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# ***Solutions to Chapter 1 Exercises***



# 1

## Chapter 1

1. On November 9, 2020, Pfizer reported early results from a randomized controlled trial of their coronavirus vaccine, based on messenger RNA technology. The report stated that the vaccine appears to be at least 90% effective. To which of Hill's nine items does this evidence of cause and effect correspond?

Item (8), experiment.

2. At the same time, Moderna was developing a coronavirus vaccine also based on messenger RNA technology. Which of Hill's nine items suggested that the Moderna vaccine would also be effective?

Item (9), analogy.

3. Second generation anti-psychotics (SGAs) are helpful treatments for mental illnesses including schizophrenia and bipolar disorder. However, they are well known to cause substantial weight gain (Beasley et al. (1997)). Additionally, Lambert et al. (2006) reported on diabetes risk associated with SGAs. Which of Hill's nine items correspond to using the weight gain evidence to substantiate the cause and effect of SGAs on diabetes risk?

Items (6) and (7), plausibility and coherence.

4. Anderson (1964) write that

“There seems little doubt whatever that cigarette smoking, and to a lesser extent other forms of tobacco smoking, are associated with mortality from lung cancer. This association has been amply demonstrated by both case history and cohort studies in a variety of countries, and has been thoroughly summarized at countless symposia and in innumerable review articles.”

Which of Hill's nine items does this evidence of causation address?

Item (2), consistency.

5. The Alpha-Tocopherol Beta Carotene Cancer Prevention Study Group (1994) reported on a randomized controlled trial of alpha-tocopherol and beta carotene in male smokers designed to validate or refute epidemiologic evidence that diets high in carotenoid-rich

fruits and vegetables, as well as high serum levels of vitamin E (alpha-tocopherol) and beta carotene, reduce the risk of lung cancer. Unexpectedly, they observed a higher incidence of lung cancer among the men who received beta carotene than among those who did not. However, they found little or no effect on the incidence of cancer other than lung cancer. Which two of Hill's nine items does this new evidence of the causal effect of beta carotene on lung cancer address?

Item (3), specificity.

6. Lee and Skerrett (2001) found that increasing levels of physical activity are more strongly protective against all-cause mortality. Which of Hill's nine items does this evidence of causation address?

Item (5), biological gradient.

7. Boden and Fergusson (2011) concludes that a review of the literature "suggests a causal linkage between alcohol use disorders and major depression, such that increasing involvement with alcohol increases risk of deression." Which of Hill's nine items presents the greatest difficulty for concluding causation in this context?

Item (4), temporality.

8. Sebat et al. (2007) found that 10% of patients with sporadic autism had de novo copy number variation (CNV), versus 1% of controls. This an example of a *case-control study*, in which the sampling is based on the outcome rather than the exposure. The authors conclude that these findings establish de novo germline mutation is a more significant risk factor for autism spectrum disorders than previously recognized. Which of Hill's nine items does this evidence of causation address?

Item (1), strength.

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## ***Bibliography***

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