**eTable 1.** List of participating countries, regions and territories in the IQVIA-MIDAS dataset and sector coverage.

|  |  |  |
| --- | --- | --- |
| **Country** | **Sectors covered** | **Percentage of market coverage** |
| Argentina | Retail | 73% |
| Australia | Retail and hospital | 90% |
| Austria | Retail and hospital | 100% |
| Belarus | Retail and hospital | 100% |
| Belgium | Retail and hospital | 100% |
| Bosnia and Herzegovina | Retail and hospital | 95% |
| Brazil | Retail and others | 97% |
| Bulgaria | Retail and hospital | 100% |
| Canada | Retail and hospital | 100% |
| Central America | Retail | 77% |
| Chile | Retail | 71% |
| Colombia | Retail | 79% |
| Croatia | Retail and hospital | 100% |
| Czechia | Retail and hospital | 95% |
| Denmark | Retail and hospital | 100% |
| Ecuador | Retail | 80% |
| Egypt | Retail | 75% |
| Estonia | Retail | 88% |
| Finland | Retail and hospital | 100% |
| France | Retail and hospital | 100% |
| French West Africa | Retail | 86% |
| Germany | Retail and hospital | 100% |
| Greece | Retail | 60% |
| Hungary | Retail and hospital | 100% |
| India | Retail, hospital and dispensing doctor | 95% |
| Ireland | Retail and hospital | 100% |
| Italy | Retail, hospital and Local Health Unit | 100% |
| Japan | Retail and hospital | 100% |
| Kazakhstan | Retail and hospital | 100% |
| Latvia | Retail and hospital | 100% |
| Lebanon | Retail | 77% |
| Lithuania | Retail and hospital | 100% |
| Luxembourg | Retail | 98% |
| Mainland China | Retail and hospital | 72% |
| Mexico | Retail and others | 100% |
| Morocco | Retail | 88% |
| Netherlands | Retail and hospital | 95% |
| New Zealand | Retail and hospital | 100% |
| Norway | Retail and hospital | 100% |
| Pakistan | Retail | 85% |
| Peru | Retail | 67% |
| Philippines | Retail and hospital | 100% |
| Poland | Retail and hospital | 100% |
| Portugal | Retail and hospital | 100% |
| Puerto Rico | Retail and hospital | NA |
| Republic of Korea | Retail and hospital | 100% |
| Romania | Retail and hospital | 100% |
| Russian Federation | Retail and hospital | 97% |
| Saudi Arabia | Retail and hospital | 95% |
| Serbia | Retail and hospital | 100% |
| Slovakia | Retail and hospital | 97% |
| Slovenia | Retail and hospital | 97% |
| South Africa | Retail and hospital | 100% |
| Spain | Retail and hospital | 100% |
| Sweden | Retail and hospital | 98% |
| Switzerland | Retail and hospital | 100% |
| Taiwan | Retail and hospital | 97% |
| Thailand | Retail and hospital | 93% |
| Tunisia | Retail and hospital | 100% |
| Turkey | Retail and hospital | 100% |
| Ukraine | Retail and hospital | 100% |
| United Arab Emirates | Retail | 45% |
| United Kingdom | Retail and hospital | 92% |
| United States | Retail and hospital | 100% |
| Uruguay | Retail and Mutuales | 71% |
| Venezuela (Bolivarian Republic of) | Retail | 78% |

NA, not available.

**eTable 2.** List of opioids and MME conversion factor

|  |  |  |
| --- | --- | --- |
| **Opioid** | **MME conversion factor** | **Strong opioid analgesic** |
| Bezitramide[1] | 60 | Y |
| Codeine[2] | 0.15 |  |
| Dextromoramide[3] | 4 | Y |
| Dextropropoxyphene[4] | 0.1 |  |
| Diamorphine[3] | Oral formulation: 1  Injection: 3 | Y |
| Dihydrocodeine[2] | 0.25 |  |
| Dipipanone[3] | 0.5 | Y |
| Fentanyl[3] | Tablet: 130  Film: 180  Nasal spray: 160  Patch: 100 | Y |
| Hydrocodone[2] | 1 | Y |
| Hydromorphone[3] | 5 | Y |
| Ketobemidone[5] | 2 | Y |
| Levorphanol[2] | 11 | Y |
| Meptazinol[3] | 0.03 |  |
| Morphine[2] | Oral formulation: 1  Injection: 2 | Y |
| Nalbuphine[2] | 1 | Y |
| Nicomorphine[5] | 1 | Y |
| Opium[2] | 1 |  |
| Oxycodone[2] | 1.5 | Y |
| Oxymorphone[2] | 3 | Y |
| Pentazocine[2] | 0.37 | Y |
| Pethidine[3] | Oral formulation: 0.1  Injection: 0.24 | Y |
| Piritramide[6] | 0.75 | Y |
| Tapentadol[2] | 0.4 | Y |
| Tilidine[7] | 0.1 |  |
| Tramadol[2] | 0.1 |  |
| Trimeperidine[8] | 0.5 | Y |

MME: milligram morphine equivalent per 1,000 inhabitant per day.

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**Subgroup analysis: strong opioids**

**eTable 3.** Worldwide, continental, and national levels of strong opioid use in 2015 and 2019 and average annual percentage change in use.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **MME/TID in 2015 (95% CI)\*** | **MME/TID in 2019 (95% CI)\*** | **Average annual percentage change (95% CI)** | **P-value** |
| **Worldwide** | 24.06  (13.77 to 42.03) | 21.65  (12.15 to 38.56) | 0.36 (-2.76 to 3.58) | 0.822 |
| **Africa** | 1.44  (0.14 to 14.85) | 0.88  (0.03 to 29.95) | -16.26 (-40.82 to 18.48) | 0.298 |
| Egypt | 0.70 | 0.61 | -4.29 (-8.09 to -0.33) | 0.041 |
| French West Africa | 0.07 | 0.01 | -61.69 (-96.82 to 362.15) | 0.308 |
| Morocco | 0.95 | 1.19 | 7.92 (-3.96 to 21.27) | 0.129 |
| South Africa | 10.51 | 11.74 | 3.00 (-0.25 to 6.36) | 0.061 |
| Tunisia | 11.65 | 12.05 | 0.99 (-0.83 to 2.84) | 0.182 |
| **America (Central and Caribbean)** | 6.49  (0.02 to 2176.99) | 6.24  (0.03 to 1544.88) | -1.89 (-7.00 to 3.51) | 0.450 |
| Central America | 1.50 | 1.32 | -6.69 (-20.08 to 8.95) | 0.250 |
| Mexico | 1.03 | 1.28 | 6.72 (0.91 to 12.86) | 0.034 |
| Puerto Rico | 176.61 | 143.84 | -5.16 (-9.82 to -0.25) | 0.044 |
| **America (North)** | 1366.22  (835.06 to 2235.45) | 800.95  (273.39 to 2346.55) | -12.93 (-15.46 to -10.34) | <0.001 |
| Canada | 1443.20 | 902.71 | -11.59 (-13.60 to -9.54) | <0.001 |
| United States of America | 1293.39 | 710.61 | -14.26 (-20.23 to -7.86) | 0.007 |
| **America (South)** | 0.51  (0.07 to 3.92) | 0.43  (0.04 to 4.70) | -3.76 (-12.07 to 5.33) | 0.393 |
| Argentina | 3.88 | 3.84 | -0.95 (-4.87 to 3.13) | 0.506 |
| Brazil | 8.23 | 6.94 | -1.75 (-12.21 to 9.97) | 0.653 |
| Chile | 0.22 | 0.33 | 10.09 (1.41 to 19.51) | 0.034 |
| Colombia | 0.73 | 0.41 | -10.87 (-26.46 to 8.02) | 0.153 |
| Ecuador | 0.13 | 0.34 | 27.63 (22.56 to 32.91) | <0.001 |
| Peru | 0.01 | 0.00 | -31.24 (-65.15 to 35.68) | 0.178 |
| Uruguay | 16.06 | 21.99 | 7.50 (4.94 to 10.13) | 0.002 |
| Venezuela (Bolivarian Republic of) | 0.03 | 0.02 | -18.32 (-50.41 to 34.53) | 0.287 |
| **Asia** | 4.06  (1.07 to 15.39) | 5.77  (1.88 to 17.66) | 9.20 (1.76 to 17.19) | 0.016 |
| India | 0.01 | 0.18 | 99.79 (24.37 to 220.95) | 0.019 |
| Japan | 139.92 | 272.09 | 14.25 (-10.10 to 45.20) | 0.175 |
| Kazakhstan | 4.99 | 5.40 | -5.52 (-32.13 to 31.54) | 0.623 |
| Lebanon | 3.65 | 7.04 | 20.34 (-1.18 to 46.54) | 0.058 |
| Mainland China | 6.42 | 8.94 | 8.58 (7.25 to 9.93) | <0.001 |
| Pakistan | 4.42 | 3.02 | -6.49 (-19.09 to 8.06) | 0.078 |
| Philippines | 0.97 | 1.23 | 5.01 (-2.34 to 12.90) | 0.121 |
| Republic of Korea | 4.33 | 11.30 | 25.74 (20.84 to 30.85) | <0.001 |
| Saudi Arabia | 4.65 | 1.24 | -24.32 (-54.68 to 26.39) | 0.182 |
| Taiwan | 63.68 | 66.50 | 2.48 (-4.04 to 9.44) | 0.321 |
| Thailand | 6.09 | 6.93 | 2.52 (-6.26 to 12.12) | 0.441 |
| Turkey | 25.37 | 24.19 | -1.19 (-2.13 to -0.24) | 0.028 |
| United Arab Emirates | 0.41 | 0.79 | 14.87 (2.81 to 28.36) | 0.029 |
| **Europe (East)** | 26.28  (11.56 to 59.76) | 33.87  (19.41 to 59.07) | 7.04 (2.79 to 11.46) | 0.002 |
| Belarus | 21.93 | 26.59 | 3.60 (-6.93 to 15.32) | 0.371 |
| Bosnia and Herzegovina | 26.61 | 30.37 | 3.90 (-0.20 to 8.18) | 0.057 |
| Bulgaria | 48.82 | 47.98 | -1.43 (-5.89 to 3.23) | 0.395 |
| Croatia | 86.72 | 71.83 | -4.50 (-6.82 to -2.13) | 0.009 |
| Romania | 46.15 | 59.63 | 6.54 (4.57 to 8.54) | 0.002 |
| Russian Federation | 5.76 | 13.88 | 30.49 (5.73 to 61.05) | 0.028 |
| Serbia | 63.63 | 66.68 | 1.30 (-1.78 to 4.47) | 0.276 |
| Ukraine | 5.44 | 11.26 | 20.78 (14.65 to 27.25) | 0.001 |
| **Europe (West and Central)** | 298.66  (207.39 to 430.14) | 310.57  (223.39 to 431.82) | 0.81 (-0.31 to 1.94) | 0.154 |
| Austria | 775.75 | 746.67 | -0.93 (-1.33 to -0.52) | 0.005 |
| Belgium | 705.01 | 692.28 | -0.66 (-2.11 to 0.82) | 0.251 |
| Czechia | 257.96 | 309.87 | 4.64 (4.19 to 5.08) | <0.001 |
| Denmark | 972.02 | 836.37 | -3.86 (-5.91 to -1.77) | 0.010 |
| Estonia | 40.33 | 70.98 | 10.98 (-4.05 to 28.37) | 0.107 |
| Finland | 404.17 | 367.57 | -2.14 (-3.33 to -0.94) | 0.011 |
| France | 412.92 | 437.95 | 1.47 (0.66 to 2.29) | 0.010 |
| Germany | 826.61 | 791.93 | -1.16 (-1.71 to -0.61) | 0.007 |
| Greece | 82.27 | 100.53 | 6.55 (1.38 to 11.99) | 0.027 |
| Hungary | 198.46 | 203.04 | 0.44 (-1.01 to 1.91) | 0.410 |
| Ireland | 324.82 | 314.72 | -1.24 (-3.02 to 0.56) | 0.115 |
| Italy | 229.44 | 252.64 | 2.63 (0.19 to 5.14) | 0.042 |
| Latvia | 75.53 | 98.25 | 7.46 (1.86 to 13.37) | 0.023 |
| Lithuania | 80.43 | 80.49 | -0.06 (-0.76 to 0.65) | 0.812 |
| Luxembourg | 339.01 | 181.42 | -14.64 (-16.35 to -12.91) | <0.001 |
| Netherlands | 614.38 | 703.39 | 3.76 (-1.09 to 8.85) | 0.091 |
| Norway | 638.12 | 687.08 | 1.60 (0.20 to 3.02) | 0.036 |
| Poland | 103.80 | 128.20 | 5.03 (0.45 to 9.82) | 0.039 |
| Portugal | 140.81 | 193.75 | 8.03 (6.68 to 9.40) | <0.001 |
| Slovakia | 166.05 | 172.99 | 0.83 (-1.16 to 2.86) | 0.278 |
| Slovenia | 228.63 | 175.36 | -6.65 (-7.96 to -5.31) | <0.001 |
| Spain | 594.06 | 695.25 | 3.86 (1.89 to 5.86) | 0.008 |
| Sweden | 596.28 | 541.15 | -2.46 (-3.23 to -1.69) | 0.002 |
| Switzerland | 740.98 | 846.36 | 3.27 (1.60 to 4.97) | 0.008 |
| United Kingdom | 694.44 | 615.73 | -3.09 (-5.29 to -0.84) | 0.023 |
| **Oceania** | 542.40  (13.80 to 21324.25) | 422.29  (30.70 to 5808.63) | -6.02 (-8.84 to -3.11) | 0.002 |
| Australia | 816.18 | 565.36 | -8.69 (-11.93 to -5.34) | 0.004 |
| New Zealand | 360.44 | 315.43 | -3.27 (-6.18 to -0.27) | 0.041 |

\*Worldwide and continental estimates with 95% CI were calculated by pooling the estimates from individual countries using a random-effects model.

CI: confidence interval; MME/TID: milligram morphine equivalent per 1,000 inhabitant per day.

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**eFigures 1.** Quarterly trends in strong opioid use at the continent level between 2015 to 2019.

MME: milligram morphine equivalent.

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**eFigure 2.** Worldwide use of strong opioid in (A) 2015; (B) 2019

MME: milligram morphine equivalent.