ILAE Symposium:
Epilepsy Treatment in North America and Around The World: Can We Learn From Each Other?

Symposium Co-Chairs:
Jacqueline A. French, M.D.
Professor of Neurology
NYU School of Medicine
New York, NY

Sheryl Haut, M.D.
Director, Adult Epilepsy Program
Director, Neurology Residency Training
Department of Neurology
Montefiore Medical Center
Bronx, NY

Tuesday, December 7, 2010
Convention Center – Lila Cockrell Theatre
10:45 am – 12:15 pm

OVERVIEW

Despite globalization of the science that underlies medical care, common issues in epilepsy are being addressed in ways that continue to reflect specific geographic and cultural approaches to provision of healthcare. This symposium will explore areas which reflect these differences: new drug development and clinical trials; epilepsy surgery; and the impact of limited resources on availability of care. New perspectives on these topics can inform both health policy and clinical decisions related to care of people with epilepsy in North America.

LEARNING OBJECTIVES

- Broaden treatment options by applying geographic and cultural differences that inform approaches to temporal lobe resections in North America and around the world
- Use complementary information from clinical trial designs from different regions in managing patients with epilepsy
- Address limited resources for epilepsy care based on the experience of health policy and treatment decisions in areas outside North America.

TARGET AUDIENCE

Intermediate: Epilepsy fellows, epileptologists, epilepsy neurosurgeons, “mid-level” providers with experience in epilepsy care (e.g., advanced practice nurses, nurses, physician assistants), neuropsychologists, psychiatrists, basic and translational researchers.

AGENDA

10:45 am – 10:55 am	Introduction and Overview Jacqueline A. French, M.D., Sheryl Haut, M.D.
10:55 am - 11:35 am	Are Placebo Controlled or Pragmatic Trials More Informative? Anthony Marson, Ph.D. and Russell Katz, M.D.
11:35 am – 12:15 pm	How Are Epilepsy Resources Allocated Around the World? Lessons From Epilepsy Surgery Frans Leijten, M.D., Ph.D. and Samuel Wiebe, M.D.

ACCREDITATION

The American Epilepsy Society is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

CREDIT DESIGNATION

The American Epilepsy Society designates this educational activity for a maximum of 1.5 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

ACKNOWLEDGEMENT

This program is supported in part by an educational grant from Pfizer Inc.

PHARMACY ACCREDITATION INFORMATION

The University of Minnesota, College of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

This knowledge-based activity provides up to 1.5 contact hours (.15 CEUs). Following attendance, completion of the activity evaluation and verification of attendance, participants will be provided an electronic statement of credit. ACPE Universal Activity Number (UAN) is 031-999-10-029-L04-P.

POLICY ON COMMERCIAL SUPPORT AND CONFLICT OF INTEREST
The American Epilepsy Society maintains a policy on the use of commercial support, which ensures that all educational activities sponsored by the AES provide in-depth presentations that are fair, balanced, independent and scientifically rigorous. All faculty, planning committee members, editors, managers and other individuals who are in a position to control content are required to disclose any relevant relationships with any commercial interests related to the activity. The existence of these interests or relationships is not viewed as implying bias or decreasing the value of the presentations. All educational materials are reviewed for fair balance, scientific objectivity and levels of evidence. Faculty disclosure will be made available through syllabus materials and faculty presentations.

FACULTY / PLANNER BIO AND DISCLOSURES
Jacqueline A. French, M.D. (Co-Chair)
Professor of Neurology
NYU School of Medicine
New York, NY
Dr. French is a professor in the Department of Neurology NYU, in the comprehensive Epilepsy Center, and Director of the Clinical Trials Consortium. Dr. French trained in Neurology at Mount Sinai Hospital in New York, and did her fellowship training in EEG and epilepsy at Mount Sinai hospital and Yale University. Dr. French has focused her research efforts on development of new therapeutics for epilepsy. She has written many articles, editorials and chapters and has edited two books on this subject. She is currently chair of the North American Commission of the ILAE.

Dr. French discloses receiving remuneration as a Consultant/Advisory Board Member for Sunovion, Novartis, and Upsher-Smith; for Contract Research from Vertex Pharma, UCB Pharma, and Sunovion.

Sheryl Haut, M.D. (Co-Chair)
Director, Adult Epilepsy Program
Director, Neurology Residency Training
Department of Neurology
Montefiore Medical Center
Bronx, NY
Dr. Haut is Director of the Adult Epilepsy Program and Director of Neurology Residency Training at AECOM. Her research interests include: the temporal distribution of seizures, with emphasis on seizure clustering; seizure prediction and pre-emption; and alternative therapies for epilepsy. Dr. Haut has a Masters in Clinical Research Methods, and completed a K23 career development award from the NIH. She is currently the Secretary of the North American Region Commission of the ILAE. She maintains an active adult epilepsy practice at Montefiore Medical Center, Bronx New York.

Dr. Haut discloses receiving remuneration as a Consultant/Advisory Board Member for Acorda, Vivus, UCB Pharma, SK Pharma; and for Contract Research from Endo.

Russell Katz, M.D.
Division Director, FDA Neuropharmacology division
Federal Drug Administration
Silver Spring, MD
Dr. Katz is the Director of the Division of Neurology Products (DNP) at the US Food and Drug Administration (FDA). Dr. Katz joined the FDA after completing his residency in Neurology at the Albert Einstein affiiliated hospitals in New York City. He has been at the FDA since 1983, and has been Director of the DNP since 1999. He has written and lectured extensively about all aspects of the development and approval of treatments for neurologic illness.

Dr. Katz has nothing to disclose.

Frans Leijten, MD, Ph.D.
Associate professor of Neurology
Rudolf Magnus Institute of Neuroscience
University Medical Center
Utrecht, The Netherlands
Dr. Frans Leijten is a member of the National Dutch Epilepsy Surgery Taskforce as an epileptologist and clinical neurophysiologist. He is the head of the Epilepsy Monitoring Unit at the University Medical Center of Utrecht, and mainly involved in epilepsy surgery diagnostics. He has published on advanced techniques such as MEG source imaging, PET and EEG-fMRI, but also on general aspects of clinical decision making and quality-of-life in epilepsy. Currently he is involved in establishing a large population-based cohort to study the aetiology of medical intractability.

Dr. Leijten discloses receiving remuneration as a Consultant/Advisory Board Member for Kendle Clinical Pharmacology Unit, Utrecht, The Netherlands.

Anthony Marson, Ph.D.
Professor of Neurology
The Walton Centre of Neurology and Neurosurgery
Liverpool, England, United Kingdom
Professor Marson is a consultant neurologist at The Walton Centre and Professor of Neurology at The University of Liverpool. His research has focussed upon the assessment of treatments and outcomes in epilepsy, with a particular focus upon informing day to day clinical decisions. He has experience of running investigator lead RCTS (MESS and SANAD) as well as systematic review, and pharmacogenetics. Current roles include Director of the UK Epilepsy Research Network, Coordinating Editor of the Cochrane Epilepsy Group, Deputy Director MRC North West Hub for Trial Methodology Research.

Dr. Marson discloses receiving remuneration as a Consultant/Advisory Board Member for UCB Pharma.

Samuel Wiebe, M.D., M.Sc. (Epidemiol)
Professor and Head
Division of Neurology
University of Calgary
Calgary, Alberta, Canada
Dr. Wiebe is Professor and Head Division of Neurology in the Department of Clinical Neurosciences, University of Calgary, Canada, Director of the Comprehensive Epilepsy Programme, and Clinical Research Director of the Hotchkiss Brain. His academic interests include surgical trials in epilepsy, epidemiological studies, and outcome assessment. Dr Wiebe is past-chair of the International League Against Epilepsy (ILAE) North American Region Commission and has been elected Secretary-General of the ILAE. Dr Wiebe has been awarded the Hopewell Professorship in Clinical Neurosciences Research.

Dr. Wiebe has nothing to disclose.

Barbara Jobst, M.D. (CME Content Reviewer)
Dartmouth-Hitchcock Medical Center
Epilepsy Program
Lebanon, NH
Practice Note: Epilepsy Surgery, Neurophysiology including Intraoperative Monitoring, Seizures and Pregnancy, Women's Health Issues in Epilepsy.

Dr. Jobst discloses receiving remuneration as a Speakers Bureau Member for Eisai and Contract Research from NeuroPace, Inc.

Paul Levisohn, M.D. (Content Specialist)
Associate Professor of Pediatrics and Neurology
University of Colorado
Denver, Colorado
Dr. Levisohn is Associate Professor of Pediatrics and Neurology at the University of Colorado, School of Medicine and The Children's Hospital, Denver. He is former medical director of the Epilepsy Monitoring Unit at The Children's Hospital. He has served as chair of the AES Practice Committee. As such, he has been involved in addressing EMU safety needs. He currently serves as consultant to AES on medical content of AES continuing medical education activities.

Dr. Levisohn discloses receiving remuneration as a Consultant for Ovation Pharmaceuticals and Novartis Pharmaceuticals and Contract Research from Lundbeck and Eisai.

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Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the American Epilepsy Society or any manufacturers of pharmaceuticals.

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The Medical Education Evaluator® allows any attendee to self-manage the process of completing course evaluations, tracking credits and printing out the appropriate certificate for either *AMA PRA Category 1 Credits*™, CE or ACPE pharmacy statement of credits.

Log on to the Evaluator via the AES website at www.aesnet.org. Once you are on the Evaluator, you will be asked to enter your AES ID # and password. The certificate(s) are saved to your personal account page which is cumulative. You may print the certificate(s) in PDF format at any time.

To help support this process, attendees who want CME will be asked to pay $35 before January 15 and $50 after January 15.

The online Evaluator will be left open through February 28, 2011. You must complete the evaluations and credit tracking by that date.

By completing this information online, attendees greatly assist the Council on Education and Annual Meeting Committee with important needs assessment data whereby the AES can further plan and address educational gaps to meet the needs of our learners.

A meeting attendance certificate will be available for international meeting attendees at the registration desk.

SYLLABUS
Paper handouts will not be provided.

Epilepsy Treatment in North America and Around the World: Can We Learn From Each Other?

December 7, 2010

North American Regional Commission
International League Against Epilepsy

Symposium Chairs:
Dr. Jacqueline French and Dr. Sheryl Haut

American Epilepsy Society Annual Meeting

Disclosures

Dr. Jacqueline French:

As Director of the Epilepsy Study Consortium (ESC), Dr French consults for a number of companies, on behalf of the Epilepsy Study consortium, and takes no personal income. Dr French is paid 20% of her academic salary for all work performed for ESC. Companies involved have included Glaxo-Smith Kline, Pfizer, UCB Pharma, Johnson and Johnson, Cyberonics, Schwarz Pharma, Ortho-McNeil, Eisai, Jazz Pharmaceuticals, Ovation Pharmaceuticals, Endo Pharmaceuticals, Bial Pharmaceuticals, Neurovista, Valeant Pharmaceuticals, Icagen, Supernus, Ikano, SK Pharmaceuticals, Taro Pharmaceuticals, Neurotherapeutics, Sepracor, Novartis, Vertex , Upsher-Smith

Dr. Sheryl Haut:

Dr. Haut has served as a consultant for Acorda, Vivus, SK Pharmaceuticals, and as a member of the Speakers Bureau for UCB. She receives unrestricted grant support from Endo.

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Members of the North American Regional Commission

Dr. Jacqueline French (Chair)
Dr. Amza Ali
Dr. Lionel Carmant
Dr. Sheryl Haut
Dr. Frances Jensen
Dr. Natalie Jette
Dr. Sharon Whiting
Dr. Samuel Wiebe (ILAE)
Dr. William Theodore (Global Campaign Liason)
Dr. John Swann (AES Liason)

The mission of the North American Regional Commission of ILAE

- Improve the care of patients with epilepsy in North America and around the world
- Participate with other regional commissions of the ILAE in a collaborative effort to improve epilepsy education and treatment globally
- Share lessons learned in North America, and integrate lessons from other regions, towards the development of global, regional and individualized approaches in epilepsy

What can we learn from each other?

- Despite globalization, common issues in epilepsy are addressed in ways that reflect specific geographic and cultural approaches to provision of healthcare
- Sometimes, this can translate to “strongly held beliefs” that are not fully based in evidence or fact
- Exposing ourselves to differing opinions will enhance our ability to deliver thoughtful, progressive epilepsy care

This symposium will focus on regional differences in two such areas

Are Placebo Controlled or Pragmatic Trials More Informative?

Dr. Russell Katz (US approach)

Dr. Anthony Marson (European approach)

Epilepsy surgery: shoestring or full-dress approach?

Dr. Samuel Wiebe (Canadian approach)

Dr. Frans Leijten (Netherlands approach)

How can we use information that we share across regions?

New perspectives on these topics can inform both health policy and clinical decisions related to care of people with epilepsy

- Use complimentary information from clinical trial designs from different regions
- Broaden treatment options by applying geographic and cultural differences that inform approaches to temporal lobe resections in North America and around the world

Pragmatic Randomised Controlled Trials In Epilepsy

Tony Marson
Professor of Neurology
University of Liverpool
&
The Walton Centre NHS
Foundation Trust

American Epilepsy Society Annual Meeting

Disclosure

UCB Pharma, GSK, Eisai,Pfizer,	Research grant
UCB Pharma	Advisory board

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Pragmatic

- Oxford English Dictionary

"Dealing with matters in accordance with practical rather than theoretical considerations or general principles; aiming at what is achievable rather than ideal; matter-of-fact, practical, down-to-earth .... ."

- Striving for the ideal can result in something that is difficult to achieve and of no practical value

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Pragmatic randomized controlled trials

- Evidence for Effectiveness
- Attempt to reflect every day clinical practice
- Motivation – to inform practice / policy
- Does the drug work in the real world?
- Broad population of subjects
- Outcomes of clinical importance, may include QOL and economic outcomes
- Long term follow-up
- Funded from the public purse

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Explanatory trials

- Provide evidence of efficacy
- Motivation – regulatory approval
- Does the drug work under ideal conditions?
- Restricted population of subjects
- Treatment compared to placebo
- Outcomes may be surrogate
- Follow-up short

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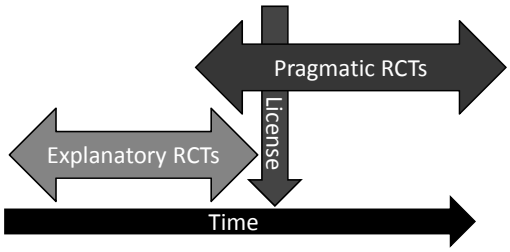
Drug evaluation timeline



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What is the most effective first line add-on treatment for refractory focal epilepsy?

- Real life treatment policies should determine the treatment groups in trials that can answer this question.
- Multiple treatment alternatives available
  - Placebo controlled trial can't answer this question
  - Head to had trial of alternatives required

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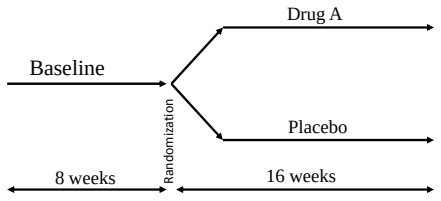
Add-on trials of new AEDs



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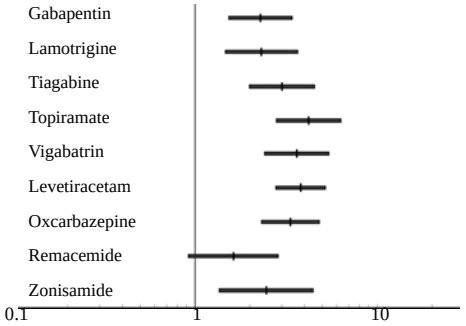
Add-on AEDs – 50% responders



The Cochrane Library, 2010

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First line add-on – further issues

- Over what duration should outcomes be measured?
  - 16 weeks of no practical value for a long term refractory condition
- What outcomes should be measured in longer term refractory epilepsy trials?
  - No international consensus!
  - Seizure freedom?
  - QOL
  - Cost effectiveness

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Consequences

- No reliable data regarding the clinical and cost effectiveness of new AEDs as add-on treatment
  - Individual clinical decisions are poorly informed
  - Guidelines are poorly informed - AAN, NICE, ILAE
  - Patients may not be offered the most effective treatment
  - Patients might be denied effective treatment
  - Resources are not used effectively

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What is the most effective first-line treatment for newly diagnosed focal epilepsy?

- Multiple treatment options
  - Head to head trials needed
- Control group should receive usual standard therapy
- This question cannot be answered by:
  - Placebo controlled trials
  - Pseudo-placebo designs
  - Withdrawal to monotherapy designs

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Levetiracetam vs Carbamazepine

Brodie et al, Neurology 2007;68:402-408

- Double blind monotherapy RCT
  - 288 levetiracetam, 291 carbamazepine slow release
- 3 dose levels
  - CBZ 400mg, 800mg, 1200mg.
  - LEV 1000mg, 2000mg, 3000mg.
- Primary outcome was proportion with 6 month remission
  - 73.0% Levetiracetam
  - 72.8% Carbamazepine
  - Analysis supports non-inferiority according to an a priori definition.

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Does this inform treatment choice?

- Is 6 month remission long enough?
  - ILAE currently recommends 12 months
- What are the effects on quality of life?
- Is levetiracetam cost effective?

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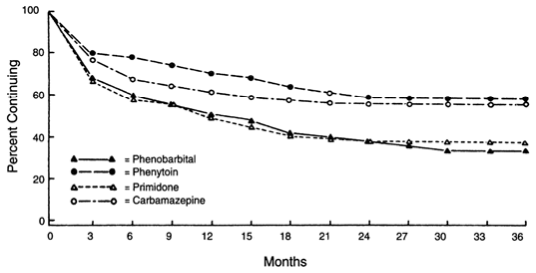
Mattson et al NEJM 1985. 313;145-51



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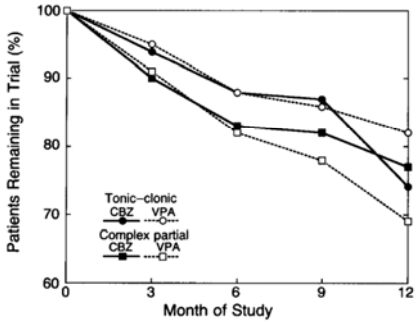
Mattson et al 1992. NEJM 327;365-71



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SANAD study

- Inclusion criteria
  - Aged 5 or over with two or more unprovoked seizures
- Un-blinded with Dosing and titration according to clinicians usual practice
- Patients followed up at 3, 6, 12 months and annually there after
- Primary
  - Time to treatment failure
  - Time to achieve a 12 month remission from seizures
- Secondary included
  - Quality of life
  - Health economic outcomes

Marson et al, Lancet 2007

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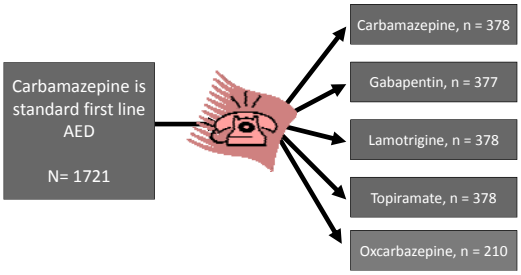
SANAD arm A



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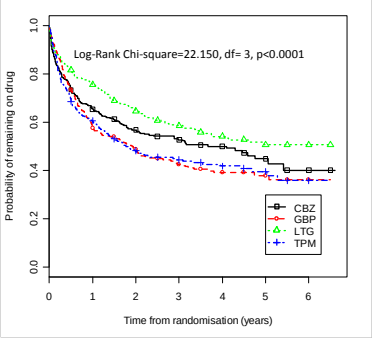
Time to treatment failure



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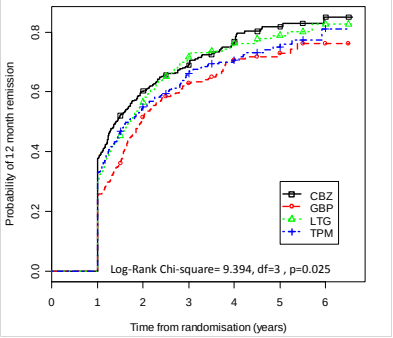
Time to 12 month remission



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Probability of cost effectiveness cost per QALY, incremental to CBZ

	Gabapentin	Lamotrigine	Topiramate	Oxcarbazepine *
£10,000	0.04	0.42	0.20	0.69
£30,000	0.31	0.82	0.47	0.86
£50,000	0.41	0.89	0.54	0.89

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Conclusions

- Most epilepsy trials are explanatory trials,
- Few pragmatic epilepsy trials have been undertaken
- As a result
  - Individual clinical decisions are poorly informed
  - Guidelines are poorly informed - AAN, NICE, ILAE
  - Resources may not be used effectively
- Our community has focussed on the needs of industry and regulators to the detriment of patients and wider society.
- More pragmatic trials are required but who should fund them?
  - Industry?
  - Public purse?

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Are Placebo Controlled or Pragmatic Trials More Informative: The Case for Placebo Controlled Trials

December 7, 2010

Russell Katz, M.D.
Division of Neurology Products
Center for Drug Evaluation and Research
Silver Spring, MD

American Epilepsy Society Annual Meeting

Disclosure

Nothing to disclose.

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Placebo Controlled Registration Trials

- It is true that "Registration" trials do not answer many questions of interest, including:
  - Extended duration of effect
  - Use as Monotherapy (at least not early)
  - Comparative effectiveness/safety (not even for controlled release products)
  - Outcomes other than seizure frequency
  - Effects in heterogeneous populations

Placebo Controlled Registration Trials

- What placebo controlled trials do offer:
- Proof of principle
- Relevant population
- But most importantly:
  - INTERPRETABILITY ("absence" of bias)

Placebo Controlled Registration Trials

- Important elements of placebo controlled trials that produce interpretability
  - Randomization (including to fixed doses)
  - Blinding
  - Prospective, "simple" statistical plans, including:
    - Requirement for a showing of superiority
    - Requirement for specific primary comparison(s)

Placebo Controlled Registration Trials

- Blinding
  - Obvious factor in decreasing bias
- Lack of blinding can have numerous unfortunate consequences, including:
  - Effects on efficacy and safety outcomes (patient and investigator dependent)

Placebo Controlled Registration Trials

- Blinding
  - In SANAD B (Marson AG, et al. The Lancet 2007;**369**:1016-1026), patients chosen based on prescribers' "belief" in VPA
  - This "belief" could clearly affect how these patients (and those on the other treatments) were treated
  - This is particularly problematic when contemplating comparative claims

Placebo Controlled Registration Trials

- Statistical issues
- Requirement for a showing of superiority
  - A showing of no difference (non-inferiority) is usually uninterpretable
  - Either both drugs worked, or both drugs did not work
  - Only way to be sure is if there is a robust database of placebo-controlled studies with comparator
  - There usually isn't

Placebo Controlled Registration Trials

- Statistical issues
  - Requirement for prospective primary comparison(s)
  - Comparisons among many treatments, many outcomes can markedly inflate Type I error rate and lead to erroneous conclusions

Placebo Controlled Registration Trials

- Randomization to dose
  - Permitting dosing according to prescribers' personal choice cannot produce useful dose-response information
  - May result in under- or overdosing
- This is independent of knowledge of treatment assignment, but that makes it worse

Placebo Controlled Registration Trials

- Comparative claims
  - A fair comparative claim must compare a range of doses, both for effectiveness and safety
  - In addition to a range of doses, a range of outcomes should be compared
  - This is VERY difficult to do adequately

Principles for A Fair Comparison

- Equi-effective doses
- Optimal use of comparator agent
  - Dose schedules
  - Titration schedules
  - Use of adjunctive medication if appropriate
- Appropriate comparator(s)
- Sensitive assessment methods
- Population studied
  - Unbiased
  - Broad sampling
- Comparisons in all important domains
- Comparisons at all relevant times
- Replication

Summary

- Registration (placebo controlled) trials do not address **many** important issues, agreed
- The one great, and critical, advantage they have over “pragmatic” trials is that they are unequivocally interpretable
- Pragmatic trials may reflect how practitioners behave, but this can reflect many biases
- Placebo controlled trials are very “pragmatic”, in that they can “quickly” get drugs to market

Epilepsy Surgery: Shoestring or Full-Dress Approach?

December 7, 2010

Frans Leijten, M.D., Ph.D.
Associate professor of Neurology
Rudolf Magnus Institute of Neuroscience
University Medical Center
Utrecht, The Netherlands
&
Samuel Wiebe, M.D.
University of Calgary
Calgary, Alberta, Canada

American Epilepsy Society Annual Meeting

TLE Surgery: Fully Dressed

Frans Leijten, M.D., Ph.D.
Rudolf Magnus Institute of Neuroscience
University Medical Center
Utrecht, The Netherlands

American Epilepsy Society Annual Meeting

Disclosure

Kendle - EEG review Phase I and II MS medication

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Goals

the rationale for a full dress approach:
- **literature**
- **survey**
- **clinical practice**

to convince your Board that you need it all

TLE surgery

- **outcome >70% seizure-free**
- **different:**
  - **surgical techniques**
  - **patient selection**
  - **amount of diagnostics**

full-dress approach

all the diagnostics available

↓

optimal patient selection

↓

best choice of surgery

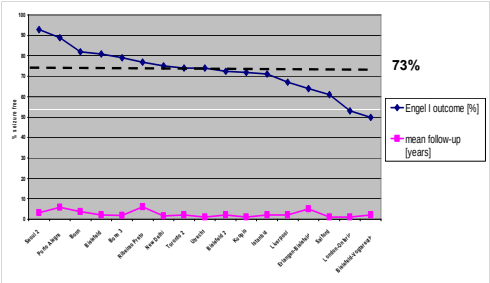
all diagnostics?

- video-EEG
- MRI (3 T)
- PET
- SPECT
- MEG
- MRS
- fMRI
- chronic invasive EEG
- intraoperative EEG
- EEG-fMRI, 7 T MRI, etc.

literature

1. outcome studies
2. a particular case: intraoperative ECoG

outcome studies

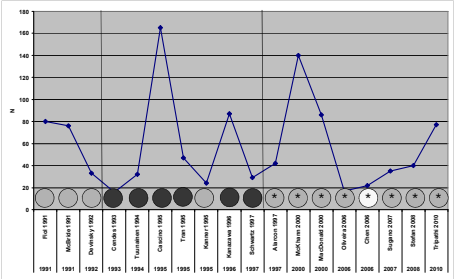


outcome studies

- 42 studies
- 17 after 1996, > 50 patients, no specific etiology
- reported outcome: 50-93%

→ some do better than others ?

value intraoperative EEG



statistics

study to settle the issue of aECoG: randomized study

suppose added value of 10%:

626 patients

313 with aECoG

313 without aECoG

survey outcome

- 7 centres
- 12-60 TLE surgeries/year
- seizure-free outcome 75-85%
- 2 extremes:
  - Lyon 85%
  - Netherlands 75%

unpublished results

	Lyon	Netherlands
Seizure free outcome (Engel 1)	85	75
Scalp EEG	100	100
Video-EEG monitoring	100	95
3 T MRI	80	100
SPECT	5	3
MRS	0	0
PET	90	25
MEG	30	5
Depth-electrodes or stereo-EEG	40	1
Subdural (grid) electrodes	5	1
Intra-operative ECoG	0	85

unpublished results

conclusions

- PET in all TLE patients
- MEG in 30%
- chronic invasive EEG in 45%

yields 10% extra seizure free

why?

- because traditional diagnostics do not predict who will have seizures after TLE surgery
- many predictors, but they do not predict much

Uijl, Epilepsia 2008

why

- TLE "plus"
- insula
- posterior temporal lobe

final conclusion

- TLE is not simple
- all diagnostics needed
- redundancy inevitable

Epilepsy Surgery: Doing it on a Shoestring

December 7, 2010

Samuel Wiebe, M.D.
University of Calgary
Calgary, Alberta, Canada

American Epilepsy Society Annual Meeting

Disclosure

Alberta Heritage Foundation for Medical Research — Clinical Research Grant

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Objectives

- Shoestring and core elements
- Validity of studies for full-dress
- Improved outcomes over time
- The way forward

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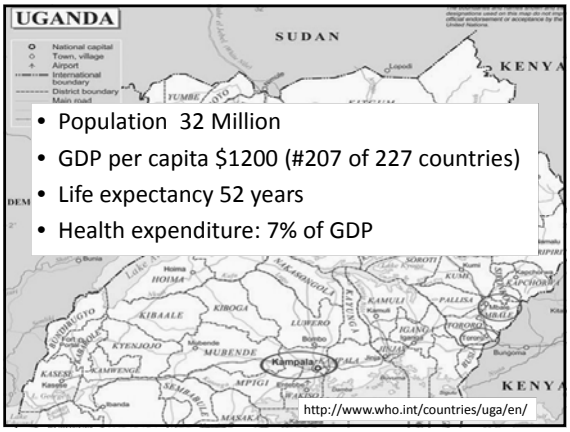

- Population 32 Million
- GDP per capita $1200 (#207 of 227 countries)
- Life expectancy 52 years
- Health expenditure: 7% of GDP

http://www.who.int/countries/uga/en/

Uganda

Surgery for pharmacoresistant epilepsy in the developing world: A pilot study

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Departments of *Neurosurgery, and †Neurology, West Virginia University, Morgantown, West Virginia, U.S.A.; ‡CURE Children's Hospital of Uganda, Mbale, Uganda; §Division of Neurosurgery, Alfred I. duPont Hospital for Children, Wilmington, Delaware, U.S.A.; ¶Department of Neurosurgery, Thomas Jefferson University Philadelphia, Pennsylvania, U.S.A.; #Department of Pathology, Wheeling Hospital, Wheeling, West Virginia, U.S.A.; Departments of **Neurology, and †† Surgery, Monash University, The Alfred Hospital, Melbourne, Australia; ‡‡Benedictine Eye Hospital, Tororo, Uganda; and §§Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, McGill University, Montreal, Quebec, Canada

Boling et al, Epilepsia 2009

The Model
-Temporal Lobe-

- 1 VEEG monitored bed in pediatric hospital
  - Applied by nurses, interpreted in USA
- MD- House officer, 4 week EEG training at MNI
- Neurosurgeon – on site apprenticeship
- CT – fine cuts with reformatting
- MMSE
- Patients
  - Age >6 years, failed ≥2 AEDs, ≥1 seizure/month
  - Simplified semiological criteria
  - No extratemporal lesions on CT

Boling et al, Epilepsia 2009

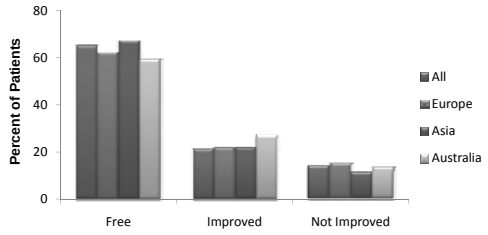
Results

Total operated (2005-2007)	10
Age, years (mean, range)	16 (12-24)
Seizure frequency	2-36/month
CT hippocampal atrophy	5
Right/Left	2/8
Follow-up, months (mean, range)	12 (8-27)
Seizure free	60%
>90 improved	20%
Not improved (less severe)	20%
Seizure free	
Normal CT	2/4
Concordant CT-EEG	4/5
Path – H Sclerosis	8

*1 memory decline, Normal CT, Left Temporal surgery, not seizure free

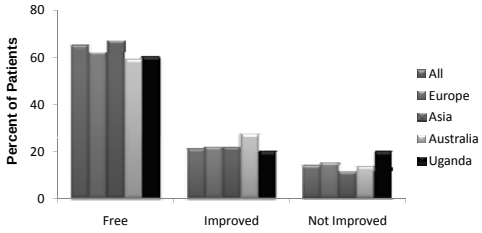
Boling et al, Epilepsia 2009

Anteromesial Temporal



Engel J Jr, et al. *Neurology.* 2003.

Anteromesial Temporal



Engel J Jr, et al. *Neurology.* 2003.

Is There a Minimum Core?

- Technology
  - MRI, VEEG
- Skilled personnel
  - Epileptologist
  - Neurosurgeon
  - Neuropsychologist
  - EEG techonologist

Campos, Epilepsia 2000; Fandino, Epilepsia 2000; Rao, Epilepsia 2000; Palmini, Epilepsia 2000

Developing Countries

- All technologies are not essential
- Collaboration with developed centres
- Staged approach
  - Entry level may include
    - Temporal Lobe
    - Lesions in non-eloquent areas
    - Corpus Callosotomy
    - Clear hemispheric syndromes

Palmini, Epilepsia 2000

Cost of epilepsy surgery

Temporal Lobe	Uganda	$100s?
	India	$1,200
	Colombia	$2,200
	Chile	$5,000
	China	$8,500
Callosotomy	Colombia	$3,500
Non-invasive	Developed Countries	$45,000

Campos, Epilepsia 2000; Fandino, Epilepsia 2000; Rao, Epilepsia 2000

ORIGINAL CONTRIBUTION

Is Ictal Recording Mandatory in Temporal Lobe Epilepsy?

Fernando Cendes, MD, PhD; Li M. Li, MD; Craig Watson, MD, PhD; Frederick Andermann, MD, FRCPC; François Dubeau, MD, FRCPC; Douglas L. Arnold, MD, FRCPC

- 184 consecutive patients at the MNI
- Volumetric assessment of H atrophy
- 100% agreement with ictal EEG if H atrophy and interictal spikes were concordant and entirely unilateral
- 97% agreement if bilateral interictal spikes

Cendes, et al, Arch Neurol 2000

Health Technology Assessment 2006; Vol. 10: No. 4

What is the Evidence?

A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery

P Whiting, R Gupta, J Burch, RE Mujica Mota, K Wright, A Marson, U Weishmann, A Haycox, J Kleijnen and C Forbes

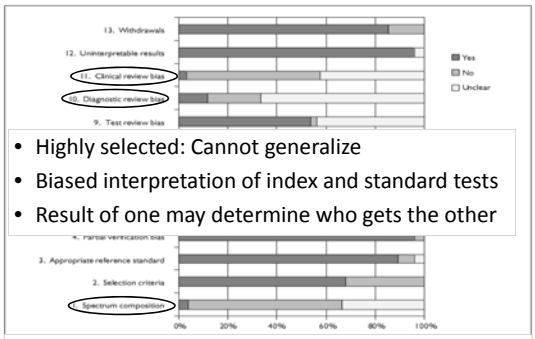
Health Technology Assessment 2006; Vol. 10: No. 4

- SPECT 39 studies
- MRI 30 studies
- PET 18 studies
- SISCOM 7 studies
- MRS 6 studies
- CT 5 studies

Localization by:
- -Ictal/Interictal EEG
- -Resection site
- -MRI
- -Combination

- Outcome 32 studies

Quality of Studies About Accuracy



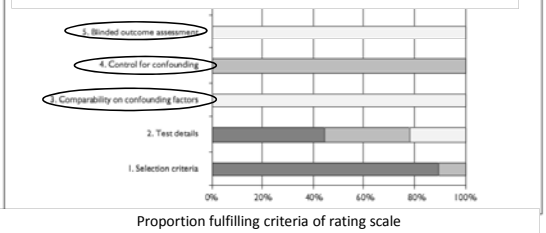
- Highly selected: Cannot generalize
- Biased interpretation of index and standard tests
- Result of one may determine who gets the other

Proportion fulfilling criteria of QUADAS rating scale

Whiting etal, HTA 2006

Quality of Studies Predicting Outcome

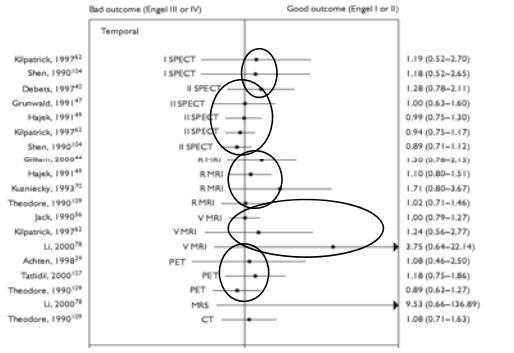
- Lowest level of evidence
- Cannot support recommendations for practice
- Small samples



Proportion fulfilling criteria of rating scale

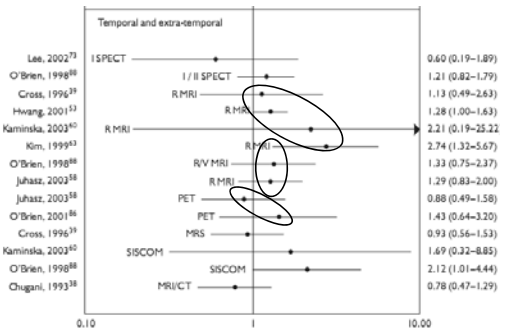
Whiting etal, HTA 2006

Test vs Outcome – Temporal



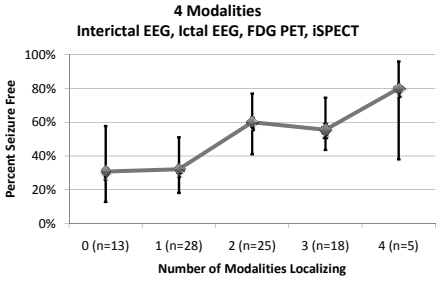
Whiting et al, HTA 2006

Test vs Outcome – Temporal Extratemporal



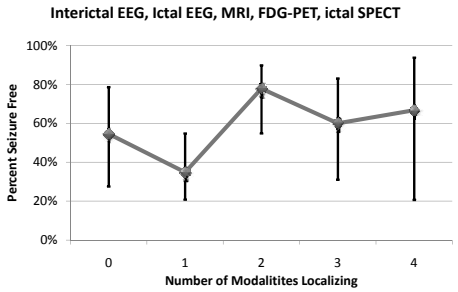
Whiting etal, HTA 2006

Surgical Outcome and Prognostic Factors of Cryptogenic Neocortical Epilepsy



Lee et al, Ann Neurol 2005

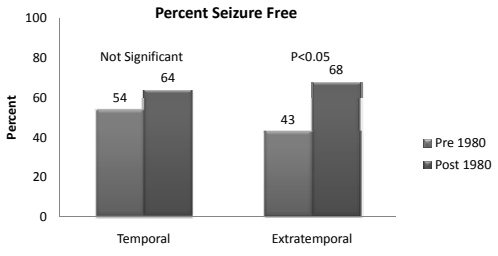
Frontal lobe epilepsy: Clinical characteristics, surgical outcomes and diagnostic modalities



Lee et al, Seizure 2008

Do outcomes improve as technology improves?

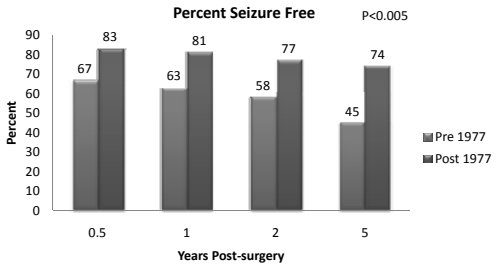
Long Term Outcome Temporal-Extratemporal



Tellez et al, Brain 2005

Improved outcomes in pediatric epilepsy surgery

The UCLA experience, 1986–2008



Hemb et al, Neurology 2010

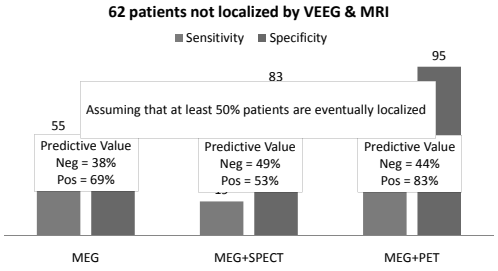
Improved Outcome Over Time

- More high end imaging (fMRI, PET, MSI)
- **But**
  - Larger surgery even if deficit, more complete resection
  - Different patients, fewer non-specific path
  - Fewer discontinued AEDs post op

How do we move forward?

- Good Quality Correlation analyses
  - New technology vs standard
  - Seizure localization
  - Outcome
- Randomized Controlled Trials
  - Decision making with and without new technology
  - Compare outcomes

Prediction of Engel I Outcome



Knowlton et al, Ann Neurol 2008

Conclusions

- We have done a poor job at assessing the incremental yield of new technologies
- **No Support for Full-Dress**: Evidence is poor, heterogeneous, difficult to apply
- Shoestring approach yields usual results (60% seizure free) in selected patients
- Be critical –Not all patients need all tests