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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

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AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

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Structured Abstract

Objectives. This report, commissioned at the request of the Centers for Disease Control and Prevention and the Social Security Administration, addresses in an evidence-based fashion diagnosis of and interventions for treatment-resistant epilepsy (TRE). It addresses drug and surgical treatments, as well as service-related interventions.

Search Strategy. We systematically searched 23 electronic databases, including PubMed® and EMBASE. Search dates ranged from 1985 to January 1, 2002 for all but drug topics, which ranged from 1975 to January 1, 2002. We employed different search strategies for each of the nine key questions addressed. Our searches identified 11,111 articles.

Selection Criteria. We retrieved 2,356 articles, and included 357, according to *a priori* criteria accounting for the quality and relevance of available studies.

Data Collection and Analysis. We employed a "best evidence" synthesis that used the best available, not the best possible evidence. Case control studies were the most common design for diagnostic topics, RCTs were most common for antiepileptic drug (AED) strategies, and the surgical literature was nearly all retrospective case series. The quality of these studies was systematically considered. We computed summary statistics in meta-analyses of RCTs of multiple AED therapy (polytherapy) and computed thresholds for effectiveness in meta-analyses of sequential AED monotherapy and uncontrolled surgical studies.

Main results. There is no widely used definition of TRE. Lack of high quality studies precludes an evidence-based determination of the most effective diagnostic for rediagnosing or re-evaluating patients. Nevertheless, up to 35 percent of patients (but probably fewer) diagnosed with TRE may also have nonepileptic seizures, or not have epilepsy at all. Not all patients diagnosed with TRE receive optimized therapy, but the number of these patients cannot be determined. Initiation of sequential monotherapy appears to result in seizure increases in many patients, and whether sequential monotherapy causes any patients to become seizure-free is not clear. Polytherapy can reduce seizure frequency, but some patients experience intolerable adverse effects. Drug reduction may cause seizure increases without additional benefit. Results of the AED studies assessed in this report may not be generalizable to drugs not examined in the studies we included. Temporal lobe surgery eliminates seizures in many patients. Hemispherectomy and frontal lobe surgery eliminate seizures in an indeterminate number of patients. Corpus callosotomy reduces seizure frequency but generally does not eliminate seizures. Vagal nerve stimulation affords some seizure reduction. There was insufficient evidence to assess other treatments. Epilepsy is associated with increased all-cause mortality and death from drowning. The link between sudden death and seizure frequency is uncertain. Generalized tonic-clonic seizures seem associated with an increased risk of death.

Conclusions. Some patients diagnosed with treatment-resistant epilepsy are misdiagnosed or not receiving optimized AED treatment. Effective treatments are available, but all have disadvantages. There are many weaknesses in the current literature, particularly in studies of diagnostics and nondrug, nonsurgical interventions. Better-designed studies in these areas are needed.

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