models with inverse probability weighted (IPW) estimation techniques to address those challenges in a single model. **METHODS:** Generalized random effect models were used with weights that are calculated as inverse of probability being uncensored. The Gaussian family and log link function were chosen. We applied a test to see if possible censoring bias exists. We also calculated the deviation from the consistent value if standard pooled ordinary least squares were used. **RESULTS:** A total of 4,824 observations were used in the analysis. We obtained Medicare claim files for the two years following a lung-cancer diagnosis. Costs had high kurtosis and skewness. Moreover, 30% of the cases were censored. Therefore, their annual costs were not observed. The total cost of all care is $60K for the two years following a lung-cancer diagnosis and $55K for incomplete cases. Results significantly diverged from the standard regression model ($p = 0.000$). **CONCLUSIONS:** This paper applies the inverse probability weighted estimation to an inception cohort of patients newly diagnosed with lung cancer. Our findings suggest that the standard regression model yields an inconsistent estimator due to censoring bias. IPW least square estimation method removes that bias.

PMC46

A REVIEW OF THE EVOLUTION OF HEALTH ECONOMIC MODELS OF SMOKING CESSATION

Fisher MI[1], Muston D[2], Knight CJ[1]

[1]Heron Evidence Development Ltd, Luton, UK, [2]Heron Evidence Development Ltd, Stopsley, Luton, UK

OBJECTIVES: To review how health economic models of the cost-effectiveness of smoking cessation interventions have evolved over the last ten years. **METHODS:** The Medline database was searched via PubMed using the keywords 'cost-effectiveness models smoking cessation'. Articles not available or dating before 1998 were excluded. The abstracts from these results were examined, and relevant studies were selected for the review. A bibliographic search was implemented on the selected studies and additional relevant studies were included. An extraction grid was built to record key comparable attributes of each included model as reported. **RESULTS:** Thirteen studies were included and extracted, dating from 1999–2008. The most common model design was Markov model simulations of hypothetical patient cohorts given various interventions (6 studies). Reported cost perspectives have widened over the period: since 2004, societal perspectives have been the most common (7/8 studies) whereas previously direct perspectives were more common (4/5 studies). Prior to 2004, 3/5 studies were of UK patients whereas since then 4 were for the US, 3 Scandinavia. The interventions included in the models were initially Nicotine Replacement Therapy (NRT) and bupropion (Zyban), but this has widened recently to also include varenicline (Champix), which was approved by the FDA in May 2006. It was not possible to draw clear conclusions as to the values of cost, health outcome and cost-effectiveness made given the wide variety of study designs, perspectives and countries modelled and the small number of studies. **CONCLUSIONS:** There is wide variety in the nature of published health economic models of smoking cessation in terms of perspective, country and model structure. Some trends have been observed. Markov models were the most common model design to use for modelling smoking cessation cost-effectiveness in the articles we reviewed.

PMC47

USE OF STABILIZED INVERSE PROPENSITY SCORES AS WEIGHTS TO DIRECTLY ESTIMATE RELATIVE RISK AND ITS CONFIDENCE INTERVALS

Xu S[1], Ross C[1], Raebel MA[1], Shetterly S[1], Blanchette CM[2], Smith DH[3]

[1]Kaiser Permanente Colorado, Denver, CO, USA, [2]Lovelace Respiratory Research Institute, Albuquerque, NM, USA, [3]Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA

OBJECTIVES: Inverse propensity scores have been used in observational studies to reduce selection bias. To obtain estimates of the main effects, a pseudo data set is created with weights copies of observations for each subject and analyzed with conventional regression models. Currently variance estimation requires specific formulas depending on type of outcomes. Our goal is to demonstrate a statistical approach to directly obtain the correct estimates of variance of the main effects (usually group difference in outcomes) in regression models. **METHODS:** We carried out theoretical and simulation studies to show that the variance of the main effects estimated directly from regressions is underestimated, and that the type I error rate is higher due to the inflated sample size in the pseudo data. We propose to use the stabilized weights to directly estimate both the main effect and its variance from conventional regression models. **RESULTS:** We applied the approach to a study examining the effectiveness of serum potassium monitoring in reducing hyperkalemia-associated adverse events among 27,362 diabetic patients newly-prescribed a renin-angiotensin-aldosterone system (RAAS) inhibitor from three HMO Research Network sites. The relative risk (with monitoring versus without monitoring) and confidence intervals were 0.52 (0.39, 0.70) using stabilized weights compared to 0.52 (0.43, 0.64) using typical inverse propensity scores. The sample size in the pseudo data using the stabilized weights was 27,312 compared to 54,632 using inverse propensity scores. The sample size in the pseudo data using the stabilized weights is slightly smaller than the original 27,362 largely due to missing covariates in the propensity score model. **CONCLUSIONS:** Our theoretical, simulation results, and real data example demonstrate that the use of the stabilized weights in the pseudo data preserves the sample size of original data, produces correct estimation of the variance of main effect, and maintains an appropriate type I error rate.

PMC48

"UNNATURAL" HISTORY: MODELING DISEASE PROGRESSION USING OBSERVATIONAL DATA

Noyes K[1], Bajorska A[1], Chappel AR[2], Schwid S[1], Mehta LR[2], Holloway R[1], Dick A[3]

[1]University of Rochester School of Medicine, Rochester, NY, USA, [2]University of Rochester, Rochester, NY, USA, [3]The RAND Corporation, Pittsburgh, PA, USA

OBJECTIVES: Cost-effectiveness analysis requires comparison of outcomes in treated and untreated populations. Data from randomized clinical trials (RCT) do not provide progression rates representative of the general population, while treatment effects in observational data may be biased due to non-randomization. We developed a novel approach for estimating untreated progression rates (controls) by using data from a nationally representative patient cohort, as well as RCT estimates. **METHODS:** We used data from the 2000–2005 Sonya Slifka multiple sclerosis (MS) cohort. Disease progression was characterized by disability-based disease states and relapses. We modeled probabilities of disease state transitions using a first-order annual Markov model that adjusted for age, gender, disease duration, recent relapse rates, prior states, and the specific disease-modifying therapy (DMT). We developed an iterative multinomial logistic regression algorithm, constraining the effects of DMT to match those reported by RCTs. **RESULTS:** After correcting for the DMT treatment effects and other observable risk factors, the probability of disability progression was greater for estimates based on all MS patients compared to the estimates based on untreated individuals only. The 95% confidence intervals using the entire cohort (including treated and untreated individuals) were narrower than the intervals based on the subsample of untreated patients. **CONCLUSIONS:** Our results indicate that the untreated patients in our study had lower estimates of disease progression than the treated patients would have had if they remained untreated. This suggests that patients who forgo treatment are likely to have milder, slower progressing forms of MS. Correcting for treatment effects in a more inclusive group of patients likely provides a more realistic estimate of disease progression than simply characterizing progression in an untreated cohort. The use of a broader cohort also improves the precision of disease progression estimates.

PMC49

A FACTORIAL SIMULATION OF THE GAINS FROM AN EMPIRICAL BAYES APPROACH OVER CLASSICAL METHODS

Murray JF[1], Fryback DG[2]

[1]Eli Lilly and Company, Indianapolis, IN, USA, [2]University of Wisconsin-Madison, Madison, WI, USA

OBJECTIVES: Classical methods assume that any and all information exists only in the data; Empirical Bayes (EB) methods assume, under certain conditions, that an informative prior can be calculated from the data. We conducted a simulation to show the gains achieved by EB over classical methods. **METHODS:** We assumed that exchangeable units of analysis are available from which to calculate prior information. A non-parametric prior was estimated as a mixture of normal distributions. The simulation used a two-level, four factor design to generate one-hundred and sixty scenarios. The factors varied were: (1) the number of units of analysis [25, 50], (2) the sample size within each unit of analysis [10 or 25], (3) the number of distributions within the mixture [2 or 4] and (4) the average effect sizes between the distributions within the prior mixture [0.2 and 0.8 standard deviations]. A prior was estimated for each scenario using the EM algorithm across all units of analysis. This prior was combined with the individual data to estimate posterior means; bootstrap methods were used to estimate Bayesian confidence intervals. The Bayesian and Classical results were compared within scenarios on four measures of "goodness": (1) Absolute difference between the "true" mean and the classical and EB estimates, (2) frequency of the EB mean being closest to the "true" mean, (3) average widths of the EB and classical intervals, and the actual probability coverage of the estimated intervals. **RESULTS:** EB methods were consistently closer in absolute difference and were more frequently closer to the "true" mean. EB confidence intervals were consistently narrower giving less uncertainty about the location of the true mean while maintaining the expected probability coverage. **CONCLUSIONS:** Using "prior" information based on certain assumptions, Empirical Bayes methods provide better estimates of means and confidence intervals compared to classical methods.

PMC50

REGRESSION ESTIMATORS FOR QUALITY OF LIFE AND QUALITY-ADJUSTED LIFE YEARS (QALYS)

Basu A[1], Manca A[2]

[1]University of Chicago, Chicago, IL, USA, [2]University of York, York, UK

OBJECTIVES: Unlike the literature on estimators for cost data, not much attention has been paid to the appropriate use of regression estimators for the analysis of health benefits in economic evaluation, i.e. EQ5D and QALYs. We explored the use of Beta regression models to address characteristics – such as ceiling effect, truncated distribution, and heteroschedasticity – typical of any quality of life data. **METHODS:** We developed both a single equation and a two-part Beta regression models (Classical and Bayesian), defined incremental and marginal effects of covariates on the mean EQ5D, and proposed relevant estimators. Using the UK multicentre EVALUATE trial as a motivating example, we compared results from OLS regression to those obtained from our Beta-based estimators in terms of estimated mean treatment effect after controlling for other covariates. We complemented the case study with a microsimulation exercise. **RESULTS:** The OLS regression fit the EVALUATE trial EQ5D data as well as any of the advanced estimators based on Beta distribution. The estimated treatment effects were 0.0099 (SE = 0.011; 90% CI: –0.022, 0.038) under standard OLS regression