PMC9

30 YEARS OF COST-EFFECTIVENESS ANALYSES: A BIBLIOMETRIC REVIEW OF ARTICLES PUBLISHED IN THE ECONOMIC AND MEDICAL LITERATURE: 1976–2005

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Cost-effectiveness analysis (CEA) presenting a cost/QALY ratio is considered the gold standard for economic evaluations in health care. Despite the proliferation of CEA research, there has been no detailed study focusing on the bibliometric properties of this literature. To describe and analyze trends in publications and co-authorship in the CEA literature from 1976–2005. We used the Tufts-New England Medical Center registry of original CEAs published through 2005 http://www.tufts-nemc.org/cearegistry/). For each article we recorded the year of publication, journal's name, the number of contributing authors and their names. Authors were assigned a credit based on their perceived contribution to the study (1 credit point for the first and last authors, $^1/_2$ point for the second author, and 1/n credit points for all other authors). We calculated the Author's Contribution Index (ACI), by dividing the total credit points by the number of studies published by the same author. Approximately 1150 studies have been published in 360 journals over the past 30 years, with an increase in the number published annually from 18(±26) in 1976–2000 to 138(±46) in 2001–2005, $p < 0.0001$. The mean number of contributing authors was 4.6(±2.4) and increased from 4.3(±2.3) to 4.8(±2.5), $p < 0.0001$ over that same time interval. Medical journals were characterized by a higher number of co-authors, as compared with the economic and health policy literature: 4.7(±2.4) vs. 4.2(±2.1), $p = 0.004$. The lowest number of co-authors (3.6) was in Value in Health and Medical Decision Making, and the highest in Circulation (7.7). The most prolific authors were affiliated with Harvard and Tufts Universities. **CONCLUSIONS:** The CEA literature continues to proliferate. Co-authorship trends seem to follow the rapid increase in the mean number of authors found in the health economics and medical literature. Further research is needed to examine journals' and authors' concentration trends, and dissemination of CEA results.

PMC10

THE DEVELOPMENT OF COST-EFFECTIVENESS INDICES WITH EQUITY IMPLICATIONS FOR THE ECONOMIC EVALUATION OF HEALTH CARE

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The incremental cost-effectiveness ratio (ICER) with number of dollars per quality-adjusted life year (QALY) has been extensively used in cost-effectiveness analysis (CEA) for improving efficiency in health care, but there is a lack of simple CEA indicators to take the equity issue in health into consideration. In this paper, by adjusting the ordinary ICERs with the quality-adjusted life expectancy (QALE) of the age- and gender-matched general population, we developed the CEA indicators based on and/or weighted by relative health gap to improve the distributive justice. If we collect the quality of life and survival data to estimate the QALY gained by a certain intervention for a specific disease, then the CEA indicators based on and/or weighted by relative health gain can also be developed to reduce the unintended inequity. The proposed six new CEA indicators with equity implications were empirically calculated for comparisons among the diseases of end stage renal disease, acquired immune deficiency syndrome, liver cancer, and breast cancer to demonstrate their applicability.

PMC11

ACCOUNTING FOR THE PLACEBO RESPONSE IN COST-EFFECTIVENESS ANALYSIS

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Defined as the psychophysiologic response associated with placebos, the placebo effect is of considerable interest to researchers and clinicians. To ensure that study participants remain blinded to treatment, a placebo must resemble the investigational product in all aspects except for physiological activity: it should have the same shape, colour, delivery mode, smell and taste. To produce a placebo with all of these qualities, the development cost and, thus, the daily cost of providing them to patients in a clinical trial, can be significant. Cost-effectiveness analyses (CEAs) typically use efficacy and safety data from RCTs. In fact, phase 3 RCT data are often considered the most robust data source in CEAs. By subtracting the clinical effect in the placebo arm from the clinical effect in the active arm, CEAs remove the placebo response from the effectiveness side of the equation. However, the same method is not applied to the cost side: instead of subtracting from the cost of active treatment, the cost of placebo is ignored. This leads to an inaccurate estimation of the incremental cost of treatment relative to the incremental effects and, consequently, of the incremental cost-effectiveness ratio (ICER). We propose a method whereby both the costs and effects of placebo are incorporated into CEA. A CEA of Sativex in oncology pain will be used to illustrate the proposed approach. Results will be presented. In recognition of the clinical benefit that can be effected via the placebo response, RCTs have been designed to measure this response and to deduce the true effect of an active therapy. CEAs, which typically use data from these RCTs, should adopt a similar approach. Economic analyses should not only consider the effect but also the costs of placebo to achieve a more accurate prediction of the ICER for an active therapy.

PMC12

MEASURING ECONOMIC AND CLINICAL OUTCOMES ASSOCIATED WITH TELE-ICU MONITORING

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OBJECTIVE: Patients in adult intensive care units (ICUs) require multidisciplinary care that frequently result in substantial morbidity, mortality, and costs. Telemedicine has been used to provide remote intensivist monitoring for ICUs. We measured the economic and clinical outcomes associated with Tele-ICU monitoring in 6 ICUs (5 hospitals) across the Houston metropolitan area. **METHODS:** We assessed the cost and effectiveness of Tele-ICU by comparing the economic and clinical outcomes in the period after the full implementation of the Tele-ICU (post period) with the economic and clinical outcomes in the baseline period before the introduction of the Tele-ICU (pre period). The cost analysis in this study adopts a hospital perspective because the decision to implement a Tele-ICU is made at the hospital or health system level. Costs were measured using hospital costs and the cost of operating the Tele-ICU. Hospital costs were computed using average daily ICU costs and floor costs for patients in each ICU during the two study periods using individual patient data (4390 patients). ICU and hospital length of stay (LOS) and ICU and hospital mortality were obtained from chart reviews. **RESULTS:** Average

daily per patient ICU costs across the six ICUs was $3060 and $3663 in the pre and the post period respectively and the average daily per patient floor costs was $1439 and $1551 in the pre and the post period respectively. The average LOS across the 6 ICUs increased from 4.5 to 5.3 days. There was no significant difference ($p > 0.05$) in the average mortality rate in the pre and the post period across the 6 ICUs. **CONCLUSION:** Unlike in previous studies, Tele-ICU monitoring increased hospital costs and length of stay.

RESEARCH ON METHODS & CONCEPTUAL PAPERS—Database Studies & Management

PMC13

USE OF POTENTIALLY INAPPROPRIATE PSYCHOACTIVE MEDICATIONS AND FALLS IN U.S. NURSING HOME RESIDENTS

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Use of Potentially Inappropriate Psychoactive Medications (PIPM) poses a serious threat of falls among elderly nursing home residents. With this objective, the study was conducted to identify the effects of PIPMs on falls among nursing home residents. The 2004 National Nursing Home Survey (NNHS) was used as the data source. Logistic regression was performed to ascertain the relationship between residents' falls in the past 180 days and use of PIPM as per Beers' criteria in the presence of other risk factors. The data analysis was performed using SAS 9.1. The 2004 NNHS includes 1174 facilities consisting of 3868 males and 9639 females. The mean age of the residents was 80.5 ± 12.97 years. The residents who fell were older than the residents who did not fall (82.46 vs. 79.5 years, $p < 0.0001$). Residents on PIPMs were at an increased risk of falling compared to those who did not take PIPMs (odds = 1.295, $p < 0.0001$). Residents suffering from mental disorders fell more compared to the other group (odds = 1.316, $p < 0.0001$). Residents' fall-risk increased with an increase in the number of impaired ADLs (odds = 1.158, $p < 0.0001$). The fall-risk also increased with advance of age (odds = 1.017, $p < 0.0001$). Use of bedrails had a protective effect on residents fall-risk (odds = 0.652, $p < 0.0001$). In addition to these factors, male gender (odds = 1.247, $p < 0.0001$) and white race (odds = 1.485, $p < 0.0001$) were also significant risk factors. Among facility factors, being a non-profit facility ($n = 467$) was associated with a higher risk of falls (odds = 1.133, $p < 0.0001$). Prevention of falls in elderly nursing home residents remains a challenge. PIPMs are still prescribed to the elderly nursing home residents. Access to appropriate psychoactive medications should be ensured. Residents with the identified risk factors should be closely monitored. Further research should be pursued to evaluate the impact of medications in other therapeutic categories and facility factors on falls.

PMC14

EXPLORING CANDIDATE DIFFERENCES BETWEEN DRUG COHORTS PRIOR TO EXPOSURE: A SYSTEMATIC APPROACH USING MULTIPLE OBSERVATIONAL DATABASES

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OBJECTIVES: To develop a systematic approach using disparate observational databases for identifying pre-exposure differences in condition incidence across drug cohorts. A case study to examine the utility of the method was conducted, comparing dutasteride with finasteride. **METHODS:** Two disparate databases an electronic health record (EHR) and an administrative claims database were used for analysis. We applied an unmatched cohort design to each source, capturing all persons within the two exposed populations. For all conditions, we calculate unadjusted incidence rates prior to exposure for each cohort and the associated incidence rate ratios (IRR) between cohorts. Three different IRR estimates were calculated using unique definitions of person-time: '6 months' prior to exposure, any time 'before' exposure, and 'variable' time based on length of exposure. Each method used statistical significance of the IRR as the threshold for identifying 'candidate differences' (CD). A composite threshold requiring significance across both sources was also used. **RESULTS:** Using the '6 months' metric, 194 CDs within the EHR and 469 within the claims database were identified, with 108 conditions occurring in both sources. Expert review found the combined list contained all concepts previously hypothesized as important to consider when designing a dutasteride-finasteride study, as well as 10 conditions not hypothesized but deemed important for any evaluation, 40 unexpected pre-exposure conditions that warranted further consideration, and 10 terms that added no value. There was good concordance across metrics, with 70 of 129 'before' CDs and 95 of 161 'variable' CDs matching the '6 months' results. **CONCLUSIONS:** Exploratory analysis of pre-exposure cohort differences can enhance design of observational evaluation studies, guiding researchers to develop their conceptual model to assess the relationship between treatment and outcome by identifying potential sources of sample selection bias. Using multiple data sources allows independent verification of exploratory findings, raising confidence that CDs identified bear consideration.

PMC15

DETERMINING THE MECHANISM OF MISSING DATA IN INCOMPLETE DATASETS

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OBJECTIVES: In any study involving individual level data, the problems associated with incomplete observations are an obstacle to analysis. For this reason methods have been developed to complete these datasets. Multiple imputation is considered the most robust method of handling missing data, however it is also the most complex and computationally intensive. Whether multiple imputation is needed depends on the mechanism of the missing data. For example, if data is missing completely at random simpler methods can be used. For this reason, we conduct an analysis to inform the appropriate imputation method by identifying the mechanism of missing data. **METHODS:** To determine the mechanism of missing data we fit a probit model to a dataset from a study comparing the use of Endovascular Repair (EVAR) versus the use of Open Surgical Repair (OSR) in repairing Abdominal Aortic Aneurisms. From this we determined the appropriate method to complete the dataset. We then ran a sensitivity analysis on the different methods to determine the potential consequence of utilizing the inappropriate method. **RESULTS:** The results of the probit model indicated that the dataset had data which was missing at random and thus the missingness is predictable by observables in the dataset. This implied that the most appropriate method is imputation by stochastic regression or multiple imputation(the stronger of the two methods). The sensitivity analysis, however, showed no statistically significant difference between the two methods in terms of QALYs—total QALY difference between EVAR and OSR: –0.09952(–0.13202,–0.0670) for SR and –0.0866(–0.12344,–0.04977) with significant deviations from other methods. **CONCLUSIONS:** This study demonstrates the