

Table e-1: ICD-9 codes used in this study**ICD-9 Code****Disease/diagnosis**

| | |
|--------------------------|---|
| 331.0 | Alzheimer's disease |
| 290.0-290.3 | 'Senile' dementias |
| 290.4-290.9 | Vascular dementia and unspecified dementias |
| 331.1-331.2 | Frontotemporal degeneration and 'senile degeneration' |
| 331.9 | Unspecified cerebral degeneration |
| 797 | 'Senility' |
| 250 | Diabetes mellitus |
| 274 | Gout |
| 295 | Schizophrenia |
| 296.2-269.3, 311 | Major Depression |
| 296.0-296.1, 296.4-296.8 | Bipolar disorder |
| 300.0 | Anxiety disorder |
| 388.3 | Tinnitus |
| 389 | Hearing loss |
| 401-405 | Hypertension |
| 410-414 | Ischemic heart disease |
| 440 | Peripheral vascular disease |
| 446 | Vasculitides |
| 530-535 | Esophageal, gastric, peptic, gastrojejunal, and other ulcer disease (gastroesophageal reflux is included in 530) |
| 555-556 | Inflammatory bowel disease |
| 578 | Upper and/or lower gastrointestinal bleeding |
| 584 | Acute renal failure |
| 585 | Chronic kidney disease |
| 586 | Renal failure, unspecified |
| 710 | Connective tissue diseases |
| 712 | Crystal arthropathies, excluding gout |
| 714 | Rheumatoid arthritis |
| 715, 721 | Osteoarthritis |
| 720 | Spondyloarthropathies |

Table e-1: Comorbid diseases in the sample

| Comorbidities | Cases (#) | Cases (%) | Controls (#) | Controls (%) |
|---|------------------|------------------|---------------------|---------------------|
| Low dose aspirin | 24,045 | 48.7 | 77,423 | 39.3 |
| Cardiovascular disease and risk factors | | | | |
| Hypertension | 40,077 | 81.2 | 158,263 | 80.4 |
| Hyperlipidemia | 27,225 | 55.2 | 117,063 | 59.5 |
| Ischemic Heart Disease | 25,693 | 52.1 | 100,075 | 50.8 |
| Diabetes mellitus | 16,989 | 34.4 | 67,051 | 34.1 |
| Congestive Heart Failure | 12,366 | 25.1 | 47,177 | 24.0 |
| Transient Ischemic Attack | 5,223 | 10.6 | 13,275 | 6.7 |
| Peripheral Vascular Disease | 4,952 | 10.0 | 19,095 | 9.7 |
| Stroke | 4,025 | 8.2 | 8,664 | 4.4 |
| Chronic obstructive pulmonary disease | 15,611 | 31.6 | 62,264 | 31.6 |
| Gastrointestinal disease | | | | |
| Ulcer Disease | 19,139 | 38.8 | 73,922 | 37.6 |
| Gastroesophageal reflux | 16,183 | 32.8 | 63,812 | 32.4 |
| Gastrointestinal Bleeding | 5,927 | 12.0 | 18,932 | 9.6 |
| Inflammatory Bowel Disease | 630 | 1.3 | 2,297 | 1.2 |
| Kidney disease | | | | |
| Chronic Renal Insufficiency | 4,187 | 8.5 | 17,623 | 9.0 |
| Acute Renal Failure | 3,212 | 6.5 | 7,677 | 3.9 |
| Unspecified Renal Failure | 1,817 | 3.7 | 7,018 | 3.6 |
| Rheumatologic disease | | | | |
| Osteoarthritis | 23,700 | 48.0 | 90,589 | 46.0 |
| Gout | 3,966 | 8.0 | 19,317 | 9.8 |
| Rheumatoid Arthritis | 1,806 | 3.7 | 7,328 | 3.7 |
| Ankylosing Spondylitis | 329 | 0.7 | 1,445 | 0.7 |
| Connective Tissue Diseases | 252 | 0.5 | 1,040 | 0.5 |
| Other Crystal Arthropathy | 196 | 0.4 | 696 | 0.4 |
| Vasculitis | 205 | 0.4 | 647 | 0.3 |
| Mental Illness | | | | |
| Major Depression | 20,071 | 40.7 | 36,713 | 18.7 |
| Anxiety Disorder | 9,035 | 18.3 | 21,712 | 11.0 |
| Bipolar Disorder | 8,223 | 16.7 | 12,894 | 6.6 |
| PTSD | 3,914 | 7.9 | 8,893 | 4.5 |
| Schizophrenia | 2,643 | 5.4 | 3,572 | 1.8 |
| Other side effects of NSAID use | | | | |
| Tinnitus | 3,361 | 6.8 | 13,716 | 7.0 |
| Hearing Loss | 18,414 | 37.3 | 67,570 | 34.3 |

Table e-3: NSAID use in the sample

| | Prescribed at Least Once (%) | | Over 1 Year of Use (%) | | Over 5 Years of Use (%) | |
|--|------------------------------|--------------|------------------------|--------------|-------------------------|-------------|
| | Cases | Controls | Cases | Controls | Cases | Controls |
| Any NSAID | 42.17 | 40.16 | 14.92 | 14.91 | 0.81 | 0.99 |
| Arylpropionic Acid Derivatives | 31.31 | 29.11 | 7.71 | 7.90 | 0.22 | 0.36 |
| Ibuprofen | 20.85 | 18.72 | 4.02 | 4.12 | 0.11 | 0.20 |
| Ketoprofen | 0.04 | 0.06 | 0.01 | 0.02 | 0.00 | 0.00 |
| Naproxen | 15.17 | 14.59 | 3.21 | 3.32 | 0.08 | 0.11 |
| Oxaprozin | 0.58 | 0.55 | 0.13 | 0.13 | 0.00 | 0.01 |
| Indolic Acid Derivatives | 10.79 | 11.08 | 2.08 | 2.08 | 0.04 | 0.06 |
| Etodolac | 5.01 | 5.22 | 1.00 | 0.93 | 0.00 | 0.00 |
| Indomethacin | 3.70 | 4.07 | 0.36 | 0.47 | 0.01 | 0.01 |
| Sulindac | 3.05 | 2.83 | 0.66 | 0.59 | 0.03 | 0.03 |
| Cox-II Inhibitors | 4.90 | 4.99 | 1.70 | 1.81 | 0.02 | 0.02 |
| Celecoxib | 3.02 | 2.99 | 0.99 | 1.02 | 0.02 | 0.02 |
| Rofecoxib | 2.37 | 2.51 | 0.64 | 0.71 | 0.00 | 0.00 |
| Valdecoxib | 0.22 | 0.27 | 0.02 | 0.02 | 0.00 | 0.00 |
| Enolic Acid Derivatives. | 3.24 | 3.30 | 0.79 | 0.82 | 0.03 | 0.05 |
| Meloxicam | 0.45 | 0.50 | 0.04 | 0.06 | 0.00 | 0.00 |
| Piroxicam | 2.16 | 2.15 | 0.59 | 0.58 | 0.02 | 0.04 |
| Nabumetone | 0.73 | 0.71 | 0.16 | 0.15 | 0.01 | 0.01 |
| Heteroarylacetic Acid Derivatives | 2.99 | 3.20 | 0.55 | 0.67 | 0.02 | 0.03 |
| Diclofenac | 2.45 | 2.70 | 0.52 | 0.63 | 0.02 | 0.03 |
| Ketorolac | 0.35 | 0.33 | 0.00 | 0.00 | 0.00 | 0.00 |
| Tolmetin | 0.23 | 0.22 | 0.04 | 0.04 | 0.00 | 0.00 |
| Non-acetylated NSAIDs | 6.90 | 5.80 | 1.57 | 1.08 | 0.06 | 0.06 |
| Diflunisal | 0.13 | 0.11 | 0.03 | 0.02 | 0.00 | 0.00 |
| Salsalate | 5.91 | 4.89 | 1.37 | 0.93 | 0.05 | 0.05 |
| Salicylates | 0.94 | 0.87 | 0.15 | 0.13 | 0.00 | 0.00 |
| High Dose ASA | 0.08 | 0.06 | 0.02 | 0.01 | 0.00 | 0.00 |

Protective effects of NSAIDs on the development of Alzheimer disease

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