**SupplementaryMaterial**

**Geographical Variation in Opioid Use in Elderly Patients with Dementia: A Nationwide Study**

**Supplementary Table 1. Diagnoses used for identification of patients with dementia**

|  |  |  |
| --- | --- | --- |
|  | **ICD-8** | **ICD-10** |
| **Alzheimer’s disease** | 290.10 | F00.0, F00.1, F00.2, F00.9, G30.0, G30.1, G30.8, G30.9 |
| **Vascular dementia** | 293.09-19 | F01.0, F01.1, F01.2, F01.3, F01.8, F01.9 |
| **Frontotemporal dementia** | 290.11 | F02.0 |
| **Other dementias** | - | G31.8 |
| **Dementia without specification** | 290.09-19 | F03, G31.9 |

ICD, International Classification of Diseases

**Supplementary Table 2. ICD-8, ICD-10 and ATC Codes Used to Identify Comorbidity\*.**

\*All subtypes are included for ICD and ATC codes unless otherwise stated.

|  |  |  |
| --- | --- | --- |
| **Disease** | **Determined by** | **Codes** |
| Diabetes | Considered present if one of the following ICD-10 codes were registered in the National Patient Register or if a prescription for an antidiabetic was filled in 2014  | ICD10: E10, E11, E12, E13, E14ATC: A10 |
| Recent fracture | Considered present if one of the following ICD-10 codes were registered the National Patient Register in 2014 | ICD10: S02, S12, S22, S32, S42, S52, S62, S72, S82, S92, T02, T08, T10, T12 |
| Cancer  | Considered present if one of the following codes were registered in the National Patient Register (excludes non-melanoma skin cancer): | ICD-8: 14xxx, 15xxx, 16xxx, 17xxx, 18xxx,19xxx, 20xxx ICD-10: C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C85, C88, C90-C97 |
| Osteoporosis | Considered present if one the following codes were registered in the National Patient Registerand/or a prescription for an antiosteoporosis drug was filled. | ICD-8: 723.09 ICD-10: M80.0-M82.8ATC: M05 |
| Pulmonary disease | Considered present if one of the following codes for chronic pulmonary disorder was registered in the National Patient Register. | ICD-8: 490-493xx, 515-518xxICD-10: J40-47, J60-67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3  |
| Vascular disease | Considered present if a diagnosis of myocardial infarction, peripheral vascular disease, cerebrovascular disease or hemiplegia was registered in the National Patient Register under one of the following codes. | Codes for myocardial infarction:ICD-8: 410.xxICD-10: I21-I23Peripheral vascular disease:ICD-8: 440-444.xxICD-10: I70-74, I77Cerebrovascular disease:ICD-8: 430-438.xxICD-10: I60-69, G45, G46Hemiplegia:ICD-8: 430-438.xxICD-10: I60-69, G45, G46 |
| Liver disease | Considered present if a liver disease diagnosis was registered in the National Patient Register under one of the following codes | Mild liver disease:ICD-8: 571.xx, 573.01+573.04ICD-10: B18, K70.0-K70.3, K70.9, K71, K73, K74, K76.0Moderate to severe liver disease:ICD-8: 070.00, 070.02, 070.04, 070.06, 070.08, 573.00, 456.00-456.09ICD-10: B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85 |
| Renal disease | Considered present if a renal disease diagnosis was registered in the National Patient Register under one of the following: | ICD-8: 403.xx, 404.xx, 580-584.xx, 590.09, 593.19, 753.10-753.19, 792xxICD-10: I12, I13, N00-N05, N07, N11, N14, N17-19, Q61 |

**Supplementary Table 3A. Baseline characteristics for elderly with dementia stratified by region.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Capital** **(n=11,367)** | **Central** **(n=6930)** | **North****(= 3412)** | **Zealand****(n= 5017)** | **Southern****(n= 9288)** |
| **Age, y** | 83.4 (77.4-88.6) | 83.2 (77.6-87.9) | 83.4 (78.2-88.1) | 82.6 (76.9-87.8) | 83.3 (77.7-88.1) \*\*\* |
| **Female**  | 7348 (64.5%) | 4424 (63.8%) | 2155 (63.2%) | 3081 (61.4%) | 5771 (62.1%) \*\*\* |
| **Married** | 3686 (32.4%) | 2508 (36.2%) | 1246 (36.5%) | 1867 (37.2%) | 3419 (36.8%) \*\*\* |
| **Nursing home resident** | 6352 (55.9%) | 4053 (58.5%) | 2093 (61.3% | 2507 (50.0%) | 4713 (50.7%) \*\*\* |
| **Pain causing comorbidity** |  |  |  |  |  |
| * Osteoporosis
 | 1801 (15.8%) | 1349 (19.5%) | 516 (15.1%) | 827 (16.5%) | 2322 (25.0%)\*\*\* |
| * Cancer
 | 2729 (24.01%) | 1339 (19.3%) | 611 (17.9%) | 1115 (22.2%) | 2094 (22.6%)\*\*\* |
| * Diabetes
 | 1470 (12.9%) | 759 (11.0%) | 376 (11.0%) | 678 (13.5%) | 1183 (12.7%)\*\*\* |
| * Fracture in 2014
 | 933 (8.2%) | 514 (7.4%) | 268 (7.9%) | 419 (8.4%) | 751 (8.1%) \*\*\* |
| * Arthritis
 | 2,446 (21.5%) | 1,299 (18.7%) | 578 (16.9%) | 944 (18.8%) | 1,863 (20.1%)\*\*\* |
| **Other comorbidity** |  |  |  |  |  |
| * Vascular disease
 | 4736 (41.7%) | 2588 (37.3%) | 1232 (36.1%) | 2113 (42.1%) | 3784 (40.7%) \*\*\* |
| * Pulmonary disease
 | 1700 (15.0%) | 856 (12.4%) | 455 (13.3%) | 759 (15.1%) | 1241 (13.4%) \*\*\* |
| * Liver disease
 | 280 (2.5%) | 126 (1.8%) | 45 (1.3%) | 111 (2.2%) | 147 (1.6%) \*\*\* |
| * Kidney disease
 | 654 (5.8%) | 413 (6.0%) | 161 (4.7%) | 308 (6.1%) | 434 (4.7%) \*\*\* |

\*\*\*p<0.001

**Supplementary Table 3B. Baseline characteristics for elderly without dementia stratified by region.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Capital** **(n=280,186)** | **Central** **(n=220,650)** | **North** **(n= 113,224)** | **Zealand****(n= 167,664)** | **Southern****(n= 230,063)** |
| **Age, y** | 72.6 (68.9-78.8) | 72.6 (68.8-78.8) | 72.8 (68.6-79.1) | 72.3 (68.6-78.2) | 72.8 (68.7-78.9) \*\*\* |
| **Female**  | 156,973 (56.0%) | 117,944 (53.5%) | 60,216 (53.1%) | 89,803 (53.6%) | 123,314 (53.6%)\*\*\* |
| **Married** | 143,397 (53.3%) | 131,547 (59.6%) | 66,883 (59.1%) | 98,671 (59.9%) | 137,324 (59.7%)\*\*\* |
| **Nursing home resident** | 8575 (3.1%) | 7587 (3.4%) | 4466 (3.9%) | 3941 (2.3%) | 6081 (2.6%)\*\*\* |
| **Pain causing comorbidity** |  |  |  |  |  |
| * Osteoporosis
 | 24,065 (8.6%) | 27,662 (12.5%) | 15,075 (13.3%) | 8870 (5.3%) | 40,613 (17.7%)\*\*\* |
| * Cancer
 | 60,847 (21.7%) | 42,296 (19.2%) | 21,675 (19.1%) | 33,578 (20.0%) | 48,123 (20.9%)\*\*\* |
| * Diabetes
 | 23,980 (8.6%) | 17,350 (7.9%) | 8619 (7.6%) | 14,599 (8.7%) | 20,394 (8.9%) \*\*\* |
| * Fracture in 2014
 | 8061 (2.9%) | 6058 (2.8%) | 2846 (2.5%) | 4422 (2.6%) | 6532 (2.8%) \*\*\* |
| * Arthritis
 | 46,310 (16.5%) | 34,274 (15.5%) | 16,390 (14.5%) | 24,612 (14.7%) | 38,985 (17.0%)\*\*\* |
| **Other comorbidity** |  |  |  |  |  |
| * Vascular disease
 | 63,004 (22.5%) | 50,577 (22.9%) | 24,830 (21.9%) | 37,867 (22.6%) | 53,497 (23.3%) \*\*\* |
| * Pulmonary disease
 | 32,968 (11.8%) | 22,343 (10.1%) | 12,229 (10.8%) | 17,718 (10.6%) | 23,452 (10.2%) \*\*\* |
| * Liver disease
 | 4670 (1.7%) | 2669 (1.0%) | 1176 (1.04%) | 2387 (1.4%) | 2926 (1.3%) \*\*\* |
| * Kidney disease
 | 10,417 (3.7%) | 8934 (4.1%) | 3602 (3.2%) | 5858 (3.5%) | 8473 (3.7%) \*\*\* |

\*\*\*p<0.001

**Supplementary Table 4A.** Logistic regression analysis of the association between opioid use and dementia among home-living elderly and step-wise adjustment for age, sex, region and comorbidity. Numbers are given as odds ratios (ORs) and 95% confidence intervals (CI).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Opioid= dementia | Opioid = dementia age sex | Opioid = dementia region | Opioid = dementia age sex region | Opioid = dementia age sex region comorbidity |
| Dementia | 1.65 (1.59-1.72) | 1.28 (1.23-1.33) | 1.65 (1.59-1.71) | 1.28 (1.24-1.33) | 1.12 (1.08-1.17) |
| Sex (male as reference) |  | 1.38 (1.36-1.39) |  | 1.38 (1.36-1.39) | 1.37 (1.35-1.38) |
| Age |  |  |  |  |  |
| 70-74 |  | 1.21 (1.19-1.23) |  | 1.21 (1.19-1.23) | 1.09 (1.07-1.11) |
| 75-79 |  | 1.53 (1.51-1.55) |  | 1.53 (1.51-1.55) | 1.25 (1.24-1.28) |
| 80-84 |  | 1.86 (1.83-1.87) |  | 1.87 (1.83-1.90) | 1.42 (1.39-1.44) |
| 85-89 |  | 2.12 (2.08-2.17) |  | 2.13 (2.08-2.17) | 1.59 (1.55-1.62) |
| 90-94 |  | 2.52 (2.44-2.60) |  | 2.52 (2.45-2.60) | 1.92 (1.86-1.99) |
| 95+ |  | 2.84 (2.68-3.02) |  | 2.85 (2.68-3.03) | 2.32 (2.18-2.48) |
| Region  |  |  |  |  |  |
| North |  |  | 1.0 (Reference) |  | 1.0 (reference) |
| Capital |  |  | 1.06 (1.04-1.08) | 1.05 (1.03-1.07) | 1.01 (0.99-1.03) |
| Central |  |  | 1.09 (1.07-1.11) | 1.10 (1.07-1.12) | 1.08 (1.06-1.10) |
| Zealand  |  |  | 1.14 (1.11-1.16) | 1.15 (1.13-1.17) | 1.18 (1.15-1.20) |
| South |  |  | 1.10 (1.07-1.12) | 1.09 (1.07-1.11) | 1.00 (0.98-1.02) |
|  |  |  |  |  |  |
| Comorbidity |  |  |  |  |  |
| Osteoporosis |  |  |  |  | 1.63 (1.60-1.66) |
| Cancer |  |  |  |  | 1.59 (1.57-1.61) |
| Arthritis |  |  |  |  | 2.73 (2.70-2.77) |
| Fracture |  |  |  |  | 1.77 (1.72-1.82) |
| Diabetes |  |  |  |  | 1.60 (1.57-1.62) |
| Liver |  |  |  |  | 1.77 (1.70-1.84) |
| Vascular |  |  |  |  | 1.53 (1.51-1.55) |
| Lung |  |  |  |  | 1.77 (1.75-1.80) |
| Kidney |  |  |  |  | 1.52 (1.48-1.56) |

**Supplementary Table 4B.** Logistic regression analysis of the association between opioid use and dementia among nursing home residents and step-wise adjustment for age, sex, region and comorbidity. Numbers are given as odds ratios (ORs) and 95% confidence intervals (CI).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Opioid=dementia | Opioid = dementia age sex | Opioid = dementia region | Opioid = dementia age sex region | Opioid = dementia age sex region comorbidity |
| Dementia | 0.83 (0.80-0.86) | 0.82 (0.79-0.85) | 0.82 (0.79-0.85) | 0.81 (0.78-0.84) | 0.87 (0.84-0.91) |
| Sex |  | 1.31 (1.26-1.36) |  | 1.31 (1.26-1.36) | 1.22 (1.17-1.27) |
| Age |  |  |  |  |  |
| 70-74 |  | 1.08 (0.97-1.20) |  | 1.08 (0.97-1.19) | 1.07 (0.97-1.19) |
| 75-79 |  | 1.14 (1.03-1.25) |  | 1.14 (1.03-1.25) | 1.08 (0.98-1.20) |
| 80-84 |  | 1.22 (1.11-1.33) |  | 1.22 (1.12-1.34) | 1.14 (1.04-1.33) |
| 85-89 |  | 1.30 (1.19-1.42) |  | 1.30 (1.19-1.43) | 1.21 (1.11-1.33) |
| 90-94 |  | 1.34 (1.23-1.47) |  | 1.35 (1.23-1.47) | 1.29 (1.18-1.47) |
| 95+ |  | 1.28 (1.16-1.42) |  | 1.28 (1.16-1.42) | 1.32 (1.19-1.47) |
| Region  |  |  |  |  |  |
| North  |  |  | 1.0 (reference) | 1.0 (reference) | 1.0 (reference) |
| Capital |  |  | 1.13 (1.06-1.20) | 1.13 (1.06-1.19) | 1.07 (1.00-1.13) |
| Central |  |  | 0.98 (0.93-1.05) | 0.99 (0.93-1.05) | 0.95 (0.89-1.01) |
| Zealand  |  |  | 1.21 (1.13-1.29) | 1.22 (1.14-1.31) | 1.20 (1.12-1.29) |
| South |  |  | 1.14 (1.07-1.21) | 1.15 (1.08-1.22) | 1.08 (1.01-1.15) |
| Comorbidity |  |  |  |  |  |
| Osteoporosis |  |  |  |  | 1.70 (1.62-1.78) |
| Cancer |  |  |  |  | 1.27 (1.22-1.32) |
| Arthritis |  |  |  |  | 1.71 (1.64-1.79) |
| Fracture |  |  |  |  | 1.36 (1.28-1.45) |
| Diabetes |  |  |  |  | 1.07 (1.02-1.13) |
| Liver |  |  |  |  | 1.16 (1.02-1.31) |
| Vascular |  |  |  |  | 1.13 (1.09-1.17) |
| Lung |  |  |  |  | 1.22 (1.16-1.28) |
| Kidney |  |  |  |  | 1.18 (1.10-1.26) |