**Online Supplemental Files**

**Supplemental Table S1. Distribution of medical conditions potential treated by gabapentinoid in osteoarthritis and matched non-osteoarthritis cohort**

$Medical conditions were recorded within 3 years prior to the index date

|  |  |  |
| --- | --- | --- |
|  | **Osteoarthritis cohort**  **(N=215,357)** | **Matched non-osteoarthritis cohort‡**  **(N=215,357)** |
| **Having any of medical conditions$ below, n (%)** | **34,069 (15.82)** | **30,524 (14.17)** |
| **Neuropathic Pain, n (%)** | **18,489 (8.59)** | **18,105 (8.41)** |
| **Menopause, n (%)** | **6,277 (2.91)** | **3,960 (1.84)** |
| **Cancer or Metastatic tumour, n (%)** | **4,015 (1.86)** | **3,981 (1.85)** |
| **Migraine, n (%)** | **3,485 (1.62)** | **2,627 (1.22)** |
| **Epilepsy, n (%)** | **1,987 (0.92)** | **1,597 (0.74)** |
| **Panic Attack, n (%)** | **1,384 (0.64)** | **1,119 (0.52)** |
| **Restless Legs Syndrome, n (%)** | **1,040 (0.48)** | **688 (0.32)** |
| **Fibromyalgia, n (%)** | **913 (0.42)** | **469 (0.22)** |
| **Bipolar Disorder, n (%)** | **348 (0.16)** | **295 (0.14)** |
| **Generalised Anxiety, n (%)** | **253 (0.12)** | **212 (0.10)** |
| **Complex Regional Pain Syndrome, n (%)** | **64 (0.03)** | **30 (0.01)** |
| **Alcohol Withdrawal Syndrome, n (%)** | **115 (0.05)** | **105 (0.05)** |
| **Attention Deficit Disorder, n (%)** | **14 (0.01)** | **9 (0.00)** |

**Supplemental Table S2. Relative incidence of first gabapentinoid prescription among diagnosed osteoarthritis patients, by having medical conditions potentially treated by ganabpentinoid**

‡ Matched 1:1 by sex, age group, region/country, GP practice, and year of diagnosis

¶ The distribution of medical conditions in OA and non-OA cohort was presented in Supplemental Table S1.

IRR Incidence rate ratio

n/person-year = number of patients with first gabapentinoid / total person-years of follow-up

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Osteoarthritis cohort** | | **Matched non-osteoarthritis cohort‡** | | **IRR (95% CI)** |
| **n** | **person-years** | **n** | **person-years** |
| **Having any of following medical conditions**¶ | **Yes** | **8,573** | **325,827** | **2,599** | **240,387** | **2.43 (2.33 to 2.54)** |
| **No** | **18,801** | **1,413,329** | **6,663** | **1,515,796** | **3.03 (2.94 to 3.11)** |

**Supplemental Table-S3**. Rate of gabapentinoid-opioid co-prescription events (±28-day window) among incident gabapentin users by opioid strength

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| Overall | 3·30 | (3·29 to 3·31) | 1·93 | (1·92 to 1·94) | 0·50 | (0·50 to 0·51) | 0·28 | (0·27 to 0·28) | 0·60 | (0·59 to 0·60) | 0·31 | (0·31 to 0·32) |
| Sex: |  |  |  |  |  |  |  |  |  |  |  |  |
| Male | 3·74 | (3·71 to 3·76) | 2·39 | (2·36 to 2·42) | 0·43 | (0·42 to 0·44) | 0·21 | (0·21 to 0·22) | 0·59 | (0·58 to 0·60) | 0·31 | (0·30 to 0·32) |
| Female | 3·13 | (3·11 to 3·14) | 1·79 | (1·78 to 1·81) | 0·53 | (0·53 to 0·54) | 0·29 | (0·29 to 0·30) | 0·60 | (0·60 to 0·61) | 0·32 | (0·31 to 0·32) |
| Age, years†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 40-44 | 6·22 | (6·10 to 6·35) | 4·82 | (4·67 to 4·96) | 0·79 | (0·75 to 0·84) | 0·33 | (0·29 to 0·37) | 0·27 | (0·25 to 0·30) | 0·19 | (0·17 to 0·22) |
| 45-54 | 4·91 | (4·88 to 4·95) | 3·59 | (3·54 to 3·64) | 0·48 | (0·47 to 0·49) | 0·36 | (0·34 to 0·38) | 0·50 | (0·49 to 0·51) | 0·32 | (0·31 to 0·34) |
| 55-64 | 3·72 | (3·69 to 3·74) | 1·89 | (1·87 to 1·92) | 0·42 | (0·41 to 0·42) | 0·22 | (0·21 to 0·23) | 0·54 | (0·53 to 0·55) | 0·29 | (0·28 to 0·30) |
| 65-74 | 2·92 | (2·90 to 2·94) | 2·03 | (2·00 to 2·06) | 0·43 | (0·43 to 0·44) | 0·30 | (0·29 to 0·31) | 0·58 | (0·58 to 0·59) | 0·35 | (0·34 to 0·36) |
| 75-84 | 2·43 | (2·41 to 2·45) | 1·56 | (1·53 to 1·59) | 0·60 | (0·59 to 0·61) | 0·37 | (0·36 to 0·38) | 0·69 | (0·68 to 0·70) | 0·45 | (0·44 to 0·47) |
| 85+ | 2·65 | (2·61 to 2·69) | 0·39 | (0·37 to 0·40) | 0·82 | (0·80 to 0·84) | 0·16 | (0·15 to 0·17) | 0·83 | (0·81 to 0·85) | 0·13 | (0·12 to 0·14) |
| Region/country: |  |  |  |  |  |  |  |  |  |  |  |  |
| North East | 4·32 | (4·23 to 4·40) | 2·06 | (1·98 to 2·13) | 0·89 | (0·85 to 0·92) | 0·24 | (0·22 to 0·27) | 0·20 | (0·19 to 0·22) | 0·12 | (0·10 to 0·13) |
| North West | 3·56 | (3·53 to 3·59) | 2·10 | (2·06 to 2·13) | 0·53 | (0·52 to 0·54) | 0·26 | (0·25 to 0·28) | 0·62 | (0·61 to 0·63) | 0·36 | (0·35 to 0·38) |
| Yorkshire & Humber | 3·70 | (3·63 to 3·76) | 2·42 | (2·34 to 2·51) | 0·44 | (0·42 to 0·46) | 0·18 | (0·16 to 0·21) | 0·69 | (0·66 to 0·72) | 0·32 | (0·29 to 0·35) |
| East Midlands | 2·82 | (2·75 to 2·88) | 1·56 | (1·48 to 1·65) | 0·46 | (0·44 to 0·49) | 0·31 | (0·28 to 0·35) | 0·56 | (0·54 to 0·60) | 0·31 | (0·27 to 0·35) |
| West Midlands | 2·94 | (2·91 to 2·97) | 1·82 | (1·77 to 1·86) | 0·41 | (0·39 to 0·42) | 0·28 | (0·26 to 0·30) | 0·59 | (0·58 to 0·61) | 0·40 | (0·38 to 0·42) |
| East of England | 2·31 | (2·27 to 2·35) | 1·56 | (1·51 to 1·61) | 0·40 | (0·38 to 0·41) | 0·24 | (0·22 to 0·26) | 0·64 | (0·62 to 0·66) | 0·32 | (0·29 to 0·34) |
| South West | 3·07 | (3·03 to 3·11) | 1·79 | (1·74 to 1·84) | 0·54 | (0·53 to 0·56) | 0·30 | (0·28 to 0·32) | 0·48 | (0·46 to 0·50) | 0·18 | (0·17 to 0·20) |
| South Central | 2·83 | (2·79 to 2·87) | 1·60 | (1·55 to 1·65) | 0·42 | (0·41 to 0·44) | 0·17 | (0·16 to 0·19) | 0·53 | (0·52 to 0·55) | 0·30 | (0·28 to 0·32) |
| London | 2·65 | (2·61 to 2·69) | 1·51 | (1·47 to 1·56) | 0·60 | (0·58 to 0·62) | 0·45 | (0·42 to 0·48) | 0·62 | (0·61 to 0·64) | 0·39 | (0·37 to 0·42) |
| South East Coast | 3·26 | (3·23 to 3·30) | 1·91 | (1·86 to 1·95) | 0·69 | (0·67 to 0·71) | 0·38 | (0·36 to 0·40) | 0·59 | (0·58 to 0·61) | 0·29 | (0·27 to 0·30) |
| Northern Ireland | 2·69 | (2·65 to 2·72) | 1·66 | (1·62 to 1·71) | 0·60 | (0·58 to 0·62) | 0·32 | (0·30 to 0·34) | 0·72 | (0·70 to 0·74) | 0·43 | (0·40 to 0·45) |
| Scotland | 3·34 | (3·31 to 3·37) | 1·84 | (1·81 to 1·87) | 0·35 | (0·34 to 0·36) | 0·17 | (0·16 to 0·18) | 0·41 | (0·40 to 0·42) | 0·18 | (0·17 to 0·19) |
| Wales | 4·56 | (4·52 to 4·59) | 2·53 | (2·49 to 2·57) | 0·49 | (0·48 to 0·50) | 0·32 | (0·31 to 0·33) | 0·8 | (0·79 to 0·82) | 0·40 | (0·38 to 0·41) |
| Calendar year†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 1995 | 0·33 | (0·24 to 0·45) | 0·08 | (0·03 to 0·17) | 0·48 | (0·36 to 0·62) | 0·00 | - | 1·06 | (0·89 to 1·26) | 0·03 | (0·00 to 0·10) |
| 1996 | 0·51 | (0·41 to 0·63) | 0·08 | (0·04 to 0·15) | 0·42 | (0·33 to 0·53) | 0·09 | (0·04 to 0·17) | 0·98 | (0·84 to 1·14) | 0·17 | (0·10 to 0·27) |
| 1997 | 1·07 | (0·92 to 1·24) | 0·24 | (0·17 to 0·32) | 0·81 | (0·68 to 0·96) | 0·01 | (0·00 to 0·04) | 1·27 | (1·11 to 1·46) | 0·30 | (0·23 to 0·39) |
| 1998 | 0·92 | (0·80 to 1·05) | 0·43 | (0·36 to 0·52) | 0·34 | (0·27 to 0·42) | 0·12 | (0·08 to 0·17) | 0·54 | (0·45 to 0·64) | 0·14 | (0·10 to 0·20) |
| 1999 | 1·07 | (0·97 to 1·16) | 0·29 | (0·23 to 0·36) | 0·39 | (0·34 to 0·45) | 0·24 | (0·19 to 0·31) | 0·61 | (0·54 to 0·69) | 0·30 | (0·24 to 0·38) |
| 2000 | 1·47 | (1·39 to 1·56) | 0·99 | (0·90 to 1·08) | 0·22 | (0·19 to 0·26) | 0·10 | (0·07 to 0·13) | 0·63 | (0·58 to 0·69) | 0·30 | (0·25 to 0·35) |
| 2001 | 2·22 | (2·13 to 2·30) | 1·91 | (1·80 to 2·03) | 0·50 | (0·46 to 0·54) | 0·41 | (0·36 to 0·46) | 0·82 | (0·77 to 0·88) | 0·48 | (0·42 to 0·54) |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| 2002 | 2·51 | (2·44 to 2·57) | 1·61 | (1·52 to 1·70) | 0·56 | (0·53 to 0·60) | 0·24 | (0·21 to 0·28) | 0·68 | (0·64 to 0·71) | 0·14 | (0·12 to 0·17) |
| 2003 | 2·48 | (2·43 to 2·53) | 1·42 | (1·36 to 1·48) | 0·35 | (0·33 to 0·37) | 0·23 | (0·20 to 0·25) | 0·74 | (0·71 to 0·77) | 0·39 | (0·36 to 0·42) |
| 2004 | 2·45 | (2·40 to 2·50) | 2·10 | (2·03 to 2·17) | 0·38 | (0·36 to 0·40) | 0·26 | (0·24 to 0·29) | 0·80 | (0·78 to 0·83) | 0·26 | (0·24 to 0·29) |
| 2005 | 2·69 | (2·65 to 2·73) | 1·99 | (1·93 to 2·05) | 0·38 | (0·36 to 0·39) | 0·30 | (0·27 to 0·32) | 0·64 | (0·62 to 0·66) | 0·48 | (0·45 to 0·51) |
| 2006 | 2·84 | (2·80 to 2·88) | 1·61 | (1·56 to 1·65) | 0·37 | (0·36 to 0·39) | 0·28 | (0·26 to 0·30) | 0·61 | (0·59 to 0·63) | 0·43 | (0·41 to 0·46) |
| 2007 | 3·10 | (3·06 to 3·14) | 1·81 | (1·76 to 1·85) | 0·35 | (0·34 to 0·36) | 0·33 | (0·31 to 0·35) | 0·62 | (0·61 to 0·64) | 0·38 | (0·36 to 0·40) |
| 2008 | 3·04 | (3·00 to 3·07) | 2·03 | (1·99 to 2·07) | 0·49 | (0·48 to 0·51) | 0·21 | (0·19 to 0·22) | 0·59 | (0·58 to 0·61) | 0·27 | (0·26 to 0·29) |
| 2009 | 3·35 | (3·31 to 3·38) | 2·53 | (2·49 to 2·58) | 0·47 | (0·46 to 0·48) | 0·28 | (0·27 to 0·30) | 0·56 | (0·54 to 0·57) | 0·34 | (0·32 to 0·36) |
| 2010 | 3·34 | (3·31 to 3·38) | 2·02 | (1·98 to 2·07) | 0·49 | (0·48 to 0·51) | 0·27 | (0·26 to 0·29) | 0·54 | (0·52 to 0·55) | 0·31 | (0·29 to 0·32) |
| 2011 | 3·44 | (3·40 to 3·47) | 1·89 | (1·85 to 1·93) | 0·55 | (0·53 to 0·56) | 0·24 | (0·23 to 0·26) | 0·46 | (0·44 to 0·47) | 0·19 | (0·18 to 0·20) |
| 2012 | 3·74 | (3·70 to 3·78) | 1·80 | (1·76 to 1·84) | 0·63 | (0·62 to 0·65) | 0·32 | (0·30 to 0·34) | 0·58 | (0·56 to 0·60) | 0·27 | (0·26 to 0·29) |
| 2013 | 3·96 | (3·91 to 4·00) | 1·82 | (1·77 to 1·87) | 0·56 | (0·54 to 0·58) | 0·27 | (0·25 to 0·28) | 0·58 | (0·57 to 0·60) | 0·33 | (0·31 to 0·35) |
| 2014 | 4·05 | (4·00 to 4·10) | 1·95 | (1·89 to 2·00) | 0·62 | (0·60 to 0·64) | 0·32 | (0·30 to 0·35) | 0·61 | (0·59 to 0·62) | 0·33 | (0·31 to 0·35) |
| 2015 | 4·45 | (4·39 to 4·52) | 2·25 | (2·17 to 2·32) | 0·67 | (0·64 to 0·69) | 0·31 | (0·28 to 0·34) | 0·58 | (0·56 to 0·60) | 0·26 | (0·23 to 0·28) |
| 2016 | 4·14 | (4·05 to 4·23) | 2·68 | (2·56 to 2·80) | 0·85 | (0·81 to 0·89) | 0·38 | (0·34 to 0·43) | 0·67 | (0·64 to 0·71) | 0·27 | (0·24 to 0·32) |
| 2017 | 5·68 | (5·48 to 5·90) | 3·29 | (3·06 to 3·53) | 1·03 | (0·95 to 1·13) | 0·66 | (0·56 to 0·77) | 0·86 | (0·78 to 0·94) | 0·59 | (0·49 to 0·70) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | | | | | |

**Supplemental Table-S4**. Rate of gabapentinoid-opioid co-prescription events (±28-day window) among incident gabapentin ***long-term users***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OA | | Non-OA | |
|  | Rate | 95% CI | Rate | 95% CI |
| Overall | 6·24 | (6·22 to 6·26) | 3·82 | (3·80 to 3·84) |
| Sex: |  |  |  |  |
| Male | 6·51 | (6·47 to 6·54) | 4·44 | (4·38 to 4·49) |
| Female | 6·12 | (6·10 to 6·14) | 3·63 | (3·60 to 3·66) |
| Age, years†: |  |  |  |  |
| 40-44 | 8·56 | (8·39 to 8·73) | 8·94 | (8·68 to 9·21) |
| 45-54 | 7·93 | (7·87 to 7·98) | 6·78 | (6·68 to 6·87) |
| 55-64 | 6·51 | (6·47 to 6·55) | 3·71 | (3·67 to 3·76) |
| 65-74 | 5·72 | (5·69 to 5·76) | 4·11 | (4·06 to 4·16) |
| 75-84 | 5·37 | (5·33 to 5·41) | 3·29 | (3·23 to 3·34) |
| 85+ | 5·80 | (5·71 to 5·88) | 0·78 | (0·75 to 0·81) |
| Region/country: |  |  |  |  |
| North East | 8·17 | (8·02 to 8·33) | 4·34 | (4·18 to 4·51) |
| North West | 6·52 | (6·47 to 6·57) | 3·94 | (3·87 to 4·00) |
| Yorkshire & Humber | 6·59 | (6·48 to 6·71) | 4·61 | (4·45 to 4·78) |
| East Midlands | 5·07 | (4·96 to 5·19) | 3·14 | (2·98 to 3·30) |
| West Midlands | 6·11 | (6·05 to 6·18) | 4·03 | (3·94 to 4·12) |
| East of England | 4·61 | (4·54 to 4·68) | 3·18 | (3·08 to 3·27) |
| South West | 5·84 | (5·76 to 5·91) | 3·31 | (3·21 to 3·40) |
| South Central | 5·38 | (5·31 to 5·45) | 3·16 | (3·07 to 3·25) |
| London | 5·48 | (5·41 to 5·56) | 3·11 | (3·02 to 3·20) |
| South East Coast | 6·35 | (6·28 to 6·41) | 3·85 | (3·76 to 3·94) |
| Northern Ireland | 5·49 | (5·42 to 5·56) | 3·37 | (3·29 to 3·46) |
| Scotland | 5·90 | (5·85 to 5·96) | 3·54 | (3·48 to 3·61) |
| Wales | 8·07 | (8·01 to 8·13) | 4·96 | (4·88 to 5·03) |
| Calendar year†: |  |  |  |  |
| 1995 | 1·81 | (1·58 to 2·06) | 0·14 | (0·06 to 0·27) |
| 1996 | 2·03 | (1·81 to 2·26) | 0·75 | (0·51 to 1·05) |
| 1997 | 2·94 | (2·69 to 3·22) | 0·63 | (0·51 to 0·77) |
| 1998 | 2·24 | (2·02 to 2·47) | 1·04 | (0·89 to 1·22) |
| 1999 | 2·50 | (2·33 to 2·68) | 0·84 | (0·72 to 0·98) |
| 2000 | 3·20 | (3·04 to 3·36) | 1·85 | (1·70 to 2·00) |
| 2001 | 4·40 | (4·26 to 4·54) | 3·83 | (3·63 to 4·04) |
| 2002 | 4·63 | (4·52 to 4·75) | 2·85 | (2·69 to 3·02) |
| 2003 | 4·64 | (4·55 to 4·73) | 3·15 | (3·03 to 3·27) |
| 2004 | 4·76 | (4·68 to 4·85) | 3·54 | (3·42 to 3·65) |
| 2005 | 5·49 | (5·42 to 5·57) | 4·66 | (4·54 to 4·78) |
| 2006 | 5·47 | (5·39 to 5·54) | 3·05 | (2·97 to 3·14) |
| 2007 | 5·81 | (5·74 to 5·87) | 3·60 | (3·52 to 3·68) |
| 2008 | 5·85 | (5·79 to 5·91) | 3·96 | (3·88 to 4·04) |
| 2009 | 6·21 | (6·14 to 6·27) | 4·82 | (4·74 to 4·91) |
| 2010 | 6·21 | (6·15 to 6·28) | 4·04 | (3·96 to 4·12) |
| 2011 | 6·68 | (6·62 to 6·75) | 3·58 | (3·51 to 3·66) |
| 2012 | 7·15 | (7·07 to 7·22) | 3·73 | (3·64 to 3·82) |
| 2013 | 7·75 | (7·67 to 7·84) | 3·83 | (3·73 to 3·93) |
| 2014 | 7·88 | (7·79 to 7·98) | 4·31 | (4·19 to 4·43) |
| 2015 | 8·00 | (7·89 to 8·12) | 4·34 | (4·19 to 4·50) |
| 2016 | 8·76 | (8·57 to 8·96) | 5·66 | (5·39 to 5·94) |
| 2017 | 10·43 | (9·95 to 10·93) | 6·36 | (5·83 to 6·92) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | |

**Supplemental Table-S5**. Rate of gabapentinoid-opioid co-prescription events (±28-day window) among incident gabapentin ***long-term users*** by strength of opioid

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| Overall | 5·14 | (5·12 to 5·16) | 3·21 | (3·19 to 3·24) | 0·75 | (0·74 to 0·76) | 0·44 | (0·43 to 0·45) | 0·90 | (0·89 to 0·91) | 0·50 | (0·49 to 0·51) |
| Sex: |  |  |  |  |  |  |  |  |  |  |  |  |
| Male | 5·51 | (5·48 to 5·55) | 3·89 | (3·84 to 3·95) | 0·61 | (0·60 to 0·62) | 0·34 | (0·32 to 0·35) | 0·86 | (0·85 to 0·88) | 0·49 | (0·47 to 0·50) |
| Female | 4·98 | (4·96 to 5·00) | 3·00 | (2·98 to 3·03) | 0·81 | (0·80 to 0·81) | 0·47 | (0·46 to 0·48) | 0·92 | (0·91 to 0·93) | 0·50 | (0·49 to 0·52) |
| Age, years†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 40-44 | 7·97 | (7·80 to 8·13) | 8·59 | (8·33 to 8·86) | 0·98 | (0·93 to 1·04) | 0·58 | (0·51 to 0·65) | 0·32 | (0·28 to 0·35) | 0·29 | (0·25 to 0·34) |
| 45-54 | 7·10 | (7·04 to 7·15) | 6·13 | (6·04 to 6·22) | 0·69 | (0·67 to 0·71) | 0·62 | (0·59 to 0·65) | 0·70 | (0·69 to 0·72) | 0·54 | (0·51 to 0·57) |
| 55-64 | 5·63 | (5·59 to 5·67) | 3·19 | (3·15 to 3·23) | 0·62 | (0·61 to 0·63) | 0·37 | (0·36 to 0·39) | 0·81 | (0·79 to 0·82) | 0·50 | (0·48 to 0·51) |
| 65-74 | 4·62 | (4·59 to 4·65) | 3·39 | (3·34 to 3·44) | 0·67 | (0·66 to 0·69) | 0·49 | (0·47 to 0·51) | 0·94 | (0·92 to 0·95) | 0·59 | (0·57 to 0·61) |
| 75-84 | 3·95 | (3·91 to 3·98) | 2·41 | (2·36 to 2·46) | 0·93 | (0·92 to 0·95) | 0·55 | (0·52 to 0·57) | 1·06 | (1·04 to 1·08) | 0·63 | (0·61 to 0·66) |
| 85+ | 3·99 | (3·92 to 4·06) | 0·53 | (0·51 to 0·56) | 1·17 | (1·13 to 1·20) | 0·16 | (0·15 to 0·18) | 1·28 | (1·24 to 1·31) | 0·18 | (0·16 to 0·19) |
| Region/country: |  |  |  |  |  |  |  |  |  |  |  |  |
| North East | 7·12 | (6·97 to 7·26) | 4·05 | (3·90 to 4·21) | 1·24 | (1·18 to 1·31) | 0·33 | (0·29 to 0·38) | 0·28 | (0·25 to 0·31) | 0·12 | (0·09 to 0·15) |
| North West | 5·34 | (5·30 to 5·39) | 3·25 | (3·20 to 3·31) | 0·78 | (0·76 to 0·80) | 0·41 | (0·39 to 0·43) | 0·94 | (0·92 to 0·96) | 0·59 | (0·56 to 0·61) |
| Yorkshire & Humber | 5·55 | (5·44 to 5·66) | 4·15 | (4·00 to 4·30) | 0·61 | (0·57 to 0·65) | 0·30 | (0·26 to 0·35) | 1·00 | (0·96 to 1·05) | 0·54 | (0·49 to 0·60) |
| East Midlands | 4·10 | (4·00 to 4·21) | 2·50 | (2·36 to 2·64) | 0·70 | (0·66 to 0·74) | 0·46 | (0·40 to 0·53) | 0·80 | (0·76 to 0·85) | 0·50 | (0·44 to 0·57) |
| West Midlands | 4·93 | (4·87 to 4·99) | 3·19 | (3·11 to 3·27) | 0·59 | (0·57 to 0·61) | 0·48 | (0·45 to 0·51) | 0·96 | (0·94 to 0·99) | 0·69 | (0·65 to 0·72) |
| East of England | 3·62 | (3·56 to 3·69) | 2·64 | (2·55 to 2·73) | 0·58 | (0·56 to 0·61) | 0·41 | (0·37 to 0·44) | 0·92 | (0·89 to 0·95) | 0·50 | (0·46 to 0·54) |
| South West | 4·91 | (4·84 to 4·98) | 2·87 | (2·78 to 2·96) | 0·82 | (0·79 to 0·84) | 0·40 | (0·37 to 0·44) | 0·63 | (0·60 to 0·65) | 0·25 | (0·23 to 0·28) |
| South Central | 4·38 | (4·32 to 4·44) | 2·71 | (2·63 to 2·80) | 0·64 | (0·61 to 0·66) | 0·26 | (0·23 to 0·29) | 0·80 | (0·78 to 0·83) | 0·48 | (0·45 to 0·52) |
| London | 4·19 | (4·12 to 4·26) | 2·29 | (2·21 to 2·36) | 0·91 | (0·88 to 0·94) | 0·62 | (0·59 to 0·67) | 0·97 | (0·94 to 1·00) | 0·61 | (0·57 to 0·65) |
| South East Coast | 5·15 | (5·09 to 5·21) | 3·24 | (3·16 to 3·32) | 0·94 | (0·91 to 0·97) | 0·57 | (0·54 to 0·61) | 0·93 | (0·90 to 0·95) | 0·46 | (0·43 to 0·50) |
| Northern Ireland | 4·30 | (4·24 to 4·36) | 2·71 | (2·63 to 2·79) | 0·96 | (0·93 to 0·99) | 0·52 | (0·49 to 0·56) | 1·12 | (1·08 to 1·15) | 0·67 | (0·63 to 0·71) |
| Scotland | 5·16 | (5·11 to 5·21) | 3·17 | (3·11 to 3·23) | 0·53 | (0·51 to 0·55) | 0·28 | (0·27 to 0·30) | 0·63 | (0·61 to 0·65) | 0·30 | (0·28 to 0·31) |
| Wales | 6·82 | (6·76 to 6·87) | 4·20 | (4·14 to 4·27) | 0·73 | (0·71 to 0·75) | 0·55 | (0·52 to 0·57) | 1·16 | (1·14 to 1·18) | 0·58 | (0·56 to 0·61) |
| Calendar year†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 1995 | 0·34 | (0·24 to 0·46) | 0·10 | (0·04 to 0·22) | 0·48 | (0·37 to 0·62) | 0·00 | (0·00 to 0·00) | 1·07 | (0·90 to 1·27) | 0·03 | (0·00 to 0·12) |
| 1996 | 0·56 | (0·45 to 0·69) | 0·14 | (0·05 to 0·30) | 0·47 | (0·37 to 0·59) | 0·23 | (0·11 to 0·43) | 1·11 | (0·95 to 1·29) | 0·44 | (0·27 to 0·69) |
| 1997 | 1·10 | (0·95 to 1·28) | 0·28 | (0·20 to 0·38) | 0·84 | (0·70 to 0·99) | 0·01 | (0·00 to 0·05) | 1·31 | (1·14 to 1·50) | 0·39 | (0·29 to 0·50) |
| 1998 | 1·22 | (1·06 to 1·39) | 0·72 | (0·59 to 0·86) | 0·45 | (0·36 to 0·56) | 0·18 | (0·12 to 0·26) | 0·70 | (0·59 to 0·84) | 0·23 | (0·16 to 0·32) |
| 1999 | 1·50 | (1·37 to 1·64) | 0·36 | (0·28 to 0·45) | 0·55 | (0·47 to 0·63) | 0·33 | (0·25 to 0·42) | 0·85 | (0·75 to 0·96) | 0·40 | (0·32 to 0·50) |
| 2000 | 2·25 | (2·12 to 2·39) | 1·37 | (1·25 to 1·51) | 0·30 | (0·26 to 0·35) | 0·10 | (0·07 to 0·15) | 0·99 | (0·91 to 1·08) | 0·44 | (0·37 to 0·52) |
| 2001 | 3·12 | (3·01 to 3·24) | 2·94 | (2·77 to 3·13) | 0·67 | (0·62 to 0·73) | 0·64 | (0·56 to 0·73) | 1·08 | (1·01 to 1·15) | 0·73 | (0·64 to 0·82) |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| 2002 | 3·48 | (3·38 to 3·58) | 2·62 | (2·47 to 2·78) | 0·77 | (0·72 to 0·81) | 0·36 | (0·31 to 0·42) | 0·93 | (0·88 to 0·98) | 0·22 | (0·18 to 0·27) |
| 2003 | 3·58 | (3·50 to 3·66) | 2·49 | (2·38 to 2·60) | 0·46 | (0·43 to 0·49) | 0·35 | (0·31 to 0·39) | 1·03 | (0·98 to 1·07) | 0·51 | (0·47 to 0·57) |
| 2004 | 3·61 | (3·54 to 3·68) | 3·14 | (3·03 to 3·25) | 0·55 | (0·53 to 0·58) | 0·38 | (0·34 to 0·42) | 1·15 | (1·11 to 1·19) | 0·37 | (0·33 to 0·40) |
| 2005 | 4·33 | (4·27 to 4·40) | 3·56 | (3·46 to 3·67) | 0·60 | (0·58 to 0·63) | 0·53 | (0·49 to 0·57) | 1·01 | (0·98 to 1·04) | 0·86 | (0·81 to 0·91) |
| 2006 | 4·41 | (4·35 to 4·48) | 2·35 | (2·28 to 2·43) | 0·57 | (0·54 to 0·59) | 0·38 | (0·35 to 0·41) | 0·95 | (0·92 to 0·98) | 0·66 | (0·62 to 0·70) |
| 2007 | 4·87 | (4·81 to 4·93) | 2·91 | (2·84 to 2·99) | 0·55 | (0·53 to 0·57) | 0·54 | (0·51 to 0·58) | 0·99 | (0·96 to 1·02) | 0·62 | (0·58 to 0·65) |
| 2008 | 4·80 | (4·74 to 4·85) | 3·44 | (3·37 to 3·51) | 0·75 | (0·72 to 0·77) | 0·35 | (0·33 to 0·38) | 0·79 | (0·77 to 0·82) | 0·44 | (0·41 to 0·46) |
| 2009 | 5·23 | (5·18 to 5·29) | 4·20 | (4·12 to 4·28) | 0·87 | (0·85 to 0·90) | 0·44 | (0·41 to 0·46) | 0·81 | (0·79 to 0·84) | 0·53 | (0·50 to 0·55) |
| 2010 | 5·24 | (5·19 to 5·30) | 3·50 | (3·42 to 3·57) | 0·77 | (0·75 to 0·80) | 0·42 | (0·40 to 0·45) | 0·83 | (0·81 to 0·86) | 0·51 | (0·48 to 0·54) |
| 2011 | 5·68 | (5·62 to 5·74) | 3·16 | (3·09 to 3·23) | 0·83 | (0·80 to 0·85) | 0·38 | (0·35 to 0·40) | 0·71 | (0·69 to 0·73) | 0·29 | (0·27 to 0·32) |
| 2012 | 5·93 | (5·87 to 6·00) | 3·08 | (3·00 to 3·16) | 0·92 | (0·89 to 0·94) | 0·61 | (0·58 to 0·65) | 0·88 | (0·86 to 0·91) | 0·47 | (0·44 to 0·51) |
| 2013 | 6·55 | (6·47 to 6·62) | 3·25 | (3·16 to 3·34) | 0·93 | (0·91 to 0·96) | 0·45 | (0·42 to 0·48) | 0·92 | (0·89 to 0·95) | 0·45 | (0·42 to 0·48) |
| 2014 | 6·58 | (6·50 to 6·67) | 3·55 | (3·44 to 3·66) | 0·95 | (0·92 to 0·98) | 0·52 | (0·48 to 0·57) | 0·96 | (0·93 to 0·99) | 0·57 | (0·53 to 0·62) |
| 2015 | 6·84 | (6·74 to 6·95) | 3·83 | (3·68 to 3·97) | 0·93 | (0·89 to 0·97) | 0·38 | (0·34 to 0·43) | 0·87 | (0·83 to 0·91) | 0·41 | (0·37 to 0·47) |
| 2016 | 6·93 | (6·75 to 7·10) | 4·85 | (4·61 to 5·11) | 1·38 | (1·30 to 1·46) | 0·64 | (0·55 to 0·74) | 1·10 | (1·03 to 1·17) | 0·44 | (0·37 to 0·52) |
| 2017 | 8·58 | (8·15 to 9·04) | 5·00 | (4·53 to 5·49) | 1·56 | (1·38 to 1·76) | 1·02 | (0·82 to 1·26) | 1·29 | (1·13 to 1·48) | 1·13 | (0·91 to 1·38) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | | | | | |

**Supplemental Table-S6**. Rate of gabapentinoid-opioid co-prescription events ***(±14-day window***) among incident gabapentin users with and without osteoarthritis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | OA | | | | Non-OA | | | |
|  | n | Person-years | Rate | 95% CI | n | Person-years | Rate | 95% CI |
| Overall | 382,837 | 106,195 | 3·61 | (3·59 to 3·62) | 92,798 | 44,440 | 2·09 | (2·07 to 2·10) |
| Sex: |  |  |  |  |  |  |  |  |
| Male | 119,848 | 30,291 | 3·96 | (3·93 to 3·98) | 25,489 | 10,198 | 2·50 | (2·47 to 2·53) |
| Female | 262,989 | 75,904 | 3·46 | (3·45 to 3·48) | 67,309 | 34,242 | 1·97 | (1·95 to 1·98) |
| Age, years†: |  |  |  |  |  |  |  |  |
| 40-44 | 9534 | 1,515 | 6·29 | (6·17 to 6·42) | 4,263 | 897 | 4·75 | (4·61 to 4·90) |
| 45-54 | 69,441 | 13,712 | 5·06 | (5·03 to 5·10) | 19,528 | 5,314 | 3·67 | (3·62 to 3·73) |
| 55-64 | 106,864 | 27,433 | 3·90 | (3·87 to 3·92) | 27,937 | 13,927 | 2·01 | (1·98 to 2·03) |
| 65-74 | 102,922 | 32,270 | 3·19 | (3·17 to 3·21) | 23,797 | 10,857 | 2·19 | (2·16 to 2·22) |
| 75-84 | 72,174 | 24,787 | 2·91 | (2·89 to 2·93) | 14,229 | 7,532 | 1·89 | (1·86 to 1·92) |
| 85+ | 21,902 | 6,479 | 3·38 | (3·34 to 3·43) | 3,044 | 5,913 | 0·51 | (0·50 to 0·53) |
| Region/country: |  |  |  |  |  |  |  |  |
| North East | 11,205 | 2,371 | 4·73 | (4·64 to 4·81) | 2,905 | 1,354 | 2·14 | (2·07 to 2·22) |
| North West | 68,724 | 17,573 | 3·91 | (3·88 to 3·94) | 15,311 | 6,646 | 2·30 | (2·27 to 2·34) |
| Yorkshire & Humber | 12,389 | 3,109 | 3·98 | (3·91 to 4·06) | 3,028 | 1,229 | 2·46 | (2·38 to 2·55) |
| East Midlands | 7,390 | 2,402 | 3·08 | (3·01 to 3·15) | 1,564 | 879 | 1·78 | (1·69 to 1·87) |
| West Midlands | 32,977 | 10,121 | 3·26 | (3·22 to 3·29) | 7,856 | 3,776 | 2·08 | (2·03 to 2·13) |
| East of England | 17,770 | 6,866 | 2·59 | (2·55 to 2·63) | 4,113 | 2,454 | 1·68 | (1·63 to 1·73) |
| South West | 23,849 | 7,143 | 3·34 | (3·30 to 3·38) | 5,018 | 2,659 | 1·89 | (1·84 to 1·94) |
| South Central | 21,730 | 7,118 | 3·05 | (3·01 to 3·09) | 4,664 | 2,767 | 1·69 | (1·64 to 1·73) |
| London | 19,832 | 6,479 | 3·06 | (3·02 to 3·10) | 4,837 | 2,652 | 1·82 | (1·77 to 1·88) |
| South East Coast | 31,663 | 8,709 | 3·64 | (3·60 to 3·68) | 7,461 | 3,586 | 2·08 | (2·03 to 2·13) |
| Northern Ireland | 23,293 | 7,610 | 3·06 | (3·02 to 3·10) | 5,825 | 3,145 | 1·85 | (1·80 to 1·90) |
| Scotland | 44,255 | 12,980 | 3·41 | (3·38 to 3·44) | 12,957 | 7,043 | 1·84 | (1·81 to 1·87) |
| Wales | 67,760 | 13,715 | 4·94 | (4·90 to 4·98) | 17,259 | 6,250 | 2·76 | (2·72 to 2·80) |
| Calendar year†: |  |  |  |  |  |  |  |  |
| 1995 | 186 | 124 | 1·51 | (1·30 to 1·74) | 4 | 75 | 0·05 | (0·01 to 0·14) |
| 1996 | 267 | 177 | 1·51 | (1·33 to 1·70) | 28 | 111 | 0·25 | (0·17 to 0·36) |
| 1997 | 392 | 167 | 2·34 | (2·12 to 2·59) | 61 | 189 | 0·32 | (0·25 to 0·41) |
| 1998 | 339 | 241 | 1·41 | (1·26 to 1·56) | 146 | 261 | 0·56 | (0·47 to 0·66) |
| 1999 | 717 | 466 | 1·54 | (1·43 to 1·66) | 142 | 268 | 0·53 | (0·45 to 0·63) |
| 2000 | 1,454 | 809 | 1·80 | (1·71 to 1·89) | 554 | 469 | 1·18 | (1·08 to 1·28) |
| 2001 | 3,473 | 1,247 | 2·79 | (2·69 to 2·88) | 1,308 | 587 | 2·23 | (2·11 to 2·35) |
| 2002 | 6,354 | 2,133 | 2·98 | (2·91 to 3·05) | 1,176 | 726 | 1·62 | (1·53 to 1·71) |
| 2003 | 9,594 | 3,332 | 2·88 | (2·82 to 2·94) | 2,495 | 1,486 | 1·68 | (1·61 to 1·75) |
| 2004 | 11,776 | 4,097 | 2·87 | (2·82 to 2·93) | 3,464 | 1,606 | 2·16 | (2·09 to 2·23) |
| 2005 | 18,905 | 6,306 | 3·00 | (2·96 to 3·04) | 5,103 | 2,196 | 2·32 | (2·26 to 2·39) |
| 2006 | 20,662 | 6,616 | 3·12 | (3·08 to 3·17) | 5,240 | 2,798 | 1·87 | (1·82 to 1·92) |
| 2007 | 27,959 | 8,364 | 3·34 | (3·30 to 3·38) | 7,132 | 3,501 | 2·04 | (1·99 to 2·09) |
| 2008 | 32,935 | 9,671 | 3·41 | (3·37 to 3·44) | 9,864 | 4,660 | 2·12 | (2·08 to 2·16) |
| 2009 | 36,758 | 10,203 | 3·60 | (3·57 to 3·64) | 12,134 | 4,521 | 2·68 | (2·64 to 2·73) |
| 2010 | 37,990 | 10,639 | 3·57 | (3·53 to 3·61) | 9,741 | 4,473 | 2·18 | (2·13 to 2·22) |
| 2011 | 39,665 | 10,765 | 3·68 | (3·65 to 3·72) | 8,868 | 4,561 | 1·94 | (1·90 to 1·99) |
| 2012 | 37,303 | 9,085 | 4·11 | (4·06 to 4·15) | 7,673 | 3,952 | 1·94 | (1·90 to 1·99) |
| 2013 | 34,313 | 8,123 | 4·22 | (4·18 to 4·27) | 6,355 | 3,198 | 1·99 | (1·94 to 2·04) |
| 2014 | 29,606 | 6,832 | 4·33 | (4·28 to 4·38) | 5,062 | 2,375 | 2·13 | (2·07 to 2·19) |
| 2015 | 20,342 | 4,343 | 4·68 | (4·62 to 4·75) | 3,435 | 1,474 | 2·33 | (2·25 to 2·41) |
| 2016 | 8,874 | 1,952 | 4·55 | (4·45 to 4·64) | 1,998 | 720 | 2·77 | (2·65 to 2·90) |
| 2017 | 2,973 | 504 | 5·90 | (5·69 to 6·12) | 814 | 231 | 3·53 | (3·29 to 3·78) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | |

**Supplemental Table-S7**. Rate of gabapentinoid-opioid co-prescription events ***(±14-day window***) among incident gabapentin users ***by strength of opioid***

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid=weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| Overall | 2·97 | (2·96 to 2·98) | 1·75 | (1·74 to 1·77) | 0·41 | (0·40 to 0·41) | 0·23 | (0·22 to 0·23) | 0·47 | (0·47 to 0·47) | 0·25 | (0·24 to 0·25) |
| Sex: |  |  |  |  |  |  |  |  |  |  |  |  |
| Male | 3·37 | (3·35 to 3·39) | 2·20 | (2·17 to 2·23) | 0·34 | (0·34 to 0·35) | 0·17 | (0·17 to 0·18) | 0·46 | (0·46 to 0·47) | 0·25 | (0·24 to 0·26) |
| Female | 2·81 | (2·80 to 2·82) | 1·62 | (1·61 to 1·64) | 0·43 | (0·43 to 0·44) | 0·24 | (0·24 to 0·25) | 0·47 | (0·47 to 0·48) | 0·25 | (0·24 to 0·25) |
| Age, years†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 40-44 | 5·85 | (5·73 to 5·97) | 4·55 | (4·42 to 4·70) | 0·68 | (0·64 to 0·73) | 0·28 | (0·24 to 0·31) | 0·22 | (0·20 to 0·25) | 0·14 | (0·11 to 0·16) |
| 45-54 | 4·54 | (4·51 to 4·58) | 3·33 | (3·29 to 3·38) | 0·40 | (0·39 to 0·41) | 0·31 | (0·29 to 0·32) | 0·39 | (0·38 to 0·40) | 0·25 | (0·24 to 0·27) |
| 55-64 | 3·38 | (3·36 to 3·40) | 1·73 | (1·71 to 1·75) | 0·34 | (0·33 to 0·34) | 0·18 | (0·17 to 0·19) | 0·44 | (0·43 to 0·45) | 0·24 | (0·23 to 0·25) |
| 65-74 | 2·59 | (2·58 to 2·61) | 1·81 | (1·78 to 1·84) | 0·34 | (0·34 to 0·35) | 0·24 | (0·23 to 0·25) | 0·46 | (0·45 to 0·46) | 0·28 | (0·27 to 0·29) |
| 75-84 | 2·13 | (2·11 to 2·14) | 1·38 | (1·35 to 1·40) | 0·48 | (0·47 to 0·49) | 0·31 | (0·30 to 0·32) | 0·54 | (0·53 to 0·55) | 0·34 | (0·33 to 0·36) |
| 85+ | 2·34 | (2·30 to 2·38) | 0·34 | (0·33 to 0·36) | 0·67 | (0·65 to 0·69) | 0·12 | (0·11 to 0·13) | 0·65 | (0·63 to 0·67) | 0·10 | (0·09 to 0·11) |
| Region/country |  |  |  |  |  |  |  |  |  |  |  |  |
| North East | 4·03 | (3·95 to 4·11) | 1·94 | (1·87 to 2·02) | 0·76 | (0·72 to 0·79) | 0·18 | (0·16 to 0·21) | 0·16 | (0·14 to 0·18) | 0·09 | (0·08 to 0·11) |
| North West | 3·23 | (3·20 to 3·26) | 1·94 | (1·90 to 1·97) | 0·43 | (0·42 to 0·44) | 0·21 | (0·20 to 0·22) | 0·50 | (0·49 to 0·51) | 0·30 | (0·28 to 0·31) |
| Yorkshire & Humber | 3·34 | (3·28 to 3·41) | 2·23 | (2·14 to 2·31) | 0·35 | (0·33 to 0·37) | 0·14 | (0·12 to 0·17) | 0·55 | (0·53 to 0·58) | 0·25 | (0·22 to 0·28) |
| East Midlands | 2·50 | (2·44 to 2·57) | 1·41 | (1·33 to 1·49) | 0·37 | (0·34 to 0·39) | 0·26 | (0·23 to 0·30) | 0·45 | (0·42 to 0·48) | 0·26 | (0·23 to 0·29) |
| West Midlands | 2·63 | (2·60 to 2·67) | 1·66 | (1·61 to 1·70) | 0·32 | (0·31 to 0·33) | 0·24 | (0·23 to 0·26) | 0·47 | (0·46 to 0·49) | 0·32 | (0·30 to 0·34) |
| East of England | 2·03 | (2·00 to 2·06) | 1·40 | (1·35 to 1·45) | 0·30 | (0·29 to 0·31) | 0·20 | (0·18 to 0·21) | 0·49 | (0·47 to 0·51) | 0·24 | (0·22 to 0·26) |
| South West | 2·74 | (2·70 to 2·78) | 1·60 | (1·55 to 1·65) | 0·44 | (0·43 to 0·46) | 0·25 | (0·23 to 0·27) | 0·39 | (0·37 to 0·40) | 0·14 | (0·12 to 0·15) |
| South Central | 2·49 | (2·46 to 2·53) | 1·44 | (1·40 to 1·49) | 0·32 | (0·31 to 0·34) | 0·13 | (0·11 to 0·14) | 0·42 | (0·41 to 0·44) | 0·24 | (0·22 to 0·26) |
| London | 2·34 | (2·30 to 2·38) | 1·34 | (1·29 to 1·38) | 0·50 | (0·48 to 0·51) | 0·37 | (0·35 to 0·40) | 0·47 | (0·46 to 0·49) | 0·30 | (0·28 to 0·32) |
| South East Coast | 2·91 | (2·88 to 2·95) | 1·71 | (1·67 to 1·76) | 0·58 | (0·56 to 0·60) | 0·33 | (0·31 to 0·34) | 0·45 | (0·44 to 0·47) | 0·23 | (0·21 to 0·25) |
| Northern Ireland | 2·39 | (2·36 to 2·42) | 1·49 | (1·45 to 1·53) | 0·48 | (0·46 to 0·49) | 0·25 | (0·24 to 0·27) | 0·56 | (0·55 to 0·58) | 0·33 | (0·31 to 0·35) |
| Scotland | 2·98 | (2·95 to 3·01) | 1·64 | (1·61 to 1·67) | 0·27 | (0·27 to 0·28) | 0·14 | (0·13 to 0·15) | 0·33 | (0·32 to 0·34) | 0·14 | (0·13 to 0·15) |
| Wales | 4·18 | (4·15 to 4·22) | 2·34 | (2·30 to 2·38) | 0·40 | (0·39 to 0·41) | 0·27 | (0·26 to 0·28) | 0·62 | (0·61 to 0·64) | 0·30 | (0·29 to 0·32) |
| Calendar year†: |  |  |  |  |  |  |  |  |  |  |  |  |
| 1995 | 0·23 | (0·15 to 0·33) | 0·04 | (0·01 to 0·12) | 0·41 | (0·31 to 0·54) | 0·00 | - | 0·89 | (0·73 to 1·07) | 0·01 | (0·00 to 0·07) |
| 1996 | 0·40 | (0·31 to 0·50) | 0·07 | (0·03 to 0·14) | 0·30 | (0·22 to 0·39) | 0·05 | (0·02 to 0·12) | 0·87 | (0·74 to 1·02) | 0·13 | (0·08 to 0·22) |
| 1997 | 0·87 | (0·74 to 1·03) | 0·16 | (0·11 to 0·23) | 0·62 | (0·50 to 0·75) | 0·01 | (0·00 to 0·03) | 1·00 | (0·85 to 1·16) | 0·17 | (0·12 to 0·24) |
| 1998 | 0·78 | (0·67 to 0·90) | 0·39 | (0·32 to 0·47) | 0·28 | (0·22 to 0·35) | 0·08 | (0·05 to 0·12) | 0·41 | (0·34 to 0·50) | 0·13 | (0·09 to 0·18) |

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid=weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| 1999 | 0·95 | (0·87 to 1·05) | 0·22 | (0·16 to 0·28) | 0·28 | (0·23 to 0·33) | 0·15 | (0·11 to 0·21) | 0·48 | (0·42 to 0·55) | 0·25 | (0·19 to 0·31) |
| 2000 | 1·25 | (1·17 to 1·33) | 0·89 | (0·81 to 0·98) | 0·18 | (0·16 to 0·22) | 0·07 | (0·04 to 0·09) | 0·52 | (0·47 to 0·57) | 0·26 | (0·21 to 0·31) |
| 2001 | 1·97 | (1·90 to 2·05) | 1·71 | (1·61 to 1·82) | 0·40 | (0·37 to 0·44) | 0·35 | (0·30 to 0·40) | 0·64 | (0·59 to 0·68) | 0·38 | (0·33 to 0·44) |
| 2002 | 2·26 | (2·20 to 2·33) | 1·49 | (1·40 to 1·58) | 0·45 | (0·43 to 0·48) | 0·18 | (0·15 to 0·21) | 0·54 | (0·51 to 0·58) | 0·11 | (0·08 to 0·13) |
| 2003 | 2·23 | (2·18 to 2·28) | 1·29 | (1·23 to 1·35) | 0·26 | (0·24 to 0·28) | 0·18 | (0·16 to 0·20) | 0·59 | (0·56 to 0·61) | 0·29 | (0·27 to 0·32) |
| 2004 | 2·17 | (2·12 to 2·22) | 1·9 | (1·83 to 1·97) | 0·31 | (0·29 to 0·33) | 0·22 | (0·20 to 0·25) | 0·66 | (0·64 to 0·69) | 0·23 | (0·20 to 0·25) |
| 2005 | 2·38 | (2·34 to 2·42) | 1·79 | (1·74 to 1·85) | 0·31 | (0·30 to 0·32) | 0·25 | (0·23 to 0·27) | 0·49 | (0·47 to 0·51) | 0·37 | (0·34 to 0·39) |
| 2006 | 2·53 | (2·49 to 2·56) | 1·43 | (1·39 to 1·48) | 0·30 | (0·28 to 0·31) | 0·23 | (0·21 to 0·24) | 0·49 | (0·47 to 0·50) | 0·36 | (0·34 to 0·39) |
| 2007 | 2·83 | (2·79 to 2·86) | 1·66 | (1·62 to 1·70) | 0·28 | (0·27 to 0·30) | 0·29 | (0·28 to 0·31) | 0·49 | (0·48 to 0·51) | 0·32 | (0·30 to 0·34) |
| 2008 | 2·75 | (2·71 to 2·78) | 1·85 | (1·81 to 1·89) | 0·41 | (0·40 to 0·42) | 0·17 | (0·16 to 0·18) | 0·47 | (0·45 to 0·48) | 0·20 | (0·19 to 0·22) |
| 2009 | 3·03 | (2·99 to 3·06) | 2·33 | (2·29 to 2·37) | 0·38 | (0·36 to 0·39) | 0·23 | (0·22 to 0·25) | 0·44 | (0·43 to 0·45) | 0·26 | (0·25 to 0·28) |
| 2010 | 3·03 | (3·00 to 3·06) | 1·88 | (1·84 to 1·92) | 0·40 | (0·39 to 0·41) | 0·22 | (0·21 to 0·24) | 0·43 | (0·41 to 0·44) | 0·24 | (0·23 to 0·26) |
| 2011 | 3·10 | (3·07 to 3·13) | 1·71 | (1·67 to 1·75) | 0·45 | (0·44 to 0·46) | 0·20 | (0·19 to 0·21) | 0·36 | (0·35 to 0·37) | 0·15 | (0·14 to 0·16) |
| 2012 | 3·39 | (3·35 to 3·43) | 1·64 | (1·60 to 1·68) | 0·52 | (0·51 to 0·54) | 0·26 | (0·25 to 0·28) | 0·45 | (0·44 to 0·47) | 0·21 | (0·20 to 0·22) |
| 2013 | 3·57 | (3·53 to 3·61) | 1·63 | (1·59 to 1·68) | 0·45 | (0·44 to 0·46) | 0·21 | (0·20 to 0·23) | 0·46 | (0·45 to 0·48) | 0·26 | (0·24 to 0·28) |
| 2014 | 3·63 | (3·58 to 3·67) | 1·74 | (1·69 to 1·79) | 0·49 | (0·48 to 0·51) | 0·26 | (0·24 to 0·28) | 0·47 | (0·45 to 0·49) | 0·26 | (0·24 to 0·28) |
| 2015 | 4·00 | (3·94 to 4·06) | 2·04 | (1·97 to 2·12) | 0·54 | (0·52 to 0·56) | 0·26 | (0·23 to 0·28) | 0·45 | (0·43 to 0·47) | 0·19 | (0·16 to 0·21) |
| 2016 | 3·59 | (3·51 to 3·68) | 2·36 | (2·25 to 2·48) | 0·68 | (0·65 to 0·72) | 0·32 | (0·28 to 0·36) | 0·52 | (0·48 to 0·55) | 0·21 | (0·18 to 0·25) |
| 2017 | 4·83 | (4·64 to 5·03) | 2·83 | (2·62 to 3·06) | 0·79 | (0·72 to 0·88) | 0·54 | (0·45 to 0·64) | 0·65 | (0·58 to 0·72) | 0·43 | (0·35 to 0·53) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | | | | | |

**Supplemental Table-S8**. Rate of gabapentinoid-opioid co-prescription events ***(±14-day window***) among incident gabapentin ***long-term users***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OA | | Non-OA | |
|  | Rate | 95% CI | Rate | 95% CI |
| Overall | 5·59 | (5·58 to 5·61) | 3·46 | (3·44 to 3·49) |
| Sex: |  |  |  |  |
| Male | 5·85 | (5·81 to 5·88) | 4·07 | (4·02 to 4·12) |
| Female | 5·49 | (5·46 to 5·51) | 3·28 | (3·25 to 3·30) |
| Age, years†: |  |  |  |  |
| 40-44 | 8·07 | (7·90 to 8·24) | 8·40 | (8·14 to 8·66) |
| 45-54 | 7·32 | (7·26 to 7·38) | 6·40 | (6·31 to 6·49) |
| 55-64 | 5·91 | (5·87 to 5·95) | 3·38 | (3·34 to 3·42) |
| 65-74 | 5·06 | (5·03 to 5·09) | 3·65 | (3·60 to 3·70) |
| 75-84 | 4·67 | (4·64 to 4·71) | 2·87 | (2·82 to 2·93) |
| 85+ | 5·11 | (5·04 to 5·19) | 0·69 | (0·66 to 0·72) |
| Region/country: |  |  |  |  |
| North East | 7·63 | (7·47 to 7·78) | 4·12 | (3·96 to 4·28) |
| North West | 5·89 | (5·84 to 5·93) | 3·61 | (3·55 to 3·68) |
| Yorkshire & Humber | 5·96 | (5·85 to 6·07) | 4·24 | (4·08 to 4·39) |
| East Midlands | 4·50 | (4·39 to 4·62) | 2·87 | (2·71 to 3·02) |
| West Midlands | 5·47 | (5·41 to 5·54) | 3·66 | (3·57 to 3·74) |
| East of England | 4·00 | (3·94 to 4·07) | 2·83 | (2·74 to 2·92) |
| South West | 5·21 | (5·14 to 5·28) | 2·94 | (2·85 to 3·03) |
| South Central | 4·74 | (4·67 to 4·81) | 2·83 | (2·75 to 2·92) |
| London | 4·84 | (4·77 to 4·92) | 2·75 | (2·67 to 2·84) |
| South East Coast | 5·65 | (5·58 to 5·71) | 3·49 | (3·41 to 3·57) |
| Northern Ireland | 4·89 | (4·82 to 4·95) | 3·00 | (2·91 to 3·08) |
| Scotland | 5·28 | (5·23 to 5·34) | 3·17 | (3·11 to 3·23) |
| Wales | 7·36 | (7·30 to 7·41) | 4·57 | (4·50 to 4·64) |
| Calendar year†: |  |  |  |  |
| 1995 | 1·52 | (1·31 to 1·76) | 0·05 | (0·01 to 0·14) |
| 1996 | 1·68 | (1·48 to 1·90) | 0·58 | (0·38 to 0·86) |
| 1997 | 2·41 | (2·18 to 2·67) | 0·39 | (0·29 to 0·50) |
| 1998 | 1·86 | (1·67 to 2·07) | 0·92 | (0·77 to 1·08) |
| 1999 | 2·16 | (2·00 to 2·33) | 0·67 | (0·56 to 0·79) |
| 2000 | 2·77 | (2·62 to 2·91) | 1·65 | (1·51 to 1·80) |
| 2001 | 3·85 | (3·72 to 3·99) | 3·61 | (3·41 to 3·82) |
| 2002 | 4·12 | (4·02 to 4·23) | 2·61 | (2·46 to 2·77) |
| 2003 | 4·13 | (4·04 to 4·21) | 2·83 | (2·72 to 2·95) |
| 2004 | 4·20 | (4·12 to 4·28) | 3·21 | (3·10 to 3·32) |
| 2005 | 4·84 | (4·77 to 4·91) | 4·18 | (4·07 to 4·30) |
| 2006 | 4·87 | (4·80 to 4·94) | 2·76 | (2·68 to 2·84) |
| 2007 | 5·27 | (5·21 to 5·33) | 3·31 | (3·24 to 3·40) |
| 2008 | 5·25 | (5·19 to 5·31) | 3·58 | (3·51 to 3·66) |
| 2009 | 5·86 | (5·80 to 5·92) | 4·41 | (4·33 to 4·49) |
| 2010 | 5·60 | (5·54 to 5·66) | 3·73 | (3·65 to 3·81) |
| 2011 | 6·04 | (5·98 to 6·10) | 3·25 | (3·18 to 3·32) |
| 2012 | 6·47 | (6·40 to 6·54) | 3·37 | (3·29 to 3·45) |
| 2013 | 6·99 | (6·91 to 7·07) | 3·46 | (3·37 to 3·55) |
| 2014 | 7·05 | (6·96 to 7·14) | 3·83 | (3·71 to 3·95) |
| 2015 | 7·20 | (7·09 to 7·31) | 3·96 | (3·81 to 4·11) |
| 2016 | 7·60 | (7·42 to 7·78) | 4·99 | (4·74 to 5·25) |
| 2017 | 9·01 | (8·56 to 9·47) | 5·57 | (5·08 to 6·10) |
| †At time of initial gabapentinoid prescription | | | | |

**Supplemental Table-S9**. Rate of gabapentinoid-opioid co-prescription events (±14-day window) among incident gabapentin ***long-term users*** by strength of opioid

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | |
| Overall | 4·64 | (4·62 to 4·66) | 2·93 | (2·91 to 2·95) | 0·61 | (0·60 to 0·62) | 0·37 | (0·36 to 0·37) | 0·71 | (0·71 to 0·72) | 0·40 | (0·39 to 0·41) | |
| Sex: |  |  |  |  |  |  |  |  |  |  |  |  | |
| Male | 4·98 | (4·95 to 5·02) | 3·59 | (3·64 to 3·64) | 0·50 | (0·49 to 0·51) | 0·28 | (0·26 to 0·29) | 0·69 | (0·68 to 0·71) | 0·39 | (0·38 to 0·41) | |
| Female | 4·49 | (4·47 to 4·51) | 2·73 | (2·70 to 2·75) | 0·66 | (0·65 to 0·67) | 0·45 | (0·44 to 0·46) | 0·72 | (0·72 to 0·73) | 0·40 | (0·39 to 0·41) | |
| Age, years: |  |  |  |  |  |  |  |  |  |  |  |  | |
| 40-44 | 7·50 | (7·35 to 7·67) | 8·13 | (7·87 to 8·38) | 0·85 | (0·80 to 0·90) | 0·49 | (0·43 to 0·56) | 0·26 | (0·23 to 0·29) | 0·21 | (0·17 to 0·26) | |
| 45-54 | 6·57 | (6·52 to 6·63) | 5·70 | (5·61 to 5·79) | 0·58 | (0·56 to 0·60) | 0·54 | (0·51 to 0·57) | 0·56 | (0·54 to 0·58) | 0·43 | (0·40 to 0·45) | |
| 55-64 | 5·13 | (5·10 to 5·17) | 2·93 | (2·89 to 2·96) | 0·50 | (0·49 to 0·51) | 0·31 | (0·29 to 0·32) | 0·66 | (0·65 to 0·68) | 0·42 | (0·40 to 0·43) | |
| 65-74 | 4·11 | (4·08 to 4·14) | 3·03 | (2·99 to 3·08) | 0·54 | (0·53 to 0·55) | 0·41 | (0·39 to 0·42) | 0·74 | (0·72 to 0·75) | 0·46 | (0·44 to 0·48) | |
| 75-84 | 3·46 | (3·43 to 3·49) | 2·14 | (2·09 to 2·18) | 0·76 | (0·74 to 0·77) | 0·46 | (0·44 to o·48) | 0·82 | (0·81 to 0·84) | 0·49 | (0·47 to 0·51) | |
| 85+ | 3·56 | (3·50 to 3·62) | 0·48 | (0·46 to 0·51) | 0·97 | (0·93 to 1·00) | 0·14 | (0·13 to 0·15) | 0·99 | (0·95 to 1·02) | 0·14 | (0·12 to 0·15) | |
| Region/country: |  |  |  |  |  |  |  |  |  |  |  |  | |
| North East | 6·66 | (6·52 to 6·81) | 3·87 | (3·72 to 4·02) | 1·07 | (1·02 to 1·13) | 0·26 | (0·22 to 0·30) | 0·22 | (0·19 to 0·24) | 0·10 | (0·08 to 0·13) | |
| North West | 4·85 | (4·81 to 4·90) | 3·01 | (2·95 to 3·07) | 0·64 | (0·62 to 0·66) | 0·33 | (0·32 to 0·35) | 0·76 | (0·74 to 0·78) | 0·48 | (0·46 to 0·51) | |
| Yorkshire & Humber | 5·05 | (4·95 to 5·15) | 3·84 | (3·70 to 3·99) | 0·49 | (0·46 to 0·52) | 0·24 | (0·20 to 0·28) | 0·82 | (0·78 to 0·86) | 0·42 | (0·38 to 0·48) | |
| East Midlands | 3·66 | (3·56 to 3·76) | 2·27 | (2·14 to 2·41) | 0·56 | (0·52 to 0·60) | 0·39 | (0·34 to 0·45) | 0·66 | (0·61 to 0·70) | 0·44 | (0·38 to 0·51) | |
| West Midlands | 4·44 | (4·38 to 4·49) | 2·92 | (2·84 to 2·99) | 0·53 | (0·51 to 0·55) | 0·43 | (0·40 to 0·46) | 0·77 | (0·75 to 0·80) | 0·55 | (0·52 to 0·59) | |
| East of England | 3·20 | (3·14 to 3·26) | 2·36 | (2·28 to 2·45) | 0·44 | (0·42 to 0·47) | 0·33 | (0·30 to 0·37) | 0·71 | (0·68 to 0·74) | 0·39 | (0·36 to 0·43) | |
| South West | 4·41 | (4·34 to 4·47) | 2·56 | (2·48 to 2·64) | 0·66 | (0·64 to 0·69) | 0·33 | (0·31 to 0·37) | 0·50 | (0·48 to 0·52) | 0·19 | (0·17 to 0·21) | |
| South Central | 3·88 | (3·82 to 3·94) | 2·46 | (2·38 to 2·54) | 0·50 | (0·47 to 0·52) | 0·19 | (0·17 to 0·22) | 0·65 | (0·62 to 0·67) | 0·39 | (0·36 to 0·42) | |
| London | 3·73 | (3·67 to 3·79) | 2·03 | (1·96 to 2·10) | 0·77 | (0·74 to 0·80) | 0·54 | (0·50 to 0·58) | 0·75 | (0·72 to 0·77) | 0·47 | (0·44 to 0·51) | |
| South East Coast | 4·61 | (4·55 to 4·67) | 2·92 | (2·84 to 2·99) | 0·79 | (0·76 to 0·81) | 0·50 | (0·47 to 0·54) | 0·71 | (0·69 to 0·73) | 0·38 | (0·35 to 0·40) | |
| Northern Ireland | 3·83 | (3·77 to 3·89) | 2·42 | (2·35 to 2·49) | 0·77 | (0·74 to 0·79) | 0·42 | (0·39 to 0·45) | 0·87 | (0·85 to 0·90) | 0·52 | (0·48 to 0·55) | |
| Scotland | 4·62 | (4·57 to 4·67) | 2·83 | (2·78 to 2·89) | 0·42 | (0·41 to 0·44) | 0·23 | (0·22 to 0·25) | 0·51 | (0·49 to 0·53) | 0·24 | (0·22 to 0·25) | |
| Wales | 6·25 | (6·19 to 6·30) | 3·91 | (3·85 to 3·98) | 0·61 | (0·59 to 0·62) | 0·47 | (0·45 to 0·49) | 0·91 | (0·89 to 0·93) | 0·45 | (0·43 to 0·48) | |
| Calendar year†: |  |  |  |  |  |  |  |  |  |  |  |  | |
| 1995 | 0·23 | (0·15 to 0·33) | 0·04 | (0·01 to 0·12) | 0·42 | (0·31 to 0·55) | 0·00 | (0·00 to 0·00) | 0·90 | (0·74 to 1·09) | 0·01 | (0·00 to 0·07) | |
| 1996 | 0·43 | (0·33 to 0·54) | 0·12 | (0·04 to 0·27) | 0·33 | (0·25 to 0·43) | 0·14 | (0·05 to 0·30) | 0·98 | (0·83 to 1·15) | 0·35 | (0·20 to 0·58) | |
| 1997 | 0·90 | (0·76 to 1·06) | 0·18 | (0·12 to 0·26) | 0·64 | (0·52 to 0·77) | 0·01 | (0·00 to 0·04) | 1·02 | (0·87 to 1·19) | 0·22 | (0·15 to 0·31) | |
| 1998 | 1·04 | (0·89 to 1·20) | 0·65 | (0·53 to 0·79) | 0·37 | (0·29 to 0·47) | 0·12 | (0·07 to 0·19) | 0·54 | (0·44 to 0·66) | 0·21 | (0·14 to 0·29) | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gabapentinoid-strong opioid | | | | Gabapentinoid-moderate opioid | | | | Gabapentinoid-weak opioid | | | |
| OA | | Non-OA | | OA | | Non-OA | | OA | | Non-OA | |
| Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI | Rate | 95% CI |
| 1999 | 1·34 | (1·22 to 1·48) | 0·26 | (0·19 to 0·34) | 0·39 | (0·32 to 0·46) | 0·21 | (0·15 to 0·28) | 0·67 | (0·58 to 0·76) | 0·32 | (0·25 to 0·41) |
| 2000 | 1·92 | (1·80 to 2·05) | 1·25 | (1·13 to 1·37) | 0·25 | (0·20 to 0·29) | 0·06 | (0·04 to 0·10) | 0·81 | (0·74 to 0·90) | 0·38 | (0·31 to 0·45) |
| 2001 | 2·79 | (2·68 to 2·91) | 2·75 | (2·58 to 2·93) | 0·55 | (0·50 to 0·60) | 0·58 | (0·50 to 0·66) | 0·82 | (0·76 to 0·88) | 0·62 | (0·54 to 0·71) |
| 2002 | 3·14 | (3·05 to 3·24) | 2·42 | (2·28 to 2·58) | 0·62 | (0·58 to 0·66) | 0·27 | (0·22 to 0·32) | 0·75 | (0·71 to 0·80) | 0·17 | (0·13 to 0·21) |
| 2003 | 3·22 | (3·15 to 3·30) | 2·28 | (2·18 to 2·38) | 0·35 | (0·33 to 0·38) | 0·29 | (0·25 to 0·33) | 0·81 | (0·78 to 0·85) | 0·40 | (0·36 to 0·45) |
| 2004 | 3·20 | (3·13 to 3·27) | 2·83 | (2·73 to 2·94) | 0·45 | (0·42 to 0·47) | 0·32 | (0·29 to 0·36) | 0·95 | (0·91 to 0·99) | 0·32 | (0·28 to 0·35) |
| 2005 | 3·84 | (3·78 to 3·91) | 3·22 | (3·12 to 3·32) | 0·50 | (0·47 to 0·52) | 0·45 | (0·42 to 0·49) | 0·78 | (0·75 to 0·80) | 0·66 | (0·62 to 0·71) |
| 2006 | 3·93 | (3·87 to 4·00) | 2·11 | (2·05 to 2·18) | 0·46 | (0·44 to 0·49) | 0·32 | (0·29 to 0·34) | 0·76 | (0·74 to 0·79) | 0·56 | (0·53 to 0·60) |
| 2007 | 4·46 | (4·40 to 4·52) | 2·69 | (2·62 to 2·76) | 0·45 | (0·43 to 0·47) | 0·48 | (0·45 to 0·52) | 0·78 | (0·76 to 0·81) | 0·52 | (0·48 to 0·55) |
| 2008 | 4·34 | (4·29 to 4·40) | 3·13 | (3·07 to 3·20) | 0·61 | (0·59 to 0·63) | 0·29 | (0·27 to 0·31) | 0·62 | (0·60 to 0·64) | 0·33 | (0·31 to 0·36) |
| 2009 | 4·97 | (4·91 to 5·03) | 3·88 | (3·80 to 3·95) | 0·60 | (0·58 to 0·62) | 0·36 | (0·34 to 0·39) | 0·68 | (0·65 to 0·70) | 0·40 | (0·38 to 0·43) |
| 2010 | 4·76 | (4·71 to 4·82) | 3·25 | (3·18 to 3·32) | 0·63 | (0·61 to 0·65) | 0·35 | (0·32 to 0·37) | 0·67 | (0·65 to 0·69) | 0·41 | (0·38 to 0·44) |
| 2011 | 5·15 | (5·09 to 5·21) | 2·86 | (2·80 to 2·93) | 0·68 | (0·66 to 0·71) | 0·32 | (0·30 to 0·35) | 0·57 | (0·55 to 0·59) | 0·24 | (0·22 to 0·26) |
| 2012 | 5·41 | (5·34 to 5·47) | 2·81 | (2·74 to 2·89) | 0·75 | (0·73 to 0·78) | 0·51 | (0·48 to 0·54) | 0·70 | (0·68 to 0·73) | 0·37 | (0·34 to 0·40) |
| 2013 | 5·93 | (5·86 to 6·00) | 2·94 | (2·85 to 3·02) | 0·76 | (0·73 to 0·79) | 0·37 | (0·34 to 0·40) | 0·74 | (0·71 to 0·77) | 0·36 | (0·33 to 0·39) |
| 2014 | 5·92 | (5·84 to 6·00) | 3·17 | (3·07 to 3·28) | 0·76 | (0·73 to 0·79) | 0·42 | (0·39 to 0·46) | 0·76 | (0·73 to 0·79) | 0·47 | (0·43 to 0·51) |
| 2015 | 6·18 | (6·08 to 6·29) | 3·50 | (3·36 to 3·64) | 0·77 | (0·73 to 0·80) | 0·32 | (0·28 to 0·37) | 0·68 | (0·65 to 0·72) | 0·31 | (0·27 to 0·36) |
| 2016 | 6·04 | (5·88 to 6·20) | 4·26 | (4·03 to 4·50) | 1·12 | (1·05 to 1·19) | 0·55 | (0·46 to 0·64) | 0·83 | (0·77 to 0·89) | 0·35 | (0·29 to 0·43) |
| 2017 | 7·43 | (7·03 to 7·86) | 4·34 | (3·91 to 4·80) | 1·24 | (1·08 to 1·42) | 0·94 | (0·75 to 1·17) | 0·99 | (0·85 to 1·15) | 0·81 | (0·63 to 1·03) |
| †At time of initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | | | | | |

**Supplemental Table-S10.** Rate of gabapentinoid-opioid co-prescription (same day) among incident gabapentin users with and without osteoarthritis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | OA | | | | Non-OA | | | |
|  | n | Person-years | Rate | 95% CI | n | Person-years | Rate | 95% CI |
| Overall | 266,407 | 106,195 | 2·51 | (2·50 to 2·52) | 65,388 | 44,440 | 1·47 | (1·46 to 1·48) |
| Sex: |  |  |  |  |  |  |  |  |
| Male | 84,796 | 30,291 | 2·80 | (2·78 to 2·82) | 18,431 | 10,198 | 1·81 | (1·78 to 1·83) |
| Female | 181,611 | 75,904 | 2·39 | (2·38 to 2·40) | 46,957 | 34,242 | 1·37 | (1·36 to 1·38) |
| Age, years†: |  |  |  |  |  |  |  |  |
| 40-44 | 7,802 | 1,515 | 5·15 | (5·04 to 5·27) | 3,494 | 897 | 3·90 | (3·77 to 4·03) |
| 45-54 | 52,735 | 13,712 | 3·85 | (3·81 to 3·88) | 14,453 | 5,314 | 2·72 | (2·68 to 2·76) |
| 55-64 | 78,351 | 27,433 | 2·86 | (2·84 to 2·88) | 20,609 | 13,927 | 1·48 | (1·46 to 1·50) |
| 65-74 | 70,127 | 32,270 | 2·17 | (2·16 to 2·19) | 16,437 | 10,857 | 1·51 | (1·49 to 1·54) |
| 75-84 | 44,319 | 24,787 | 1·79 | (1·77 to 1·80) | 8,616 | 7,532 | 1·14 | (1·12 to 1·17) |
| 85+ | 13,073 | 6,479 | 2·02 | (1·98 to 2·05) | 1,779 | 5,913 | 0·30 | (0·29 to 0·32) |
| Region/country: |  |  |  |  |  |  |  |  |
| North East | 8,536 | 2,371 | 3·60 | (3·52 to 3·68) | 2,299 | 1,354 | 1·70 | (1·63 to 1·77) |
| North West | 50,450 | 17,573 | 2·87 | (2·85 to 2·90) | 11,392 | 6,646 | 1·71 | (1·68 to 1·75) |
| Yorkshire & Humber | 9,007 | 3,109 | 2·90 | (2·84 to 2·96) | 2,372 | 1,229 | 1·93 | (1·85 to 2·01) |
| East Midlands | 5,421 | 2,402 | 2·26 | (2·20 to 2·32) | 1,191 | 879 | 1·35 | (1·28 to 1·43) |
| West Midlands | 24,420 | 10,121 | 2·41 | (2·38 to 2·44) | 6,038 | 3,776 | 1·60 | (1·56 to 1·64) |
| East of England | 12,063 | 6,866 | 1·76 | (1·73 to 1·79) | 3,042 | 2,454 | 1·24 | (1·20 to 1·28) |
| South West | 15,610 | 7,143 | 2·19 | (2·15 to 2·22) | 3,288 | 2,659 | 1·24 | (1·19 to 1·28) |
| South Central | 14,769 | 7,118 | 2·07 | (2·04 to 2·11) | 3,177 | 2,767 | 1·15 | (1·11 to 1·19) |
| London | 12,937 | 6,479 | 2·00 | (1·96 to 2·03) | 3,074 | 2,652 | 1·16 | (1·12 to 1·20) |
| South East Coast | 21,349 | 8,709 | 2·45 | (2·42 to 2·48) | 5,169 | 3,586 | 1·44 | (1·40 to 1·48) |
| Northern Ireland | 13,216 | 7,610 | 1·74 | (1·71 to 1·77) | 3,404 | 3,145 | 1·08 | (1·05 to 1·12) |
| Scotland | 29,379 | 12,980 | 2·26 | (2·24 to 2·29) | 8,905 | 7,043 | 1·26 | (1·24 to 1·29) |
| Wales | 49,250 | 13,715 | 3·59 | (3·56 to 3·62) | 12,036 | 6,250 | 1·93 | (1·89 to 1·96) |
| Calendar year†: |  |  |  |  |  |  |  |  |
| 1995 | 162 | 124 | 1·31 | (1·11 to 1·52) | 1 | 75 | 0·01 | (0·00 to 0·07) |
| 1996 | 209 | 177 | 1·18 | (1·03 to 1·35) | 18 | 111 | 0·16 | (0·10 to 0·26) |
| 1997 | 308 | 167 | 1·84 | (1·64 to 2·06) | 33 | 189 | 0·17 | (0·12 to 0·25) |
| 1998 | 251 | 241 | 1·04 | (0·92 to 1·18) | 125 | 261 | 0·48 | (0·40 to 0·57) |
| 1999 | 451 | 466 | 0·97 | (0·88 to 1·06) | 118 | 268 | 0·44 | (0·36 to 0·53) |
| 2000 | 1028 | 809 | 1·27 | (1·19 to 1·35) | 477 | 469 | 1·02 | (0·93 to 1·11) |
| 2001 | 2651 | 1247 | 2·13 | (2·05 to 2·21) | 1049 | 587 | 1·79 | (1·68 to 1·90) |
| 2002 | 4793 | 2133 | 2·25 | (2·18 to 2·31) | 793 | 726 | 1·09 | (1·02 to 1·17) |
| 2003 | 7270 | 3332 | 2·18 | (2·13 to 2·23) | 1829 | 1486 | 1·23 | (1·18 to 1·29) |
| 2004 | 8469 | 4097 | 2·07 | (2·02 to 2·11) | 2494 | 1606 | 1·55 | (1·49 to 1·62) |
| 2005 | 13913 | 6306 | 2·21 | (2·17 to 2·24) | 3856 | 2196 | 1·76 | (1·70 to 1·81) |
| 2006 | 14911 | 6616 | 2·25 | (2·22 to 2·29) | 3842 | 2798 | 1·37 | (1·33 to 1·42) |
| 2007 | 20337 | 8364 | 2·43 | (2·40 to 2·47) | 5130 | 3501 | 1·47 | (1·43 to 1·51) |
| 2008 | 22913 | 9671 | 2·37 | (2·34 to 2·40) | 7280 | 4660 | 1·56 | (1·53 to 1·60) |
| 2009 | 25874 | 10203 | 2·54 | (2·51 to 2·57) | 8902 | 4521 | 1·97 | (1·93 to 2·01) |
| 2010 | 26199 | 10639 | 2·46 | (2·43 to 2·49) | 6714 | 4473 | 1·50 | (1·47 to 1·54) |
| 2011 | 27927 | 10765 | 2·59 | (2·56 to 2·62) | 6407 | 4561 | 1·40 | (1·37 to 1·44) |
| 2012 | 25754 | 9085 | 2·83 | (2·80 to 2·87) | 5063 | 3952 | 1·28 | (1·25 to 1·32) |
| 2013 | 23647 | 8123 | 2·91 | (2·87 to 2·95) | 4129 | 3198 | 1·29 | (1·25 to 1·33) |
| 2014 | 19676 | 6832 | 2·88 | (2·84 to 2·92) | 3319 | 2375 | 1·40 | (1·35 to 1·45) |
| 2015 | 13309 | 4343 | 3·06 | (3·01 to 3·12) | 2195 | 1474 | 1·49 | (1·43 to 1·55) |
| 2016 | 4885 | 1952 | 2·50 | (2·43 to 2·57) | 1135 | 720 | 1·58 | (1·49 to 1·67) |
| 2017 | 1470 | 504 | 2·92 | (2·77 to 3·07) | 479 | 231 | 2·07 | (1·89 to 2·27) |
| †At time of initial gabapentinoid prescription  n/person-year = number of co-prescription events / total person-years of follow-up from initial gabapentinoid prescription  OA Osteoarthritis | | | | | | | | |