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Commentary

Interaction in Medical Sciences; How Far is the Truth?

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Abstract

Interaction, or effect modification, is vital in understanding complex relationships between risk factors and health outcomes. While often studied between two variables, multiple variables actually interact simultaneously, shaping health events. However, detecting these interactions is challenging due to sample size, dataset, and software limitations, leading to incomplete predictions in research.

To bridge this gap, large-scale studies considering multiple health variables and advanced software are needed. Uncovering interactions can greatly improve personalized medicine and interventions. Temporal aspects matter too, as interaction effects change over time. Longitudinal studies tracking changes offer insights into dynamic interactions.

New data collection methods like wearables offer real-time exposure data. Merging these with traditional designs enhances interaction detection. Embracing temporal dimensions and novel data methods can yield a nuanced understanding of effective interventions, better clinical choices, and improved health outcomes.

Conclusion: The systematic review aims to provide evidence-based insights into the impact of virtual simulation on nurses' knowledge enhancement. By synthesizing data from RCTs, the study intends to guide educational practices and policy decisions for optimizing nursing education through innovative methods.

Keywords: Interaction, Statistical Software, Truth.

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1. Interaction in Medical Sciences; How Far is the Truth?

The term effect modification (interaction) in epidemiology is used to describe a situation in which two or more risk factors modify each other's effects. A variable that is associated with both exposure (x) and outcome (y) of interest is responsible for all or part of the association between exposure and outcome and is known as a confounder. Whereas effect modification is a fact that refers to the effect of the exposure on the outcome varies depending on the presence or different level of another variable (the effect modifier). [1] An important issue in the evaluation of interaction is how to measure effect. The effect can be measured by either attributable risk (additive model) or a relative difference, for example, the relative risk (multiplicative model). The conceptual basis for the evaluation of interaction is the same for both models. Theoretically, at least three factors are required for the phenomenon to occur. Effect modification refers to variation in the magnitude of an effect measure across levels of a third variable [2, 3]. Effect modification is a phenomenon that occurs among different variables quantitatively or qualitatively. Effect modification is a fact, and the only task of the researcher is to identify and report it. In general, in most studies and statistical methods, effect modification is considered for only two variables. A survey of 225 cohorts and case–control studies showed that 61% of the studies addressed effect modification or interaction in their publications in this way [4].

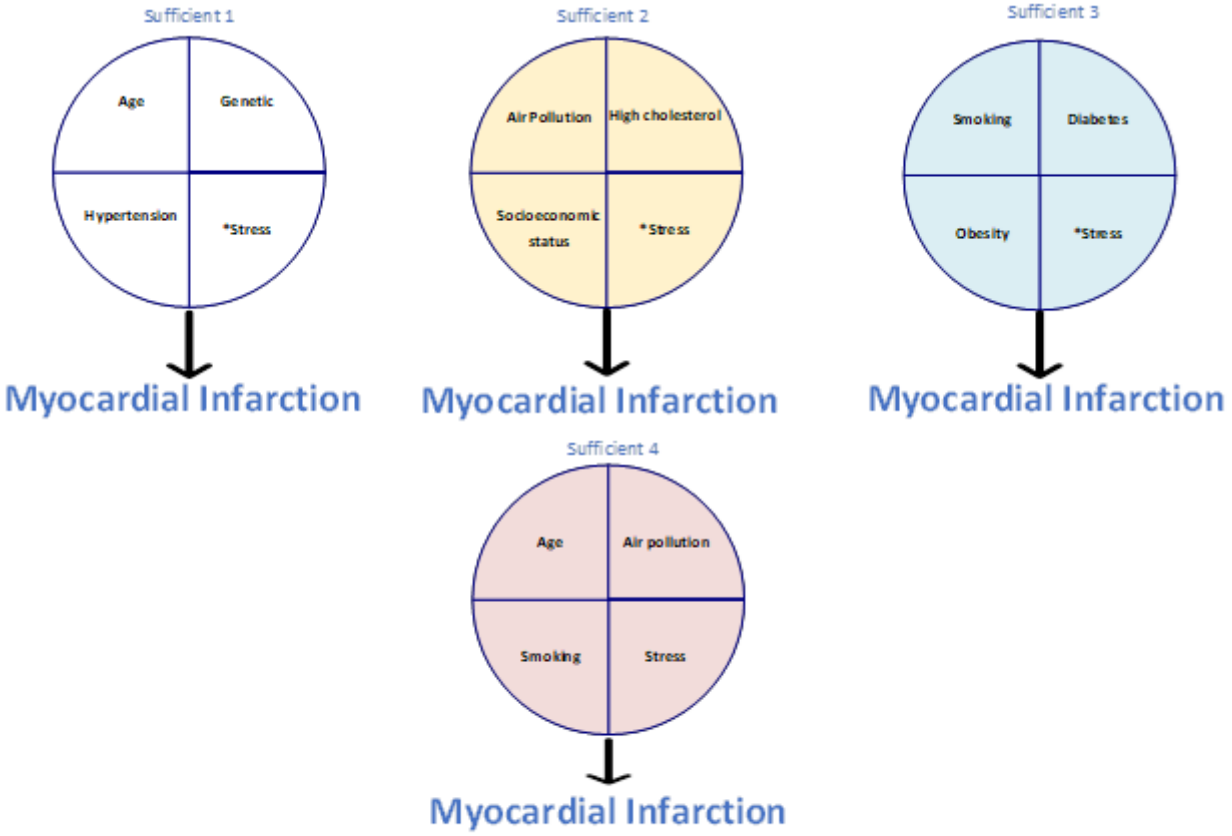
When the association between factor A and outcome Y exists and is of the same direction in each stratum formed by Z but the strength of the association varies across strata, quantitative interaction is said to exist. On the other hand, qualitative interaction is regarded as present when either the effects of A on the outcome Y are in opposite directions (crossover) according to the presence of the third variable Z or there is an association in one of the strata formed by Z but not in the other. In other words, the nature of A is dependent on the presence of the effect modifier Z.

However, in reality, there are effect modifications among more than two variables or an infinite number of variables. The farther we go from detecting effect modification among variables, the farther we get from the reality of the true association. It is noticeable that there are a lot of necessary and sufficient causes to interact with each other for a special effect. For example, for the occurrence of Myocardial Infarction (MI), there are a lot of necessary and sufficient causes including (hypertension, diabetes, stress, obesity, dyslipidemia, smoking, history of disease, and so on) to intricate with each other (Figure1). Interaction among components of three sufficient causes can create other sufficient causes. By ignoring and not detecting the interaction among all components, in fact, we have missed many of the causes related to MI. Therefore, we have actually moved away from the reality. (Figure 1).

In reality, numerous variables at different levels including genetic, organ, tissue, person (age, sex, lifestyle, personality types and etc.), population (socioeconomic status, cultural and political factors), environmental level (air pollution, climate change) interact with each other simultaneously for the occurrence of a health event. Interestingly, any of those studies could not detect such inactions. Regarding that, this limitation in detecting such interaction between numerous variables causes vulnerable and even harmful results in health aspects. It is noticeable that ignoring the effects of interaction among variables is fundamentally harmful in prediction models and causes vulnerable results in clinical research.

Clinical investigators running RCTs usually examine whether the observed treatment effect is the same in various subsets of patients. The qualitative interaction, which means that the treatment is beneficial in some subsets and harmful in others, is of major importance [5]. Taking into account the effect of reporting interaction in the main message of public health research and especially in prediction studies is highly important. Despite the importance of detecting interaction in public health and clinical research, small sample sizes and lack of genetic and environmental variables in the available datasets on one side, and lack of statistical software on another side, the interaction between these variables (environmental and genetic) in the real world are ignored. As a result, despite the fact that numerous studies have been conducted to focus on the importance of interaction, serious debates on the subject are still ongoing. Noticeably, most of the study's findings are far from the truth occurring in the real world.

Large sample sizes considering all related health variables and also designing software to be able to detect both quantitative and qualitative interactions among more than two variables are necessary. Interestingly, after detecting interaction, personalized medicine in clinical and interventions in public health would be done bet



*Stress: Stress was defined as a necessary cause because of its effect on making myocardial infarction

Figure 1. Interaction of age, air pollution, and smoking as components of three different sufficient causes for the occurrence of Myocardial Infarction

done better. In fact, without assessing interaction and its effects on the probability of outcomes or public and clinical interventions, decision-making and prediction in public and clinical research [6-8] would not be accessible.

In summary, considering the temporal aspect is crucial for comprehending the role of interaction and its impact on health outcomes. The effects of interaction are not static but can vary over time, resulting in dynamic relationships between risk factors and outcomes. Longitudinal studies that track changes in exposure and effect modifiers over time can offer valuable insights into the temporal dynamics of interactions.

By examining how the strength and direction of interaction evolve across different time points, researchers can gain a deeper understanding of the underlying mechanisms and pathways involved. This knowledge has practical implications, as it can guide the development of targeted interventions and personalized treatment strategies that can adapt to individuals' changing risk profiles.

Moreover, advancements in data collection methods, such as wearable devices and mobile health technologies, present new possibilities for capturing real-time data on exposures and effect modifiers. Integrating these innovative data sources with traditional study designs can enhance our ability to detect and comprehend complex interactions in a more comprehensive and timely manner.

By acknowledging the temporal dimension of interactions and incorporating novel data collection methods, future research holds the potential to provide a more nuanced understanding of the true associations and interactions that manifest in the real world. This enhanced

understanding can lead to more effective public health interventions, improved clinical decision-making, and ultimately better health outcomes for individuals and populations.

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