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

Badamgarav E1, Borenstein J2, Song PJ1, Dubois RW1

1Cerner Health Insights, Beverly Hills, CA, USA; 2Cedars-Sinai Health System, Los Angeles, CA, USA

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 effect 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

Song PJ1, Badamgarav E1, Dubois RW1, Borenstein J2

1Cerner Health Insights, Beverly Hills, CA, USA; 2Cedars-Sinai Health System, Los Angeles, CA, USA

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

Steinbach SL1, Harpe SE2, Foud M3, Ohsfeldt RL4

1Ohio State University, Columbus, OH, USA; 2Virginia Commonwealth University, Richmond, VA, USA; 3University of Alabama at Birmingham, Birmingham, AL, USA; 4The University of Iowa College of Public Health, Iowa City VAMC, IA, USA

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, −0.696, −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

Singer ME1, Asche CV2, Rose J1

1Case School of Medicine, Cleveland, OH, USA; 2University of Utah, Salt Lake City, UT, USA

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...
emergency department visits in 1999–2001 by individuals aged 25–64 with primary diagnosis of pneumonia, antibiotic prescription within three-days, chest x-ray on index date, continuous enrollment for 12-months prior, 30-days after index visit. Exclusion criteria: antibiotic prescription, pneumonia diagnosis, or hospitalization in prior 30-days; initial therapy with multiple antibiotics; in prior 12-months residence in a long-term care facility or diagnosis of cancer of bronchus or lung, secondary malignancy, HIV/AIDS, cystic fibrosis, immunity disorders. We considered the following comorbid illnesses: chronic liver, renal, or lung disease; cerebrovascular disease; cardiac disease; diabetes mellitus; malignancy. RESULTS: A total of 5748 cases met criteria, 13.9% initially seen in the emergency department. Of these, 18.8% had one comorbidity, 3.3% had multiple comorbidities. Macrolides were the most common initial therapy (66.5%), followed by quinolones (17.9%). Quinolone use more than doubled from 1999 to 2001, from 11.8% to 24.3% in patients without comorbidity, from 12.1% to 20.9% for one comorbidity, 24.9% for one comorbidity, 28.6% for multiple comorbidities. Hospitalization without secondary malignancy. Macrolides were the most common therapy, quinolone usage was substantial and rising rapidly regardless of comorbidity. Hospitalization for patients failing therapy was fairly common even in patients without comorbidity.

**OBJECTIVE:** Infections due to P. aeruginosa are associated with increased likelihood of death and morbidity. Empiric therapy is often difficult due to increased resistance noted with this organism. The purpose of this study was to determine the impact of inappropriate initial empiric therapy on health outcomes of patients with P. aeruginosa bacteremia. METHODS: Retrospective cohort study of hospitalized patients with their first episode of P. aeruginosa bacteremia. Patients were stratified based on appropriateness of antipseudomonal therapy. Inappropriate initial empiric therapy was defined as receipt of antibiotic therapy to which the isolate displayed in vitro resistance. Data collected included discharge mortality, new ICU admission, mortality; in hospital stay. RESULTS: A total of 87 patients (71% males/29% females) aged 58 ± 17 years (mean ± SD) were identified between January, 2002 to April, 2004. Overall mortality was 44%. Forty-nine percent of patients’ received inappropriate antibiotic therapy. ApacheII score were significantly higher in patients that died (p = 0.003). Mortality rates were significantly higher in patients treated with inappropriate empiric therapy (63%) compared to patients treated appropriately (39%, OR = 2.97, p = 0.024). New requirements for ICU admission, hemodialysis, or ventilator did not differ between the two groups. CONCLUSIONS: Inappropriate initial empiric therapy in patients with P. aeruginosa bacteremia significantly increased mortality rates.