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EPIDEMIOLOGY COUNCIL NEWSLETTER – APRIL 2020

From the Co-Chairs

Hi members

Welcome to the second newsletter of the Epidemiology Council. The Epidemiology Council has been very active in the last few months, with two articles recently published in the Journal of Physical Activity and Health and two projects underway.

Be sure to check out our two articles in the January 2020 issue of JPAH. In these articles we outline the purpose and goals of the Epidemiology Council and approaches to improving causal inference in physical activity epidemiology. In this newsletter we feature another method called the 'E-value', which can be used to estimate the effect of unmeasured confounding in observational studies. Our flagship project, the Physical Activity Cohort Study Repository (PACE), is well underway and an update is provided in this newsletter. The protocol of our other current project, a review of covariate selection in physical activity epidemiology, is being finalised and we will be moving to the literature search and data extraction stages soon. If you would like more information or are interested in being involved in this project, please email Terry Boyle (email below). We're planning an online journal club via Twitter in late April and we hope you can join us for that. More details will follow. We're also making plans for ISPAH 2020 in Vancouver. We'll share more details when they are finalized, and hope to see you some of you in October!

With best wishes
Brigid and Terry
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E-values to support epidemiological enquiry: An overview

Investigations of causality can be subject to bias from different sources. Performing sensitivity analyses to explore these biases, and to attempt to quantitatively assess their magnitude and direction of effect, is good practice in epidemiology[1] but not universally applied. These sensitivity analyses encourage researchers to make measured claims about their results, and may reduce misinterpretation or misapplication of study findings.

One common source of bias is residual confounding arising from confounders (factors associated with exposure and outcome which may be responsible for some of an observed exposure-outcome association) which are unmeasured or poorly measured. The E-value was recently proposed by two causal methodologists, Tyler VanderWeele (Harvard University) and Peng Ding (University of California, Berkeley), as a user-friendly tool to estimate the extent to which unmeasured confounding could influence an observed association.[2]

The E-value estimates how strongly associated an unmeasured confounder must be with both the exposure and the outcome to explain away the exposure-outcome association, on the risk ratio scale. Its derivation is:

E-value = $RR + \sqrt{RR * (RR - 1)}$ for relative risks [RR] above 1;

E-value = $(\frac{1}{RR}) + \sqrt{\frac{1}{RR} * (\frac{1}{RR} - 1)}$ for RRs below 1.

The same formula should be applied to the confidence limit nearest to the null. A smaller E-value suggests the effect estimate is vulnerable to unmeasured confounding, as even relatively weak confounders could explain the association. A larger E-value provides more confidence that unmeasured confounding is unlikely to have produced the association.

E-values can be obtained with a calculator, but VanderWeele and colleagues have also developed an R package and online calculator (details overleaf). E-values (for the effect estimate and confidence limit) could be reported alongside standard output from epidemiological studies.

The E-value is just one of many approaches available to help researchers evaluate whether their estimated associations are likely to be causal. It does not assess the likelihood of bias from sources other than unmeasured confounding, so a large E-value does not guarantee that a reported effect estimate is an accurate reflection of the relationship under study. There have been some critiques of the E-value's utility and interpretation[3], but its citation history (over 200 in under 3 years [PubMed]) suggests that at least some researchers are starting to consider it a potentially useful tool. The E-value would ideally be estimated and interpreted alongside other bias analyses, and was not intended to replace careful thinking about confounding and alternative threats to causal inference.

Written by: Suzanne Dixon-Suen, Secretary of the Epidemiology Council

References:

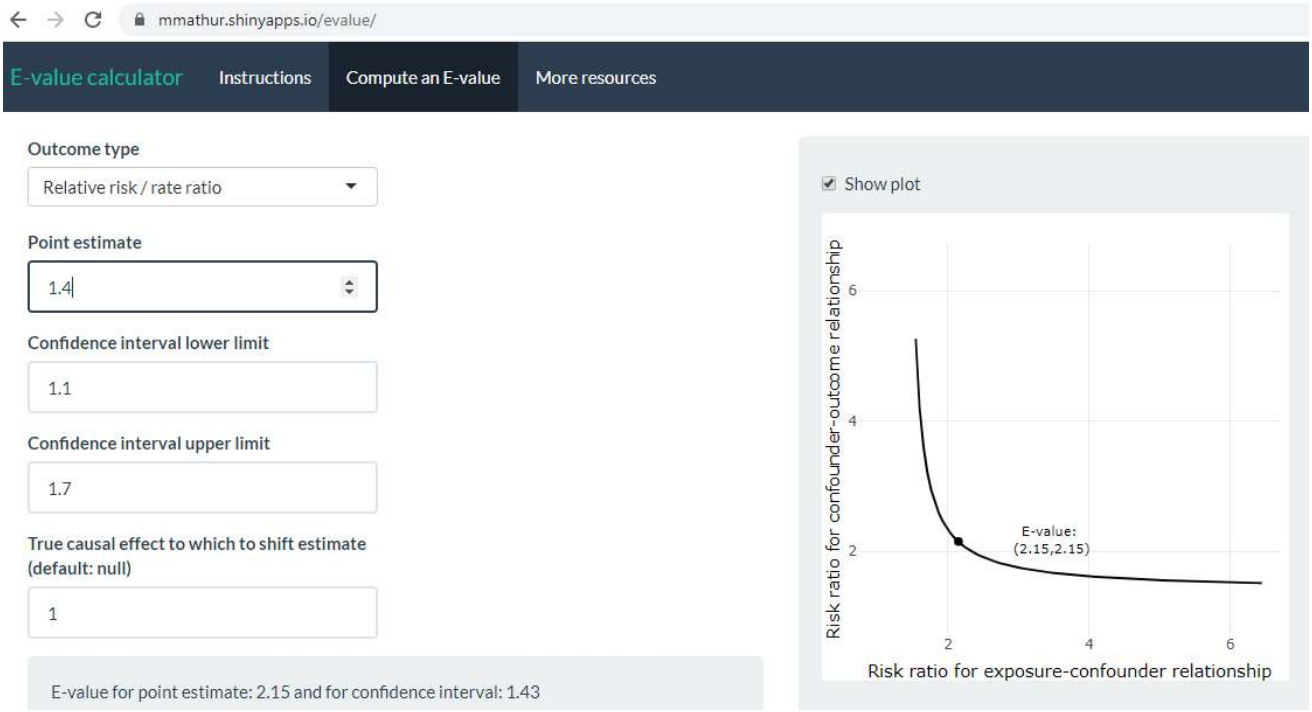
1. Lash T.L, Fox M.P., MacLehose R.F., Maldonaldo G., McCandless L.C., Greenland S., 2014. Good practices for quantitative bias analysis. *International Journal of Epidemiology* 43(6): 1969-1985.
2. VanderWeele, T.J. and Ding, P., 2017. Sensitivity analysis in observational research: Introducing the E-value. *Annals of Internal Medicine* 167: 268-274.
3. Ioannidis J.P.A., Tan Y.J., and Blum M.R., 2019. Limitations and misinterpretations of E-values for sensitivity analyses of observational studies. *Annals of Internal Medicine* 170: 108-111.

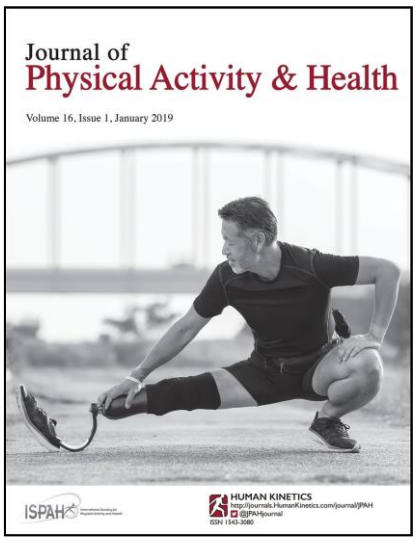
Tools to calculate E-values:

R package: https://cran.r-project.org/web/packages/EValue/index.html

Stata package: https://ideas.repec.org/c/boc/bocode/s458592.html

Online calculator https://mmathur.shinyapps.io/evalue/ **(sample output below)**





Click here to see the Epidemiology Council's article "Approaches to improve causal inference in physical activity epidemiology" published in the Journal of Physical Activity and Health.

Update from the Physical Activity Cohort Repository (PACE)

PACE core working group members Leonessa Boing and Brigid Lynch

The Physical Activity Cohort Repository (PACE) project was initiated by the Epidemiology Council of International Society of Physical Activity (ISPAH). This project aims to identify cohort studies with measures of physical activity and/or sedentary behaviour (self-report and/or device-based measurement) at two or more timepoints through a scoping review of the literature.

The longer-term goal is to produce an online, searchable repository containing information about these cohort studies to assist physical activity research worldwide. This repository will be housed and managed by ISPAH, and made freely available to members. We hope the PACE will contribute to building a stronger evidence base for physical activity and health, but it will facilitate international collaborations that will help build capacity in low- and middle-income countries.

The PACE project is lead by Andrea Ramirez Varela (Colombia), working closely with Leonessa Boing (Brazil/Australia), Brigid Lynch (Australia) and Terry Boyle (Australia). The project working group consists of twelve ISPAH members, Philip von Rosen (Sweden), Jakob Tarp (Norway), Elli Kontostoli (UK), Derrick Bennett (UK), Jacqueline Louise Mair (Scotland), Jenny Rossen (Sweden), Kirstie Tew (UK), Jorge Mota (Portugal), Clare Hume (Australia), Saud Abdulaziz M Alomairah (Denmark), Paul Mackie (Australia) and Sigríður Lára (Iceland).

The initial literature search was conducted in PubMed and Web of Science. Additionally, we searched for cohort profiles published in the International Journal of Epidemiology. Our inclusion criteria were: (i) The study must be a cohort study with two or more waves of data collection that include measures of physical activity and/or sedentary behavior. (ii) Physical activity and/or sedentary behavior measurements can be self-reported, or device-measured. (iii) No restrictions on sample size or populations and outcomes, nor on participant age, dates of publication or language of publication. Currently, we are screening titles and abstracts from the 8,992 references found. The title and abstract screening are being completed by the working group (paired up so that each article is independently reviewed twice), using systematic review management software (Covidence).

Our aim is to finish the review by June 2020, as the results of PACE will be presented at ISPAH 2020. The PACE protocol will soon be available on the Epidemiology Council page of the ISPAH website. We also plan to publish the scoping review of PACE in a peer-reviewed journal.

The PACE team

Core working group

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