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Table e-1a. Quality assessment of cross-sectional studies

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| First author | Questions | | | | | | |
| Q1 | Q2 | Q3 | Q4 | Q1 | Q1 | Q2 |
| Sormani et al 12 | a\* | a\* | c | a\*\* | a\* | a\*\* | b |
| Ciampi et al e1 | a\* | a\* | c | a\*\* | a\* | c\* | b |
| Barzegar et al 14 | a\* | a\* | b | a\*\* | a\* | a\*\* | b |
| Montero-Escribano et al e2 | c | b | c | b\* | a\* | b\*\* | b |
| Safavi et al 13 | a\* | a\* | b | a\*\* | a\*\* | c\* | a\* |
| Crescenzo et al e3 | a\* | a\* | c | a\*\* | a\* | c\* | b |
| Moss et al e4 | a\* | a\* | b | a\*\* | a\*\* | c\* | a\* |
| Mantero et al e5 | c | b | c | b\* | a\*\* | c\* | a\* |
| Sahraian et al 16 | a\* | a\* | a\* | a\*\* | a\*\* | c\* | a\* |
| Álvarez et al 15 | a\* | a\* | c | a\*\* | a\* | a\*\* | b |
| Nesbitt et al e6 | a\* | a\* | c | c | N/A | c\* | b |
| Vogel et al e7 | a\* | a\* | b | a\*\* | a\*\* | c\* | a\* |
| Capasso et al e8 | a\* | a\* | c | b\* | a\*\* | a\*\* | a\* |

Table e-1b. Quality assessment of cohort studies

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First author | Questions | | | | | | | |
| Q1 | Q2 | Q3 | Q4 | Q1 | Q1 | Q2 | Q3 |
| Louapre et al 20 | a\* | c | a\* | b | a\* | a\* | a\* | a\* |
| Parrotta et al 19 | a\* | c | a\* | b | a\* | a\* | a\* | a\* |
| Loonstra et al 21 | b | c | a\* | b | a\* | a\* | a\* | a\* |
| Costa et al 23 | a\* | c | a\* | b | a\* | a\* | a\* | a\* |
| Chaudhry et al 22 | b | c | a\* | b | a\* | a\* | b | d |
| Evangelou et al 47 | a\* | c | a\* | a\* | a\*\* | a\* | a\* | a\* |
| Kovvuru et al 24 | a\* | c | a\* | b | a\* | a\* | b | d |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Table e2-a. Characteristics of original studies included in the investigation | | | | | | | | | | | | | | |
| First Author | Location | Date of first publication | Type of study | Confirmed/suspected | Positive PCR | Age,  Mean or median (SD or range) | Sex | Disease duration,  Mean or (SD or range) | EDSS,  Mean or median (SD or range) | Course of disease | DMTs | Comorbidity | Symptoms | Severity of COVID-19 |
| Louapre et al 20 | France | 6/26/2020 | Cohort | 347 | 146/191 | 44.60 (12.80) | F 249  M 98 | 13.50 (10.00) | 2.0  (0.0-9.5) | RRMS 276  SPMS 48  PPMS 17  CIS 6 | IFN 20  GA 33  RTX 17  OCR 38  Fingolimod 42  Natalizumab 57  DMF 35  TFL 33  Cladribine 3  Alemtuzumab 1  MMF 3  CP 1  MTX 1  No treatment 63 | Any comorbidity: 113  CVD 23  DM 16  Lung Diseases: 15  Obesity 24  Smoking 33 | Asthenia 290  Cough 266  Fever 260  Headache 180  Dyspnea 162  Anosmia/Ageusia 150  GI Symptoms: 88  Dizziness 54  Asymptomatic 2 | Hospitalized 73 (21.0)  Death 12 (3.5) |
| Parrotta et al 19 | USA | 07/09/2020 | Cohort | 76 (72 MS) | 37 | 44 .9 (15.2) | F 47  M 29 | 15.20 (10.70) | NR | RRMS 55  SPMS 15  PPMS 2  NMO 1  MOGAD 1  Neurosarcoidosis 1  CRION 1 | IFN 3  GA 6  RTX 18  OCR 16  Fingolimod 8  Natalizumab 4  DMF 4  Siponimod 2  IVIG 3  No treatment 12 | CAD 3  HTN 17  Malignancy 4  Smoking 2  Obesity 23  VTE 4  DM 8 | Fever 52  Cough 52  Fatigue 29  Dyspnea 24  Myalgia/arthralgia 20  Anosmia 17  Ageusia 15  Headache 16  Neurological worsening 16 | Hospitalized 15/72 (20.8)  Death 6/72 (8.3) |
| Parrotta et al 19# | USA | 07/09/2020 | Cohort | 9 | 4 | 19.44 (4.12) | F 7  M 2 | 6.11 (3.55) | NR | RRMS 9 | GA 1  RTX 4  OCR 2  Natalizumab 1  No treatment 1 | DM 2  Lung Diseases 1  Obesity 3 | NR | Hospitalized 2 (22.3)  Death 0 |
| Loonstra et al 21 | Netherlands | 7/14/2020 | Cohort | 86 | 37 | 45.50 (20-71) | F 60  M 26 | NR | 3.0 (0-8) | RRMS 69  SPMS 9  PPMS 5  Baló’s MS 1  Unknown 2 | IFN 5  GA 4  OCR 19  Fingolimod 15  Natalizumab 5  DMF 18  TFL 5  Alemtuzumab 1  IVIG 1  Stem cell 1  No treatment 12 | Any comorbidity: 23 | NR | Hospitalized 22 (25.6)  death 4 (4.6) |
| Costa el al 23 | Multicenter | 07/02/2020 | Cohort | 52 | 4 | NR | NR | NR | NR | NR | NR | NR | NR | Hospitalized 1 (2.0%)  Death 0 |
| Evangelou el al 47 | UK | 08/27/2020 | Cohort | 237 | 37 | NR | NR | NR | NR | NR | Interferon 11  GA 18  OCR 14  Fingolimod 15  Natalizumab 19  DMF 32  TFL 2  Cladribine 2  Alemtuzumab 5  No treatment 116 | NR | NR | Hospitalized 3 (1.3%)  Death 0 |
| Chaudhry el al 22 | USA | 09/19/2020 | Cohort | 40 | 40 | 52.0 (45.5-61) | F 24  M 16 | 12 (6.5-19) | NR | RRMS 30  Progressive 9 | Interferon 2  GA 3  OCR 12  Fingolimod 2  Natalizumab 2  DMF 6  TFL 3  Alemtuzumab 1  No treatment 8 | HTN 16  DM 9  Lung diseases 2  Smoking 6  HLP 7 | Fever 26  Cough 26  Dyspnea 20  Headache 7  Myalgia 14  Sore throat 4  Diarrhea 4  Altered Mental Status 4 | Hospitalized 19 (47.5%)  Death 4 (10%) |
| Kovvuru et al 24 | USA | 11/27/2020 | Cohort | 115 | NR | 52 (15.5) | F 83  M 32 | NR | NR | NR | DMF 12  OCR 15  Interferon beta-1a ≤10  Interferon beta-1b ≤10  GA ≤10  Fingolimod ≤10  TFL ≤10  Natalizumab ≤10  Alemtuzumab ≤10  Mitoxantrone ≤10 | NR | NR | Hospitalized 38 (33.0%)  Death 5 (4.3%) |
| Sormani et al 12 | Italy | 4/30/2020 | Cross-sectional | 232 | 57 | 44.00 (19-82) | F 159  M 73 | 11.6 (0-38) | 2.60 (0-9) | RRM 204  SPMS 21  PPMS 7 | IFN 22  GA 24  RTX 2  OCR 26  Fingolimod 31  Natalizumab 25  DMF 57  TFL 16  Cladribine 5  Alemtuzumab 1  Azathioprine 1  Ponesimod 1  No treatment 21 | NR | NR | Hospitalized: NR  Death 5 (2.1) |
| Ciampi et al e1 | Chile | 07/12/2020 | Cross-sectional | 14 | 11 | 34.71 (17-57) | F 10  M 4 | 6.46 (2-14) | 1.428 (0-4) | RRMS 14 | IFN 1  OCR 2  Fingolimod 5  Natalizumab 1  DMF 2  TFL 2  Alemtuzumab 2\* | Any comorbidity: 14  Insulin resistance 4  Depression 5  Migraine 3  Hypothyroidism 3  HTN 1  DM 1  Thyroiditis 1  Obesity 2  cutaneous amyloidosis 1  Lung diseases 1 | Fever 6  Cough 1  Dyspnea 1  Myalgia/arthralgia 7  Anosmia 4  Sore throat 1  Headache 3  Diarrhea 1  Rhinorrhea 1  Pneumonia 2  Asymptomatic 2 | Hospitalized 3 (21.4)  Death 0 |
| Barzegar et al 14 | Iran | 06/08/2020 | Cross-sectional | 9 | 2 | 38.55 (29-50) | F 8  M 1 | 10.30 (1-27) | 1.83 (0-8) | RRMS 6  SPMS 2  CIS 1 | IFN 4  GA 1  RTX 1  Fingolimod 1  No treatment 2 | Any comorbidity: 4  Hashimoto's disease 1  Epilepsy 1  Amnesia 1  Hypothyroidism 1 | Fever 5  Cough 4  Dyspnea 6  Anosmia 1  Sore throat 3  Diarrhea 2 | Hospitalized 2 (22.3)  Death 1 (11.2) |
| Montero-Escribano e2 | Spain | 05/07/2020 | Cross-sectional | 8 | 2 | 46.0 (41-55) | F 6  M 2 | NR | NR | RRMS 4  SPMS 1  PPMS 3 | RTX 6  OCR 2 | NR | Fever 6  Cough 4  Fatigue 2  Dyspnea 2  Anosmia 3  Ageursia 2  GI symptoms 3  Myalgia/arthralgia 1  Odynophagia 2  Chest pain 1  Pneumonia 1 | Hospitalized 1 (12.5)  Death 0 |
| Safavi et al 13 | Iran | 05/13/2020 | Cross-sectional | 34 | No PCR | 34.8 (8) | F 27  M 7 | 6.6 (4.2) | NR | RRMS 27  Progressive 7 | IFN 3  RTX 21  Fingolimod 5  DMF 2  TFL 1  No DMT 2 | NR | Fever 32  Cough 29  Dyspnea 16  Sore throat 16  Sneezing 18  Diarrhea 6  Nausea/vomiting 11 | Hospitalized 2 (5.3)  Death 0 |
| Crescenzo et al e3 | Italy | 07/04/2020 | Cross-sectional | 29 | 11 | 39 (10) | F 15  M 14 | 9.2 (6.7) | 2.5 (0-7.5) | RRMS 23  Progressive 6 | OCR 7  Fingolimod 4  Natalizumab 2  DMF 12  TFL 2  Azathioprine 1  No treatment 1 | Any comorbidity 13 | NR | Hospitalized 2 (6.9)  Death 0 |
| Moss et al e4 | Multicenter | 08/10/2020 | Cross-sectional | 77 | 17 | 46.79 (10.84) | F 62  M 15 | 16.60 (10.15) | 2.30 (1.97) | RRMS 57  Progressive MS 20 | NR | Any comorbidity: 37  Smoking 16 | NR | Hospitalized 5 (6.5%)  Death 0 |
| Álvarez el al 15 | Spain | 10/01/2020 | Cross-sectional | 12 | 9 | 47.91 (22-74) | F 9  M 3 | NR | 1.92 (0-8) | RRMS 9  Progressive 3 | Interferon 2  Fingolimod 1  DMF 2  TFL 2  Cladribine 1  Alemtuzumab 1  No treatment 3 | NR | Fever 8  Anosmia 1  Dyspnea 1  Headache 3  Asthenia 4  Myalgia 5  Sore throat 7 | Hospitalized: NR  Death 1 (8.3%) |
| Mantero el al e5 | Italy | 11/01/2020 | Cross-sectional | 15 | 1 | 40.5 (13.7) | F 10  M 5 | 11.5 (9.2) | 2.0 (1.5, 3.0) | RRMS 14  Progressive 1 | Interferon 3  Fingolimod 1  Natalizumab 1  DMF 7  TFL 2  No treatment 1 | NR | NR | Hospitalized 0  Death 0 |
| Sahraian et al 16 | Iran | 08/29/2020 | Cross-sectional | 68 | NR | 37.27 (9.10) | F 56  M 12 | 6.86 (6.21) | NR | RRMS 60  Progressive 3 | Interferon 10  GA 5  RTX 38  OCR 1  Fingolimd 4  Natalizumab 2  DMF 2  TFL 2  Azathioprine 1  No treatment 2 | NR | NR | Hospitalized 17 (25%)  Death 2 (2.9%) |
| Nesbitt et al e6 | Multicenter | 06/24/2020 | Cross-sectional | 25 | NR | 41.4 (13.2) | F 11  M 4 | NR | 6.7 (1.0) | RRMS 4  Progressive 3 | IFN 2  GA 2  RTX 1  OCR 6  Fingolimod 4  DMF 2  TFL 1  Natalizumab 1  Cladribine 4  Alemtuzumab 3 | NR | NR | Hospitalized 7 (28%)  Death 0 |
| Vogel et ale7 | USA | 19/09/2020 | Cross-sectional | 7 | 7 | 43 (29-64) | F 5  M 2 | NR | NR | NR | RTX 1  OCR 1  DMF 2  No treatment 2 | HTN 3  CVD 1  DM 2  Lung diseases 1 | NR | Hospitalized 0  Death 0 |
| Capasso et al e8 | Italy | 12/16/2020 | Cross-sectional | 9 | NR | 41.4 (12.8) | F 6  M 3 | NR | 3.0 (1.0-6.5) | NR | TFL 1  Natalizumab 3  Almtuzumab 3  Cladribine 1  No DMT 1 | Any comorbidity: 0 | Cough 1  Fever 1  Anosmia 1  Asymptomatic 7 | Hospitalized 0  ICU 0  Ventilation 0  Death 0 |
| Jack el al e9 | Merck KGaA  Global Patient Safety Database | 08/27/2020 | Pharmacovigilance study | 46 | 15 | NR | F 26  M 12 | NR | NR | NR | Cladribine 46 | NR | Asymptomatic 2 | Hospitalized 4 (8.7%)  Death 0 |
| Hughes et al e10 | Roche/Genentech global safety databases | 05/16/2020 | Pharmacovigilance study | 100 | 32 | 42.3 (23-59) | F 48  M 28 | NR | NR | RRMS 30  Progressive 15 | OCR 100 | NR | Asymptomatic 1 | Hospitalized 26 (26)  Death 0 |
| Meca-Lallana et al e11 | Spain | 06/15/2020 | Case report/series | 7 | 5 | 46.71 (25-60) | F 3  M 4 | 10.71 (5-19) | 4.42 (1.0-8) | RRMS 4  Progressive 3 | OCR 6  RTX 1 | Any comorbidity: 1  Smoking 1 | Fever 5  Cough 4  Fatigue 1  Dyspnea 3  Myalgia/arthralgia 1  Anosmia 1  Headache 2  Asymptomatic 2 | Hospitalized 3 (42.9)  Death 0 |
| Bowen et al 8 | USA | 05/26/2020 | Case report/series | 8 | 7 | 51.5 (11.4) | F 6  M 2 | NR | 3.62  (1-8.5) | RRMS 5  SPMS 3 | IFN 1  GA 1  Fingolimod 2  DMF 2  TFL 1  No treatment 1 | Any comorbidity: 4  CAD 1  HTN 1  DM 2  Lung diseases 2  Obesity 1  Myotonic dystrophy 1  Cardiomyopathy 1 | Fever 7  Cough 6  Fatigue 2  Dyspnea 2  Anosmia 2  Sneezing 2  Headache 4  disequilibrium 1  Altered mental status 2  Chills 1  Nausea 1 | Hospitalized 3ˠ (37.5)  Death 2 (25) |
| Mantero et al e12 | Italy | 06/25/2020 | Case report/series | 7 | No PCR | 35.90  (11.4) | F 5  M 2 | 6.71 (5.6) | 1.5 (1.5-2.0) | RRMS 7 | DMF 7 | Any comorbidity: 0 | Fever 6  Cough 4  Dyspnea 2  Anosmia 5  Ageusia 1  Asthenia 2  Pseudo-relapse 1 | Hospitalized 0  Death 0 |
| Matías-Guiu et al e13 | Spain | 06/11/2020 | Case report/series | 2 | No PCR | 52.50 (51-54) | F 2 | 29.50 (23-36) | 6.5 (6.5-6.5) | RRMS 2 | Alemtuzumab 2 | NR | Fever 2  Anosmia 1  Ageusia 1  Asthenia 1  Headache 1  Diarrhea 2 | Hospitalized 0  Death 0 |
| Maghzi et al e14 | USA | 05/21/2020 | Case report/series | 5 | 4 | 53.6 (38-79) | F 2  M 3 | 12.80 (2-28) | 2.5 (0.0-6.0) | RRMS 3  SPMS 1  RIS 1 | TFL 5 | Any comorbidity : 3  HTN 1  ADHD 1  Anxiety 1  HLP 1  Sleep apnea 1  Recurrent UTI 1 | Fever 5  Cough 2  Fatigue 1  Dyspnea 1  Myalgia/arthralgia 1  Anosmia 2  Sore throat 2  Asthenia 1  Headache 2  Diarrhea 2  Nausea 1 | Hospitalized 0  Death 0 |
| Luca et al e15 | Italy | 07/04/2020 | Case report/series | 2 | 2 | 46.0 (34-58) | F 2  M 0 | 4.5 (4-5) | 2.5 (2.5-2.5) | RRMS 2 | TFL 1  Fingolimod 1 | NR | Fever 2  Sore throat 1  Diarrhea 1 | Hospitalized 2  Death 0 |
| Guevara et al e16 | Chile | 06/20/2020 | Case report/series | 1 | 1 | 35.0 | M | 2 | 1.0 | RRMS | Alemtuzumab | No comorbidity | Fever 1  Cough 1 | Hospitalized 0  Death 0 |
| Thornton et al e17 | USA | 06/26/2020 | Case report/series | 2 | 2 | 40.5 (39-42) | F 1  M 1 | 4.5 (4-5) | NR | RRMS 2 | OCR 2 | No comorbidity | Fever 1  Cough 2  Dyspnea 1  Ageusia 1 | Hospitalized 0  Death 0 |
| Mallucci et al e18 | Italy | 07/19/2020 | Case report/series | 2 | 2 | 43.0 (37-49) | NR | 19.0 (15-23) | 2.5 (2.5-2.5) | NR | Fingolimod 2 | NR | Asymptomatic 2 | Hospitalized 0  Death 0 |
| Mohn et al e19 | Germany | 05/28/2020 | Case report/series | 1 | 1 | 42.0 | M | 7.0 | NR | RRMS | TFL | No comorbidity | Fever  Sore throat  Nausea  Vomiting  general weakness  Neurological worsening | Hospitalized 1  Death 0 |
| Valencia-Sanchez et al e20 | USA | 05/08/2020 | Case report/series | 1 | 1 | 58 | F | 13 | 6.0 | RRMS | Fingolimod | HTN  DM  Obesity  HLP  TIA  Migraine | Fever  Cough  Anosmia  Hyposmia Dysgeusia Dyspnea | Hospitalized 1  Death 0 |
| Rejdak et al e21 ‡ | Poland | 04/30/2020 | Case report/series | 10 | 10 | 38.0  (10) | F 7  M 3 | 9.0  (4.0) | NR | NR | GA 2  Fingolimod 2  Natalizumab 2  DMF 4 | NR | Asymptomatic 10 | Hospitalized 0  Death 0 |
| Carandini et al e22 | Italy | 05/28/2020 | Case report/series | 1 | 1 | 25 | F | NR | NR | RRMS | Alemtuzumab 1 | NR | Fever  Cough  Fatigue | Hospitalized 0  Death 0 |
| Gemcioglu et al e23 | Turkey | 05/16/2020 | Case report/series | 1 | 1 | 31 | M | 2 | NR | NR | IFN | Seasonal allergic rhinitis | Cough  Dyspnea | Hospitalized 1  Death 0 |
| Conte et al e24 | USA | 06/20/2020 | Case report/series | 1 | 1 | 48 | F | NR | NR | NR | OCR | NR | Fever  Dyspnea  Upper respiratory  Malaise | Hospitalized 1  Death 0 |
| Suwanwongse et al e25 | USA | 05/15/2020 | Case report/series | 1 | 1 | 31 | M | NR | NR | NR | OCR | Obesity | Cough  Dyspnea  Diarrhea  Nausea  Vomiting | Hospitalized 1  Death 0 |
| Gomez-Mayordomo et al e26 | Spain | 07/09/2020 | Case report/series | 1 | 1 | 57 | M | 24 | 6 | RRMS | Fingolimod | NR | Fever  Dyspnea  Malaise | Hospitalized 1  Death 0 |
| Devogelaere et al e27 | Belgium | 06/20/2020 | Case report/series | 1 | 1 | 33 | F | 16 | 8 | NR | RTX | No comorbidity | Fever 1  Cough 1  Dyspnea 1  Headache 1 | Hospitalized 1  Death 0 |
| Fernandez-Dıaz et al e28 | Spain | 07/17/2020 | Case report/series | 2 | 2 | 36.5 (30-43) | F 1  M 1 | 8.25 (2.5-14) | 1.25 (0.0-2.5) | RRMS 2 | Alemtuzumab 2 | No comorbidity | Fever 2  Cough 2  Dyspnea 1  Myalgia/arthralgia 1 | Hospitalized 1  Death 0 |
| Novi et al e29 | Italy | 04/15/2020 | Case report/series | 1 | 1 | 58 | M | 12 | 6 | PPMS 1 | OCR | Allergic rhinitis, Asthma  Peptic ulcer | Fever  Cough | Hospitalized 1  Death 0 |
| Aguirre et al e30 # | Spain | 06/03/2020 | Case report/series | 1 | 1 | 18 | M | 7 | 1.5 | NR | Natalizumab | No comorbidity | Fever  Cough  Malaise | Hospitalized 1  Death 0 |
| Barzegar et al e31 | Iran | 05/05/2020 | Case report/series | 1 | 1 | 42 | F | 19 | 1 | RRMS | Fingolimod | Hypothyroidism Recurrent UTI MDD  PTE  Myasthenia gravis | Fever 1  Cough 1  Dyspnea 1  Neurological worsening | Hospitalized 1  Death 0 |
| Borriello et al e32 | Italy | 04/30/2020 | Case report/series | 1 | 1 | 28 | M | 20 | 1.5 | RRMS | Natalizumab | No comorbidity | Fever  Dyspnea | Hospitalized 1  Death 0 |
| Ghajarzadeh et al e33 | Iran | 05/23/2020 | Case report/series | 1 | 1 | 39 | F | 10 | 2.0 | RRMS | OCR | Epilepsy | Fever  Dyspnea | Hospitalized 0  Death 0 |
| Chiarini et al e34 | Italy | 05/29/2020 | Case report/series | 1 | 1 | 45 | F | 24 | 6.5 | RRMS | Fingolimd | Obesity | Fever  Asthenia | Hospitalized 1  Death 0 |
| Lucchini et al e35 | Italy | 06/22/2020 | Case report/series | 1 | 1 | 60 | F | 8 | 2.5 | RRMS | OCR | NR | Fever  Cough  Sore throat  Nasal congestion | Hospitalized 0  Death 0 |
| Foerch et al e36 | Germany | 05/06/2020 | Case report/series | 1 | 1 | 57 | F | 10 | 2.0 | RRMS | Fingolimd | Any comorbidity: 1  (not available in detail) | Fever  Cough  Dyspnea | Hospitalized 1  Death 0 |
| Woo et al e37 | Germany | 07/11/2020 | Case report/series | 1 | 1 | 44 | F | 21 | 2.0 | RRMS | RTX | History of malignancy | Fever  Cough  Dyspnea  Malaise  Muscle ache | Hospitalized 1  Death 0 |
| Ciardi et al e38 | Italy | 07/15/2020 | Case report/series | 1 | 1 | 62 | F | NR | 6.0 | RRMS | TFL | NR | Fever  Cough  Dyspnea  Fatigue  Diarrhea | Hospitalized 1  Death 0 |
| Louapre et al e39 | France | 06/08/2020 | Case report/series | 2 | 2 | 54.5 (53-56) | F 2 | 24.5 (21-28) | 7.0 (6-8) | RRMS 1  SPMS 1 | OCR 1  Natalizumab 1 | Any comorbidity: 2  HTN  Acute pancreatitis Cholecystectomy  COPD  Epilepsy  Smoking | Asymptomatic 1  Fever 1  Cough 1 | Hospitalized 1  Death 0 |
| Iannetta et al e40 | Italy | 08/04/2020 | Case report/series | 2 | 2 | 45.0 (36-54) | F 1  M 1 | 14.5 (2-17) | 6.25 (5.5-7.0) | RRMS 1  SPMS 1 | OCR 2 | Any comorbidity: 2  Malignancy 1  DVT 1 | Fever 2  Cough 1  Sneezing 1  Coryza 1 | Hospitalize 2  Death 0 |
| Wurm et al e41 | Germany | 08/07/2020 | Case report/series | 1 | 1 | 59 | F | 4 | 6.0 | Progressive | RTX | NR | Fever  Cough  Fatigue  Dyspnea  Headache  Nausea | Hospitalize 1  Death 0 |
| Dersch et al e42 | Germany | 08/07/2020 | Case report/series | 1 | 1 | 55 | M | 4 | NR | RRMS | Cladribine | NR | Fever  Malaise  Thoracic pain Respiratory symptoms | Hospitalize 1  Death 0 |
| Fiorella et al e43 | Chile | 08/10/2020 | Case report/series | 1 | 1 | 24 | F 1 | 2 | 0.0 | RRMS | Alemtuzumab | Depression | Cough  Myalgia  Sore throat | Hospitalize 0  Death 0 |
| Gazca et al e44 | Mexico | 08/12/020 | Case report/series | 4 | 0 | 46.25 (6.18) | F 3  M 1 | NR | NR | NR | Autologous transplants 4 | NR | Fever 3  Cough 4  Dyspnea 3  Headache 3  Diarrhea 1 | Hospitalized 1  Death 0 |
| Mantero et al e45 | Italy | 08/31/2020 | Case report/series | 6 | 3 | 45 (8.6) | F 4  M 2 | 15.8 (9.6) | 1.75 (1-4.5) | RRMS 6 | TFL 6 | Any comorbidity: 0 | NR | Hospitalized 0  Death 0 |
| Angelis et al e46 | Italy | 08/16/2020 | Case report/series | 2 | 2 | 45.00 (29-61) | F 1  M 1 | 9.00 (2-26) | 2.00 (1.5-2.5) | RRMS 2 | Cladribine 2 | Any comorbidity: 1  HTN 1  Dyslipidemia 1 | Fever 1  Anosmia 1  dysgeusia 1  Diarrhea 1  Asymptomatic 1 | Hospitalized 0  Death 0 |
| Celius et al e47 | Norway | 08/29/2020 | Case report/series | 1 | 1 | 35 | F | 2.0 | NR | NR | Cladribine 1 | NR | Fever 1  Anosmia 1  Common cold | Hospitalized 0  Death 0 |
| Șerban e48 | Romania | 09/29/2020 | Case report/series | 1 | 1 | 45 | M | 7 | 5.5 | NR | Natalizumab | NR | Fever  Cough  Headache  Arthralgia | Hospitalized 1  Death 0 |
| Kataria et al e49 | USA | 11/02/2020 | Case report/series | 3 | 3 | 62 (8.88) | F 1  M 2 | 17.3 (4.6) | 3.8 (2.3) | RRMS 3 | GA 1  OCR 1  DMF 1 | Any comorbidity: 3  HTN 3  DM 1  HLP 1  Smoking 1 | Fever 3  Cough 2  Dyspnea 2  Fatigue 1  Neurological worsening 2 | Hospitalized 2  Death 0 |
| Moghadasi et al e50 | Iran | 10/28/2020 | Case report/series | 1 | 1 | 34 | F | 15 | NR | Progressive 1 | CP | Recurrent tract infection | Fever  Cough  Dyspnea  Nausea  Generalized weakness | Hospitalized 1  Death 0 |
| Rimmer et al 9 | USA | 08/10/2020 | Case report/series | 1 | 1 | 51 | F | 14 | 6.5 | RRMS | Natalizumab 1 | HTN  Recurrent tract infection | Fever  Cough  Neurological worsening | Hospitalized 1  Death 1 |
| Margoni et al e51 # | Italy | 10/12/2020 | Case report/series | 1 | 0 | NR | NR | NR | NR | NR | Natalizumab 1 | NR | Fever  Cough | Hospitalized 0  Death 0 |
| Preziosa et al e52 | Italy | 11/20/2020 | Case report/series | 2 | NR | 35 (30-40) | F 1  M 1 | 7.4 (1.4-13.4) | 2.5 (1.5-3.5) | RRMS 2 | Cladribine 2 | Any comorbidity: 0 | Fever 2  Anosmia 1  Ageusia 2  Cough 2  Dyspnea 1  Fatigue 2 | Hospitalized 0  Death 0 |
| Florea et al e53 | Romania | 11/26/10 | Case report/series | 1 | 1 | 40 | F | 8 | NR | RRMS | No treatment | Any comorbidity: 0 | Asymptomatic | Hospitalized 1  Death 0 |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Table e2-a. Characteristics of conference abstracts included in the investigation | | | | | | | | | | | | | | |
| First Author | Location | Date of first publication | Type of study | Confirmed/suspected | Positive PCR | Age,  Mean or median (SD or range) | Sex | Disease duration,  Mean or (SD or range) | EDSS,  Mean or median (SD or range) | Course of disease | DMTs | Comorbidity | Symptoms | Severity of COVID-19 |
| Meca-Lallana et al e54 | Spain | 2020 | Cohort | 41 | 18 | 39.4 (10.3) | F 21  M 20 | 9.0 (1.4) | 2.5 (0.7) | RRMS 38  Progressive 3 | IFN 2  GA 2  OCR 4  RTX 1  TFL 10  DMF 3  Fingolimod 3  Cladribine 3  Natalizumab 9  No treatment 2 | Any comorbidity: 3 | Asymptomatic 6 | Hospitalized 7 (17.1%)  Death 0 |
| Radaelli et al e55 | Italy | 2020 | Cohort | 153 | 7 | 45 (20-71) | F 124  M 29 | NR | 2.5 (1-8.5) | NR | NR | NR | NR | Hospitalized 3 (2.0%)  Death 0 |
| Guevara et al  e56 | Chile | 2020 | Cohort | 5 | 5 | 43.25 (6.97) | F 3  M 2 | NR | 2.14 (1.3) | RRMS 5 | GA 2  Fingolimod 1  Alemtuzumab 2 | Obesity 1  No comorbidity 4 | Fever 4  Cough 3  Dyspnea 1  Headache 2  Anosmia 1  Ageusia 1  Myalgia 3  Malaise 1  Pneumonia 2  Sneezing 1  Nasal congestion 1  Odynophagia 1  Pseudo relapse 1 | Hospitalized 2  Death 0 |
| Moreno-Torres et al 25 | Spain | 2020 | Cohort | 219 | 88 | 45.3 (12.4) | F 138  M 81 | 11.9 (8.9) | 2.74 (2.28) | RRMS 181  SPMS 23  PPMS 15 | IFN 16  GA 10  RTX 13  OCR 16  Fingolimod 18  Natalizumab 27  TFL 33  DMF 32  Alemtuzumab 11  Cladribine 9  No DMT 30 | DM 5/83  Lung disease 2/85  CVD 2/85  HTN 11/76  Cancer 4/83  Smoking 7/62 | Fever 65/87  Cough 63/87  Fatigue 42/86  Dyspnea 37/86  Anosmia 19/79  Ageusia 16/79  Diarrhea 12/86  Myalgia 44/85  Sore throat 23/85  Pneumonia 53/74 | Hospitalized 51 (23.3%)  Death 5 |
| Zabalza1 et al 26 | Spain | 2020 | Cohort | 93 | 47 | NR | NR | 14.45 (13.1) | NR | NR | NR | Any comorbidity 33 | NR | Hospitalized 19 (20.4%)  Death 2 (2.1%) |
| Klineova et al 27 | USA | 2020 | Cohort | 349 | NR | 45 (13-76) | F 247  M 102 | 11.5 (9.1) | NR | NR | NR | NR | NR | Hospitalized 48 (13.7%)  Death 13 (3.7%) |
| Schreiner et al  e57 # | USA | 2020 | Cohort | 17 | 12 | 20.6 | F 13  M 4 | NR | NR | MS 14  CIS 1 | GA 1  RTX6  OCR 1  Fingolimod 3  Natalizumab 1  DMF 1  MF 1  No DMT 2 | Any comorbidity 4  DM 1  Other 3 | Fever 9  Cough 9  Fatigue 9  Dyspnea 5  Anosmia 8  Ageusia 6  Diarrhea 4  Chills 5  Headache 1  Sore throat 2  Asymptomatic 1 | Hospitalized 4 (23.5%)  Death 0 |
| Mendes et al 28 | Brazil | 2020 | Cohort | 94 | 32 | 40.6 (10.2) | F 73  M 21 | 9.9 (8.6) | NR | NR | IFN 9  GA 5  Natalizumab 20  TFL 5  DMF 17  Fingolimod 16  OCR 5  RTX 2  Alemtuzumab 1  No treatment 14 | Any comorbidity: 19  DM 1  HTN 8  Dyslipidemia 6  CAD 1  Lung disease 3  Obesity 2  Thyroid disease 2  Cancer 2  Smoker 9 | Fever 68  Cough 55  Dyspnea 36  Headache 51  Fatigue 43  Diarrhea 17  Anosmia or Ageusia 43  Myalgia 55 | Hospitalized 12 (12.8%)  Death 1 (1.1%) |
| Salter et al 29 | North America | 2020 | Cohort | 734 | NR | 48.2 (13.5) | F 539  M 195 | 13.8 (9.9) | NR | NR | NR | NR | NR | Hospitalized 229 (31.2%)  Death 45 (6.1%) |
| Dillon et al 30 O | USA  (Optum® de-identified COVID-19 Electronic  Health Record dataset) | 2020 | Cohort | 47 | NR | 47 | F 32  M 15 | NR | NR | NR | OCR 47 | NR | NR | Hospitalized 12 (25.5%)  Death 1 (2.1%) |
| Dillon et al 30 | (USA  Optum® de-identified COVID-19 Electronic  Health Record dataset) | 2020 | Cohort | 357 | NR | NR | F 266  M 91 | NR | NR | NR | NR | HTN 193  DM 85  Obesity 93  Malignancy 79  Lung disease 103  CAD 43  Liver disease 21  Renal disease 47 | NR | Hospitalized 87 (24.4%)  Death 13 (3.6%) |
| Omerhoca et al e58 | Turkey | 2020 | Cross sectional | 7 | 7 | 38.8 (7.5) | F 5  M 2 | NR | 1.7 (0.5) | RRMS 7 | IFN 4  GA 1  DMF 1  No treatment 1 | Any comorbidity 2 | NR | Hospitalized 0  Death 0 |
| Kieseier et al 17 | USA  ( IBM ® Explorys ® dataset) | 2020 | Cross sectional | 170 | NR | NR | F 128  M 42 | NR | NR | NR | NR | HTN 95  DM 56  CAD 25  Cancer 33  COPD 32  Kidney disease 26 | NR | Hospitalized 51 (30%)  Death 5 (3.0%) |
| Poursadeghfard et al 18 | Iran | 2020 | Cross sectional | 76 | 8 | 38.08 | F 53  M 23 | NR | NR | RRMS 60  PPMS 9  SPMS 1  CIS 2 | IFN 27  GA 5  DMF 8  TFL 1  RTX 12  Fingolimod 11  No DMT 12 | HTN 5  DM 2  Hypothyroidism 6  Hyperthyroidism 2  Lung disease 3  CAD 7 | Fever 28  Cough 29  Dyspnea 20  Sore throat 30  Headache 10  Diarrhea 2  Anosmia 1  Ageusia 1 | Hospitalized 12 (15.8%)  Death 2 (2.6%) |
| Mallucci et al e59 | Italy | 2020 | Cross sectional | 37 | NR | NR | NR | NR | NR | NR | Natalizumab 22  Fingolimod 15 | NR | Asymptomatic 13 | Hospitalized 0  Death 0 |
| Hervás-García et al e60 | Spain | 2020 | Cross sectional | 19 | NR | 42.7 | NR | NR | NR | NR | IFN 3  RTX 2  OCR 3  Fingolimod 2  Natalizumab 2  DMF 5  Cladribine 1  Alemtuzumab 1 | NR | Asymptomatic 17 | Hospitalized 2 (11.8%)  Death 0 |
| Freedman et al 10 | Merck KGaA  Global Patient Safety Database | 2020 | Pharmacovigilance case series | 102 | NR | NR | F 70  M 24 | NR | NR | NR | IFN 102 | NR | NR | Hospitalized 12 (11.8%)  Death 2 |
| Reder et al 11 | Bayer database | 2020 | Pharmacovigilance case series | 23 | NR | 49 (27-65) | F 17  M 5 | NR | NR | NR | IFN 23 | NR | NR | Hospitalized NR  Death 2 (8.7%) |
| Wallach et al e61 | USA | 2020 | Case report/series | 11 | 9 | 50.5 (34-64) | F 10  M 1 | NR | NR | NR | IFN 1  RTX 1  OCR 6  TFL 1  No treatment 2 | NR | NR | Hospitalized 4 (36.4%)  Death 0 |
| Oreja-Guevara et al e62 | Spain | 2020 | Case report/series | 14 | 6 | 40.1 (12.0) | F 9  M 5 | 9.7 (8.9) | 2 (1.9) | RRMS 13  SPMS 1 | Cladribine 14 | Any comorbidity 5  HBP 1  DM 1  Obesity 2  Smoking 1  Anxiety 1  Depression 1  Hypothyroidism 1  Talassemia trait 1  DLP 2 | Fever 9  Cough 8  Dyspnea 1  Anosmia 7  Ageusia 3  Asthenia 4  Myalgia 6  Diarrhea 1  Rash 1  Pneumonia 1  Asymptomatic 2 | Hospitalized 1 (7.1%)  Death 0 |
| Karan et al e63 | CLARIFY-MS and MAGNIFY-MS studies | 2020 | Case report/series | 3 | 1 | 40.0 (14.7) | F 3 | 10.0 (9.8) | 2.5 (1.8) | RRMS 3 | Cladribine 3 | Any comorbidity 2  Asthma 1  CVD 1  DVT 1 | NR | Hospitalized 2  Death 0 |

Note: ND: not determine, F: female, M: male, NR: not-report, EDSS: Expanded Disability Status Scale, CVD: cardiovascular disease, HT: hypertension, DM: diabetes mellitus, RRMS: relapsing-remitting MS, SPMS: secondary-progressive MS, PPMS, primary-progressive MS, CIS: clinically isolated syndrome, RIS: radiologically isolated syndrome VTE: Venous thromboembolism, IFN: interferon, GA: glatiramer acetate, RTX: rituximab, OCR: ocrelizumab, DMF: dimethyl fumarate, TFL: teriflunomide, MMF: mycophenolate mofetil MTX: methotrexate, CP: cyclophosphamide

\*One patients receive both ocrelizumab and alemtuzumab

ˠ One patient hospitalized for primary observation

🟓 One patient self-confirmed

★One patient nor reported

‡ All patients received Amantadine

# Studies on MS patients with pediatric onset

O All atients received OCR

Table e3-a. Demographic and clinical characteristics of COVID-19 infection in patients with MS from published articles

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | N (%) or Mean (SD) | Number of patients | Study reporting characteristics |
| Age | 44.25 (4.85) | 1358 | 63 |
| Sex, female/male | 987/422 (2.34:1) | 1447 | 63 |
| Disease duration | 12.20 (3.10) | 1025 | 49 |
| EDSS | 2.51 (0.98) | 923 | 43 |
| **Course of MS** |  | | |
| Relapsing | 950 (75.9) | 1251 | 52 |
| progressive | 210 (16.8) |
| CIS | 7 (0.6) |
| **Comorbidity** |  | | |
| Patients with any comorbidity | 230 (36.2) | 636 | 36 |
| HTN | 45 (7.9) | 569 | 34 |
| CAD | 28 (4.9) |
| DM | 42 (7.4) |
| Malignancy | 6 (1.0) |
| Lung diseases | 24 (4.2) |
| **Symptoms** |  | | |
| Fever | 462 (71. 7) | 644 | 53 |
| Cough | 432 (67.1) | 644 | 53 |
| Fatigue/asthenia | 340 (52.8) | 644 | 53 |
| Shortness of breath | 263 (40.8) | 644 | 53 |
| Headache | 224 (34.8) | 644 | 53 |
| GI complication | 112 (18.4) | 610 | 52 |
| Anosmia\* | 42 (14.5) | 289 | 51 |
| Ageusia\* | 24 (8.3) | 289 | 51 |
| Asymptomatic | 31 (3.9%) | 790 | 55 |
| **DMTs** |  | | |
| B-cell depleting agents | 391 (24.3) | 1610 | 65 |
| Dimethyl fumarate | 209 (13.0) |
| Fingolimod | 150 (9.3) |
| Natalizumab | 131 (8.1) |
| Glatiramer acetate | 101 (6.3) |
| Interferon | 90 (5.6) |
| Teriflunomide | 87 (5.4) |
| Cladribine | 68 (4.2) |
| Alemtuzumab | 25 (1.5) |
| No DMT | 249 (15.5) |
| PCR positive test | 541 (36.5) | 1481 | 58 |
| Hospitalized | 279 (18.7) | 1495 | 64 |
| Death | 39 (2.2) | 1739 | 67 |

Table e3-b. Demographic and clinical characteristics of COVID-19 infection in patients with MS from conference abstracts

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | N (%) or Mean (SD) | Number of patients | Study reporting characteristics |
| Age | 45.41 (3.80) | 1891 | 16 |
| Sex, female/male | 1751/662 (2.64:1) | 2413 | 19 |
| Disease duration | 12.52±1.42 | 1454 | 7 |
| EDSS | 2.58 (0.20) | 442 | 7 |
| **Course of MS** |  | | |
| Relapsing | 291 (83.6) | 348 | 5 |
| progressive | 51 (14.6) |
| CIS | 3 (0.9) |
| **Comorbidity** |  | | |
| Patients with any comorbidity | 69 (25.2) | 274 | 8 |
| HTN | 312 (29.7) | 1052 | 10 |
| CAD | 79 (7.5) |
| DM | 151 (14.3) |
| Malignancy | 118 (11.2) |
| Lung diseases | 144 (13.7) |
| **Symptoms** |  | | |
| Fever | 183 (62.5) | 293 | 6 |
| Cough | 167 (57.0) | 293 | 6 |
| Fatigue/asthenia | 98 (46.4) | 211 | 4 |
| Shortness of breath | 100 (36.4) | 275 | 6 |
| Headache | 64 (33.3) | 192 | 5 |
| GI complication | 36 (12.3) | 292 | 6 |
| Anosmia | 36 (18.8) | 191 | 5 |
| Ageusia | 27 (14.1) | 191 | 5 |
| Asymptomatic | 39 (7.5) | 522 | 9 |
| **DMTs** |  | | |
| B-cell depleting agents | 119 (16.6) | 715 | 15 |
| Dimethyl fumarate | 67 (9.4) |
| Fingolimod | 69 (9.6) |
| Natalizumab | 81(11.3) |
| Glatiramer acetate | 26 (3.6) |
| Interferon | 187 (26.1) |
| Teriflunomide | 50 (7.0) |
| Cladribine | 30 (4.2) |
| Alemtuzumab | 15 (2.1) |
| No DMT | 63 (8.8) |
| PCR positive test | 222 (32.1) | 692 | 11 |
| Hospitalized | 558 (21.9) | 2548 | 19 |
| Death | 91 (3.5) | 2571 | 20 |

Table e4-a. Risk of hospitalization by DMTs class

|  |  |  |  |
| --- | --- | --- | --- |
|  | Published articles | Conference abstracts | All studies |
| B-cell depleting agents | 29.3% (98/334) | 28.8% (19/66) | 29.2% (117/400) |
| Dimethyl fumarate | 13.9% (14/101) | 14.3% (1/7) | 13.9% (15/108) |
| Fingolimod | 17.0% (17/101) | 4.8% (1/21) | 14.7% (18/122) |
| Natalizumab | 13.1% (11/84) | 0 (0/25) | 10.1% (11/109) |
| Glatiramer acetate | 13.8% (8/58) | 25.0% (1/4) | 14.5% (9/62) |
| Interferon | 9.3% (5/54) | 11.8% (13/110) | 11.0% (18/164) |
| Teriflunomide | 20.1% (13/62) | 0 (0/1) | 20.6% (13/63) |
| Cladribine | 11.9% (7/59) | 16.7% (3/18) | 13.0% (10/77) |
| Alemtuzumab | 13.3% (2/15) | 0 (0/3) | 11.1% (2/18) |
| No DMT | 44.9% (48/107) | 0 (0/5) | 42.9% (48/112) |

Note: Sixty published articles and 10 conference abstracts were included

DMT: disease modifying therapies

Table e4-b. Risk of mortality by DMTs class

|  |  |  |  |
| --- | --- | --- | --- |
|  | Published articles | Conference abstracts | All studies |
| B-cell depleting agents | 2.1% (8/376) | 3.6% (4/112) | 2.5% (12/488) |
| Dimethyl fumarate | 1.0% (2/194) | 0 (0/42) | 0.8% (2/236) |
| Fingolimod | 0.7% (1/150) | 0 (0/42) | 0.5 (1/192) |
| Natalizumab | 1.6% (2/128) | 0 (0/61) | 1.1% (2/189) |
| Glatiramer acetate | 0.9% (1/101) | 0 (0/16) | 0.8% (1/117) |
| Interferon | 0 (0/90) | 2.6% (4/151) | 1.7% (4/241) |
| Teriflunomide | 2.4% (2/83) | 0 (0/44) | 1.6% (2/127) |
| Cladribine | 0/67 (0) | 0 (0/30) | 0 (0/97) |
| Alemtuzumab | 0 (0/22) | 0 (0/14) | 0 (0/36) |
| No DMT | 7.3% (18/248) | 16.2% (6/37) | 8.4% (24/285) |

DMT: disease modifying therapies

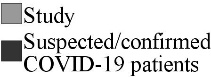
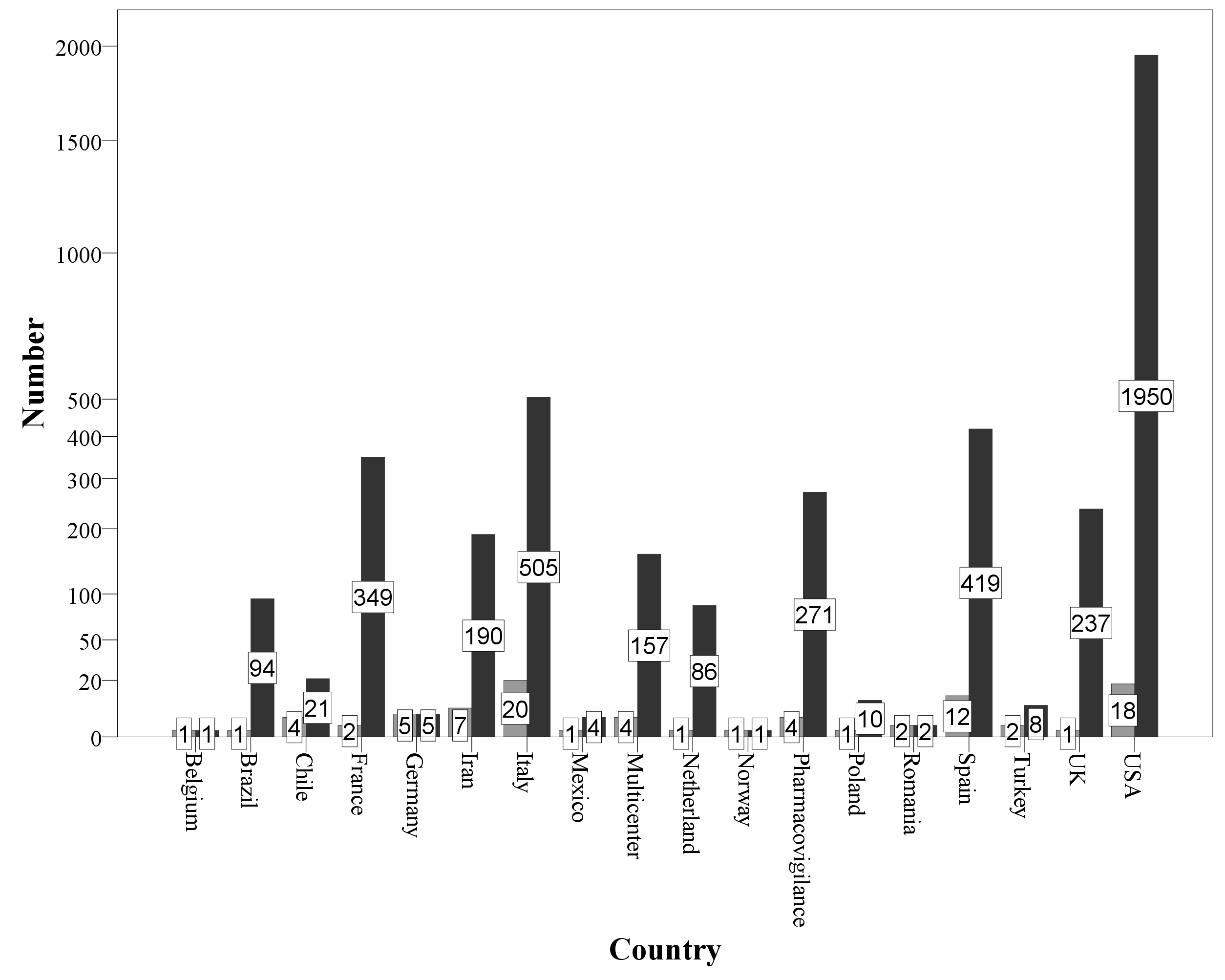
 

Figure e-1. Number of study and confirmed/suspected COVID-19 patients in each country

Number of study and patients were extracted from abstract. USA: 6 studies and 1685 patients; Turkey: 1 study and 7 patients; Spain: 5 studies and 386 patients; Italy: 2 studies and 190 patients; Iran: 1 study and 76 patients; Chile: 1 study and 5 patients; Brazil: 1 study and 94 patients; Multicenter: 1 study and 3 patients; pharmacovigilance: 2 studies and 125 patients