

## Supplementary Online Content

Kunchok A, Aksamit AJ Jr, Davis JM III, et al. Association between tumor necrosis factor inhibitor exposure and inflammatory central nervous system events. *JAMA Neurol*. Published online May 18, 2020. doi:10.1001/jamaneurol.2020.1162

**eFigure 1.** Case-Control Inclusion Criteria

**eFigure 2.** Study Design

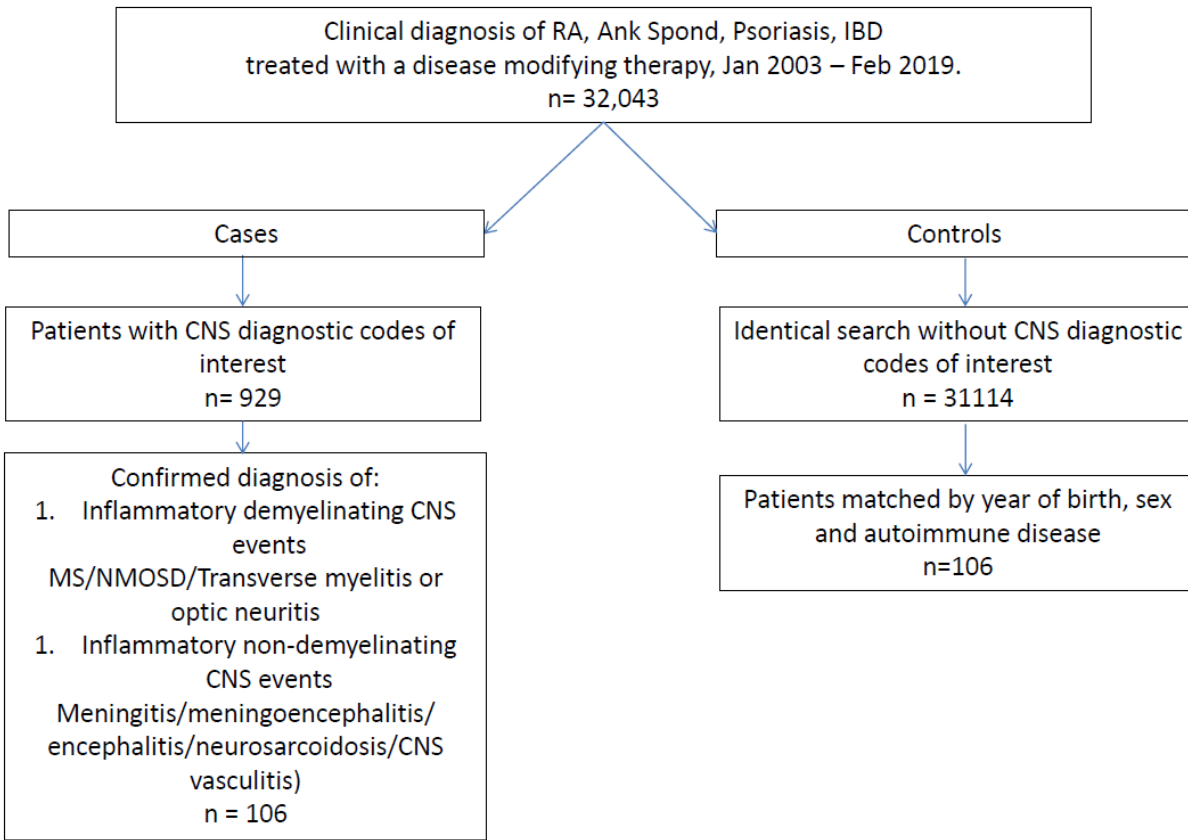
**eTable 1.** Disease Modifying Therapies Used by the Study Population at Any Point in Their Disease Course

**eTable 2.** Exclusions from CNS Diagnostic Code Search for Cases

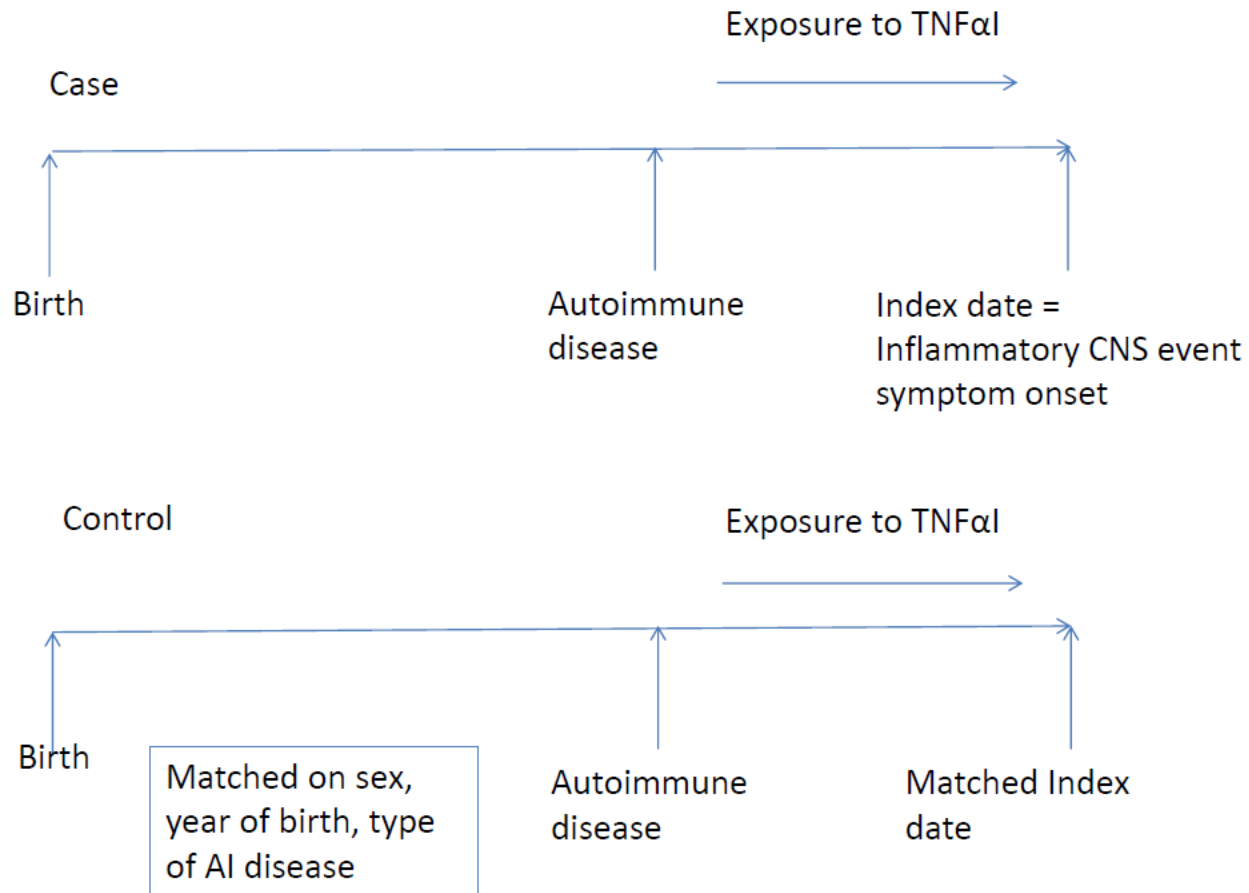
**eTable 3.** Cases Stratified by Inflammatory Demyelinating and Non-demyelinating CNS Events for Each Systemic Autoimmune Disease

This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1: Case-Control Inclusion Criteria**



eFigure 2: Study Design



**eTable 1: Disease Modifying Therapies Use by the Study Population at Any Point in Their Disease Course**

<b>Disease modifying therapies:</b>
Leflunomide
Azathioprine
Methotrexate
Hydroxychloroquine
Minocycline
Sulfasalazine
Gold
Cyclophosphamide
Mycophenolate
Cyclosporine
Anakinra
Sekukinumab
Ustekinumab
Abatacept
Rituximab
Tocilizumab
Natalizumab
Vedolizumab
Apremilast
Secukinumab
Ixekizumab
Brodalumab
Guselkumab
Tilrakizumab
Mesalamine
Etanercept
Infliximab
Adalimumab
Golimumab
Certolizumab

**eTable 2: Exclusions From CNS Diagnostic Code Search for Cases**

<b>Reason for exclusion</b>	<b>n</b>
<b>Cases not occurring during study period:</b> (prior to 2003 or prior to autoimmune disease onset)	148
<b>Malignancy:</b> Primary CNS malignancy (glioma, lymphoma, meningioma); paraneoplastic CNS disease; systemic malignancy (solid organ or haematological); secondary CNS (metastatic) disease	22
<b>Non-neurological diagnosis:</b> evaluation for MS negative, influenza, infectious mononucleosis, postural hypotension, spondylitis, chronic pain, systemic sarcoidosis but evaluation for CNS disease negative, systemic vasculitis but evaluation for CNS disease negative	437
<b>Other neurological disorder:</b> ALS; myasthenia gravis, cerebral palsy; CIDP; migraines; myositis; peripheral neuropathy; CNS ischaemia; leukodystrophy; leukoencephalopathy; epilepsy (non-autoimmune); PRES; pachymeningitis due to CSF leak or IgG4 disease; skull base osteomyelitis; trigeminal neuralgia; tremor; haemangioma; cavernoma; osmotic demyelination syndrome; depression; narcolepsy; dementia; PML; toxic-metabolic encephalopathy; arachnoiditis; compressive myelopathy; infectious transverse myelitis; meningitis secondary to drugs, bacterial or viral meningitis; surgical meningitis(post ENT or neurosurgical intervention); optic neuropathy secondary to other causes (drugs, ischaemia, glaucoma, non-arteritic ischaemic, sellar lesions, trauma, IgG4)	155
<b>Lacking ancillary confirmative tests:</b> lack of confirmatory CSF or MRI	7
<b>Autoimmune disease not confirmed:</b> autoimmune diagnosis removed or alternative autoimmune disease	23
<b>Immunodeficiency or immunocompromised:</b> solid organ transplant, stem cell transplant, congenital (common variable) or acquired immunodeficiency (HIV)	28
<b>Cases meeting inclusion criteria but consent for research refused</b>	3
<b>Total</b>	<b>823</b>

**eTable 3: Cases Stratified by Inflammatory Demyelinating and Non-demyelinating CNS Events for Each Systemic Autoimmune Disease**

<b>Autoimmune disease</b>	<b>Total cases</b>	<b>Inflammatory demyelinating CNS events</b>	<b>Inflammatory non-demyelinating CNS events</b>
	n	n (%)	n (%)
Rheumatoid arthritis	48	26 (54)	22 (45)
Ankylosing spondylitis	4	1 (25)	3 (75)
Psoriasis and Psoriatic arthritis	21	12 (57)	9 (43)
Crohn's disease	27	14 (53)	13 (48)
Ulcerative colitis	6	3 (50)	3 (50)