Developing EPHT Modules for Neurodegenerative Diseases: Opportunities and Challenges

Mark A. Werner, Ph.D.

Wisconsin Division of Public Health

Presentation Objectives

○ Describe these conditions and the basis for interest in environmental etiologies

○ Characterize the features of WI mortality data for ALS

○ Discuss progress to date on establishing EPHT modules for MS and ALS in Wisconsin

Collaborators

- WI DPH: Katrina Boyd, Marni Bekkedal, Kristen Malecki, Henry Anderson;

- UW SMPH: Ben Brooks, Marty Kanarek

- Jeremy Otte, NMSS WI

Multiple Sclerosis

- Autoimmune disease that primarily affects the central nervous system
- Chief feature is loss of myelin leading to sclerosis
- Symptoms stem from impaired neural impulse conduction

Symptoms of MS

- Primary symptoms:
  - Impaired balance, coordination, ability to walk
  - Reduced visual and cognitive function
  - Impaired bowel and bladder control
  - Chronic neck, head and body pain
- Secondary symptoms
  - Headache, hearing loss, tremor, difficulty swallowing.
- Relapse and remission are common

Amyotrophic Lateral Sclerosis

- A progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord

- Degeneration of motor neurons leads to loss of voluntary motor function and virtual paralysis

- Mean survival time: 3-5 years

	MS	ALS
New Annual Diagnoses (US)	10,000	5600
Gender (M/F)	30/70	60/40
Mean Age of Onset	30-35	55

MS and the Environment

- More frequently diagnosed in temperate climates than in subtropical or tropical climates
  - Orkney Islands (Scotland): 250 per 100,000
  - Japan: 2 per 100,000
- People born in high-prevalence areas who move to low-prevalence areas have reduced prevalence (e.g., if before age 15)
- Evidence for genetic and viral etiologies

ALS and the Environment

- Excesses observed among Gulf War veterans
  - Recognized as 'service-related illness' by VA
  - 40 cases among 700,000 veterans
- High rates of ALS-like syndrome linked to cyanobacterial neurotoxin exposure in Guam
- ALS-like syndrome induced in rabbit model upon injection of aluminum

MS and ALS
Barriers to Surveillance

- Low incidence and prevalence
- Relationship between diagnosis and date of onset is variable
- Differences in diagnostic criteria among physicians
- Lack of well-developed disease registries

Registries

○ Used to aggregate case data for disease surveillance and to obtain patients for clinical trials

○ Examples:

- NARCOMS (North American Research Committee On Multiple Sclerosis) Registry
- VA ALS Registry

MS, ALS and EPHT

- Standardized data collection across states needed to assemble sufficient case numbers for meaningful surveillance

- EPHT networks = platforms to explore relationships between new and emerging registry data and environmental data

ALS Mortality in WI

- Goals:
  - Summarize how ALS deaths were classified and characterize utility of available geographically-specific data
- Review of records from 1989-1998
- Records included with ALS as underlying cause of death (UCOD) or primary cause of death

ALS Mortality in WI

- Total of 1047 deaths recorded for which ALS was UCOD or primary cause of death (ICD-9 = 335.2)
  - UCOD
    - ALS = 508
    - Respiratory Arrest = 229
    - Pneumonia = 65
   - Inhalation of Food or Vomitus = 35
    - Cardiac Arrest = 31

ALS Mortality in WI

| Place of Death	Number	Percent
Primary Care Hospital	389	37.2
Nursing Home	*280*	*26.7*
Other (private residence, etc.)	378	36.1

ALS Mortality in WI

- Use of administrative mortality data offers some insight into coding and geographical case distribution
- Debilitating nature of condition decreases the ability to use death address as a useful site for assessing pre-diagnosis exposure

Case Definitions
Diagnostic Criteria

○ Until recently, both MS and ALS diagnoses were made on the basis of widely-variable criteria

○ El Escorial criteria have emerged for ALS

○ MS
- Three primary criteria:
  - CSF findings
  - MRI
  - Clinical observation

A2

Did you have a lumbar puncture?

Yes → Was it abnormal consistent with MS?

Yes: A A1 A3 A4 A5

No: A A1 A3 A4 A5 B

No: A A1 A4 A5

MacDonald Criteria

Poser Criteria

Schumacher Criteria

B

El Escorial Criteria - 1994

B2

Did you have an electromyogram or EMG?

Yes

No

Stop

Was it abnormal consistent with motor neuron disease or ALS?

Yes

No

Stop

Bulbar

Arms

Legs

Yes | No

Yes | No

Yes | No
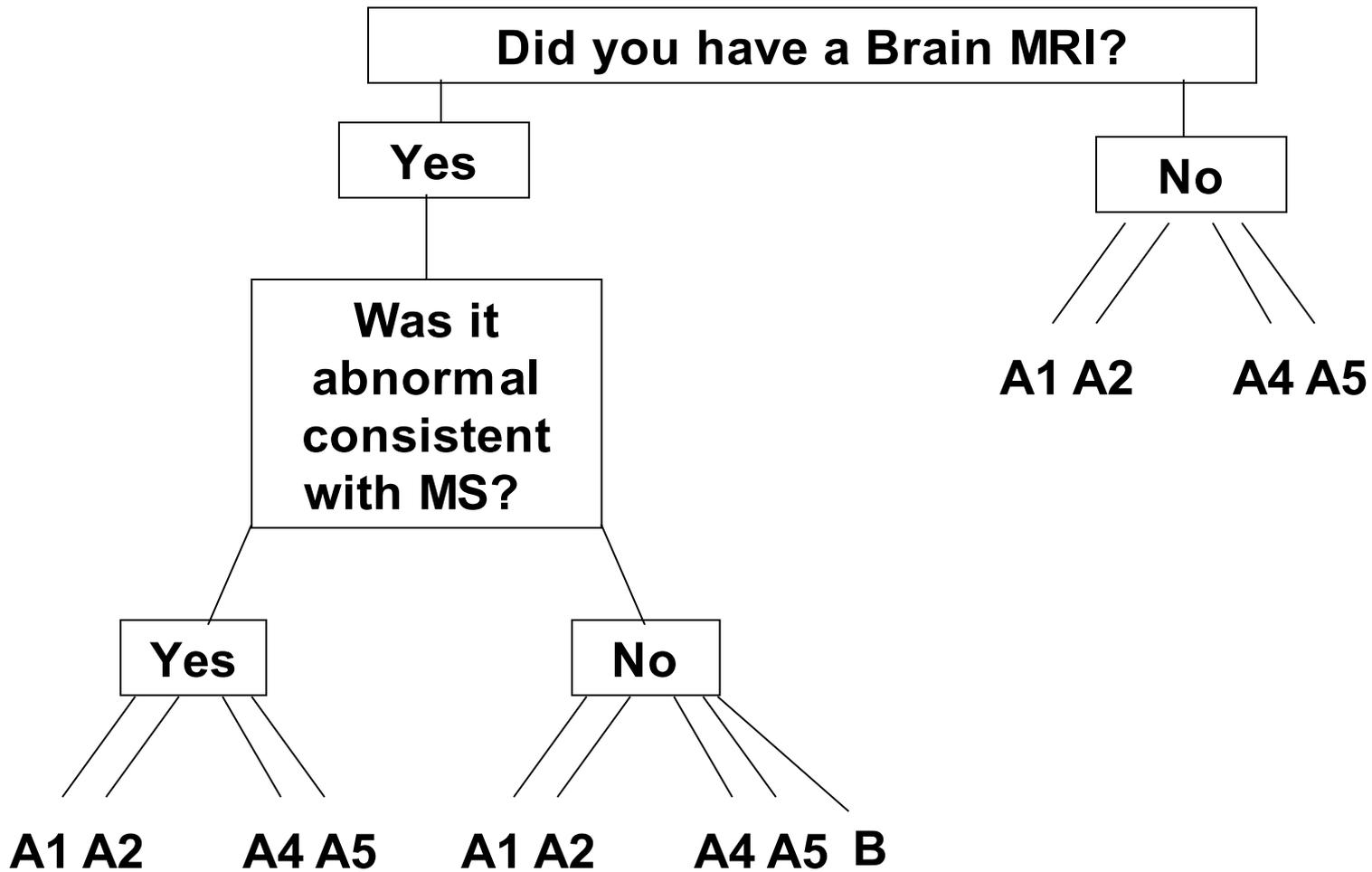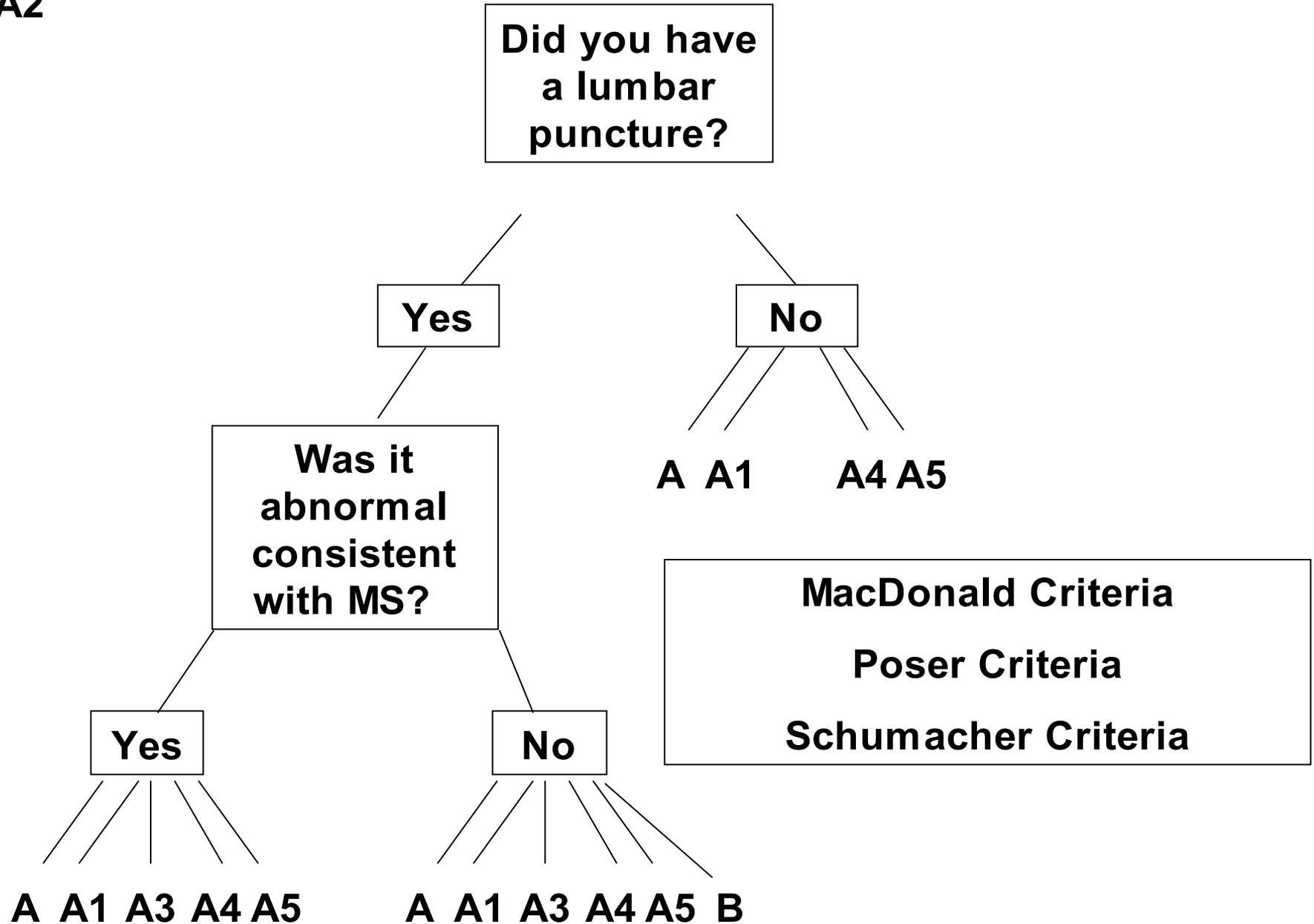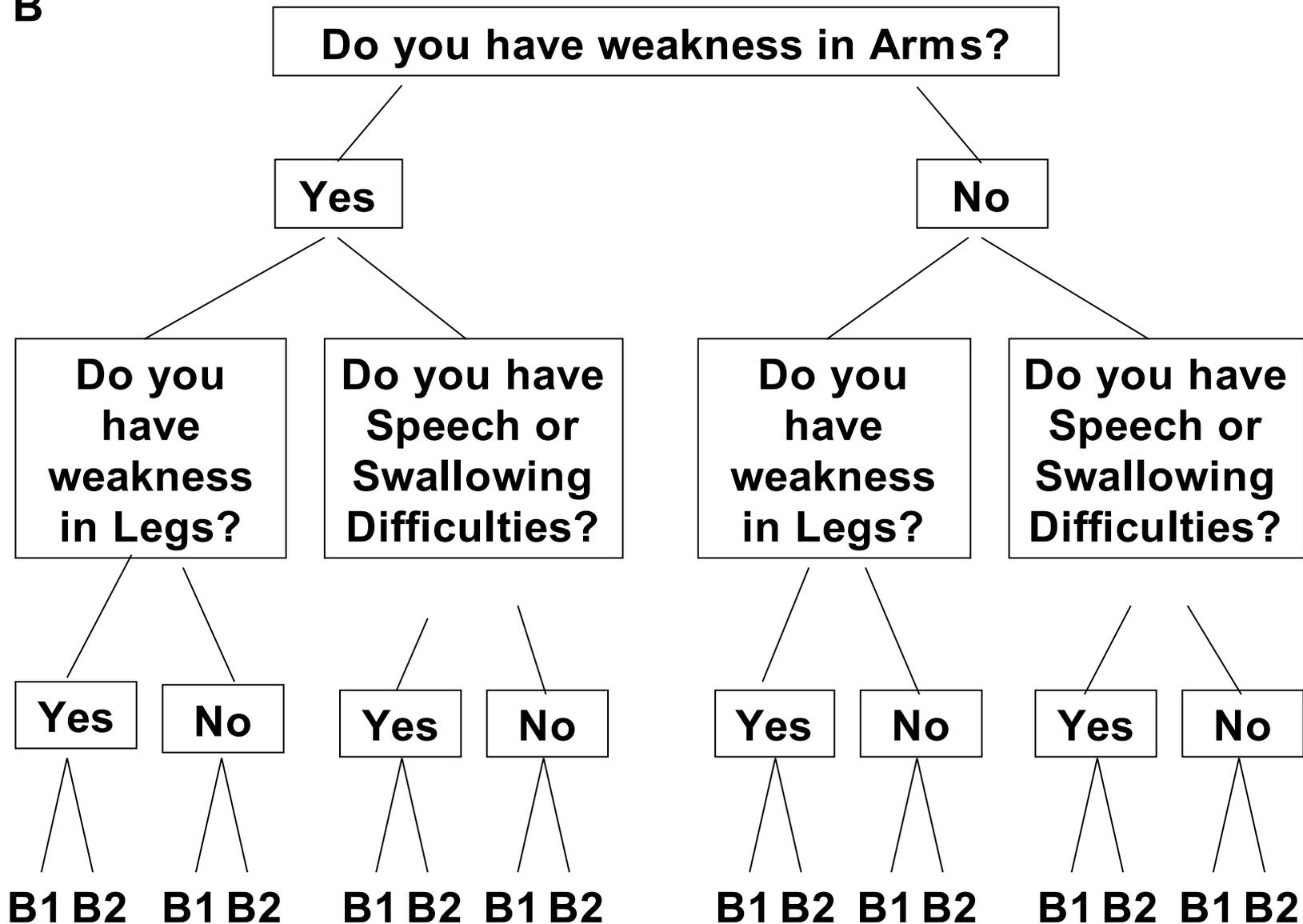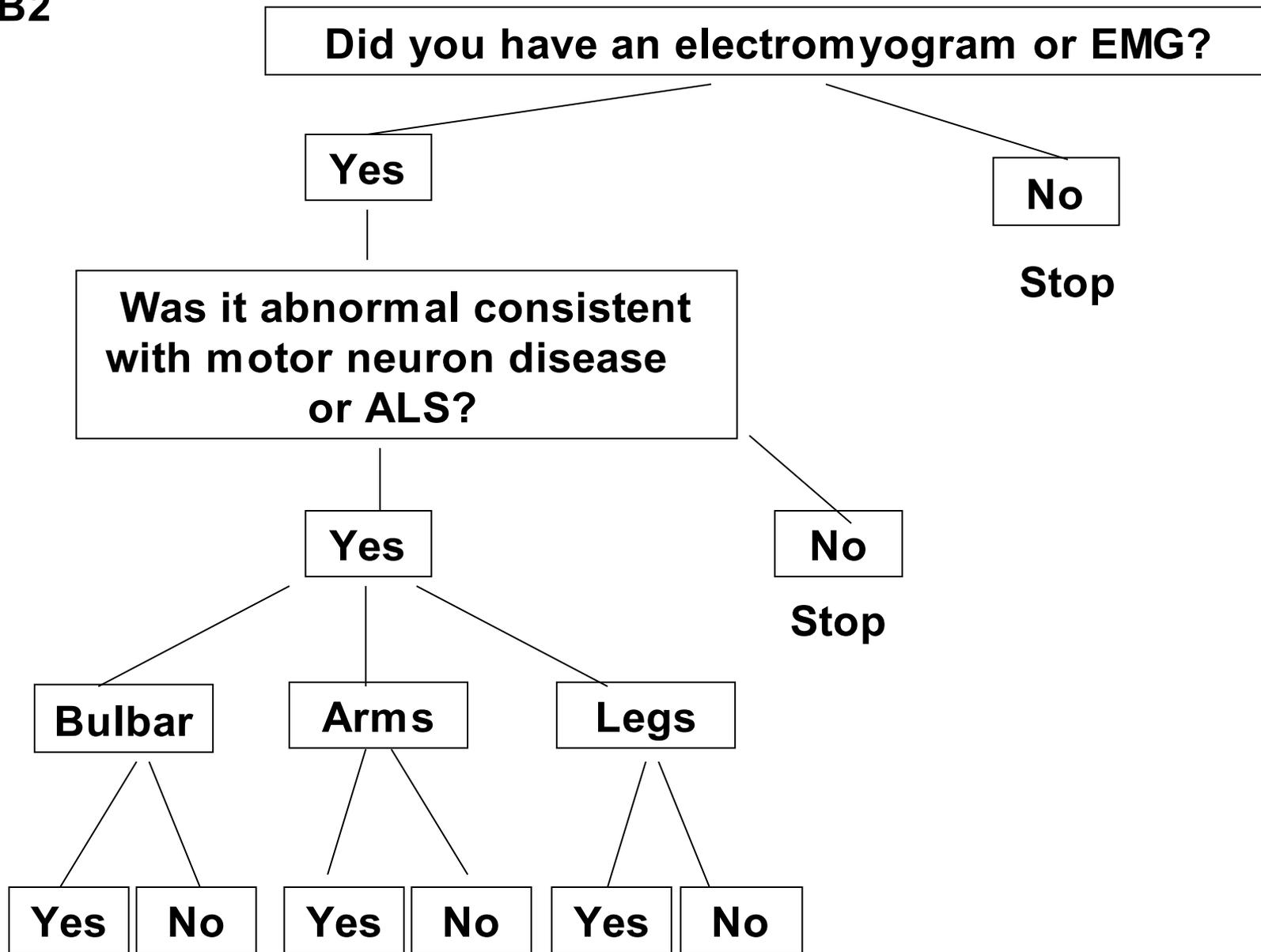
El Escorial Criteria - 1994

Current Approach

- Obtain case information from advocacy group records
  - Develop approach to confirm diagnosis in subset of patient population
- For ALS, consider supplementation with clinic-based case ascertainment outside Milwaukee service area
- Describe risk profile based on statewide environmental hazard data

Summary

- Administrative data can be informative, but currently-available data are insufficient as a sole basis for useful EPHT network content

- Lack of well-developed disease registries hampers ability to assess surveillance

- National MS/ALS surveillance plan under development

Do you have any abnormal sensations, e.g. aching, numbness, tingling, burning?

Do you have any abnormal disorder of vision, e.g. double vision, loss of vision in one eye?

Do you have any difficulty controlling your bladder or bowel function?

Do you have any difficulty drinking a glass of water or writing due to a tremor?

Do you have any trouble with speech or swallowing?

Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
/	I	/	I	/	I	/	I	I	**Stop**
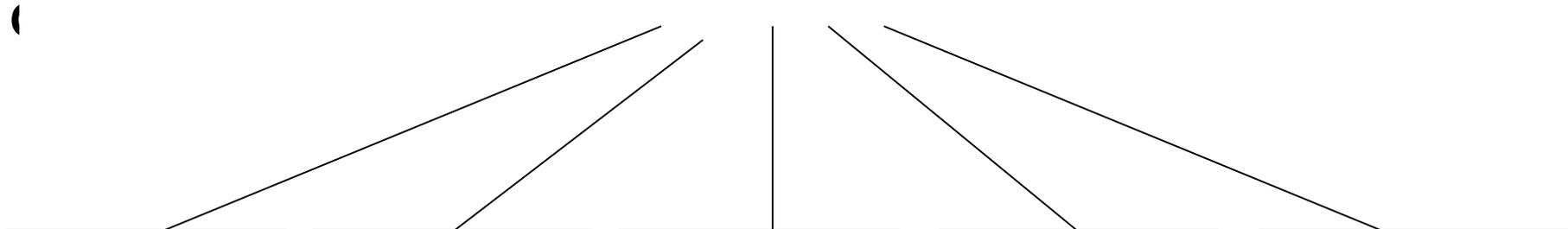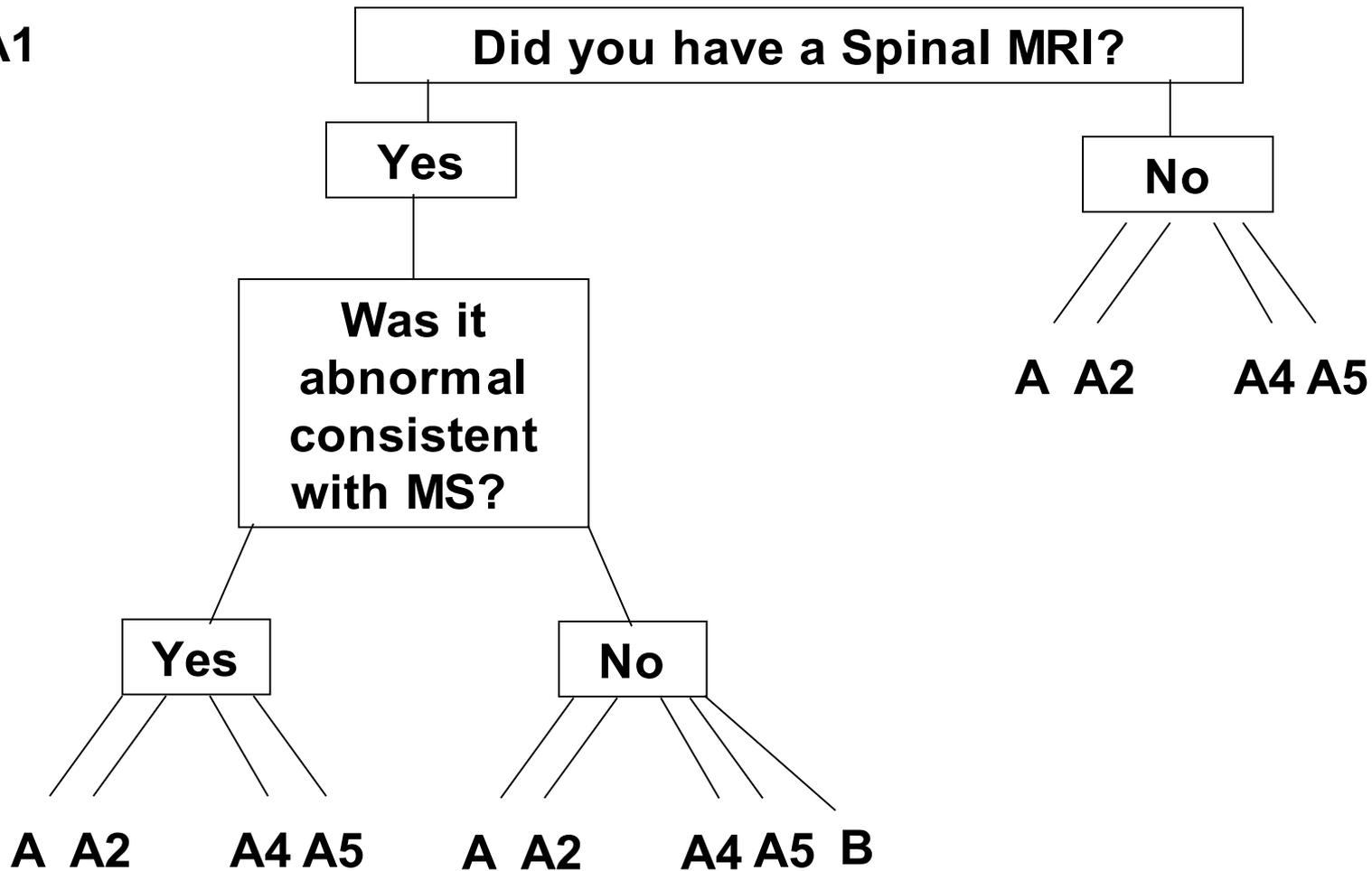
A3

Was lumbar puncture positive for elevated CSF IgG Index or immunoglobulin?	Was lumbar puncture positive for elevated CSF Oligoclonal Bands?	Was lumbar puncture positive for elevated CSF Myelin Basic Protein?
Yes No	Yes No	Yes No

MacDonald Criteria

Poser Criteria

Schumacher Criteria

A4

Did you have a special eye examination
named visual evoked response?

Yes

No

Was it
abnormal
consistent
with MS?

A   A1 A2   A5

Yes

No

MacDonald Criteria

Poser Criteria

Schumacher Criteria
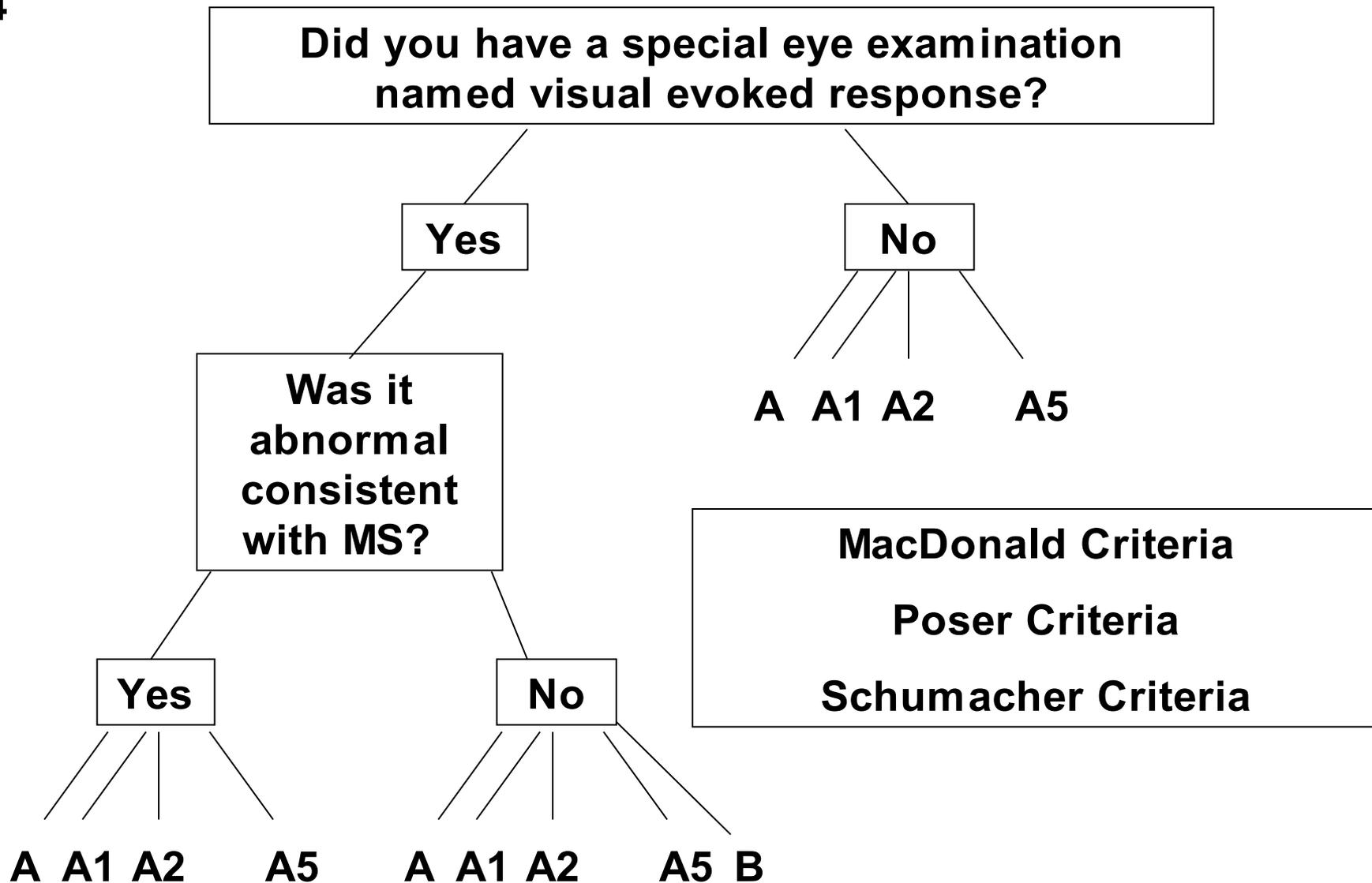
A A1 A2   A5

A A1 A2   A5 B

A5

Did you have a electrical stimulation examination of your arms and/or legs named somatosensory evoked response?

Yes

No

Was it abnormal consistent with MS?

A A1 A2   A4

MacDonald Criteria

Poser Criteria

Schumacher Criteria

Yes

No

A A1 A2   A4

A A1 A2   A4 B

B1

Did you have increased reflexes [hyperreflexia] or increased muscle stiffness[spasticity] or a Babinksi sign [upgoing toe]?

Yes

No

Were any of these signs consistent with the diagnosis of motor neuron disease or ALS?

Yes

No

Stop

Bulbar

Arms

Legs

Yes   No

Yes   No

Yes   No

El Escorial Criteria - 1994