Original quantitative research

Canadian trends in opioid-related mortality and disability from opioid use disorder from 1990 to 2014 through the lens of the Global Burden of Disease Study

Heather M. Orpana, PhD (1,2)*; Justin J. Lang, PhD (1)*; Maulik Baxi, MD, MPH (3); Jessica Halverson, MPH, MSW (1); Nicole Kozloff, MD, SM (4,5); Leah Cahill, PhD (6,7,8); Samiah Alam, MSc (6); Scott Patten, MD, PhD (9); Howard Morrison, PhD (1)

This article has been peer reviewed.

Abstract

Introduction: Several regions in Canada have recently experienced sharp increases in opioid overdoses and related hospitalizations and deaths. This paper describes opioid-related mortality and disability from opioid use disorder in Canada from 1990 to 2014 using data from the Global Burden of Disease (GBD) study.

Methods: We used data from the GBD study to describe temporal trends (1990–2014) in opioid-related mortality and disability from opioid use disorder using common metrics: disability-adjusted life years (DALY), deaths, years of life lost (YLL) and years lived with disability (YLD). We also compared age-standardized YLL and DALY rates per 100,000 population between Canada, the USA and other regions.

Results: The age-standardized opioid-related DALY rate in Canada was 355.5 per 100,000 population in 2014, which was higher than the global rate of 193.2, but lower than the rate of 767.9 in the United States. Between 1990 and 2014, the age-standardized opioid-related YLL rate in Canada increased by 142.2%, while globally this rate decreased by 10.1%. In comparison with YLL, YLD accounted for a larger proportion of the overall opioid-related burden across all age groups. Health loss was greater for males than females, and highest among those aged 25 to 29 years.

Conclusion: The health burden associated with opioid-related mortality and disability from opioid use disorder in Canada is significant and has increased dramatically from 1990 to 2014. These data point to a need for public health action including enhanced monitoring of a range of opioid-related harms.

Keywords: opioids, substance use, health burden, DALY, dependence, mortality, years of life lost, disability-adjusted life years, death, years lived with disability

Highlights

- Long-term national trends data on opioid-related mortality and disability from opioid use disorder have not been previously presented for Canada.
- From 1990 to 2014, the age-standardized years of life lost rate due to opioid-related mortality increased by 142.2%, compared to a 10.1% global decrease.
- These estimates of the health burden of disability and mortality related to opioid use are likely an underestimate. More work is needed to capture the full range of health and social consequences of opioid use.

Introduction

Canada is experiencing a public health crisis; significant and sharp increases in opioid-related overdoses and mortality in multiple regions over the last few years have prompted federal, provincial/territorial and municipal responses. The most recent count of apparent opioid-related...
The Canadian Tobacco, Alcohol and Drugs Survey, which reports biennially on national drug-related behaviour, does not include information on all opioids, and prevalence or frequency information does not support a full understanding of the health burden associated with drug consumption. For example, in 2015, 2% of respondents reported using psychoactive substances, including cocaine or crack, ecstasy, speed or methamphetamine, hallucinogens or heroin, but this does not include other forms of opioids. Of those reporting taking prescription opioids, 2% reported abusing them, which represents about 0.3% of Canadians aged 15 years and older. However, survey sources of data on illegal drug use likely provide underestimates of the true magnitude of the issue because of respondents’ concerns around reporting drug use and the associated stigma. In addition, household survey methods do not reach some of the populations who may be more likely to use substances. This is particularly important when measuring the health burden disproportionately present in socially disadvantaged groups, such as people experiencing homelessness. Based on other sources of data, the number of people using heroin, fentanyl and other synthetic opioids is steadily rising, representing a shift from prescription to non-prescription opioid use. Apart from the direct health impacts of opioid use, including deaths and overdoses, other health and social harms related to opioid use include increased risk of chronic and infectious diseases and a higher risk of family problems, self-harm, problems at work and school, and contact with the criminal justice system.

The Global Burden of Disease (GBD) study is an international collaborative effort to systematically quantify health loss due to more than 300 diseases, injuries and risk factors in 195 countries from 1990 to 2016. In this paper, we use the GBD framework to quantify the health burden of opioid-related mortality and disability from opioid use disorder in Canada from 1990 to 2014 to allow comparisons across time and regions. The purpose of this paper is to describe the burden of opioid-related mortality and disability from opioid use disorder in Canada over the last quarter century, through the lens of the GBD study, by sex and by age. A secondary goal is to compare levels and trends in Canada with those in the United States of America (USA) and those in GBD study super-regions (i.e. Southeast Asia, East Asia and Oceania; Central Europe, Eastern Europe and Central Asia; High Income; Latin America and Caribbean; North Africa and Middle East; South Asia; and Sub-Saharan Africa).

Methods

The GBD 2016 estimates and analyses adhere to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER). Comprehensive details on the GBD methodology are available in the 2016 GBD capstone papers and Degenhardt et al. (2014) provide further details on GBD methods related to the modelling of opioid-related mortality and disability from opioid use disorder. All GBD results can be accessed online through the GBD Data Visualization Hub (https://vizhub.healthdata.org/gbd-compare/).

Data sources

The GBD study identifies data through comprehensive systematic reviews of published and grey literature and through environmental scans of national and sub-national data sources. The full list of data sources used to model Canadian GBD estimates can be found at http://ghdx.healthdata.org/geography/canada.

Estimation of mortality and years of life lost

Opioid-related mortality estimates were modelled using the Cause of Death Ensemble modelling (CODEm) statistical package. CODEm uses the best available data to model consistent estimates by using ensemble models of various techniques (linear mixed effects models, spatial–temporal models and Gaussian process regression) that incorporate temporal trends of the estimate.

The GBD study undertakes a standard process to ensure that international data are comparable and to correct for “garbage codes” (i.e. deaths that are coded to causes that cannot cause death or are intermediate causes of death). Because of the low number of deaths due to opioid dependence (International Classification of Diseases [ICD-10] code F11), it is difficult to obtain internally consistent models that capture all mortality associated with opioid use. As a result, deaths due to accidental poisoning from narcotics were reclassified as deaths associated with opioid use, thereby collapsing ICD-10 Codes X42 and F11 into a single category (as described by Degenhardt et al., 2014). Because not all jurisdictions capture detailed information about the specific drugs associated with drug-related deaths, the higher-level category—mortality due to drug use disorders—was modelled first. When data on specific drug-related deaths were available, such as in Canada, these data were used to distribute deaths between different types of drug-related deaths. When data on specific drug deaths were not available, other methods were used to proportionally distribute drug-related deaths between each drug included in the GBD framework. Garbage codes, including unintentional poisoning by exposure to other and unspecified drugs (ICD-10 X44), are redistributed proportionally to specific drugs as described in the GBD causes of death capstone paper.

We did not distinguish between prescription and non-prescription opioid use in relation to opioid mortality.

Mortality estimates were then combined with time-invariant world standard life expectancy tables to calculate years of life lost (YLL), describing the number of years lost to premature mortality.
incorporating ICD-10 codes X42 (Accidental poisoning due to narcotics and hallucinogens)\textsuperscript{7} and F11 (Mental disorders due to the use of opioids).\textsuperscript{24} We extracted deaths associated with these codes and combined them into a single category—deaths related to opioid use—in order to provide data consistent with the presentation of the GBD opioid-related mortality data. Age-standardized rates were calculated using the GBD world standard population. While more recent vital statistics data for Canada are available, we have reported these to correspond with the date range of GBD estimates that we are reporting.

Estimation of years lived with disability

To estimate the prevalence of opioid use disorder in order to calculate the associated disability, we defined opioid use disorder in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; code 304.00)\textsuperscript{25} and the ICD-10 (code F11.2)\textsuperscript{26} diagnostic criteria (as described by Degenhardt et al., 2014\textsuperscript{4}). This case definition means that people experiencing morbidity associated with opioid use, but not opioid dependence, are excluded in our disability estimates.

Prevalence estimates for opioid use disorder were calculated using the Disease Modelling - Meta-Regression II (DisMod-MR II) software, which implements Bayesian meta-regression techniques to obtain internally consistent estimates.\textsuperscript{27} Obtaining accurate estimates of illegal drug use prevalence remains a major challenge because of the associated stigma and difficulties with accessing marginalized populations. As a result, indirect estimates of prevalence, based on methods such as the multiplier methods, capture-recapture and back-projection estimates, were preferred over direct sources such as surveys.\textsuperscript{28} The modelled High Income North America (i.e., Canada, USA and Greenland) estimates are based on 27 prevalence studies and two studies on remission.\textsuperscript{18}

To provide a more global sample, the GBD study developed disability weights using community-based surveys conducted in five countries and open-access Internet-based surveys.\textsuperscript{29,30} Epidemiological data from a US national study were used to adjust each disability weight by severity,\textsuperscript{31} and microsimulation methods were used to account for comorbidity.\textsuperscript{18} After all corrections, the disability weight for opioid use disorder was set by the GBD study at 0.50 (95% uncertainty interval [UI]: 0.33–0.69) on a scale from 0 (no disability) to 1.0 (severe disability).\textsuperscript{18} Final prevalence estimates were multiplied by their corresponding disability weights to obtain YLD, described as the number of years that individuals lived with disability.

Disability-adjusted life years

DALYs were calculated as the sum of YLD and YLD, representing the overall burden of opioid-related mortality and disability from opioid use disorder.

Age-standardized rates for DALY were calculated using the GBD, time-invariant, world standard population. Crude (all-age) and age-standardized analyses are presented, and trend analyses use age-standardized estimates. Analyses were conducted for both sexes together and by sex. YLL and DALY are also presented for the USA and each of the seven GBD super-regions.

Uncertainty intervals

Uncertainty intervals (UIs) were established by running 1000 draws and identifying the 2.5th and 97.5th percentiles for each estimate. The level of uncertainty is related to the quality of the available data and the data coverage. Narrow UIs indicate high certainty in the estimate, whereas wide UIs indicate low certainty in the estimate.

Results

General results and international comparisons

In 2014, there were 131,057.8 (95% UI: 104,713.8–159,793.1) crude DALYs from opioid-related mortality and disability from opioid use disorder. Of these, 80,893.3 (63,579.9–100,891.3) were among males and 50,164.5 (37,340.4–62,727.8) among females (data not shown).

The age-standardized DALY rate for Canadian males and females combined was 355.5 per 100,000 population (95% UI: 230.8–436.3), a burden associated with opioid-related mortality and disability from opioid use disorder that was significantly higher than the global rate of 193.2 (147.5–232.5; Table 1). The burden of opioid-related mortality and disability from opioid use disorder in 2014 was concentrated in the High Income region (which includes Canada and the USA); North Africa and the Middle East; and the Central Europe, Eastern Europe and Central Asia regions (see Figure 1). The USA demonstrates the largest rates of opioid burden for both males (968.6 DALYs per 100,000; 95% UI: 746.6–1167.2) and females (565.7 DALYs per 100,000; 95% UI: 435.2–684.3), more than double the burden estimated in Canada in 2014.

Age-standardized opioid-related mortality rates increased substantially among males, from 1.3 per 100,000 (95% UI: 1.0–1.7) in 1990 to 3.1 (2.3–4.1) in 2014, whereas rates among females rose from 0.5 (0.4–0.7) to 1.3 (1.0–1.8) between 1990 and 2014 (Figure 2). The crude opioid-related mortality count increased from 201.1 per 100,000 (157.0–271.9) in 1990 to 606.6 (454.3–805.6) in 2014 among males, and from 76.7 (59.9–105.6) in 1990 to 279.2 (210.9–361.7) in 2014 among females. For the most part, observed Canadian data from vital statistics fall within the GBD estimates of 95% UIs. However, in 2011, the observed data for males surpassed the GBD modelled estimates, and this trend continued through the rest of the time series.

The age-standardized YLL rate for Canadians (both sexes combined) was 103.1 per 100,000 (95% UI: 83.5–129.9) (Table 2). This rate was much higher among males (146.3; 109.6–195.9) than among females (59.8; 45.1–79.4). Figure 2 highlights the increasing trends in YLL and YLD for both males and females, which together demonstrate a slow but steady increase from 1990 to 2014, resulting in large overall percentage increases. The increase is greater in YLL, reflecting the impact of an increasing number of deaths at younger ages. For both sexes, the YLL rate in Canada increased by 142.2% between 1990 and 2014, with a 28.2% increase between 2004 and 2014. In contrast, the global YLL rate decreased by 10.1% from 1990 to 2014, with an 8.6% decrease between 2004 and 2014 (Table 2).

Figure 3 shows the age distribution of DALY’s as the sum of YLL and YLD, for males and females, as rates per 100,000 population and counts. The DALY rate among infants is low because of the small number of deaths contributing a relatively higher number of YLL in this age group. This is consistent with vital statistics data for this age group, which show a small
and variable number of deaths due to accidental narcotic poisoning each year. The highest number of DALY total counts and highest DALY age-standardized rates are among males in their 20s, whereas those aged 65 years and over contribute a relatively small number of opioid-related DALY overall. YLD contribute the greatest proportion of DALY in all age categories except the neonatal period; however, this proportion varies by age group. There is a relatively higher contribution of YLD to DALY among those aged 70 years and over, compared to younger age groups, and YLD contribute a relatively higher proportion to DALY among younger females, compared to younger men.

**Discussion**

Estimates from the GBD study demonstrate that the health burden associated with opioid-related mortality and disability from opioid use disorder in Canada is significant and has increased from 1990 to 2014. The 142% increase in YLLs and 63% increase in DALYs from 1990 to 2014 demonstrate a slowly developing epidemic of opioid-related harms over a quarter of a century.

The Special Advisory Committee on the Epidemic of Opioid Overdose reported 2861 apparent opioid-related deaths in 2016 in Canada. While not directly comparable because of the differences in case definitions, this nevertheless indicates a recent, rapid acceleration of this public health problem. Patterns observed in the USA may foreshadow what is to come for Canada, as the vital statistics data used to model estimates in the USA are current to 2015. Early patterns of opioid-related mortality seen in the USA have been observed in Canada, albeit later.

The burden of opioid-related health loss in Canada disproportionately affects males. The estimated prevalence of opioid use disorder and the DALY rate in males is 1.6 times that in females; their death rate, 2.3 times; their YLD rate, 1.3 times; and their YLL rate, almost 2.5 times. There is a need to understand what drives these sex differences and how interventions can address health inequity. Similarly, opioid-related harms are disproportionately higher among young adults, which could have lasting repercussions throughout the life course. The nature of opioid-related disability and mortality varies according to age group. While deaths in younger age groups likely reflect a higher proportion of non-prescription opioid use, mortality in the older age groups may reflect a significant proportion of opioid toxicity.

It is important to note that while the trends from 1990 to 2014 show large increases in opioid-related mortality and disability from opioid use disorder, these estimates are almost certainly conservative and underestimate the true burden of opioid use in Canada. When calculating prevalence, used to estimate YLD and DALY, only opioid use disorder is captured. Not all opioid use in the population meets the criteria for opioid use disorder,

### TABLE 1

<table>
<thead>
<tr>
<th>Region</th>
<th>Total</th>
<th></th>
<th></th>
<th>Females</th>
<th></th>
<th></th>
<th></th>
<th>Males</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DALY rate per 100 000 population</td>
<td>95% UI</td>
<td>Per cent change in age-standardized rates 1990–2014 (%)</td>
<td>DALY rate per 100 000 population</td>
<td>95% UI</td>
<td>Per cent change in age-standardized rates 1990–2014 (%)</td>
<td>Per cent change in age-standardized rates 2004–2014 (%)</td>
<td>DALY rate per 100 000 population</td>
<td>95% UI</td>
<td>Per cent change in age-standardized rates 1990–2014 (%)</td>
</tr>
<tr>
<td>Canada</td>
<td>355.5</td>
<td>280.8–436.3</td>
<td>54.7</td>
<td>14.8</td>
<td>270.5</td>
<td>202.0–343.5</td>
<td>42.8</td>
<td>15.1</td>
<td>440.7</td>
<td>341.2–554.7</td>
</tr>
<tr>
<td>USA</td>
<td>767.9</td>
<td>612.3–915.7</td>
<td>47.5</td>
<td>18.1</td>
<td>565.7</td>
<td>435.2–684.3</td>
<td>41.8</td>
<td>18.2</td>
<td>968.6</td>
<td>746.6–1167.2</td>
</tr>
<tr>
<td>Global</td>
<td>193.2</td>
<td>147.5–232.5</td>
<td>−4.4</td>
<td>−0.9</td>
<td>136.5</td>
<td>102.7–166.1</td>
<td>−7.2</td>
<td>−0.9</td>
<td>249.2</td>
<td>192.0–299.4</td>
</tr>
<tr>
<td>Southeast Asia, East Asia and Oceania</td>
<td>145.0</td>
<td>111.5–176.1</td>
<td>−27.9</td>
<td>−8.0</td>
<td>108.4</td>
<td>83.2–133.1</td>
<td>−33.0</td>
<td>−6.6</td>
<td>181.2</td>
<td>138.4–217.3</td>
</tr>
<tr>
<td>Central Europe, Eastern Europe and Central Asia</td>
<td>298.6</td>
<td>254.8–344.5</td>
<td>−8.9</td>
<td>−18.2</td>
<td>151.4</td>
<td>119.9–179.2</td>
<td>−10.9</td>
<td>−16.3</td>
<td>452.0</td>
<td>385.7–522.4</td>
</tr>
<tr>
<td>High Income</td>
<td>346.4</td>
<td>274.9–417.1</td>
<td>36.3</td>
<td>14.4</td>
<td>252.3</td>
<td>193.6–304.2</td>
<td>34.9</td>
<td>15.6</td>
<td>440.1</td>
<td>347.8–530.3</td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>116.3</td>
<td>86.8–145.7</td>
<td>13.6</td>
<td>3.8</td>
<td>88.9</td>
<td>64.7–113.1</td>
<td>10.0</td>
<td>4.5</td>
<td>144.6</td>
<td>109.9–179.2</td>
</tr>
<tr>
<td>North Africa and Middle East</td>
<td>330.7</td>
<td>234.1–414.0</td>
<td>13.5</td>
<td>−0.0</td>
<td>216.8</td>
<td>153.2–288.8</td>
<td>8.4</td>
<td>3.2</td>
<td>430.8</td>
<td>310.5–534.9</td>
</tr>
<tr>
<td>South Asia</td>
<td>147.8</td>
<td>107.6–185.6</td>
<td>13.0</td>
<td>10.2</td>
<td>111.8</td>
<td>80.4–141.6</td>
<td>13.4</td>
<td>9.1</td>
<td>182.2</td>
<td>133.4–230.1</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>136.5</td>
<td>102.3–168.2</td>
<td>−7.9</td>
<td>−5.6</td>
<td>93.2</td>
<td>67.3–120.8</td>
<td>−10.5</td>
<td>−8.6</td>
<td>180.8</td>
<td>139.6–218.2</td>
</tr>
</tbody>
</table>

**Abbreviations:** DALY, disability-adjusted life years; UI, uncertainty interval.

yet all levels of non-prescription opioid use have the potential to cause harm and disability. Including use that does not meet the criteria for disorder would provide a more comprehensive picture of the true burden of opioid use in Canada. As noted in the methods section of this paper, the 2016 iteration of the GBD calculated estimates using 2012 Canadian vital statistics data. Given that vital statistics data for 2013 and 2014 show an increasing trend in opioid-related mortality, based on public health surveillance, we anticipate that the number of opioid-related deaths will be significantly higher in 2016 and 2017 in Canada. When the GBD process is able to capture this increase, deaths, YLD, YLL and DALY will be higher than the estimates for 2014, which are the focus of this paper.

**Strengths and limitations**

The strengths of this study include the rigorous approach to modelling estimates used to quantify health loss associated with opioid use in a manner that is comparable across time, across causes and between countries. This paper provides a more comprehensive account of the health burden associated with opioid-related mortality and disability from opioid use disorder in Canada than previously published results. However, along with this comparability come limitations. The data presented here have been truncated at 2014 in order to align with the date range of the estimates we report from the GBD, as explained in the previous section. The GBD produces estimates through a modelling process that includes standardizing across countries and recoding some causes of death that are known to be unreliable. As such, some GBD estimates may not be fully aligned with the observed data for Canada. Nonetheless, these estimates provide a more robust picture of health loss due to opioid use in Canada, including temporal trends. Comparison of the GBD estimates and observed data from 2000 to 2014 indicate high concordance once categories of deaths are collapsed in a consistent fashion. Deaths due to opioid use disorder, which are relatively rare in Canada (observed deaths between 2000 and 2014 ranged from 1 to 13), were combined with deaths due to accidental poisoning by narcotics and other hallucinogens to create total deaths due to opioid use. This approach may overestimate deaths related to opioid use due to the inclusion of “other hallucinogens” in ICD code X42. However, this is likely to be small because of the low toxicity of hallucinogens. Furthermore, some deaths recorded as accidental poisoning may, in fact, have been intentional poisonings, thus representing deaths by suicide.

Because only disability associated with opioid use disorder was estimated, these
FIGURE 2
(a) Age-standardized opioid-related mortality rates per 100,000 population, males and females, 1990–2014, global and Canada; (b) crude mortality counts, modelled Global Burden of Disease and Vital Statistics data, males and females, 1990–2014, Canada; and (c) age-standardized YLL and YLD rates, males and females, 1990–2014, Canada

Abbreviations: CANSIM, Canadian Socio-Economic Information Management System; GBD, Global Burden of Disease; YLD, years lived with disability; YLL, years of life lost.

Note: Vertical bars represent the 95% uncertainty intervals.
analyses do not take into account disability associated with other forms of use, such as acute opioid intoxication or harmful use that does not meet the criteria for disorder. Other studies may include ICD codes not referenced in the present study. The actual burden of disability associated with a broader range of opioid use is likely to be higher than the estimates reported here. Disability weights derived from surveys in a limited number of countries may not be entirely applicable to the Canadian context, and the underlying level of disability for opioid use disorder may vary significantly over time and between contexts.  

Finally, the GBD method does not account for indirect effects of opioid use and losses that are not health-related. Opioid use may impact negatively on other facets of life, such as relationships, educational attainment and work life, thus having indirect health effects through these social determinants.  

Further refinement of analyses by characteristics other than sex and age was not possible with the GBD data. Opioid-related health loss is likely not evenly distributed across the Canadian population, and further analyses of inordinately affected subgroups should be conducted. Examples of these subgroups include those who have other mental health problems, low school involvement, a prior history of substance use disorder, chronic homelessness, a history of abuse and neglect and substance use during adolescence. The relationship of medical opioid-prescribing patterns due to patterns of health loss due to opioid use should also be further elucidated. Subnational estimates were not provided, but may be available in future iterations of the GBD study, in a manner similar to those for the USA and the United Kingdom.  

Conclusion

Health loss due to opioid use is significant and has increased dramatically in Canada from 1990 to 2014. When the GBD study produces estimates with updated vital registration data on opioid-related deaths for 2013 and later, we expect estimates for the period 2014 to 2016 to be even greater than those reported here. Furthermore, they will more accurately reflect the health loss associated with opioid use in Canada. Even then, these estimates will not fully account for the burden of disease associated with opioid use. Canada has a higher level of health loss associated with opioid use than all other high-income countries except for the USA. Well-coordinated public health action to prevent problematic opioid use and related harms is indicated to mitigate the unnecessary death and disability associated with this problem in Canada.

Acknowledgements

This research has been conducted as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), led by the Institute for Health Metrics and Evaluation. The GBD was partially funded by the Bill & Melinda Gates Foundation; the funders had no role in the study design, data analysis, data interpretation, or writing of the report.

The authors would like to thank Emily Wolfe Phillips for her thorough review of the final manuscript.

### TABLE 2

<table>
<thead>
<tr>
<th>Region</th>
<th>Total</th>
<th>Females</th>
<th>Males</th>
<th>Per cent change in (total) age-standardized YLL rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YLL rate per 100 000</td>
<td>95% UI</td>
<td>Prevalence</td>
<td>95% UI</td>
</tr>
<tr>
<td>Canada</td>
<td>103.1</td>
<td>83.5–129.9</td>
<td>0.7</td>
<td>0.6–0.8</td>
</tr>
<tr>
<td>USA</td>
<td>265.0</td>
<td>123.2–294.5</td>
<td>1.3</td>
<td>1.2–1.5</td>
</tr>
<tr>
<td>Global</td>
<td>47.6</td>
<td>39.8–51.0</td>
<td>0.4</td>
<td>0.3–0.4</td>
</tr>
<tr>
<td>Southeast Asia, East Asia and Oceania</td>
<td>35.9</td>
<td>30.5–48.6</td>
<td>0.3</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Central Europe, Eastern Europe and Central Asia</td>
<td>150.8</td>
<td>129.7–179.1</td>
<td>0.4</td>
<td>0.3–0.4</td>
</tr>
<tr>
<td>High Income*</td>
<td>107.5</td>
<td>60.0–116.5</td>
<td>0.6</td>
<td>0.6–0.7</td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>19.9</td>
<td>17.8–24.6</td>
<td>0.2</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>North Africa and Middle East</td>
<td>41.3</td>
<td>30.1–49.5</td>
<td>0.7</td>
<td>0.6–0.9</td>
</tr>
<tr>
<td>South Asia</td>
<td>20.3</td>
<td>17.2–24.2</td>
<td>0.3</td>
<td>0.3–0.4</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>30.5</td>
<td>24.2–37.7</td>
<td>0.3</td>
<td>0.2–0.3</td>
</tr>
</tbody>
</table>

**Abbreviations:** YLL, years of life lost; UI, uncertainty interval.

NK is supported by a NARSAD Young Investigator Grant from the Brain & Behavior Research Foundation.

**Conflicts of interest**

The authors declare that they have no conflicts of interest.

**Authors’ contributions and statement**

HMO and JJL conceived the research questions and objectives for this study. HMO and JJL led the synthesis and interpretation of results. HMO, JJL and MB drafted the manuscript. All co-authors contributed to interpreting data and reviewing and revising the manuscript for intellectual content. All authors read and approved the final manuscript.

The content and views expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

**References**


