Similarly, the same principle can be applied for time-dependent outcomes. In this context, the aAF could be obtained from a time-dependent regression predicting the administration of a secondary treatment and multiplied for the cost of the secondary treatment. Going back to the PCa example, one could estimate the effect of a PSM on the administration over time of salvage RT for recurrence, if an expectant management had been offered post-surgery.

In conclusion, the concept of the AF can be applied for cost estimation, after having extrapolated the AF from a multivariable regression predicting the administration of additional treatment(s) and multiplying it by the cost of the additional treatment(s).

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was a free submission to the journal. The article has undergone external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tau-20-1146). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Mansournia MA, Altman DG. Population attributable fraction. BMJ 2018;360:k757.
2. Doll R, Hill AB. A study of the aetiology of carcinoma of the lung. Br Med J 1952;2:1271-86.
3. Levin ML. The occurrence of lung cancer in man. Acta Unio Int Contra Cancrum 1953;9:531-41.
4. Benichou J. A review of adjusted estimators of attributable risk. Stat Methods Med Res 2001;10:195-216.
5. Black CD, Thavorn K, Coyle D, et al. Health system costs of potentially inappropriate prescribing in Ontario, Canada: a protocol for a population-based cohort study. BMJ Open 2018;8:e021727.
6. Martini A, Cumarasamy S, Haines KG III, et al. An updated approach to incremental nerve sparing for robot-assisted radical prostatectomy. BJU Int 2019;124:103-8.
7. Martini A, Falagario UG, Villers A, et al. Contemporary Techniques of Prostate Dissection for Robot-assisted Prostatectomy. Eur Urol 2020;78:583-91.
8. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2017;71:618-29.
9. Mohler JL, Antonarakis ES, Armstrong AJ, et al. Prostate Cancer, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2019;17:479-505.
10. Martini A, Marqueen KE, Falagario UG, et al. Estimated Costs Associated With Radiation Therapy for Positive Surgical Margins During Radical Prostatectomy. JAMA Netw Open 2020;3:e201913.

Cite this article as: Martini A. On the use of the "*Population Attributable Fraction*": application in cost estimation. Transl Androl Urol 2021;10(1):22-23. doi: 10.21037/tau-20-1146