

**Supplemental Table 1. Studies reporting the incidence of seizure disorders (epilepsy) in multiple sclerosis**

| Study (Year)                  | Region/ Sub-Region                | Source/ Population  | Prevalence Day/Period                       | Diagnostic Criteria: MS/ Established By     | Diagnostic Criteria: Epilepsy/ Established By | Crude Overall Incidence (95%CI)                             | Age-Standardized Overall Incidence (95%CI) | Crude Incidence (95%CI) |         | Standardized Incidence (95%CI) |         | Quality Score |
|-------------------------------|-----------------------------------|---|---|---|---|---|--|-------------------------|---------|--------------------------------|---------|---------------|
|                               |                                   |   |   |   |   |   |  | Males                   | Females | Males                          | Females |               |
| Allen <sup>13</sup> (2013)    | England                           | HES and ORLS/ Hospital admission or record of day case care for MS                  | ORLS (1963-1998)<br><br>HES (1999-Feb 2011) | ICD-10 G35, ICD-7 340, ICD-8 340, ICD-9 340 | ICD10 G40–G41, ICD 7-9 345                    | ORLS<br>62/3,913 = 1.58%<br><br>HES<br>2,580/85,772 = 3.01% | NR   | NR                      | NR      | NR                             | NR      | 4/8           |
| Catenoix <sup>15</sup> (2011) | France/ Lyon City and Rhone-Alpes | EDMUS Lyon MS Cohort, Lyon Neurology Clinic/ all MS patients examined at least once | 1976-2007                                   | Neurologist diagnosed: Poser                | EDMUS database/recorded as a symptom of MS    | Epileptic seizure after MS onset<br>69/5,041 = 1.83%        | NR   | NR                      | NR      | NR                             | NR      | 6/8           |
| Drake <sup>18</sup> (1961)    | United States/ California         | Department of Neurology,  | NR  | NR  | Clinical observation                          | Seizures<br>13/289 = 4.50%                                  | NR   | NR                      | NR      | NR                             | NR      | 0/9           |

|                                  |                    |   |                   |                                      |   |   |    |    |    |    |    |     |
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|                                  |                    | University of California School of Medicine                     |                   |                                      |   |   |    |    |    |    |    |     |
| Eriksson <sup>21</sup> (2002)    | Sweden/ Gothenburg | MS incidence cohort, clinically definite or probable MS         | 1950-1989         | Neurologist diagnosed: Poser         | Patient chart review and EEG when available       | Epilepsy 349 ± 153 /100,000/year              | NR | NR | NR | NR | NR | 7/8 |
| Etemadi far <sup>23</sup> (2012) | Iran/ Isfahan      | Isfahan MS Society/ Pediatric onset MS (symptoms ≤16 years old) | Apr 2003-Jul 2010 | Neurologist diagnosed: McDonald 2005 | Clinical record review/ILAE criteria, EEG and MRI | Epilepsy after MS onset 7/117 = 5.98%         | NR | NR | NR | NR | NR | 7/8 |
| Etemadi far <sup>22</sup> (2013) |                    | Adult onset MS  |                   |                                      |   | Adult MS Epilepsy at MS onset 5/3,522 = 0.14% |    |    |    |    |    |     |
|                                  |                    |   |                   |                                      |   | Epilepsy after MS onset 64/3,522 = 1.82%      |    |    |    |    |    |     |
| Ghezzi <sup>25</sup>             | Italy/             | MS centre/  | Jan 1, 1982-      | Neurologist                          | ILAE 1981   | Epilepsy                                      | NR | NR | NR | NR | NR | 7/8 |

|   |   |   |                   |  |  |   |                             |    |    |    |    |    |     |
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| (1990)  | Milano  | all patients with MS onset $\geq 1$   | Jun 30, 1988      | diagnosed: MacAlpine                         | criteria, EEG, cranial CT scan and MRI in some cases   | after MS onset<br>$23/2,353 = 0.98\%$                   |                             |    |    |    |    |    |     |
| Kinnunen <sup>28</sup><br>(1986)                | Finland/<br>Uusimaa                                 | All MS patients in the province of Uusimaa  | Jan 1, 1979       | Neurologist diagnosed: Schumacher            | ILAE criteria, EEG and CSF   | Epilepsy after MS onset<br>$8/599 = 1.34\%$             | NR                          | NR | NR | NR | NR | NR | 8/8 |
| Martinez -<br>Lapiscina <sup>30</sup><br>(2013) | Spain/<br>Pamplona<br>City and<br>Navarra<br>Region | MS Clinic Complejo Hospitalario de Navarra/electronic database                        | Jan 2010-May 2010 | Neurologist diagnosed: McDonald 2001 or 2005 | Medical chart review/ ILAE criteria, EEG and MRI<br><br>Epileptic seizures occurring at any point after MS onset | Epileptic seizures after MS onset<br>$13/428 = 3.04\%$  | NR                          | NR | NR | NR | NR | NR | 5/8 |
| Nicoletti <sup>5</sup> (2003)                   | Italy/<br>Catania                                   | Patients identified from previous epidemiological study determining MS prevalence and | 1975-1994         | Neurologist diagnosed: Poser                 | ILAE 1993 criteria, and treated with antiepileptic drugs   | Epilepsy<br>$285/100,000$ person-year at risk (119-684) | Epilepsy<br>$147.8/100,000$ | NR | NR | NR | NR | NR | 8/8 |

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|   |  | incidence/<br>MS Centers,<br>IMSA,<br>private<br>neurologist<br>and family<br>physicians |                             |                                 |   |   |   |   |  |    |    |     |
| Nyquist <sup>3</sup><br><sup>4</sup> (2001) | United States/<br>Minnesota<br>(Olmsted<br>County) | Mayo Clinic  | Jan 1, 1990-<br>Jan 1, 1998 | Neurologist<br>diagnosed: Poser | Medical Record<br>Review/<br>ILAE<br>classification, EEG<br>and MRI | Epileptic<br>seizures after<br>MS diagnosis<br>37/5,715 =<br>0.65%<br><br>Epileptic<br>seizures after<br>first signs of<br>MS but before<br>diagnosis<br>6/5,715 =<br>0.10% | NR  | NR  | NR   | NR | NR | 7/8 |
| Nyquist <sup>3</sup><br><sup>3</sup> (2002) | United States/<br>Minnesota<br>(Olmsted<br>County) | Incident<br>cases<br>identified<br>from<br>Rochester<br>Epidemiolo<br>gy                 | 1935-1991                   | Neurologist<br>diagnosed: Poser | Medical Record<br>Review/<br>ILAE 1993<br>classification            | Epilepsy after<br>definite MS<br>diagnosis<br>5/208 = 2.40%   | Epilepsy after<br>definite MS<br>diagnosis<br>61/100,000<br>person years<br>(7-114) | Epilep<br>sy<br>after<br>definit<br>e MS<br>diagno<br>sis | Epilepsy<br>after<br>definite<br>MS<br>diagnosis<br>4/144 =<br>2.78% | NR | NR | 8/8 |

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|---|------------------|---|----------------------|--|---|---|--|-----------------|----|----|----|----|-----|
|   |                  | Project,<br>Mayo Clinic   |                      |  |   | Epilepsy after<br>first MS<br>symptoms<br>8/208 = 3.85%   | Epilepsy after<br>first MS<br>symptoms<br>80/100,000<br>person years<br>(24-135) | 1/64 =<br>1.56% |    |    |    |    |     |
| Olafsson<br><sup>35</sup><br>(1999)     | Iceland          | Neurology<br>clinic/medic<br>al records   | 1965-1989            | Neurologist<br>diagnosed: Poser            | Medical Record<br>Review/<br>ILAE<br>classification   | Epilepsy<br>After MS onset<br>4/188 = 2.13%<br><br>Epilepsy<br>After MS<br>diagnosis<br>3/188 = 1.60% | NR   | NR              | NR | NR | NR | NR | 7/8 |
| Shayan<br>nejad <sup>36</sup><br>(2013) | Iran/<br>Isfahan | MS clinic of<br>the Kashani<br>hospital/ all<br>patients with<br>definite MS<br>diagnosis | Mar 2007-Jun<br>2011 | Neurologist<br>diagnosed:<br>McDonald 2005 | Medical Record<br>Review/<br>ILAE<br>classification,<br>EEG, MRI and<br>antiepileptic drug<br>use | Seizures after<br>onset of MS<br>22/920 = 2.39%   | NR   | NR              | NR | NR | NR | NR | 6/8 |
| Shiraishi<br><sup>37</sup> (2005)       | Japan/<br>Kyoto  | Department<br>of<br>Neurology,<br>Utano<br>National<br>Hospital/                          | 1979-2001            | Neurologist<br>diagnosed:<br>McDonald 2001 | Medical Record<br>Review  | Symptomatic<br>Epilepsy during<br>course of MS<br>9/27 = 33.3%  | NR   | NR              | NR | NR | NR | NR | 4/8 |

|                                 |                  |  |  |                                      |   |   |    |  |  |    |    |     |
|---------------------------------|------------------|--|--|--------------------------------------|---|---|----|--|--|----|----|-----|
|                                 |                  | MS onset ≤ 15 years  |  |                                      |   |   |    |  |  |    |    |     |
| Sokic <sup>38</sup><br>(2001)   | Serbia           | Institute of Neurology, Belgrade School of Medicine/ consecutive hospitalized patients | 1996-1997  | Neurologist diagnosed: Poser         | Medical Record Review/ ILAE 1981 classification, EEG and MRI<br><br>Chronic Epilepsy/ Spontaneously repeating seizures occurring regardless of clinical phase of MS | Chronic Epilepsy After MS onset<br>8/268 = 2.99%<br><br>Seizures or epilepsy after MS onset<br>16/268 = 5.97% | NR | NR   | NR   | NR | NR | 6/8 |
| Striano <sup>39</sup><br>(2003) | Italy/<br>Naples | MS clinic  | Retrospectively from 1995-1997, prospectively from 1998-2002 | Neurologist diagnosed: McDonald 2001 | ILAE 1989 classification, EEG<br><br>Chronic epilepsy/ seizures in ≥ 2 different periods of time; a single cluster of seizures was considered a unique episode      | Chronic epilepsy after MS onset<br>10/270 = 3.70%   | NR | Chronic epilepsy after MS onset<br>1/50 = 2.0% | Chronic epilepsy after MS onset<br>9/220 = 4.09% | NR | NR | 4/8 |
| Uribe-San                       | Chile            | MS centre, Universidad   | 2009-2012  | Neurologist diagnosed:               | Medical Record Review/  | Epilepsy after MS onset   | NR | Epilepsy                                       | Epilepsy after                                   | NR | NR | 6/8 |

|                                |                           |  |           |   |   |   |    |                                   |  |    |    |     |
|--------------------------------|---------------------------|--|-----------|---|---|---|----|-----------------------------------|--|----|----|-----|
| Martin <sup>41</sup><br>(2014) |                           | Catolica of Chile/MS and CIS patients                                  |           | McDonald 2010                                 | ILAE 1981 classification, EEG and MRI                           | 9/280 = 3.21%<br><br>Epilepsy after onset (MS and CIS patients)<br>10/310 = 3.23% |    | after onset (MS and CIS patients) | onset (MS and CIS patients)<br>5/215 = 2.33% |    |    |     |
| Viveiros <sup>42</sup> (2010)  | Brazil/<br>Rio de Janeiro | SIAPEM database/all patients followed up at a private neurology clinic | 1997-2007 | Neurologist diagnosed: McDonald 2001 and 2005 | Medical Record Review/<br>ILAE 1989 classification, EEG and MRI | Epileptic seizures after MS onset<br>3/160 = 1.88%                                | NR | NR                                | NR   | NR | NR | 4/8 |

NR: Not Reported, HES: English National Hospital Episode Statistics, ORLS: Oxford Record Linkage Study, EDMUS: European Database for Multiple Sclerosis, ILAE: International League against Epilepsy, IMSS: Isfahan Multiple Sclerosis Society, EOMS: Early Onset Multiple Sclerosis, IMSA: Italian Multiple Sclerosis Association, SIAPEM: Brazilian Software Database for Multiple Sclerosis Research in Tropical Countries.