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Original Research

An evaluation of three statistical estimation methods for assessing health policy effects on prescription drug claims

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Abstract

Background: While the choice of analytical approach affects study results and their interpretation, there is no consensus to guide the choice of statistical approaches to evaluate public health policy change.
Objectives: This study compared and contrasted three statistical estimation procedures in the assessment of a U.S. Food and Drug Administration (FDA) suicidality warning, communicated in January 2008 and implemented in May 2009, on antiepileptic drug (AED) prescription claims.
Methods: Longitudinal designs were utilized to evaluate Oklahoma (U.S. State) Medicaid claim data from January 2006 through December 2009. The study included 9289 continuously eligible individuals with prevalent diagnoses of epilepsy and/or psychiatric disorder. Segmented regression models using three estimation procedures [i.e., generalized linear models (GLM), generalized estimation equations (GEE), and generalized linear mixed models (GLMM)] were used to estimate trends of AED prescription claims across three time periods: before (January 2006–January 2008); during (February 2008–May 2009); and after (June 2009–December 2009) the FDA warning.
Results: All three statistical procedures estimated an increasing trend ($P < 0.0001$) in AED prescription claims before the FDA warning period. No procedures detected a significant change in trend during (GLM: −30.0%, 99% CI: −60.0% to 10.0%; GEE: −20.0%, 99% CI: −70.0% to 30.0%; GLMM: −23.5%, 99% CI: −58.8% to 1.2%) and after (GLM: 50.0%, 99% CI: −70.0% to 160.0%; GEE:

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80.0%, 99% CI: −20.0% to 200.0%; GLMM: 47.1%, 99% CI: −41.2% to 135.3%) the FDA warning when compared to pre-warning period.
Conclusions: Although the three procedures provided consistent inferences, the GEE and GLMM approaches accounted appropriately for correlation. Further, marginal models estimated using GEE produced more robust and valid population-level estimations.

Keywords: Generalized linear model; Generalized estimation equations; Generalized linear mixed models; FDA alert; Antiepileptic drugs

Introduction

Studies evaluating health care regulatory actions are common. However, certain types of data, in particular longitudinal data, require health service researchers to use statistical procedures that obtain robust and valid estimates to provide accurate assessments of the outcomes of these actions.[1,2] There is no consensus to guide the choice of statistical approaches to formally evaluate a public health policy change.[3,4] For example, some studies have used relatively simple generalized linear models (GLM), which use maximum likelihood estimation (MLE), to estimate policy effect without accounting for correlation induced by repeatedly measuring observations from the same individual over time.[5–11] Analyzing longitudinal data without taking into account the correlation between the outcomes[12] causes standard errors to be underestimated or overestimated, which may lead to making either a type I or II error.[13] Ultimately, ignoring correlation produces inaccurate inferences about the effect of policies evaluated.

Generalized estimation equations (GEE) calculate standard errors for their parameter estimates by incorporating a "sandwich estimator".[14] Because the parameter estimates are robust, GEE estimation is gaining popularity among health service researchers[15–17] although it has not been widely used to evaluate FDA policy changes.[4] While GEE estimates a population-level policy effect, it does not attempt to quantify heterogeneity of responses in the effect across individual subjects. In contrast, the generalized linear mixed model (GLMM), which uses a pseudo-likelihood estimation technique, accounts for autocorrelation via the introduction of random effect and allows for subject-specific inferences.[18] Because of limited accessibility to the software, GLMM has not been commonly employed by health service researchers.[19]

The three aforementioned analytical approaches may yield different results and subsequent policy interpretations when applied to the same data to answer a common research question. It is known that the absolute magnitude of the parameter estimates derived from GLMM are generally larger than those derived from GEE estimation.[20]

In January 2008, the U.S. FDA issued an alert, followed later (May 2009) by a warning of an increased risk of suicidality, defined as suicidal ideation and behavior, among users of antiepileptic drugs (AEDs).[21] Using this policy change as an example case, the objective of this study was to compare and contrast the results and conclusions of three estimation procedures (i.e., GLM, GEE and GLMM) used to assess the association between the FDA suicidality warning and AED prescription claims among Oklahoma Medicaid individuals diagnosed with epilepsy and/or psychiatric disorder(s), from 2006 through 2009. Oklahoma is a state located in south-central U.S., and Medicaid is a federal program providing medical insurance primarily to indigent, and to other populations.

Methods

Study design

A longitudinal segmented regression analysis of Oklahoma Medicaid claims data from January 2006 through December 2009 was used to evaluate the change in AED prescription claims before and after the FDA suicidality alert and warning. A time-series of 48 consecutive months was created using person level data as a unit of analysis. For each month, the proportion of individuals with an AED prescription claim was calculated. This study was reviewed and approved by the Institutional Review Board at the University of Oklahoma Health Sciences Center.