ADJUSTMENT FOR PUBLICATION BIAS CHANGES THE APPARENT EFFICACY OF HORMONE TREATMENT: UNADJUSTED DATA MIGHT DISTORT THE RISK–BENEFIT TRADE OFF

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OBJECTIVES: To determine the impact of publication bias on the magnitude of the treatment effect in clinical studies evaluating hormone therapy (HT) on the frequency of hot flashes among menopausal women. METHODS: We searched computerized databases for English language articles from 1966 to April, 2004. Two reviewers evaluated 5840 published titles, identified placebo-controlled observations that met explicit inclusion criteria, and extracted data pertaining to study characteristics, interventions used, and outcomes measured. Studies evaluating the effects of HT in cancer patients were excluded. The impact of HT on the frequency of hot flashes was calculated using a random-effects model. The effects of publication bias were assessed using the trim and fill method. RESULTS: Based on our criteria, a total of 29 studies were included in the meta-analysis. A funnel plot examining the presence of publication bias was asymmetric, suggesting that small non-significant studies were missing. The trim and fill method suggested that four studies were missing. The standardized mean difference between unadjusted and adjusted point estimates was 0.8 (CI 0.3–1.2). CONCLUSIONS: When evaluating the efficacy and safety of therapeutic interventions, the validity of findings from a meta-analysis is questionable if publication bias is present. Given that restricting a meta-analysis to published literature can distort the effects under investigation by as much as 30%, researchers should try to detect and correct for publication bias when synthesizing the evidence. Our meta-analysis confirmed that HT is effective in relieving menopause-related hot flashes but less than originally suggested. For therapies with significant risk-benefit tradeoffs, the clinical decision could vary upon a complete and unbiased assessment.

NEW INSIGHTS INTO THE PLACEBO EFFECTS: A CASE STUDY OF THE EFFECTIVENESS OF HORMONE THERAPY ON THE FREQUENCY OF HOT FLASHES

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OBJECTIVES: To determine the magnitude of the placebo effect in studies examining the impact of hormone therapy (HT) on the frequency of hot flashes among menopausal women. We also examined the influence of data type on point estimates. METHODS: We searched computerized databases for English language articles from 1966 to April, 2004. Two reviewers evaluated 5840 published titles, identified placebo-controlled observations that met explicit inclusion criteria, and extracted data pertaining to study characteristics, interventions used, and outcomes measured. Studies evaluating the effects of HT in cancer patients were excluded. The magnitude of the placebo effect on frequency of hot flashes was calculated using a random-effects model. The effects of outcome type (binary and continuous) were assessed separately. RESULTS: Based on our criteria, a total of 25 studies were included in the meta-analysis. When the effects of data type were assessed, studies with continuous outcomes (N = 18) reported a larger placebo effect than studies using binary outcomes (N = 7). The difference in standardized mean difference (SMD) = 2.52 (CI: 2.17–2.8). A larger placebo effect was observed in weekly hot flashes. The difference between weekly and daily SMD = 0.5 (CI: 0.15–0.85). CONCLUSIONS: Placebos are used to control for natural remission and provide a standard for comparison to active treatment. However, it is difficult to distinguish a true placebo effect from reporting bias when studying hot flashes; patients tend to please investigators by reporting positive changes when no improvement took place. Overall, we found a greater placebo effect in studies with continuous outcomes possibly due to the systematic differences in the self-recording of symptoms or the natural decline of symptoms. These findings may apply to other patient reported outcomes in other conditions.

HEALTH PREFERENCES AND WILLINGNESS TO PAY TO REDUCE EXPOSURE TO POST-MENOPAUSAL RISK FACTORS

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OBJECTIVES: This study uses conjoint analysis to examine women’s health preferences toward three post-menopausal risk factors: osteoporosis, heart disease, and breast cancer. Willingness to pay (WTP) to reduce the risk of exposure was also examined. METHODS: A questionnaire containing three parts: conjoint analysis to assess health preferences toward the easiest (hardest) condition to live with (levels: 25%, 50%, 75%), WTP to reduce risk factor exposure 0%, 50%, 25%, respectively, and demographic characteristics was administered to a random sample of women currently participating in a large observational study at the University of Alabama Birmingham, School of Medicine. Of the 99 responses obtained, 83 were suitable for conjoint analysis. Visual analog scales established validity and quality of life measures assessed current health status. RESULTS: Overall utilities for the best possible preferences were 1.573, −0.694, −0.877 for osteoporosis, heart disease, and breast cancer, respectively, with Log likelihood = −1077.21, X² = 671.4, P < 0.001. Pseudo R = 0.24 for the binary logit model. Similar patterns were observed for the worst possible preferences. Average WTP values to reduce exposure to the three risk factors levels that were the easiest to live with ranged from $224.50 to $3500. Alternatively, WTP values to reduce exposure for risk factor levels that were the hardest to live with ranged from $425.00 to $6500. Patient preferences were consistent with the assumptions of decision theory and income levels. CONCLUSIONS: Findings from this study reveal the usefulness of conjoint analysis to assess health preferences with respect to disease severity, risk, and the possibility of future encounters.

INFECTION

OUTPATIENT COMMUNITY-ACQUIRED PNEUMONIA IN NON-ELDERLY ADULTS: TREATMENT AND OUTCOMES

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OBJECTIVE: To examine antibiotic prescribing and outcomes in outpatient treatment of community-acquired pneumonia in non-elderly adults. METHODS: We analyzed claims from eight managed care organizations. Index claims were outpatient or