Question 5

Which methods of nondrug treatment for epilepsy after initial treatment failure lead to improved outcomes for patients with treatment-resistant epilepsy?

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Bouilleret (2002)	✓							
Alsaadi (2001)	✓							
Bauer (2001)								✓
Boling (2001)	✓							
Carreno (2001)						✓		
Ferrier (2001)		✓						
Hennessy (2001)	✓							
Hennessy (2001)	✓							
Hodaie (2001)							✓	
Jan (2001)	✓							
Kanemoto (2001)	✓							
Kohler (2001)	✓							
Kral (2001)		✓						
Kumlien (2001)								✓
Kwan (2001)							✓	
Maehara (2001)							✓	
Miranda (2001)	✓							
Mulligan (2001)					✓			
Nees (2001)	✓							
Orbach (2001)					✓			
Schramm (2001)	✓							
Schramm (2001)						✓		
Siegel (2001)		✓						
Sotero de Menezes (2001)	✓							
Verma (2001)	✓							
Wiebe (2001)	✓							✓
Wilson (2001)	✓							

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined (continued)

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Anhoury (2000)	✓							
Canizares (2000)	✓							
Derry (2000)	✓							
Di Rocco (2000)						✓		
Dupont (2000)	✓							
Eberhardt (2000)	✓							
Fandino-Franky (2000)							✓	
Foldvary (2000)	✓							
Holmes (2000)	✓							
Hong (2000)		✓						
Iannelli (2000)	✓							
Markand (2000)	✓							✓
Mosewich (2000)		✓						
Rao (2000)	✓							
Robinson (2000)	✓							
Shimizu (2000)						✓		
Shimizu (2000)					✓			
Westerveld (2000)	✓							
Wurm (2000)	✓							
Altshuler (1999)	✓							
Assaf (1999)	✓							
Battaglia (1999)						✓		
Chassoux (1999)		✓						
Eriksson (1999)	✓	✓						
Ferrier (1999)		✓						
Henry (1999)	✓							
Holmes (1999)	✓							
Leung (1999)	✓							
Mathern (1999)	✓							
Matsuzaka (1999)							✓	
McInerney (1999)							✓	

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined (continued)

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Mitchell (1999)	✓							
Parrent (1999)	✓							
Pinard (1999)							✓	
Rossi (1999)	✓							
Salanova (1999)	✓							
Son (1999)	✓							
Visudhiphan (1999)	✓							
Wennberg (1999)		✓						
Blumer (1998)	✓							
Carmant (1998)							✓	
Helmstaedter (1998)		✓						
Holmes (1998)								✓
Maher (1998)	✓							
Radhakrishnan (1998)	✓							
Ring (1998)	✓							
Smith (1998)					✓			
Swartz (1998)		✓						
Szabo (1998)	✓							
Wolf (1998)								✓
Wyllie (1998)	✓					✓		
Bizzi (1997)	✓							
Blume (1997)	✓							
Cappabianca (1997)	✓	✓						
Casazza (1997)	✓							
Ho (1997)	✓							
Hufnagel (1997)					✓			
Keene (1997)	✓							
Kilpatrick (1997)	✓							
McLachlan (1997)	✓							✓
Pacia (1997)					✓			
Patil (1997)					✓			

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined (continued)

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Reeves (1997)	✓							
Schwartz (1997)	✓							
Silander (1997)	✓							
Sisodiya (1997)	✓							
Smith (1997)		✓						
Sorenson (1997)							✓	
Vining (1997)						✓		
Adam (1996)	✓							
Andersen (1996)							✓	
Goldstein (1996)	✓							
Hermanns (1996)								✓
Holmes (1996)	✓							
Peacock (1996)						✓		
Rose (1996)	✓							
Rossi (1996)							✓	
Sakas (1996)							✓	
Sirven (1996)	✓							
Acciarri (1995)	✓	✓						
Berkovic (1995)	✓							
Claverie (1995)							✓	
Davies (1995)	✓							
Jooma (1995a)	✓							
Jooma (1995b)	✓							
Liu (1995)	✓							
Morrell (1995)					✓			
Renowden (1995)	✓							
Salanova (1995)			✓					
Salanova (1995)			✓					
Sawhney (1995)					✓			
Schramm (1995)						✓		
Sperling (1995)	✓							

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined (continued)

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Thadani (1995)	✓							
Vickrey (1995)								✓
Vossler (1995)	✓							
Wyler (1995)	✓							
Blume (1994)	✓							
Guldvog (1994a)	✓							
Guldvog (1994b)	✓							
Naylor (1994)	✓							
Chelune (1993)	✓							
Reutens (1993)							✓	
Bladin (1992)	✓							
Salanova (1992)				✓				
Adler (1991)		✓						
Berkovic (1991)	✓							
Blume (1991)				✓				
Cohen (1991)							✓	
Elwes (1991)	✓							
Fuiks (1991)							✓	
Garcia Sola (1991)		✓						
Guldvog (1991)								✓
Hopkins (1991)	✓							
Nordgren (1991)							✓	
Oguni (1991)							✓	
Palmini (1991)		✓						
Rasmussen (1991)		✓						
Rasmussen (1991)	✓							
Shimizu (1991)					✓			
Wieser (1991)	✓							
Bidzinski (1990)	✓							
Huttenlocher (1990)								✓
Mackenzie (1990)	✓							

Evidence Table 102. All studies meeting the inclusion criteria for surgical interventions and the interventions examined (continued)

Reference	Temporal Lobe Surgery	Frontal Lobe Surgery	Parietal Lobe Surgery	Occipital Lobe Surgery	Multiple Subpial Transections	Hemispherectomy	Corpus Callosotomy	Surgical Control Patients
Marino (1990)							✓	
Mizrahi (1990)	✓							
Provinciali (1990)							✓	
Sass (1990)							✓	
Walczak (1990)	✓							
Yeh (1990)	✓							
So (1989)	✓							
Sperling (1989)	✓							
Estes (1988)	✓							
Ivnik (1988)	✓							
Murro (1988)							✓	
Purves (1988)							✓	
Spencer (1988)							✓	
Tinuper (1988)						✓		
Bladin (1987)	✓							
Cutfield (1987)	✓							
Drake (1987)	✓							
Garcia-Flores (1987)							✓	
Gates (1987)							✓	
Harbord (1987)								✓
Lindsay (1987)						✓		
King (1986)	✓							
Lieb (1986)	✓							
Meyer (1986)	✓							
Carey (1985)	✓							
Delgado-Escueta (1985)	✓							
Ojemann (1985)	✓							
Powell (1985)	✓							

Evidence Table 103. Studies of temporal lobe surgery – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Bouilleret (2002)	18	1993-2000	France		No	Prospective	Nested case-control with individual patient data
Alsaadi (2001)	49	1989-1994	United States	Department of Neurology, University of California San Francisco, 400 Parnassus Avenue, Room A889, San Francisco, California 94143, USA.	No	Retrospective	Nested case-control
Boling (2001)	18	1981-1999	Canada	Dr. W. Boling, Department of Neurosurgery, Montreal Neurol. Inst. and Hospital, Montreal, Que. H3A 2B4. Canada	No	Retrospective	Case series
Hennessy (2001)	116	1975-1995	England	Epilepsy Centre, Kings College Hospital, Denmark Hill, London SE5, Department of Biostatistics and Computing, Institute of Psychiatry, de Crespigny Park, London SE5.	No	Retrospective	Nested case-control
Hennessy (2001)	80	1975-1995	England	Epilepsy Centre, King's College Hospital, Denmark Hill, London SE5, UK. Michael@hennessy72.fsnet.co.uk	No	Retrospective	Nested case-control
Jan (2001)	29	1990-1996	Canada		No	Retrospective	Case series
Kanemoto (2001)	52	1987-1999	Japan		No	Retrospective	Case series
Kohler (2001)	58	1986-1999	United States	Neuropsychiatry Section, Department of Psychiatry, University of Pennsylvania, Philadelphia 19104-4283, USA. kohler@bblmail.psycha.upenn.edu	No	Retrospective	Case series
Miranda (2001)	50	1976-1998	Canada		No	Retrospective	Case series
Nees (2001)	50	1992-1994	England		No	Retrospective	Case series
Schramm (2001)	61	1993-1999	Germany	Department of Neurosurgery, University of Bonn, Germany. schrammj@mailer.meb.uni-bonn.de	No	Prospective	Case series

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Sotero de Menezes (2001)	15	1978-1993	United States	Department ofNeurology, Children's Hospital and Regional Medical Center, University of Washington, Seattle 98105, USA. msoter@chmc.org	No	Retrospective	Nested case-control with individual patient data
Verma (2001)	13	1989-1996	United States	Department of Medicine (Neurology), Duke University Medical Center, 27710, Durham, NC, USA	No	Retrospective	Nested case-control with individual patient data
Wiebe (2001)	40	1996-2000	Canada	Department of Clinical Neurological Sciences, University of Western Ontario, and London Health Sciences Centre, Canada. swiebe@uwo.ca	No	Prospective	RCT
Wilson (2001)	90	1990-1993	Australia	Comprehensive Epilepsy Program, Epilepsy Research Institute, Austin & Repatriation Medical Centre (A&RMC), Melbourne, Australia. s.wilson@psych.unimelb.edu.au	No	Retrospective	Case series
Anhoury (2000)	121	1988-1997	England	Raymond Way Neuropsychiatry Research Group, University Department of Clinical Neurology, Institute of Neurology, London, England.	No	Retrospective	Case series
Canizares (2000)	33	1998-1999	Spain	Department of Psychiatry and Clinical Psychobiology of the University of Barcelona, Spain.	No	Prospective	Case series
Derry (2000)	39	1996-1998	Canada	Department of Psychology, London Health Sciences Centre, University of Western Ontario, Canada. pderry@julian.uwo.ca	No	Prospective	Case series
Dupont (2000)	30	1994-1999	France	Service Hospitalier Frederic Joliot, Commissariat a l'Energie Atomique, 91401 Orsay Cedex, France. dupont@shfj.cea.fr	No	Not reported	Nested case-control
Eberhardt (2000)	26	1995-1999	Germany	Department of Neurosurgery, University of Erlangen-Nuremberg, Germany. neoruradiologie@rzmail.uni-erlangen.de	No	Prospective	Nested case-control with individual patient data
Foldvary (2000)	79	1962-1984	United States	Department of Neurology, Duke University Medical Center, Durham, NC, USA.	No	Retrospective	Nested case-control

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Holmes (2000)	23	1993-1997	United States	Regional Epilepsy Center, University of Washington, Seattle, 98104, USA. mdholmes@u.washington.edu	No	Retrospective	Nested case-control
Iannelli (2000)	37	1981-1997	Italy	Institute of Neurosurgery, Section of Pediatric Neurosurgery, Catholic University, Rome, Italy. Iannel@tiscalinet.it	No	Retrospective	Case series
Markand (2000)	53	1994-1997	United States	Department of Neurology, Division of Biostatistics, Indiana University School of Medicine, Indianapolis, Indiana, USA. omarkand@iupui.edu	No	Prospective	Controlled
Rao (2000)	119	1995-1998	India	R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India.	No	Retrospective	Case series
Robinson (2000)	22	1993-1998	United States	Department of Neurosurgery, Epilepsy Center, St. Louis Children's Hospital, Washington University School of Medicine, Missouri 63110, USA.	No	Prospective	Nested case-control
Westerveld (2000)	82		United States	Department of Neurosurgery, Yale University School of Medicine, New Haven, Connecticut 06520-8082, USA. westerm@msn.com	Yes	Retrospective	Case series
Wurm (2000)	16	1997-1998	Austria	Department of Neurosurgery, OO Landesnervenklinik Wagner Jauregg, Linz, Austria. gabriele.wurm@lkh.ooe.gv.at	No	Not reported	Case series
Altshuler (1999)	49	1974-1990	United States	UCLA Department of Psychiatry and Biobehavioral Sciences, Mood Disorders Research Program 90095-7057, USA.	No	Retrospective	Case series
Assaf (1999)	75	1989-1995	United States	Department of Neurology, Saint Louis University, Missouri 63110, USA.	No	Retrospective	Case series
Eriksson (1999)	75	1987-1995	Sweden	Institute of Clinical Neuroscience, Dept. of Neurology, Sahlgrenska University Hospital, Goteborg, Sweden.	No	Retrospective	Case series
Henry (1999)	38	1991-1994	United States	Department of Neurology, Emory University School of Medicine, Atlanta, Georgia 30322, USA.	No	Retrospective	Case series

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Holmes (1999)	13	1992-1996	United States	Department of Neurology, University of Washington School of Medicine, Seattle, USA.	No	Retrospective	Nested case-control with individual patient data
Leung (1999)	11	1994-1998	Hong Kong	Division of Neurosurgery, Department of Surgery, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong.	No	Retrospective	Case series
Mathern (1999)	31	1986-1997	United States	Division of Neurosurgery, The Mental Retardation Research Center, University of California, Los Angeles, USA. gmathern@ucla.edu	No	Prospective	Case series
Mitchell (1999)	45	1993-1995	Australia	Brain Imaging Research Institute, Austin and Repatriation Medical Centre, Heidelberg, Victoria, Australia.	No	Retrospective	Case series
Parrent (1999)	19	1994-1997	Canada	London Health Sciences Centre, Ontario, Canada. andrew.parrent@lhsc.on.ca	No	Retrospective	Case series
Rossi (1999)	28	1980-1996	Italy	Institute of Neurosurgery, Catholic University, Medical School, Rome, Italy.	No	Retrospective	Case series
Salanova (1999)	145	1984-1995	United States	Department of Neurology, Indiana University School of Medicine, Indianapolis 46202, USA. vsalanov@iumc.iupui.edu	No	Retrospective	Nested case-control
Son (1999)	71	1994-1999	South Korea	Department of Neurosurgery, Seoul National University College of Medicine, Korea.	No	Retrospective	Case series
Visudhiphan (1999)	14	1993-1998	Thailand	Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.	No	Retrospective	Case series
Blumer (1998)	44	1994-1995	United States	Department of Psychiatry, University of Tennessee, and Epi-Care Center, Memphis 38103, USA.	No	Prospective	Case series
Maher (1998)	93	1994-1996	Canada	Department of Medicine, University of Manitoba, Winnipeg, Canada.	Yes	Retrospective	Case series
Radhakrishnan (1998)	175	1988-1991	United States	Department of Neurology, Mayo Clinic, Rochester, MN 55905, USA.	No	Retrospective	Nested case-control

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Ring (1998)	60	1995-1996	England	National Hospital for Neurology and Neurosurgery, London, UK.	No	Prospective	Case series
Szabo (1998)	14	1989-1994	United States	Department of Neurology, The Cleveland Clinic Foundation, Ohio 44195, USA.	No	Retrospective	Nested case-control with individual patient data
Wyllie (1998)	72	1990-1996	United States	Department of Neurology, The Cleveland Clinic Foundation, OH 44195, USA.	No	Retrospective	Case series
Bizzi (1997)	19	1990-1994	United States	Columbia Children's Hospital and Children's Medical Center, Dallas, Tex., USA.	No	Retrospective	Case series
Blume (1997)	14	1977-1994	Canada	University Hospital, University of Western Ontario, London, Canada.	No	Retrospective	Case series
Cappabianca (1997)	10	1985-1994	Italy	Department of Neurosurgery, University Federico II School of Medicine, Naples, Italy.	No	Retrospective	Case series
Casazza (1997)	40	1988-1994	Italy	Istituto Nazionale Neurologico C. Besta, Milano, Italy.	No	Retrospective	Case series
Ho (1997)	63	1989-1993	Australia	Department of Neurology, Austin and Repatriation Medical Centre, Melbourne, Australia.	No	Retrospective	Case series
Keene (1997)	44	1975-1996	Canada	Department of Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Canada.	No	Retrospective	Case series
Kilpatrick (1997)	36	1993-1995	Australia	Department of Neurology, The Melbourne Neuroscience Centre, The Royal Melbourne Hospital, Victoria, Australia.	No	Not reported	Nested case-control with individual patient data
McLachlan (1997)	56	1992-1995	Canada	Department of Clinical Neurological Sciences, University of Western Ontario, London, Canada.	No	Prospective	Controlled
Reeves (1997)	190	1988-1991	United States	Department of Neurology, Mayo Clinic, Rochester, Minnesota 55905, USA.	No	Retrospective	Case series
Schwartz (1997)	29	1992-1994	United States	Department of Neurological Surgery, Columbia-Presbyterian Medical Center, New York, New York, USA.	No	Prospective	Nested case-control with individual patient data

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Silander (1997)	94	1980-1990	Sweden	Dr. H.C. Silander, Department of Neurosurgery, University Hospital, S-751 85 Uppsala. Sweden	Yes	Retrospective	Case series
Sisodiya (1997)	27	1993-1995	England	Department of Clinical Neurology, National Hospital for Neurology and Neurosurgery, London, UK.	No	Retrospective	Nested case-control with individual patient data
Adam (1996)	30	1991-1994	France	Service de Neurophysiologie, Hopital de la Pitie-Salpetriere, Paris, France.	No	Prospective	Nested case-control with individual patient data
Goldstein (1996)	33	1985-1993	United States	Comprehensive Epilepsy Center, University of Miami School of Medicine, FL, USA.	No	Retrospective	Nested case-control
Holmes (1996)	45	1982-1986	United States	Department of Medicine (Neurology), University of Washington, School of Medicine, Seattle, USA.	No	Prospective	Case series
Rose (1996)	56	1992-1994	Canada	Department of Psychology, University Hospital, London, Ontario, Canada.	No	Prospective	Case series
Sirven (1996)	174	1985-1992	United States	Comprehensive Epilepsy Center, Graduate Hospital, Philadelphia, PA 19146, USA.	No	Retrospective	Case series
Acciarri (1995)	10	1975-1992	Italy	2nd Division of Neurosurgery, Bellaria Hospital, Bologna, Italy.	No	Retrospective	Nested case-control with individual patient data
Berkovic (1995)	135	1986-1991	Australia	Department of Neurology, Austin Hospital, Heidelberg, Melbourne, Australia.	No	Not reported	Case series
Davies (1995)	12	1969-1988	England	Department of Neurosurgery, University Hospital of Wales, Cardiff, UK.	No	Retrospective	Case series
Jooma (1995a)	30	1985-1992	United States	Department of Neurosurgery, University of Cincinnati College of Medicine, Ohio, USA.	No	Retrospective	Nested case-control with individual patient data
Jooma (1995b)	62	1992-1994	United States	Department of Neurosurgery, University of Cincinnati College of Medicine, Ohio, USA.	No	Retrospective	Case series

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Liu (1995)	12	1983-1990	United States	Department of Neurosurgery, University of Cincinnati College of Medicine, Mayfield Neurological Institute, OH 45267-0515.	No	Retrospective	Nested case-control with individual patient data
Renowden (1995)	67	1983-1992	England	Department of Neuroradiology, Radcliffe Infirmary NHS Trust, Oxford, United Kingdom.	No	Retrospective	Case series
Sperling (1995)	73	1986-1990	United States	Comprehensive Epilepsy Center, Graduate Hospital, Philadelphia, PA 19146, USA.	No	Retrospective	Case series
Thadani (1995)	22	1983-1992	United States	Section of Neurology, Dartmouth-Hitchcock Medical Center, Lebonon, NH 03756.	No	Retrospective	Case series
Vossler (1995)	31	1979-1989	United States	Epilepsy Center, Swedish Medical Center, 801 Broadway,Seattle, WA 98122. United States	No	Retrospective	Nested case-control with individual patient data
Wyler (1995)	70	1990-1992	United States	Epilepsy Center, Swedish Medical Center, Seattle, Washington, USA.	No	Prospective	RCT
Blume (1994)	125	1974-1989	Canada	Epilepsy Unit, University Hospital, The University of Western Ontario, London, Ontario, Canada	No	Retrospective	Nested case-control
Guldvog (1994b)	79	1949-1988	Norway	Foundation for Health Services Research, Nordbyhagen, Norway.	Yes	Retrospective	Case series
Guldvog (1994a)	35	1952-1988	Norway	Foundation for Health Services Research, Nordbyhagen, Norway.	Yes	Retrospective	Case series
Naylor (1994)	37	1987-1991	Denmark	Department of Psychiatry, Rigshospitalet, Blegdamsvej 9,DK-2100 Copenhagen O. Denmark	No	Retrospective	Case series
Chelune (1993)	96	1990-1991	United States		No	Prospective	Case series
Bladin (1992)	115	1975-1991	Australia	Comprehensive Epilepsy Program, Austin Hospital, Melbourne, Australia.	No	Retrospective	Case series

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Berkovic (1991)	10	1985-1986	Canada	Montreal Neurological Institute and Hospital, Quebec, Canada.	No	Retrospective	Nested case-control with individual patient data
Elwes (1991)	108	1976-1987	England	Institute of Psychiatry, De Crespigny Park, London, UK.	No	Prospective	Case series
Hopkins (1991)	11	1978-1988	Australia	Royal Children's Hospital, Melbourne, Australia.	No	Retrospective	Nested case-control with individual patient data
Rasmussen (1991)	100	1961-1980	Canada	Montreal Neurology Institute and Hospital, Department of Neurology and Neurosurgery, McGill University, Quebec, Canada.	No	Retrospective	Case series
Wieser (1991)	215	1975-1990	Switzerland	Department of Neurology, University Hospital, Zurich, Switzerland.	No	Retrospective	Case series
Bidzinski (1990)	320	1957-1988	Poland	Department of Neurosurgery, Warsaw Medical Academy, Poland.	No	Retrospective	Case series
Mackenzie (1990)	30	1983-1989	Australia	Prince Henry Hospital, Little Bay, NSW.	No	Retrospective	Case series
Mizrahi (1990)	22	1980-1986	United States	Department of Neurology, Baylor College of Medicine, Houston, TX 77030.	No	Retrospective	Nested case-control with individual patient data
Walczak (1990)	100	1964-1985	United States	Department of Medicine, Duke University Medical Center, Durham, NC 27710.	No	Retrospective	Case series
Yeh (1990)	12	1982-1986	Japan	Department of Neurosurgery, University of Cincinnati College of Medicine, Ohio.	No	Retrospective	Nested case-control with individual patient data
So (1989)	48	1973-1987	Canada	Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec, Canada.	No	Retrospective	Nested case-control
Sperling (1989)	39	1976-1983	United States	Department of Neurology, University of Pennsylvania, Philadelphia.	No	Retrospective	Case series

Evidence Table 103. Studies of temporal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Estes (1988)	46	1979-1984	United States		No	Retrospective	Nested case-control with individual patient data
Ivnik (1988)	142	1972-1987	United States	Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN 55905.	No	Retrospective	Case series
Bladin (1987)	63	1985-1987	Australia	Department of Neurology, Austin Hospital, Melbourne, Vic.	No	Retrospective	Case series
Cutfield (1987)	26	1961-1980	New Zealand	North Shore Hospital.	No	Retrospective	Nested case-control
Drake (1987)	16	1974-1986	Canada	Division of Neurosurgery, Hospital for Sick Children, Toronto, Ontario.	No	Retrospective	Nested case-control with individual patient data
King (1986)	23	1981-1983	United States		No	Prospective	Case series
Lieb (1986)	75	1961-1977	United States		No	Retrospective	Case series
Meyer (1986)	50	1970-1983	United States		No	Retrospective	Case series
Carey (1985)	24	1975-1984	Ireland		No	Retrospective	Case series
Delgado-Escueta (1985)	15	1972-1983	United States		No	Retrospective	Nested case-control with individual patient data
Ojemann (1985)	14	1983-1983	United States		No	Not reported	Case series
Powell (1985)	59	1973-1984	England		No	Prospective	Case series

Evidence Table 104. Studies of frontal lobe surgery – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Ferrier (2001)	35	1975-1996	England	Institute of Epileptology, King's College Hospital, London, UK.	No	Retrospective	Nested case-control
Kral (2001)	32	1989-2000	Germany	Department of Neurosurgery, University of Bonn, Medical Center, Sigmund Freud Strasse 25, 53105 Bonn, Germany.	No	Retrospective	Case series
Siegel (2001)	14	1992-1999	United States	Sections of Neurology, Neurosurgery, and Nuclear Medicine, Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, U.S.A; and Department of Neurology, University Hospital Zurich, Switzerland.	No	Retrospective	Case series
Hong (2000)	18	1995-1999	South Korea	Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea. schong@smc.samsung.co.kr	No	Retrospective	Nested case-control with individual patient data
Mosewich (2000)	68	1987-1994	United States	Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.	No	Retrospective	Case series
Chassoux (1999)	120	1964-1995	France	Department of Neurosurgery, Sainte Anne Hospital Center, Paris, France.	No	Retrospective	Case series
Eriksson (1999)	25	1987-1995	Sweden	Institute of Clinical Neuroscience, Dept. of Neurology, Sahlgrenska University Hospital, Goteborg, Sweden.	No	Retrospective	Case series
Ferrier (1999)	42	1975-1996	England	Institute of Epileptology, King's College Hospital, London, UK.	No	Retrospective	Case series
Wennberg (1999)	22	1970-1994	Canada	Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, McGill University, Quebec, Canada.	No	Retrospective	Nested case-control with individual patient data
Helmstaedter (1998)	33	1995-1996	Germany	University Hospital of Epileptology, Bonn, Germany. psych@mailer.meb.uni-bonn.de	No	Retrospective	Case series

Evidence Table 104. Studies of frontal lobe surgery – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Swartz (1998)	19	1986-1995	United States	B.E. Swartz, UCLA Neurology Department, W127B Epilepsy Center, 11301 Wilshire Blvd., Los Angeles, CA 90073. United States	No	Retrospective	Nested case-control with individual patient data
Cappabianca (1997)	13	1985-1994	Italy	Department of Neurosurgery, University Federico II School of Medicine, Naples, Italy.	No	Retrospective	Case series
Smith (1997)	53	1995-1997	United States	Section of Neurosurgery, Medical College of Georgia, Augusta, USA. depatientsurg.jsmith@mail.mcg.edu	No	Retrospective	Nested case-control
Acciarri (1995)	13	1975-1992	Italy	2nd Division of Neurosurgery, Bellaria Hospital, Bologna, Italy.	No	Retrospective	Nested case-control with individual patient data
Adler (1991)	14	1972-1987	United States	Department of Surgery, (Neurosurgery), Stanford University Medical School, Calif.	No	Retrospective	Case series
Garcia Sola (1991)	18	1978-1990	Spain	Department of Clinical Neurophysiology, Hospital Puerta de Hierro, Madrid, Spain.	No	Retrospective	Case series
Palmini (1991)	12	1975-1990	Canada	Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec, Canada.	No	Retrospective	Case series
Rasmussen (1991)	283	1928-1980	Canada	Montreal Neurological Institute and Hospital, Quebec, Canada.	No	Retrospective	Case series

Evidence Table 105. Studies of multiple subpial transection – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Mulligan (2001)	12	1990-1999	United States	Department of Neurosurgery, Yale University School of Medicine, New Haven, CT 06520, U.S.A.	No	Retrospective	Case series
Orbach (2001)	54	1992-2000	United States	Dr. O. Devinsky, NYU-Mt. Sinai Compreh. Epilepsy Ctr., 403 E. 34th St., New York, NY 10016. United States	No	Retrospective	Case series
Shimizu (2000)	31	1983-1998	Japan	Department of Neurosurgery, Tokyo Metropolitan Neurological Hospital, Japan. smz-h@qb3.so-net.ne.jp	No	Retrospective	Case series
Smith (1998)	84		United States	Department of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612-3824, USA.	No	Retrospective	Case series
Hufnagel (1997)	22	1993-1996	Germany	Dr. A. Hufnagel, Department of Neurology, University of Essen, Hufelandstr. 55, D-45122 Essen. Germany	No	Retrospective	Nested case-control with individual patient data
Pacia (1997)	21	1992-1994	United States	Departments of Neurology and Neurosurgery, New York University School of Medicine, Hospital for Joint Diseases, New York, NY, USA	No	Retrospective	Nested case-control with individual patient data
Patil (1997)	19	1991-1995	United States	Epilepsy Care Center, Immanuel Medical Center, Omaha, Nebraska, USA.	No	Retrospective	Nested case-control with individual patient data
Morrell (1995)	14	1987-1994	United States	Department of Neurological Science, Rush-Presbyterian-St Luke's Medical Center, Chicago, IL 60612, USA.	No	Retrospective	Nested case-control with individual patient data
Sawhney (1995)	21	1989-1993	England	Department of Clinical Neurophysiology, Maudsley Hospital, London UK.	No	Retrospective	Nested case-control with individual patient data
Shimizu (1991)	12	1989-1990	Japan	Department of Neurosurgery, Tokyo Metropolitan Neurological Hospital, Japan.	No	Retrospective	Case series

Evidence Table 106. Studies of hemispherectomy – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Carreno (2001)	13	1992-1999	United States	Departments of Neurology (Drs. Carreno, Wyllie, and Kotagal), Neurosurgery (Drs. Bingaman and Comair), and Neuroradiology (Dr. Ruggieri), The Cleveland Clinic Foundation, OH.	No	Retrospective	Case series
Schramm (2001)	20	1991-1999	Germany	Dr. J. Schramm, Department of Neurosurgery, University of Bonn Medical Center, Sigmund-Freud-Strasse 25, 53105 Bonn. Germany	No	Retrospective	Case series
Di Rocco (2000)	15	1985-1996	Italy	Pediatric Neurosurgery, Catholic University Medical School, Rome, Italy. cdirocco@RM.Unicatt.it	No	Retrospective	Nested case-control with individual patient data
Shimizu (2000)	34	1993-1999	Japan	Department of Neurosurgery, Tokyo Metropolitan Neurological Hospital, Japan. smzh@tmnh.fuchu.tokyo.jp	No	Retrospective	Case series
Battaglia (1999)	10	1987-1998	Italy	Child Neurology and Psychiatry Unit, UCSC, Rome, Italy.	No	Retrospective	Case series
Wyllie (1998)	16	1990-1996	United States	Department of Neurology, The Cleveland Clinic Foundation, OH 44195, USA.	No	Retrospective	Case series
Vining (1997)	58	1968-1996	United States	Pediatric Epilepsy Center, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA.	No	Retrospective	Case series
Peacock (1996)	58	1986-1995	United States	Department of Surgery, UCLA Medical Center 90095-7039, USA.	No	Retrospective	Case series
Schramm (1995)	13	1992-1994	Germany	Neurosurgical Department, University of Bonn, Germany.	No	Retrospective	Case series
Tinuper (1988)	14	1974-1987	Canada	Montreal Neurological Hospital and Institute, McGill University, Quebec, Canada.	No	Retrospective	Nested case-control with individual patient data
Lindsay (1987)	17	1948-1986	England	National Centre for Children with Epilepsy, Park Hospital for Children, Headington, Oxford.	No	Retrospective	Nested case-control with individual patient data

Evidence Table 107. Studies of corpus callosotomy – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Hodaie (2001)	17	1992-1999	Canada	Division of Neurosurgery, Hospital for Sick Children and University of Toronto, Ont., Canada.	No	Retrospective	Case series
Kwan (2001)	61	1989-1996	Taiwan	Section of Epilepsy, Neurological Institute, Taipei Veterans General Hospital, Taiwan, ROC. sykwan@vghtpe.gov.tw	No	Retrospective	Nested case-control
Maehara (2001)	52	1991-1998	Japan	Department of Neurosurgery, Tokyo Metropolitan Neurological Hospital, Fuchu, Tokyo, Japan. maehara.nsrg@tmd.ac.jp	No	Retrospective	Nested case-control
Fandino-Franky (2000)	97	1989-1997	Colombia	Neurological Hospital, Colombian League Against Epilepsy, Cartagena.	No	Prospective	Case series
Matsuzaka (1999)	22	1989-1994	Japan	Department of Pediatrics, Nagasaki University School of Medicine, Sakamoto, Japan. neuro@net.nagasaki-u.ac.jp	No	Retrospective	Case series
McInerney (1999)	47	1972-1999	United States	Sections of Neurosurgery and Neurology, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, USA.	No	Retrospective	Case series
Pinard (1999)	17	1989-1995	France	Unite de Neurochirurgie Pediatrique, Fondation Rothschild, Hopital Saint Vincent de Paul, Paris, France.	No	Retrospective	Nested case-control with individual patient data
Carmant (1998)	28	1989-1993	United States	Department of Neurology, Harvard Medical School, Children's Hospital, Boston, Massachusetts	No	Retrospective	Case series
Sorenson (1997)	23	1991-1994	United States	Department of Neurology, Texas Comprehensive Epilepsy Program, University of Texas, Houston 77225-0708, USA.	No	Retrospective	Case series
Andersen (1996)	20	1988-1994	Denmark	University Clinic of Neurology, Hvidovre Hospital, Denmark.	No	Retrospective	Case series
Rossi (1996)	20	1988-1995	Italy	Institute of Neurosurgery, Catholic University School of Medicine, Rome, Italy.	No	Retrospective	Case series
Sakas (1996)	20	1984-1993	Ireland	National Centre for Neurosurgery, Beaumont Hospital, Dublin, Ireland.	No	Retrospective	Nested case-control

Evidence Table 107. Studies of corpus callosotomy – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Claverie (1995)	20	1983-1993	France	University of Bordeaux 2, B. P. 40 Carreire,F33076 Bordeaux Cedex. France	No	Retrospective	Nested case-control with individual patient data
Reutens (1993)	64	1973-1991	Australia	Department of Neurology, Austin Hospital,Heidelberg, Vic. 3084. Australia	Yes	Retrospective	Case series
Cohen (1991)	10	1987-1989	United States	Section of Pediatric Neurology, Medical College of Georgia, 1120 15th Street, Augusta, GA 30912.United States	No	Prospective	Nested case-control
Fuiks (1991)	80	1985-1990	United States	EpiCare Center, Baptist Memorial Hospital, University of Tennessee, Memphis.	No	Retrospective	Nested case-control
Nordgren (1991)	18	1972-1987	United States	Section of Neurology, Dartmouth-Hitchcock Medical Center, Hanover, NH 03756.	No	Retrospective	Nested case-control with individual patient data
Oguni (1991)	43	1981-1989	Canada	Montreal Neurological Hospital, Canada.	No	Retrospective	Case series
Marino (1990)	28	1978-1985	Brazil	Division of Functional Neurosurgery, Hospital das Clinicas, Sao Paulo, Brazil.	No	Retrospective	Nested case-control with individual patient data
Provinciali (1990)	15	1987-1988	Italy	Neurological Clinic, University of Ancona, Italy.	No	Prospective	Case series
Sass (1990)	32	1985-1987	United States	Section Neurological Surgery, Yale Univ. School of Medicine, 333 Cedar Street,New Haven, CT 06510. United States	No	Retrospective	Case series
Murro (1988)	25	1980-1986	United States	Department of Neurology, Medical College of Georgia, Augusta 30912.	No	Retrospective	Nested case-control with individual patient data
Purves (1988)	24	1977-1987	Canada	Division of Neurosciences and Neurology, University of British Columbia, Vancouver, Canada.	No	Retrospective	Nested case-control with individual patient data
Spencer (1988)	22	1979-1983	United States	Department of Neurology, Yale University School of Medicine, New Haven, CT 06510.	No	Retrospective	Nested case-control with individual patient data

Evidence Table 107. Studies of corpus callosotomy – general study information (continued)

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Garcia-Flores (1987)	14	1980-1986	Mexico	Osler Clinic, Monterrey, Mexico.	No	Retrospective	Case series
Gates (1987)	24	1979-1985	United States	Comprehensive Epilepsy Program and Department of Neurosurgery, University of Minnesota, Minneapolis, Minnesota, U.S.A.	No	Retrospective	Nested case-control

Evidence Table 108. Studies with epilepsy surgery control patients – general study information

Reference	Number of Patients	Years	Country	Author Affiliation	Multicenter Study	Method of Patient Selection	Study Design
Bauer (2001)	63	1970-1989	Germany	Department of Epileptology, University of Bonn, Germany	No	Retrospective	Case series
Kumlien (2001)	47	1993-1999	United States	Minnesota Epilepsy Group, St. Paul, MN, U.S.A.	No	Retrospective	Case series
Wiebe (2001)	40	1996-2000	Canada	Department of Clinical Neurological Sciences, University of Western Ontario, and London Health Sciences Centre, Canada. swiebe@uwo.ca	No	Prospective	RCT
Markand (2000)	37	1994-1997	United States	Department of Neurology, Division of Biostatistics, Indiana University School of Medicine, Indianapolis, Indiana, USA. omarkand@iupui.edu	No	Prospective	Controlled
Holmes (1998)	35	1977-1997	United States	Department of Neurology, University of Washington, Seattle, USA.	No	Prospective	Case series
Wolf (1998)	15	1987-1992	Germany	Epilepsiezentrum Bethel, Bielefeld, Germany.	No	Prospective	Case series
McLachlan (1997)	21	1992-1995	Canada	Department of Clinical Neurological Sciences, University of Western Ontario, London, Canada.	No	Prospective	Controlled
Hermanns (1996)	74	1992-1994	Germany	Bethel Epilepsy Centre, Bielefeld, Germany.	No	Prospective	Case series
Vickrey (1995)	46	1974-1990	United States	Department of Neurology, University of California, Los Angeles, USA.	No	Retrospective	Case series
Guldvog (1991)	185	1960-1989	Norway	National Center for Epilepsy, Sandvika, Norway.	Yes	Retrospective	Matched controls
Huttenlocher (1990)	155	1970-1989	United States	Department of Pediatrics, University of Chicago, IL 60637.	No	Retrospective	Case series
Harbord (1987)	38	1969-1985	Australia	Department of Neurology, Adelaide Children's Hospital, South Australia.	No	Retrospective	Case series

Evidence Table 109. Studies excluded from the evidence base for seizure-free outcomes after temporal lobe surgery

Reference	N	Reason for Exclusion
So (1989)	48	Only patients with bitemporal epileptiform abnormalities were enrolled in this study. Because foci are seen in both temporal lobes, surgery for this condition can be expected to produce poor results compared to patients in whom only one lobe is involved

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements

Reference	Type of Surgery	Pathology	Mean Age at Treatment (Years)	SD of Age at Treatment	Mean Age at First Seizure (Years)	SD of Age at First Seizure	Mean Duration of Condition Before Surgery (Years)	SD of Duration Before Surgery (Years)
Bouilleret (2002)	Standard	MTS	26.4	7.1	8.6	3.8	17.9	9.1
Alsaadi (2001)	Not Described	Not reported						
Boling (2001)	AH	Various (no tumors)	54		18		34.9	12.1
Hennessy (2001)	Standard	MTS	24					
Hennessy (2001)	Standard	Non-MTS focal lesions	19					
Jan (2001)	Not Described	Various	28	6.9				
Kanemoto (2001)	Standard	Not reported	27.1	5.9	9.7	5.3	17.5	7.8
Schramm (2001)	Neocortex	Various	27.9		14.4		13.6	
Sotero de Menezes (2001)	Tailored	Various	8.3	3.1				
Verma (2001)	Standard	Various	34.3	11.7	8.5	8.9	25.8	14.1
Wilson (2001)	Standard	Not reported	32.7	11.3	11.1	9.5		
Dupont (2000)	Partial	Various	29					
Eberhardt (2000)	Tailored	Various	34.6	7.8				
Foldvary (2000)	Tailored	Various	23.9	9			12.9	8.5
Holmes (2000)	Tailored	Various	33		16		17	
Iannelli (2000)	Neocortex	Tumor	9.1	5			2.8	
Markand (2000)	Tailored	Not reported	31	10.8	12.3	9.7	18.7	11.7
Rao (2000)	Standard	Various	25.6				16.1	

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Type of Surgery	Pathology	Mean Age at Treatment (Years)	SD of Age at Treatment	Mean Age at First Seizure (Years)	SD of Age at First Seizure	Mean Duration of Condition Before Surgery (Years)	SD of Duration Before Surgery (Years)
Robinson (2000)	AH	Various	15.4		5.2		10.3	
Assaf (1999)	Partial	Various						
Eriksson (1999)	Tailored	Various	34		14		18	
	Tailored	Various	9.9		1.5		5.5	
Henry (1999)	Not Described	Not reported						
Holmes (1999)	Not Described	Various	35.2	10.9				
Mathern (1999)	Tailored	Various	11.7	0.8	5.3	0.8	6.4	0.7
Mitchell (1999)	Not Described	Various	31					
Rossi (1999)	Not Described	Tumor	20.8				7	
Salanova (1999)	Tailored	Various	30.4		10.5		19.7	
Son (1999)	Standard	MTS	28.9					
Maher (1998)	Not Described	Various	32	10				
Radhakrishnan (1998)	Tailored	Various	31		8		19	
Szabo (1998)	Standard	Various	9.4	1.7	3.6	2.2	5.8	2.3
Bizzi (1997)	Partial	Various	11.9	4.6				
Cappabianca (1997)	Neocortex	Vascular malformation	28.8					
Casazza (1997)	Neocortex	Tumor	30.9	8.9	21	9.6	9.9	6.8
Ho (1997)	Partial	Various	31	10				
Keene (1997)	Neocortex	Various	13	3.6	6	4.6		
Kilpatrick (1997)	Standard	Various	36.8	11.5	15			

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Type of Surgery	Pathology	Mean Age at Treatment (Years)	SD of Age at Treatment	Mean Age at First Seizure (Years)	SD of Age at First Seizure	Mean Duration of Condition Before Surgery (Years)	SD of Duration Before Surgery (Years)
McLachlan (1997)	Tailored	Various	31.9	10.9	12.1	9.8		
Schwartz (1997)	Partial	MTS	26.8	10.2				
Silander (1997)	Tailored	Various	32				18	
	Tailored	Various	14				7.5	
Sisodiya (1997)	Standard	MTS	28.2	6.9				
Adam (1996)	Standard	MTS			9.4	4.1		
Goldstein (1996)	Tailored	Various	9.3		3.2		6.1	
Holmes (1996)	Tailored	Various	29.6					
Sirven (1996)	Standard	Various						
Acciarri (1995)	Neocortex	Vascular malformation	34.8	12.5	33.3	12.8	1.6	1.2
Berkovic (1995)	Partial	Various	29	10				
Davies (1995)	Tailored	Various	23				8	
Jooma (1995b)	Tailored	Various					19	
Jooma (1995a)	Tailored	Tumor	34.1	10	14.4	7.3	19.7	7.7
	Neocortex	Tumor	26.5	17.3	23.8	18.6	2.7	3.1
Liu (1995)	Tailored	Other	37.2	13.7	17.8	9.5	19.3	8.2
Renowden (1995)	AH	MTS	23.6				12	
	Standard	MTS	21.3				12	
Thadani (1995)	Standard	MTS	33		10			
Vossler (1995)	Tailored	Various	14.3	3.9	5	4.4	9.3	4.4

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Type of Surgery	Pathology	Mean Age at Treatment (Years)	SD of Age at Treatment	Mean Age at First Seizure (Years)	SD of Age at First Seizure	Mean Duration of Condition Before Surgery (Years)	SD of Duration Before Surgery (Years)
Blume (1994)	Standard	Various						
Guldvog (1994a)	Standard	Various					8	
Guldvog (1994b)	Standard	Various					11.5	
Berkovic (1991)	Standard	MTS	22.5	6	6.3	4.1	16.2	5.9
Hopkins (1991)	Standard	Various	5.5	2.2	2	1.4	3.6	2.1
Rasmussen (1991)	Standard	Not reported						
Wieser (1991)	AH	Various	29.7	13.7	18.8	15.3	11	10.2
Bidzinski (1990)	Standard	Not reported	23		8		13	
Mizrahi (1990)	Tailored	Various	21	8.4	5.9	2.3	15.1	8.1
Walczak (1990)	Standard	Not reported	25				15	
Yeh (1990)	Neocortex	Vascular malformation	36.3	11.9	25.3	8.3	11	8.2
Sperling (1989)	Standard	Not reported						
Estes (1988)	Tailored	Various						
Bladin (1987)	Standard	Not reported						
Cutfield (1987)	Tailored	Various	22				12	
Drake (1987)	Tailored	Tumor	12.7	2.7	6.3	4.3	6.5	3.9
Lieb (1986)	Standard	Not reported						
Meyer (1986)	Tailored	Not reported	15.8		7.5		8.3	
Delgado-Escueta (1985)	Standard	Various	26.5	6.9	15.8	8	10.7	4.9

AH Amygdalohippocampectomy
MTS Mesial temporal sclerosis

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Males	Females	Number of Patients With Simple Partial Seizures	Number of Patients With Complex Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Bouilleret (2002)	10	8	5	13	16	18	
Alsaadi (2001)						49	12
Boling (2001)			9	9			
Hennessy (2001)							
Hennessy (2001)	42	38	39	41	23	73	31
Jan (2001)	14	15	13	16			
Kanemoto (2001)	22	30	28	24			
Schramm (2001)	26	35	27	34	14	57	33
Sotero de Menezes (2001)	9	5			10	14	
Verma (2001)	7	6	7	6			
Wilson (2001)			38	52		90	
Dupont (2000)			13	17			
Eberhardt (2000)	9	11	12	8			
Foldvary (2000)	34	45	45	34	62	79	48
Holmes (2000)	7	16	8	15			
Iannelli (2000)	16	21	27	10	2	21	2
Markand (2000)	26	27	33	20		53	48
Rao (2000)			60	59		119	
Robinson (2000)	8	14	13	9		22	
Assaf (1999)							
Eriksson (1999)	Adults		31	29			
	Children		7	8			
Henry (1999)						38	

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Males	Females	Number of Patients With Simple Partial Seizures	Number of Patients With Complex Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Holmes (1999)	8	5	3	10			
Mathern (1999)	16	15	22	9			
Mitchell (1999)							
Rossi (1999)							
Salanova (1999)	71	74					
Son (1999)			45	26			
Maher (1998)	50	43	45	48			
Radhakrishnan (1998)	68	107	77	98		175	
Szabo (1998)	7	7	7	7		14	
Bizzi (1997)			11	8			
Cappabianca (1997)							
Casazza (1997)					35	33	16
Ho (1997)	28	35	30	33		63	
Keene (1997)	29	15	28	16			
Kilpatrick (1997)	8	10	11	7			
McLachlan (1997)	26	25	24	27		51	
Schwartz (1997)	6	7	9	4		13	
Silander (1997)	Adults		34	34	20	63	32
	Children		11	13	5	27	11
Sisodiya (1997)	16	11	11	16			
Adam (1996)	7	8					
Goldstein (1996)	16	17	17	16			
Holmes (1996)						45	
Sirven (1996)					174	174	
Acciarri (1995)	5	5	5	5		10	0
Berkovic (1995)							

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Males	Females	Number of Patients With Simple Partial Seizures	Number of Patients With Complex Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Davies (1995)							
Jooma (1995b)							
Jooma (1995a)	Tailored					12	6
	Neocortex					12	6
Liu (1995)	5	7	5	7	0	12	8
Renowden (1995)	3	14	6	11			
	33	17	26	24			
Thadani (1995)	11	11			19	22	4
Vossler (1995)	13	17	19	11			
Blume (1994)			64	61		125	
Guldvog (1994a)	25	10					
Guldvog (1994b)							
Berkovic (1991)	3	7	5	5	1	10	4
Hopkins (1991)	5	6	8	3		11	
Rasmussen (1991)							
Wieser (1991)	114	101	120	95			
Bidzinski (1990)							
Mizrahi (1990)	10	12					
Walczak (1990)	45	55	59	41		100	
Yeh (1990)	3	9	8	4	3	9	10
Sperling (1989)						39	
Estes (1988)	12	13					

Evidence Table 110. Patient characteristics for studies of temporal lobe surgery reporting seizure-free outcome measurements (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Males	Females	Number of Patients With Simple Partial Seizures	Number of Patients With Complex Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Bladin (1987)							
Cutfield (1987)	17	9	11	15		26	
Drake (1987)			8	3	3	11	7
Lieb (1986)	46	29	40	35		75	
Meyer (1986)	27	23	29	21			
Delgado-Escueta (1985)	5	10	12	3	1	15	12

Evidence Table 111. Studies of temporal lobe surgery that reported patients as seizure-free with no auras[a]

Reference	N	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Seizure Free with No Auras	Percentage	Cohen's h Effect Sizes	Effect Size CI	P Values for Effect Sizes	Standardized Residuals for Effect Sizes
Bouilleret (2002)	18	4.8	2	7	12	66.7	1.91	1.26—2.56	<0.000001	0.73
Wilson (2001)	90		2		47	52.2	1.62	1.32—1.91	<0.000001	-0.40
Dupont (2000)	30	3.5	2.1	5.3	14	46.7	1.50	1.00—2.01	<0.000001	-0.66
Eberhardt (2000)	20	3	2.2	3.7	7	35.0	1.27	0.65—1.89	0.000062	-1.30
Holmes (2000)	23	3	2	6	11	47.8	1.53	0.95—2.11	<0.000001	-0.50
Markand (2000)	51		2		30	58.8	1.75	1.36—2.14	<0.000001	0.40
Rao (2000)	68		2		46	67.6	1.93	1.60—2.27	<0.000001	1.59
Holmes (1999)	13	3	2	5	7	53.8	1.65	0.88—2.42	0.000027	-0.06
Rossi (1999)	28		2		21	75.0	2.09	1.57—2.62	<0.000001	1.62
Maher (1998)	93		2		53	57.0	1.71	1.42—2.00	<0.000001	0.29
Szabo (1998)	14	2.8	2	4	10	71.4	2.01	1.27—2.75	<0.000001	0.92
Casazza (1997)	40	4.6	2		19	47.5	1.52	1.08—1.96	<0.000001	-0.69
McLachlan (1997)	40	2	2	2	18	45.0	1.47	1.03—1.91	<0.000001	-0.92
Schwartz (1997)	13	2.4	2	3.3	7	53.8	1.65	0.88—2.42	0.000027	-0.06
Sisodiya (1997)	27	2.5	2	4	15	55.6	1.68	1.15—2.22	<0.000001	0.04

[a] Seizure-free with no auras means that patients are free of complex and simple partial seizures

Evidence Table 111. Studies of temporal lobe surgery that reported patients as seizure-free with no auras[a] (continued)

Reference	N	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Seizure Free with No Auras	Percentage	Cohen's h Effect Sizes	Effect Size CI	P Values for Effect Sizes	Standardized Residuals for Effect Sizes
Adam (1996)	15	2.7	2	3.7	7	46.7	1.50	0.79—2.22	0.000038	-0.46
Holmes (1996)	45	4.5	4	5	27	60.0	1.77	1.36—2.19	<0.000001	0.50
Renowden (1995)	17 - AH		2		8	47.1	1.51	0.84—2.18	0.000010	-0.47
	50 – Standard lobectomy		2		25	50.0	1.57	1.18—1.96	<0.000001	-0.52
Meyer (1986)	24	5	5		10	41.7	1.40	0.84—1.97	0.000001	-0.94
Delgado-Escueta (1985)	15	6	2	11	9	60.0	1.77	1.06—2.49	0.000001	0.28

[a] Seizure-free with no auras means that patients are free of complex and simple partial seizures

AH Amygdalohippocampectomy

Evidence Table 112. Studies of temporal lobe surgery that reported patients as seizure-free with auras[a]

Reference	N	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Seizure Free With Auras	Percentage	Cohen's h Effect Sizes	Effect Size CI	P Values for Effect Sizes	Standardized Residuals for Effect Sizes
Hennessy (2001)	116	5	2		78	67.2	1.92	1.67—2.18	<0.000001	-0.21
Hennessy (2001)	80		2		52	65.0	1.88	1.57—2.19	<0.000001	-0.48
Jan (2001)	29		2		23	79.3	2.2	1.68—2.71	<0.000001	0.95
Sotero de Menezes (2001)	14	5	2	10	6	42.9	1.43	0.69—2.17	0.000159	-1.39
Verma (2001)	13		2		9	69.2	1.97	1.20—2.73	0.000001	0.04
Wilson (2001)	90		2		60	66.7	1.91	1.62—2.20	<0.000001	-0.27
Eberhardt (2000)	20	3	2.2	3.7	13	65.0	1.88	1.26—2.50	<0.000001	-0.23
Markand (2000)	51		2		37	72.5	2.04	1.65—2.43	<0.000001	0.46
Assaf (1999)	75		2		52	69.3	1.97	1.65—2.29	<0.000001	0.12
Eriksson (1999)	15 – children		2		9	60.0	1.77	1.06—2.49	0.000001	-0.49
	60 - adults				34	56.7	1.70	1.35—2.06	<0.000001	-1.37
Mitchell (1999)	45		2		26	57.8	1.73	1.31—2.14	<0.000001	-1.07
Radhakrishnan (1998)	175	3.6	2	5.7	134	76.6	2.13	1.92—2.34	<0.000001	1.82
Ho (1997)	63	4.1	2	6.2	38	60.3	1.78	1.43—2.13	<0.000001	-0.98

[a] Seizure-free with auras means the patients are free of complex seizures but may have simple partial seizures

Evidence Table 112. Studies of temporal lobe surgery that reported patients as seizure-free with auras[a] (continued)

Reference	N	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Seizure Free With Auras	Percentage	Cohen's h Effect Sizes	Effect Size CI	P Values for Effect Sizes	Standardized Residuals for Effect Sizes
Kilpatrick (1997)	18	2.5	2	3.2	13	72.2	2.03	1.38—2.68	<0.000001	0.25
Reeves (1997)	134	4.2	2.5	6.5	107	79.9	2.21	1.97—2.45	<0.000001	2.25
Schwartz (1997)	13	2.4	2	3.3	9	69.2	1.97	1.20—2.73	0.000001	0.04
Sisodiya (1997)	27	2.5	2	4	16	59.3	1.76	1.22—2.29	<0.000001	-0.71
Adam (1996)	15	2.7	2	3.7	12	80.0	2.21	1.50—2.93	<0.000001	0.73
Liu (1995)	12	5.3	2.2	8.5	6	50.0	1.57	0.77—2.37	0.000119	-0.93
Vossler (1995)	30	6.4	2.3	14.8	20	66.7	1.91	1.40—2.42	<0.000001	-0.15
Blume (1994)	125	5.5	2	16	87	69.6	1.97	1.73—2.22	<0.000001	0.20
Walczak (1990)	100		2		63	63.0	1.83	1.56—2.11	<0.000001	-0.85
Yeh (1990)	12	3.7	2	6	10	83.3	2.30	1.50—3.10	<0.000001	0.86
Estes (1988)	25	4.1	2.2	7	9	36.0	1.29	0.73—1.84	0.000005	-2.36
Meyer (1986)	24	5	5		18	75.0	2.09	1.53—2.66	<0.000001	0.51
Delgado-Escueta (1985)	15	6	2	11	11	73.3	2.06	1.34—2.77	<0.000001	0.29

[a] Seizure-free with auras means the patients are free of complex seizures but may have simple partial seizures

Evidence Table 113. Studies of surgery control patients reporting seizure-free outcome measurements

Reference	N	Years	Country	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients and Percentage							
							Seizure-Free (undefined)	%	Seizure-Free (no auras)	%	Seizure-Free (with auras)	%	Engel Class I	%
Bauer (2001)	63	1970-1989	Germany	8.7	3.7	19	9	14.3						
Kumlien (2001)	47	1993-1999	USA	3.4	2		11	23.4						
Wiebe (2001)	40	1996-2000	Canada		1				1	2.5	3	7.5		
Markand (2000)	33	1994-1997	USA		1				0	0.0				
Holmes (1998)	35	1977-1997	USA		10		2	5.7						
Wolf (1998)	15	1987-1992	Germany		4				3	20.0	4	26.7	4	26.7
McLachlan (1997)	21	1992-1995	Canada		2		0	0.0						
Hermanns (1996)	74	1992-1994	Germany	1.3	0.9	2	0	0.0						
Vickrey (1995)	43	1974-1990	USA	5.7	1	17			2	4.7	4	9.3		
Guldvog (1991)	185	1960-1989	Norway	9	2	31	Reported changes in seizure frequency only							
Huttenlocher (1990)	155	1970-1989	USA	13	5	20	0	0.0						
Harbord (1987)	38	1969-1985	Australia	6.6	2	15	4	10.5						

Evidence Table 114. Studies with epilepsy surgery control patients – reasons for patients not to receive surgery

Reference	Number of Patients	Control Group	Number of Patients Who Refused Surgery	Number of Patients Who Were Unsuitable For Surgery	Number of Patients Who Were Actual Surgical Candidates
Bauer (2001)	63	Medical management control			
Kumlien (2001)	47	Temporal lobe - nonsurgical control		47	
Wiebe (2001)	40	Temporal lobe - nonsurgical control	0	0	40
Markand (2000)	37	Temporal lobe - nonsurgical control	5	32	
Holmes (1998)	35	Medical management control	35		
Wolf (1998)	15	Medical management control	15		
McLachlan (1997)	21	Temporal lobe - nonsurgical control	8	13	
Hermanns (1996)	74	Medical management control			
Vickrey (1995)	46	Medical management control	2	44	
Guldvog (1991)	185	Medical management control			38
Huttenlocher (1990)	155	Medical management control			
Harbord (1987)	38	Medical management control			

Evidence Table 115. Comparisons of summary estimates based on study level characteristics for temporal lobe surgery studies reporting seizure-free with no auras [a]

Study Level Characteristics	Number of Studies	Cohen's h Summary Estimate	95% Confidence Intervals		Back-transformed Percentage Estimate	95% Confidence Intervals	
			Lower	Upper		Lower	Upper
United States	8	1.69	1.50	1.89	56%	46%	66%
Other countries	13	1.66	1.54	1.78	54%	48%	60%
Mesial temporal sclerosis only	6	1.63	1.39	1.86	53%	41%	64%
Various other pathologies	15	1.68	1.57	1.79	55%	50%	61%
Standard temporal lobectomy	11	1.74	1.61	1.88	58%	52%	65%
Tailored temporal lobectomy	6	1.59	1.39	1.78	51%	41%	60%
Other surgical procedures	4	1.53	1.25	1.81	48%	34%	62%

[a] Studies were regrouped according to the selected study level characteristics and new summary estimates were calculated.

Evidence Table 116. Comparisons of summary estimates based on study level characteristics for temporal lobe surgery studies reporting seizure-free with auras. [a]

Study Level Characteristics	Number of Studies	Cohen's h Summary Estimate	95% Confidence Intervals		Back-transformed Percentage Estimage	95% Confidence Intervals	
			Lower	Upper		Lower	Upper
United States	13	2.00	1.90	2.11	71%	66%	76%
Other countries	14	1.90	1.79	2.00	66%	61%	71%
Mesial temporal sclerosis only	4	1.93	1.71	2.14	68%	57%	77%
Various other pathologies	23	1.95	1.87	2.03	69%	65%	72%
Standard temporal lobectomy	11	1.97	1.87	2.07	69%	65%	74%
Tailored temporal lobectomy	10	1.93	1.79	2.06	68%	61%	73%
Other surgical procedures	6	1.92	1.74	2.10	67%	58%	75%

[a] Studies were regrouped according to the selected study level characteristics and new summary estimates were calculated.

Evidence Table 117. Studies of temporal lobe surgery that reported patients as Engel class I

Reference	Number of Patients Evaluated	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients in Engel Class I	Percentage	Cohen's h Effect Sizes	Effect Size CI	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Bouilleret (2002)	18	4.8	2	7	16	88.9	1.63	1.32—1.95	<0.000001	1.59
Alsaadi (2001)	49		2		37	75.5	2.09	1.29—2.89	<0.000001	0.87
Boling (2001)	18	5.3	2		11	61.1	1.50	1.18—1.82	<0.000001	-0.42
Kanemoto (2001)	52	7	2	12	42	80.8	1.43	0.69—2.17	<0.000001	1.56
Schramm (2001)	32	2	2	2	26	81.3	1.66	1.24—2.08	<0.000001	1.26
Sotero de Menezes (2001)	14	5	2	10	6	42.9	1.97	1.73—2.22	0.000159	-1.34
Dupont (2000)	30	3.5	2.1	5.3	24	80.0	1.76	1.52—2.00	<0.000001	1.10
Eberhardt (2000)	20	3	2.2	3.7	13	65.0	1.60	1.15—2.04	<0.000001	-0.18
Foldvary (2000)	79		2		42	53.2	2.62	1.90—3.33	<0.000001	-1.93
Iannelli (2000)	32	6	2	14	26	81.3	2.11	1.71—2.50	<0.000001	1.26
Markand (2000)	51		2		37	72.5	1.79	1.14—2.45	<0.000001	0.54
Robinson (2000)	17	2.7	2	5.5	11	64.7	2.23	1.85—2.62	<0.000001	-0.19
Salanova (1999)	144		2		91	63.2	2.25	1.76—2.74	<0.000001	-0.85
Son (1999)	71	3.2	2	5	66	93.0	1.84	1.61—2.07	<0.000001	4.09
Maher (1998)	93		2		73	78.5	2.01	1.27—2.75	<0.000001	1.71
Szabo (1998)	14	2.8	2	4	10	71.4	2.01	1.27—2.75	<0.000001	0.21
Bizzi (1997)	14	4.8	2	7	10	71.4	1.72	1.28—2.16	<0.000001	0.21

Evidence Table 117. Studies of temporal lobe surgery that reported patients as Engel class I (continued)

Reference	Number of Patients Evaluated	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients in Engel Class I	Percentage	Cohen's h Effect Sizes	Effect Size CI	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Casazza (1997)	40	4.6	2		23	57.5	1.67	1.43—1.91	<0.000001	-0.96
Keene (1997)	44	7.7	2		24	54.5	1.05	0.25—1.85	<0.000001	-1.29
Kilpatrick (1997)	18	2.5	2	3.2	13	72.2	2.56	1.76—3.36	<0.000001	0.30
Sisodiya (1997)	27	2.5	2	4	16	59.3	2.26	1.67—2.85	<0.000001	-0.65
Adam (1996)	15	2.7	2	3.7	15	100.0	2.21	1.34—3.09	<0.000001	3.32
Berkovic (1995)	135	3.7	2	6.8	74	54.8	2.03	1.38—2.68	<0.000001	-2.29
Davies (1995)	12	7.4	2		9	75.0	1.76	1.22—2.29	<0.000001	0.40
Jooma (1995b)	62		2		40	64.5	3.14	2.43—3.86	<0.000001	-0.39
Jooma (1995a)	12 – lesionectomy	3.4	2	7	3	25.0	1.87	1.51—2.22	0.010315	-2.18
	12 – tailored surgery	5	2.5	7	11	91.7	2.46	1.81—3.12	<0.000001	1.53
Thadani (1995)	22	4	3	9	18	81.8	2.25	1.76—2.74	<0.000001	1.09
Blume (1994)	125	5.5	2	16	87	69.6	2.21	1.71—2.72	<0.000001	0.33
Berkovic (1991)	10	2.8	2.4	3.3	8	80.0	1.88	1.26—2.50	0.000001	0.63
Wieser (1991)	138		2		82	59.4	2.04	1.65—243	<0.000001	-1.51
Sperling (1989)	39	5.7	3	9	20	51.3	1.87	1.20—2.54	<0.000001	-1.51
Lieb (1986)	75	8	2	21	35	46.7	2.60	2.28—2.93	<0.000001	-2.70
Delgado-Escueta (1985)	15	6	2	11	14	93.3	2.18	1.89—2.46	<0.000001	1.89

Evidence Table 118. Studies of temporal lobe surgery reporting Engel class I – data used in meta-regression

Reference	N	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	United States
Bouilleret (2002)	18	2.46	9	1993	2000	No
Alsaadi (2001)	49	2.11	24.5	1989	1994	Yes
Boling (2001)	18	1.79	9	1981	1999	No
Kanemoto (2001)	52	2.23	26	1987	1999	No
Schramm (2001)	32	2.25	16	1993	1999	No
Sotero de Menezes (2001)	14	1.43	7	1978	1993	Yes
Dupont (2000)	30	2.21	15	1994	1999	No
Eberhardt (2000)	20	1.88	10	1995	1999	No
Foldvary (2000)	79	1.63	39.5	1962	1984	Yes
Iannelli (2000)	32	2.25	16	1981	1997	No
Markand (2000)	51	2.04	25.5	1994	1997	Yes
Robinson (2000)	17	1.87	8.5	1993	1998	Yes
Salanova (1999)	144	1.84	72	1984	1995	Yes
Son (1999)	71	2.60	35.5	1994	1999	No
Maher (1998)	93	2.18	46.5	1994	1996	No
Szabo (1998)	14	2.01	7	1989	1994	Yes
Bizzi (1997)	14	2.01	7	1990	1994	Yes
Casazza (1997)	40	1.72	20	1988	1994	No
Keene (1997)	44	1.66	22	1975	1996	No
Kilpatrick (1997)	18	2.03	9	1993	1995	No
Sisodiya (1997)	27	1.76	13.5	1993	1995	No
Adam (1996)	15	3.14	7.5	1991	1994	No
Berkovic (1995)	135	1.67	67.5	1986	1991	No
Davies (1995)	12	2.09	6	1969	1988	No
Jooma (1995b)	62	1.87	31	1992	1994	Yes
Jooma (1995a)	12 – lesionectomy	1.05	6	1985	1992	Yes
	12 – tailored surgery	2.56	6	1985	1992	Yes

Evidence Table 118. Studies of temporal lobe surgery reporting Engel class I – data used in meta-regression (continued)

Reference	N	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	United States
Thadani (1995)	22	2.26	11	1983	1992	Yes
Blume (1994)	125	1.97	62.5	1974	1989	No
Berkovic (1991)	10	2.21	5	1985	1986	No
Wieser (1991)	138	1.76	69	1975	1990	No
Sperling (1989)	39	1.60	19.5	1976	1983	Yes
Lieb (1986)	75	1.50	37.5	1961	1977	Yes
Delgado-Escueta (1985)	15	2.62	7.5	1972	1983	Yes

Evidence Table 119. Results of meta-regression of studies of temporal lobe surgery reporting Engel class I

Parameter	Qe	p value for Qe	Intercept	CI of Intercept	p Value for Intercept	Coefficient	CI of Coefficient	p Value for Coefficient
One predictor models								
Year study ended	55.7	0.006	-58.5	-83.7 — –33.3	.0000006	0.030	0.017 — 0.044	0.000009
Year study started	56.7	0.005	-30.7	-44.6 — -16.7	0.000016	0.016	0.009 — 0.024	0.00001
United States	72.1	0.00006	1.8	1.7 — 1.9	<0.000001	0.174	0.030 — 0.318	0.018
Two predictor models								
Year study ended,	54.4	0.006	-50.4	-79.1 — -21.7	0.006	0.019	-0.005 — 0.042	0.12
Year study started						0.008	-0.006 — 0.021	0.26
Year study started,	54.8	0.005	-28.4	-42.7 — -14.1	0.0001	0.015	0.007 —0.002	0.00007
United States						-0.105	-0.250 — 0.040	0.16
Year study ended,	55.0	0.005	-54.5	-81.3 — -27.7	0.00007	0.028	-0.220 — 0.090	0.39
United States						0.028	0.020 — 0.040	0.00003
Three predictor model								
Year study started,	53.4	0.005	-44.9	-75.6 — -14.3	0.004	0.015	-0.01 — 0.04	0.24
Year study started,						0.008	-0.005 — 0.020	0.21
United States						-0.079	-0.07 — 0.23	0.31

Evidence Table 120. Studies of temporal lobe surgery that reported patients as seizure-free undefined

Reference	Number of Patients Evaluated	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Seizure Free Undefined	Percentage	Cohen's h Effect Sizes	Effect Size CI	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Henry (1999)	38	6.2	5	7.2	27	71.1	2.01	1.56—2.46	<0.000001	0.90
Mathern (1999)	20		2		13	65.0	1.88	1.26—2.50	<0.000001	0.23
Cappabianca (1997)	10		2		8	80.0	2.21	1.34—3.09	0.000001	0.92
Silander (1997)	25 children		2		12	48.0	1.64	1.28—1.99	<0.000001	-0.97
	62 adults				33	53.2	1.53	0.98—2.09	<0.000001	-0.98
Goldstein (1996)	33	4.7	2	10	15	45.5	1.48	1.00—1.96	<0.000001	-1.34
Sirven (1996)	174	2.7	2.3	8	136	78.2	2.17	1.96—2.38	<0.000001	3.76
Acciarri (1995)	10	5.2	2	14	10	100.0	3.14	2.27—4.02	<0.000001	3.01
Guldvog (1994b)	53 adults	7	2	26	29	54.7	1.67	1.28—2.05	<0.000001	-0.73
Guldvog (1994a)	34 children	7	2		23	67.6	1.93	1.46—2.41	<0.000001	0.54
Hopkins (1991)	11	3.6	2	7.5	8	72.7	2.04	1.21—2.88	0.000002	0.56
Rasmussen (1991)	100	12	2	24	55	55.0	1.67	1.39—1.95	<0.000001	-0.99
Bidzinski (1990)	286	16	2	30	140	49.0	1.55	1.39—1.71	<0.000001	-3.61
Mizrahi (1990)	22	5.3	2	8	14	63.6	1.85	1.26—2.44	<0.000001	0.15
Bladin (1987)	63		2		51	81.0	2.24	1.89—2.59	<0.000001	2.52
Cutfield (1987)	25	12	5	17	13	52.0	1.61	1.06—2.17	<0.000001	-0.69
Drake (1987)	11	2.7	2	5	7	63.6	1.85	1.01—2.68	0.000015	0.10

Evidence Table 121. Studies of temporal lobe surgery reporting seizure-free undefined – data used in meta-regression.

Reference	N	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	United States
Henry (1999)	38	2.01	19	1991	1994	Yes
Mathern (1999)	20	1.88	10	1986	1997	Yes
Cappabianca (1997)	10	2.21	5	1985	1994	No
Silander (1997)	25 children	1.64	31	1980	1990	No
	62 adults	1.53	12.5	1980	1990	No
Goldstein (1996)	33	1.48	16.5	1985	1993	Yes
Sirven (1996)	174	2.17	87	1985	1992	Yes
Acciarri (1995)	10	3.14	5	1975	1992	No
Guldvog (1994b)	53 adults	1.67	26.5	1949	1988	No
Guldvog (1994a)	34 children	1.93	17	1952	1988	No
Hopkins (1991)	11	2.04	5.5	1978	1988	No
Rasmussen (1991)	100	1.67	50	1961	1980	No
Bidzinski (1990)	286	1.55	143	1957	1988	No
Mizrahi (1990)	22	1.85	11	1980	1986	Yes
Bladin (1987)	63	2.24	31.5	1985	1987	No
Cutfield (1987)	25	1.61	12.5	1961	1980	No
Drake (1987)	11	1.85	5.5	1974	1986	No

Evidence Table 122. Results of meta-regression of studies of temporal lobe surgery reporting seizure-free undefined

Parameter	Q_e	p value for Q_e	Intercept	CI of Intercept	p value for Intercept	Coefficient	CI of Coefficient	p value for Coefficient
One predictor models								
Year study started	26.2	0.036	-24.7	-37.3 — -12.2	0.0001	0.013	0.007 — 0.019	0.000008
United States	33.6	0.004	1.7	1.6 — 1.8	<0.000001	0.311	0.116 — 0.506	0.002
Year study ended	37.8	0.001	-51.9	-96.2 — -7.6	0.022	0.027	0.004 — 0.049	0.017
Two predictor models								
Year study started	26.1	0.025	-23.3	-41.2 — -5.4	0.011	0.013	0.004 — 0.021	0.004
United States						0.032	-0.247 — 0.310	.824
Year study started	26.2	0.025	-24.9	-71.8 — 22.0	.298	0.013	0.006 — 0.020	0.0002
Year study ended						0.0001	-0.027 — 0.027	0.996
Year study ended	33.3	0.003	-14.1	-70.6 — 42.5	0.626	0.008	-0.020 — 0.036	0.579
United States						0.267	0.018 — 0.516	0.036
Three predictor model.								
Year study started	26.1	0.016	-21.0	-77.8 — 35.8	0.469	0.036	-0.264 — 0.337	0.812
Year study started						0.013	0.003 — 0.002	0.010
United States						-0.001	-0.028 — 0.030	0.932

Evidence Table 123. Studies of temporal lobe surgery reporting relationships between patient or study characteristics and treatment outcome

Reference	N	Seizure Outcome Measurement	Statistical Method	Patient or Study Characteristics Examined									
				Age at Surgery	Age at Seizure Onset	Duration of Epilepsy Prior to Surgery	Length of Followup	Gender	Side of Surgery	Complex Partial Seizures	Simple Partial Seizures	Secondarily Generalized Seizures	Mesial Temporal Sclerosis
Hennessy (2001)	80	Seizure-free with auras	Univariate	Sig.	NS	Sig.		NS	NS	NS	NS	NS	
Hennessy (2001)	116	Seizure-free with auras	Univariate	NS	NS	NS						Sig.	
Foldvary (2000)	79	Engel class I	Univariate	NS		NS		NS	NS				
Holmes (2000)	23	Seizure-free no auras	Univariate	NS	NS	NS		NS	NS				NS
Robinson (2000)	22	Engel class I	Univariate	NS	NS	NS			NS				
Radhakrishnan (1998)	175	Seizure-free with auras	Univariate	NS	NS	NS	NS						Sig.
Goldstein (1996)	33	Seizure-free (undefined)	Univariate	NS	NS	NS			NS				NS
Blume (1994)	125	90% Reduction in Seizure Frequency	Multiple regression	Sig.									NS
Cutfield (1987)	26	Seizure-free (undefined)	Multiple regression		NS	NS							NS

Sig. Statistically significant according to authors
NS Not statistically significant according to authors

Evidence Table 124. Studies of temporal lobe surgery reporting relationships between patient characteristics and treatment outcome – other study variables

Reference	Number of Patients	Seizure Outcome Measurement	Statistical Method	Other Study Variables
Alsaadi (2001)	49	Engel class I	Univariate	Ictal and postictal clinical manifestations (NS)
Hennessy (2001)	80	Seizure-free with auras	Univariate	Special schooling (Sig.), Developmental dysplastic lesions (Sig.), Perinatal complications (NS), Delayed developmental milestones (NS), Family history of epilepsy (NS), Febrile convulsion (NS), EEG spikes confined to temporal lobe (NS), Neoplasms (NS)
Hennessy (2001)	116	Seizure-free with auras	Univariate	Perinatal complications (Sig.), EEG interictal spikes confined to operated temporal lobe (Sig.), Febrile convulsion (NS), Developmental delay (NS), Special schooling (NS), Psychiatric history (NS), Family history of epilepsy (NS), Lateralized abnormality on physical examination (NS)
Dupont (2000)	30	Seizure-free no auras	Multiple regression	PET determined metabolism of the temporal pole, basofrontal cortex, anterior part of the lateral temporal neocortex, and medial temporal cortex (Sig.)
Foldvary (2000)	79	Engel class I	Univariate	Monthly frequency of CPS less than 20 (Sig.), Recorded seizures during routine or prolonged EEG (NS)
Holmes (2000)	23	Seizure-free no auras	Univariate	EEG finding of basal-temporal ictal onset (Sig.), EEG finding of unilateral basal-temporal interictal epileptiform patterns (Sig.)
Robinson (2000)	22	Engel class I	Univariate	History of febrile seizures (NS), IAP memory localization (NS), Unilateral hypometabolism (Sig.)
Salanova (1999)	144	Engel class I	Univariate	History of febrile seizures (Sig.), MTS or discrete lesion (Sig.), Availability of PET scan and volumetric MRI (Sig.), Unitemporal interictal spiking (NS), Bitemporal interictal spiking (NS)
Radhakrishnan (1998)	175	Seizure-free with auras	Univariate	Scalp interictal epileptiform discharges concordant with ictal onset (Sig.), Seizure-free during first year (Sig.), No epileptiform discharge at 3 mo (Sig.), Symptomatic epilepsy etiology (NS), History of febrile seizure (NS), Lesions other than MTS on neuroimaging (NS), No epileptiform discharge at 1 wk (NS),
Goldstein (1996)	33	Seizure-free (undefined)	Univariate	Generalized motor seizures (NS) Mental retardation (NS), Unitlateral temporal interictal activity (NS), Unilateral temporal ictal activity (NS), Significant etiological history (NS)
Blume (1994)	115	Seizure-free with auras	Multiple regression	Febrile convulsions as etiology (NS), No generalized motor seizures (Sig.), Lateralized temporal spikes (Sig.), No extra-anterior temporal spikes on any record (Sig.), No postoperative seizures within one week of surgery (Sig.)
So (1989)	48	Engel class I	Univariate	Stereotactic depth EEG unilateral (seizure onset in the resected lobe) (Sig.), History of early convulsion (<3 yr) (Sig.), Extent of hippocampal removal (Sig.), Residual ECoG epileptiform abnormalities (Sig.), Early postoperative seizures (<2 mo) (Sig.), Pathology (NS), Major etiological factor (NS)
Cutfield (1987)	26	Seizure-free (undefined)	Multiple regression	EEG findings (NS)

Sig. Statistically significant according to authors NS Not statistically significant according to authors

Evidence Table 125. Studies of temporal lobe surgery reporting individual patient age at surgery

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Bouilleret (2002)	18	Seizure-free no auras	0.27	-0.23	0.65	0.97
Sotero de Menezes (2001)	14	Seizure-free with auras	-0.37	-0.75	0.20	-1.42
Verma (2001)	13	Seizure-free with auras	-0.29	-0.73	0.31	-1.07
Eberhardt (2000)	20	Seizure-free no auras	0.07	-0.39	0.49	0.15
Holmes (1999)	13	Seizure-free no auras	0.23	-0.37	0.69	0.65
Szabo (1998)	14	Seizure-free with auras	-0.03	-0.55	0.51	-0.20
Kilpatrick (1997)	18	Seizure-free with auras	-0.16	-0.58	0.33	-0.75
Schwartz (1997)	13	Seizure-free no auras	0.05	-0.52	0.58	0.06
Sisodiya (1997)	27	Engel class I	-0.07	-0.44	0.32	-0.52
Jooma (1995a)	12 lesionectomy	Seizure-free with auras	-0.19	-0.69	0.43	-0.64
	12 tailored		-0.03	-0.59	0.55	-0.14
Liu (1995)	12	Seizure-free with auras	0.37	-0.26	0.78	1.09
Vossler (1995)	30	Seizure-free with auras	0.15	-0.22	0.48	0.66
Berkovic (1991)	10	Seizure-free (undefined)	0.31	-0.40	0.79	0.77
Hopkins (1991)	11	Seizure-free (undefined)	0.34	-0.33	0.78	0.93
Mizrahi (1990)	22	Seizure-free (undefined)	0.16	-0.28	0.55	0.61
Yeh (1990)	12	Seizure-free with auras	-0.23	-0.71	0.40	-0.79
Drake (1987)	11	Seizure-free (undefined)	-0.23	-0.73	0.43	-0.74
Delgado-Escueta (1985)	15	Seizure-free no auras	-0.21	-0.65	0.34	-0.85

[a] A positive correlation indicates more successful surgeries with an older age at surgery.

Evidence Table 126. Sensitivity analysis of studies of temporal lobe surgery reporting individual patient age at surgery for successful and nonsuccessful patients

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.02	-0.11	0.14	0.814	10.71	0.906
Removing study with largest negative correlation	0.03	-0.09	0.16	0.601	8.84	0.945
Removing study with largest positive correlation	0.00	-0.13	0.13	0.991	9.41	0.926
Removing study with smallest N	0.01	-0.12	0.13	0.926	10.04	0.902
Removing study with largest N	0.00	-0.14	0.13	0.978	10.15	0.897

[a] A positive correlation indicates more successful surgeries with an older age at surgery.

Evidence Table 127. Studies of temporal lobe surgery reporting individual age at seizure onset

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Bouilleret (2002)	18	Seizure-free no auras	-0.18	-0.60	0.31	-0.16
Verma (2001)	13	Seizure-free with auras	0.21	-0.38	0.68	1.16
Szabo (1998)	14	Seizure-free with auras	-0.34	-0.74	0.23	-0.74
Adam (1996)	15	Seizure-free no auras	0.01	-0.51	0.52	0.53
Jooma (1995a)	12 lesionectomy	Seizure-free with auras	-0.18	-0.68	0.44	-0.22
	12 tailored		0.06	-0.53	0.61	0.53
Liu (1995)	12	Seizure-free with auras	0.13	-0.48	0.65	0.84
Vossler (1995)	30	Seizure-free with auras	-0.16	-0.49	0.22	-0.09
Berkovic (1991)	10	Seizure-free (undefined)	-0.48	-0.85	0.22	-1.02
Hopkins (1991)	11	Seizure-free (undefined)	-0.11	-0.66	0.53	0.10
Mizrahi (1990)	22	Seizure-free (undefined)	-0.15	-0.54	0.29	-0.06
Yeh (1990)	12	Seizure-free with auras	-0.35	-0.77	0.28	-0.69
Drake (1987)	11	Seizure-free (undefined)	0.42	-0.24	0.81	1.70
Delgado-Escueta (1985)	15	Seizure-free no auras	-0.20	-0.64	0.35	-0.21

[a] A positive correlation indicates more successful surgeries with an older age at seizure onset.

Evidence Table 128. Sensitivity analysis of studies of temporal lobe surgery reporting individual patient age at seizure onset

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	-0.11	-0.26	0.04	0.158	7.23	0.890
Removing study with largest negative correlation [b]	-0.09	-0.24	0.06	0.249	6.00	0.916
Removing study with largest positive correlation	-0.14	-0.29	0.02	0.083	4.64	0.969
Removing study with smallest N	-0.09	-0.24	0.06	0.249	6.00	0.916
Removing study with largest N	-0.10	-0.26	0.07	0.238	7.16	0.847

[a] A positive correlation indicates more successful surgeries with an older age at seizure onset.
[b] The study with the largest negative effect size also had the smallest N.

Evidence Table 129. Studies of temporal lobe surgery reporting individual patients duration of epilepsy prior to surgery

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation[a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Bouilleret (2002)	18	Seizure-free no auras	0.28	-0.21	0.66	0.21
Verma (2001)	13	Seizure-free with auras	-0.38	-0.77	0.22	-2.08
Szabo (1998)	14	Seizure-free with auras	0.31	-0.26	0.72	0.29
Jooma (1995a)	12 lesionectomy	Seizure-free with auras	-0.01	-0.58	0.57	-0.50
	12 tailored		-0.10	-0.63	0.51	-0.77
Liu (1995)	12	Seizure-free with auras	0.47	-0.15	0.82	0.82
Vossler (1995)	30	Seizure-free with auras	0.29	-0.08	0.59	0.36
Berkovic (1991)	10	Seizure-free (undefined)	0.64	0.02	0.90	1.40
Hopkins (1991)	11	Seizure-free (undefined)	0.42	-0.24	0.82	0.62
Mizrahi (1990)	22	Seizure-free (undefined)	0.21	-0.23	0.58	-0.11
Yeh (1990)	12	Seizure-free with auras	0.03	-0.56	0.59	-0.66
Drake (1987)	11	Seizure-free (undefined)	-0.62	-0.89	-0.03	-2.79
Delgado-Escueta (1985)	15	Seizure-free no auras	0.03	-0.49	0.53	-0.75

[a] A positive correlation indicates more successful surgeries with a longer duration of epilepsy prior to surgery.

Evidence Table 130. Sensitivity analysis of studies of temporal lobe surgery reporting individual patient duration of epilepsy prior to surgery

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.15	-0.01	0.30	0.058	15.90	0.195
Removing study with largest negative correlation	0.20	0.04	0.35	0.015	9.44	0.581
Removing study with largest positive correlation [b]	0.12	-0.04	0.28	0.133	13.24	0.278
Removing study with smallest N	0.12	-0.04	0.28	0.133	13.24	0.278
Removing study with largest N	0.12	-0.05	0.29	0.172	15.19	0.174

[a] A positive correlation indicates more successful surgeries with a longer duration of epilepsy prior to surgery.
[b] The study with the largest effect size also had the smallest N.

Evidence Table 131. Studies of temporal lobe surgery reporting number of male and female patients with successful and nonsuccessful surgery

Reference	Seizure Outcome Measurement	Number of Male Patients	Number of Male Successes	Number of Female Patients	Number of Female Successes	Cohen's h Effect Sizes	95% Confidence Interval		p Values for Effect Sizes	Standardized Residuals for Effect Sizes
							Lower	Upper		
Bouilleret (2002)	Seizure-free no auras	5	4	13	8	0.41	-0.62	1.44	0.435201	0.92
Hennessy (2001)	Seizure-free with auras	39	27	41	25	0.17	-0.26	0.61	0.438003	1.23
Verma (2001)	Seizure-free with auras	7	5	6	4	0.10	-0.99	1.19	0.853018	0.30
Eberhardt (2000)	Seizure-free no auras	12	1	8	6	-1.51	-2.40	-0.61	0.000948	-3.29
Holmes (1999)	Seizure-free no auras	3	1	10	6	-0.54	-1.83	0.75	0.411001	-0.74
Szabo (1998)	Seizure-free with auras	7	6	7	4	0.65	-0.40	1.70	0.222367	1.37
Kilpatrick (1997)	Seizure-free with auras	11	9	7	4	0.55	-0.40	1.49	0.258407	1.29
Schwartz (1997)	Seizure-free no auras	9	4	4	3	-0.63	-1.81	0.54	0.290693	-0.98
Sisodiya (1997)	Engel class I	11	6	16	9	-0.03	-0.80	0.73	0.930230	0.07
Liu (1995)	Seizure-free with auras	5	1	7	5	-1.09	-2.23	0.06	0.063539	-1.79
Vossler (1995)	Seizure-free with auras	19	12	11	8	-0.21	-0.95	0.54	0.587416	-0.41
Berkovic (1991)	Seizure-free (undefined)	5	3	5	5	-1.37	-2.61	-0.13	0.030367	-2.11
Yeh (1990)	Seizure-free with auras	8	7	4	3	0.32	-0.88	1.52	0.596218	0.64
Drake (1987)	Seizure-free (undefined)	8	6	3	1	0.86	-0.46	2.19	0.202175	1.39
Delgado-Escueta (1985)	Seizure-free no auras	12	8	3	1	0.68	-0.59	1.94	0.292366	1.17

Evidence Table 132. Studies of temporal lobe surgery reporting number of male and female patients with successful and nonsuccessful surgery – data used in meta-regression

Reference	Number of Patients	Cohen's h Effect Size	Weight	Mesial Temporal Sclerosis Patients Only	Tumor Patients Only	Standard Temporal Lobectomy	Tailored Temporal Lobectomy
Bouilleret (2002)	18	0.4106	3.6111	Yes	No	Yes	No
Hennessy (2001)	80	0.1735	19.9875	No	No	Yes	No
Verma (2001)	13	0.1031	3.2308	No	No	Yes	No
Eberhardt (2000)	20	-1.5087	4.8	No	No	No	Yes
Holmes (1999)	13	-0.5412	2.3077	No	No	Yes	No
Szabo (1998)	14	0.6523	3.5	No	No	Yes	No
Kilpatrick (1997)	18	0.5464	4.2778	No	No	Yes	No
Schwartz (1997)	13	-0.6349	2.7692	Yes	No	No	No
Sisodiya (1997)	27	-0.0343	6.5185	Yes	No	Yes	No
Liu (1995)	12	-1.0864	2.9167	No	No	No	Yes
Vossler (1995)	30	-0.2056	6.9667	No	No	No	Yes
Berkovic (1991)	10	-1.3694	2.5	Yes	No	Yes	No
Yeh (1990)	12	0.3245	2.6667	No	Yes	No	No
Drake (1987)	11	0.8634	2.1818	No	Yes	No	Yes
Delgado-Escueta (1985)	15	0.6797	2.4	No	No	Yes	No

Evidence Table 133. Results of meta-regression of studies of temporal lobe surgery reporting percentage of male and female patients among patients with successful and nonsuccessful surgery

One predictor models Bolded = statistically significant coefficient						
Covariate	**Intercept (CI)**	**P (intercept) =**	**Coefficient (CI)**	**P (coefficient)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	-0.11 (-0.35 to 0.13)	0.359016	-0.03 (-0.31 to 0.26)	0.853727	24.615	0.026
End year (centered)	-0.04 (-0.28 to 0.20)	0.726323	-0.02 (-0.07 to 0.04)	0.592742	27.642	0.010
Mesial temporal sclerosis (MTS=0)	-0.26 (-0.75 to 0.24)	0.316342	0.25 (-0.32 to 0.81)	0.387887	27.177	0.009
Tumor (Tumor = 0)	0.57 (-0.32 to 1.46)	0.211983	-0.67 (-1.60 to 0.25)	0.152673	25.882	0.018
Standard (St = 0)	**0.14 (-0.14 to 0.42)**	**0.340748**	**-0.62 (-1.13 to –0.12)**	**0.014820**	**21.985**	**0.056**
Tailored (Tailored = 0)	**-0.59 (-1.07 to –0.11)**	**0.015064**	**0.70 (0.15 to 1.24)**	**0.0124402**	**21.683**	**0.060**
Treatment age (centered)	**-0.12 (-0.36 to 0.12)**	**0.338682**	**-0.03 (-0.05 to 0.00)**	**0.053711**	**24.239**	**0.029**
United States (USA = 0)	-0.14 (-0.54 to 0.26)	0.491480	0.12 (-0.37 to 0.61)	0.629453	27.693	0.010
Left side (centered)	**-0.09 (-0.33 to 0.15)**	**0.454805**	**-0.02 (-0.03 to 0.01)**	**0.075197**	**24.697**	**0.025**

Average start year = 1985.7
Average end year = 1992.3
Average treatment age = 26.68
Average left = 50.6

Evidence Table 133. Results of meta-regression of studies of temporal lobe surgery reporting percentage of male and female patients among patients with successful and nonsuccessful surgery (continued)

Two predictor models: Standard and year plus one other variable					Bolded in this table = homogeneous				
Covariate: B_1	**Covariate: B_2**	**Intercept (CI)**	**P (intercept) =**	**Coefficient B_1 (CI)**	**P (B_1) =**	**Coefficient B_2 (CI)**	**P(B_2)**	**Q_e =**	**P (Q_e) =**
Standard (St = 0)	Start year (centered)	0.08 (-0.21 to 0.37)	0.579398	-0.60 (-1.10 to –0.10)	0.019348	-0.02 (-0.05 to 0.00)	0.097903	19.135	0.084
Standard (St = 0)	End year (centered)	0.23 (-0.08 to 0.54)	0.146365	-0.76 (-1.29 to –0.22)	0.005391	-0.04 (-0.10 to 0.02)	0.149786	19.870	0.070
Standard (St = 0)	MTS (MTS=0)	-0.13 (-0.64 to 0.38)	0.607917	-0.67 (-1.18 to –0.17)	0.009323	0.37 (-0.20 to 0.94)	0.208745	20.405	0.060
Standard (St = 0)	**Tumor (tumor = 0)**	**1.48 (0.44 to 2.53)**	**0.005361**	**-0.92 (-1.46 to –0.37)**	**0.001012**	**-1.35 (-2.35 to –0.34)**	**0.008741**	**15.108**	**0.236**
Standard (St = 0)	Tailored (tailored = 0)	-0.29 (-1.30 to 0.72)	0.573474	-0.30 (-1.19 to 0.58)	0.504500	0.43 (-0.54 to 1.39)	0.387611	21.238	0.047
Standard (St = 0)	Treatment age (centered)	0.07 (-0.22 to 0.76)	0.618834	-0.58 ()-1.09 to –0.08)	0.023037	-0.02 (-0.05 to 0.00)	0.093667	19.076	0.087
Standard (St = 0)	United States (USA = 0)	0.20 (-0.28 to 0.69)	0.413259	-0.65 (-1.18 to –0.12)	0.015872	-0.09 (-0.61 to 0.43)	0.745048	21.880	0.039
Standard (St = 0)	Left (left = 0)	0.09 (-0.21 to 0.40)	0.561171	-0.52 (-1.08 to 0.04)	0.067680	-0.08 (-0.09 to –0.06)	<0.000001	21.368	0.045
Tailored (Tailored = 0)	**Start year (centered)**	**-0.65 (-1.13 to –0.17)**	**0.008273**	**0.70 (0.16 to 0.00)**	**0.011632**	**-0.30 (-0.06 to 0.00)**	**0.061406**	**18.245**	**0.108**
Tailored (Tailored = 0)	End year (centered)	-0.61 (-1.09 to –0.13)	0.012149	0.77 (0.21 to 1.34)	0.007076	-0.03 (-0.09 to 0.02)	0.255782	20.376	0.060
Tailored (Tailored = 0)	MTS (MTS=0)	-1.10 (-1.86 to –0.34)	0.004654	0.84 (0.27 to 1.42)	0.003879	0.51 (-0.08 to 1.10)	0.092632	18.861	0.092
Tailored (Tailored = 0)	Tumor (tumor = 0)	0.15 (-0.79 to 1.09)	0.760981	0.77 (0.21 to 1.32)	0.006644	-0.85 (-1.78 to 0.09)	0.074982	18.507	0.101
Tailored (Tailored = 0)	**Treatment age (centered)**	**-0.67 (-1.16 to –0.19)**	**0.006435**	**0.72 (0.18 to 1.27)**	**0.009648**	**-0.03 (-0.06 to 0.00)**	**0.042434**	**17.518**	**0.131**

Evidence Table 133. Results of meta-regression of studies of temporal lobe surgery reporting percentage of male and female patients among patients with successful and nonsuccessful surgery (continued)

Two predictor models: Standard and year plus one other variable					Bolded in this table = homogeneous				
Covariate: B_1	**Covariate: B_2**	**Intercept (CI)**	**P (intercept)=**	**Coefficient B_1 (CI)**	**P (B_1) =**	**Coefficient B_2 (CI)**	**P(B_2)**	**Q_e =**	**P (Q_e) =**
Tailored (Tailored = 0)	United States (USA = 0)	0.56 (-1.09 to –0.04)	0.034766	0.72 (0.15 to 1.29)	0.013569	-0.07 (-0.58 to 0.45)	0.801865	21.620	0.042
Tailored (Tailored = 0)	Left (centered)	-0.54 (-1.02 to –0.05)	0.029525	0.60 (0.03 to 1.17)	0.038490	-0.01 (-0.03 to 0.01)	0.269959	20.490	0.060
Treatment age (centered)	Start year (centered)	-0.13 (-0.37 to 0.11)	0.300278	-0.02 (-0.05 to 0.02)	0.289714	-0.02 (-0.05 to 0.02)	0.403631	23.516	0.024
Treatment age (centered)	End year (centered)	-0.11 (-0.36 to 0.14)	0.386278	-0.03 (-0.05 to 0.00)	0.060675	0.00 (-0.06 to 0.05)	0.883014	24.217	0.019
Treatment age (centered)	MTS (MTS=0)	-0.26 (-0.76 to 0.24)	0.312923	-0.03 (-0.05 to 0.00)	0.069978	0.18 (-0.39 to 0.75)	0.531492	23.846	0.021
Treatment age (centered)	Tumor (tumor = 0)	0.54 (-0.35 to 1.43)	0.235524	-0.03 (-0.06 to 0.00)	0.049363	-0.71 (-1.63 to 0.22)	0.133582	21.989	0.038
Treatment age (centered)	United States (USA = 0)	-0.22 (-0.63 to 0.19)	0.257560	-0.03 (-0.06 to 0.00)	0.057296	0.16 (0.34 to 0.65)	0.5432915	23.851	0.021
Treatment age (centered)	Left (centered)	-0.17 (-0.42 to 0.07)	0.168086	-0.03 (-0.06 to –0.01)	0.016665	-0.02 (-0.04 to 0.00)	0.020548	18.996	0.089
Left (centered)	**Start year (centered)**	**-0.19 (-0.43 to 0.06)**	**0.138223**	**-0.02 (-0.04 to –0.01)**	**0.007930**	**-0.04 (-0.07 to –0.01)**	**0.008234**	**17.845**	**0.120**
Left (centered)	End year (centered)	0.85 (0.60 to 1.10)	<0.000001	-0.02 (-0.04 to 0.00)	0.022466	-1.02 (-1.99 to 0.05)	0.038476	20.411	0.0597
Left (centered)	MTS (MTS=0)	-0.28 (-0.79 to 0.22)	0.269997	-0.02 (-0.03 to 0.00)	0.070488	0.25 (-0.32 to 0.82)	0.390991	23.952	0.020
Left (centered)	Tumor (tumor = 0)	-0.04 (-0.28 to 0.20)	0.717057	-0.02 (-0.05 to 0.00)	0.017863	-0.06 (-0.12 to 0.01)	0.086814	21.3701	0.041
Left (centered)	United States (USA = 0)	-0.10 (-0.50 to 0.31)	0.641064	-0.02 (-0.03 to 0.00)	0.089033	0.01 (-0.50 to 0.52	0.971889	24.695	0.016

Evidence Table 134. Studies of temporal lobe surgery reporting the number of left-sided and right-sided operations with successful and nonsuccessful surgery outcome measurements

Reference	N	Seizure Outcome Measurement	Left Side	Left Side Successes	Right Side	Right Side Successes	Cohen's h Effect Sizes	95% Confidence Interval		p Values for Effect Sizes	Standardized Residuals for Effect Sizes
								Lower	Upper		
Bouilleret (2002)	18	Seizure-free no auras	8	7	10	5	0.85	-0.08	1.78	0.073797	1.98
Hennessy (2001)	80	Seizure-free with auras	38	25	42	27	0.03	-0.41	0.47	0.887980	0.50
Sotero de Menezes (2001)	14	Seizure-free with auras	5	2	9	4	-0.09	-1.18	1.00	0.871789	-0.04
Verma (2001)	13	Seizure-free with auras	6	3	7	6	-0.80	-1.89	0.29	0.152705	-1.33
Eberhardt (2000)	20	Seizure-free no auras	11	3	9	4	-0.36	-1.24	0.52	0.422490	-0.66
Holmes (1999)	13	Seizure-free no auras	5	2	8	5	-0.45	-1.57	0.66	0.425779	-0.69
Szabo (1998)	14	Seizure-free with auras	7	5	7	5	0.00	-1.05	1.05	1.000000	0.13
Kilpatrick (1997)	18	Seizure-free with auras	10	6	8	7	-0.65	-1.58	0.28	0.172765	-1.25
Schwartz (1997)	13	Seizure-free no auras	7	4	6	3	0.14	-0.95	1.23	0.796671	0.39
Sisodiya (1997)	27	Engel class I	11	7	16	8	0.28	-0.49	1.04	0.480658	0.91
Adam (1996)	15	Seizure-free no auras	8	4	7	3	0.14	-0.87	1.16	0.781800	0.42
Goldstein (1996)	33	Seizure-free (undefined)	17	6	16	9	-0.42	-1.11	0.26	0.223648	-1.06
Liu (1995)	12	Seizure-free with auras	7	4	5	2	0.34	-0.80	1.49	0.556065	0.72
Vossler (1995)	30	Seizure-free with auras	17	12	13	8	0.19	-0.53	0.91	0.603189	0.74
Berkovic (1991)	10	Seizure-free (undefined)	7	5	3	3	-1.13	-2.48	0.22	0.102162	-1.55

Evidence Table 134. Studies of temporal lobe surgery reporting the number of left-sided and right-sided operations with successful and nonsuccessful surgery outcome measurements (continued)

Reference	N	Seizure Outcome Measurement	Left Side	Left Side Successes	Right Side	Right Side Successes	Cohen's h Effect Sizes	95% Confidence Interval		p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Mizrahi (1990)	22	Seizure-free (undefined)	12	6	10	8	-0.64	-1.48	0.20	0.132866	-1.38
Yeh (1990)	12	Seizure-free with auras	9	8	3	2	0.55	-0.76	1.86	0.408278	0.94
Estes (1988)	25	Seizure-free with auras	13	4	12	5	-0.23	-1.01	0.56	0.570101	-0.41
Delgado-Escueta (1985)	15	Seizure-free no auras	10	7	5	2	0.61	-0.46	1.69	0.263161	1.27

Evidence Table 135. Sensitivity analysis of studies of temporal lobe surgery reporting the number of left side and right side surgeries among patients with successful and nonsuccessful surgery

Sensitivity Adjustment	Cohen's h Summary Estimate [a]	95% Confidence Interval		p value for Summary Estimate	Q	p value for Q	Back-transformed Percentage Estimate [b]	95% Confidence Interval	
		Lower	Upper					Lower	Upper
Original analysis	-0.07	-0.27	0.13	0.49	17.88	0.46	0%	-2%	0%
Removing study with smallest effect size [c]	-0.05	-0.25	0.15	0.65	15.47	0.56	0%	-2%	1%
Removing study with largest effect size	-0.11	-0.32	0.09	0.27	13.96	0.67	0%	-3%	0%
Removing study with smallest N	-0.05	-0.25	0.15	0.65	15.47	0.56	0%	-2%	1%
Removing study with largest N	-0.10	-0.32	0.13	0.40	17.62	0.41	0%	-3%	0%

[a] A positive summary estimate favors left side surgery patients achieving more successful surgeries.
[b] The back-transformed percentage estimate is the difference between the percentage of left side surgery patients who achieved successful surgery and the percentage of right side surgery patients who achieved successful surgery. A positive percentage favors left side surgeries and a negative percentage favors right side surgeries. A difference of 0% indicates no differences between left side and right side patients in achieving successful surgery.
[c] The study with the smallest effect size also had the smallest N.

Evidence Table 136. Studies of temporal lobe surgery reporting number of simple partial seizure (SPS) patients with successful and nonsuccessful surgery.

Reference	N	Seizure Outcome Measurement	SPS Patients	SPS Successes	Non-SPS Patients	Non-SPS Successes	Cohen's h Effect Sizes	95% Confidence Interval		p Values for Effect Sizes	Standardized Residuals for Effect Sizes
								Lower	Upper		
Bouilleret (2002)	18	Seizure-free no auras	16	10	2	2	-1.32	-2.79	0.15	0.078835	-1.97
Hennessy (2001)	80	Seizure-free with auras	23	18	57	34	0.41	-0.08	0.89	0.099855	2.24
Berkovic (1991)	10	Seizure-free (undefined)	9	7	1	1	-0.98	-3.05	1.08	0.351655	-1.05
Yeh (1990)	12	Seizure-free with auras	3	2	9	8	-0.55	-1.86	0.76	0.408278	-1.03
Drake (1987)	11	Seizure-free (undefined)	3	2	8	5	0.09	-1.24	1.41	0.897564	-0.02

Evidence Table 137. Sensitivity analysis of studies of temporal lobe surgery reporting the percentage of patients with simple partial seizures among patients with successful and nonsuccessful surgery

Sensitivity Adjustment	Cohen's h Summary Estimate [a]	95% Confidence Interval		p value for Summary Estimate	Q	p value for Q	Back-transformed Percentage Estimate [b]	95% Confidence Interval	
		Lower	Upper					Lower	Upper
Original analysis	0.10	-0.30	0.51	0.62	7.12	0.13	0%	-2%	6%
Removing study with smallest effect size	0.22	-0.20	0.64	0.31	3.25	0.36	1%	-1%	10%
Removing study with largest effect size [c]	-0.60	-1.34	0.13	0.11	2.08	0.55	-9%	-39%	0%
Removing study with smallest N	0.14	-0.27	0.56	0.49	6.02	0.11	0%	-2%	8%
Removing study with largest N [c]	-0.60	-1.34	0.13	0.11	2.08	0.55	-9%	-39%	0%

[a] A positive summary estimate favors patients who have simple partial seizures achieving more successful surgeries.
[b] The back-transformed percentage estimate is the difference between the percentage of patients with simple partial seizures who achieved successful surgery and the percentage of patients without simple partial seizures who achieved successful surgery. A positive percentage favors patients with simple partial seizures and a negative percentage favors patients without simple partial seizures. A difference of 0% indicates no differences between patients with or without simple partial seizures in achieving successful surgery.
[c] The study with the largest effect size also had the largest N.

Evidence Table 138. Studies of temporal lobe surgery reporting number of secondarily generalized seizure (SGS) patients with successful and nonsuccessful surgery

Reference	N	Seizure Outcome Measurement	SGS Patients	SGS Successes	Non-SGS Patients	Non-SGS Successes	Cohen's h Effect Sizes	95% Confidence Interval		p Values for Effect Sizes	Standardized Residuals for Effect Sizes
								Lower	Upper		
Hennessy (2001)	80	Seizure-free with auras	31	22	49	30	0.21	-0.24	0.66	0.368647	2.15
Hennessy (2001)	116	Seizure-free with auras	57	31	59	47	-0.55	-0.91	-0.18	0.003215	-2.61
Liu (1995)	12	Seizure-free with auras	8	3	4	3	-0.78	-1.98	0.42	0.204920	-0.96
Berkovic (1991)	10	Seizure-free (undefined)	4	4	6	4	1.23	-0.03	2.50	0.056521	2.26
Yeh (1990)	12	Seizure-free with auras	10	8	2	2	-0.93	-2.45	0.59	0.231255	-0.95
Drake (1987)	11	Seizure-free (undefined)	7	3	4	4	-1.71	-2.94	-0.49	0.006241	-2.47
Delgado-Escueta (1985)	15	Seizure-free no auras	12	9	3	0	2.09	0.83	3.36	0.001176	3.63

Evidence Table 139. Studies of temporal lobe surgery reporting number of secondarily generalized seizure (SGS) patients with successful and nonsuccessful surgery – data used in meta-regression

Reference	Number of Patients	Cohen's h Effect Size	Weight	Mesial Temporal Sclerosis Patients Only	Tumor Patients Only	Standard Temporal Lobectomy	Tailored Temporal Lobectomy
Hennessy (2001)	80	0.2063	18.9875	No	No	Yes	No
Hennessy (2001)	116	-0.5472	28.9914	Yes	No	Yes	No
Liu (1995)	12	-0.7763	2.6667	No	No	No	Yes
Berkovic (1991)	10	1.231	2.4	Yes	No	Yes	No
Yeh (1990)	12	-0.9273	1.6667	No	Yes	No	No
Drake (1987)	11	-1.7141	2.5455	No	Yes	No	Yes
Delgado-Escueta (1985)	15	2.0944	2.4	No	No	Yes	No

Evidence Table 140. Results of meta-regression of studies of temporal lobe surgery reporting the number of patients with secondarily generalized seizures among patients with successful and nonsuccessful surgery

One predictor variable	Bolded = statistically significant coefficient					
Covariate	**Intercept (CI)**	**P (intercept)**	**Coefficient (CI)**	**P (coefficient)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	-1.96 (-2.28 to -1.64)	<0.000001	0.00 (-0.09 to 0.09)	0.966950	31.779	<0.0000017
End year (centered)	0.06 (-0.35 to 0.47)	0.780259	-0.06 (-0.13 to 0.01)	0.116190	29.312	0.000020
MTS (MTS=0)	**-0.41 (-0.76 to -0.06)**	**0.021420**	**0.45 (-0.06 to 0.95)**	**0.086312**	**28.831**	**0.000020**
Tumor (Tumor = 0)	**-1.40 (-2.36 to -0.45)**	**0.003970**	**1.29 (0.30 to 2.28)**	**0.010444**	**25.277**	**0.000126**
Standard (St = 0)	**-0.08 (-0.34 to 0.19)**	**0.584601**	**-1.09 (-1.88 to -0.29)**	**0.007470**	**24.620**	**0.000165**
Tailored (Tailored = 0)	**-1.23 (-2.09 to -0.38)**	**0.004862**	**1.13 (0.23 to 2.03)**	**0.013471**	**25.674**	**0.000103**
Treatment age (centered)	-0.24 (-0.52 to 0.05)	0.101922	-0.01 (-0.07 to 0.04)	0.574820	31.462	0.000008
United States (USA = 0)	**0.58 (-0.29 to 1.45)**	**0.189245**	**-0.86 (-1.77 to 0.05)**	**0.065196**	**28.380**	**0.000031**
Percent male (centered)	-0.23 (-0.50 to 0.04)	0.096627	-0.01 (-0.04 to 0.02)	0.543944	31.413	0.000008
Percent simple partial seizures	-0.20 (-0.47 to 0.08)	0.164976	0.00 (-0.03 to 0.03)	0.916759	31.770	0.000007
Percent generalized seizures	-0.29 (-0.65 to 0.06)	0.107075	-0.01 (-0.03 to 0.01)	0.462774	31.251	0.000008

Evidence Table 140. Results of meta-regression of studies of temporal lobe surgery reporting the number of patients with secondarily generalized seizures among patients with successful and nonsuccessful surgery (continued)

Two predictor variables: start year plus one variable

Bolded in this table = both coefficients significant, Italicized and bolded = both coefficients significant and MR homogeneous

Covariate: B_1	Covariate: B_2	Intercept (CI)	P (intercept)	Coefficient B_1 (CI)	P (B_1) =	Coefficient B_2 (CI)	P(B_2)	Q_e =	P (Q_e) =
MTS (MTS = 0)	**Tumor (Tumor = 0)**	**-2.10 (-3.19 to –1.01)**	**0.000166**	**0.70 (0.17 to 1.23)**	**0.010168**	**1.69 (0.65 to 2.72)**	**0.001381**	**18.611**	**0.000937**
MTS (MTS = 0)	Standard (St = 0)	-0.41 (-0.76 to –0.06)	0.021115	0.83 (0.28 to 1.38)	0.003086	-1.58 (-2.44 to –0.72)	0.000318	15.869	0.0032
MTS (MTS = 0)	**Tailored (Tailored = 0)**	**-1.97 (-2.98 to –0.95)**	**0.000143**	**0.73 (0.19 to 1.27)**	**0.007651**	**1.56 (0.60 to 2.57)**	**0.001340**	**18.594**	**0.000964**
MTS (MTS = 0)	Treatment age (centered)	-0.42 (-0.78 to –0.06)	0.022014	0.43 (-0.09 to 0.95)	0.101515	-0.01 (-0.06 to 0.05)	0.834629	28.787	0.000009
MTS (MTS = 0)	United States (USA = 0)	0.26 (-0.76 to 1.28)	0.621027	0.33 (-0.221 to 0.86)	0.235274	-0.67 (-1.63 to 0.29)	0.172392	26.968	0.000020
MTS (MTS = 0)	Percent male (centered)	-0.41 (-0.76 to –0.06)	0.021216	0.44 (-0.10 to 0.97)	0.107418	0.00 (-0.03 to 0.03)	0.936807	28.824	0.000009
MTS (MTS = 0)	Percent simple	-0.42 (-0.77 to –0.07)	0.018427	0.62 (0.03 to 1.20)	0.0404442	-0.02 (-0.06 to 0.02)	0.266268	27.575	0.000015
MTS (MTS = 0)	Percent CGE	-0.52 (-0.96 to –0.09)	0.019117	0.46 (-0.05 to 0.97)	0.077299	-0.01 (-0.03 to 0.01)	0.401950	28.129	0.000012
MTS (MTS = 0)	Start year (centered)	-0.41 (-0.81 to –0.01)	0.046672	0.45 (-0.06 to 0.95)	0.086060	0.00 (-0.09 to 0.09)	0.980949	28.830	0.000009
MTS (MTS = 0)	End year (centered)	-0.18 (-0.72 to 0.36)	0.521359	0.36 (-0.18 to 0.89)	0.189704	-0.04 (-0.12 to 0.003)	0.267427	27.596	0.000015
Tumor (Tumor = 0)	Standard (St = 0)	0.70 (-2.26 to 0.85)	0.376850	0.63 (-0.91 to 2.16)	0.423728	-0.70 (-1.93 to 0.53)	0.264120	23.979	0.000081
Tumor (Tumor = 0)	Tailored (Tailored = 0)	-1.69 (-2.73 to –0.65)	0.001444	0.89 (-0.26 to 2.04)	0.128514	0.73 (-0.32 to 1.77)	0.172070	23.361	0.000107

Evidence Table 140. Results of meta-regression of studies of temporal lobe surgery reporting the number of patients with secondarily generalized seizures among patients with successful and nonsuccessful surgery (continued)

Two predictor variables: start year plus one variable (continued)

Bolded in this table = both coefficients significant, Italicized and bolded = both coefficients significant and MR homogeneous

Covariate: B_1	Covariate: B_2	Intercept (CI)	P (intercept)	Coefficient B_1 (CI)	P (B_1) =	Coefficient B_2 (CI)	P(B_2)	Q_e =	P (Q_e) =
Tumor (Tumor = 0)	Treatment age (centered)	-1.46 (-2.43 to –0.49)	0.003117	1.31 (0.32 to 2.30)	0.009589	-0.02 (-0.07 to 0.03)	0.490667	24.753	0.000056
Tumor (Tumor = 0)	United States (USA = 0)	-0.64 (-1.96 to 0.68)	0.341773	1.22 (0.23 to 2.22)	0.015783	-0.76 (-1.68 to 0.15)	0.102166	22.554	0.000156
Tumor (Tumor = 0)	Percent male (centered)	-1.50 (-2.52 to –0.49)	0.003679	1.44 (0.33 to 2.54)	0.010665	0.01 (-0.02 to 0.04)	0.563892	24.896	0.000053
Tumor (Tumor = 0)	Percent simple	-1.49 (-2.50 to –0.48)	0.003880	1.36 (0.34 to 2.38)	0.009061	0.01 (-0.02 to 0.04)	0.608476	24.964	0.000051
Tumor (Tumor = 0)	Percent CGE	-1.52 (-2.52 to –0.52	0.002871	1.55 (0.37 to 2.72)	0.010040	0.01 (-0.02 to 0.04)	0.434255	24.625	0.000060
Tumor (Tumor = 0)	Start year (centered)	-1.39 (-2.35 to –0.43)	0.004522	1.32 (0.32 to 2.32)	0.00961	0.02 (-0.07 to 0.11)	0.697709	25.077	0.000049
Tumor (Tumor = 0)	**End year (centered)**	**-1.83 (-2.77 to –0.89)**	**0.000142**	**2.52 (1.38 to 3.67)**	**0.000016**	**-0.16 (-0.24 to –0.08)**	**0.000140**	**12.157**	**0.016221**
Standard (St = 0)	Tailored (Tailored = 0)	-0.38 (-2.15 to 1.38)	0.671466	-0.85 (-2.39 to 0.69)	0.278810	0.31 (-1.44 to 2.05)	0.730062	24.501	0.000063
Standard (St = 0)	Treatment age (centered)	-0.04 (-0.36 to 0.29)	0.830962	-1.16 (-2.01 to –0.30)	0.007991	0.01 (-0.04 to 0.07)	0.655440	24.423	0.000066
Standard (St = 0)	**United States (USA = 0)**	**1.44 (0.46 to 2.42)**	**0.004075**	**-1.63 (-2.49 to –0.76)**	**0.000222**	**-1.59 (-2.58 to –0.60)**	**0.001663**	**14.728**	**0.005300**
Standard (St = 0)	Percent male (centered)	-0.09 (-0.38 to 0.20)	0.529649	-1.07 (-1.87 to –0.27)	0.008599	0.00 (-0.04 to 0.03)	0.745227	24.513	0.000063
Standard (St = 0)	Percent simple	-0.04 (-0.34 to 0.25)	0.781214	-1.12 (-1.92 to –0.31	0.006384	-0.01 (-0.04 to 0.02)	0.596896	24.337	0.000068

Evidence Table 140. Results of meta-regression of studies of temporal lobe surgery reporting the number of patients with secondarily generalized seizures among patients with successful and nonsuccessful surgery (continued)

Two predictor variables: start year plus one variable (continued)

Bolded in this table = both coefficients significant, Italicized and bolded = both coefficients significant and MR homogeneous

Covariate: B_1	Covariate: B_2	Intercept (CI)	P (intercept)	Coefficient B_1 (CI)	P (B_1) =	Coefficient B_2 (CI)	P(B_2)	Q_e =	P (Q_e) =
Standard (St = 0)	Percent CGE	0.20 (-0.29 to 0.68)	0.426228	-1.54 (-2.59 to –0.50)	0.003776	-0.02 (-0.05 to 0.01)	0.179913	22.870	0.00134
Standard (St = 0)	Start year (centered)	0.13 (-0.26 to 0.51)	0.521675	-1.39 (-2.29 to –0.49)	0.002344	0.07 (-0.03 to 0.18)	0.147246	22.531	0.000157
Standard (St = 0)	**End year (centered)**	**0.82 (0.28 to 1.35)**	**0.002696**	**-2.17 (-3.14 to –1.20)**	**0.000012**	**-0.17 (-0.25 to –0.08)**	**0.000146**	**22.531**	**0.038118**
Tailored (Tailored = 0)	Treatment age (centered)	-1.24 (-2.09 to 0.38)	0.004783	1.12 (0.21 to 2.03)	0.015741	-0.01 (-0.06 to 0.05)	0.836505	25.631	0.000038
Tailored (Tailored = 0)	**United States (USA = 0)**	**-0.35 (-1.35 to 0.64)**	**0.487119**	**1.98 (0.96 to 3.00)**	**0.000147**	**-1.81 (-2.84 to –0.77)**	**0.000619**	**13.960**	**0.007424**
Tailored (Tailored = 0)	Percent male (centered)	-1.26 (-2.13 to –0.40)	0.004135	1.13 (0.23 to 2.03)	0.013545	-0.01 (-0.04 to 0.02)	0.548722	25.317	0.000043
Tailored (Tailored = 0)	Percent simple	-1.27 (-2.13 to –0.41)	0.003935	1.22 (0.29 to 2.15)	0.010041	-0.01 (-0.05 to 0.02)	0.461415	25.137	0.000047
Tailored (Tailored = 0)	Percent CGE	-1.26 (-2.13 to –0.39)	0.004449	1.22 (0.22 to 2.22)	0.016733	0.00 (-0.2 to 0.03)	0.698106	25.521	0.000040
Tailored (Tailored = 0)	Start year (centered)	-1.26 (-2.12 to –0.40)	0.004139	1.26 (0.31 to 2.20)	0.009042	0.04 (-0.05 to 0.13)	0.400510	24.967	0.000051
Tailored (Tailored = 0)	**End year (centered)**	**-1.32 (-2.18 to –0.45)**	**0.002739**	**1.83 (0.82 to 2.84)**	**0.000369**	**-0.12 (-0.20 to –0.40)**	**0.002625**	**16.626**	**0.00285**
United States (USA = 0)	**Treatment age (centered)**	**1.00 (0.03 to 1.96)**	**0.042543**	**-1.48 (-2.59 to –0.38)**	**0.008544**	**-0.06 (-0.12 to 0.00)**	**0.051456**	**24.549**	**0.000062**
United States (USA = 0)	Percent male (centered)	0.58 (-0.29 to 1.45)	0.190020	-0.90 (-1.81 to 0.02)	0.054632	-0.01 (-0.04 to 0.02)	0.412989	27.716	0.000014

Evidence Table 140. Results of meta-regression of studies of temporal lobe surgery reporting the number of patients with secondarily generalized seizures among patients with successful and nonsuccessful surgery (continued)

Two predictor variables: start year plus one variable (continued)

Bolded in this table = both coefficients significant, Italicized and bolded = both coefficients significant and MR homogeneous

Covariate: B_1	Covariate: B_2	Intercept (CI)	P (intercept)	Coefficient B_1 (CI)	P (B_1) =	Coefficient B_2 (CI)	P(B_2)	Q_e =	P (Q_e) =
United States (USA = 0)	Percent simple	0.96 (-0.06 to 1.99)	0.066008	-1.38 (-2.55 to –0.20)	0.021714	0.03 (-0.01 to 0.07)	0.169206	26.506	0.000025
United States (USA = 0)	**Percent CGE**	**1.05 (0.10 to 1.99)**	**0.029933**	**-1.81 (-2.99 to –0.62)**	**0.002728**	**-0.04 (-0.07 to –0.01)**	**0.014582**	**22.274**	**0.000177**
United States (USA = 0)	Start year (centered)	0.58 (-0.29 to 1.45)	0.191861	-0.89 (-1.83 to 0.04)	0.060169	-0.02 (-0.11 to .007)	0.715934	28.248	0.000011
United States (USA = 0)	End year (centered)	0.53 (-0.36 to 1.41)	0.245352	-0.65 (-1.75 to 0.45)	0.244482	-0.03 (-0.11 to 0.06)	0.516362	27.956	0.000013

Evidence Table 141. Studies of temporal lobe surgery reporting quality of life outcome measurements

Epilepsy Surgery Inventory					
Reference	**Number of Patients**	**Surgery**	**Followup (Years)**	**Mean Overall Quality of Life Score**	**SD of Overall Score**
Rose (1996)	47	Standard temporal lobectomy	0	60.5	19.0
			2	57.7	20.7

The study found no significant difference in overall quality of life scores measured prior to or 2 years after surgery, but reported that patients with low preoperative scores showed the greatest improvement in postoperative scores.

Quality of Life in Epilepsy					
Reference	**Number of Patients**	**Surgery**	**Followup (Years)**	**Mean Global Score**	**SD of Global Score**
Markand (2000)	53	Tailored temporal lobectomy	0	47	10
	51		2	54	12
	37	Control	0	42	10.1
	33		2	40	12

The study found that the baseline overall score was significantly higher in the surgery group. At 2 years after surgery the overall score was significantly improved in the surgery group compared to baseline and the control group. The improvement in the surgery group was almost entirely due to patients who became completely seizure-free. Patients who were free of complex partial seizures but still had auras or who still experienced complex partial seizures had no significant improvement in overall score after surgery.

Evidence Table 142. Studies of temporal lobe surgery reporting employment data

Reference	Number of Patients Evaluated	Mean Followup Time in Years	Minimum Followup	Maximum Followup	Number of Patients Not Able to Obtain Work Prior to Surgery	Number of Patients Able to Obtain Work After Surgery	Number of Patients Working Prior to Surgery	Number of Patients Able to Remain at Work After Surgery
Boling (2001)	18	5.3	2		1	0	13	9
Reeves (1997)	134	4.2	2.5	6.5	20	7	67	57
Sperling (1995)	73	2			28	15	33	30
Mizrahi (1990)	22	5.3	2	8	5	3	4	3
Delgado-Escueta (1985)	15	6	2	11	3	3	8	7

Evidence Table 143. Studies of temporal lobe surgery reporting the ability to attend or remain in school after surgery

Reference	N	Surgery	Followup (Years)	Minimum Followup	Maximum Followup	Number of Patients			
						Did Not Attend School Prior to Surgery	Able to Attend School After Surgery	Attending School Prior to Surgery	Able to Remain in School or Obtain Employment After Surgery
Mizrahi (1990)	22	Tailored temporal lobectomy	5.3	2	8	0	0	11	11
Delgado-Escueta (1985)	15	Standard temporal lobectomy	6	2	11	1	1	2	2

In Mizrahi, all eleven patients attending school at the time of surgery showed improvement in school or obtained employment at the time of followup. In Delgado-Escueta, only three patients were of school age; all showed improvement in schoolwork after surgery.

Evidence Table 144. Studies of temporal lobe surgery reporting ability to obtain a driver's license after surgery

Reference	Number of Patients	Surgery	Followup (Years)	Minimum Followup Time	Maximum Followup Time	Number of Patients Able to Obtain a Drivers License After Surgery
Reeves (1997)	134	Standard	4.2	2.5	6.5	89 (66%)

The number of patients who were driving increased significantly after surgery; 16% compared to 66%.

Evidence Table 145. Studies reporting new cases of depression after temporal lobe surgery

Reference	Number of Patients	Years	Country	Method of Diagnosis
Kanemoto (2001)	52	1987-1999	Japan	Mood disorder due to a general medical condition that fulfilled the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) criteria
Kohler (2001)	58	1986-1999	United States	Neurologic and neuropsychological evaluations were used to determine the presence of psychiatric symptoms meeting the severity criteria for mood and anxiety disorders as classified in the DSM-IV, including major depression and depression not otherwise specified.
Nees (2001)	50	1992-1994	England	Data derived from standard interviews on all patients by a clinical psychiatrist were used to make a diagnosis of depression.
Wiebe (2001)	36	1996-2000	Canada	Depression was assessed with the depression scale of the Center for Epidemiological Studies-Depression Scale (CES-D)
Anhoury (2000)	109	1988-1997	England	Clinical diagnoses of mood disorders were made by experienced psychiatrists with an interest in epilepsy.
Derry (2000)	39	1996-1998	Canada	The CES-D was used to define clinical depression for the purposes of this study.
Altshuler (1999)	49	1974-1990	United States	Patients were administered the Structured Clinical Interview for DSM-III-R that assesses current and past psychopathology for evidence of depression.
Ring (1998)	60	1995-1996	England	Depression was defined according to DSM-IV criteria, but as if there were no associated general medical condition.
Naylor (1994)	37	1987-1991	Denmark	Patients were diagnosed as having moderate or severe depressive episodes before or after surgery using the criteria of the International Classification of Diseases-10th revision.
Bladin (1992)	107	1975-1991	Australia	DSM-III criteria were used to diagnose depression.

Evidence Table 146. Patient characteristics for studies of temporal lobe surgery reporting new cases of depression

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Kanemoto (2001)	52	Standard	Not reported	27.1	5.9	9.7	5.3	17.5	7.8
Kohler (2001)	58	Standard	Various	32.3	10.6			17.7	10.3
Nees (2001)	50	Not described	Various	26		8.8			
Wiebe (2001)	36	Standard	Various	34.4	9.9	16.2	10		
Anhoury (2000)	109	Not described	Various	30.1	7.4				
Derry (2000)	39	Standard	Not reported	31.2	1	12.1	10	18.8	9.2
Altshuler (1999)	49	Standard	Mesial temporal sclerosis	40	5.5	11.4	8.3	17.6	4.3
Ring (1998)	60	Not described	Not reported	27	7.4				
Naylor (1994)	37	AH	Various	29.1	9.1	11.5	10.3	17.6	8.2
Bladin (1992)	107	Standard	Not reported						

AH Amygdalohippocampectomy

Evidence Table 146. Patient characteristics for studies of temporal lobe surgery reporting new cases of depression (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Number of Patients With Simple Partial Seizures
Kanemoto (2001)	22	30	28	24	
Kohler (2001)	27	31	20	38	44
Nees (2001)	31	19	17	33	
Wiebe (2001)	12	24	21	19	
Anhoury (2000)			50	71	
Derry (2000)	18	21	16	23	
Altshuler (1999)	23	26	23	26	
Ring (1998)	36	24	21	39	
Naylor (1994)			22	15	
Bladin (1992)	62	48	46	64	

Evidence Table 147. Results of meta-analysis of studies of temporal lobe surgery reporting new cases of depression after surgery

Reference	Number of Patients	Number of New Cases of Depression After Treatment	Percentage	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Kanemoto (2001)	52	2	3.8	0.39	0.01—0.78	0.044109	-1.66
Kohler (2001)	58	6	10.3	0.65	0.29—1.02	0.000421	-0.29
Nees (2001)	50	14	28.0	1.12	0.72—1.51	<0.000001	2.14
Wiebe (2001)	36	7	19.4	0.91	0.45—1.38	0.000107	0.91
	40 – control patients	8	20.0	---	---	---	---
Anhoury (2000)	109	26	23.9	1.02	0.76—1.29	<0.000001	2.57
Derry (2000)	39	4	10.3	0.65	0.21—1.10	0.003988	-0.25
Altshuler (1999)	49	5	10.2	0.65	0.25—1.05	0.001288	-0.29
Ring (1998)	60	7	11.7	0.70	0.34—1.06	0.000134	-0.05
Naylor (1994)	37	2	5.4	0.47	0.01—0.92	0.043542	-1.05
Bladin (1992)	107	5	4.7	0.44	0.17—0.70	0.001436	-2.18

Evidence Table 148. Studies of temporal lobe surgery reporting new cases of depression after surgery – data used in meta-regression

Reference	Number of Patients	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	Mesial Temporal Sclerosis Patients Only	Standard Temporal Lobectomy	Age at Surgery	Conducted in the United States
Kanemoto (2001)	52	0.3948	26	1987	1999	No	Yes	27.1	No
Kohler (2001)	58	0.6549	29	1986	1999	No	Yes	32.3	Yes
Nees (2001)	50	1.1152	25	1992	1994	No	Yes	26	No
Wiebe (2001)	36	0.9133	18	1996	2000	No	Yes	34.4	No
Anhoury (2000)	109	1.0205	54.5	1988	1997	No	Yes	30.1	No
Derry (2000)	39	0.652	19.5	1996	1998	No	Yes	31.2	No
Altshuler (1999)	49	0.6503	24.5	1974	1990	Yes	Yes	40	Yes
Ring (1998)	60	0.6972	30	1995	1996	No	Yes	27	No
Naylor (1994)	37	0.4693	18.5	1987	1991	No	No	29.1	No
Bladin (1992)	107	0.4358	53.5	1975	1991	No	Yes	30.8	No

Evidence Table 149. Results of meta-regression of studies of temporal lobe surgery reporting new cases of depression after surgery

One predictor variable Bolded = statistically significant coefficient						
Covariate	**Intercept (CI)**	**P (intercept) =**	**Coefficient (CI)**	**P (coefficient)**	**Q_e =**	**P (Q_e) =**
Start year (centered)t	**0.73 (0.61 to 0.84)**	**<0.000001**	**0.02 (0.00 to 0.03)**	**0.034561**	**13.400**	**0.099**
End year (centered)	0.71 (0.60 to 0.83)	<0.000001	0.02 (-0.01 to 0.06)	0.163850	16.060	0.042
Mesial temporal sclerosis (MTS=0)	0.65 (0.25 to 1.05)	0.001318	0.06 (-0.35 to 0.47)	0.773529	17.940	0.022
Standard (St = 0)	0.72 (0.60 to 0.84)	<0.000001	-0.25 (-0.72 to 0.22)	0.293673	16.910	0.031
Treatmet age (centered)	0.71 (0.59 to 0.82)	<0.000001	-0.01 (-0.04 to 0.03)	0.689034	17.964	0.021
United States (USA = 0)	0.65 (0.39 to 0.92)	0.000002	0.06 (-0.23 to 0.36)	0.666754	17.8370	0.022
% Males (centered)	0.70 (0.58 to 0.81)	<0.000001	-0.01 (-0.02 to 0.01)	0.347664	17.0790	0.029

Evidence Table 149. Results of meta-regression of studies of temporal lobe surgery reporting new cases of depression after surgery (continued)

Two predictor variables: Start year plus one variable Bolded = homogeneous only (2nd predictor variable not significant)									
Covariate: B_1	**Covariate: B_2**	**Intercept (CI)**	**P (intercept)**	**Coefficient B_1 (CI)**	**P (B_1) =**	**Coefficient B_2 (CI)**	**P(B_2)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	End year (centered)	0.73 (0.62 to 0.84)	<0.000001	0.02 (0.00 to 0.04)	0.094916	-0.01 (-0.05 to 0.04)	0.821843	13.4900	0.061
Start year (centered)	MTS (MTS=0)	0.92 (0.46 to 1.38)	0.000084	0.02 (0.00 to 0.04)	0.025968	-0.20 (-0.67 to 0.27)	0.397550	12.6830	0.080
Start year (centered)	Standard (St = 0)	0.75 (0.63 to 0.86)	<0.000001	0.02 (0.00 to 0.03)	0.029075	-0.27 (-0.74 to 0.21)	0.268487	12.1720	0.095
Start year (centered)	Treatmet age (centered)	0.74 (0.62 to 0.85)	<0.000001	0.02 (0.00 to 0.04)	0.028560	0.01 (-0.02 to 0.05)	0.464442	12.8680	0.075
Start year (centered)	United States (USA = 0)	0.78 (0.49 to 1.07)	<0.000001	0.02 (0.00 to 0.03)	0.030205	-0.06 (-0.37 to 0.26)	0.729666	13.2810	0.066
Start year (centered)	% Males (centered)	0.72 (0.61 to 0.84)	<0.000001	0.02 (0.00 to 0.03)	0.032570	-0.01 (-0.02 to 0.01)	0.430557	12.7630	0.078

Evidence Table 150. Studies reporting new cases of psychosis after temporal lobe surgery

Reference	N	Years	Country	Exclusion from Surgery	Method of Diagnosis
Kanemoto (2001)	52	1987-1999	Japan	Patients were excluded from surgery if they had chronic psychosis	Psychotic disorder due to a general medical condition that fulfilled the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) criteria
Wiebe (2001)	36	1996-2000	Canada	Patients were excluded from surgery if they had chronic psychosis	Psychopathology was assessed with the General Health Questionnaire
Anhoury (2000)	109	1988-1997	England	Patients were not excluded for psychiatirc disorders	Clinical diagnoses of psychosis were made by experienced psychiatrists with an interest in epilepsy.
Blumer (1998)	44	1994-1995	United States	Patients were not excluded for psychiatirc disorders	Patients were evaluated by a psychiatrist using a standardized psychiatric evaluation developed specifically for patients with epilepsy
Naylor (1994)	37	1987-1991	Denmark	Patients were not excluded for psychiatirc disorders	Patients were diagnosed as having acute psychotic disorder before or after surgery using the criteria of the International Classification of Diseases-10th revision.
Bladin (1992)	107	1975-1991	Australia	Patients were not excluded for psychiatirc disorders	DSM-III criteria were used to diagnose psychoses.

Evidence Table 151. Patient characteristics for studies of temporal lobe surgery reporting new cases of psychosis

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Kanemoto (2001)	52	Standard	Not reported	27.1	5.9	9.7	5.3	17.5	7.8
Wiebe (2001)	36	Standard	Various	34.4	9.9	16.2	10		
Anhoury (2000)	109	Not described	Various	30.1	7.4				
Blumer (1998)	44	Not described	Various	36				20.5	13.2
Naylor (1994)	37	AH	Various	29.1	9.1	11.5	10.3	17.6	8.2
Bladin (1992)	107	Standard	Not reported						

AH Amygdalohippocampectomy

Patient characteristics for studies of temporal lobe surgery reporting new cases of psychosis (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females
Kanemoto (2001)	22	30	28	24
Wiebe (2001)	12	24	21	19
Anhoury (2000)			50	71
Blumer (1998)	22	22	19	25
Naylor (1994)			22	15
Bladin (1992)	62	48	46	64

Evidence Table 152. Studies of temporal lobe surgery reporting new cases of psychosis after surgery

Reference	Number of Patients	New Cases of Psychosis After Treatment	Percentage	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Kanemoto (2001)	52	7	13.5	0.75	0.37—1.14	0.000128	2.09
Wiebe (2001)	36	1	2.8	0.33	-0.13—0.80	0.155362	-0.16
	40 – control patients	1	2.5	---	---	---	---
Anhoury (2000)	109	3	2.8	0.33	0.07—0.60	0.013860	-0.32
Blumer (1998)	44	2	4.5	0.43	0.01—0.85	0.043855	0.30
Naylor (1994)	37	0	0.0	0.00	-0.46—0.46	1.000000	-1.67
Bladin (1992)	107	3	2.8	0.34	0.07—0.60	0.013852	-0.29

Evidence Table 153. Studies of temporal lobe surgery reporting both the number of patients with IQ changes after surgery and the pre-treatment and post-treatment mean IQ

Reference	N	Years	Country	Test Used to Determine IQ	Method Used to Determine Significant Change in IQ
Miranda (2001)	50	1976-1998	Canada	Wechsler Intelligence Scale for Children—Revised, Wechsler Intelligence Scale for Children—III, Wechsler Adult Intelligence Scale—Revised. Used Verbal IQ data for analysis.	A significant change following surgery for epilepsy was defined as two times the value of the average standard error of measurement for each scale.
Robinson (2000)	21	1993-1998	United States	Wechsler Intelligence Scale for Children—III, Wechsler Adult Intelligence Scale—Revised. Used Verbal IQ data for analysis.	A significant individual change was defined as a difference between pre- and postoperative scores greater than 0.5 SDs (>8 points)
Westerveld (2000)	82		United States	Wechsler Intelligence Scale for Children. Used Verbal IQ data for analysis.	The frequency of changes in IQ exceeding two times the value of the standard error of the measurement from each scale was used to determine significant changes (seven points for VIQ).
Chelune (1993)	96	1990-1991	United States	Wechsler Adult Intelligence Scale—Revised. Used Verbal IQ data for analysis.	A significant individual change between pretest and posttest scores was defined as exceeding the reliable change interval of 90% after correction for expected practice effects.
Ivnik (1988)	141	1972-1987	United States	Wechsler Adult Intelligence Scale—Revised. Used Verbal IQ data for analysis.	Changes that are larger than the standard error of the measuring instrument represent cases in which true cognitive change occurred for a specific patient.
Powell (1985)	59	1973-1984	England	Wechsler Adult Intelligence Scale—Revised. Used Verbal IQ data for analysis.	Change in pretest to posttest scores of more than 10 points.

Evidence Table 154. Patient characteristics for studies of temporal lobe surgery reporting individual patient changes in IQ

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Miranda (2001)	50	Not described	Various	13.3	3.4	6.1	4.6	7.3	4.5
Robinson (2000)	22	AH	Various	15.4		5.2		10.3	
Westerveld (2000)	82	Not described	Various	14.4		5.4			
Chelune (1993)	96	Standard	Not reported	29.4	7.4	13.2	9.2	16.5	8.4
Ivnik (1988)	141	Tailored	Not reported	28	7.8	12.9	9.4		
Powell (1985)	59	Standard	Not reported	25.5	9.6	9.6	8		

AH Amygdalohippocampectomy

Patient characteristics for studies of temporal lobe surgery reporting individual patient changes in IQ (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Patients With Secondarily Generalized Seizures
Miranda (2001)	25	25	21	29	
Robinson (2000)	8	14	13	9	
Westerveld (2000)			48	34	
Chelune (1993)	49	47	60	36	
Ivnik (1988)			68	74	54
Powell (1985)	30	29	34	15	

Evidence Table 155. Studies of temporal lobe surgery reporting individual patient changes in verbal IQ after surgery

Reference	Number of Patients	Significant Decrease in IQ					Significant Increase in IQ				
		N	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes	N	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Miranda (2001)	50	7	0.77	0.37—1.16	0.000126	0.61	7	0.77	0.37—1.16	0.000126	0.12
Robinson (2000)	21	1	0.44	-0.16—1.04	0.153959	-0.71	4	0.90	0.30—1.51	0.003424	0.53
Westerveld (2000)	82	8	0.64	0.33—0.94	0.000047	-0.12	7	0.59	0.29—0.90	0.000146	-1.07
Chelune (1993)	96 surgery	8	0.59	0.30—0.87	0.000050	-0.52	8	0.59	0.30—0.87	0.000050	-1.24
	40 control	2	---	---	---	---	2	---	---	---	---
Ivnik (1988)	141	13	0.62	0.38—0.85	<0.000001	-0.36	27	0.91	0.67—1.14	<0.000001	1.63
Powell (1985)	59	10	0.85	.049—1.21	0.000004	1.14	8	0.75	0.39—1.12	0.000042	0.06

Evidence Table 156. Studies of temporal lobe surgery reporting individual patient changes in verbal IQ – changes in mean IQ

Reference	Number of Patients	Mean Pre-surgery IQ	SD of the Pre-surgery IQ	Mean Post-surgery IQ	SD of the Post-surgery IQ	Hedges' d Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Miranda (2001)	50	86	17	87	16	-0.06	-0.45—0.33	0.763796	-0.05
Robinson (2000)	21	87	9	89	12	-0.09	-0.70—0.51	0.764497	-0.14
Westerveld (2000)	82	93	16	93	14	0.00	-0.31—0.31	1.000000	0.38
Chelune (1993)	96 surgery	90	11	91	12	-0.17	-0.46—0.11	0.231396	-1.02
	40 control	92.1	12.9	93.0	12.8	---	---	---	---
Ivnik (1988)	141	95	NR	96	NR	---	---	---	---
Powell (1985)	59	100	20	98	19	0.10	-0.26—0.46	0.580321	0.92

Evidence Table 157. Sensitivity analysis of studies of temporal lobe surgery reporting mean IQ

Sensitivity Adjustment	Hedges' d Summary Estimate	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	-0.05	-0.21	0.11	0.53	1.53	0.82
Removing study with smallest effects size [a]	0.00	-0.19	0.20	0.96	0.48	0.92
Removing study with largest effect size	-0.09	-0.26	0.09	0.34	0.68	0.88
Removing study with smallest N	-0.05	-0.21	0.12	0.57	1.51	0.68
Removing study with largest N	0.00	-0.19	0.20	0.96	0.48	0.92

[a] The study with the smallest effect size also had the largest N.

Evidence Table 158. Studies of temporal lobe surgery reporting individual changes in patient memory after surgery

Reference	Number of Patients	Years	Country	Wechsler Memory Scale Used in Study
Canizares (2000)	33	1998-1999	Spain	General Memory Score
Chelune (1993)	96	1990-1991	United States	Verbal
Ivnik (1988)	141	1972-1987	United States	Memory quotient
Ojemann (1985)	13	1983-1983	United States	Verbal
Powell (1985)	59	1973-1984	England	Logical Memory percent Recall

Evidence Table 159. Studies of temporal lobe surgery reporting individual patient changes in memory function

Reference	Number of Patients	Wechsler Memory Scale Used in Study	Number of Patients With a Significant Decrease in Memory Score	Percentage of Patients Experiencing a Decrease	Number of Patients With a Significant Increase in Memory Score	Percentage of Patients Experiencing an Increase	Baseline Mean Memory Score	Baseline SD of the Mean Memory Score	Mean Memory Score After Surgery	SD of the Mean Memory Score After Surgery
Canizares (2000)	33	General Memory Score	3	9.1%	10	30.3%	80	15	88	19
Chelune (1993)	96 surgery patients	Verbal	28	29.2%	1	1.0%	90	14	87	14
	40 control patients	Verbal	1	2.5%	2	5%	94.5	17.4	102.5	18.3
Ivnik (1988)	141	Memory quotient	48	34.0%	48	34.0%	100		100	
Ojemann (1985)	13	Verbal	8	61.5%	3	23.1%	23		17	
Powell (1985)	59	Logical Memory percent Recall	8	13.6%	13	22.0%	70	28	74	25

Evidence Table 160. Patient characteristics for studies of temporal lobe surgery reporting complications due to surgery

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Epilepsy Before Surgery (Years)
Boling (2001)	18	AH	Various (no tumors)	54		18		34.9	12.1
Schramm (2001)	61	Neocortex	Various	27.9		14.4		13.6	
Sotero de Menezes (2001)	15	Tailored	Various	8.3	3.1				
Wiebe (2001)	36	Standard	Various	34.4	9.9	16.2	10		
Iannelli (2000)	37	Neocortex	Tumor	9.1	5			2.8	
Rao (2000)	164	Standard	Various	25.6				16.1	
Robinson (2000)	21	AH	Various	15.4		5.2		10.3	
Wurm (2000)	16	AH	Various	35.7					
Altshuler (1999)	49	Standard	MTS	40	5.5	11.4	8.3	17.6	4.3
Leung (1999)	11	Standard	MTS	28				17.2	
Parrent (1999)	19	AH	Not reported	34.1					
Salanova (1999)	145	Tailored	Various	30.4		10.5		19.7	
Son (1999)	71	Standard	MTS	28.9					
Visudhiphan (1999)	14	Standard	Various	13.1	3.6	6.7	3.8	6.4	4.5
Radhakrishnan (1998)	175	Tailored	Various	31		8		19	
Wyllie (1998)	72	Standard	Various			4.4			
Bizzi (1997)	14	Partial	Various	11.9	4.6				
Blume (1997)	14	Tailored	Various	8.5		2.6		6	
Kilpatrick (1997)	36	Standard	Various	36.8	11.5	15			
Adam (1996)	30	Standard	MTS	29		9			
Acciarri (1995)	10	Neocortex	Vascular malformation	34.8	12.5	33.3	12.8	1.6	1.2

Evidence Table 160. Patient characteristics for studies of temporal lobe surgery reporting complications due to surgery (continued)

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Epilepsy Before Surgery (Years)
Davies (1995)	12	Tailored	Various	23				8	
Jooma (1995a)	14	Tailored	Tumor	34.1	10	14.4	7.3	19.7	7.7
	16	Neocortex	Tumor	26.5	17.3	23.8	18.6	2.7	3.1
Liu (1995)	22	Tailored	Other	37.2	13.7	17.8	9.5	19.3	8.2
Wyler (1995)	70	Standard	Various	30.9		10.5			
Blume (1994)	125	Standard	Various						
Guldvog (1994b)	64	Standard	Various					11.5	
Guldvog (1994a)	35	Standard	Various					8	
Hopkins (1991)	11	Standard	Various	5.5	2.2	2	1.4	3.6	2.1
Bidzinski (1990)	320	Standard	Not reported	23		8		13	
Mackenzie (1990)	30	Standard	Not reported						
Mizrahi (1990)	22	Tailored	Various	21	8.4	5.9	2.3	15.1	8.1
Walczak (1990)	100	Standard	Not reported	25				15	
So (1989)	48	Tailored	Bitemporal epileptiform abnormalities	27.5					
Cutfield (1987)	26	Tailored	Various	22				12	
Drake (1987)	16	Tailored	Tumor	12.7	2.7	6.3	4.3	6.5	3.9

Evidence Table 160. Patient characteristics for studies of temporal lobe surgery reporting complications due to surgery (continued)

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Epilepsy Before Surgery (Years)
King (1986)	23	Not described	Various	28.7	9.2	12.9	10.5	15.7	7.6
Meyer (1986)	50	Tailored	Not reported	15.8		7.5		8.3	
Carey (1985)	24	Standard	Various	21		10.8		14.7	
Delgado-Escueta (1985)	15	Standard	Various	26.5	6.9	15.8	8	10.7	4.9

AH Amygdalohippocampectomy
MTS Mesial temporal sclerosis

Evidence Table 160. Patient characteristics for studies of temporal lobe surgery reporting complications due to surgery (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Number of Patients With Simple Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Boling (2001)			9	9		
Schramm (2001)	26	35	27	34	14	33
Sotero de Menezes (2001)	9	5			10	
Wiebe (2001)	12	24	21	19		
Iannelli (2000)	16	21	27	10	2	2
Rao (2000)			60	59		
Robinson (2000)	8	14	13	9		
Wurm (2000)	3	13	7	9		
Altshuler (1999)	23	26	23	26		
Leung (1999)	8	3	4	7		
Parrent (1999)	7	12	10	9		
Salanova (1999)	71	74				
Son (1999)			45	26		
Visudhiphan (1999)	4	10	7	7		
Radhakrishnan (1998)	68	107	77	98		
Wyllie (1998)						
Bizzi (1997)			11	8		
Blume (1997)	6	8	7	7	13	
Kilpatrick (1997)	8	10	11	7		
Adam (1996)	15	15	11	19	19	17
Acciarri (1995)	5	5	5	5		0
Davies (1995)						
Jooma (1995b)						6
Liu (1995)	5	7	5	7	0	8
Wyler (1995)	23	47	37	33		
Blume (1994)			64	61		

Evidence Table 160. Patient characteristics for studies of temporal lobe surgery reporting complications due to surgery (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Number of Patients With Simple Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Guldvog (1994b)						
Guldvog (1994a)	25	10				
Hopkins (1991)	5	6	8	3		
Bidzinski (1990)						
Mackenzie (1990)					18	19
Mizrahi (1990)	10	12				
Walczak (1990)	45	55	59	41		
Cutfield (1987)	17	9	11	15		
Drake (1987)			8	3	3	7
King (1986)			12	11		
Meyer (1986)	27	23	29	21		
Carey (1985)			11	13	3	12
Delgado-Escueta (1985)	5	10	12	3	1	12

Evidence Table 161. Complications due to surgery reported in studies of temporal lobe surgery

Reference	N	Number of Patients with a Serious Permanent Complication	Percentage of Permanent Complications	List of Permanent Complications [a]	Number of Patients with a Mild or Transient Complication	Percentage of Transient Complications	List of Transient Complications [a]
Boling (2001)	18	0	0.00		1	5.56	Scalp wound infection (1)
Schramm (2001)	61	0	0.00		3	4.92	Meningitis (2), Dysphasia (1)
Sotero de Menezes (2001)	15	1	6.67	Hemiparesis (1)	3	20.00	4th cranial nerve palsy (1), Speech delay (1), Attention-deficit disorder (1)
Wiebe (2001)	36	2	5.56	Sensory abnormality of the thigh due to a small thalamic infarct (1)	1	2.78	Wound infection (1)
Iannelli (2000)	37	1	2.70	Hemiparesis (1)	2	5.41	Skin flap infection (1), Dysphasia (1)
Rao (2000)	164	1	0.61	Hemiplegia due to injury to the anterior choroidal artery (1)			Complications were not reported per patient. Hemiparesis (5), Dysphasia (2), Meningitis (2), Wound infection (2), Oculomotor nerve palsy (1)
Robinson (2000)	41	2	9.09	Partial peripheral nerve palsy (1), Dysnomia (1)	6	14.6	Partial peripheral nerve palsy (2), Dysnomia (2), Facial nerve palsy (1), Dysnomia (1)
Wurm (2000)	16	1	6.25	Hemiparesis (1)	0	0.00	
Altshuler (1999)	49	5	10.20	Hemiparesis (3), Cranial nerve palsy (1), Dysplagia (1)			Not reported
Leung (1999)	11	1	9.09	Paralysis of the frontalis muscle due to facial nerve injury (1)	1	9.09	Vocal cord palsy (1)

Evidence Table 161. Complications due to surgery reported in studies of temporal lobe surgery (continued)

Reference	N	Number of Patients with a Serious Permanent Complication	Percentage of Permanent Complications	List of Permanent Complications [a]	Number of Patients with a Mild or Transient Complication	Percentage of Transient Complications	List of Transient Complications [a]
Parrent (1999)	19	0	0.00		1	5.26	Hematoma
Salanova (1999)	145	2	1.38	Hemiparesis (1), Homonymous hemianopsia (1)	1	0.69	Hemiparesis (1)
Son (1999)	71	2	2.82	Hemiparesis (2)	2	2.82	Surgical wound infection (2)
Visudhiphan (1999)	14	0	0.00		0	0.00	
Radhakrishnan (1998)	175	2	1.14	Hemiparesis (1), Dysphasia (1)			Not reported
Wyllie (1998)	72	0	0.00		2	2.78	Language disturbance after venous infraction (1), Ipsilateral superior oblique paresis (1)
Bizzi (1997)	14	1	7.14	Basal ganglia infarction (1)	3	21.43	Micrographia (1), Hemiparesis (1), Bone flap osteomyelitis (1)
Blume (1997)	14	0	0.00				Not reported
Kilpatrick (1997)	36	0	0.00		3	8.33	Mild dysphasia (3)
Adam (1996)	30	2	6.67	Upper limb deficient due to infarction (1), Hemiparesis (1)	0	0.00	
Acciarri (1995)	10	0	0.00		0	0.00	
Davies (1995)	12	1	8.33	Worsening of preoperative hemiparesis (1)	3	25.00	Persistent mild dysphasia (1), Bone flap infection (2)
Jooma (1995b)	30	2	12.50	Hemiparesis (2)			Not reported
Liu (1995)	22	2	9.09	Moderate increase in preexisting hemiparesis (2)	0	0.00	

Evidence Table 161. Complications due to surgery reported in studies of temporal lobe surgery (continued)

Reference	N	Number of Patients with a Serious Permanent Complication	Percentage of Permanent Complications	List of Permanent Complications [a]	Number of Patients with a Mild or Transient Complication	Percentage of Transient Complications	List of Transient Complications [a]
Wyler (1995)	70	3	4.29	Subgaleal cerebrospinal fluid fistula (3)	1	1.43	Nerve paresis (1)
Blume (1994)	125	1	0.80	Hemiparesis (1)	1	0.80	Hemiparesis (1)
Guldvog (1994a)	35	0	0.00		6	17.14	Minor hemiparesis (3), Minor partial facial paresis (2), Dysphasia (1)
Guldvog (1994b)	64	6	9.38	Memory deficit and Dysphasia (1), Long-term slow cerebration (1), Facial paresis and Dysphasia (1), Memory deficit and Hemiparesis (1), Hemiparesis and Hypalgesia (1), Paresis of the left arm and ataxia (1)	5	7.81	Facial paresis (4), Hemiparesis (1)
Hopkins (1991)	11	0	0.00		2	18.18	Hemiparesis, mild (2)
Bidzinski (1990)	320	2	0.63	Hemiparesis (2)			Not reported
Mackenzie (1990)	30	0	0.00		2	6.67	Mild word-finding difficulty (1), Mild hemiparesis (1)
Mizrahi (1990)	22	0	0.00		0	0.00	
Walczak (1990)	100	1	1.00	Hemiplegia (1)	9	9.00	Bone flap infection (1), Decrease spontaneous speech or anomias (7), Hemiparesis (1)
So (1989)	48	0	0.00		3	6.25	Dysphasia (2), Wound infection (1)

Evidence Table 161. Complications due to surgery reported in studies of temporal lobe surgery (continued)

Reference	N	Number of Patients with a Serious Permanent Complication	Percentage of Permanent Complications	List of Permanent Complications [a]	Number of Patients with a Mild or Transient Complication	Percentage of Transient Complications	List of Transient Complications [a]
Cutfield (1987)	26	0	0.00		1	3.85	Dysphasia (1)
Drake (1987)	16	0	0.00		4	25.00	Mild contralateral hemiparesis (3), Contralateral increase in tone only (1)
King (1986)	23	0	0.00		3	13.04	Dysphasia (3)
Meyer (1986)	50	0	0.00		6	12.00	Infected bone flaps (2), Rhinorrhea (1), Upper-extremity paresis (2), Expressive Dysphasia (1)
Carey (1985)	24	0	0.00		2	8.33	Hemiparesis, mild (1), Dysphasia (1)
Delgado-Escueta (1985)	15	1	6.67	Cerebral anoxic episode causing a drop in mental quotient (1)	2	13.33	Dysphasia and mild right arm clumsiness (1), Mild naming disorder (1)

[a] The number of patients with each specific complication is in parenthesis

Evidence Table 162. Patient characteristics for studies of temporal lobe surgery reporting surgery related mortality

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Boling (2001)	18	AH	Various (no tumors)	54		18		34.9	12.1
Schramm (2001)	61	Neocortex	Various	27.9		14.4		13.6	
Wiebe (2001)	36	Standard	Various	34.4	9.9	16.2	10		
Iannelli (2000)	37	Neocortex	Tumor	9.1	5			2.8	
Rao (2000)	164	Standard	Various	25.6				16.1	
Robinson (2000)	22	AH	Various	15.4		5.2		10.3	
Wurm (2000)	16	AH	Various	35.7					
Altshuler (1999)	49	Standard	MTS	40	5.5	11.4	8.3	17.6	4.3
Leung (1999)	11	Standard	MTS	28				17.2	
Parrent (1999)	19	AH	Not reported	34.1					
Salanova (1999)	145	Tailored	Various	30.4		10.5		19.7	
Son (1999)	71	Standard	MTS	28.9					
Visudhiphan (1999)	14	Standard	Various	13.1	3.6	6.7	3.8	6.4	4.5
Wyllie (1998)	72	Standard	Various			4.4			
Bizzi (1997)	14	Partial	Various	11.9	4.6				
Blume (1997)	14	Tailored	Various	8.5		2.6		6	
Kilpatrick (1997)	36	Standard	Various	36.8	11.5	15			
Adam (1996)	30	Standard	MTS	29		9			

Evidence Table 162. Patient characteristics for studies of temporal lobe surgery reporting surgery related mortality (continued)

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Acciarri (1995)	10	Neocortex	Vascular malformation	34.8	12.5	33.3	12.8	1.6	1.2
Berkovic (1995)	135	Partial	Various	29	10				
Davies (1995)	12	Tailored	Various	23				8	
Liu (1995)	22	Tailored	Other	37.2	13.7	17.8	9.5	19.3	8.2
Wyler (1995)	70	Standard	Various	30.9		10.5			
Blume (1994)	125	Standard	Various						
Guldvog (1994b)	64	Standard	Various					11.5	
Guldvog (1994a)	35	Standard	Various					8	
Bladin (1992)	107	Standard	Not reported						
Elwes (1991)	108	Standard	Various	23					
Hopkins (1991)	11	Standard	Various	5.5	2.2	2	1.4	3.6	2.1
Bidzinski (1990)	320	Standard	Not reported	23		8		13	
Mizrahi (1990)	22	Tailored	Various	21	8.4	5.9	2.3	15.1	8.1
Yeh (1990)	12	Neocortex	Vascular malformation	36.3	11.9	25.3	8.3	11	8.2
So (1989)	48	Tailored	Bitemporal epileptiform abnormalities	27.5					
Cutfield (1987)	26	Tailored	Various	22				12	

Evidence Table 162. Patient characteristics for studies of temporal lobe surgery reporting surgery related mortality (continued)

Reference	N	Surgery	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Drake (1987)	16	Tailored	Tumor	12.7	2.7	6.3	4.3	6.5	3.9
Meyer (1986)	50	Tailored	Not reported	15.8		7.5		8.3	
Carey (1985)	24	Standard	Various	21		10.8		14.7	

AH Amygdalohippocampectomy
MTS Mesial temporal sclerosis

Evidence Table 162. Patient characteristics for studies of temporal lobe surgery reporting surgery related mortality (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Number of Patients With Simple Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Boling (2001)			9	9		
Schramm (2001)	26	35	27	34	14	57
Wiebe (2001)	12	24	21	19		
Iannelli (2000)	16	21	27	10	2	21
Rao (2000)			60	59		119
Robinson (2000)	8	14	13	9		22
Wurm (2000)	3	13	7	9		
Altshuler (1999)	23	26	23	26		49
Leung (1999)	8	3	4	7		11
Parrent (1999)	7	12	10	9		
Rossi (1999)						
Salanova (1999)	71	74				
Son (1999)			45	26		
Visudhiphan (1999)	4	10	7	7		14
Wyllie (1998)						
Bizzi (1997)			11	8		
Blume (1997)	6	8	7	7	13	14
Kilpatrick (1997)	8	10	11	7		
Adam (1996)	15	15	11	19	19	30
Acciarri (1995)	5	5	5	5		10
Berkovic (1995)						
Davies (1995)						
Liu (1995)	5	7	5	7	0	12
Wyler (1995)	23	47	37	33		

Evidence Table 162. Patient characteristics for studies of temporal lobe surgery reporting surgery related mortality (continued)

Reference	Right Side Surgeries	Left Side Surgeries	Number of Males	Number of Females	Number of Patients With Simple Partial Seizures	Number of Patients With Secondarily Generalized Seizures
Blume (1994)			64	61		125
Guldvog (1994b)						
Guldvog (1994a)	25	10				
Bladin (1992)	62	48	46	64		
Elwes (1991)	53	49	54	48		
Hopkins (1991)	5	6	8	3		11
Bidzinski (1990)						
Mizrahi (1990)	10	12				
Yeh (1990)	3	9	8	4	3	9
Cutfield (1987)	17	9	11	15		26
Drake (1987)			8	3	3	11
Meyer (1986)	27	23	29	21		
Carey (1985)			11	13	3	20

Evidence Table 163. Corpus callosotomy studies excluded from the evidence base for seizure frequency outcomes

Reference	N	Reason for Exclusion
Pinard (1999)	14	Patients with West Syndrome are different from the patients in the other studies of corpus callosotomy because of the spasms that are characteristic of this syndrome. The main measure of surgical success for these patients is a reduction in spasms and is not comparable to the seizure-free and seizure frequency reduction outcome measurements reported in the other studies in the evidence base.

Evidence Table 164. Patient characteristics in studies of corpus callosotomy reporting seizure frequency outcomes

Reference	N	Pathology	Mean Age at Treatment (Years)	SD of Age at Treatment (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Duration of Condition Before Treatment (Years)	SD of Duration Before Treatment (Years)
Kwan (2001)	61	Lennox-Gastaut	7.9					
Maehara (2001)	52		18		5.1		12.9	
Matsuzaka (1999)	22		19		5.6		13.3	
McInerney (1999)	47		13.6		3.8		9.8	
Sakas (1996)	20		25.7	1.4	8.8	1.4		
Claverie (1995)	20		22.8	9.7				
Reutens (1993)	64		20		5.2		14.8	
Marino (1990)	28		21.4	10.1	6.5	5.7	14.9	8.2
Murro (1988)	25		25.8	11.8	6.2	3.6	19.6	11.3
Purves (1988)	24		25.9	10.9	6.3	6.8	19.6	10.2
Spencer (1988)	22		20.5	6.6	5.6	3.8	14.9	7
Gates (1987)	24							

Evidence Table 164. Patient characteristics in studies of corpus callosotomy reporting seizure frequency outcomes (continued)

Reference	N	Males	Females	Simple Partial Seizures	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Kwan (2001)	61	47	14				
Maehara (2001)	52	34	18	24	5		52
Matsuzaka (1999)	22			9	7		17
McInerney (1999)	47	28	19	18	19		47
Sakas (1996)	20	14	6		8		20
Claverie (1995)	20						
Reutens (1993)	64	38	26	14	20		64
Marino (1990)	28			25	23		25
Murro (1988)	25	7	6	1	5		10
Purves (1988)	24	12	12	8	19	5	12
Spencer (1988)	22	17	5	13	21		22
Gates (1987)	24	15	7	1	19	22	22

Evidence Table 165. Studies of corpus callosotomy reporting a percentage reduction in seizure frequency

Reference	N	Type of Seizure Evaluated	Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients				
						90% or Greater Reduction	75% to 90% Reduction	50% to 75% Reduction	Less than 50% Reduction	No Change or Worse
Kwan (2001)	61	All seizure types		2		11	0	27	7	16
Maehara (2001)	52	Disabling generalized seizures	3.3	2	6.8	32				
Matsuzaka (1999)	22	Most disabling seizures	4.8	2.1	8.4	4	10	3	5	0
McInerney (1999)	43	Most disabling seizures	12.3	2	27	13	11	6	3	10
Sakas (1996)	20	Drop attacks and generalized tonic-clonic seizures	6.7			6	0	10	0	4
Claverie (1995)	15	All seizure types	4.5	2	10	4	1	2	2	6
Reutens (1993)	27	All seizure types		2				14	13	
Marino (1990)	28	All seizure types	8.7	4	11	22	3	2	0	1
Murro (1988)	13	All seizure types	3.1	2.3	5.6	3	4	2	1	3
Purves (1988)	24	All seizure types	5.1	2	11		17			3
Spencer (1988)	22	All seizure types	2			2	5	5	7	3
Gates (1987)	22	All seizure types	3.7	2.1	6.6	8	3	5	5	1

Evidence Table 166. Studies of corpus callosotomy reporting a 90% or greater reduction in frequency of all seizure types

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients With a 90% or Greater Reduction in Seizure Frequency	Percentage	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Kwan (2001)	61		2		11	18.0	0.88	0.52—1.23	0.000001	-0.46
Claverie (1995)	15	4.5	2	10	4	26.7	1.09	0.37—1.80	0.002957	0.43
Murro (1988)	13	3.1	2.3	5.6	3	23.1	1.00	0.23—1.77	0.010616	0.17
Spencer (1988)	22		2		2	9.1	0.61	0.02—1.20	0.042193	-1.18
Gates (1987)	22	3.7	2.1	6.6	8	36.4	1.29	0.70—1.89	0.000018	1.29

Evidence Table 167. Studies of corpus callosotomy reporting patients who received no benefit from surgery

Patients' seizure frequencies were unchanged or become worse; all seizure types were considered

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	No Change or Worse	Percentage	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Kwan (2001)	61		2		16	26.2	1.08	0.72—1.43	<0.000001	1.67
Claverie (1995)	15	4.5	2	10	6	40.0	1.37	0.65—2.09	0.000177	1.55
Marino (1990)	28	8.7	4	11	1	3.6	0.38	-0.14—0.90	0.154803	-1.82
Murro (1988)	13	3.1	2.3	5.6	3	23.1	1.00	0.23—1.77	0.010616	0.46
Purves (1988)	24	5.1	2	11	3	12.5	0.72	0.16—1.29	0.012293	-0.39
Spencer (1988)	22		2		3	13.6	0.76	0.17—1.35	0.012112	-0.25
Gates (1987)	22	3.7	2.1	6.6	1	4.5	0.43	-0.16—1.02	0.154113	-1.41

Evidence Table 168. Studies of corpus callosotomy reporting patients as completely seizure-free

Reference	Number of Patients Evaluated	Type of Seizure Evaluated	Mean Followup Period in Years	Minimum Followup	Maximum Followup	Patients Completely Seizure-Free (No Auras)	Percentage
Marino (1990)	28	All seizure types	8.7	4	11	1	3.6
Murro (1988)	13	All seizure types	3.1	2.3	5.6	0	0.0
Spencer (1988)	22	All seizure types		2		1	4.5
Gates (1987)	22	All seizure types	3.7	2.1	6.6	3	13.6

Evidence Table 169. Studies of corpus callosotomy reporting pre- and postsurgery seizure frequency [a]

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Pre-surgery Seizure Frequency		Post-surgery Seizure Frequency		Results of Paired t-test [b]		
					Mean	SD	Mean	SD	t	df	p value
Murro (1988)	13	3.1	2.3	5.6	110	164.6	20	35	2.0	12	0.065
Spencer (1988)	22		2		159	210	78	130	2.7	21	0.014
Gates (1987)	22	3.7	2.1	6.6	178.3	273.6	40	49	2.6	21	0.015

[a] Seizure frequency is presented as seizures per month
[b] Calculated by ECRI

Evidence Table 170. Studies of corpus callosotomy reporting relationships between patient or study characteristics and treatment outcome

Reference	N	Seizure Outcome Measurement	Statistical Method	Patient Characteristics Examined		
				Age at Treatment	Age at Seizure Onset	Other Study Variables
Kwan (2001)	61	Seizure-free or seizure reduction by more than 50% of all seizure types	Univariate			Bisynchronous anterior-dominant epileptiform discharges vs. posterior-dominant epileptiform discharges (NS)
Maehara (2001)	52	90% reduction in frequency of disabling generalized seizures	Multiple regression			Total callosotomy was independently predictive of satisfactory reduction in drop attacks and disabling generalized seizures (Sig.)
Sakas (1996)	20	Completely free of drop attacks and generalized tonic-clonic seizures or significantly improved	Univariate	NS	Sig. Younger age of onset showed better improvement	Extent of resection (NS), Pre-operative electroencephalographic patterns (NS), Neuro-imaging finding (NS)
Spencer (1988)	22	Seizure-free with auras	Univariate		NS	Full scale IQ scores less than 45 were associated with poor outcome (Sig.), Hemiparetic patients vs. normal physical examine (NS)

NS Not statistically significant
Sig. Statistically significant according to the authors

Evidence Table 171. Studies of corpus callosotomy reporting individual patient age at surgery

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Claverie (1995)	15	90% reduction in seizure frequency	-0.18	-0.63	0.37	-1.19
Nordgren (1991)	18	80% reduction in seizure frequency	0.17	-0.32	0.59	0.13
Marino (1990)	28	90% reduction in seizure frequency	0.20	-0.18	0.54	0.38
Murro (1988)	13	90% reduction in seizure frequency	-0.22	-0.69	0.38	-1.21
Purves (1988)	24	80% reduction in frequency and severity of all seizure types	0.15	-0.27	0.52	0.07
Spencer (1988)	22	Seizure-free with auras	0.39	-0.04	0.69	1.29

[a] A positive correlation coefficient indicates more successful surgeries with an older age at surgery.

Evidence Table 172. Sensitivity analysis of studies of corpus callosotomy reporting individual patient age at surgery

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.14	-0.05	0.32	0.16	4.05	0.54
Removing study with largest negative effect size [b]	0.18	-0.03	0.37	0.09	2.59	0.63
Removing study with largest positive effect size	0.13	-0.08	0.33	0.21	4.03	0.40
Removing study with smallest N	0.18	-0.03	0.37	0.09	2.59	0.63
Removing study with largest N	0.14	-0.08	0.34	0.22	4.04	0.40

[a] A positive correlation coefficient indicates more successful surgeries with an older age at surgery.
[b] The study with the largest negative effect size had the smallest N

Evidence Table 173. Studies of corpus callosotomy reporting individual patient age at seizure onset

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Nordgren (1991)	18	80% reduction in seizure frequency	0.26	-0.24	0.65	0.95
Marino (1990)	28	90% reduction in seizure frequency	-0.17	-0.51	0.22	-1.23
Murro (1988)	13	90% reduction in seizure frequency	0.18	-0.42	0.66	0.46
Purves (1988)	24	80% reduction in frequency and severity of all seizure types	0.16	-0.26	0.53	0.63
Spencer (1988)	22	Seizure-free with auras	-0.07	-0.48	0.36	-0.53

[a] A positive correlation coefficient indicates more successful surgeries with an older age at seizure onset.

Evidence Table 174. Sensitivity analysis of studies of corpus callosotomy reporting individual patient age at seizure onset

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.04	-0.16	0.24	0.70	2.55	0.64
Removing study with largest negative effect size [b]	0.12	-0.12	0.35	0.33	1.05	0.79
Removing study with largest positive effect size	0.00	-0.23	0.22	0.97	1.65	0.65
Removing study with smallest N	0.02	-0.19	0.24	0.83	2.34	0.51
Removing study with largest N	0.12	-0.12	0.35	0.33	1.05	0.79

[a] A positive correlation coefficient indicates more successful surgeries with an older age at seizure onset.
[b] The study with the largest negative effect size also had the largest N.

Evidence Table 175. Studies of corpus callosotomy reporting individual patient duration of epilepsy prior to surgery

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Interval		Standardized Residuals for Effect Sizes
				Lower	Upper	
Nordgren (1991)	18	80% reduction in seizure frequency	-0.14	-0.57	0.35	-1.25
Marino (1990)	28	90% reduction in seizure frequency	0.36	-0.01	0.65	1.35
Murro (1988)	13	90% reduction in seizure frequency	-0.28	-0.72	0.32	-1.49
Purves (1988)	24	80% reduction in frequency and severity of all seizure types	0.06	-0.36	0.45	-0.51
Spencer (1988)	22	Seizure-free with auras	0.40	-0.02	0.70	1.34

[a] A positive correlation coefficient indicates more successful surgeries with a longer duration of epilepsy prior to surgery.

Evidence Table 176. Sensitivity analysis of studies of corpus callosotomy reporting individual patient duration of epilepsy prior to surgery

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.15	-0.05	0.34	0.15	6.21	0.18
Removing study with largest negative effect size [b]	0.21	-0.01	0.40	0.06	3.98	0.26
Removing study with largest positive effect size	0.08	-0.15	0.30	0.50	4.41	0.22
Removing study with smallest N	0.21	-0.01	0.40	0.06	3.98	0.26
Removing study with largest N	0.06	-0.18	0.30	0.60	4.40	0.22

[a] A positive correlation coefficient indicates more successful surgeries with a longer duration of epilepsy prior to surgery.
[b] The study with the largest negative effect size also had the smallest N.

Evidence Table 177. Studies of corpus callosotomy reporting patients who were free of their most disabling seizures

Reference	N	Type of Seizures Evaluated	Followup Period in Years	Minimum Followup	Maximum Followup	Number of Patients Free of Disabling Seizures	Percentage	Cohen's h Effect Size	95% Confidence Interval
Matsuzaka (1999)	22	Most disabling seizures	4.8	2.1	8.4	4	18.2	0.88	0.29—1.47
McInerney (1999)	43	Most disabling seizures	12.3	2	27	13	30.2	1.16	0.74—1.59
Sakas (1996)	20	Drop attacks and generalized tonic-clonic seizures	6.7	2		4	20.0	0.93	0.31—1.55
Marino (1990)	23	Drop attacks and generalized tonic-clonic seizures	8.7	4	11	7	30.4	1.17	0.59—1.75
Murro (1988)	13	Tonic, Atonic, Tonic-clonic, Complex partial	3.1	2.3	5.6	1	7.7	0.56	-0.21—1.33
Spencer (1988)	22	Tonic, Atonic, Tonic-clonic, Complex partial		2		9	40.9	1.39	0.80—1.98
Gates (1987)	22	Tonic, Atonic, Tonic-clonic, Complex partial	3.7	2.1	6.6	6	27.3	1.10	0.51—1.69

Evidence Table 178. Studies of corpus callosotomy reporting patients who were free of generalized tonic-clonic seizures.

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Patients with Generalized Tonic-Clonic Seizures			Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
					N	Free	% Free				
Kwan (2001)	61		2		23	3	13.0	0.74	0.16—1.32	0.012206	-2.04
Maehara (2001)	52	3.3	2	6.8	16	2	12.5	0.72	0.03—1.42	0.040934	-1.71
McInerney (1999)	43	12.3	2	27	35	10	28.6	1.13	0.66—1.60	0.000002	-0.80
Sakas (1996)	20	6.7			18	6	33.3	1.23	0.58—1.88	0.000222	-0.21
Marino (1990)	28	8.7	4	11	21	11	52.4	1.62	1.01—2.22	<0.000001	1.12
Murro (1988)	13	3.1	2.3	5.6	10	1	10.0	0.64	-0.23—1.52	0.150175	-1.51
Spencer (1988)	22		2		21	16	76.2	2.12	1.52—2.73	<0.000001	2.87
Gates (1987)	22	3.7	2.1	6.6	15	11	73.3	2.06	1.34—2.77	<0.000001	2.19

Evidence Table 179. Studies of corpus callosotomy reporting patients who were free of generalized tonic-clonic seizures – data used in meta-regression

Reference	Number of Patients	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	Conducted in the United States	Mean Age at Surgery
Kwan (2001)	61	0.74	11.50	1989	1996	No	7.9
Maehara (2001)	52	0.72	8.00	1991	1998	No	18
McInerney (1999)	43	1.13	17.50	1972	1999	Yes	13.6
Sakas (1996)	20	1.23	9.00	1984	1993	No	25.7
Marino (1990)	28	1.62	10.50	1978	1985	No	21.4
Murro (1988)	13	0.64	5.00	1980	1986	Yes	25.8
Spencer (1988)	22	2.12	10.50	1979	1983	Yes	20.5
Gates (1987)	22	2.06	7.50	1979	1985	Yes	19

Evidence Table 180. Results of the meta-regression for studies of corpus callosotomy reporting patients who were free of generalized tonic-clonic seizures after surgery

One predictor variables Bolded = statistically significant coefficient						
Covariate	**Intercept (CI)**	**P (intercept) =**	**Coefficient (CI)**	**P (coefficient)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	**1.265 (1.043 to 1.487)**	**<0.000001**	**-0.033 (-0.068 to 0.0009)**	**0.055932**	**17.7957**	**0.006764**
End year (centered)	**1.359 (1.136 to 1.582)**	**<0.000001**	**-0.060 (-0.094 to -0.026)**	**0.000563**	**9.554118**	**0.144729**
United States (USA = 0)	**1.497 (1.189 to 1.805)**	**<0.000001**	**-0.411 (-0.85 to 0.027)**	**0.066393**	**18.07976**	**0.006036**
Age at treatment (centered)	**1.335 (1.111 to 1.560)**	**<0.000001**	**0.034 (-0.004 to 0.072)**	**0.085921**	**18.50058**	**0.005096**
Lennox-Gastaut (all others = 0)	**1.389 (1.152 to 1.627)**	**<0.000001**	**-0.650 (-1.275 to -0.02)**	**0.041219**	**17.28277**	**0.008298**
Percentage male (centered)	1.269 (1.047 to 1.491)	<0.000001	0.029 (-0.006 to 0.065)	0.104512	18.81447	0.004489

Average N = 19.88
Average start year: 1981.5
Average end year: 1990.63
Average age at treatment: 18.987
Average percentage male: 68.106

Evidence Table 180. Results of the meta-regression for studies of corpus callosotomy reporting patients who were free of generalized tonic-clonic seizures after surgery (continued)

Two predictor variables									
Covariate: B_1	**Covariate: B_2**	**Intercept (95% CI's)**	**P (intercept) =**	**Coefficient B_1 (95% CI's)**	**P (B_1) =**	**Coefficient B_2 (95% CI's)**	**P(B_2)**	**Q_e =**	**P (Q_e) =**
End year (centered)	Start year (centered)	1.332 (1.106 to 1.557)	<0.001	-0.058 (-0.092 to -0.023)	0.001	-0.028 (-0.063 to 0.007)	0.112	7.028	0.219
End year (centered)	United States (USA = 0)	1.499 (1.191 to 1.807)	<0.001	-0.057 (-0.092 to -0.022)	0.001	-0.292 (-0.738 to 0.153)	0.198	7.9	0.162
End year (centered)	Age at treatment (centered)	1.353 (1.128 to 1.578)	<0.001	-0.066 (-0.109 to -0.023)	0.003	-0.01 (-0.059 to 0.038)	0.673	9.376	0.095
End year (centered)	Lennox-Gastaut (all others= 0)	1.408 (1.17 to 1.646)	<0.001	-0.055 (-0.091 to -0.019)	0.003	-0.374 (-1.025 to 0.276)	0.26	8.283	0.141
End year (centered)	Percentage male (centered)	1.338 (1.112 to 1.564)	<0.001	-0.058 (-0.092 to -0.023)	0.001	0.02 (-0.016 to 0.057)	0.269	8.332	0.139

Evidence Table 181. Studies of corpus callosotomy reporting patients who became free of atonic seizures after surgery

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Patients with Atonic Seizures			Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
					N	Free	% Free				
Kwan (2001)	61		2		11	6	54.5	1.66	0.83—2.50	0.000097	-0.35
Maehara (2001)	52	3.3	2	6.8	52	42	80.8	2.23	1.85—2.62	<0.000001	2.71
McInerney (1999)	43	12.3	2	27	30	17	56.7	1.70	1.20—2.21	<0.000001	-0.44
Sakas (1996)	20	6.7			13	7	53.8	1.65	0.88—2.42	0.000027	-0.42
Marino (1990)	28	8.7	4	11	18	9	50.0	1.57	0.92—2.22	0.000002	-0.76
Gates (1987)	22	3.7	2.1	6.6	22	8	36.4	1.29	0.70—1.89	0.000018	-1.84

Evidence Table 182. Studies of corpus callosotomy reporting employment data

Reference	Number of Patients	Followup in Years	Number of Patients Not Able to Obtain Employment Prior to Surgery	Number of Patients Able to Obtain Employment or Begin Training After Surgery	Number of Patients With a 50% or Better Reduction in Drop Attacks and Generalized Tonic-Clonic Seizures
Sakas (1996)	20	6.7	20	16	16

Patients in this study were between the ages of 15 and 37 years and no patients had regular employment or training prior to surgery. After surgery, 7 patients had full-time employment and 9 were in training.

Evidence Table 183. Studies of corpus callosotomy reporting changes in IQ

Reference	Number of Patients	Number of Patient With a Decrease in IQ	Number of Patient With an Increase in IQ	Baseline IQ		IQ After Surgery	
				Mean	SD	Mean	SD
Cohen (1991)	10	1	2	43	18	42	19

All patients were 18 years old or younger. The authors concluded that a majority of patients did not appear to experience any significant change in cognitive functioning.

Evidence Table 184. Patient characteristics from studies of corpus callosotomy reporting complications due to surgery

Reference	N	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration Before Surgery (Years)
Hodaie (2001)	17		10.5					
Maehara (2001)	52		18		5.1		12.9	
Fandino-Franky (2000)	97		14					
Pinard (1999)	17	West Syndrome	6.9	3.5	0.5	0.3	6.4	3.5
Carmant (1998)	28		13.8	6.5				
Sorenson (1997)	23		16.6		5.5		12.2	1.5
Andersen (1996)	20		20.8					
Rossi (1996)	20		23				15	
Sakas (1996)	20		25.7	1.4	8.8	1.4		
Reutens (1993)	64		20		5.2		14.8	
Fuiks (1991)	80		18.3		5.3			
Nordgren (1991)	18		13.1	3.2	3.6	3.5	9.1	3.9
Oguni (1991)	43		23.5				18.8	
Marino (1990)	28		21.4	10.1	6.5	5.7	14.9	8.2
Provinciali (1990)	15		26.2	7.6				
Sass (1990)	32		24	6.6	7.4	5	16.7	8.3
Murro (1988)	25		25.8	11.8	6.2	3.6	19.6	11.3
Purves (1988)	24		25.9	10.9	6.3	6.8	19.6	10.2
Garcia-Flores (1987)	14		17.8	9	6.5	8.8		
Gates (1987)	24							

Evidence Table 184. Patient characteristics from studies of corpus callosotomy reporting complications due to surgery (continued)

Reference	Males	Females	Simple Partial Seizures	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Hodaie (2001)	8	9				
Maehara (2001)	34	18	24	5		52
Fandino-Franky (2000)	59	38				
Pinard (1999)						
Carmant (1998)						
Sorenson (1997)						
Andersen (1996)	13	7				
Rossi (1996)	14	6	9	13		20
Sakas (1996)	14	6		8		20
Reutens (1993)	38	26	14	20		64
Fuiks (1991)	44	36		9		69
Nordgren (1991)	11	7	13	8	8	16
Oguni (1991)	20	23	5	8	24	43
Marino (1990)			25	23		25
Provinciali (1990)	9	6				
Sass (1990)	21	11			32	
Murro (1988)	7	6	1	5		10
Purves (1988)	12	12	8	19	5	12
Garcia-Flores (1987)			3	3	3	6
Gates (1987)	15	7	1	19	22	22

Evidence Table 185. Studies of corpus callosotomy reporting complications – list of complications

Reference	N	Years	Country	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Hodaie (2001)	17	1992-1999	Canada	0		2	Wound infection (2)
Maehara (2001)	52	1991-1998	Japan	0		17	Acute epidural hematoma without neurological deficit (1), Akinetic state (14), Marked disconnect syndrome (2)
Fandino-Franky (2000)	97	1989-1997	Colombia	0		12	Leg weakness (10), Mutism (2)
Pinard (1999)	17	1989-1995	France	2	Deteriorated language (2)	0	
Carmant (1998)	28	1989-1993	United States	0		3	Acute disconnection problems (3)
Sorenson (1997)	23	1991-1994	United States	1	Right frontal infarction related to venous thrombosis (1)	13	Complications were not identified per patient. Meningitis (3), Diabetes insipidus (1), Postoperative disconnection syndrome (13)
Andersen (1996)	20	1988-1994	Denmark	7	Seven patients had persistent interhemispheric disconnection syndrome with the following symptoms: Mild hemiapraxia (3), Severe cognitive and neurologic sequelae (language impairment, hemisphere competition, apraxia) (4)	5	Interhemispheric disconnection syndrome (5)
Rossi (1996)	20	1988-1995	Italy	1	Mild leg weakness (1)	12	Mutism (8), Mild hemiparesis (2), Dysarthria (2)
Sakas (1996)	20	1984-1993	Ireland	0		7	Hemiparesis (3), Disconnection syndrome (3), Hemiparesis and Akinetism (1)

Evidence Table 185. Studies of corpus callosotomy reporting complications – list of complications (continued)

Reference	N	Years	Country	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Reutens (1993)	64	1973-1991	Australia	4	Hemiparesis (2), Persistent disturbance in behavior (2)		Complications were not identified per patient. Meningitis (4), Wound infections (4), Extradural hematoma (1), Hemiparesis (13), Akinesia or mutism (20), Postoperative aggression (6), Persistent mild disconnection syndrome (1)
Fuiks (1991)	80	1985-1990	United States	0		5	Subdural hemotoma (1), Deep wound infection (1), Left hemiparesis (1), Epidural hematoma (2)
Nordgren (1991)	18	1972-1987	United States	1	Hemiparesis worsened (1)	3	Aseptic meningitis (2), hydrocephalus and shut (1)
Oguni (1991)	43	1981-1989	Canada	0		16	Epidural hematoma with hemiparesis (1), Cranial infection (1), Collection of blood between the galea and bone flap (1), Contralateral weakness of the leg (2), Decreased output of speech (4), Minor confusional state (3), Mild fever (2), Drowsiness (2)
Marino (1990)	28	1978-1985	Brazil	1	Hemiplegia (1)	1	Meningitis (1)
Provinciali (1990)	15	1987-1988	Italy	0		8	Broncho-pneumonia (1), Meningitis (1), Deficit in naming objects held in the left hand (1), Hemiparesis (1), Arachnoiditis (1), Apraxia and/or slight paresis of left arm (3)
Sass (1990)	32	1985-1987	United States	4	Clinically significant language impairments (4)	1	Venous hemorrhagic infarction (1)
Murro (1988)	25	1980-1986	United States	0		6	Intracranial hemorrhage (2), Wound infection (2), Bone flap infection (1), Mild hemiparesis (1)

Evidence Table 185. Studies of corpus callosotomy reporting complications – list of complications (continued)

Reference	N	Years	Country	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Purves (1988)	24	1977-1987	Canada	0		11	Reduced speech output and left hemiparesis (7), Subdural hematoma (2), Meningitis and abscess (1), Diabetes insipidus (1)
Garcia-Flores (1987)	14	1980-1986	Mexico	0		1	Hemiparesis (1)
Gates (1987)	24	1979-1985	United States	3	Stuttering disorders (2), Lower extremity weakness resulting from cerebral infarction (1)	4	Hematomas (2), Steroid-dependent cerebral edema (1), Bone flap infection (1)

Evidence Table 186. Patient characteristics from studies of frontal lobe surgery reporting seizure outcome measurements

Reference	N	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Epilepsy Before Surgery (Years)
Ferrier (2001)	35		17.3	8.5	6.2	4.1	11.1	7.2
Siegel (2001)	14	Various	31.3		12.2		19.2	
Hong (2000)	18	Cortical dysplasia	18.3	9.8	5.6	4.1	12.6	7.4
Eriksson (1999)	12	Various	34		14		18	
	13	Various	9.9		1.5		5.5	
Wennberg (1999)	22	Foreign tissue lesion	23.2	12.8				
Swartz (1998)	19	Various	31.3	12.3	17.8	13.3	13.5	9.7
Cappabianca (1997)	13		28.8					
Smith (1997)	53	Various						
Acciarri (1995)	13	Vascular malformation	31.7	14.4	27.7	10.2	4	5
Adler (1991)	14	Various	12.2		3		7.8	
Garcia Sola (1991)	18	Various	18.7					
Palmini (1991)	12	Neuronal migration disorder	17.5				11.9	
Rasmussen (1991)	283	Non-tumoral lesion						

Evidence Table 186. Patient characteristics from studies of frontal lobe surgery reporting seizure outcome measurements (continued)

Reference	Right Side Surgery	Left Side Surgery	Males	Females	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Ferrier (2001)							
Siegel (2001)							
Hong (2000)	3	8	7	4			
Eriksson (1999)	Adults		6	6			
	Children		6	7			
Wennberg (1999)	10	9					
Swartz (1998)	6	7					
Cappabianca (1997)							
Smith (1997)							
Acciarri (1995)	3	8	7	4	1	2	8
Adler (1991)	11	3	8	6			
Garcia Sola (1991)							
Palmini (1991)							
Rasmussen (1991)							

Evidence Table 187. Studies of frontal lobe surgery reporting seizure-free undefined

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Patients Seizure Free Undefined	Percentage	Cohen's h Effect Sizes	95% Confidence Interval	p Values for Effect Sizes	Standardized Residuals for Effect Sizes
Ferrier (2001)	35	6	2	19.5	21	60.0	1.77	1.30—2.24	<0.000001	2.26
Cappabianca (1997)	13		2		11	84.6	2.34	1.57—3.10	<0.000001	2.80
Smith (1997)	24		2		15	62.5	1.82	1.26—2.39	<0.000001	2.03
Acciarri (1995)	11	6.7	2	13	11	100.0	3.14	2.31—3.98	<0.000001	4.48
Garcia Sola (1991)	18	9	5	12.5	6	33.3	1.23	0.58—1.88	0.000222	-0.08
Rasmussen (1991)	283	16	2	49	68	24.0	1.02	0.86—1.19	<0.000001	-5.40

Evidence Table 188. Studies of frontal lobe surgery reporting patients who were seizure-free undefined – data used in meta-regression

Reference	N	Cohen's h Effect Size	Weight	Year Study Started	Year Study Ended	Conducted in the United States	Vascular Malformation Patients Only
Ferrier (2001)	35	1.77	17.5	1975	1996	No	No
Cappabianca (1997)	13	2.34	6.5	1985	1994	No	No
Smith (1997)	24	1.82	12	1995	1997	Yes	No
Acciarri (1995)	11	3.14	5.5	1975	1992	No	Yes
Garcia Sola (1991)	18	1.23	9	1978	1990	No	No
Rasmussen (1991)	283	1.02	141.5	1928	1980	No	No

Evidence Table 189. Results of the meta-regression for studies of frontal lobe surgery reporting patients who were seizure-free undefined

One predictor variable Bolded = statistically significant coefficient						
Covariate	**Intercept (CI)**	**P (intercept) =**	**Coefficient (CI)**	**P (coefficient)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	**1.743 (1.514 to 1.973)**	**<0.000001**	**0.015 (0.010 to 0.0218)**	**<0.000001**	**15.33792**	**0.004049**
End year (centered)	**1.711 (1.492 to 1.930)**	**<0.000001**	**0.059 (0.037 to 0.080)**	**<0.000001**	**14.93439**	**0.004839**
United States (USA = 0)	**1.823 (1.257 to 2.389)**	**<0.000001**	**-0.603 (-1.188 to -0.019)**	**0.042828**	**39.13536**	**<0.000001**
Tumor (all others=0)	**3.141 (2.305 to 3.977)**	**<0.000001**	**-1.939 (-2.787 to -1.091)**	**0.000007**	**23.13496**	**0.000119**

Two predictor variables									
Covariate: B_1	**Covariate: B_2**	**Intercept (CI)**	**P (intercept)**	**Coefficient B_1 (CI)**	**P (B_1) =**	**Coefficient B_2 (CI)**	**P(B_2)**	**Q_e =**	**P (Q_e) =**
Start year (centered)	End year (centered)	1.726 (1.492 to 1.961)	<0.001	0.005 (-0.024 to 0.035)	0.725	0.04 (-0.068 to 0.148)	0.468	14.81	0.002
Start year (centered)	United States (USA = 0)	1.412 (0.824 to 2)	<0.001	0.018 (0.011 to 0.026)	<0.001	0.436 (-0.275 to 1.147)	0.23	13.894	0.003
Start year (centered)	Tumor (all others=0)	3.11 (2.274 to 3.946)	<0.001	0.013 (0.007 to 0.02)	<0.001	-1.483 (-2.356 to -0.611)	0.001	4.239	0.237
End year (centered)	USA (USA = 0)	1.466 (0.883 to 2.049)	<0.001	0.065 (0.04 to 0.091)	<0.001	0.312 (-0.374 to 0.998)	0.373	14.14	0.003
End year (centered)	Tumor (all others=0)	3.116 (2.28 to 3.952)	<0.001	0.051 (0.028 to 0.073)	<0.001	-1.513 (-2.381 to -0.644)	0.001	3.278	0.351
United States (USA = 0)	Tumor (all others=0)	3.806 (2.786 to 4.826)	<0.001	-0.664 (-1.249 to -0.079)	0.026	-1.983 (-2.831 to -1.134)	<0.001	18.178	<0.001

Average N = 64
Average year started = 1972.67
Average year ended = 1991.5

Evidence Table 190. Studies of frontal lobe surgery reporting patients with seizure-free outcomes

Reference	Number of Patients	Followup Period in Years	Minimum Followup	Maximum Followup	Seizure Free Outcome	Number of Patients with Outcome	Percentage
Siegel (2001)	14		2		Engel Class I	8	57.1
Hong (2000)	11	3.5	2.1	4.7	Engel Class I	6	54.5
Eriksson (1999)	12 - adults	2			Seizure-free with auras	3	25.0
	13 - children					4	30.8
Wennberg (1999)	19	6.5	2	17	Engel Class I	11	57.9
Swartz (1998)	14	4.1	2	9	Seizure-free with no auras	8	57.1
Adler (1991)	14	8.2	3.6	19	Seizure-free with no auras	8	57.1
Palmini (1991)	12	5.8	2	15	Seizure-free with auras	2	16.7

Evidence Table 191. Studies of frontal lobe surgery reporting relationships between patient or study characteristics and treatment outcome

Reference	N	Seizure Outcome Measurement	Statistical Method	Patient or Study Characteristic Examined				
				Age at Treatment	Age at Seizure Onset	Duration of Epilepsy Prior to Treatment	Length of Followup	Other Study Variables
Ferrier (2001)	35	Seizure-free with auras	Univariate					Abolition of seizure patterns (Sig.), Abolition of sporadic spikes or their presence in the postsurgery electrocorticograms (NS), Location of residual sporadic discharges (NS), Incomplete removal of abnormal tissue (NS)
Smith (1997)	53	Seizure-free (undefined)	Univariate	NS	NS	NS	NS	Seizure frequency (NS), Completeness of lesion resection (NS), Lesional cases had better outcomes than nonlesional cases (Sig.)

Sig. Statistically significant
NS Not statistically significant

Evidence Table 192. Patient characteristics from studies of frontal lobe surgery reporting complications due to surgery

Reference	N	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration of Epilepsy Before Surgery (Years)
Kral (2001)	32	Various	10.8		4.6		6.1	
Mosewich (2000)	68		28.5	12.4	12.1	9.9	16.5	10.6
Chassoux (1999)	120	Various	21	8.2	9.2	7.3	11.9	7.3
Ferrier (1999)	42	Various	16.8	10.4	6.1	5.2	10.6	7.9
Helmstaedter (1998)	33	Various	29.8	10	15	11	15.2	9
Swartz (1998)	19	Various	31.3	12.3	17.8	13.3	13.5	9.7
Smith (1997)	53	Various						
Acciarri (1995)	13	Vascular malformation	31.7	14.4	27.7	10.2	4	5

Patient characteristics from studies of frontal lobe surgery reporting seizure outcome measurements (continued)

Reference	Right Side Surgery	Left Side Surgery	Males	Females	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Kral (2001)			22	10	20	12	4
Mosewich (2000)	39	29	45	23			
Chassoux (1999)	75	44	77	43			79
Ferrier (1999)			18	19		16	
Helmstaedter (1998)	16	17	21	12			
Swartz (1998)	6	7					
Smith (1997)							
Acciarri (1995)	3	8	7	4	1	2	8

Evidence Table 193. Studies of frontal lobe surgery reporting complications – list of complications

Reference	N	Years	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Kral (2001)	32	1989-2000	0			Complications were not identified per patient. Meningitis (1), Wound infection (2), Subdural hygroma (1), Weakness of the contralateral hand (3), Hemiparesis (1)
Mosewich (2000)	68	1987-1994	0		3	Mild to moderate hemiparesis (2), Mild hemiparesis and expressive dyphasia (1)
Chassoux (1999)	120	1964-1995	27	One year or more after surgery: Spastic hemiparesis or pronounced worsening of the preoperative deficit (27)	72	Minor motor deficit or a worsening of the preoperative motor deficit (19), Isolated facial paresis (6), Motor inertia (5), Hemiparesis or hemiplegia (42)
Ferrier (1999)	37	1975-1996	0		19	Complications were not identified per patient, but 18 of 37 patients had no postoperative complications. Hemiparesis (8), Mild dysphasia (2), Bone flap infection (8), CSF leak (1), Buzzing sensation in the left ear (1), Monoplegia with mild weakness (1)
Helmstaedter (1998)	33	1995-1996	0		14	Motor aphasia and paresis (3), transcortical aphasia and paresis (4), Cortical dysarthria (2) Severe psychomotor slowing (3), Anosmia (1)
Swartz (1998)	15	1986-1995	0		6	Decreased verbal fluency (2), Incontinence (1), Abulia (2), Monoparesis (1)
Smith (1997)	53		4	Disabling hemipareses (2), Diabetes insipidus (1), Steroid-induced diabetes mellitus (1)	6	Osteomyelitis (1), Epidural hematoma (1), Hemiparesis (1), Aphasia (1), Aspiration pneumonitis (1), Mild dysnomia (1)
Acciarri (1995)	11	1975-1992	0		0	

Evidence Table 194. Patient characteristics from studies of frontal lobe surgery reporting surgery related mortality

Reference	N	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration of Epilepsy Before Surgery (Years)
Kral (2001)	32	Mixed	10.8		4.6		6.1	
Smith (1997)	53	Mixed						
Acciarri (1995)	13	Vascular malformation	31.7	14.4	27.7	10.2	4	5

Patient characteristics from studies of frontal lobe surgery reporting surgery related mortality (continued)

Reference	Right Side Surgery	Left Side Surgery	Males	Females	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Kral (2001)			22	10	20	12	4
Smith (1997)							
Acciarri (1995)	3	8	7	4	1	2	8

Evidence Table 195. Patient characteristics from studies of hemispherectomy reporting seizure-free outcome measurements

Reference	N	Years	Country	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration of Epilepsy Before Surgery (Years)
Di Rocco (2000)	15	1985-1996	Italy	2.4	2.8				
Tinuper (1988)	14	1974-1987	Canada	14.5	10.2	4.7	5.6	9.8	9.5
Lindsay (1987)	17	1948-1986	England	12	2.9	5.1	2.4	7	2

Patient characteristics from studies of hemispherectomy reporting seizure-free outcome measurements (continued)

Reference	Right Side Surgery	Left Side Surgery	Males	Females	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Di Rocco (2000)	9	6	11	4			
Tinuper (1988)	6	8					
Lindsay (1987)	8	7	7	8			

Evidence Table 196. Studies of hemispherectomy reporting seizure outcome measurements

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Seizure-free With No Auras	Percentage	Seizure Free (Undefined)	Percentage
Di Rocco (2000)	15	5.5	3.5	14	6	40.0	---	---
Tinuper (1988)	14	6.9	4	13	---	---	10	71.4
Lindsay (1987)	15	14.1	2	36	---	---	9	60.0

Studies of hemispherectomy reporting seizure outcome measurements (continued)

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Engel Class I	Percentage	Engel Class IV	Percentage
Di Rocco (2000)	15	5.5	3.5	14	10	66.7	1	6.7
Tinuper (1988)	14	6.9	4	13	---	---	---	---
Lindsay (1987)	15	14.1	2	36	11	73.3	1	6.7

Evidence Table 197. Studies of hemispherectomy reporting education data

Reference	N	Mean Followup in Years	Minimum Followup	Maximum Followup	Number of Patients Going to School Prior to Surgery	Number of Patients Able to Remain at School or Obtain Employment After Surgery
Lindsay (1987)	15	14.1	2	36	1	8

Evidence Table 198. Studies of hemispherectomy reporting changes in IQ

Reference	N	Mean Followup in Years	Minimum Followup	Maximum Followup	Number of Patients with a Decrease in IQ	Number of Patients with an Increase in IQ	Baseline IQ		IQ After Surgery	
							Mean	SD	Mean	SD
Lindsay (1987)	15	14.1	2	36	2	6	59	14	66	Not reported

Evidence Table 199. Patient characteristics from studies of hemispherectomy reporting complications

Reference	N	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration of Epilepsy Before Surgery (Years)
Carreno (2001)	13						
Schramm (2001)	20	14.3	12.4	3.3	3.8	10.5	10.9
Di Rocco (2000)	15	2.4	2.8				
Shimizu (2000)	34	6.9		5.5		5.5	
Battaglia (1999)	10	1.7	1.7				
Wyllie (1998)	16			1.5			
Vining (1997)	58	6.8					
Peacock (1996)	58	4.8		0.8		3.9	
Schramm (1995)	13	12		3.7		9	
Tinuper (1988)	14	14.5	10.2	4.7	5.6	9.8	9.5
Lindsay (1987)	17	12	2.9	5.1	2.4	7	2

Evidence Table 199. Patient characteristics from studies of hemispherectomy reporting complications (continued)

Reference	Number of Patients	Right Side Surgery	Left Side Surgery	Males	Females	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Carreno (2001)	13							
Schramm (2001)	20			11	9			
Di Rocco (2000)	15	9	6	11	4			
Shimizu (2000)	34			21	13			
Battaglia (1999)	10			7	3	9	3	4
Wyllie (1998)	16							
Vining (1997)	58	32	26	18	40			
Peacock (1996)	58	25	33	31	27			
Schramm (1995)	13			11	2			
Tinuper (1988)	14	6	8					
Lindsay (1987)	17	8	7	7	8			

Evidence Table 200. Studies of hemispherectomy reporting complications – list of complications

Reference	N	Years	Country	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Carreno (2001)	13	1992-1999	United States	0		4	Bone flap infection (1), Placement of shunt for hydrocephalus (3)
Schramm (2001)	20	1991-1999	Germany	0		3	Subgaleal cerebrospinal fluid effusion (1), Meningitis (1), Deep infection (1)
Di Rocco (2000)	15	1985-1996	Italy	0		12	Five patients had more than one complication. Fever (6), Skin infection (2), Osteomyelitis and meningitis (1), Hemiparesis (2), Dystonia (2), Unilateral third cranial nerve deficit (1), Anemia (1), Hydrocephalus requiring a CSF shunt (5), Subdural hematoma (1)
Shimizu (2000)	34	1993-1999	Japan	1	Severe disability due to bilateral brain swelling (1)	5	Placement of shunts to treat CSF accumulation or hydrocephalus (5)
Battaglia (1999)	10	1987-1998	Italy	0		5	Hydrocephalus (3), Subdural hematoma (1), Hyperthermia (1)
Wyllie (1998)	16	1990-1996	United States	0		2	Deep vein thrombosis with secondary staphylococcus infection (1), Contralateral subdural hematoma (1)
Vining (1997)	58	1968-1996	United States	1	Coma (1)		Complications were not identified per patient. Severe intraoperative bleeding (8), Shunts (16), Septic meningitis (2), Bone infection (1), Deep venous thrombosis in the leg (2)
Peacock (1996)	58	1986-1995	United States	0		6	3 of 27 patients receiving a functional hemispherectomy developed hydrocephalus requiring a shunt (3), Mild cerebrospinal fluid infections treated with antibiotics (3)
Schramm (1995)	13	1992-1994	Germany	0		2	Placement of a shunt (1), Subgaleal cerebrospinal fluid effusion (1)
Tinuper (1988)	14	1974-1987	Canada	0		2	Hydrocephalus corrected with a shunt (1), Abscess in the removal cavity treated with antibiotics (1)

Evidence Table 201. Patient characteristics in studies of multiple subpial transection

Reference	N	Pathology	Mean Age at Surgery (Years)	SD of Age at Surgery (Years)	Mean Age at Seizure Onset (Years)	SD of Age at Seizure Onset (Years)	Mean Duration of Epilepsy Before Surgery (Years)	SD of Duration of Epilepsy Before Surgery (Years)
Mulligan (2001)	12		29.4		12.5		13.8	
Orbach (2001)	54							
Shimizu (2000)	31		9.3					
Smith (1998)	84							
Hufnagel (1997)	22		25.7	10.4	8.7	8.4	17	9.8
Pacia (1997)	21	Various	30.6	8.8				
Patil (1997)	19		21.7	14.1	8.3	6.9	13.3	9.4
Morrell (1995)	14	Landau-Kleffner syndrome	7	2.2	3.8	1.1	3.2	1.4
Sawhney (1995)	21		16	9.4	7	4.3	9	9.3
Shimizu (1991)	12		29					

Patient characteristics in studies of multiple subpial transection (continued)

Reference	Males	Females	Simple Partial Seizures	Complex Partial Seizures	Secondarily Generalized Seizures	Generalized Convulsive Seizures
Mulligan (2001)	4	8				
Orbach (2001)						
Shimizu (2000)	24	7				
Smith (1998)						
Hufnagel (1997)	12	10	8	14		16
Pacia (1997)	13	8				
Patil (1997)	6	13		14	16	
Morrell (1995)	4	10				
Sawhney (1995)	5	16				
Shimizu (1991)	9	3				

Evidence Table 202. Studies of multiple subpial transection reporting seizure frequency outcomes

Reference	N	Followup Period in Years	Minimum Followup	Maximum Followup	Seizure-free Outcome	Number of Patients with Outcome	Percentage
Mulligan (2001)	12	1.5	0.5	3	Seizure-free (undefined)	0	0.0
					90% reduction in seizure frequency	3	25.0
Orbach (2001)	54	4.7	2.3	7.4	Seizure-free with auras	20	37.0
					Engel Class I	20	37.0
					90% reduction in seizure frequency	20	37.0
Shimizu (2000)	25		1		Engel Class I	5	20.0
Smith (1998)	84		2		Engel Class I	42	50.0
Hufnagel (1997)	22	1.5	0.7	3.1	Seizure-free with auras	9	40.9
					90% reduction in seizure frequency	15	68.2
Pacia (1997)	21	1.8	1	2.8	Seizure-free with auras	12	57.1
					Engel Class I	12	57.1
Patil (1997)	19	2.6	1.3	4.5	Seizure-free (undefined)	5	26.3
					90% reduction in seizure frequency	17	89.5
Morrell (1995)	14	3.7	1.1	6.5	Seizure-free (undefined)	11	78.6
Sawhney (1995)	21	2.9	0.8	5	Seizure-free (undefined)	0	0.0

Evidence Table 203. Studies of multiple subpial transection reporting individual patient age at surgery

Reference	Number of Patients	Seizure Outcome Measurement	Point-Biserial Correlation [a]	95% Confidence Intervals		Standardized Residuals for Effect Sizes
				Lower	Upper	
Hufnagel (1997)	22	Seizure-free (undefined)	-0.18	-0.56	0.26	-1.63
Pacia (1997)	21	Seizure-free (undefined)	0.16	-0.29	0.55	0.08
Patil (1997)	19	Seizure-free (undefined)	0.20	-0.28	0.60	0.26
Morrell (1995)	14	Seizure-free (undefined)	0.17	-0.40	0.64	0.09
Sawhney (1995)	21	Improved	0.38	-0.06	0.70	1.25

[a] A positive correlation coefficient indicates more successful surgeries with an older age at surgery.

Evidence Table 204. Sensitivity analysis of studies of multiple subpial transection reporting individual patient age at surgery

Sensitivity Adjustment	Point-Biserial Correlation [a]	95% Confidence Interval		p Value for Summary Estimate	Q	p Value for Q
		Lower	Upper			
Original analysis	0.14	-0.07	0.34	0.196	3.33	0.504
Removing study with larest negative effect size [b]	0.24	-0.01	0.45	0.055	0.68	0.879
Removing study with largest positive effect size	0.07	-0.17	0.30	0.579	1.76	0.63
Removing study with smallest N	0.14	-0.09	0.36	0.243	3.32	0.344
Removing study with largest N	0.24	-0.01	0.45	0.055	0.68	0.879

[a] A positive correlation coefficient indicates more successful surgeries with an older age at surgery.
[b] The same study had the largest negative effect size and the largest N

Evidence Table 205. Studies of multiple subpial transection reporting successful surgery among male and female patients

Reference	N	Seizure Outcome Measurement	Number of Male Patients	Number of Male Successes	Number of Female Patients	Number of Female Successes	Cohen's h Effect Size [a]	95% Confidence Intervals		p Value for the Effect Size	Standardized Residuals for Effect Sizes
								Lower	Upper		
Hufnagel (1997)	22	Seizure-free (undefined)	12	5	10	4	0.03	-0.81	0.87	0.936876	-0.56
Pacia (1997)	21	Seizure-free (undefined)	13	7	8	5	-0.18	-1.06	0.71	0.695827	-1.05
Patil (1997)	19	Seizure-free (undefined)	6	2	13	3	0.23	-0.74	1.20	0.642986	-0.02
Morrell (1995)	14	Seizure-free (undefined)	4	4	10	7	1.16	0.00	2.32	0.050049	1.67
Sawhney (1995)	21	Improved	5	4	16	10	0.39	-0.61	1.40	0.445580	0.33

[a] A positive effect size favors male patients achieving more successful surgeries.

Evidence Table 206. Sensitivity analysis of studies of multiple subpial transection reporting successful surgery among male and female patients

Sensitivity Adjustment	Cohen's h Summary Estimate [a]	95% Confidence Interval		p value for Summary Estimate	Q	p value for Q	Back-transformed Percentage Estimate [b]	95% Confidence nterval	
		Lower	Upper					Lower	Upper
Original analysis	0.24	-0.19	0.66	0.272	3.59	0.464	1%	-1%	11%
Removing study with smallest effect size	0.37	-0.12	0.85	0.141	2.48	0.479	3%	0%	17%
Removing study with largest effect size [c]	0.10	-0.36	0.55	0.684	0.79	0.852	0%	-3%	7%
Removing study with smallest N	0.10	-0.36	0.55	0.684	0.79	0.852	0%	-3%	7%
Removing study with largest N	0.31	-0.18	0.80	0.219	3.28	0.350	2%	-1%	15%

[a] A positive summary estimate favors male patients achieving more successful surgeries.
[b] The back-transformed percentage estimate is the difference between the percentage of malr patients who achieved successful surgery and the percentage of female patients who achieved successful surgery. A positive percentage favors male patients and a negative percentage favors female patients. A difference of 0% indicates no differences between male and female patients in achieving successful surgery.
[c] The same study had the largest effect size and the smallest N

Evidence Table 207. Studies of multiple subpial transection reporting no benefit [a]

Reference	Number of Patients	Followup Period in Years	Minimum Followup	Maximum Followup	No Benefit	Percentage
Mulligan (2001)	12	1.5	0.5	3	5	41.7
Hufnagel (1997)	22	1.5	0.7	3.1	3	13.6
Pacia (1997)	21	1.8	1	2.8	1	4.8
Patil (1997)	19	2.6	1.3	4.5	0	0.0

[a] Patients had no change in seizure frequency or experienced an increase in seizure frequency after surgery

Evidence Table 208. Studies of multiple subpial transection reporting complications

Reference	N	Years	Country	Number of Patients with a Serious Permanent Complication	List of Permanent Complications	Number of Patients with a Mild or Transient Complication	List of Transient Complications
Mulligan (2001)	12	1990-1999	USA	0		0	
Shimizu (2000)	31	1983-1998	Japan	0		0	
Smith (1998)	84		USA	7	Aphasia, weakness, parietal sensory loss, worsening of a preexisting language disorder (7)	8	Eight patients experienced transient complications. Weakness (3), Cortical sensory loss (1), Dyslexia (1), Meningitis (1), Phlebitis (1), Orchitis (1), VIth cranial nerve palsy (1)
Hufnagel (1997)	22	1993-1996	Germany	4	Dysphasia (2), Global aphasia (1), Erethism and hyperkinesia (1)	10	Neurological deficits involving motor impairment (10)
Pacia (1997)	21	1992-1994	USA	1	Moderate dysphasia (1)	9	Mild higher corticosensory loss (1), Decreased left hand proprioception (1), Mild dysnomia and Dyslexia (1), Mild dysnomia (6)
Patil (1997)	19	1991-1995	USA	0		3	Hemiparesis (3)
Morrell (1995)	14	1987-1994	USA	0		2	Two small infarcts with one patient having right arm weakness (2)
Sawhney (1995)	21	1989-1993	England	2	Worsening of existing hemiplegia (2)	12	Neurological deficit (12), Arterial bleeding (1), Pulmonary embolism (1)
Shimizu (1991)	12	1989-1990	Japan	0		1	Intracerebral hematoma (1)

Evidence Table 209. Studies addressing nondrug, nonsurgery interventions

Reference	Country	Vagal-Nerve Stimulation	Ketogenic Diet	Magnetic Therapy	Vitamin B_6 Therapy	Herbal Medicine	Acupuncture	Elecrical Brain Stimulation	Chiropractic Therapy	Crainial Realignment	Hyperbaric Oxygen Therapy
Aldenkamp (2001)	Holland	✓									
Andriola (2001)		✓									
Chayasirisobhon (2001)	United States	✓									
Ergene (2001)	United States	✓									
Hoppe (2001)	Germany	✓									
Liporace (2001)		✓									
Pulsifer (2001)	United States		✓								
DeGiorgio (2000) Followup of ClinicalTrial EO5	United States	✓									
Hosain (2000)	United States	✓									
Ohtsuka (2000)	Japan					✓					
Valesco (2000a)	Mexico							✓			
Velasco (2000b)	Mexico							✓			
Ben-Menachem (1999)	Sweden	✓									
Boon (1999)	Belgium	✓									
Clinical Trial EO4 Labar (1999)	United States	✓									
Kloster (1999)	Norway						✓				
Mak (1999)			✓								
Parker (1999)	United Kingdom	✓									
Sirven (1999)	United States		✓								
Clinical Study EO5 Handforth (1998)	United States	✓									

Evidence Table 209. Table listing studies addressing each nondrug, nonsurgery intervention (continued)

Reference	Country	Vagal-Nerve Stimulation	Ketogenic Diet	Magnetic Therapy	Vitamin B_6 Therapy	Herbal Medicine	Acupuncture	Elecrical Brain Stimulation	Chiropractic Therapy	Crainial Realignment	Hyperbaric Oxygen Therapy
Freeman (1998)	United States		✓								
Lundgren (1998)	Sweden	✓									
Vining (1998)	United States		✓								
Salinski (1996) Followup of ClinicalTrial EO3	Multi-national	✓									
Tiancai (1996)	China					✓					
Clinical Trial EO3 The VNS Group (1995)	Multi-national	✓									
Nagakubo (1993)	Japan					✓					
Fisher (1992)	United States							✓			
Sramka (1990)	Russia							✓			
Ogunmekan (1989)	Canada					✓					
Schwartz (1989)			✓								
Ziyu (1987)	China						✓				
Sills (1986)			✓								
Trauner (1985)	United States		✓								
Total Number of Studies		**16**	**8**	**0**	**0**	**4**	**2**	**4**	**0**	**0**	**0**

Evidence Table 210. Articles addressing vagal nerve stimulation (VNS) excluded for quality reasons

Study	Reason for Exclusion
Liporace (2001)	This study was designed to assess the effects of making program adjustments to the VNS device on side effects without reducing the effectiveness of the device. Patient characteristics poorly described. Seizure type and severity information not presented. Followup time not presented.

Evidence Table 211. Quality of reporting in studies of vagal nerve stimulation

Reference	Sampling methodology described?	Clinical setting clearly described?	Inclusion/exclusion criteria stated?	Criteria used to categorize patients reported?	Basic demographic data for patients presented?	Information on comorbidities presented?	Information on method of data collection presented?	Analytic methods clearly described?	Information on sample size requirements presented?	Outcome data clearly presented?	Individual patient data presnted?
RCTs performed in the United States											
Clinical Study EO5 (1998)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No
Clinical Trial EO3 (1995)	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No
Long-term followups of RCT's performed in the United States											
DiGiorgio (2000) Followup of Clinical Trial EO5	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No
Salinski (1996) Followup of Clinical Trial EO3	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No
Case-series performed in the United States											
Chayasirisobhon (2001)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes
Ergene (2001)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No
Hosain (2000)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No
Clinical Trial EO4 Labar (1999)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes
Case-series performed outside of the United States											
Aldenkamp (2001)	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	No
Hoppe (2001)	No	Yes	Yes	No	No	No	NA	NA	No	Yes	No
Ben-Menachem (1999)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Boon (1999)	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No
Parker (1999)	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes
Lundgren (1998)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes

Evidence Table 212. Primary characteristics of included studies on vagal nerve stimulation

Reference	Start	End	Country	N	Longitudinal Study	Number of Study Groups	Number of Treatment Arms	Cross-Over Design	If Cross-Over Design, Was Washout Period Included
Aldenkamp (2001)	NR	NR	Holland	16	Yes	1	1	No	NA
Chayasirisobhon (2001)	1998	1999	United States	24	Yes	1	1	No	NA
Ergene (2001)	NR	NR	United States	17	Yes	1	1	NA	NA
Hoppe (2001)	1998	1999	Germany	36	Yes	1	1	No	NA
DiGiorgio (2000) Follow-up of Clinical Trial EO5	1995	1996	United States	199	Yes	1	1	No	NA
Hosain (2000)	NR	NR	United States	13	Yes	1	1	No	NA
Ben-Menachem (1999)	1992	1997	Sweden	64	Yes	1	1	No	NA
Boon (1999)	1995	1999	Belgium	25	Yes	1	1	No	NA
Clinical Trial EO4 Labar (1999)	NR	NR	United States	25	Yes	1	1	No	NA
Parker (1999)	1995	1996	United Kingdom	16	Yes	1	1	No	NA
Clinical Study EO5 Handforth (1999)	1995	1996	United States	199	Yes	2	2	No	NA
Lundgren (1998)	NR	NR	Sweden	16	Yes	1	1	No	NA
Salinski (1996) Follow-up of Clinical Trial EO3	NR	NR	Multi-national[a]	114	Yes	1	1	No	NA
Clinical Trial EO3 The VNS Group (1995)	NR	NR	Multi-national[a]	114	Yes	2	2	No	NA

[a] United States / Germany / Sweden / Canada / Holland

Evidence Table 212. Primary characteristics of included studies on vagal nerve stimulation (continued)

Reference	Type of Control Group	Randomized	Randomization Method Described	Method of Randomization Acceptable	Patients Blinded	2nd or 3rd Party Raters Blinded	Multi-center	Number of Centers	Industry Funded
Aldenkamp (2001)	NA	NA	NA	NA	No	No	No	1	NR
Chayasirisobhon (2001)	NA	NA	NA	NA	No	No	No	1	Yes
Ergene (2001).	NA	NA	NA	NA	No	No	No	1	NR
Hoppe (2001)	NA	NA	NA	NA	No	No	No	1	Yes
DiGiorgio (2000) Follow-up of Clinical Trial EO5	NA	NA	NA	NA	No	No	Yes	20	Yes
Hosain (2000)	NA	NA	NA	NA	No	No	No	1	NR
Ben-Menachem (1999)	NA	NA	NA	NA	No	No	No	1	No
Boon (1999)	NA	NA	NA	NA	No	No	No	1	No
Clinical Trial EO4 Labar (1999)	NA	NA	NA	NA	No	No	Yes	NR	Yes
Parker (1999)	NA	NA	NA	NA	No	No	No	1	No
Clinical Study EO5 Handforth (1999)	Concurrent Active	Yes	Yes	Yes	Yes	Yes	Yes	20	Yes
Lundgren (1998)	NA	NA	NA	NA	No	No	No	1	NR
Salinski (1996) Follow-up of Clinical Trial EO3	NA	NA	NA	NA	No	No	Yes	17	Yes
Clinical Trial EO3 The VNS Group (1995)	Concurrent Active	Yes	No	NA	Yes	Yes	Yes	17	Yes

Evidence Table 213. Study characteristics: data collection and analysis for studies of vagal nerve stimulation

Reference	Long Term Followup of Previous Controlled Trial	Subgroup Analysis of a Larger Trial	A Priori Power Calculations Performed	Pretreatment Baseline Data Reported	Baseline Observation Period	Method For Seizure Frequency Measurement
RCTs performed in United States [a]						
Clinical Study EO5 Handforth (1999)	No	No	Yes	Yes	12 to 16 weeks	Patient or caregiver maintained seizure diary
Clinical Trial EO3 The VNS Group (1995)	No	No	No	Yes	12 weeks	Patient or caregiver maintained seizure diary
Long-term followup of RCTs performed in United States						
DiGiorgio (2000) Followup of Clinical Trial EO5	Yes	No	No	Yes	12 to 16 weeks	Patient or caregiver maintained seizure diary
Salinski (1996) Followup of Clinical Trial EO3	Yes	No	No	Yes	12 weeks	Patient or caregiver maintained seizure diary
Case series performed in United States						
Chayasirisobhon (2001)	No	No	No	Yes	4 weeks	Patient or caregiver maintained seizure diary
Ergene (2001)	No	No	No	Yes	NR	Patients asked to subjectively describe change in seizure frequency and severity
Hosain (2000)	No	No	No	Yes	1 month	Unclear
Clinical Trial EO4 Labar (1999)	No	Yes	No	Yes	1 month	Patient or caregiver maintained seizure diary
Case series performed outside United States						
Aldenkamp (2001)	No	No	No	Yes	NR	NR
Hoppe (2001)	No	No	No	Yes	None	Patient or caregiver maintained seizure diary

Evidence Table 213. Study characteristics: data collection and analysis for studies of vagal nerve stimulation (continued)

Reference	Long Term Followup of Previous Controlled Trial	Subgroup Analysis of a Larger Trial	A Priori Power Calculations Performed	Pretreatment Baseline Data Reported	Baseline Observation Period	Method For Seizure Frequency Measurement
Ben-Menachem (1999)	No	No	No	Yes	3 months	Patient or caregiver maintained seizure diary (n = 57) Unknown (n = 7)
Boon (1999)	No	No	No	Yes	2 years[c]	Patient or caregiver maintained seizure diary (and for baseline retrospective review of diary plus medical records)
Parker (1999)	No	No	No	Yes	8 weeks	Patient or caregiver maintained seizure diary
Lundgren (1998)	No	No	No	Yes	6 months	Patient or caregiver maintained seizure diary

Evidence Table 213. Study characteristics: data collection and analysis for studies of vagal nerve stimulation (continued)

Reference	Followup [b]			Total Attrition: N (%)	Patient Data Stratified by Seizure Type	Compliance Monitored	Individual Patient Data Presented	Statistical Methods Reported	Statistical Methods Appropriate	AED Regimes Fixed During Followup Period
	Multiple	Longest	Times							
RCTs performed in United States										
Clinical Study EO5 Handforth (1999)	Yes	16 wks	12 to 16 wks	5 (2.5)	No	Yes	No	Yes	Yes	Yes
Clinical Trial EO3 The VNS Group (1995)	No	14 wks	14 wks	0 (0.0)	No	NR	No	Yes	Yes	Yes
Long-term followup of RCTs performed in United States										
DiGiorgio (2000) Followup of Clinical Trial EO5	Yes	1 yr	3 mos 12 mos	31 (15.9)	No	NR	No	Yes	Yes	No
Salinski (1996) Followup of Clinical Trial EO3	Yes	1 yr	3 mos 6 mos 9 mos 12 mos	14 (12.3)	No	NR	No	Yes	Yes	No
Case series performed in United States										
Chayasirisobhon (2001)	No	6 mos	6 mos	0 (0.0)	No	NR	Yes	No (none performed)	NA	Yes
Ergene (2001)	Yes	12 mos	1 to 3 wks 5 to 7 wks 3 mos 6 mos 9 to 12 mos	0 (0.0)	No	NR	No	Yes	Yes	Yes
Hosain (2000)	No	6 mos	6 mos	0 (0.0)	No	NR	Yes	Yes	Yes	No
Clinical Trial EO4 Labar (1999)	No	3 mos	3 mos	1 (4.0)	No	Yes	No	Yes	Yes	Yes

Evidence Table 213. Study characteristics: data collection and analysis for studies of vagal nerve stimulation (continued)

Reference	Followup [b]			Total Attrition: N (%)	Patient Data Stratified by Seizure Type	Compliance Monitored	Individual Patient Data Presented	Statistical Methods Reported	Statistical Methods Appropriate	AED Regimes Fixed During Followup Period
	Multiple	Longest	Times							
Case series performed outside United States										
Aldenkamp (2001)	No	6 mos	6 mos	0 (0.0)	Yes	NR	No	Yes	Yes	No
Hoppe (2001)	No	>6 mos	Mean: 8.0 (SD: 2.8) mos	0 (0.0)	No	NR	No	Yes	Yes	Yes
Ben-Menachem (1999)	No	5 yrs	Mean: 20 mos Rng: 3 to 64 mos	0 (0.0)	Yes	NR	Partial	No (none performed)	NA	NR
Boon (1999)	No	4 yrs 2 mos	Mean: 26 mos Rng: 3 to 64 mos	0 (0.0)	No	NR	Yes	Yes	Yes	No
Parker (1999)	Yes	12 mos	6 mos 12 mos	1 (6.25) 1 (6.25)	No	NR	Yes	Yes	Yes	No [d]
Lundgren (1998)	Yes	24 mos	4 to 6 mos 10 to 12 mos 16 to 18 mos 22 to 24 mos	0 (0.0) 0 (0.0) 5 (31.3) 14 (87.5)	No	NR	Yes	Yes	Yes	No [e]

[a] Multinational studies in which the majority of study centers were based in the United States are included in this section
[b] Followup time refers to time after activation of device or in case of followup studies the followup time refers to time after completion of controlled phase of study
[c] Based on a retrospective review of medical records and patient seizure diaries
[d] Dosage of phenytoin increased in one patient with a >50% increase in seizures at 9 months. Authors report that this had no effect on seizure frequency. Remaining 14 patients maintained on same drugs and dosage for remainder of study.
[e] One patient received concomitant transient add-on treatment with felbamate. The dosage of clonazepam was increased from 1.25 to 1.50 mg daily in patient 1 during the eighth month of VNS treatment. The dosage of lamotrigine was increased in one patient after 11 months of vagal nerve stimulation treatment.
Mos = Months NA = Not applicable Wks = weeks NR = Not reported Rng = Range

Evidence Table 214. Study characteristics: attrition rates in studies of vagal nerve stimulation

Reference	Attrition in the Whole Study (at Longest Followup)[a]							
	Total: N (%)	Due to Death: N (%)	Due to Adverse Event: N (%)	Due to Unrelated Illness: N (%)	Due to Treatment Dissatisfaction: N (%)	Due to Other Treatment: N (%)	Due to Other[b] Causes: N (%)	Due to Censorship[c] N (%)
RCTs performed in United States								
Clinical Study EO5 Handforth (1999)	5 (2.5)[d]	0 (0.0)	3 (1.5)[d]	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)
Clinical Trial EO3 The VNS Group (1995)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Long-term followup of RCTs performed in United States								
DiGiorgio (2000) Followup of Clinical Trial EO5	31 (15.9)	2 (1.0)	2 (1.0)	0 (0.0)	18 (9.2)	0 (0.0)	9 (4.6)	0 (0.0)
Salinski (1996) Followup of Clinical Trial EO3	14 (12.3)	2 (1.8)	0 (0.0)	1 (0.9)	9 (7.9)	0 (0.0)	2 (1.8)	0 (0.0)
Case series performed in United States								
Chayasirisobhon (2001)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ergene (2001)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hosain (2000)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Clinical Trial EO4 Labar (1999)	1 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)	0 (0.0)
Case series performed outside United S tates								
Aldenkamp (2001)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hoppe (2001)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ben-Menachem (1999)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Boon (1999)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Parker (1999)	1 (6.25)	0 (0.0)	1 (6.25)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lundgren (1998)	5 (31.3)[g] 14 (87.5)[h]	NR	NR	NR	NR	NR	NR	NR

Evidence Table 214. Study characteristics: attrition rates in studies of vagal nerve stimulation (continued)

Reference	Attrition in Per Treatment Arm (at Longest Followup)[a]							
	Treatment Arm	Total: N (%)	Due to Death: N (%)	Due to Adverse Event: N (%)	Due to Unrelated Illness: N (%)	Due to Treatment Dissatisfaction: N (%)	Due to Other Treatment: N (%)	Due to Other Causes: N (%)
RCTs performed in United States								
Clinical Study EO5 Handforth (1999)	High	3 (3.2)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)[e]
	Low	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)[f]
Clinical Trial EO3 The VNS Group (1995)	High	NA	NA	NA	NA	NA	NA	NA
	Low	NA	NA	NA	NA	NA	NA	NA

[a] Exact attrition figures at different followup times and for different outcome measures are presented in the results table
[b] "Other" refers to patients lost to followup for unspecified reasons
[c] Censored patients are those who had not yet reached follow-up time at time of analysis
[d] Includes one patient who was not randomized because of surgical infection
[e] Poor compliance (n = 1); Uninterruptible patient diary
[f] Withdrawal of consent (n = 1)
[g] At 18 months
[h] At 24 months
NA = Not applicable
NR = Not reported

Evidence Table 215. Study characteristics: confirmation of diagnosis and definition used in studies of vagal nerve stimulation

Reference	Method(s) Used toEnsure That Patients Were Correctly Diagnosed	Patient Description
RCT's performed in the United States		
Clinical Study EO5 Handforth (1999)	Not reported	Patients with medically refractory seizures defined as a frequency of ≥6 seizures per month
Clinical Trial EO3 The VNS Group (1995)	Not reported	Patients with medically refractory seizures defined as a frequency of ≥6 seizures per month
Long-term followup of RCT's performed in the United States		
DiGiorgio (2000) Followup of Clinical Trial EO5	As Clinical Study EO5 above	As Clinical Study EO5 above
Salinski (1996) Followup of Clinical Trial EO3	As Clinical Study EO3 above	As Clinical Study EO3 above
Case-series performed in the United States		
Chayasirisobhon (2001)	Not reported	Patients with seizures refractory to antiepilpetic drugs given alone or in various combinations
Ergene (2001)	Not reported	Patients with persistant, frequent seizures despite appropriate medical management
Hosain (2000)	Clinical evaluation Routine EEG Video-EEG	Patients with severe, medication resistant mixed seizures
Clinical Trial EO4 Labar (1999)	Retrospective review of clinical notes, EEG data, neroimaging data	Patients with medication resistant generalized epilepsy
Case-series performed outside the United States		
Aldenkamp (2001)	Clinical evaluation EEG evidence	Patients with Lennox-Gestaut syndrome whose seizures were unacceptable to patient because of impact on dailiy function Patients seizures were resistant to treatment with antiepileptic drugs and patients were inelligable for resective surgery
Hoppe (2001)	Not reported	Patients with pharmacoresistant complex-partial seizures
Ben-Menachem (1999)	Clinical evaluation Routine EEG Ictal video-EEG in patients with partial seizures MRI	Patients with seizuers refractory to available antiepileptic drugs

Evidence Table 215. Study characteristics: confirmation of diagnosis and definition used in studies of vagal nerve stimulation (continued)

Reference	Method(s) Used to Ensure That Patients Were Correctly Diagnosed	Patient Description
Boon (1999)	Extensive pre-surgical evaluation which included: Clinical evaluation Video-EEG monitoring (+2 patients underwent intracranial video-EEG monitoring) MRI FDG-PET	Patients with medically refractory partial seizures considered for resective surgery but, following an extensive evaluation, were found not to be suitable candidates because a confined or resectable epileptogenic zone could not be identified
Parker (1999)	Clinical assessment Interictal EEG activity conjusive with generalized seizures Normal MRI (no evidence of focal lesion) PET (no evidence of focal lesion or focal lesion with absence of interical focal abnormality)	Patients with cryptogenic epileptic enecepahlopathy
Lundgren (1998)	Not reported	Patients with intractable epilepsy

Evidence Table 216. Study characteristics: patient selection criteria in studies of vagal nerve stimulation

Reference	Reasons for Patient Selection						Minimum Seizure Rate to be Eligible	Side Effects Included in Definition of Treatment Resistant Epilepsy	Study Reported Prior AEDs Failed at Maximum Tolerated Dose
	Subpopulation of Patients Who Received VNS	Children	Adults	Particular Syndrome	Particular Seizure Type	Mentally Retarded or Have Deveolpmental Disability			
RCTs performed in United States									
Clinical Study EO5 Handforth (1999)	Yes	No	No	No	Yes	No	6 per month	No	No
Clinical Trial EO3 The VNS Group (1995)	Yes	No	No	No	Yes	No	6 per month	No	No
Long-term followup of RCTs performed in United States									
DiGiorgio (2000) Followup of Clinical Trial EO5	Yes	No	No	No	Yes	No	6 per month	No	No
Salinski (1996) Followup of Clinical Trial EO3	Yes	No	No	No	Yes	No	6 per month	No	No
Case series performed in United States									
Chayasirisobhon (2001)	No	No	No	No	No	No	6 per month	No	No
Ergene (2001)	Yes	No	No	No	Yes	No	Not reported	No	No
Hosain (2000)	Yes	No	No	Yes	No	No	Not reported	No	No
Clinical Trial EO4 Labar (1999)	Yes	No	No	No	Yes	No	≥1 per month	No	No
Case series performed outside United States									
Aldenkamp (2001)	Yes	Yes	No	Yes	No	Yes	Not reported	No	No
Hoppe (2001)	Yes	No	Yes	No	Yes	No	Not reported	No	No
Ben-Menachem (1999)	No	No	No	No	No	No	Not reported	No	No
Boon (1999)	Yes	No	No	No	Yes	No	Not reported	No	No
Parker (1999)	Yes	Yes	No	No	No	No	Not reported	No	No
Lundgren (1998)	Yes	Yes	No	No	No	No	Not reported	No	No

[a] See The Vagus Nerve Stimulation Study

Evidence Table 216. Study characteristics: patient selection criteria in studies of vagal nerve stimulation (continued)

Reference	Inclusion Critiera	Excusion Criteira	Patient Sampling Method
RCTs performed in United States			
Clinical Study EO5 Handforth (1999)	≥6 seizures in a 30 day period Age 12 to 65 years Use acceptable AX-contraception if fertile female Take 1 to 3 marketed AEDs on a stable regimen for >1 month	Deteriorating medical or neurological conditions Pregnancy Cardiac or pulmonary disorder Active peptic ulcer History of non-epilpetic seizures >1 episode of status epilepticus in previous 12 mos Prior cervical vagotomy Prior brain stimulation Prior VNS Prior resective epilepsy surgery Inability to perform pulmonary function tests Unable to comply with clinical visits	Not reported
Clinical Trial EO3 The VNS Group (1995)	Partial seizures Seizures not adequatley controlled with medication ≥6 seizures per month Age ≥12 years	Progressive or unstable-medical condition Eitiology best treated by surgery Use of >3 AED's at study entry Use of an experimental AED at time of entry Pregnancy ≥20% variation in serum AED levels during baseline.	Consecutive

Evidence Table 216. Study characteristics: patient selection criteria in studies of vagal nerve stimulation (continued)

Reference	Inclusion Critiera	Excusion Criteira	Patient Sampling Method
Long-term followup of RCTs performed in United States			
DiGiorgio (2000) Followup of Clinical Trial EO5	See Clinical Trial EO3	See Clinical Trial EO5	See Clinical Trial EO5
Salinski (1996) Followup of Clinical Trial EO3	See Clinical Trial EO3	See Clinical Trial EO3	See Clinical Trial EO3
Case series performed in United States			
Chayasirisobhon (2001)	Refractory response to AED's given alone or in combination ≥ 6 seizures per mo Patients are unsuitable-for epilepsy surgery	Evidence of non-epilpetic seizures Previous left cervical vagotomy	All patients who met inclusion criteria implanted with VNS at study center
Ergene (2001)	Partial onset seizures Persistant, frequent seizues despite appropriate medical management Not candidates for surgical treatment	Not reported	Not reported
Hosain (2000)	Patients with Lennox Gestaut syndrome Severe medication resistant mixed seizures Static encephalopathy Generalized slow spike-and-wave discharges seen on EEG Undergone video-EEG to confirm diagnosis	Not reported	All patients with Lennox-Gastaut syndrome
Clinical Trial EO4 Labar (1999)	Age >3 years ≥1 seizure per month	Cardiac or progressive neurologic disease	All patients with generalized seizures who met inclusion criteria of study EO4[b]

[b] This report contains a subgroup of patients with generalized seizures who entered Clinical Study EO4. Data from whole study population is not available

Evidence Table 216. Study characteristics: patient selection criteria in studies of vagal nerve stimulation (continued)

Reference	Inclusion Critiera	Excusion Criteira	Patient Sampling Method
Case series performed outside United States			
Aldenkamp (2001)	Multiple seizure types consistent with Lennox-Gastaut syndrome Mental retardation or developmental delay Seizures unacceptable-to patients or parent because of impact on daily life functions and development due to frequency or severity Resistance to existing pharmacological treatments and ineligibility for surgical alternatives (resective surgery, callosotomy) Written and signed informed consent	Progressive neurological disease Bad physical condition that would not allow the surgical implantation procedure Any risk for complications due to the implanataion procedure (cardiac disease, restrictive pulmonary disease, stomach ulcers)	All patients with Lennox-Gastaut syndrome
Hoppe (2001)	Patients with pharmacoresistant complex-partial seizures Patients able to participate in neuropsychological assessment.	Not reported	Consecutive
Ben-Menachem (1999)	Refractory to available AED's Patients deemed unsuitable-for epilepsy surgery or had received unsuccessful surgery	Not reported	Not reported
Boon (1999)	Patients with partial seizures refractory to available AED's who had undergone extensive pre-surgical evaluation but were consequently deemed unsutiable candidates for surgery	Not reported	All patients with >6 mos followup.
Parker (1999)	Mixed generilized seizures refractory to treatment with AED's Age ≤18 yrs	Not reported	All children receiving VNS device at study center who met inclusion criteria
Lundgren (1998)	Not reported	Not reported	Unclear

Evidence Table 217. Study characteristics: settings in studies of vagal nerve stimulation

All studies used the NeuroCybernetic Prosthesis Generator

Reference	Study Arm	Output Current (mA)	Ramp Up Period	Frequency (Hz)	Pulse Width (ms)	On Time (sscs)	Off Time (min)	Manual Activation Mode
RCTs performed in United States								
Clinical Study EO5 Handforth (1999)	High	0.25 to 3.5 (maximum tolerable)	2 weeks	30	500	30	5	Enabled
	Low	0.25 to 3.5 (minimum level consistent sensation of stimulation)	2 weeks	1.0	130	30	180	Disabled
Clinical Trial EO3 The VNS Group (1995)	High	1.5 (range: 0.25 to 3.0 (max tolerable)	NR	30 (range: 20 to 50)	500	30 (range: 30 to 90)	5 (range: 5 to 10)	Enabled
	Low	1.25 (range: 0.25 to 2.75) (minimum level consistent a sensation stimulation)	NR	1 (range: 1 to 2)	130	30	90 (range: 60 to 180)	Disabled
Long-term followup of RCTs performed in United States								
DiGiorgio (2000) Followup of Clinical Trial EO5	High	0.25 to 3.5 (maximum tolerable)	2 weeks	20 to 30	500 to 750	7 to 60	1.1 to 180	Enabled
Salinski (1996) Followup of Clinical Trial EO3	High	1.5 (range: 0.25 to 3.0 (maximum tolerable)	NR	30 (range: 20 to 50)	500	30 (range: 30 to 90)	5 (range: 5 to 10)	Enabled
Case series performed in United States								
Chayasirisobhon (2001)	NA	1.75 to 3.5 (maximum tolerable)	6 weeks	30	500	30	5	Enabled
Ergene (2001)	NA	1.0 to 2.5 (maximum tolerable)	2 to 3months	30	500	30	5	NR
Hosain (2000)	NA	0.50 to 1.75 (maximum tolerable)	2 weeks to 2 months	30	500	30	5	Enabled
Clinical Trial EO4 Labar (1999)	NA	0.25 to 3.5 (maximum tolerable)	3 months	30	500	30	5	Enabled

Evidence Table 217. Study characteristics: settings in studies of vagal nerve stimulation (continud)

Reference	Study Arm	Output Current (mA)	Ramp Up Period	Frequency (Hz)	Pulse Width (ms)	On Time (seconds)	Off Time (minutes)	Manual Activation Mode
Case series performed outside United States								
Aldenkamp (2001)	NA	1.5 to 2.0 (maximum tolerable)	3 months	30	500	30 (or 7 if patient did not respond)	5 (or 18 secs if patient did not respond)	NR
Hoppe (2001)	NA	0.5 to 2.0 (maximum tolerable)	8 weeks	30	500	30 (or 7 if patient did not respond	5 (or 30 secs if patient did not respond)	NR
Ben-Menachem (1999)	NA	1.0 to 1.5 (maximum tolerable)	NR	30	500	30 (or 7 if patient did not respond)	5 (or 20 secs if patient did not respond)	NR
Boon (1999)	NA	1.0 to 2.7 (maximum tolerable)	NR	30	500	30	5 to 10	Enabled
Parker (1999)	NA	1.25 to 2.0 (maximum tolerable)	NR	NR	NR	30	5	NR
Lundgren (1998)	NA	1.25 to 2.0 (maximum tolerable)	2 to 12 weeks	30	500	30 (or 7 if patient did not respond)	5 (or 12 to 30 secs if patient did not respond)	Yes

[a] Information on VNS device settings extracted from Labar (1999)
NA Not applicable
NR Not reported

Evidence Table 218. Patient characteristics: baseline demographics in studies of vagal nerve stimulation

Reference	Presented Baseline Demographic Data For All Patients Who Entered Study	Study Arm	% Male	Mean Age at Implantation in Years (SD)	Age Range in Years	Mean Duration of Disease in Years (SD)	Range of Disease Duration
RCTs performed in United States							
Clinical Study EO5 Handforth (1999)	Yes	High	51.6	32.1 (10.8)	13 to 54	22.1 (11.5)	2 to 48
		Low	42.7	34.2 (10.1)	15 to 60	23.7 (10.8)	2 to 52
Clinical Trial EO3 The VNS Group (1995)	No	High	61	33.1 (NR)	NR	23.1 (NR)	NR
		Low	63.9	33.5 (NR)	NR	20.0 (NR)	NR
Long-term followup of RCTs performed in United States							
DiGiorgio (2000) Followup of Clinical Trial EO5	Yes	NA	46.7	34 (NR)	NR	Median: 22	NR
Salinski (1996) Followup of Clinical Trial EO3	Yes	NA	NR	33 (NR)	13 to 52	NR	NR
Case series performed in United States							
Chayasirisobhon (2001)	Yes	NA	58.3	27.1 (17.2)	6 to 70	20.1 (14.1)	1 to 43
Ergene (2001)	Yes	NA	64.7	33.8 (NR)	11 to 55	NR	NR
Hosain (2000)	Yes	NA	76.9	18.9 (10.8)	4 to 44	NR	NR
Clinical Trial EO4 Labar (1999)	No	NA	54.2	NR (NR)	4 to 40	NR (NR)	4 to 35

Evidence Table 218. Patient characteristics: baseline demographics in studies of vagal nerve stimulation (continued)

Reference	Presented Baseline Demographic Data For All Patients Who Entered Study	Study Arm	% Male	Mean Age at Implantation in Years (SD)	Age Range in Years	Mean Duration of Disease in Years (SD)	Range of Disease Duration
Case series performed outside United States							
Aldenkamp (2001)	Yes	NA	81.3	11.1 (NR)	6 to 17	8.5 (NR)	NR
Hoppe (2001)	Yes	NA	NR	33.6 (9.8)	NR	NR	NR
Ben-Menachem (1999)	No	NA	NR	NR	NR	NR	NR
Boon (1999)	Yes	NA	40.0	30.2 (9.0)	12 to 45	17.0 (8.0)	5 to 35
Parker (1999)	Yes[a]	NA	NR	11.3 (3.1)	5 to 17	10.0 (3.4)	3 to 16
Lundgren (1998)	Yes	NA	62.5	11.0 (4.5)	4 to 19	8.1 (4.3)	3.5 to 18.6

Evidence Table 218. Patient characteristics: baseline demographics in studies of vagal nerve stimulation (continued)

Reference	Mean Age at Onset (SD)	Range of Age at Onset	Postsurgical Patients (%)	AED's Taken by Each Patient	Patients With IQ <70 (%)
RCTs performed in United States					
Clinical Study EO5 Handforth (1999)	NR	NR	0 (0.0)	1 to 3	NR
	NR	NR	0 (0.0)	1 to 3	NR
Clinical Trial EO3 The VNS Group (1995)	NR	NR	0 (0.0)	Mean: 2.09	NR
	NR	NR	0 (0.0)	Mean: 2.08	NR
Long-term followup of RCTs performed in United States					
DiGiorgio (2000) Followup of Clinical Trial EO5	Median: 9 years	NR	0 (0.0)	1 to 3	NR
Salinski (1996) Followup of Clinical Trial EO3	NR	NR	0 (0.0)	1 to 3	NR
Case series performed in United States					
Chayasirisobhon (2001)	7.0 (8.9) years	1 day to 31 years	NR	1 to 3	11 (45.8)
Ergene (2001)	NR	NR	0 (0.0)	2 or 3	NR
Hosain (2000)	NR	NR	3 (23.1)	Median: 6 (range: 4 to 12	NR
Clinical Trial EO4 Labar (1999)	NR (NR)	0 to 14 yrs	NR	1 to 5	NR
Case series performed outside United States					
Aldenkamp (2001)	2.6 (NR)	0 to 8 yrs	0	NR	NR
Hoppe (2001)	NR	NR	NR	NR	0 (0.0)
Ben-Menachem (1999)	NR	NR	NR	1 to 4	NR
Boon (1999)	13.3 (7.8) years	2 to 29 years	0 (0.0)	NR	NR
Parker (1999)	1.3 (1.6) years	1 mo to 3 years	0	NR	NR
Lundgren (1998)	2.9 (2.7) years	1 mos to 9 years	6 (37.5)	1 to 3	14 (87.5)

[a] Demographic data presented for the 15 of 16 patients in whom device was who initiated. Data from one patient who had device removed because of infection prior to device initiation was not presented.
NA = Not applicable
NR = Not reported

Evidence Table 219. Patient characteristics: seizure types and etiology in studies of vagal nerve stimulation

Reference	Treatment Arm	Number of Patients With Each Seizure Type (%)								
		Primary Partial	Primary Generalized	Complex Partial	Simple Partial	Secondary Generalized	Generalized Tonic, Clonic, or Tonic-Clonic	Generalized Absence	Lennoz-Gastaut Syndrome	Generalized Atonic
RCTs performed in United States										
Clinical Study EO5 Handforth (1999)	High	95 (100.0)	NR	NR	NR	NR	NR	NR	NR	NR
	Low	103 (100.0)	NR	NR	NR	NR	NR	NR	NR	NR
Clinical Trial EO3 The VNS Group (1995)	High	54 (100.0)	NR	50 (92.6)	24 (44.4)	38 (70.4)	NR	NR	NR	NR
	Low	60 (100.0)	NR	58 (96.7)	25 (41.7)	33 (55.0)	NR	NR	NR	NR
Long-term followup of RCTs performed in United States										
DiGiorgio (2000) Followup of Clinical Trial EO5	NA	195 (100.0)	NR	191 (98.0)	NR	NR	96 (49.2)	NR	NR	NR
Salinski (1996) Followup of Clinical Trial EO3	NA	114 (100.0)	NR	NR	NR	NR	NR	NR	NR	NR
Case series performed in United States										
Chayasirisobhon (2001)	NA	14 (58.3)	?	10 (41.7)	12 (50.0)	?	21 (87.5)	8 (33.3)	6 (25.0)	7 (29.2)
Ergene (2001)	NA	17 (100.0)	0 (0.0%)	NR	NR	NR	NR	NR	NR	NR
Hosain (2000)	NA	13 (100.0)	4 (30.8)	4 (30.8)	0 (0.0)	3 (23.1)	9 (69.2)	12 (92.3)	13 (100.0)	4 (30.8)
Clinical Trial EO4 Labar (1999)	NA	0 (0.0)	24 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	22 (88.0)	12 (48.0)	NR	NR

Evidence Table 219. Patient characteristics: seizure types and etiology in studies of vagal nerve stimulation (continued)

Reference	Treatment Arm	Number of Patients With Each Seizure Type (%)								
		Primary Partial	Primary Generalized	Complex Partial	Simple Partial	Secondary Generalized	Generalized Tonic, Clonic, or Tonic-Clonic	Generalized Absence	Lennoz-Gastaut Syndrome	Generalized Atonic
Case series performed outside United States										
Aldenkamp (2001)	NA	NR	NR	5 (31.3)	0 (0.0)	1 (6.3)	10 (62.5)[a] 9 (56.3)[b]	10 (62.5)	12 (75.0) (+4 patients (25.0%) with LG like syndromes)	3 (18.8)
Hoppe (2001)	NA	36 (100.0)	0 (0.0)	36 (100.0)	0 (0.0)	NR	NR	NR	NR	NR
Ben-Menachem (1999)	NA	47 (73.4)	17 (26.6)	47 (73.4)	NR	NR	9 (14.1)	NR	8 (12.5)	NR
Boon (1999)	NA	0 (0.0)	20 (100)	4 (20.0)	18 (90.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Parker (1999)	NA	0 (0.0)	16 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (62.5)	0 (0.0)
Lundgren (1998)	NA	8 (50.0)	8 (50.0)	NR	NR	2 (12.5)	4 (25.0)	0 (0.0)	4 (25.0)	0 (0.0)

[a] Generalized tonic seizures
[b] Generalized tonic-clonic seizures
NA Not applicable
NR Not reported

Evidence Table 219. Patient characteristics: seizure types and etiology in studies of vagal nerve stimulation (continued)

Reference	Treatment Arm	Etiology / Syndrome / History	
RCTs performed in United States			
Clinical Study EO5 Handforth (1999)	High	NR	
	Low	NR	
Clinical Trial EO3 The VNS Group (1995)	High	NR	
	Low	NR	
Long-term followup of RCTs performed in United States			
DiGiorgio (2000) Followup of Clinical Trial EO5	NA	NR	
Salinski (1996) Followup of Clinical Trial EO3	NA	NR	
Case series performed in United States			
Chayasirisobhon (2001)	NA	Lennox-Gestaut syndrome (n = 6)	Epidermoid tumor (n = 1)
		Tuberous sclerosis (n = 3)	Caernous angioma (n = 1)
		Encephalitis (n = 2)	Porencephalopathy (n = 1)
		Head injury (n = 2)	Prenatal encephalopathy (n = 1)
		Oligodendrioma (n = 1)	Unknown (n = 5)
		Meningoencephalitis (n = 1)	
Ergene (2001)	NA	Cerebral palsy/ perinatal brain injury (n = 5 (29.4%)	Subarachnoid hemorrhage (n = 2 (11.8%)
		Mesial temporal sclerosis (n = 3 (17.7%)	History of meningitis (n = 1 (5.9%)
		Head injury (n = 2 (11.8%)	Unknown (n = 4 (23.5%)
Hosain (2000)	NA	Lennox Gestaut syndrome (n = 13)	
Clinical Trial EO4 Labar (1999)	NA	Cryptogenic (n = 10)	Congenital brain injury (n = 3)
		Postinfectious (n = 4)	Unknown (n = 7)

Evidence Table 219. Patient characteristics: seizure types and etiology in studies of vagal nerve stimulation (continued)

Reference	Treatment Arm	Etiology / Syndrome / History	
Case series performed outside United States			
Aldenkamp (2001)	NA	Lennox-Gestaut syndrome (n = 12) Doose syndrome (n = 3)	Myoclonic absence epilepsy (n = 1)
Hoppe (2001)	NA	NR	
Ben-Menachem (1999)	NA	Lennox-Gestaut syndrome (n = 8) NR (n = 56)	
Boon (1999)	NA	History of head injury (n = 5) History of encephalitis (n = 2) History of premature birth (n = 1) History of meningitis (n = 5)	History of forceps delivery (n =1) History of fibrile seizures (n = 6) History of ventricular atrial drainage (n = 1) No history (n = 4)
Parker (1999)	NA	Lennox-Gestaut (n = 10) Juvenile myoclonic epilepsy (n = 6)	
Lundgren (1998)	NA	Lennox-Gestaut (n = 4) NR (n = 12)	

Evidence Table 220. Subpopulations of patients with treatment-resistant epilepsy in whom vagal nerve stimulation was assessed

Reference	Patients Recruited Because of Seizure Type	Patients Recruited Because of Syndrome	Seizure Type or Syndrome (if Applicable)	Patients Chosen Because They Were Children	Patients Chosen Because They Were Adults
RCTs performed in United States					
Clinical Study EO5 Handforth (1999)	✓		Partial seizures		
Clinical Trial EO3 The VNS Group (1995)	✓		Partial seizures		
Followup studies of RCTs					
DiGiorgio 2000) Followup of Clinical Trial EO5	✓		Partial seizures		
Salinski (1996) Followup of Clinical Trial EO3	✓		Partial seizures		
Case series performed in United States					
Chayasiriobhon (2001)			Mixed		
Ergene (2001)	✓		Partial seizures		
Hosain (2000)		✓	Lennox-Gestaut Syndrome		
Clinical Trial EO4 Labar (1999)	✓		Generalized seizures		
Case series performed outside of the United States					
Aldenkamp (2001)		✓	Lennox-Gestaut Syndrome	✓	
Hoppe (2001)	✓		Complex-partial seizures		
Ben-Menachem (1999)			Mixed		
Boon (1999)	✓		Partial seizures		
Parker (1999)	✓		Primary or secondary generlaized seizures	✓	
Lundgren (1998)			Mixed	✓	

Evidence Table 221. Individual patient data extracted from Boon (1999)

Patient	Sex	Age	Seizure Type	Age at Onset of Disease (Years)[a]	Duration of Disease (Years)	History
1	M	36	CPS, SG	14	22	Febrile seizures, head trauma
2	F	34	CPS, SG, SPS	29	5	Head trauma
3	M	39	CPS, SG	26	13	Head trauma
4	F	32	CPS, SG	14	18	Encephalitis
5	M	30	CPS, SG, SPS	12	18	Premature birth, callosotomy
6	M	21	CPC, SG	3	18	Febrile seizures
7	M	29	CPS, SG	7	22	Head trauma
8	F	23	CPS, SG, SPS	5	18	Febrile seizures, head trauma
9	F	32	CPS, SG	23	9	Febrile seizuers
10	F	25	CPS, SG	2	23	Febrile seizures, encephailitis
11	F	39	CPS, SG	8	31	Forceps birth
12	F	44	CPS, SG	9	35	Meningitis, ventricular atrial drainage
13	F	17	CPS, SG, SPS	6	11	None
14	F	25	CPS, SG (atonic)	12	13	None
15	M	20	CPS	14	6	Meningitis, head trauma
16	M	38	CPS, SG	18	20	None
17	F	12	CPS, SG	7	5	None
18	F	37	CPS, SG	23	14	Meningitis
19	M	26	CPS	12	14	Meningitis
20	F	45	CPS, SG	21	24	Meningitis, febrile seizures

[a] Calculated from available data by ECRI
CPS Complex partial seizure
SG Secondary generalized
SPS Simple partial seizure

Evidence Table 221. Individual patient data extracted from Boon (1999) (continued)

Patient	VNS Output Current (mA)	Baseline Mean Seizure Frequency (Seizures Per Month)	Followup Time (Months)	Post VNS Mean Seizure Frequency (Seizures Per Month)	% Reduction In Mean Seizure Rate[a]
1	2.25	8	50	0	100
2	1.75	3	50	0	100
3	1.5	4	45	0	100
4	2.75	40	43	25	37.5
5	2.5	4	38	3	25.0
6	2.5	4	38	1	75.0
7	2.0	30	37	20	33.3
8	1.5	4	31	0	100
9	1.75	16	28	4	25.0
10	3.0	35	26	30	14.3
11	2.75	8	23	2	25.0
12	1.75	2	20	0	100
13	1.5	200	20	0	100
14	1	30	19	30	0.0
15	2.75	4	15	1	25.0
16	2	30	12	30	0.0
17	2	12	10	9	25.0
18	2	3	9	0.5	83.3
19	2.25	20	8	12	40.0
20	1	10	6	6	40.0

[a] Calculated from available data by ECRI

Evidence Table 222. Individual patient data extracted from Chayasirisobhon (2001)

Patient	Sex	Age at Device Implantation (Years)	Age at Onset of Epilepsy	Etiology/Syndrome	Type of Seizures
1	F	43	8 years	Encephalitis	PS, PCS, GS
2 [a]	M	24	6 months	Lennox-Gastaut syndrome	AB, AS, GS, MS, TS
3 [a]	M	11	2 months	Lennox-Gastaut syndrome	AB, AS, GS, MS, TS
4	M	22	2 years	Oligodendroglioma	PS, PCS, GS
5	M	54	12 years	Unknown	PS, PCS, GS
6	M	18	12 years	Head injury	PS, PCS, GS
7	F	45	5 years	Unknown	PS, PCS
8 [a]	M	16	2 months	Meningoencephalitis	PS, GS
9	F	70	17 years	Unknown	AB, AS, GS, MS, TS
10 [a]	M	9	8 years	Encephalitis	PS, GS
11 [a]	F	10	2 years	Tuberous sclerosis	AB, AS, GS, MS, TS
12	F	23	18 years	Head injury	PS, PCS, S
13 [a]	F	12	1 day	Tuberous sclerosis	AB, AS, GS, MS, TS
14	M	41	7 years	Unknown	AB, GS
15	F	45	31 years	Epidermoid tumor	PS, PCS
16	M	32	15 years	Cavernous angioma	PS, PCS, GS
17 [a]	M	13	11 months	Lennox-Gastaut syndrome	AB, AS, GS, MS, TS
18 [a]	M	27	3 months	Lennox-Gastaut syndrome	AB, AS, GS, TS
19	F	46	27 years	Unknown	PCS, GS
20 [a]	M	14	11 months	Lennox-Gastaut syndrome	TS, GS
21	M	43	1 day	Porenephaly	PS, GS
22 [a]	M	6	2 years	Lennox-Gastaut syndrome	AB, AS, GS, MS, TS
23	F	15	6 months	Prenatal encephalopathy	PS, GS
24 [a]	F	12	2 months	Tuberous sclerosis	AB, GS

[a] Mentally retarded

AB Absence seizure
AS Atonic seizure
GS Generalized tonic-clonic seizure
MS Myoclonic seizure
PS Partial seizure
PCS Partial complex seizure
TS Tonic seizure

Evidence Table 222. Individual patient data extracted from Chayasirisobhon (2001) (continued)

Patient	Medications	Current Settings (mA)	Type and Baseline Seizure Rate	Type and Baseline Seizure Rate at Followup	% Decrease in Seizure Frequency
1	CBZ, PRM	2.75	PCS 127	PCS 122	3.9
2	CBZ, VPA	2.25	GS 24 / TS 12	GS 12 / TS 2	50.0 / 83.3
3	VPA	2.50	AS 241 / GS 74	AS 4 / GS 7	98.3 / 90.5
4	CBZ, PRM	2.00	PS 34 / GS 6	PS 3 / GS 1	91.2 / 83.3
5	CBZ, PRM	2.50	PCS 18 / PS 10	PCS 7 / PS 5	61.1 / 50.0
6	CBZ, TGB	3.00	PCS 6	PCS 4	33.3
7	CBZ, TPM	1.75	PCS 31	PCS 12	61.3
8	CBZ, VPA	2.75	PS/GS 63	PS/GS 4	93.7
9	PHT, TGB	2.75	PCS 6	PCS 4	33.3
10	VPA	3.5	PS/GS 30	PS/GS 25	16.7
11	PHT, VPA	2.5	AS 1072 /GS 231	AS 78 / GS41	92.7 / 82.3
12	ETT, LTG	2.0	CPS 10 / GS 2	PCS 4 / GS 0	60.0 / 100.0
13	PRM, TPM, TGB	3.25	AS 1204 / GS 56	AS 84 / GS 4	93.0 / 89.3
14	VPA	2.35	AB 136 / GS 14	AB 66 / GS 0	51.5 / 100.0
15	CBZ	2.0	PS 11 / PCS 8	PS 1 / PCS 0	90.9 / 100.0
16	CBZ, TPM	3.25	PCS 28	PCS 25	10.7
17	CBZ, VPA	3.25	MS 60 / GS 74	MS 56 / GS 60	6.7 / 19.0
18	PB, VPA	3.5	AB 30 / GS 12	AB 15 / GS 11	50.0 / 8.3
19	CNZ, GBP	2.75	PCS 84	PCS 15	82.1
20	VPA, TPM	3.0	TS 126	TS 98	22.2
21	PRM, LTG, TGB	3.0	PS 75 / GS 43	PS 95 / GS 57	-32.6 / -26.7
22	LEV	2.5	TS 168	TS 32	81.0
23	PHT, TPM, LEV	3.25	PCS 5 / GS 6	PCS 2 / GS 2	60.0 / 66.7
24	CBZ, VPA	3.25	AB 71	AB 5	93.0

CBZ	Carbamazepine	PB	Phenobarbital
CNZ	Clonzapam	PHT	Phenytoin
ETT	Ethotoin	PRM	Primodome
GBP	Gabapentin	TGB	Tiagabine
LEV	Levetiracetam	TPM	Topiramate
LTG	Lamotrigine	VPA	Valproate

Evidence Table 223. Individual patient data extracted from Hosain (2000)

Patient	Age at Implant	Sex	Etiology	Seizure Types	Neuroimaging	Baseline Seizure Frequency	% Reduction in Seizures at 6 Months
1	10	M	Cryptogenic	GTC, MY	Atrophy	22	84
2	14	F	Cryptogenic	GTC, MY, ATA	Diffuse atrophy	>100	0
3	14	M	Hypoxic-ischemic encephalopathy	AT, T, ATA, CP, CP/2nd gen	Difuse atrophy	22	54
4	13	M	CNS infection	ATA, MY, CP, GTC	Diffuse atrophy, calcifications	77	77
5	9	M	Tuberous sclerosis	ATA, AT, GTC, CP/2nd gen	Cortical tubers	96	93
6	16	M	Cryptogenic	CP, CP/2nd gen, ATA, MY	Atrophy CC section	123	40
7	15	M	Cryptogenic	ATA, MY, GTC	CC section	19	47
8	4	M	Tuberous sclerosis	ATA, AT, GTC, MY	Cortical tubers	21	37
9	23	M	Immunization-induced encephalopathy	GTC, ATA, T	CC section	118	78
10	26	M	Cryptogenic	ATA	Normal	29	52
11	29	F	Cryptogenic	ATA	Normal	75	43
12	29	F	Encephalitis	ATA, GTC	Atrophy	94	42
13	44	M	Trauma	ATA, AT	Atrophy	54	89

ATA Atypical absence seizure
AT Atonic seizure
GTC Generalized tonic-clonic seizure
MY Myoclonic seizure
CP Partial complex seizure
T Tonic seizure
CP/2nd generation Partial complex seizure with secondary generalization

Evidence Table 224. Individual patient data extracted from Parker (1999)

Patient	Diagnosis	Age at Onset	Age at Implant	Seizure Types	Concurrent Treatment	Seizure Rate (Per Month)	% Change From Baseline at 6 months	% Change From Baseline at 12 months
1	LGS	1 month	13 years 6 months	CPS, secondary generalized, NCS	Carbamazepine, Sodium Valproate	68	-15.0	-34.0
2	LGS	3 months	10 years 9 months	CPS, Atonic	Carbamazepine, Clobazam, Gabapentin	43	-32.0	-17.0
3	LGS	6 months	11 years 11 months	Atonic, CPS	Carbamazepine, Clobazam	72	-19.0	+7.0
4	LGS	1 months	11 years 2 months	GTCS, NCS	Carbamazepine, Vigabatrin, Lamotrigine	6	-41.0	-50.0
5	LGS	3 months	6 years 11 months	Myoclonic, GTCS	Carbamazepine, Clobazam, Lamotrigine	166	-63.0	-80.0
6	LGS	8 months	13 years 9 months	CPS, secondary generalized, atonic, atypical, absence	Carbamazepine, Phenytoin, Clobazam	26	-8.0	+27.0
7	LGS	6 months	16 years 6 months	Myoclonic, atonic, GTCS, NCS	Carbamazepine, Phenytoin, Gabapentin	288	-54.0	-46.0
8	De Novo LGS	3 years	6 years 3 months	CPS	Lamotrigine, Sodium Valproate	4	-25.0	-100.0
9	De Novo LGS	3 years	10 years 7 months	Atonic, atypical, absence, GTCS	Lamotrigine, Sodium Valproate	Device removed after implant		
10	De Novo LGS	2 years	9 years 7 months	GTCS, atonic	Carbamazepine, Clonazepam, Gabapentin	5	+100.0	+40.0

Evidence Table 224. Individual patient data extracted from Parker (1999) (continued)

Patient	Diagnosis	Age at Onset	Age atImplant	Seizure Types	Concurrent Treatment	Seizure Rate (Per Month)	% Change From Baseline at 6 months	% Change From Baseline at 12 months
11	SME	7 months	14 years 11 months	Secondary generalized, CPS, atypical, absences	Lamotrigine, Sodium Valproate, Primidone	26	+165.0	+62.0
12	SME	2 months	11 years 3 months	CPS, secondary generalized	Carbamazepine, Lamotrigine, Phenytoin, Heminevrin	23	+17.0	+65.0
13	SME	12 months	11 years 4 months	GTCS, NCS	Carbamazepine, Vigabatrin, Diazepam	9	-23.0	-23.0
14	SME	3 months	5 years 1 months	Secondary generalized	Phenytoin, Clobazam, Lamotrigine, Vigabatrin	20	0.0	0.00
15	MAE	2 years	12 years 6 months	Atypical, absences, secondary generalized	Sodium Valproate, Lamotrigine, Nitrazepam	7	+14.0	0.00
16	MAE	11 months	14 years 2 months	CPS, secondary generalized	Lamotrigine, Sodium Valproate, Vigabatrin	85	-40.0	-67.0

CPS Complex partial seizures
GTCS Generalized tonic clonic seizures
LGS Lennox-Gastaut Syndrome
MAE Myoclonic astatic epilepsy
NCS Non-convulsive status eplilepticus
SME Severe myoclonic epilepsy

Evidence Table 225. Individual patient data extracted from Lundgren (1998)

Patient	Sex	Age at Onset	Cause	Type of Epilepsy	Seizure Type	Pevious Surgery Type	Mentally Retarded (IQ <70)?	Age at Implant (years)
1	M	3 months	Cryptogenic	JME	TA, MYO, ABS	Anterior callosotomy	Yes	10
2	F	2 years 6 months	Cryptogenic	Partial	SPS	None	No	11
3	M	1 years 8 months	Malformation	Partial	TA, GTCS	Anterior callosotomy	Yes	14
4	F	1 month	Cryptogenic	Partial	CPS	None	Yes	8
5	M	3 years 3 months	Unknown granulomatous tumor	Partial	CPS	Frontal and temporal lobe resection	Yes	7
6	M	5 months	Malformation	LGS	TA, MYO, CPS	Frontal and occipital lobe resection	Yes	4
7	F	5 months	Malformation	LGS	GTCS, ATO	Subtotal hemispherectomy, Anterior callosotomy	Yes	19
8	M	4 years 3 months	Malformation	Partial	CPS	Temproal and frontal lobe resection	Yes	15
9	M	6 months	Cryptogenic	Generalized	ABS, MYO, GTCS	None	Yes	6
10	M	9 years	Malformation	Partial	CPS	None	Yes	15
11	M	4 months	Malformation	LGS	TA, CPS	None	Yes	9
12	F	2 years	Malformation	Partial	CPS	None	Yes	6
13	M	6 years	Idiopathic	Generalized	TA, GTCS	Anterior callosotomy		16
14	F	7 years 6 months	Unknown WM disease	Generalized	TA	None	Yes	11
15	F	4 years	Malformation	Partial	SPS, CPS, TA	None	Yes	17
16	M	4 years	Idiopathic	Generalized	GTCS	None	Yes	8

ABS Absence seizures
CPS Complex partial seizures
GTCS Generalized tonic clonic seizures
PGS Primary generalized seizures
LGS Lennox Gastaut syndrome
MYO Myoclonic seizures
SME Severe myoclonic epilepsy of infancy
SCS Simple partial seizures
TA Tonic-axial seizures
WM White matter

Evidence Table 225. Individual patient data extracted from Lundgren (1998) (continued)

Patient	Number of Seizures Per Month					Quality of Life (Nonvalidated Visual Analog Instrument)				
	Baseline	4 to 6 Months	10 to 12 Months	20 to 18 Months	22 to 24 Months	Baseline	4 to 6 Months	10 to 12 Months	20 to 18 Months	22 to 24 Months
1	26	10	16	14	27	70	75	65	65	70
2	46	0	0	3	15	100	99	99	99	50
3	45	57	68	59		20	15	10	10	
4	24	43	50	75		0	0	0	0	
5	203	300	56	135		60	65	0	0	
6	1195	210	135	160		50	50	50	50	
7	25	23	8	16		30	50	55	55	
8	11	14	14			10	10			
9	>100	>100	>100	>100		0	0	0	0	
10	11	4	4	5		75	75	75	75	
11	25	18	18			10	10			
12	29	7	7	8		0	25	25	25	
13	40	35	35	30		0	0	0	0	
14	30	30	30			0	0			
15	100	80	80			25	30			
16	115	60	70			25	25			

Evidence Table 226. Percentage reduction in seizure frequency from baseline in studies of vagal nerve stimulation

Reference	How Determined	Study Arm	N	Mean Pretreatment Absolute Seizure Frequency (SD)	Evidence of Selection Bias	Followup Time	Used Intent-to-Treat
RCTs performed in United States							
Clinical Study EO5 Handforth (1999)	Patient or caregiver maintained seizure diary	High	95	1.59 (3.26) per day Median: 0.51 (NR) per day	No	3 months	Yes
		Low	103	0.97 (1.13) per day Median: 0.49 (NR) per day			
Clinical Trial EO3 The VNS Group (1995)	Patient or caregiver maintained seizure diary	High	54	Median: 1.49 (Range: NR) per day	No	14 wks	NA
		Low	60	Median: 1.71 (Range: NR) per day			
Long-term followup of RCTs performed in United States							
DiGiorgio (2000) Followup of Clinical Trial EO5	Patient or caregiver maintained seizure diary		195	Median: 0.54 per day		3 months	Yes
						6 months	Yes
Salinski (1996) Followup of Clinical Trial EO3	Patient or caregiver maintained seizure diary		114	Median: 0.79 (Range: NR)		3 months	
						6 months	
						9 months	
						12 months	
Case series performed in United States							
Chayasirisobhon (2001)	Patient or caregiver maintained seizure diary		24	175.3 (348.6) per month Median: 52.5 (Range: 6 to 1303)		6 months	
Hosain (2000)	Unclear		13	65.4 (39.4) per month Median: 75 (Range: 19 to 123)		6 months	NA
Clinical Trial EO4 Labar (1999)	Patient or caregiver maintained seizure diary		24	Median: 48 (2 to 1650) per month		3 months	NA

Evidence Table 226. Percentage reduction in seizure frequency from baseline in studies of vagal nerve stimulation (continued)

Reference	How Determined	Study Arm	N	Mean Pretreatment Absolute Seizure Frequency (SD)	Evidence of Selection Bias	Followup Time	Used Intent-to-Treat
Case series performed outside United States							
Aldenkamp (2001)	NR		16	3906 (NR)		6 months	
Hoppe (2001)	Patient or caregiver maintained seizure diary		36	42.0 (95.0) per month		6 months	NA
Boon (1999)	Patient or caregiver maintained seizure diary		20	23.4 (43.4) per month Median: 9.0 (Range: 2 to 200)		Mean: 26.4 (SD: 14.4)	
Parker (1999)	Patient or caregiver maintained seizure diary		15	72.5 (93.7) per month		6 months	NA
Lundgren (1998)	Patient or caregiver maintained seizure diary		16	Median: 35.5 (Range: 11 to 1195)		4 to 6 months	
						10 to 12 months	
						12 months	NA

Evidence Table 226. Percentage reduction in seizure frequency from baseline in studies of vagal nerve stimulation (continued)

Reference	Study Arm	N	Mean % Change From Baseline (SD)	Reported P = (Within Groups)	Reported P = (Between Groups)	Within Groups[a]			Between Groups[b]		
						% Change From Reduction (CI)	P =	Minimum Detectable Change (Power = 0.8; P = 0.05)	% Reduction From Baseline Differnece (CI)	P =	Minimum Detectable Difference (Power = 0.8; P = 0.05)
RCTs performed in United States											
Clinical Study EO5 Handforth (1999)	High	54	-27.9 (34.3)	<0.0001	0.04	27.9 (18.5 to 37.65)	0.00000	NA	12.70 (2.35 to 23.1)	0.017	NA
	Low	102	-15.2 (39.2)	<0.0001		15.2 (7.6 to 22.80)	0.00090	NA			
Clinical Trial EO3 The VNS Group (1995)	High	54	-24.5 (CI: – 14.1 to -34.9)	<0.01	0.01	24.5 (9.79 to 39.21)	0.001094	NA	18.4 (4.5 to 32.3)	0.009	NA
	Low	60	-6.1 (CI: 3.6 to -15.8)	=0.21		6.1 (-3.6 to 15.8)	0.21780	NA			
Long-term followup of RCTs performed in United States											
DiGiorgio (2000) Followup of Clinical Trial EO5		195	Median: -34.0	<0.0001		NC	NC	NA			
		195	Median: -45	<0.0001		NC	NC	NA			
Salinski (1996) Followup of Clinical Trial EO3		114	Median: -20.2	<0.01		NC	NC	NA			
			Median: -24.7	<0.01		NC	NC	NA			
			Median: -25.7	<0.01		NC	NC	NA			

			Median: -31.9	<0.01		NC	NC	NA			

Evidence Table 226. Percentage reduction in seizure frequency from baseline in studies of vagal nerve stimulation (continued)

Reference	Study Arm	N	Mean % Change From Baseline (SD)	Reported P = (Within Groups)	Reported P = (Between Groups)	Within Groups[a]			Between Groups[b]		
						% Change From Reduction (CI)	P =	Minimum Detectable Change (Power = 0.8; P = 0.05)	% Reduction From Baseline Differnece (CI)	P =	Minimum Detectable Difference (Power = 0.8; P = 0.05)
Case series performed in United States											
Chayasirisobhon (2001)		24	-55.1 (35.5) Median: -61.2 (-96.5 to +28.8)			55.1 (30.5 to 79.70)	0.000011	NA			
Hosain (2000)		13	-56.6 (26.4) Median: -52 (0 to 93)	0.04		56.6 (36.30 to 76.90)	0.00000	NA			
Clinical Trial EO4 Labar (1999)		24	Median: -46 (-100 to + 350%)	0.004		NC	NC	NA			
Case series performed outside United States											
Aldenkamp (2001)		16	-26.9 (NR)	0.005		NC	NC	NA			
Hoppe (2001)		36	Median: -20%	NR		NC	NC	NC			
Boon (1999)		20	-52.4 (37.5) Median: -38.75 (0 to -100)	NR		52.4 (28.55 to 76.25)	0.000017	NA			
Parker (1999)		15	-19 (NR)	0.083		NC	NC				
Lundgren (1998)		16	-19.9 (50.2)	NR		19.9 (-4.7 to 44.5)	0.11282				
		16	-26.3 (55.4)	NR		26.3 (-12.90 to 64.69)	0.179357				
		15	-17 (NR)	0.264		NC	NC				

[a] Only applicable if individual patient data available
[b] Only applicable for studies that included ≥2 treatment arms

Evidence Table 227. Percentage change from baseline data in studies of vagal nerve stimulation (results of fixed effects meta-analysis of single treatment arm data)

Reference	N	Percentage Change From Baseline (CI)	P-Value	Standardized Residual	Outlier by Standardized Residual	Outlier by Q
Data from treatment arm of RCT						
Clinical Study EO5 Handforth (1999)	95	27.9 (18.5 to 37.65)	<0.000001	-1.82	Yes	No
Clinical Trial EO3 The VNS Group (1995)	54	24.5 (9.79 to 39.21)	0.001094	-1.49	No	No
Data from case series						
Chayasirisobhon (2001)	16	55.1 (30.5 to 79.7))	0.000011	1.72	Yes	No
Hosain (2000)	13	56.6 (36.3 to 76.9)	<0.000001	2.27	Yes	Yes
Boon (1999)	19	52.4 (28.55 to 76.25)	0.000017	1.54	No	No
Lundgren (1998)	16	26.3 (-12.90 to 64.69)	0.179357	-0.42	No	No
Test of Homogeneity of Fixed Effects Model [b]		**Q = 13.12**	**0.022256**			
Fixed Effects Summary Effect Size		Not applicable due to statistically signficiant test for homogeneity				
Random Effects Summary Effect Size [c]		**39.27 (26.58 to 51.97)**	**<0.000001**			

[a] By convention a positive effect size indicates treatment benefit.
[b] Critical Q (df = 5) = 11.07
[c] The random effects summary effect size is provided as an alternative when the fixed effects model has statistically significant heterogeneity.

Evidence Table 228. Univariate meta-regression analyses of percentage change from baseline data in studies of vagal nerve stimulation

Covariate	Intercept (CI)	P Value for Intercept	Coefficient (CI)	P Value for Coefficient	Q_e =	P (Q_e) =
Study RCT or not?	26.86 (18.73 to 34.99)	<0.000001	25.07 (10.25 to 39.89)	0.000911	2.124000	0.712965
Attrion rate	40.55 (31.07 to 50.02)	<0.000001	-5.06 (-10.50 to 0.38)	0.068322	9.800000	0.043935
Followup time[a]	37.91 (30.18 to 45.63)	<0.000001	1.07 (-0.05 to 2.19)	0.061703	9.630000	0.047143
Age at surgery[a]	40.12 (31.52 to 48.72)	<0.000001	-1.35 (-2.59 to –0.11)	0.033487	8.602000	0.071855
Proportion male	12.21 (-29.62 to 54.03)	0.567343	0.39 (-0.34 to 1.13)	0.290400	12.01100	0.017270
Partial seizures only	54.64 (33.28 to 75.99)	0.000001	-0.23 (-0.46 to 0.00)	0.050799	9.288000	0.054290
Lennox-Gastaut only	30.61 (23.25 to 37.97)	<0.000001	0.29 (0.07 to 0.50)	0.008567	6.187000	0.185611

[a] Mean centered

Evidence Table 229. Difference in absolute seizure frequency in studies of vagal nerve stimulation

Reference	How Determined	Study Arm	N	Mean Pretreatment Seizure Frequency (SD)	Followup Time	Mean Posttreatment Seizure Frequency (SD)	Reported P = (Within Groups)	Reported P = (Between Groups)
Aldenkamp (2001)	NR		16	3906 (NR)	6 months	3172 (NR)	0.005	
Chayasirisobhon (2001)	Patient or caregiver maintained seizure diary		24	1.78 (0.61) log per month[b] [Median: 52.5 (Range: 6 to 1303)]	6 months	1.24 (0.62) log per month[b] [Median: 14.5 (Range: 1 to 152)]	<0.001[c] [<0.001[d]]	
Hoppe (2001)	Patient maintained seizure diary		36	42.0 (95.0) per month	Mean: 8.0 (SD: 2.8)	33.0 (86.3) per month	0.09	
Boon (1999)	Patient or caregiver maintained seizure diary		19[f]	14.0 (12.7) per month [Median: 8.0 (Range: 2 to 40)] per month[f]	Mean: 26.4 (SD: 14.4)	9.1 (11.6) per month [Median: 3.0 (Range: 0 to 30)] per month[g]	0.0003	
Lundgren (1998)	Patient or caregiver maintained seizure diary		16	1.69 (0.51) log per month[c] [Median: 35.5 (Range: 11 to 1195)]	4 to 6 months	1.54 (0.53) log per month[b] [Median: 33.0 (0 to 300)]	0.073[c] [0.140[d]]	
Clinical Trial EO3 The VNS Group (1995)	Patient or caregiver maintained seizure diary	High	54	Median: 0.73 (Range: NR) per day	12 weeks	Median: 0.42 (Range: NR) per day	<0.01	0.02
		Low	60	Median: 0.82 (Range: NR) per day		Median: 0.80 (Range: NR) per day	0.19	
					10 to 12 month	1.48 (0.46) log per month[b] [Median: 33. (0 to 135)]	0.030[c] [0.041[d]]	

Evidence Table 229. Difference in absolute seizure frequency in studies of vagal nerve stimulation (continued)

Reference	How Determined	Study Arm	N	Minimum Detecatble Change (Power = 0.8, P = 0.05)	Minimum Detectable Difference (Power = 0.8, P = 0.05)	Pre-Post Within Groups Summary Effect Size (Hedges' d)[a]	Post-Treatment Between Groups Summary Effect Size (Hedges'd)	Individual Patient Data Availabale
Aldenkamp (2001)	NR		16	NA		NC		No
Chayasirisobhon (2001)	Patient or caregiver maintained seizure diary		24	NA		0.88 (0.48 to 1.27)[e]		Yes
Hoppe (2001)	Patient maintained seizure diary		36	NC		NC		No
Boon (1999)	Patient or caregiver maintained seizure diary		19[f]	NA		0.39 (0.21 to 0.58)[e]		Yes
Lundgren (1998)	Patient or caregiver maintained seizure diary		16			0.27 (-0.02 to 0.56)[e]		Yes
Clinical Trial EO3 The VNS Group (1995)	Patient or caregiver maintained seizure diary	High	54	NA	NA	NC	NC	No
		Low	60	NC		NC		
				NA		0.41 (0.05 to 0.77)[e]		

[a] Only calculated if individual patient data presented
[b] Calculated from raw data. Data are log transformed because pre-treatment data were non-normally distributed (Kolmogorov-Smirnov test)
[c] Based on a paired t-test of log transformed seizure frequency data
[d] Based on Wilcoxon Rank-Paired Test
[e] Calculated from raw data using method of Dunlap (1996)
[f] Does not include patient 13 who was excluded from analysis because her seizures only occurred in clusters
[g] Calculated from individual patient data presented by Boon (199)
NC = Not calculated. Data not sufficient to calculate an effect size (missing dispersion data, OR, data were presented as median and range, OR, individual patients data not presented)

Evidence Table 230. Proportion of patients seizure-free in studies of vagal nerve stimulation.

Reference	How Determined	N	Seizure Frequency at Baseline (SD)	Followup Time	Number of Patients Seizure Free Posttreatment (%)	Used an Intent-to-Treat Doctrine	Reported P = (Within Groups)	Pre-Post Effect Size (Cohen's h (CI))	Minimum Detectable Change (Power = 0.8; P = 0.05)
Case series performed outside United States									
Boon (1999)	Patient or caregiver maintained seizure diary	20	23.4 (43.4) per month [Median: 9.0 (Range: 2 to 200)]	Mean: 26.4 (SD: 14.4) months	6 (30.0)	Yes	NR	1.16 (0.54 to 1.78)	NA

NA Not applicable
NR Not reported

Evidence Table 231. Proportion of patients with >50% reduction in seizure frequency in studies of vagal nerve stimulation

Reference	How Determined	Study Arm	N	Mean Pretreatment Absolute Seizure Frequency (SD)	Evidence of Selection Bias	Followup Time	Used Intent-To-Treat Doctrine
RCTs performed in United States							
Clinical Study EO5 Handforth (1999)	Patient or caregiver maintained seizure diary	High	95	1.29 (3.26) per day	No	3 months	No[d,e]
		Low	103	0.97 (1.13) per day			
Clinical Trial EO3 The VNS Group (1995)	Patient or caregiver maintained seizure diary	High	54	Median: 0.73 (Range: NR) per day	No	12 weeks	Yes
		Low	60	Median: 0.82 (Range: NR) per day			
Long-term followup of RCTs performed in United States							
DiGiorgio (2000) Followup of Clinical Trial EO5	Patient or caregiver maintained seizure diary		195	Median: 0.54 per day		3 months	Yes
						6 months	
Salinski (1996) Followup of Clinical Trial EO3	Patient or caregiver maintained seizure diary		114	Median 0.79 per day		3 months	Yes
						6 months	
						9 months	
						12 months	
Case series performed in United States							
Chayasirisobhon (2001)	Patient or caregiver maintained seizure diary		24	[Median: 52.5 (Range: 6 to 1303) per months]		6 months	Yes
Hosain (2000)	Unclear		13	65.4 (39.4) per month [Median: 75 (Range: 19 to 123) per months]		6 months	NA[e]
Clinical Trial EO4 Labar (1999)	Patient or caregiver maintained seizure diary		25	[Median: 48 (Range: 2 to 1650) per months]		3 months	Yes

Evidence Table 231. Proportion of patients with >50% reduction in seizure frequency in studies of vagal nerve stimulation (continued)

Reference	How Determined	Study Arm	N	Mean Pretreatment Absolute Seizure Frequency (SD)	Evidence of Selection Bias	Followup Time	Used Intent-To-Treat Doctrine
Case series performed outside United States							
Aldenkamp (2001)	NR		16	3906 (NR)		6 months	Yes
Hoppe (2001)	Patient maintained seizure diary		36	42.0 (95.0) per month		Mean: 8.0 (SD: 2.8)	Yes
Ben-Menachem (1999)	Patient or caregiver maintained seizure diary (n = 57) Unknown (n = 7)		64	NR		Mean: 20 (Range: 3 to 64 months)	Yes
Boon (1999)	Patient or caregiver maintained seizure diary		20	23.4 (43.4) per month [Median: 9.0 (Range: 2 to 200)]		Mean: 26.4 (SD: 14.4)	Yes
Parker (1999)	Patient or caregiver maintained seizure diary		16	[Median:26.0 (Range: 4 to 288)]			Yes
Lundgren (1998)	Patient or caregiver maintained seizure diary		16	[Median: 35.5 (Range: 11 to 1195)]		4 to 6 months 10 to 12 months	Yes Yes

Evidence Table 231. Proportion of patients with >50% reduction in seizure frequency in studies of vagal nerve stimulation (continued)

Reference	Study Arm	N	Number of Patients With >50% Reduction in Seizure Frequency (%)	Reported P = (Within Groups)	Reported P = (Between Groups)	Calculated by ECRI [a]			
						Minimum Detectable Change (Power = 0.8; P = 0.05)	Within Groups Summary Effect Size, Cohens' h (CI)	Minimum Detectable Difference (Power = 0.8; P = 0.05)	Between Groups Summary Effect Size, Cohens'h (CI)
RCTs performed in United States									
Clinical Study EO5 Handforth (1999)	High	95	22 (23.1)	NR	0.172 [f]	NC	1.00 (0.72 to 1.29)		0.19 (-0.09 to 0.47)
	Low	103	16 (15.5)	NR			0.81 (0.54 to 1.08)		
Clinical Trial EO3 The VNS Group (1995)	High	54	17 (31.5)	NR	0.02[g]	NC	0.91 (0.81 to 1.57)	NA	0.44 (0.08 to 0.81)
	Low	60	8 (13.3)	NR			0.75 (0.39 to 1.11)		
Long-term followup of RCTs performed in United States									
DiGiorgio (2000) Followup of Clinical Trial EO5		195	66 (33.8)	NR		NA	1.24 (1.04 to 1.44)		
			68 (34.9)	NR		NA	1.26 (1.07 to 1.47)		
Salinski (1996) Followup of Clinical Trial EO3		114	28 (24.6)	NR		NA	1.04 (0.78 to 1.30)		
			24 (21.1)	NR		NA	0.95 (0.69 to 1.22)		
			25 (21.9)	NR		NA	0.98 (0.72 to 1.23)		
			31 (27.2)	NR		NA	1.10 (0.84 to 1.36)		
Case series performed in United States									
Chayasirisobhon (2001)		24	15 (62.5)	NR		NA	1.82 (0.57 to 1.26)		
Hosain (2000)		13	7 (53.9)	NR		NA	1.65 (0.88 to 2.42)		
Clinical Trial EO4 Labar (1999)		24	11 (45.8)	NR		NA	1.45 (0.90 to 2.01)		

Evidence Table 231. Proportion of patients with >50% reduction in seizure frequency in studies of vagal nerve stimulation (continued)

Reference	Study Arm	N	Number of Patients With >50% Reduction in Seizure Frequency (%)	Reported P = (Within Groups)	Reported P = (Between Groups)	Calculated by ECRI [a]			
						Minimum Detectable Change (Power = 0.8; P = 0.05)	Within Groups Summary Effect Size, Cohen's h (CI)	Minimum Detectable Difference (Power = 0.8; P = 0.05)	Between Groups Summary Effect Size, Cohen's h (CI)
Case series performed outside United States									
Aldenkamp (2001)		16	4 (25.0)	NR		NA	1.05 (0.35 to 1.74)		
Hoppe (2001)		36	11 (30.6)	NR		NA	1.17 (0.71 to 1.63)		
Ben-Menachem (1999)		63	29 (46.0)	NR		NA	1.48 (1.13 to 1.82)		
Boon (1999)		20	8 (40.0)	NR		NA	1.37 (0.75 to 1.99)		
Parker (1999)		16	4 (25.0)	NR		NA	1.05 (0.35 to 1.74)		
Lundgren (1998)		16	5 (31.3)	NR		NA	1.19 (0.49 to 1.88)		
		16	6 (37.5)	NR		NA	1.32 (0.63 to 2.01)		

[a] All calculations performed using intent-to-treat doctrine
[b] 1-tailed 2-sample arcsine binomial power analysis
[c] Between groups if a controlled trial. If case series based on comparison with a synthetic control group of equal size where no patients spontaneously had a >50% reduction in seizure frequency from baseline
[d] Does not include one patient who was withdrawn during ramp-up stage due to uninterruptible seizure diary
[e] Does not include one patient who withdrew consent during ramp up stage
[f] Chi-Squared test
[g] Fishers exact test
[h] Not an outcome measure reported by Hosain et al.. Data were extracted from individual patient data presented in Evidence Table
[I] Not applicable because this was a case series with no control group
NA = Not applicable
NC = Not calculated
NR = Not reported

Evidence Table 232. Quality of life in studies of vagal nerve stimulation

Reference	Instrument and Followup Time	Domain	Treatment Arm			Control Arm		
			N	Outcome Mean (SD)		N	Outcome Mean (SD)	
				Pretreatment	Posttreatment		Pretreatment	Posttreatment
Clinical Trial EO5 (Data extracted from Dodrill 2001)	QOLIE-31 6 months	Seizure worry	78	51.9 (26.8)	60.7 (23.7)	82	50.9 (25.2)	
		Overall QoL		67.0 (14.7)	67.9 (13.4)		62.1 (15.3)	
		Emotional well-being		68.3 (17.3)	71.5 (16.3)		65.0 (19.3)	
		Energy/fatigue		57.1 (19.2)	58.6 (18.9)		54.7 (19.7)	
		Cognitive function		53.4 (23.2)	59.5 (21.9)		57.6 (21.9)	
		Medication effects		54.1 (31.2)	58.5 (30.2)		57.9 (29.5)	
		Social functioning		53.2 (24.6)	59.1 (24.0)		54.6 (22.0)	
		Overall score		58.1 (15.0)	62.0 (14.1)		57.8 (14.3)	
	SF-36 6 months	Physical function	78	83.3 (17.1)	89.7 (11.7)	82	83.7 (18.4)	
		Role physical		68.5 (34.3)	76.2 (27.2)		62.2 (33.0)	
		Bodily pain		71.9 (22.4)	72.7 (21.0)		68.41 (25.0)	
		General health		66.2 (19.3)	69.3 (16.3)		61.9 (21.5)	
		Vitality		57.1 (19.2)	58.6 (18.9)		54.7 (19.7)	
		Social function		68.9 (27.2)	75.5 (19.7)		68.0 (21.3)	
		Role emotional		76.1 (27.4)	85.9 (21.5)		72.7 (32.0)	
		Mental health		68.3 (17.3)	71.5 (16.3)		65.0 (19.3)	
		Summary: Physical		48.3 (9.4)	49.9 (6.84)		47.1 (6.8)	
		Summary: Emotional		45.4 (10.1)	48.1 (9.12)		44.3 (10.8)	
Ergene (2001)	QOLIE-10[a] 2 weeks	Overall score	17	32.8 (standard error: 2.0)	26.0 (9.5)			
	6 weeks				25.6 (9.9)			
	12 weeks				25.7 (9.9)			
	24 weeks				24.3 (8.7)			
	48 weeks				24.9 (14.8)			

Evidence Table 232. Quality of life in studies of vagal nerve stimulation (continued)

Reference	Instrument and Followup Time	Domain	Reported P Value		ECRI Calculated Effect Sizes Hedges' d (CI)	
			Within Groups	Posttreatment Between Groups	Pretreatment Between Groups	Posttreatment Between Groups
Clinical Trial EO5 (Data extracted from Dodrill 2001)	QOLIE-31 6 months	Seizure worry	NR	0.261	0.04 (-0.27 to 0.35)	0.15 (-0.16 to 0.46)
		Overall QoL	NR	0.991	0.32 (0.01 to 0.64)	0.26 (-0.05 to 0.57)
		Emotional well-being	NR	0.316	0.18 (-0.13 to 0.49)	0.30 (-0.01 to 0.61)
		Energy/fatigue	NR	0.313	0.12 (-0.19 to 0.43)	0.24 (-0.07 to 0.55)
		Cognitive function	NR	0.279	-0.19 (-0.50 to 0.13)	-0.03 (-0.34 to 0.28)
		Medication effects	NR	0.990	-0.12 (-0.43 to 0.19)	-0.19 (-0.50 to 0.12)
		Social functioning	NR	0.283	-0.06 (-0.37 to 0.25)	0.14 (-0.17 to 0.45)
		Overall score	NR	0.274	0.02 (-0.29 to 0.33)	0.15 (-0.17 to 0.46)
	SF-36 6 months	Physical function	NR	0.105	-0.02 (-0.33 to 0.29)	0.28 (-0.03 to 0.59)
		Role physical	NR	0.037	0.19 (-0.12 to 0.50)	0.40 (0.09 to 0.71)
		Bodily pain	NR	0.376	0.15 (-0.16 to 0.46)	0.27 (-0.04 to 0.58)
		General health	NR	0.457	0.21 (-0.10 to 0.52)	0.28 (-0.04 to 0.59)
		Vitality	NR	0.313	0.12 (-0.19 to 0.43)	0.24 (-0.04 to 0.55)
		Social function	NR	0.473	0.04 (-0.27 to 0.35)	0.23 (-0.08 to 0.54)
		Role emotional	NR	0.026	0.11 (-0.20 to 0.42)	0.42 (0.10 to 0.73)
		Mental health	NR	0.316	0.18 (-0.13 to 0.49)	0.30 (-0.01 to 0.62)
		Summary: Physical	NR	0.127	0.15 (-0.16 to 0.46)	0.34 (0.03 to 0.65)
		Summary: Emotional	NR	0.202	0.10 (-0.21 to 0.41)	0.31 (-0.01 to 0.62)
Ergene (2001)	QOLIE-10[a]	Overall score				
	2 weeks		<0.01			
	6 weeks		<0.01			
	12 weeks		<0.01			
	24 weeks		<0.01			
	48 weeks		<0.01			

[a] This is a short form (10-item) version of QOLIE-31, which is in turn a short-form version of QOLIE-89.

NC Not calculated
QOLIE Quality of Life in Epilepsy
SF-36 Short-Form 36

Evidence Table 233. Adverse events in studies of vagal nerve stimulation

Reference	Adverse Event	Treatment Group		Control Group		Reported P = (Between Groups)	Effect Size Cohen's h (CI)
		N	Patients Affected (%)	N	Patients Affected (%)		
RCTs performed in United States							
Clinical Study EO5 Handforth (1999)	Voice alteration	95	63 (66.3)	103	31 (30.1)	0.001	0.74 (0.46 to 1.02)
	Cough		43 (45.3)		44 (42.7)	ns	0.05 (-0.23 to 0.33)
	Pharyngitis		33 (34.7)		26 (25.2)	ns	0.21 (-0.07 to 0.49)
	Pain		27 (28.4)		31 (30.1)	ns	-0.04 (-0.32 to 0.24)
	Dyspnea		24 (25.3)		11 (10.7)	0.007	0.39 (0.11 to 0.67)
	Headache		23 (24.2)		24 (23.3)	ns	0.02 (-0.26 to 0.30)
	Dyspepsia		17 (17.9)		13 (12.6)	ns	0.15 (-0.13 to 0.43)
	Vomiting		17 (17.9)		14 (13.6)	ns	0.12 (-0.16 to 0.40)
	Paresthesia		17 (17.9)		26 (25.2)	ns	-0.18 (-0.46 to 0.10)
	Nausea		14 (14.7)		21 (20.4)	ns	-0.15 (-0.43 to 0.13)
	Accidental injury		12 (12.6)		13 (12.6)	ns	0.00 (-0.28 to 0.28)
	Fever		11 (11.6)		19 (18.4)	ns	-0.19 (-0.47 to 0.09)
	Infection		11 (11.6)		12 (11.7)	ns	0.00 (-0.28 to 0.28)

Evidence Table 233. Adverse events in studies of vagal nerve stimulation (continued)

Reference	Adverse Event	Treatment Group		Control Group		Reported P = (Between Groups)	Effect Size Cohen's h (CI)
		N	Patients Affected (%)	N	Patients Affected (%)		
Clinical Trial EO3 The VNS Group (1995)	Hoarseness/voice change	54	20 (37.2)	60	8 (13.3)	<0.01	0.56 (0.19 to 0.93)
	Throat pain		6 (11.0)		7 (11.7)	1.00	-0.02 (-0.39 to 0.35)
	Coughing		4 (7.4)		5 (8.3)	1.00	-0.03 (-0.40 to 0.33)
	Dyspnea		3 (5.6)		1 (1.7)	0.34	0.22 (-0.15 to 0.58)
	Paresthesia		3 (5.6)		2 (3.3)	0.67	0.11 (-0.26 to 0.48)
	Muscle pain		3 (5.6)		1 (1.7)	0.34	0.22 (-0.15 to 0.58)
	Headache		1 (1.8)		5 (8.3)	0.21	-0.31 (-0.68 to 0.05)
Long-term followup of RCTs performed in United States							
Salinski (1996) Followup of Clinical Trial EO3	Accidental injury	195	30 (15.4)				
	Cough, increased		29 (14.9)				
	Voice alteration		107 (54.9)				
	Dyspnea		25 (12.8)				
	Pain		30 (15.4)				
	Parasthesia		30 (15.4)				
	Headache		31 (15.9)				
	Pharyngitis		20 (10.3)				
	Depression		10 (5.1)				
	Infection		12 (6.2)				
Salinski (1996) Followup of Clinical Trial EO3	Device malfunction	114	2 (1.8)				
	Myocardial infaction		1 (0.9)				
Case series performed in the United States							
Chayasirisobhon (2001)	Vocal cord paralysis	24	2 (8.3)				
	Hoarseness		12 (50.0)				

Evidence Table 233. Adverse events in studies of vagal nerve stimulation (continued)

Reference	Adverse Event	Treatment Group		Control Group		Reported P = (Between Groups)	Effect Size Cohen's h (CI))
		N	Patients Effected (%)	N	Patients Effected (%)		
Ergene (2001)	Throat irritation	17	4 (23.5)				
	Difficulty breathing		1 (5.9)				
	Difficulty speaking		1 (5.9)				
	Epigastric discomfort		1 (5.9)				
	Increased snoring		1 (5.9)				
Hosain (2000)	Hoarseness	13	3 (23.1)				
	Excessive coughing		3 (23.1)				
	Infection		1 (7.7)				
Clinical Trial EO4 Labar (1999)	Incisional parasthesias	24	2 (8.3)				
	Incisional pain		2 (8.3)				
	Cough		6 (25.0)				
	Abdominal pain		2 (8.3)				
	Anorexia		1 (4.2)				
	Hiccups		1 (4.2)				
	Dysphagia		1 (4.2)				
	Emesis		1 (4.2)				
	Fatigue		1 (4.2)				
Case series performed outside United States							
Ben-Menachem (1999)	Hoarseness	64	11 (17.2)				
	Dyspnea		1 (1.6)				
	Cord paresis		1 (1.6)				
	Throat pain		3 (4.7)				
	Generator placement problem		1 (1.6)				
Boon (1999)	Throat parestaesias	20	1 (5.0)				
	Hoarseness or voice change		4 (20.0)				
	Exercise dyspnea		1 (5.0)				

Evidence Table 233. Adverse events in studies of vagal nerve stimulation (continued)

Reference	Adverse Event	Treatment Group		Control Group		Reported P = (Between Groups)	Effect Size Cohen's h (CI)
		N	Patients Affected (%)	N	Patients Affected (%)		
Lundgren (1998)	Aspiration	16	2 (12.5)				
	Hoarseness		6 (37.5)				
	Throat pain		1 (6.3)				
	Increased salivation		2 (12.5)				
	Tiredness		2 (12.5)				
	Electrical line fracture		1 (6.3)				
	Premature current failure		5 (31.3)				

Evidence Table 234. Mortality in studies of vagal nerve stimulation

Reference	Treatment Group			Control Group		
	N	Number of Deaths (%)	Cause of Death	N	Number of Deaths (%)	Cause of Death
RCTs performed in United States						
Clinical Study EO5 Handforth (1999)	95	0 (0.0)	NA	103	0 (0.0)	
Clinical Trial EO3 The VNS Group (1995)	54	0 (0.0)	NA	60	0 (0.0)	
Followup studies of RCT's performed in the United States (case-series)						
DiGiorgio (2000) Followup of Clinical Trial EO5	195	2 (1.0)	1 patient: Pneumonia, sepsis and respiratory failure related to untreated infection. Authors state that death was a direct result of VNS implantation and/or use. 1 patient: Suden unexpected death			
Salinski (1996) Followup of Clinical Trial EO3	114	2 (1.8)	1 patient: Thrombotic thrombocytopenic purpura 1 patient: Drowning. Authors state that deaths were unlikely to be related to VNS.			
Case series performed in the United States						
Chayasirisobhon (2001)	24	0 (0.0)				
Ergene (2001)	17	0 (0.0)				
Hosain (2000)	13	0 (0.0)				
Clinical Trial EO4 Labar (1999)	24	0 (0.0)				
Case series performed outside of the United States						
Aldenkamp (2001)	16	0 (0.0)				
Hoppe (2001)	36	0 (0.0)				
Ben-Menachem (1999)	64	4 (6.3)	3 patients: Status epilepticus 1 patient: Sudden unexpected death			
Boon (1999)	20	0 (0.0)				
Parker (1999)	16	0 (0.0)				
Lundgren (1998)	16	0 (0.0)				

Evidence Table 235. Articles addressing the ketogenic diet excluded for quality reasons

Study	Reason for Exclusion
Pulsifier (2001)	The aim of this study was to evaluate effects of ketogenic diet on behavior and cognitive function. Study only evaluated patients who had successfully completed 1 year of treatment. According to the authors 40% of patients who started ketogenic diet had discontinued it by 1 year due to treatment disatisfaction. This study provides a highly biased estimate of the effects of ketogenic diet on behavior and cognitive function because it is based entirely on data from patients who are satisfied with the treatment.
Mak (1998)	Although authors state that outcome data were recorded at 1 month followup, they refer to a table that states that seizure frequency data was recorded at least three months after discontinuation of the ketogenic diet in 10 of the 13 patients included in study. This flaw precludes determining whetehr there was a causal relationship between diet and outcome.
Edelstein (1996)	Efficacy and adverse event outcome data were poorly described. Changes in seizure frequency were only subjectively described (e.g. "deminished seizure activity occurred in 16 patients." No empirical data presented).
Schwartz (1988)	59 patients allocated to one of three ketogenic diets (Classical 4:1, MCT, modified MCT). If seizure control was unsatifactory or if major diet problems were encountered, patients were offered the option to change to alternative diet. If patient opted to try another diet, the child was readmitted, existing diet discontinued and new diet commenced. Four patients withdrew. Eight patients opted to try a new diet and data from both diets in the same patient were included in analysis resulting in an assessment of efficacy of treatment based on 63 studies originating from 55 patients. Data for three separate diets were not analyzed seperately but instead were combined leading to double counting of data from some patients. Double counting of data from a single patient is a fatal flaw.

Question 6

Which social, psychological or psychiatric services for treatment-resistant epilepsy lead to, or can be expected to lead to improved patient outcomes?

Evidence Table 236. Excluded studies of nondrug, nonsurgical treatments for treatment-resistant epilepsy

Reference	Intervention	Reason for Exclusion
Uhlmann (2001)	EEG Biofeedback and End-tidal CO_2 biofeedback	Patients were treated with one of two interventions. Outcomes were reported for all patients combined, regardless of treatment group.
Andrews (2000)	Comprehensive multidisciplinary neurobehavioral treatment	Fewer than five studies reported on this intervention.
Reiter (2000)	Comprehensive multidisciplinary neurobehavioral treatment	Patients changed their AED regimen during treatment, making this trial subject to a strong extraneous events bias. Therefore, outcomes cannot be separately associated with either the result of the training or the change in AEDs.
Sidorenko (2000)	Medical Resonance Therapy Music	Fewer than five studies reported on this intervention.
Kotchoubey (1999)	EEG Biofeedback	Fewer than five studies reported on this intervention.
Kotchoubey (1999)	EEG Biofeedback	Fewer than five studies reported on this intervention.
Schmid-Schonbein (1998)	Self-control training	Patients changed their AED regimen during treatment, making this trial subject to a strong extraneous events bias. Therefore, outcomes cannot be separately associated with either the result of the training or the change in AEDs.
Kotchoubey (1996)	EEG Biofeedback	Patients received behavioral therapy during treatment, making this trial subject to a strong extraneous events bias. Therefore, outcomes cannot be separately associated with either the result of the biofeedback or the behavioral therapy.
Panjwani (1996)	Sahaja yoga	Fewer than five studies reported on this intervention.
Deepak (1994)	Meditation	Fewer than five studies reported on this intervention.
Eriksen (1994)	Physical Exercise	Fewer than five studies reported on this intervention.
Becu (1993)	Self-Help Group (Group Therapy)	Fewer than five studies reported on this intervention.
Rockstroh (1993)	EEG Biofeedback	Fewer than five studies reported on this intervention.

Evidence Table 236. Excluded studies of nondrug, nonsurgical treatments for treatment-resistant epilepsy (continued)

Reference	Intervention	Reason for Exclusion
Usiskin (1993)	Counseling	Fewer than five studies reported on this intervention.
Andrews (1992)	Comprehensive multidisciplinary neurobehavioral treatment	Fewer than five studies reported on this intervention.
Puskarich (1992)	Progressive muscle relaxation	Fewer than five studies reported on this intervention.
Fried (1990) and Fried (1993)	End-Tidal CO_2 Biofeedback	Fewer than five studies reported on this intervention.
Gillham (1990)	Comprehensive multidisciplinary neurobehavioral and psychological treatment	Fewer than five studies reported on this intervention.
Nakken (1990)	Physical Exercise	Fewer than five studies reported on this intervention.
Whitman (1990)	Progressive muscle relaxation	Fewer than five studies reported on this intervention.
Denio (1989)	Physical Exercise	Fewer than five studies reported on this intervention.
Lantz (1988)	EEG Biofeedback	Fewer than five studies reported on this intervention.
Dahl (1987)	Contingent relaxation with neurobehavioral training	Fewer than five studies reported on this intervention.
Fraser (1986)	Vocational Services	Fewer than five studies reported on this intervention.
Virudhagirinathan (1986)	Systematic Desensitization	Fewer than five studies reported on this intervention.

Question 7

What characteristics of treatment-resistant epilepsy interfere with ability to obtain and maintain employment, or attend and perform well in school?

Evidence Table 237. Excluded studies of employment and schooling

Reference	Reason for Exclusion
Clemmons (1987)	No data are reported on patient characteristics. The number of patients who are treatment-resistant cannot be determined, and other factors such as the presence of severe neurological disorders are not considered.
Fraser (1986)	This study involved highly specialized patients: those with suspected brain impairment who enrolled in an intensive vocational intervention program. The reported data are unlikely to be generalizable to the greater population of patients with treatment-resistant epilepsy.

Question 8

What is the mortality rate in patients with treatment-resistant epilepsy?

Evidence Table 238. Excluded studies of mortality rate in patients with treatment-resistant epilepsy

Reference	Reason for Exclusion
Dashieff (1991)	Length of followup not reported, therefore person-years of exposure cannot be determined and mortality rate cannot be calculated.
Tudehope (1988)	Article does not provide enough information to determine whether patients had treatment-resistant epilepsy. Also not clear that all patients had epilepsy.
Derby (1996)	Patients with epilepsy identified through AED prescriptions in databases rather than by clinical diagnosis. Since AEDs may be prescribed for conditions other than epilepsy, this increases the likelihood of including patients who were never diagnosed with epilepsy.
Tennis (1995)	Patients with epilepsy identified through AED prescriptions in databases rather than by clinical diagnosis. Since AEDs may be prescribed for conditions other than epilepsy, this increases the likelihood of including patients who were never diagnosed with epilepsy.

Evidence Table 239. Design and conduct of included studies mortality rate in patients with treatment-resistant epilepsy

Reference	Country	N	Epilepsy Diagnosis Determined	Study Design	Standardized Mortality Ratio Reported (or Calculable)	Standardized Mortality Ratio Adjusted For Factors Other Than Age	Compliance Reported
Physician's desk reference Gabapentin trial data (2001)	United States	2203	Clinical diagnosis	Retrospective case series	No	Not applicable	No
Racoosin (2001)	United States	9144	Clinical diagnosis	Retrospective case series[a]	Yes	Gender (only for male vs. female standardized mortality ratio)	No
Wong (2001)	United Kingdom	1050	Clinical diagnosis	Retrospective double cohort	Yes	Gender	Yes
Annegers (2000)	United States	1819	Clinical diagnosis	Retrospective double cohort	Yes	Gender	Not applicable
Hennessy (1999)	United Kingdom	305	Clinical diagnosis	Retrospective double cohort	Yes	None	Not applicable
Sperling (1999)	United States	393	Clinical diagnosis	Prospective double cohort	Yes	Gender	Not applicable
Vickrey (1997)	United States	248	Clinical diagnosis	Retrospective case series	No	Not applicable	Not applicable
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	Clinical diagnosis	Retrospective case series	No	Not applicable	No
Leppik (1995)	United States, Europe, Australia	2600	Clinical diagnosis	Retrospective case series	No	Not applicable	No
Klenerman (1993)	United Kingdom	Reported as person-years	Clinical diagnosis	Retrospective double cohort	Yes	Gender	No

[a] ECRI was able to calculate standardized mortality ratios using a general reference population. For our purposes, this study became a retrospective double cohort study.

Evidence Table 240. Overall mortality rates in studies of treatment-resistant epilepsy patients

Comparison to mortality rates of general population in studies with reported standardized mortality ratios or from which standardized mortality ratios could be calculated

Reference	Country	N	Treatment	Subgroup	Overall Mortality Rate Per 1000 Person-Years (CI)		Standardized Mortality Ratio (CI)
					Study Population	General Reference Population	
Racoosin (2001)	United States	9144	AEDs	All patients	9.11 (7.64-10.85)[c]	2.53[a]	3.60 (2.99-4.29)[d]
				Male	11.3 (9.2-13.9)	3.20[a]	3.6 (2.9-4.4)[d]
				Female	6.1 (4.4-8.5)	1.75[a]	3.5 (2.5-4.8)[d]
				Ages:			
				1-14	4.1 (1.7-9.8)	0.25[a]	16.4 (4.5-41.5)[d]
				15-34	7.2 (5.4-9.5)	1.01[a]	7.1 (5.3-9.6)[d]
				35-54	9.6 (7.2-12.9)	3.23[a]	3.0 (1.4-5.5)[d]
				55-72	32.1 (21.5-47.8)	14.56[a]	2.2 (1.5-3.1)[d]
Wong[f] (2001)	United Kingdom	1050	AEDs	All patients	16.6 (12.1-22.6)[c]	1.59[c]	10.4 (7.1-13.7)
Annegers (2000)	United States	1819	Vagal nerve stimulation	All patients	7.87 (5.34-11.59)[c]	2.18[a]	3.62 (2.34-5.35)
				Male	8.1		2.80 (1.53-4.70)
				Female	7.7		5.79 (2.89-10.37)
				Ages:			
				<25			11.4 (4.9-22.5)
				25-34			6.1 (2.6-11.9)
				≥35			1.8 (0.8-3.5)
Hennessy (1999)	United Kingdom	305	Surgery	All patients	7.33 (4.75-11.29)[c] (includes some patients seizure-free after surgery)	1.62	4.52 (2.76-6.99)[e]
Sperling (1999)	United States	194[b]	Surgery	All patients	13.72 (7.68-24.41)[c]	2.90[a]	4.69 (2.34-8.41)[e]
Klenerman (1993)	United Kingdom	Not reproted	AEDs	All patients	33.31 (27.78-39.90)[c]	17.19[c]	1.94 (1.60-2.34)[e]

[a] Calculated by ECRI from U.S. Census Bureau, Statistical Abstract of the United States, 2000.
[b] This study followed a total of 393 patients after surgery; 199 became seizure free and were not included in the mortality analysis (none of these patients died).
[c] Calculated by ECRI from Mortality Statistics (England and Wales, 1999).
[d] Calculated by ECRI
[e] 95% CI calculated by ECRI
[f] The study by Wong (2001) reported mortality data for groups of patients receiving different AEDs (lamotrigine, gabapentin, and/or vigabatrin). Because many patients received more than one of these drugs, they were included in more than one group. Therefore, we have evaluated only the patients receiving lamotrigine (the largest group, n = 1,050) to avoid double counting.

Evidence Table 241. Sudden unexpected death rates in studies of treatment-resistant epilepsy patients

Reference	Country	N	Treatment	Subgroup	Sudden Unexpected Death Rate Per 1000 Person-Years (CI)	Percentage of Total Deaths Represented by SUDEP
Physician's desk reference (PDR) Gabapentin trial data (2001)	United States	2203	AEDs	All patients	3.80 (1.93-7.49)[a]	Cannot be calculated
Racoosin (2001)	United States	9144	AEDs	All patients Male Female Ages: 1-14 15-34 35-54 55-72	3.82 (2.91-5.00)[a] 4.4 (3.2-6.2) 3.0 (1.8-4.8) 2.4 (0.8-7.6) 3.2 (2.1-4.8) 4.9 (3.3-7.4) 5.3 (2.0-14.2)	41.9%
Wong (2001)	United Kingdom	1050	AEDs	All patients	7.64 (4.84-12.05)[a]	46.1%
Annegers (2000)	United States	1819	Vagal nerve stimulation	All patients	4.09 (2.39-6.99)[a]	52%
Sperling (1999)	United States	194	Surgery	All patients	7.49 (3.44-16.24)[a]	54.5%
Hennessy (1999)	United Kingdom	305	Surgery	All patients	2.20 (1.01-4.79)[a]	30%
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients	3.13 (1.98-4.95)[a]	40%
Leppik (1995)	United States, Europe, Australia	2600	AEDs	All patients	3.87 (1.87 to 7.96)[a]	29.2%
Klenerman (1993)	United Kingdom	NR	AEDs	All patients	2.06 (1.00-4.25)[a]	6.2%

[a] Calculated by ECRI

Evidence Table 242. Drowning rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Drowning Rate Per 1000 Person-Years (All Patients)				
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]	Highest Age-Specific Rate in General Reference Population	Crude Mortality Ratio (CI)[c]
Hennessy (1999)	United Kingdom	305	Surgery	1.10 (0.37-3.23)	0.005[e]	214 (43.07-626.11)	0.0196[e]	56.18 (11.29-165.39)
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	0.35 (0.10- 1.27)	0.013[d]	26.67 (3.00-96.29)	0.0196[e]	17.70 (1.99-63.91)
Vickrey (1997)	United States	248	Surgery or AEDs	0.67 (0.12-3.80)	0.013[d]	51.81 (0.68-259.67)	0.0196[r]	34.48 (0.45-170.14)
Klenerman (1993)	United Kingdom	NR (reported as patient-years)	AEDs	0.59 (0.16- 2.15)	0.005[e]	117.65 (13.21-424.80)	0.0196[e]	30.30 (3.40-109.42)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] Study population rate / highest age-specific rate in general reference population, calculated by ECRI
[d] From U.S. Census Bureau, Statistical Abstract of the United States, 2000
[e] Calculated by ECRI from Mortality Statistics (England and Wales, 1999)

Evidence Table 243. Accident-related mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Accident-Related Mortality Rate Per 1000 Person-Years				
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]	Highest Rate in General Reference Population	Crude Mortality Ratio (CI)[c]
Racoosin (2001)	United States	9144	AEDs	All patients: 1.47 (0.95-2.27)	Age-adjusted: 0.29[d]	5.06 (3.09-7.83)	0.92[d]	1.60 (0.98-2.47)
Hennessy (1999)	United Kingdom	305	Surgery	All patients: 1.47 (0.57-3.76) (includes some patients seizure-free after surgery)	All patients: 0.21[e]	6.98 (1.86-17.88)	0.25[e]	5.87 (1.57-15.02)
Sperling (1999)	United States	194	Surgery	All patients: 1.25 (0.22-7.03)[a]	Age-adjusted: 0.29[d]	4.31 (0.06-23.97)	0.37[d]	3.37 (0.04-18.73)
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients: 0.52 (0.18-1.53)	Age-adjusted: 0.29[d]	1.80 (0.36-5.26)	0.92[d]	0.57 (0.11-1.67)
Leppik (1995)	United States, Europe, Australia	2600	AEDs	All patients: 1.66 (0.56 to 4.86)	Age-adjusted: 0.29[d]	5.71 (1.15-16.70)	0.92[d]	1.80 (0.36-5.26)
Klenerman (1993)	United Kingdom	NR	AEDs	All patients: 0.88 (0.30-2.60)	All patients: 0.21[e]	4.21 (0.85-12.32)	2.57[e]	0.34 (0.07-1.01)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] Study population rate / highest rate in general reference population, calculated by ECRI
[d] From U.S. Census Bureau, Statistical Abstract of the United States, 2000. The standard population for age-adjustment was the U.S. population in 1940.
[e] Calculated by ECRI from Mortality Statistics (England and Wales, 1999).

Evidence Table 244. Automobile accident-related mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Automobile-Accident-Related Mortality Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Sperling (1999)	United States	194	Surgery	All patients: 1.25 (0.22-7.03)	Age-adjusted: 0.16[c]	7.81 (0.10-43.47)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] From U.S. Census Bureau, Statistical Abstract of the United States, 2000. The standard population for age-adjustment was the U.S. population in 1940.

Evidence Table 245. Aspiration-related mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Aspiration-Related Mortality Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Racoosin (2001)	United States	9144	AEDs	All patients: 0.29 (0.11- 0.76)	Not reported	Cannot be calculated
Hennessy (1999)	United Kingdom	305	Surgery	All patients: 0.73 (0.20-2.67) (includes some patients seizure-free after surgery)	Not reported	Cannot be calculated
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients: 0.17 (0.03-0.99)	Not reported	Cannot be calculated
Klenerman (1993)	United Kingdom	Not reported (reported as patient-years)	AEDs	All patients: 1.77 (0.81- 3.85)	Not reported	Cannot be calculated

[a] Calculated by ECRI
[b] Available studies did not report any deaths from aspiration.

Evidence Table 246. Pneumonia-related mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Pneumonia Mortality Rate Per 1000 Person-Years				
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]	Highest Rate in General Reference Population	Crude Mortality Ratio (CI)[c]
Sperling (1999)	United States	194	Surgery	All patients: 1.25 (0.22- 7.03)	Age-adjusted: 0.13[d]	9.62 (0.13-53.53)[a]	Not applicable[f]	Not applicable[f]
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients: 0.17 (0.03- 0.99)	Age-adjusted: 0.13[d]	1.34 (0.02-7.45)[a]	2.28[e]	0.08 (0.01-0.42)
Klenerman (1993)	United Kingdom	Not reported (reported as patient-years)	AEDs	All patients: 8.25 (5.72- 11.90)	All patients: 0.34[e]	24.28 (16.13-35.10)[a]	34.12[e]	0.24 (0.16-0.35)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] Study population rate / highest rate in general reference population, calculated by ECRI
[d] From U.S. Census Bureau, Statistical Abstract of the United States, 2000.
[e] From Mortality Statistics (England and Wales, 1999).
[f] The highest value for an individual age group was not higher than the value for the overall reference population, so no sensitivity analysis could be performed.

Evidence Table 247. Cardiovascular mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Cardiovascular Mortality Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Hennessy (1999)	United Kingdom	305	Surgery	Crude: 0.37 (0.06-2.07)	0.42[c]	0.87 (0.01-4.87)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] Calculated from age-specific rates in Mortality Statistics (England and Wales, 1999).

Evidence Table 248. Cerebrovascular mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Cerebrovascular Mortality Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Racoosin (2001)	United States	9144	AEDs	All patients: 0.51 (0.25- 1.06)	Age-adjusted: 0.25[c]	2.06 (0.55- 4.24)
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients: 0.17 (0.03- 0.99)	Age-adjusted: 0.25[c]	0.70 (0.01- 3.87)
Klenerman (1993)	United Kingdom	Not reported (reported as patient-years)	AEDs	All patients: 1.77 (0.81- 3.85)	All patients: 1.01[d]	1.75 (0.64-3.81)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] From U.S. Census Bureau, Statistical Abstract of the United States, 2000. The standard population for age-adjustment was the U.S. population in 1940.
[d] From Mortality Statistics (England and Wales, 1999).

Evidence Table 249. Cancer-related mortality rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Cancer Mortality Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Klenerman (1993)	United Kingdom	Not reported (reported as patient-years)	AEDs	All patients: 8.55 (5.96-12.25)[a]	4.28[c]	SMR cancer: 2.0 (1.3-2.9) Lung: 3.3 (1.7-5.9) Pancreas: 6.2 (1.7-15.8) Lymphatic/ Haemopoetic: 3.3 (0.7-9.3) Hepatobiliary: 17.6 (3.6-51.5)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] Calculated by ECRI from age-specific rates in Mortality Statistics (England and Wales, 1999).

Evidence Table 250. Suicide rates among patients with treatment-resistant epilepsy

Reference	Country	N	Treatment	Suicide Rate Per 1000 Person-Years		
				Study Population Rate (CI)[a]	General Reference Population Rate	Crude Mortality Ratio (CI)[b]
Sperling (1999)	United States	194	Surgery	All patients: 1.25 (0.22 to 7.03)	Age-adjusted: 0.10[c]	12.5 (0.16 to 69.53)
Hennessy (1999)	United Kingdom	305	Surgery	All patients: 0.37 (0.06-2.07)	0.11[d]	3.33 (0.37-18.55)
Leestma (1997)	United States, United Kingdom, Europe, Australia, South Africa	4700	AEDs	All patients: 0.17 (0.03 to 0.99)	Age-adjusted: 0.10[c]	1.74 (0.02 to 9.68)

[a] Calculated by ECRI
[b] Study population rate / general reference population rate, calculated by ECRI
[c] From U.S. Census Bureau, Statistical Abstract of the United States, 2000. The standard population for age-adjustment was the U.S. population in 1940.
[d] From Mortality Statistics (England and Wales, 1999).

Question 9

Is there a correlation between the number and/or type of seizure and sudden death?

Evidence Table 251. Design and conduct of included studies of sudden unexpected death from epilepsy (SUDEP)

Reference	Country	N	Epilepsy Diagnosis	Study Reported Criteria For Diagnosis of SUDEP	Proportion (Percent) SUDEP Cases Determined by Autopsy
Walczak (2001)	United States	4578	Clinical diagnosis	Yes	10/20 (50%)
McKee (2000)	United States	180	Clinical diagnosis plus AED treatment	Yes	4/11 (36.4%)
Kloster (1999)	Norway	79	Clinical diagnosis	Yes	42/42 (100%)
Nilsson (1999)	United Kingdom	228	Clinical diagnosis	Yes	52/57 (91.2%)
Sperling (1999)	United States	393	Clinical diagnosis	Yes	Not reported
Nashef (1995)	United Kingdom	601	Clinical diagnosis	No	10/11 (90.9%)
Timmings (1993)	United Kingdom	1820	Clinical diagnosis	No	Not reported
Jick (1992)	United States	3280 (only 31 were relevant to this question)	Anticonvulsant usage and other information on file (based on random review of only 5% of records)	Yes	11/11 (100%)
Birnbach (1991)	United States	108	Clinical diagnosis	No	Not reported

Evidence Table 251. Design and conduct of included studies of sudden unexpected death from epilepsy (continued)

Reference	Study Design	Controls	Controls Matched to Cases	Methods Used to Correlate Seizure Type/Frequency And SUDEP	Study Adjusted For Potential Confounding Variables
Walczak (2001)	Prospective nested case-control	Living patients	Yes (matched by time of enrollment and epilepsy center)	Multiple logistic regression	Yes
McKee (2000)	Retrospective nested case-control	Living patients	No	t-test	No
Kloster (1999)	Retrospective nested case-control	Deceased	No	Student's t-test or Pearson's χ^2 test	No
Nilsson (1999)	Retrospective nested case-control	Living patients	Yes (matched for year of birth, gender, and assessment period)	Multiple logistic regression	Yes
Sperling (1999)	Prospective nested case-control	All patients in cohort (living and dead)	No	No statistical comparison (only for overall mortality)	No (only in overall mortality analysis, not for sudden death)
Nashef (1995)	Retrospective nested case-control	All patients in cohort (living and deceased)	No	No statistical comparison	No
Timmings (1993)	Retrospective nested case-control	Unclear, but could be all other patients in cohort	No	χ^2 test	No
Jick (1992)	Retrospective nested case-control	Living patients	Yes (matched on age at index date and gender)	No statistical comparison	No
Birnbach (1991)	Retrospective nested case-control	Deceased and living patients	No	Student's t-test, χ^2 test	No

Evidence Table 252. Correlation between SUDEP and seizure frequency

Studies adjusted for potential confounding variables

Reference	Country	N	Seizure Frequency	SUDEP (N)	Control (N)	Published Results	Statistically Significant Association	Other Variables Adjusted For in Multiple Regression Analysis
Walczak (2001)	United States	4578 (only 100 were relevant to this question)	Monthly average:			OR[a] (CI) Multiple regression	No (possibly for females, but the publication did not specifically report that the gender-specific ratios were derived from a multivariate analysis)	Frequency of tonic-clonic seizures, number of AEDs used
			0	2	23	1.1 (0.3-4.0)		
			≤1	3	16			
			>1 to ≤15	10	30			
			>15 to ≤50	2	5			
			>50	3	3			
			Unknown	0	3			
			Males					
			<1	2	17	1.0[b]		
			1-5	3	11	3.4 (0.5-22)		
			>5	3	16	1.0 (0.1-7.9)		
			Unknown	0	0			
			Females					
			<1	2	19	1.0[b]		
			1-5	5	5	5.7 (0.6-43.9)		
			>5	5	9	7.4 (1.3-43.0)		
			Unknown	0	3			
Nilsson (1999)	United Kingdom	228	Seizures/year			Multiple regression RR[c] (CI)	Yes	Age at epilepsy onset, epilepsy type, number of AEDs, changes in AED dose per year
			0-2	5	87	1.00[b]		
			3-12	16	33	4.47 (1.33-15.03)		
			>12	24	39	4.64 (1.22-17.63)		
			Males			Unadjusted RR[c]		
			0-2	2	56	1.00[b]		
			3-12	12	18	14.8 (3.1-69.7)		
			13-50	7	12	15.1 (2.8-81.2)		
			>50	4	7	14.8 (2.3-96.1)		
			Unknown	9	9	24.1 (4.2-138.6)		
			Females			Unadjusted RR[c]		
			0-2	3	31	1.00[b]		
			3-12	4	15	2.5 (0.5-12.0)		
			13-50	8	14	4.7 (1.1-19.6)		
			>50	5	6	6.5 (1.2-34.3)		
			Unknown	3	3	7.2 (0.9-56.6)		

[a] Odds ratio
[b] Used as a reference value for the other seizure frequencies
[c] Relative risk

Evidence Table 253. Correlation between SUDEP and seizure frequency

Studies did not adjust for potential confounding variables

Reference	Country	N	Seizure Frequency	SUDEP (N)	Control (N)	Published Results	Odds Ratio (CI)[a]	Statistically Significant Association If Not, What W as The Minimum Detectable Difference
McKee (2000)	United States	180	Yearly mean SUDEP: 143 Control: 27	NA	NA	p = 0.07	Cannot be calculated	No Cannot be calculated
Kloster (1999)	Norway	79	Seizures per year ≤1 2-12 >12 No data	 4 3 32 3	 6 1 26 4	p = 0.56	 0.54 (0.14-2.10) 2.77 (0.28-27.85) 1.35 (0.50-3.68) 0.63 (0.13-3.04)	No 6.28
Sperling (1999)	United States	393	Seizures: 0 >0	 0 6	 199 188	None[b]	 0.07 (0.00-1.30) 13.76 (0.77-245.93)	No 15.1
Timmings (1993)	United Kingdom	1820	Seizures per month <1 1-4 5-60 Unknown	 4 5 4 1	NR	p = NS[c]	Cannot be calculated	No Cannot be calculated

[a] Calculated by ECRI
[b] No statistical analysis
[c] Specific p-value not reported
NA Not applicable
NR Not reported
NS Not statistically significant

Evidence Table 253. Correlation between SUDEP and seizure frequency (continued)

Reference	Country	N	Seizure Frequency	SUDEP (N)	Control (N)	Published Results	Odds Ratio (CI)[a]	Statistically Significant Association If Not, What Was The Minimum Detectable Difference
Jick (1992)	United States	3280 (only 31 were relevant to this question)	Seizures per month ≤1 >1 Unknown	 6 3 2	 13 4 3	None[b]	 0.65 (0.14-2.90) 1.50 (0.27-8.38) 1.26 (0.18-8.97)	No 6.36
Birnbach (1991)	United States	48	Mean ±SD generalized seizures per month SUDEP: 1.86 ± 3.47 Non-SUDEP deaths: 1.24 ± 1.52 Living: 0.43 ± 0.80	NA	NA	SUDEP vs. Non-SUDEP deaths: t = 0.70[d] p = 0.255[a] SUDEP vs. Living controls: t = 2.57[a] p = 0.013[a]	Cannot be calculated	No (SUDEP vs. Non-SUDEP deaths) 1.56 Yes (SUDEP vs. Living controls)

[a] Calculated by ECRI
[b] No statistical analysis
[d] Student's t-test
NA Not applicable

Evidence Table 254. Correlation between SUDEP and seizure type

Studies adjusted for potential confounding variables

Reference	Country	N	Seizure Type	SUDEP (N)	Control (N)	Published Results	Statistically Significant Association	Other Variables Adjusted For In Multiple Regression Analysis
Walczak (2001)	United States	4578 (only 100 were relevant to this question)	All patients Tonic-clonic 0 1-3 >3 Unknown			Multiple Regression OR (CI) 7.0 (2.0-24.2)	Yes	Overall seizure frequency, number of AEDs used
				4 6 9 1	54 11 15 0			
			Males Tonic-clonic 0 1-3 >3 Unknown			OR (CI) 1.0[b] 4.3 (0.5-37.3) 3.3 (0.5-22.1)		
				2 2 3 1	26 6 12 0			
			Females Tonic-clonic 0 1-3 >3 Unknown			1.0[b] 11.2 (1.6-78.4) 28.0 (3.8-205.8)		
				2 4 6 0	28 5 3 0			
Nilsson (1999)	United Kingdom	228	Generalized idiopathic	7	12	Multiple regression RR (CI) 1.00	No	Seizure frequency during last year, age at epilepsy onset, number of AEDs, changes in AED dose per year
			Partial symptomatic	26	92	1.15 (0.18-7.17)		
			Partial cryptogenic	17	45	1.94 (0.27-13.71)		
			Undetermined	7	22	1.17 (0.14-9.78)		

[a] Calculated by ECRI
[b] Used as a reference value for the other seizure frequencies
OR Odds ratio
RR Relative risk

Evidence Table 255. Correlation between SUDEP and seizure type

Studies did not adjust for potential confounding variables

Reference	Country	N	Seizure Type	SUDEP (N)	Control (N)	Published Results	Odds Ratio (CI)[a]	Statistically Significant Association If Not, What Was The Minimum Detectable Difference
Kloster (1999)	Norway	79	Generalized motor seizures Partial seizures	42 0	35 2	p = 0.07 (χ^2 test)	5.99 (0.28-128.8) 0.17 (0.01-3.59)	No 10.27
Sperling (1999)	United States	393	Non-tonic-clonic Tonic-clonic	2 4	297 90	None[b]	0.15 (0.03-0.84) 6.60 (1.19-36.63)	Yes
Nashef (1995)	United Kingdom	601	Partial cryptogenic/ symptomatic Generalized idiopathic Generalized cryptogenic/ symptomatic Undetermined	5 1 3 2	396 75 44 63	None[b]	0.41 (0.12-1.35) 0.69 (0.09-5.44) 4.65 (1.19-18.17) 1.86 (0.39-8.80)	Yes
Timmings (1993)	United Kingdom	1820	Idiopathic generalized tonic clonic Partial seizures (with or without secondary generalization)	10 4	Not reported Not reported	p <0.05 (χ^2 test)	Cannot be calculated	Yes
Jick (1992)	United States	3280 (only 31 were relevant to this question)	Primary generalized Primary partial Unknown	6 2 3	10 5 5	None[b]	1.20 (0.27-5.25) 0.67 (0.11-4.18) 1.13 (0.21-5.97)	No 9.71
Birnbach (1991)	United States	108	Generalized convulsive Other	24 1	Non-SUDEP 22 1	None[b]	1.09 (0.06-18.52) 0.92 (0.05-15.56)	No
			Generalized convulsive Other	24 1	Living 47 13	None[b]	6.64 (0.82-53.81) 0.15 (0.02-1.22)	No 7.34

[a] Calculated by ECRI
[b] No statistical analysis