World Health Organization

The need for standards for vaccine effectiveness studies

Phil Krause

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Motivation

Many public health decisions related to vaccines during the COVID pandemic relied upon observational studies

Public health authorities may not have always realized the risk of misinterpreting observational studies

Some decisions may have been based on flawed interpretations of observational studies

However, there also is no doubt that observational studies are absolutely necessary, and in many cases are the sole source of data that could inform important decisions, whether during or between pandemics

Thus, it is critical that the scientific community consider ways to increase the reliability and interpretability of observational studies

In this meeting, we'd like to discuss whether standards for design, conduct, analysis, and/or reporting of vaccine efficacy observational studies could decrease the risk that study results are misinterpreted

Observational studies of vaccine effectiveness are often performed in order to:

obtain data when randomization is perceived as not feasible or has not been done

obtain data on rare outcomes

provide data in real-time

Types of observational studies of vaccine effectiveness

- Cohort
  - Prospective
  - Retrospective
- Case control
  - Test negative design

Features that make results of observational studies more credible

Large effects

Strategies to reduce bias

Strategies to quantify bias

Strategies to allow further investigation of bias

However, the potential biases in observational studies can be appreciable. Uncertainties in such studies (e.g., if actual effect is little or zero) need to be weighed against potential benefits and harms

Sources of bias

- Confounding
- Healthy vaccinee bias
- Misclassification
- Selection bias
- Biases specific to test negative designs
- Differential depletion of susceptibles
- Waning immunity

Methods to address bias

Design- database selection

Design- strategies to avoid bias

Conduct

Analysis

Potential to use randomization:

e.g.,randomization during deployment

simple randomized trials

Strategies to assure that trial reporting and synthesis accounts for bias

- Results and data sharing
- Transparent discussion of limitations
- Reproducibility and generalizability considerations

This meeting is organized in order to inspire further discussions that will ensure that future observational studies are as well-designed, conducted, analyzed, and reported as possible.