Prevalence and Cost Impact of Nonadherence with Antiepilepsy Drugs Among Adults in a Managed Care Population

Dichotomous indicator for nonadherence

**BACKGROUND**

Medication nonadherence is widespread in chronic diseases and is a significant problem faced by medical practice. Nonadherence results in reduced treatment benefits and therefore may lead to an increased financial burden on patients, payers, and society. This burden has been estimated to be $100 billion per year across all chronic diseases in the United States (6,9). The issue of nonadherence in epilepsy and its cost implications, particularly for third-party payers, has not been widely investigated.

**OBJECTIVES AND PURPOSE**

In this study, we evaluated the prevalence and cost impact of antiepilepsy drug (AED) nonadherence among adults with epilepsy in a US managed care population.

**METHODS**

**Study Design**

A retrospective, prospective database analysis.

**Data Source**

Data were pulled from the PharMetrics database, which comprises longitudinal insurance claims data from 15 health plans, covering diverse geographic regions and more than 40 million patients in the US.

**Inclusion Criteria**

Subjects included in the study met the following inclusion criteria:

- Age ≥ 18 years
- At least one diagnosis of epilepsy (ICD-9 345.x or nonbifurcated comorbidities ICD-9 702.0 or 703.0) between 1/1/2000 and 12/31/2000
- At least two AED prescriptions between 1/1/2000 and 12/31/2000
- At least one reimbursement claim with a diagnosis of epilepsy or nonbifurcated comorbidities
- Continuous plan enrollment for at least 6 months pre-AED initiation and at least 12 months post-AED initiation

**Primary Outcomes**

- AED adherence was assessed via the medication possession ratio (MPR), which was defined as follows:
  - Overall MPR: Total AED days supplied divided by days between AED initiation and follow-up of AED refill
  - AED-specific MPR: Total days supplied for AED of interest divided by days between first prescription and expiration of last refill for that AED
- Adherence status: MPR ≥ 0.80 = Adherent, MPR < 0.80 = Non-adherent

**Other Outcomes**

- Incidence of accident or injury, as defined by relevant ICD-9 codes (2), including the following:
  - Motor vehicle accident (MVA)
  - Injury due to fall
  - Traumatic brain injury (TBI)
- Adherence and utilization cost outcomes for elderly subcohort

**Statistical Analyses**

- Descriptive statistics are presented for patient characteristics and all outcome variables.
- Regression models were estimated to formally assess the impact of overall AED nonadherence and continuous MPR on utilization and costs.
- Utilization and cost outcomes were estimated as a function of alternative adherence measures, including the following:
  - Dichotomous indicators for nonadherence (1 = MPR < 0.80, 0 = MPR ≥ 0.80)
  - Continuous MPR
- Additional covariates include age, gender, the Charlson Comorbidity Index (CCI), and follow-up duration.
- The continuous MPR specification includes a squared MPR term to capture a nonlinear relationship between MPR and outcomes.

**RESULTS**

**Patient Characteristics**

- Overall, 10,892 patients qualified for study inclusion.
- The mean age was 44 years, and 58% of patients were female. The mean CCI was 0.93, and the mean follow-up exceeded 27 months (Table 1).

**Antiepilepsy Drug Adherence**

- Results indicate that 28.3% of patients were nonadherent with overall AED therapy (Figure 1).
- Nonadherence rates were lowest for phenytoin (31.9%), levetiracetam (22.1%), and lamotrigine (32.2%) and highest for gabapentin (62.7%) (Table 2).
- Mean MPR was highest for lamotrigine (MPR = 0.80), fenrifenac (MPR = 0.74), and phenytoin (MPR = 0.62) (Figure 2).

**Health Care Utilization and Costs**

- Nonadherence to AED therapy was associated with an 11% increased likelihood of hospitalization (OR = 1.11, P < 0.001), number of inpatient admissions (+0.083 admissions, P < 0.001), and costs (+$260, P < 0.001) per patient per year (Table 3).
- Larger effect of AED nonadherence on total health care costs remained (+$1,466, P < 0.001) despite expected offset from reduced prescription drug costs (Table 3).
- Impact of refill, and total health care costs decrease significantly for every 1 percentage point increase in MPR (Table 3).
- Squared MPR coefficient in all models was negative and significant, indicating a diminishing effect as MPR increases (e.g., MPR improvement from 0.8 to 0.9 results in a greater reduction in costs than improvement from 0.7 to 0.8).

**LIMITATIONS**

- The MPR measure assumes complete medication ingestion, causing possible overestimation of actual adherence.
- Therapy may be interrupted for clinically appropriate reasons, causing MPR to possibly underestimate actual adherence.
- It may be difficult to measure the cost impact of nonadherence (i.e., “breakthrough” seizure) as there is no direct resource utilization unless the patient is seriously injured.
- Our study does not address costs paid by noncommercial payers (e.g., Medicare or Medicaid). Direct total health care costs are therefore underestimated.
- Our study does not address costs incurred by the patient and employers due to lost wages from disability or missed worktime.

**CONCLUSIONS**

- We estimated an AED nonadherence prevalence of 28%, which is consistent with previous studies of self-reported data that suggest a nonadherence rate between 30% and 60%. (5,9)
- Adherence with AEDs is suboptimal.
- AED nonadherence is associated with increased utilization and costs. For example, every 1 percentage point increase in nonadherence is associated with a 1.11 fold increased likelihood of having an MVA. Efforts to promote AED adherence may lead to cost savings for managed care payers.

**REFERENCES**


**CONTACT INFORMATION**

Keith Davis, M.A.
RTI Health Solutions, RTI International
3344 Cornwallis Road, PO Box 13194
Research Triangle Park, NC 27709-2194
Phone: 919.541.1273
E-mail: kldavis@rti.org
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Davil K, Candrilli SD, Edin HM.
"RTI Health Solutions, Research Triangle Park, North Carolina, USA" "GlaxoSmithKline R&D, Research Triangle Park, North Carolina, USA"