

## **Appendices e-4 through e-7**

### **Appendix e-4: Exclusion and inclusion criteria for article selection**

#### *Exclusion criteria*

Exclusion criteria comprise the following:

- Letters and case reports
- Non–English-language studies.
- Animal studies
- Pharmacodynamic/pharmacokinetic studies
- Studies dealing primarily with patients with established or chronic epilepsy
- Studies dealing primarily with acute provoked seizures

#### *Inclusion criteria*

- Study designs: observational (prospective, retrospective, and cross-sectional), or interventional (randomized, controlled trials [RCTs], nonrandomized, controlled trials [nRCTs], and uncontrolled case series [UCS])
- At least 10 patients, adults, with a first seizure, a first presentation with epilepsy or seizures, or a first diagnosis of epilepsy
- Patients should be over the age of 18 or the study should include a substantial proportion of subjects over the age of 18
- Studies reported in English only
- Studies dealing primarily with apparent unprovoked first seizures

## **Appendix e-5: Classification of evidence schemes**

### *A. Classification of therapeutic evidence*

**Class I.** Randomized controlled clinical trial (RCT) in a representative population. Masked or objective outcome assessment. Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences. Also required: Concealed allocation. Primary outcomes clearly defined. Exclusion/inclusion criteria clearly defined. Adequate accounting for dropouts.

**Class II.** Cohort study meeting criteria for Class I or a RCT that lacks one or two of those other criteria. All relevant baseline characteristics are present and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. Masked or objective outcome assessment.

**Class III.** Controlled studies (including well-defined natural history controls or patients serving as their own controls). A description of major confounding differences between treatment groups that could affect outcome. Outcome assessment masked, objective or preformed by someone who is not a member of the treatment team.

**Class IV.** Did not include patients with the disease. Did not include patients receiving different interventions. Undefined or unaccepted interventions or outcome measures. No measures of effectiveness or statistical precision present or calculable.

### *B. Classification of prognostic evidence*

**Class I.** Cohort survey with prospective data collection. Includes a spectrum of persons at risk for developing the outcome. Outcome measurement is objective or determined without knowledge of risk for developing the outcome. Also required: a. Inclusion criteria defined b. At least 80% of enrolled subjects have both the risk factor and outcome measured.

**Class II.** Cohort study with retrospective data collection or case-controlled study. Study meets criteria a and b (see Class I). Includes a broad spectrum of persons with and without the risk factor and the outcome. The presence of the risk factor and outcome are determined objectively or without knowledge of one another.

**Class III.** Cohort or case control study. Narrow spectrum of persons with or without the disease. The presence of the risk factor and outcome are determined objectively or without knowledge of the other or by different investigators.

**Class IV.** Did not include patients at risk for the outcome. Did not include patients with and without the risk factor. Undefined or unaccepted measures of risk factor or outcomes. No measures of association or statistical precision presented or calculable.

## **Appendix e-6: 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, 2) the magnitude of effect is large (relative rate improved outcome  $> 5$  and the lower limit of the confidence interval is  $> 2$ ).

## **Appendix e-7: All accepted articles**

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