**Electronic Supplementary Material 3**

**The Association of Potentially Inappropriate Medication Use on Health Outcomes and Hospital Costs in Community-Dwelling Older Persons: A Longitudinal 12-year Study**

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**Online Resource 3.** Table 1: Associated risk of mortality within 1, 3 and 6 months after the initiation of PIM use in time-varying cox proportional hazards regression stratified by gender.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Male** |  | **Female** |  | **Male** |  | **Female** |  | **Male** |  | **Female** |  |
|  | **1 month** |  | **1 month** |  | **3 months** |  | **3 months** |  | **6 months** |  | **6 months** |  |
|  | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** |
| **The first PIM use perioda** |  |  |  |  |  |  |  |  |  |  |  |  |
| Non-users | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| PIM-users | 4.01\*\*\* | (3.11–5.17) | 3.12\*\*\* | (2.37–4.11) | 3.52\*\*\* | (3.04–4.07) | 2.92\*\*\* | (2.51–3.39) | 2.53\*\*\* | (2.28–2.81) | 1.97\*\*\* | (1.77–2.19) |
| Number of deaths | **1,974** |  | **2,373** |  | **2,111** |  | **2,507** |  | **2,343** |  | **2,723** |  |
| **PH-assumption test** | **0.0322** |  | **<0.001** |  | **0.0266** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  |
| **PIM use** |  |  |  |  |  |  |  |  |  |  |  |  |
| Non-users | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| PIM-users | 1.49\*\*\* | (1.28–1.75) | 1.29\*\* | (1.11–1.50) | 1.89\*\*\* | (1.72–2.09) | 1.49\*\*\* | (1.35–1.64) | 2.07\*\*\* | (1.90–2.25) | 1.62\*\*\* | (1.49–1.76) |
| **Ageb** |  |  |  |  |  |  |  |  |  |  |  |  |
| 65–74 years | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| 75–84 years | 2.07\*\*\* | (1.94–2.22) | 2.88\*\*\* | (2.69–3.08) | 2.06\*\*\* | (1.93–2.21) | 2.88\*\*\* | (2.69–3.07) | 2.06\*\*\* | (1.92–2.20) | 2.88\*\*\* | (2.69–3.07) |
| ≥85 years | 5.23\*\*\* | (4.53–6.05) | 8.05\*\*\* | (7.25–8.95) | 5.16\*\*\* | (4.46–5.96) | 8.02\*\*\* | (7.22–8.90) | 5.10\*\*\* | (4.42–5.90) | 7.98\*\*\* | (7.19–8.87) |
| **Socioeconomic status (income)c** |  |  |  |  |  |  |  |  |  |  |  |  |
| <9,999 € | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| 10,000–19,999 € | 0.94 | (0.87–1.03) | 0.92\* | (0.86–0.98) | 0.95 | (0.88–1.04) | 0.92\* | (0.86–0.98) | 0.96 | (0.88–1.04) | 0.92\* | (0.86–0.98) |
| 20,000–29,999 € | 0.72\*\*\* | (0.63–0.83) | 0.90 | (0.79–1.03) | 0.72\*\*\* | (0.63–0.83) | 0.90 | (0.79–1.03) | 0.72\*\*\* | (0.63–0.83) | 0.90 | (0.79–1.03) |
| >30,000 € | 0.67\*\*\* | (0.56–0.79) | 0.77\* | (0.62–0.95) | 0.67\*\*\* | (0.56–0.80) | 0.77\* | (0.63–0.95) | 0.67\*\*\* | (0.56–0.80) | 0.77\* | (0.63–0.95) |
| **Living alonec** | 1.29\*\*\* | (1.19–1.40) | 1.00 | (0.94–1.07) | 1.28\*\*\* | (1.18–1.39) | 1.00 | (0.94–1.07) | 1.28\*\*\* | (1.18–1.39) | 1.00 | (0.94–1.07) |
| **Medication used** |  |  |  |  |  |  |  |  |  |  |  |  |
| Antidiabetics | 1.42\*\*\* | (1.28–1.58) | 1.66\*\*\* | (1.50–1.82) | 1.40\*\*\* | (1.26–1.55) | 1.65\*\*\* | (1.50–1.81) | 1.39\*\*\* | (1.25–1.55) | 1.64\*\*\* | (1.49–1.81) |
| Psychotropics | 1.23\*\*\* | (1.13–1.33) | 1.17\*\*\* | (1.09–1.25) | 1.21\*\*\* | (1.12–1.32) | 1.16\*\*\* | (1.09–1.24) | 1.21\*\*\* | (1.11–1.31) | 1.16\*\*\* | (1.08–1.24) |
| Cardiovascular medications | 1.22\*\*\* | (1.13–1.32) | 1.37\*\*\* | (1.28–1.48) | 1.22\*\*\* | (1.13–1.32) | 1.37\*\*\* | (1.27–1.48) | 1.22\*\*\* | (1.13–1.32) | 1.37\*\*\* | (1.27–1.47) |
| Opioids | 1.29\*\*\* | (1.13–1.47) | 1.40\*\*\* | (1.24–1.58) | 1.29\*\*\* | (1.13–1.47) | 1.40\*\*\* | (1.24–1.58) | 1.29\*\*\* | (1.13–1.47) | 1.39\*\*\* | (1.24–1.57) |
| NSAIDs | 0.87\*\*\* | (0.81–0.94) | 0.87\*\*\* | (0.82–0.93) | 0.87\*\*\* | (0.81–0.93) | 0.87\*\*\* | (0.82–0.93) | 0.87\*\*\* | (0.81–0.93) | 0.87\*\*\* | (0.81–0.92) |
| **Excessive polypharmacyd** | 1.60\*\*\* | (1.45–1.76) | 1.42\*\*\* | (1.31–1.54) | 1.58\*\*\* | (1.44–1.75) | 1.42\*\*\* | (1.31–1.53) | 1.58\*\*\* | (1.43–1.74) | 1.41\*\*\* | (1.30–1.53) |
| Number of deaths | **3,639** |  | **4,394** |  | **3,639** |  | **4,394** |  | **3,639** |  | **4,394** |  |
| Number of subjects | **7,786** |  | **12,880** |  | **7,786** |  | **12,880** |  | **7,786** |  | **12,880** |  |
| **PH-assumption test** | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  |
| \*p<0.05 \*\*p<0.01 \*\*\*p<0.001  PSM, propensity score matching; PIM, potentially inappropriate medication; HR, hazard ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug; PH, proportional hazard  aAdjusted for age, gender, socioeconomic status (income), living situation, morbidity (the use of antidiabetics, psychotropics, cardiovascular medications, opioids and nonsteroidal anti-inflammatory drugs) and excessive polypharmacy.  bAt the start of the follow-up (1 Jan 2002)  cYear 2000  dAt the washout period (years 2000–2001) | | | | | | | | | | | | |

**Online Resource 3.** Table 2: Associated risk of mortality within 1, 3 and 6 months after the initiation of PIM use in time-varying cox proportional hazards regression stratified by age.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **<75 years** |  | **≥75 years** |  | **<75 years** |  | **≥75 years** |  | **<75 years** |  | **≥75 years** |  |
|  | **1 month** |  | **1 month** |  | **3 months** |  | **3 months** |  | **6 months** |  | **6 months** |  |
|  | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** | **PSM adjusted HR** | **95% CI** |
| **The first PIM use perioda** |  |  |  |  |  |  |  |  |  |  |  |  |
| Non-users | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| PIM-users | 4.62\*\*\* | (3.52–6.06) | 3.06\*\*\* | (2.37–3.96) | 4.32\*\*\* | (3.71–5.03) | 2.69\*\*\* | (2.33–3.11) | 2.88\*\*\* | (2.58–3.22) | 1.90\*\*\* | (1.72–2.11) |
| Number of deaths | **1,809** |  | **2,538** |  | **1,941** |  | **2,677** |  | **2,145** |  | **2,921** |  |
| **PH-assumption test** | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  |
| **PIM use (all exposure periods)** |  |  |  |  |  |  |  |  |  |  |  |  |
| Non-users | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| PIM-users | 1.71\*\*\* | (1.46–1.99) | 1.18\* | (1.01–1.38) | 2.20\*\*\* | (2.00–2.42) | 1.35\*\*\* | (1.22–1.48) | 2.37\*\*\* | (2.18–2.58) | 1.49\*\*\* | (1.37–1.62) |
| **Gender** |  |  |  |  |  |  |  |  |  |  |  |  |
| Male | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| Female | 0.46\*\*\* | (0.43–0.49) | 0.65\*\*\* | (0.61–0.69) | 0.46\*\*\* | (0.43–0.49) | 0.65\*\*\* | (0.61–0.70) | 0.46\*\*\* | (0.43–0.49) | 0.65\*\*\* | (0.61–0.70) |
| **Socioeconomic status (income)c** |  |  |  |  |  |  |  |  |  |  |  |  |
| <9,999 € | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  | 1.00 (reference) |  |
| 10,000–19,999 € | 0.83\*\*\* | (0.77–0.91) | 0.99 | (0.92–1.06) | 0.84\*\*\* | (0.77–0.91) | 0.99 | (0.92–1.06) | 0.84\*\*\* | (0.77–0.91) | 0.99 | (0.92–1.06) |
| 20,000–29,999 € | 0.68\*\*\* | (0.59–0.78) | 0.93 | (0.82–1.05) | 0.68\*\*\* | (0.59–0.78) | 0.93 | (0.82–1.05) | 0.68\*\*\* | (0.59–0.78) | 0.93 | (0.82–1.05) |
| >30,000 € | 0.56\*\*\* | (0.46–0.68) | 0.84\* | (0.70–1.00) | 0.56\*\*\* | (0.46–0.69) | 0.84 | (0.70–1.00) | 0.56\*\*\* | (0.46–0.68) | 0.84 | (0.70–1.00) |
| **Living aloneb** | 1.17\*\*\* | (1.08–1.27) | 1.13\*\*\* | (1.06–1.21) | 1.18\*\*\* | (1.08–1.28) | 1.13\*\*\* | (1.06–1.21) | 1.18\*\*\* | (1.09–1.28) | 1.13\*\*\* | (1.06–1.21) |
| **Medication usec** |  |  |  |  |  |  |  |  |  |  |  |  |
| Antidiabetics | 1.64\*\*\* | (1.48–1.82) | 1.40\*\*\* | (1.27–1.54) | 1.61\*\*\* | (1.45–1.79) | 1.39\*\*\* | (1.26–1.53) | 1.60\*\*\* | (1.44–1.78) | 1.39\*\*\* | (1.26–1.53) |
| Psychotropics | 1.25\*\*\* | (1.15–1.37) | 1.20\*\*\* | (1.12–1.28) | 1.23\*\*\* | (1.13–1.34) | 1.20\*\*\* | (1.12–1.28) | 1.22\*\*\* | (1.12–1.33) | 1.19\*\*\* | (1.12–1.27) |
| Cardiovascular medications | 1.30\*\*\* | (1.20–1.41) | 1.30\*\*\* | (1.21–1.40) | 1.29\*\*\* | (1.20–1.40) | 1.30\*\*\* | (1.21–1.40) | 1.29\*\*\* | (1.20–1.40) | 1.30\*\*\* | (1.21–1.40) |
| Opioids | 1.39\*\*\* | (1.21–1.60) | 1.31\*\*\* | (1.17–1.47) | 1.38\*\*\* | (1.20–1.59) | 1.31\*\*\* | (1.17–1.47) | 1.38\*\*\* | (1.20–1.59) | 1.31\*\*\* | (1.17–1.47) |
| NSAIDs | 0.85\*\*\* | (0.79–0.92) | 0.90\*\*\* | (0.84–0.95) | 0.85\*\*\* | (0.79–0.91) | 0.89\*\*\* | (0.84–0.95) | 0.84\*\*\* | (0.78–0.91) | 0.89\*\*\* | (0.84–0.95) |
| **Excessive polypharmacyc** | 1.62\*\*\* | (1.46–1.79) | 1.43\*\*\* | (1.32–1.54) | 1.59\*\*\* | (1.43–1.76) | 1.42\*\*\* | (1.32–1.54) | 1.57\*\*\* | (1.42–1.74) | 1.42\*\*\* | (1.32–1.54) |
| Number of deaths | **3,427** |  | **4,606** |  | **3,427** |  | **4,606** |  | **3,427** |  | **4,606** |  |
| Number of subjects | **12,360** |  | **8,306** |  | **12,360** |  | **8,306** |  | **12,360** |  | **8,306** |  |
| **PH-assumption test** | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  | **<0.001** |  |
| \*p<0.05 \*\*p<0.01 \*\*\*p<0.001  PSM, propensity score matching; PIM, potentially inappropriate medication; HR, hazard ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug; PH, proportional hazard  aAdjusted for age, gender, socioeconomic status (income), living situation, morbidity (the use of antidiabetics, psychotropics, cardiovascular medications, opioids and nonsteroidal anti-inflammatory drugs) and excessive polypharmacy.  bYear 2000  cAt the washout period (years 2000–2001) | | | | | | | | | | | | |