

**Population Attributable Fraction Based on Sufficient Causal Framework for
Mediation Settings - Evaluation of Resource Distribution on Prevention and
Treatment for Stroke**

Sheng-Hsuan Lin

Methodology for assessing mediation and interaction has been developed rapidly over the past decade and shed light on mechanisms. Population attributable fraction (PAF) is an important measurement in epidemiology for the potential impact of exposure effect in population and benefit to allocate the resources on intervention strategies. In the case with multiple exposures along with interaction, PAF does not work well to account for intervention. An alternative definition of PAF is proposed based on sufficient cause framework to address this difficulty. In this study, we improve the previous methods in several directions. We first use a formal statistical definition to illustrate the relation between causal pies and PAFs. We also develop an approach to quantify the PAF of pathways along with the corresponding model for adjusting confounders. We apply the proposed method to explore the mechanism of a hepatitis C virus (HCV)-induced hepatocellular carcinoma (HCC) mediated by and/or interacted with abnormal alanine aminotransferase (ALT) and high hepatitis B virus (HBV) viral load. When treating ALT as mediator, 56.77% of diseased subjects can be attributable to either HCV or abnormal ALT. There are significant indirect effect and synergism. It reveals that HCC is mainly induced by abnormal ALT which occurs regardless of the presence of HCV infection. When treating viral load of HBV as mediator, more than 85% of diseased subjects are attributable to three paths: neither HCV nor high HBV viral load induces HCC; high HBV viral load always occurs regardless of the presence of HCV, and then high HBV viral load induces HCC solely;

high HBV viral load is induced by an absence of HCV, and consequently high HBV viral load induces HCC solely. We also show that the previous methods are the special cases of the proposed method without agonism or mediation. The proposed method can identify the potential impact of exposure and pathway effects in population and benefit to allocate the resources on intervention strategies more precisely.