**Supplementary Material**

**The Use of Opioids and Antipsychotics in Elderly with Dementia: Have Opioids Replaced Antipsychotics in Treating Behavioral Symptoms in Dementia?**

# **Supplementary Table 1A. 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 2A. Algorithm for Calculation of Morphine Equivalents**

Equivalent doses of oral morphine were calculated as number of defined daily doses (DDD) filled in the year multiplied by a factor based on content of one DDD [1, 2] and published guidelines for calculation of morphine equivalents [3-5]. One DDD of oral morphine is equivalent to 100 mg of morphine [5]. This formula is calculated for the subtypes of opioids: Morphine equivalents = Number of DDD x factor

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ATC Code** | **Drug Name** | **Administration Route** | **Content of 1 DDD (mg)** | **Equianalgesic Ratio** | **Oral Morphine Equivalents (mg) in 1 DDD (Factor)** |
| N02AA01 | Morphine [2, 4, 5] | Oral | 100 | 1 | 100 |
|  |  | Parenteral | 30 | 3 | 90 |
| N02AA03 | Hydromorphone | Oral [5] | 20 | 6 | 120 |
|  |  | Parenteral [3] | 4 | 15 | 60 |
| N02AA04 | Nicomorphine [4] | Oral | 30 | 1 | 30 |
|  |  | Parenteral | 30 | 3 | 90 |
| N02AA05 | Oxycodone | Oral [4, 5] | 75 | 1.5 | 112.5 |
|  |  | Parenteral [3] | 30 | 3 | 90 |
| N02AA55 | Oxycodone, combinations [4, 5] | Oral | Equivalent to 75 mg oxycodone | 1.5 | 112.5 |
| N02AA59 | Codeine, combinations excluding psychoepileptica [4, 5] | Oral | 90/120 | 0.1 | 10.8 |
| N02AB02 | Pethidine | Oral [4, 5] | 400 | 0.1 | 40 |
|  |  | Parenteral [4] | 400 | 0.4 | 160 |
| N02AB03 | Fentanyl [5] | Transdermal | 1.2 | 100 | 120 |
|  |  | Sublingual | 0.6 | 50 | 30 |
| N02AC04 | Dextropropoxyphene [5] | Oral | 300 | 0.15 | 45 |
| N02AE01 | Buprenorphine [5] | Transdermal | 1.2 | 110 | 132 |
|  |  | Sublingual | 1.2 | 50 | 60 |
| N02AG02 | Ketobemidone and antispasmodics [5] | Oral | 50 | 1 | 50 |
|  |  | Parenteral | 50 | 3 | 150 |
| N02AX02 | Tramadol [4, 5] | Oral | 300 | 0.2 | 60 |

ATC, Anatomical Therapeutic Chemical

# **Supplementary Table 3. ICD-8, ICD-10 and ATC Codes Used to Identify Comorbidity.**

|  |  |  |
| --- | --- | --- |
| **Disease** | **Determined by** | **Codes** |
| Diabetes | Considered present if one of the following ICD-10 codes was registered in the National Patient Registry or if a prescription for an antidiabetic was filled in the previous year | ICD10: E10, E11, E12, E13, E14  ATC: A10 |
| Recent fracture | Considered present if one of the following ICD-10 codes was registered the National Patient Registry in the previous year | ICD10: S02, S12, S22, S32, S42, S52, S62, S72, S82, S92, T02, T08, T10, T12 |
| Cancer | Considered present if one of the following codes was registered in the National Patient Registry (excludes non-melanoma skin cancer) | ICD-8: 14xx, 15xx, 16xx, 17xx, 18xx,19xx, 20xx  ICD-10: C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C85, C88, C90-C97 |
| Osteoporosis | Considered present if one the following codes was registered in the National Patient Registry and/or a prescription for an antiosteoporosis drug was filled | ICD-8: 723.09  ICD-10: M80.0-M82.8  ATC: M05 |
| Pulmonary disease | Considered present if one of the following codes for chronic pulmonary disorder was registered in the National Patient Registry | ICD-8: 490-493xx, 515-518xx  ICD-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 Registry under one of the following codes | ICD-8: 410.xx, 440-444.xx, 430-438.xx, 430-438.xx  ICD-10: I21-I23, I60-69, I70-74, I77, G45, G46, I60-69 |
| Liver disease | Considered present if a liver disease diagnosis was registered in the National Patient Registry under one of the following codes | ICD-8: 070.00, 070.02, 070.04, 070.06, 070.08, 573.00, 456.00-456.09, 571.xx, 573.01, 573.04  ICD-10: B15.0, B16.0, B16.2, B18, B19.0, K70.0-K70.4, K70.9, K71, K72 K73, K74, K76.0, K76.6, I85 |
| Renal disease | Considered present if a renal disease diagnosis was registered in the National Patient Registry under one of the following codes | ICD-8: 403.xx, 404.xx, 580-584.xx, 590.09, 593.19, 753.10-753.19, 792xx  ICD-10: I12, I13, N00-N05, N07, N11, N14, N17-19, Q61 |

ICD, International Classification of Diseases; ATC, Anatomical Therapeutic Chemical

# **Supplementary Table 4A. Logistic Regression Analysis Results for Elderly with Dementia**

This table compares results for elderly with dementia in 2000 versus 2005, 2010, and 2015 in five-year age groups. Numbers are given as odds ratios (ORs) and 95% confidence intervals (CI). The adjusted ORs include adjustment for age, sex, and all comorbidity.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **2005** | | | **2010** | | | **2015** | | |
| **Age (y)** | **Crude OR (95% CI)** | **Adjusted OR (95% CI)** | **Crude OR (95% CI)** | | **Adjusted OR (95% CI)** | **Crude OR (95% CI)** | | **Adjusted OR (95% CI)** |
| 65-69 | 1.11 (0.91-1.36) | 1.11 (0.90-1.36) | 1.30 (1.08-1.57) | | 1.17 (0.96-1.42) | 1.34 (1.11-1.61) | | 1.23 (1.02-1.49) |
| 70-74 | 1.18 (1.03-1.35) | 1.11 (0.97-1.28) | 1.44 (1.27-1.64) | | 1.29 (1.13-1.47) | 1.34 (1.19-1.52) | | 1.15 (1.01-1.32) |
| 75-79 | 1.15 (1.05-1.27) | 1.11 (1.00-1.22) | 1.35 (1.23-1.48) | | 1.23 (1.12-1.36) | 1.36 (1.24-1.49) | | 1.18 (1.07-1.30) |
| 80-84 | 1.09 (1.01-1.19) | 1.06 (0.98-1.16) | 1.39 (1.28-1.50) | | 1.30 (1.20-1.41) | 1.34 (1.24-1.46) | | 1.21 (1.11-1.32) |
| 85-89 | 1.16 (1.07-1.27) | 1.13 (1.04-1.24) | 1.54 (1.42-1.67) | | 1.45 (1.34-1.58) | 1.59 (1.47-1.72) | | 1.44 (1.32-1.56) |
| 90-94 | 1.26 (1.11-1.43) | 1.24 (1.09-1.40) | 1.76 (1.57-1.98) | | 1.69 (1.50-1.91) | 1.94 (1.73-2.17) | | 1.77 (1.57-1.98) |
| 95-99 | 1.50 (1.14-1.97) | 1.47 (1.11-1.93) | 1.84 (1.42-2.38) | | 1.79 (1.38-2.33) | 2.15 (1.66-2.78) | | 2.05 (1.58-2.67) |

# **Supplementary Table 4A. Results from the Logistic Regression Analysis Results for Elderly without Dementia**

This table compares results for elderly with dementia in 2000 versus 2005, 2010 and 2015 in five-year age groups. Numbers are given as odds ratios (ORs) and 95% confidence intervals (CI). The adjusted ORs include adjustment for age, sex, and all comorbidity.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **2005** | | | **2010** | | | **2015** | | |
| **Age (y)** | **Crude OR (95% CI)** | **Adjusted** **OR (95% CI)** | **Crude OR (95% CI)** | | **Adjusted OR (95% CI)** | **Crude OR (95% CI)** | | **Adjusted OR (95% CI)** |
| 65-69 | 1.14 (1.12-1.16) | 1.06 (1.04-1.08) | 1.24 (1.21-1.26) | | 1.06 (1.04-1.08) | 1.21 (1.19-1.23) | | 0.98 (0.96-1.00) |
| 70-74 | 1.16 (1.14-1.19) | 1.08 (1.06-1.10) | 1.29 (1.27-1.32) | | 1.10 (1.08-1.12) | 1.19 (1.17-1.21) | | 0.95 (0.93-0.97) |
| 75-79 | 1.15 (1.13-1.17) | 1.07 (1.05-1.09) | 1.27 (1.25-1.29) | | 1.07 (1.05-1.09) | 1.20 (1.18-1.22) | | 0.95 (0.93-0.96) |
| 80-84 | 1.15 (1.13-1.17) | 1.07 (1.05-1.10) | 1.25 (1.23-1.28) | | 1.07 (1.05-1.09) | 1.22 (1.20-1.25) | | 0.95 (0.93-0.98) |
| 85-89 | 1.13 (1.10-1.16) | 1.08 (1.05-1.11) | 1.30 (1.26-1.33) | | 1.13 (1.10-1.16) | 1.23 (1.20-1.26) | | 0.99 (0.96-1.02) |
| 90-94 | 1.15 (1.10-1.20) | 1.12 (1.07-1.16) | 1.34 (1.28-1.39) | | 1.22 (1.17-1.27) | 1.41 (1.36-1.46) | | 1.15 (1.10-1.19) |
| 95-99 | 1.26 (1.15-1.37) | 1.22 (1.12-1.33) | 1.47 (1.35-1.59) | | 1.37 (1.26-1.49) | 1.50 (1.38-1.62) | | 1.31 (1.20-1.42) |

# **REFERENCES**

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