Appendices e-1 through e-7

Appendix e-1: Mission Statement of GDS

The mission of the GDS is to prioritize, develop, and publish evidence-based guidelines related to the diagnosis, treatment, and prognosis of neurological disorders.

The GDS is committed to using the most rigorous methods available within our budget, in collaboration with other available AAN resources, to most efficiently accomplish this mission.

Appendix e-2: 2011–2013 Guideline Development Subcommittee (GDS) Members

John D. England, MD, FAAN (Chair); Cynthia Harden, MD (Vice-Chair); Melissa Armstrong, MD; Eric Ashman, MD; Misha-Miroslav Backonja, MD; Richard L. Barbano, MD, PhD, FAAN; Diane Donley, MD; Terry Fife, MD, FAAN; David Gloss, MD; John J. Halperin, MD, FAAN; Cheryl Jaigobin, MD; Andres M. Kanner, MD; Jason Lazarou, MD; Steven R. Messé, MD, FAAN; David Michelson, MD; Pushpa Narayanaswami, MD, MBBS; Anne Louise Oaklander, MD, PhD, FAAN; Tamara Pringsheim, MD; Alexander Rae-Grant, MD; Michael Shevell, MD, FAAN; Theresa A. Zesiewicz, MD, FAAN; Jonathan P. Hosey, MD, FAAN (Ex-Officio); Stephen Ashwal, MD, FAAN (Ex-Officio); Deborah Hirtz, MD, FAAN (Ex-Officio)

Appendix e-3: EMBASE Search Strategy

Database: EMBASE <1980 to 2007 Week 22>
Search Strategy:
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1 "seizure, epilepsy and convulsion"/ or exp epilepsy/ (68803)
2 mood disorder/ or affective neurosis/ or affective psychosis/ or blunted affect/ or major affective disorder/ or minor affective disorder/ or schizoaffective psychosis/ (19815)
3 exp Depression/ (130200)
4 (epileps: or depression or depressive disorder? or mood disorder?).mp. (241632)
5 or/1-4 (271536)
6 vagus nerve stimulation/ (3130)
7 (vagus nerve stimulat$4 or vagus neuro stimulat$4).mp. (3287)
8 cohort analysis/ or meta analysis/ (71823)
9 follow up/ (224221)
10 case control study/ or longitudinal study/ or prospective study/ or retrospective study/ or randomized controlled trial/ (278323)
11 case study/ (4801)
12 n=1:.ab. (38330)
13 and/11-12 (14)
14 "Review"/ (809874)
15 (randomi?ed control$3 trial? or cohort: or case control: or case series or review? or meta-analys?s or metanalys?s or metaanalys?s).mp. (1286411)
16 or/8-10,13-14,15 (1534416)
17 or/6,7 (3287)
18 and/5,17 (831)
19 limit 18 to (human and english language and yr="1999 - 2007" and "review") (181)
20 and/16,18 (370)
21 limit 20 to (human and english language and yr="1999 - 2007") (310)

Appendix e-4: Medline Search Strategy

Database: Ovid MEDLINE(R) <1996 to May Week 4 2007>
Search Strategy:
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1 exp epilepsy/ (36274)
2 vagus nerve stimulat:.mp. (465)
3 exp Electric Stimulation Therapy/ (11746)
4 exp vagus nerve/ (5689)
5 and/3-4 (491)
6 vagus neuro stimulat:.mp. (0)
7 or/2,5 (651)
8 Depression/ (20485)
9 exp depressive disorder/ (27123)
10 mood disorders/ or affective disorders, psychotic/ or bipolar disorder/ or cyclothymic disorder/ (12752)
11 and/1,7 (405)
12 or/8-10 (56355)
13 and/7,12 (114)
14 or/11,13 (494)
15 limit 14 to (humans and english language and systematic reviews and yr="1999 - 2007") (7)
16 limit 14 to (humans and english language and yr="1999 - 2007" and (meta analysis or practice guideline or randomized controlled trial or "review")) (148)
17 exp case-control studies/ or exp cohort studies/ or randomized controlled trials/ (583879)
18 (randomi?ed control$3 trial? or cohort: or case control: or review? or meta-analys?s or metanalys?s or metaanalys?s).mp. (1176180)
19 case series.mp. (10625)
20 n=1:.mp. (31970)
21 and/19-20 (72)
22 or/17-18,21 (1490658)
23 and/14,22 (273)
24 limit 23 to (humans and english language and yr="1999 - 2007") (235)
25 or/15-16,24 (235)
26 from 25 keep 1-235 (235)

Appendix e-5: Web of Science Search Strategy

# 11	32	#9 OR #7 Refined by: Languages=(ENGLISH) AND Document Type=(ARTICLE OR REVIEW) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 10	51	#9 OR #7 *Databases=SCI-EXPANDED Timespan=1997-1998*
# 9	8	#8 AND #6 *Databases=SCI-EXPANDED Timespan=1997-1998*
# 8	13,366	Topic=(depression OR depressive disorder* OR mood disorder* OR psychotic affective disorder* OR bipolar disorder* OR cyclothymic disorder* OR seasonal affective disorder*) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 7	44	#6 AND #1 *Databases=SCI-EXPANDED Timespan=1997-1998*
# 6	338	#5 OR #4 OR #3 OR #2 *Databases=SCI-EXPANDED Timespan=1997-1998*
# 5	3	Topic=(vagus neuro stimulat*) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 4	5	Topic=(vagal neuro stimulat*) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 3	234	Topic=(vagal nerve stimulat*) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 2	230	Topic=(vagus nerve stimulat*) *Databases=SCI-EXPANDED Timespan=1997-1998*
# 1	7,408	Topic=(seizure* OR epileps*) *Databases=SCI-EXPANDED Timespan=1997-1998*

Appendix e-6: Classification of Evidence for Therapeutic Interventions

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

The following are also required:

a. concealed allocation

b. primary outcome(s) clearly defined

c. exclusion/inclusion criteria clearly defined

d. adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.

e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:

1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.

2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).

3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.

4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized, controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b-e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.**

Class IV: Studies not meeting Class I, II, or III criteria, including consensus or expert opinion.

* Note that numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Appendix e-7: Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an “A” recommendation if 1) all criteria are met, and 2) the magnitude of effect is large (relative rate improved outcome > 5 and the lower limit of the confidence interval is > 2).