Geographical and socioeconomic disparities in opioid access in Mexico, 2015–19: a retrospective analysis of surveillance data

David Goodman-Meza, Joseph Friedman, Mariah M Kalmin, Emmanuel Aguilar-Posada, Marissa J Seamans, Sara Velazquez-Moreno, Clara Fleiz, Michael Shin, Jaime Arredondo-Sanchez, Steffanie A Strathdee, Steve Shoptaw

Summary

Background In 2015, Mexico implemented regulatory changes and an electronic system to improve access to prescription opioids. We aimed to investigate trends in opioid dispensing after the implementation of these changes and assess how opioid dispensing varied geographically and by socioeconomic status.

Methods In this retrospective analysis of prescription medication surveillance data, we analysed dispensing data for group 1 medications (all opioids, including morphine, methadone, hydromorphone, oxycodone, tapentadol, fentanyl, sufentanil, and remifentanil) obtained from the Federal Commission for the Protection against Sanitary Risk database for 32 states and six large metropolitan areas in Mexico. We calculated crude annual opioid prescriptions per 10 000 people at the national, state, and municipal levels. Adapting methods from the report of the *Lancet* Commission on Palliative Care and Pain Relief, we calculated the need for palliative opioids by state, and then assessed the observed opioid dispensing rates as a percentage of expected need by geographical socioeconomic status. Within the six major metropolitan areas, we mapped the geocoded location of opioid prescriptions and assessed the association between opioid dispensing and socioeconomic status as well as the association between opioid dispensing and time to US border crossing for areas on the US–Mexico border.

Findings Between June 25, 2015, and Oct 7, 2019, opioid dispensing rates increased by an average of 13% (95% CI 6·8–19·6) per quarter (3 months). The overall national opioid dispensing rate during the study period was 26·3 prescriptions per 10 000 inhabitants. States with a higher socioeconomic status had higher opioid dispensing rates than states with lower socioeconomic status (rate ratio [RR] 1·88, 95% CI 1·33–2·58, p=0·00016) after controlling for the estimated opioid requirement per state, the presence of methadone clinics, and the presence of tertiary hospitals and cancer centres. The same association between opioid dispensing and socioeconomic status was observed in the metropolitan areas, and in those metropolitan areas on the US–Mexico border a 20% decrease (RR 0·80, 95% CI 0·75–0·86) in opioid dispensation was observed per each SD increase (SD 17·1 min) in travel time to the border.

Interpretation Measures introduced by the Mexican federal Government to increase opioid access for patients with palliative care needs were only marginally successful in raising opioid prescription rates. Opioid access should be improved for patients with palliative care needs who live in geographical areas of lower socioeconomic status.

Funding US National Institutes of Health.

Lancet Public Health 2021; 6: e88–96

See **Comment** page e83

Division of Infectious Diseases (D Goodman-Meza MD) **and Department of Family Medicine** (M M Kalmin PhD, Prof S Shoptaw PhD), **David Geffen School of Medicine, Center for Social Medicine and Humanities** (J Friedman MPH, E Aguilar-Posada MPH), **Department of Epidemiology, Fielding School of Public Health** (M J Seamans PhD), **and Department of Geography** (Prof M Shin PhD), **University of California, Los Angeles, CA, USA; Department of Medicine, University of California San Diego, San Diego, CA, USA** (Prof S A Strathdee PhD); **Programa de Política de Drogas, Centro de Investigación y Docencia Económicas, Aguascalientes, Mexico** (S Velazquez-Moreno JD, J Arredondo-Sanchez PhD); **Dirección de Investigaciones Epidemiológicas y Psicosociales, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz, Mexico City, Mexico** (C Fleiz PhD)

Correspondence to:
Dr David Goodman-Meza, Division of Infectious Diseases, David Geffen School of Medicine, University of California, Los Angeles, CA 90095, USA
dgoodman@mednet.ucla.edu

Introduction

Mexico was ranked last in terms of opioid availability among the 37 member nations of the Organisation for Economic Co-operation and Development between 2011 and 2016.[1] Furthermore, the *Lancet* Commission on Palliative Care and Pain Relief indicated that Mexico provided only 36% of the opioids that patients needed for palliative care between 2010 and 2013.[2]

Reasons for tight restrictions on opioid prescriptions are varied and include: fears of diversion for illicit use, side-effects, and addiction; paucity of training for providers; costs; logistical and regulatory considerations; and cultural attitudes towards pain treatment.[2–5] Before 2015, the Mexican Health Foundation, Human Rights Watch, and palliative care organisations criticised the inadequate provision of opioids for patients.[3,4] In response, the Mexican Government improved regulations to facilitate opioid prescribing in 2015. A new electronic system was introduced for providers to obtain prescriptions and track opioid dispensation at pharmacies. The Mexican Government also increased the limit on the number of prescriptions per provider from 50 to 200, decreased the wait time for obtaining prescriptions, and introduced a QR code on prescriptions to encrypt the prescriber's personal data.[5,6] Additionally, Seguro Popular, Mexico's largest health insurer, which covers the proportion of the population employed in the informal sector and those who are unemployed, included coverage for opioids such as morphine, oxycodone, tramadol, and buprenorphine.[7]

Research in context

Evidence before this study

Disparities in access to opioids in high-income countries such as the USA are well documented; however, evidence from low-income and middle-income countries (LMICs), including Mexico, is scarce. We searched PubMed from database inception to May 25, 2020, for analyses published in English that assessed disparities in the availability and accessibility of opioids in LMICs. We included search terms associated with opioid availability ("opioid availability" or "opioid accessibility"), disparities ("disparities"), and socioeconomic status ("SES" or "socioeconomic status"), as well as the full list of LMIC names and standard terms for the LMIC setting (appendix pp 6–7). We excluded studies on access to methadone maintenance programmes for the treatment of opioid use disorder. Our search yielded three studies (two at the national level and one at the subnational level). Two studies analysed disparities in opioid access at the national level. One study using data from the International Narcotics Control Board found that human development index and opioid use were closely correlated. In a separate analysis, the *Lancet* Commission on Palliative Care and Pain Relief estimated that, between 2010 and 2013, the poorest 10% of countries met less than 2% of estimated palliative care needs, whereas the wealthiest 10% of countries met more than 24 times their estimated palliative care needs. At the subnational level, with the exception of reviews and commentaries, our search yielded only one study. This study of oral morphine use in Kerala, India, showed that morphine dispensing increased between 2012 and 2015, but substantial variation was observed between regions. The authors concluded that, despite the increase in dispensing, substantial unmet needs for palliative care with oral morphine persisted. To date, no studies have assessed opioid dispensing by socioeconomic status and disease burden at a subnational level in Mexico. In 2015, Mexico implemented regulatory changes and an electronic system to increase access to prescription opioids; however, the effects of these changes have not previously been assessed.

Added value of this study

We compared opioid needs and access at the state level across Mexico and by regional socioeconomic status. We used methodology based on the *Lancet* Commission report on Palliative Care and Pain Relief and robust estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 to inform our models. We found that opioid access increased in Mexico after the country reduced logistical barriers for providers to prescribe opioids and implemented an electronic prescribing system. However, increases in opioid dispensation have been marginal, and significant disparities exist at the geographical level and by socioeconomic status. For example, the median observed opioid dispensing rates in states with very low, low, and medium socioeconomic status were 69·2%, 45·5%, and 56·2%, respectively—lower than the expected rates for each group. For states with high and very high socioeconomic status, the median observed rates of dispensed opioids were 79·3% and 24·6%, respectively—higher than the expected rates. This is the first in-depth analysis of opioid access in Mexico, and provides insights into the changes in opioid dispensing since implementation of regulatory changes and a national electronic prescribing system in 2015.

Implications of all the available evidence

Our findings show significant disparities by socioeconomic status at the geographical level. Mexico must continue to expand access to opioids for individuals with medical necessity. Expansion should be targeted to close existing gaps in opioid access between areas with high and low socioeconomic status to ensure equity, while maintaining surveillance to avoid the public health harms associated with the overprescription that is prevalent in other countries.

Disparities in opioid access might be especially prevalent in low-income and middle-income countries (LMICs).[2,8] To our knowledge, only one study to date has assessed socioeconomic disparities in opioid accessibility at the subnational level in an LMIC. The study found that oral morphine use increased between 2012 and 2015 in Kerala, India; however, regional disparities persisted despite this increase.[9] In higher-income countries such as the USA, poorly regulated access to opioid prescriptions, primarily in socioeconomically disadvantaged areas, contributed to the first wave of the opioid epidemic in the country.[10–13] As Mexico aims to increase opioid access to individuals with pain-related conditions, socioeconomic disparities in access might ensue, since individuals in the lowest socioeconomic strata have unequal access to health-care services.[14,15]

In this study, we aimed to estimate rates of opioid prescribing and dispensing by region, and assess potential sociodemographic disparities by region in Mexico, between 2015 and 2019. Our hypothesis was that locations with lower socioeconomic status would be associated with lower opioid medication dispensing than locations with higher socioeconomic status. In urban areas situated on the US–Mexico border, we hypothesised that travel time to the main border crossing would be a predictor of opioid dispensing, because of demand from the medical tourism industry for medicines and hospitalisation services and potential diversion towards the USA.

Methods

Data sources

We obtained prescription medication surveillance data from the Federal Commission for the Protection against Sanitary Risk (COFEPRIS). Data were obtained through a federal request for information via the National Institute

for Transparency, Access to Information and Personal Data Protection (INAI; request 1215100531719). Data provided were for medications listed in group 1 (narcotics and opioids) under the Mexican General Health law.[16] Relevant group 1 medications were all opioids and included morphine, methadone, hydromorphone, oxycodone, tapentadol, fentanyl, sufentanil, and remifentanil. Two databases were provided: the first database included group 1 opioid medications dispensed and the date dispensed at public and private pharmacies nationally between June 25, 2015, and Oct 7, 2019. For our analyses, we included only entries with complete data for group 1 medications. The second database was aggregated at the pharmacy level by municipality and state per month between June, 2015, and November, 2019. Due to inconsistent reporting by state, we included data between August, 2015, and October, 2019, only.

We analysed data at the national, state, municipal, and basic geostatistical unit levels. The basic geostatistical area is the smallest unit published by the Mexican National Institute of Statistics and Geography (INEGI). To provide a granular analysis at the metropolitan area level, we analysed data by urban basic geostatistical areas for the three largest metropolitan areas in Mexico (Mexico City, Guadalajara, and Monterrey), and the three largest metropolitan areas located on the US–Mexico border (Tijuana, Mexicali, and Ciudad Juarez).

As no participants were included in this study, ethical approval was waived by the ethics review board at the University of California, Los Angeles (CA, USA).

Outcomes

We calculated crude annual opioid prescriptions per 10 000 people at the national, state, and municipal levels based on population census measures available from the 2015 Intercensal Survey by INEGI.[17] This survey did not include municipalities with populations of less than 50 000, so we did not calculate dispensing rates for those municipalities. Opioid dispensation data were available for 248 of 2465 municipalities; however, we excluded 58 municipalities that had a population of less than 50 000 people.

We calculated opioid dispensing densities by medication at the national level to visualise differences in opioid dispensing rates over time using kernel density estimation.[18] Dispensing densities were calculated for morphine, methadone, hydromorphone, oxycodone, tapentadol, and fentanyl. Due to small dispensing numbers (1%) and similar uses as surgical anaesthetics, we grouped sufentanil and remifentanil with fentanyl.

We adapted methodology from the report of the *Lancet* Commission on Palliative Care and Pain Relief[2] to calculate an overall summary of need for palliative opioids by state. For conditions expected to require opioids, we extracted number of deaths and disease prevalence from the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 for each Mexican state.[19] We used published weights provided in the appendix of the *Lancet* Commission report on Palliative Care and Pain Relief[2] to aggregate a composite score of mg of morphine needed per capita based on the disease burden in each state. A full list of illnesses and weights included in our analysis is available in the appendix (pp 7–8).

See Online for appendix

We used an index calculated by the Mexican National Population Council that captures the socioeconomic status of a geographical area to assess disparities in opioid access by geographical socioeconomic status.[20,21] Lower numbers indicate less marginalisation and higher numbers indicate more marginalisation. We reversed the order of the variable so that higher numbers corresponded with higher socioeconomic status, and lower numbers corresponded with lower socioeconomic status. We classified the socioeconomic status of geographical areas using the following categories: lowest, low, medium, high, and highest. Cutoffs used for each category are listed in the appendix (p 9). We used 2015 data for state-level analyses and 2010 data for basic geostatistical area-level analyses, because they were the most recent available indicators at each geographical level.

For each border metropolitan area, we calculated the travel time to the main border crossing by car. We calculated the geocoordinates for the centroid of each basic geostatistical area within each metropolitan area. We used an algorithm to calculate the travel time using the Google Maps application programming interfaces from each centroid to the main border crossing within each border city, assuming no traffic (appendix p 9).

We included the number of methadone clinics in a state and number of public tertiary hospital centres and medical centres that provided cancer care. We obtained the number of methadone clinics by state from a COFEPRIS database that contained all the pharmacies licensed in Mexico to provide controlled substances. We filtered pharmacy entries that had a licence to dispense methadone and aggregated the number within each state.[22] We obtained the number of tertiary hospitals and medical centres that provided cancer care from National System of Health Information databases[23,24] and aggregated the number within each state.

Statistical analysis

All statistical analyses were done using R (version 3.6) and Joinpoint Software Version (4.7.0.0; National Cancer Institute, Washington, USA).[25] We used Joinpoint regression to analyse whether changes in opioid dispensing rates over time were statistically significant at the national geographical level in aggregate, and for the individual medications.

Following the implementation of the electronic registry on June 15, 2015, there was an expected implementation scale-up period at the different geographical levels as local pharmacies adopted the new electronic platform. We therefore calculated the average quarterly percentage change over the whole study period, as well as the

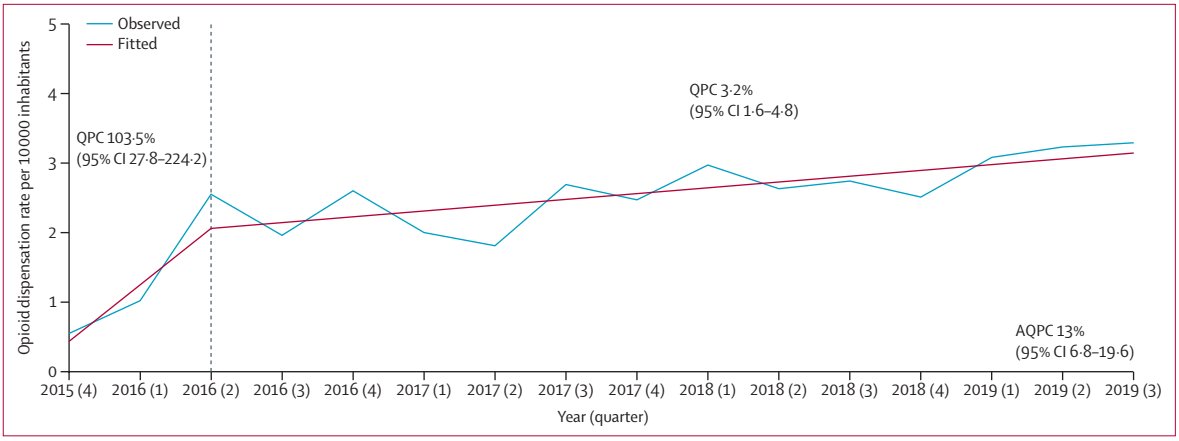

Figure 1: **Dispensing rates for group 1 opioids in Mexico**
National quarterly rates of group 1 opioid dispensing in Mexico. The vertical dotted line shows the breakpoint, which separates the initial scale-up period (when changes were expected to reflect the adoption of the electronic registry) from the remainder of the study period. QPC=quarterly percentage change. AQPC=average quarterly percentage change.

quarterly percentage change before and after the initial breakpoint (ie, the point that separates the initial scale-up period [when changes were expected to reflect the adoption of the electronic registry] from the remainder of the study period) to provide a perspective of change since full adoption of the electronic system. For this purpose, each year was divided into four quarters representing 3 months each (ie, quarter one covers January to March). We used 95% CIs as estimates of precision for each quarterly percentage change and average quarterly percentage change.

We did several analyses to identify and compare geographical variation in opioid dispensing rates. We did this observational assessment at multiple ecological levels to assess the generalisability of our findings. At the state level, we constructed a negative binomial regression model with the opioid dispensing count by state as the outcome, using state population as an offset variable, which enabled the opioid dispensing rate to be modelled as a per-capita rate. We did a stepwise regression: model 1 included only disease burden associated with palliative care need; model 2 included socioeconomic status; model 3 controlled for the number of methadone clinics in a state; and model 4 included tertiary hospital centres and cancer centres. To assess whether states had an observed opioid dispensing rate that was higher or lower than expected, we estimated the expected counts of dispensed opioid medications for each state from model 1, and then calculated the expected rates on the basis of opioid need for each state. We then calculated the observed rate as a percentage of the expected rate for each state and plotted these values to visually compare geographical areas.

We did additional analyses in six metropolitan areas to test our hypothesis of the association of socioeconomic status and opioid dispensing at a more granular level. We used a negative binomial model of opioid dispensing counts and socioeconomic status at the basic geostatistical area level in these six metropolitan areas, using the population of each basic geostatistical area as the offset variable. For the three border metropolitan areas, we also included the calculated travel time to the main international border crossing for each basic geostatistical area. For the six metropolitan areas, we were unable to calculate an opioid need score because disease prevalence and mortality data were not available at the basic geostatistical area level from the Global Burden of Disease Study 2017. For all analyses, a p value of less than 0·05 was considered to indicate statistical significance.

Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to the data in the study and had final responsibility for the decision to submit for publication.

Results

Between June 25, 2015, and Oct 7, 2019, 458 182 dispensed medication entries were recorded in the surveillance database. We excluded 1015 (0·2%) entries because the entry was incomplete or referred to a medication that was not a group 1 opioid. Therefore, 457 167 records were included in the final analysis. Nationally, group 1 opioid dispensing rates increased during the study period. Between quarter four of 2015 and quarter two of 2016, a significant increase in opioid dispensing rate was observed (quarterly percentage change 103·5%, 95% CI 27·8–224·2). Subsequently, the dispensing rate continued to increase between quarter two of 2016 and quarter three of 2019 (quarterly percentage change 3·2% [1·6–4·8]). The average quarterly percentage change between quarter 4 of 2015, and quarter three of 2019, was 13% (6·8–19·6). The overall national opioid dispensing rate during the study

period was 26·3 prescriptions per 10 000 people (figure 1). Overall, the most frequently dispensed medication was fentanyl (163 651 [35·7%] of 457 167 prescriptions), followed by methadone (121 445 [26·5%]), morphine (105 903 [23·1%]), tapentadol (33 500 [7·3%]), oxycodone (31 734 [6·9%]), and hydromorphone (910 [0·2%]; appendix p 1). Density plots for each medication showed linear increases, with the exception of methadone, which increased and decreased several times over the study period (appendix p 1).

States with the highest opioid dispensing rate were Baja California (234·5 prescriptions per 10 000 people), Mexico City (65·8), Nuevo Leon (58·7), Sonora (56·5), and Jalisco (51·9). States with the lowest dispensing rate were Tlaxacala (0 prescriptions per 10 000 people), Guerrero (0·6), Durango (2·7), Mexico State (4·3), and Tabasco (4·4; figure 2). Opioid dispensing rates by states and municipality are shown in the appendix (pp 2, 3, 10–12).

Some states had greater observed than expected opioid dispensing rates; the greatest differences were in Yucatan (243·9%), Baja California (235·1%), Aguascalientes (198·3%), Chihuahua (133·3%), and Jalisco (109·9%; appendix p 5). By contrast, other states had lower observed than expected opioid dispensing rates; the greatest differences were in Tlaxcala (–99·0%), Guerrero (–93·2%), Veracruz (–81·0%), Morelos (–74·5%), and Hidalgo (–71·1%; appendix p 5). When socioeconomic status was sequentially added to the model, the estimated opioid requirement per state variable was no longer a significant predictor of dispensing rate (p=0·13). States with a higher socioeconomic status had higher opioid dispensing rates than states with lower socioeconomic status (rate ratio [RR] 1·88, 95% CI 1·33–2·58, p=0·00016) after controlling for estimated opioid requirement per state, the presence of methadone clinics, and the presence of tertiary hospitals and cancer centres (appendix pp 13–14).

The median observed opioid dispensing rates in states with very low, low, and medium socioeconomic status were 69·2%, 45·5%, and 56·2%, which were lower than

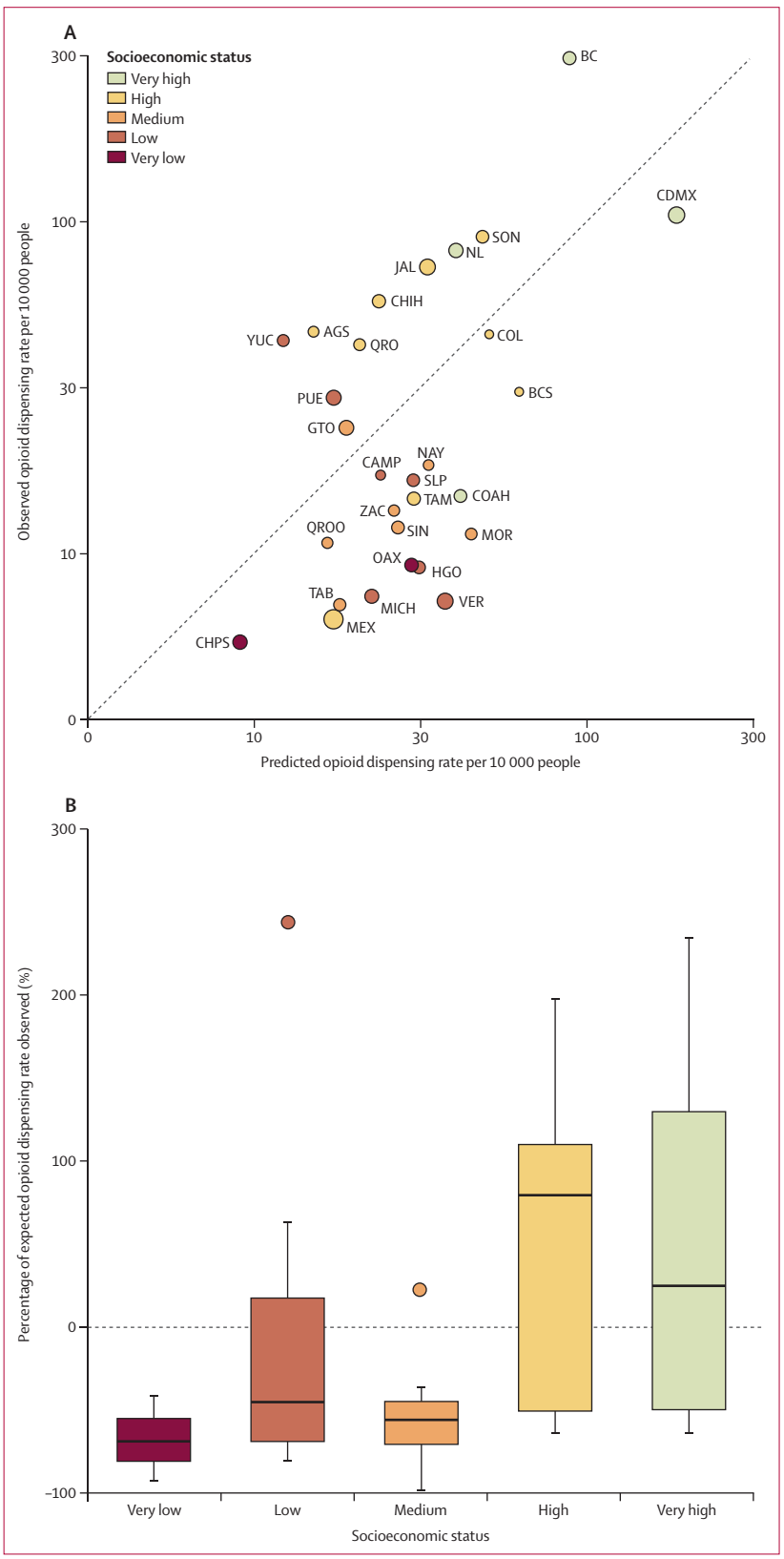

***Figure 2*: Comparison of observed versus predicted opioid dispensing rates in Mexico**

(A) Scatter plot of observed versus predicted rate of dispensed opioids by state in Mexico between August, 2015, and October, 2019; predicted rates were estimated on the basis of estimated opioid need for each state; X and Y axes are on a logarithmic scale; the diagonal dashed line is a hypothetical equality line, where the observed and expected values are equal; circle sizes are proportional to the population size for each state; the opioid dispensing rate for Tlaxcala was almost zero, thus this state is not shown. (B) The boxplot shows the observed dispensing rate as a percentage of the expected dispensing rate, by state socioeconomic status. Boxes show IQRs, horizontal lines within the boxes show the median, upper and lower whiskers indicate 1·5 × IQR, and dots indicate outliers. BC=Baja California. SON=Sonora. CDMX=Mexico City. JAL=Jalisco. NL=Nuevo Leon. YUC=Yucatan. AGS=Aguascalientes. CHIH=Chihuahua. PUE=Puebla. QRO=Queretaro. COL=Colima. GTO=Guanajuato. BCS=Baja California South. CAMP=Campeche. SLP=San Luis Potosi. NAY=Nayarit. COAH=Coahuila. SIN=Sinaloa. ZAC=Zacatecas. TAM=Tampico. QROO=Quintana Roo. OAX=Oaxaca. MOR=Morelos. TAB=Tabasco. MICH=Michoacan. HGO=Hidalgo. CHPS=Chiapas. MEX=Mexico State. VER=Veracruz.

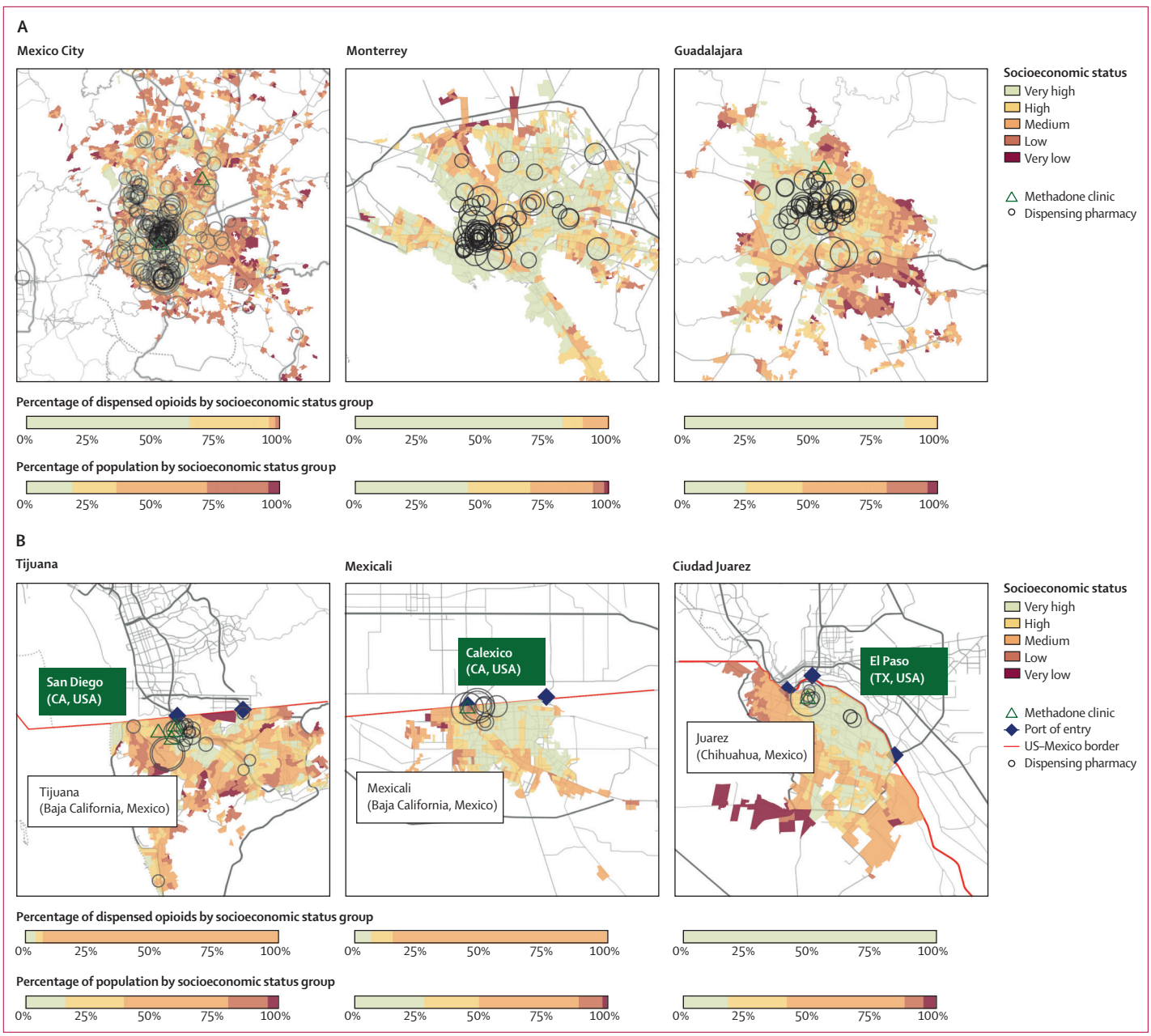

Figure 3: **Percentage of dispensed opioids by socioeconomic status in the six metropolitan areas**
(A) Percentage of dispensed opioids by socioeconomic status in the three largest metropolitan areas in Mexico. (B) Percentage of dispensed opioids by socioeconomic status in the three largest metropolitan areas in Mexico situated on the US–Mexico border. Circles indicate the location of pharmacies that dispensed opioids during the study period; the size of the circles are proportional to the number of opioids dispensed.

the expected rates for each group. For states with high and very high socioeconomic status, the median observed rates of dispensed opioids were 79·3% and 24·6%, respectively, which were higher than the expected rates.

At a more granular level, socioeconomic status was also positively associated with opioid dispensing rates in the three largest cities: Mexico City (p<0·0001), Guadalajara (p<0·0001), and Monterrey (p<0·0001; figure 3A; appendix p 15). In the border cities, socioeconomic status was positively associated with opioid dispensing (p=0·00072), whereas travel time to the main port of entry was negatively associated with opioid dispensing, suggesting that more opioids were prescribed in geographical areas closer to the port of entry than those further from the port of entry (p<0·0001; figures 3B, 4; appendix pp 16–17). Overall, in the border cities, a 20% decrease (RR 0·80, 95% CI

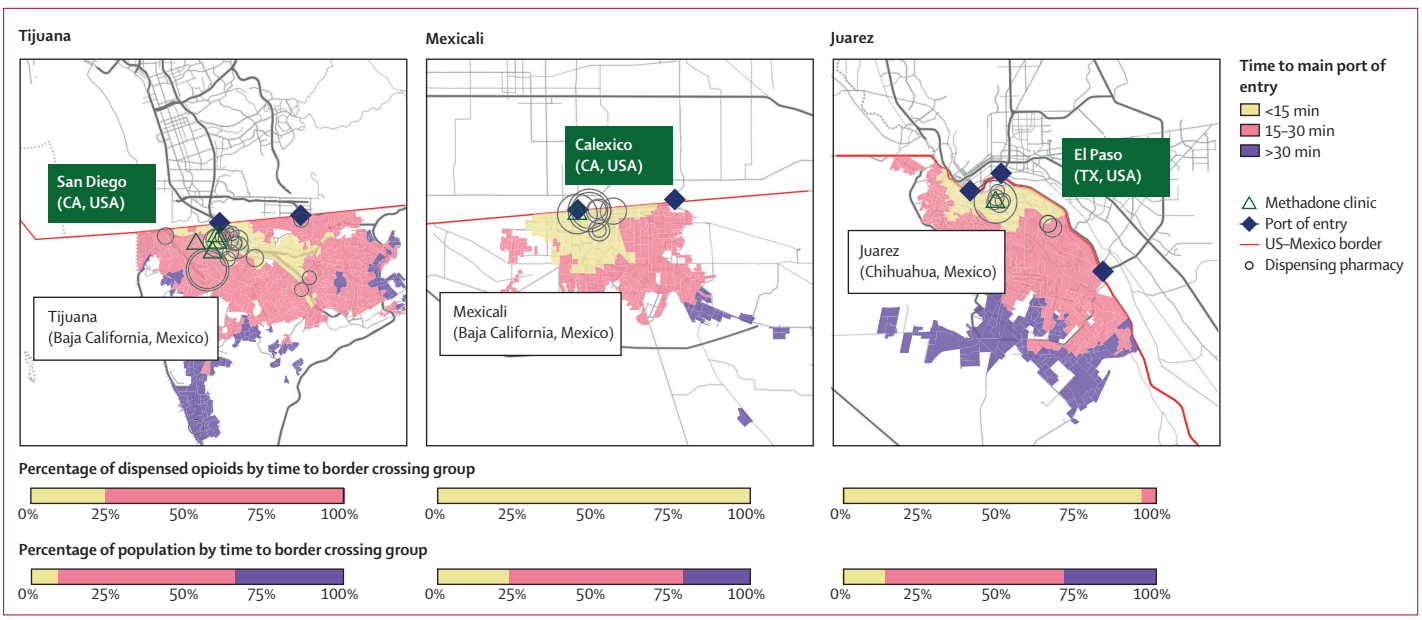

Figure 4: **Percentage of dispensed opioids by time to border crossing in the three largest metropolitan areas in Mexico situated on the US–Mexico border**
Circles indicate the location of pharmacies that dispensed opioids during the study period; the size of the circles are proportional to the number of opioids dispensed.

0·75–0·86) in opioid dispensation was observed per each SD increase (SD 17·1 min) in time to the border.

Discussion

We assessed national surveillance data for opioid dispensing in Mexico at multiple geographical levels. We found that opioid dispensing in Mexico has increased since implementation of regulatory changes associated with opioid prescription, the introduction of an electronic prescribing platform, and increased coverage from medical insurers since 2015. However, opioid dispensing remains low compared with other middle-income and high-income countries. Based on 2018 data, the International Narcotics Control Board ranked Mexico 104th in narcotic consumption among the 180 member nations.[26]

Socioeconomic status was a significant predictor of opioid dispensing rates across geographical areas, highlighting important disparities in access to medications included on the WHO list of essential medicines.[27] These socioeconomic inequalities were evident both at the state level and across metropolitan areas. Our geospatial assessment identified higher rates of opioids dispensing in areas with high and very high socioeconomic status than areas with very low, low, and medium socioeconomic status. Many reasons for this disparity in socioeconomic status exist. From a structural perspective, large referral hospitals are concentrated in the larger, more prosperous cities and states; these hospitals are typically where patients with advanced stage diseases receive treatment. Additionally, within those larger cities, different health systems are concentrated in the same geographical areas, leading to further disparities in care.[28] From an economic perspective, the additional costs to stock and store opioids and protect them from theft, and the limited affordability of these medications in poorer areas, might disincentivise pharmacies in poorer areas to make opioids available. From the perspective of patients and health-care providers, differences in cultural perceptions about pain and its treatment might also exist along socioeconomic strata. These potential differences should be further explored in the Mexican context.

Most states with the highest opioid dispensing rates were in the northern region of Mexico, on the US–Mexico border. Socioeconomic prosperity was highest in areas situated on the US–Mexico border, and this was associated with higher opioid dispensing rates compared with other Mexican states. However, more nuanced explanations exist. The US–Mexico border is a dynamic area; a complicated interdependent relationship exists between inhabitants on both sides. Since opioids are commonly prescribed on the US side of the border, local demand for opioids might influence inhabitants on the Mexican side to seek more opioids or providers to prescribe more opioids in comparison to other areas of Mexico. Moreover, access to opioids in the USA has become more difficult, which might lead inhabitants on the US side of the border to seek opioids in Mexican border cities.[29] This is supported by the heavy concentration of pharmacies observed near the ports of entry at these border cities.

Dispensing rates for methadone fluctuated over time in our analysis, which highlights inconsistent access to medications for opioid use disorder. Methadone clinics in

the country are mostly concentrated in the northern regions, although data on methadone availability in Mexico are sparse.[30,31] Methadone has been available largely through private clinics; however, a subsidised public option is available through Centros de Integracion Juvenil. A report in the grey literature highlighted recent closures of methadone clinics in several Mexican cities.[32] The report underscores the low capacity for methadone production in Mexico, noting the presence of only one licensed manufacturer in the country, and the highly regulated, time consuming, and burdensome process of importing manufacturing supplies. This led to shortages in the methadone supply chain that might explain the sudden increases and decreases observed. Decreases in supply, arbitrary policing around clinics,[33,34] and economic barriers[30,31] also restrict patient access to methadone therapy.

Our analysis has several limitations. First, analyses were done at the ecological level and no patient-level or provider-level data were included. Surveys at the patient and provider level in distinct geographical areas are needed to provide context to opioid use patterns and elucidate patient-level contributions to facilitators and barriers to opioid access and dispensing. Many other factors might also mediate the disparity in opioid access and should be further explored. Second, although data before 2015 were requested from COFEPRIS, data were not provided, and we were unable to compare changes in opioid dispensing before the implementation of the electronic system and regulatory changes. Third, we were not provided with data on medications in groups 2 or 3. These data would be informative in providing the full scope of use of opioids and other controlled substances in Mexico. Access to medications in groups 2 and 3 might be higher in areas of lower socioeconomic status, and might explain the gap in group 1 medication dispensing; however, this is unknown. Fourth, we did not analyse differences among the many medical systems that provide care in Mexico during the study period. These systems included public systems such as Seguro Popular and the Mexican Institute of Social Security, and the private sector. Availability of the different systems and variations in their quality of care might also be important factors in opioid access. Fifth, we assumed no traffic for our calculation of travel time to the main border crossing. In real-world conditions, traffic might influence time to travel and could have affected opioid access. Sixth, it is possible that some institutions might not have complied with the regulatory requirements to submit data to COFEPRIS. However, considering the diverse geographical and institutional representation within the database, we believe this database provides a broad representation of opioid dispensing practices in Mexico.

For **study code and data** see https://github.com/Joseph-Friedman/MEX_Opoids

Based on our findings, interventions are needed in Mexico to improve opioid access among patients in palliative care settings or who require opioids for pain management. General medical providers need universal training in palliative care and pain management during medical school and in continuing education. Mexican guidelines exist for the management of palliative care and opioids provided by the Secretary of Health and the National Institute of Cancer;[35] these guidelines should be widely disseminated to practitioners. Fellowship programmes for specialty training in palliative care are being established in Mexico, but incentives for doctors and other structural changes are likely to be necessary to provide this type of care in low socioeconomic status settings to prevent the widening of disparities in opioid access. Fear of opioids among Mexican patients with cancer is common,[36] and educational interventions for wider acceptance of opioids are needed. Universal coverage of opioids for patients with evidence-based needs is necessary. Seguro Popular, a government programme aimed at the provision of universal health care, evolved since its inception in 2003 and included palliative care. However, Seguro Popular was replaced in early 2020 with the Health Institute for Welfare (INSABI). The health benefits of INSABI have yet to be defined and its initial operation has been marred by public dissatisfaction.[37,38] This new health-care system should fulfil a promise of quality service and medication access to all of its beneficiaries, while maintaining surveillance on opioid use to avoid inadvertent public health crises associated with opioid overprescription.

Contributors

DG-M and JA-S conceived the study. DG-M, JA-S, and SV-M obtained the data. DG-M, JF, MMK, MJS, JA-S and MS analysed and interpreted the data. DG-M wrote the first draft of the report. JF, EA-P, MJS, CF, SAS, SS contributed to the writing of the report. All authors agreed with report results and conclusions. DG-M and JF accessed and verified the data and the code.

Declaration of interests

DG-M reports grants from Gilead, outside the submitted work. All other authors declare no competing interests.

Data sharing

The study code and study data are available online.

Acknowledgments

DG-M received funding from the US National Institute on Drug Abuse (grant number K08DA048163). JF received funding from from the University of California, Los Angeles Medical Scientist Training programme (National Institute of General Medical Sciences training grant GM008042). SS received funding from from the US National Institute of Mental Health (grant number P30-MH58107). SAS received funding from the US National Institute on Drug Abuse (grant R01DA049644). The content is solely the responsibility of the authors and does not necessarily represent the official views of the US National Institutes of Health or the authors' employing institutions. We thank the Mexican National Institute for Transparency, Access to Information and Personal Data Protection (Mexico City, Mexico) and the Mexican COFEPRIS (Mexico City, Mexico) for their support, cooperation, assistance, and provision of the data.

References

1 Organisation for Economic Co-operation and Development. Governance frameworks to counter illicit trade. March 1, 2018. https://www.oecd-ilibrary.org/governance/governance-frameworks-to-counter-illicit-trade_9789264291652-en (accessed April 2, 2020).

2 Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief–an imperative of universal health coverage: the *Lancet* Commission report. *Lancet* 2017; **391:** 1391–454.

3 Lohman D, Herrera García A. Care when there is no cure. New York: Human Rights Watch. https://www.hrw.org/report/2014/10/28/care-when-there-no-cure/ensuring-right-palliative-care-mexico (accessed Sept 27, 2020).

4 Goodman-Meza D, Medina-Mora M-E, Magis-Rodríguez C, Landovitz RJ, Shoptaw S, Werb D. Where Is the opioid use epidemic in Mexico? A cautionary tale for policymakers south of the US–Mexico border. *Am J Public Health* 2019; **109:** 73–82.

5 Solorzano JCG. Reglas generales para la tramitación electrónica de permisos para el uso de recetarios especiales con código de barras para medicamentos de la fracción I del artículo 226 de la Ley General de Salud. Mexico City: Comision Federal para la Proteccion contra Riesgos Sanitarios, 2015. https://www.dof.gob.mx/nota_detalle.php?codigo=5411543&fecha=14/10/2015 (accessed Dec 2, 2020).

6 Comision Nacional de Poblacion. En seis meses, aumenta sustancialmente en méxico la disponibilidad de medicamentos para el dolor. Mexico City: Comision Federal para la Proteccion contra Riesgos Sanitarios, 2016. https://www.gob.mx/cofepris/prensa/en-seis-meses-aumenta-sustancialmente-en-mexico-la-disponibilidad-de-medicamentos-para-el-dolor (accessed Dec 2, 2020).

7 Comision Nacional de Proteccion Social en Salud. Catálogo universal de servicios de salud. Mexico City: Secretaria de Salud, 2016. https://www.gob.mx/cms/uploads/attachment/file/280285/ANEXO_I_2016.pdf (accessed March 13, 2018).

8 Seya M-J, Gelders SFAM, Achara OU, Milani B, Scholten WK. A first comparison between the consumption of and the need for opioid analgesics at country, regional, and global levels. *J Pain Palliat Care Pharmacother* 2011; **25:** 6–18.

9 Rajagopal MR, Karim S, Booth CM. Oral morphine use in South India: a population-based study. *J Glob Oncol* 2017; **3:** 720–27.

10 McDonald DC, Carlson K, Izrael D. Geographic variation in opioid prescribing in the U.S. *J Pain* 2012; **13:** 988–96.

11 Guy GP Jr, Zhang K, Bohm MK, et al. Vital signs: changes in opioid prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017; **66:** 697–704.

12 Schieber LZ, Guy GP Jr, Seth P, et al. Trends and patterns of geographic variation in opioid prescribing practices by state, United States, 2006–2017. *JAMA Netw Open* 2019; **2:** e190665.

13 Monnat SM, Peters DJ, Berg MT, Hochstetler A. Using census data to understand county-level differences in overall drug mortality and opioid-related mortality by opioid type. *Am J Public Health* 2019; **109:** 1084–91.

14 Gutiérrez JP, García-Saisó S, Espinosa-de la Peña R, Balandrán DA. Monitoring of inequality in financial protection and healthcare in Mexico: an analysis of health surveys 2000, 2006 and 2012. *Salud Publica Mex* 2016; **58:** 639–47 (in Spanish).

15 Gutiérrez JP, García-Saisó S, Espinosa-de la Peña R, Balandrán DA. Health inequality on results and access indicators for children in Mexico: analysis of national health surveys. *Salud Publica Mex* 2016; **58:** 648–56 (in Spanish).

16 Secretaria de Salud. Listado de medicamentos de referencia. Mexico City; Secretaria de Salud, 2019. https://www.gob.mx/cms/uploads/attachment/file/441323/Listado_de_medicamentos_de_Referencia_.pdf (accessed April 13, 2020).

17 National Institute of Statistics and Geography. Intercensal Survey 2015. 2015. http://en.www.inegi.org.mx/programas/intercensal/2015/ (accessed April 2, 2020).

18 Davies TM, Marshall JC, Hazelton ML. Tutorial on kernel estimation of continuous spatial and spatiotemporal relative risk. *Stat Med* 2018; **37:** 1191–1221.

19 Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392:** 1736–88.

20 Flores-Jimenez P, Tejeida-Padilla R, Morales-Matamoros O. Structural equation model for the multidimensional measurement of the poverty in Mexico. Proceedings of the 54th Meeting of the International Society for the Systems Sciences; Waterloo, ON, Canada; July 18–23, 2010 (abstr 1388).

21 Comision Nacional de Poblacion. Índice de marginación por entidad federativa y municipio 2015. 2016. http://www.gob.mx/conapo/documentos/indice-de-marginacion-por-entidad-federativa-y-municipio-2015 (accessed April 2, 2020).

22 Comision Nacional de Proteccion Social en Salud. Bases de datos de licencias sanitarias de farmacias. Mexico City: Gobierno de Mexico, 2016. http://www.gob.mx/cofepris/documentos/bases-de-datos-de-licencias-sanitarias-de-farmacias (accessed Sept 27, 2020).

23 Sistema Nacional de Información en Salud. Catalogo de establecimientos de salud. Mexico City: Gobierno de Mexico, 2020. http://gobi.salud.gob.mx/historico_clues/ESTABLECIMIENTO_SALUD_202008.xlsx?v=1.1 (accessed Sept 27, 2020).

24 Secretaria de Salud. Datos Abiertos de México–Recursos en salud, nivel central–Recursos en Salud 2017. Mexico City: Gobierno de Mexico. https://datos.gob.mx/busca/dataset/recursos-en-salud-nivel-central (accessed Oct 2, 2020).

25 Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000; **19:** 335–51.

26 International Narcotics Control Board. Narcotic drugs 2019. Vienna: UN, 2019. https://www.incb.org/documents/Narcotic-Drugs/Technical-Publications/2019/Narcotic_Drugs_Technical_Publication_2019_web.pdf (accessed May 11, 2020).

27 WHO. World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization, 2019. https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf (accessed May 10, 2020).

28 Gómez Dantés O, Sesma S, Becerril VM, Knaul FM, Arreola H, Frenk J. The health system of Mexico. *Salud Publica Mex* 2011; **53** (suppl 2)**:** s220–32 (in Spanish).

29 Wagner KD, Moynihan MJ, Strathdee SA, et al. The social and environmental context of cross-border drug use in Mexico: findings from a mixed methods study of young injection drug users living in San Diego, CA. *J Ethn Subst Abuse* 2012; **11:** 362–78.

30 Burgos JL, Cepeda JA, Kahn JG, et al. Cost of provision of opioid substitution therapy provision in Tijuana, Mexico. *Harm Reduct J* 2018; **15:** 28.

31 Fleiz C, Villatoro J, Domínguez M, Bustos M, Medina-Mora M-E. Opioid crisis along Mexico's northern border: treatment needs Mexican opioid crisis. *Arch Med Res* 2019; **50:** 527–34.

32 Ospina-Escobar A. El desabasto de metadona en México: la política del dolor. Nexos. 2019. https://economia.nexos.com.mx/?p=2110 (accessed May 11, 2020).

33 Werb D, Wagner KD, Beletsky L, González-Zúñiga P, Rangel G, Strathdee SA. Police bribery and access to methadone maintenance therapy within the context of drug policy reform in Tijuana, Mexico. *Drug Alcohol Depend* 2015; **148:** 221–25.

34 Werb D, Strathdee SA, Vera A, et al. Spatial patterns of arrests, police assault and addiction treatment center locations in Tijuana, Mexico. *Addiction* 2016; **111:** 1246–56.

35 Consejo de Salubridad General, Instituto Nacional de Cancerologia, Early Institute. Guía de manejo integral de cuidados paliativos. Mexico City: Diario Oficial de la Federación, 2018. http://www.geriatria.salud.gob.mx/descargas/publicaciones/Guia_cuidados_paliativos_completo.pdf (accessed Sept 27, 2020).

36 Allende-Pérez S, Verástegui-Avilés E, Mohar-Betancourt A, Meneses-García A, Herrera-Gómez A. Integrated oncology and palliative care: five years experience at the National Cancer Institute of Mexico. *Salud Publica Mex* 2016; **58:** 317–24.

37 Reich MR. Restructuring health reform, Mexican style. *Health Syst Reform* 2020; **6:** 1–11.

38 Frenk J, Gómez-Dantés O, Knaul FM. A dark day for universal health coverage. *Lancet* 2019; **393:** 301–03.