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Opioid and related health consequences in East Asian communities with high population density: An empirical case of Hong Kong

Hung Chak Ho PhD MHKIOEH MRSTMH

Assistant Professor, Department of Public and International Affairs, City University of Hong Kong, Hong Kong

Dr Ho is a population health scientist with expertise in social determinants of health. His interests include biopsychosocial impacts on pain and drug use.

Chi Wai Cheung MBBS (HK) MD (HKU) FHKCA FFPMANZCA FHKCA (Pain Med) FHKAM (Anaesthesiology) Dip Pain Mgt (HKCA)

Clinical Professor, Department of Anaesthesiology, School of Clinical Medicine, The University of Hong Kong, Hong Kong

Honorary Consultant in Anaesthesiology and Specialist in Anaesthesiology, Department of Anaesthesiology, Hong Kong Sanatorium & Hospital, Hong Kong

Professor Cheung, Chi Wai is the former chairperson and current Clinical Professor of the Department of Anaesthesiology at the University of Hong Kong (HKU). He was the Peter Hung Professor in Pain Research in 2022 to 2023 at HKU. He was the former Chair of Specialty for Anaesthesiology and Adult Intensive Care Services, Gleneagles Hospital, as well as the former Chief of Service, Department of Anaesthesiology, HKU-Shenzhen Hospital. He was also the former Division Chief in Pain Medicine of the Department of Anaesthesiology, Queen Mary Hospital (Hong Kong). Professor Cheung has published extensively in peer-reviewed scientific journals in anaesthesiology and pain medicine. He is a regularly invited journal reviewer for many international peer-reviewed journals. He is the section editor of *Pain Practice*. He is the past president of the Hong Kong College of Anaesthesiologists and the past president of the Society of Anaesthetists of Hong Kong. Correspondance to: cheucw@hku.hk

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INTRODUCTION

The use of opioids has a global impact on health risk. In 2019, a review found that the prevalence of prescription opioids has been rising globally.[1] According to a 2022 longitudinal study, sales of opioid analgesics increased from 2015 to 2019.[2] They went from 27.52 milligrams of morphine equivalent per 1000 people per day (MME per 1000/day) in 2015 to 29.51 MME per 1000/day in 2019. Despite lower sales in North America and Oceania, this longitudinal analysis indicated increases in opioid analgesic sales in South America, Eastern Europe, Asia, and Western/Central Europe. These increases were influenced by country-level Human Development Index and cancer death rates.

On the extreme end of the spectrum, some countries are experiencing a serious epidemic of opioid misuse with numerous fatal cases (e.g. the United States and Canada).[3-5] The COVID-19 pandemic also altered the pattern of opioid use and its associated health impacts. It significantly increased overdose mortality in the United States, particularly in suburban White communities with wealthier residents as well as urban districts with poorer subpopulations (e.g. Black and Hispanic communities).[6] Understanding opioid usage, problems and associated health effects is crucial for medical treatment and reducing risk because of the inequity of opioid consumption and access globally. Notably, cultural norms and therapeutic approaches differ significantly in East Asian communities with dense populations (such as Hong Kong) from those in European and American countries. Opioid issues and their effects on health risks among these East Asian communities are typically underreported. As a result, this study uses the particular situation in Hong Kong as a case for global comparison.

OPIOID CONSUMPTION IN HONG KONG

In comparison to other areas, Hong Kong has a decreased risk of opioid abuse due to its tight drug consumption legislation. Oxycodone, an opioid pain medication, was not registered as a medicine appropriate for medical treatment until 13 May 2010.[7] As of 14 April 2023, there were only 455 registered

opioid-containing pain medications in Hong Kong, including seven products containing buprenorphine, 356 products containing codeine, 16 products containing fentanyl, 16 products containing morphine, 18 products containing oxycodone, and 42 products containing tramadol. These are pharmaceutical products that can only be obtained with a prescription and are sold under strict control. There are no registered medications containing hydrocodone, hydromorphone, or oxymorphone in Hong Kong.

Hong Kong has minimal opioid consumption not only in comparison to European and American countries, but also in comparison to adjacent East Asian communities. A recent study analysed trends in opioid use for pain in six adjacent communities (South Korea, Japan, Taiwan, Singapore, Hong Kong, and China) using World Health Organization (WHO) data from 2015 to 2017.[8] Hong Kong had the second-lowest opioid consumption rate of the six communities, with just 218 defined daily doses for statistical purposes (S-DDDs) per million inhabitants per day (S-DDD/m/d) for six types of opioids (fentanyl, morphine, oxycodone, hydromorphone, codeine and pethidine). This is critical because daily opioid intake in Hong Kong was just 9.4% of the intake recorded for South Korea and 15.9% compared to Japan. Daily consumption in Hong Kong was 1.8% of that in North America (12,255 S-DDD/m/d), 2.6% of that in Oceania (8246 S-DDD/m/d), and 3.3% of that in South America (6648 S-DDD/m/d) between 2015 and 2017.

Despite its low opioid usage, Hong Kong's opioid consumption trends differed slightly from those of the other areas. Fentanyl was the most often used opioid across most regions between 2015 and 2017, followed by oxycodone. However, morphine (94 S-DDD/m/d) had the largest local usage per day in Hong Kong, followed by fentanyl (76 S-DDD/m/d). Despite 356 recognised pharmaceutical items containing codeine for pain relief in Hong Kong, daily codeine intake was just 1 S-DDD/m/d. Interestingly, this daily codeine intake in Hong Kong was believed to be used primarily for cough treatment, rather than for pain reduction. This pattern of opioid intake had an impact on health outcomes and medical treatment strategies in Hong Kong.

OPIOID UTILISATION PATTERNS IN HONG KONG

Due to differences in opioid consumption trends between Hong Kong and other locations, a 2018 study evaluated opioid utilisation patterns, in terms of opioid order, after head and neck procedures in the United States and Hong Kong.[9] Based on 253 cases from a representative hospital in Hong Kong and 567 cases from a representative hospital in the United States, it was found that the hospital in the United States used a substantially greater opioid order the day before surgery (PRE1), postoperative day 6 (POD6), and postoperative day 14 (POD14) (see Table 1).

The orders of acetaminophen or paracetamol, NSAIDs, and anxiolytics did not differ significantly between hospitals in the United States and Hong Kong.

Table 1. Frequency of opioid and tramadol orders in US and Hong Kong hospitals

	Frequency of opioid orders in US hospital	Frequency of opioid orders in Hong Kong hospital	Frequency of tramadol orders in US hospital	Frequency of tramadol orders in Hong Kong hospital
PRE1	15.3%	1.6%	0.4%	4.7%
POD6	86.8%	0.4%	0.9%	13.4%
POD14	71.4%	0.8%	4.0%	9.5%

Using data from Li et al. (2018)[9]

A comparative study in 2019 also discovered a difference in opioid intake owing to cultural background and healthcare setting.[10] This research studied patients who underwent major abdominal surgery and were given patient-controlled analgesia with intravenous morphine for postoperative pain treatment, comparing patients in Hong Kong with those from surrounding regions. Educational attainment, place of residence, and ability to understand English were used to define the level of Western cultural influences. One hundred and twenty-eight Chinese patients in rural China and 134 patients in Hong Kong with a high influence from Western culture were compared, based on a total opioid requirement up to 48 hours after surgery as the primary endpoint. Postoperative opioid requirements were substantially higher among patients in Hong Kong. Estimated by morphine equivalent, the average cumulative opioid demand among patients in Hong

Kong was 42.0 mg ([CI: 38.3–45.6], p-value < 0.0001), whereas patients in rural China required just 18.8 mg (CI: 15.7–22.0). More notably, ethnicity was a significant influence on opioid requirement in addition to operation duration and severity of pain upon admission to the post-anaesthetic care unit. These findings confirmed the causes for regional differences in opioid consumption, with an underlying assumption regarding the potential influences of regional socioeconomic status, cost of healthcare, and utilisation.

Another notable example is the use of opioids for palliative care in Hong Kong, particularly among cancer patients. Opioid medication for chronic non-cancer pain is uncommon and lacks established regulatory/practice guidelines in Hong Kong.[11] Specifically, guidelines are published in Hong Kong, but medical doctors are not required to follow them. Interestingly, opioids are widely utilised among cancer patients, particularly those whose situations are deteriorating. A retrospective study conducted in Hong Kong in the early 2000s discovered high usage of opioids among patients receiving palliative care.[12] This study included 494 cancer deaths to examine the utilisation of public healthcare by advanced cancer patients in their last six months of life and their end-of-life process within the last two weeks of life. This cohort included 247 patients who received palliative care and died in palliative care units (PCS-PCD), 86 patients who received palliative care but died in non-palliative care wards (PCS-NPCD), and 161 patients who did not receive palliative care (NPCS-NPCD).

Although all groups received a similar amount of mild opioids during the last two weeks of life, individuals in PCS-PCD received much more fentanyl and morphine than the other groups. The difference between groups was not significant for fentanyl; however, it was for morphine (p-value = 0.001). Patients in PCS-PCD received significantly more morphine than patients in PCS-NPCD, while PCS-NPCD patients received significantly more morphine than patients in NPCS-NPCD. Although opioid usage patterns in Hong Kong have evolved lately, these traditions of using morphine for palliative care have remained notable.

MORTALITY RISK FROM OPIOID USE IN HONG KONG

A recent analysis for drug poisoning deaths (2001–2016) in Hong Kong indicated a considerable decline in mortality from other opioids (codeine or morphine) between 2001 and 2004, and a stable declining trend between 2005 and 2010,[7] owing to rigorous drug registration laws and specific patterns of opioid use. However, as with prescription opioid difficulties in other countries, the number of deaths has steadily climbed since 2011, shortly after the certification of prescription opioids for medicinal purposes (e.g. oxycodone). A population-based retrospective cohort study for opioid-naive individuals who underwent surgical operations between 1 January 2000 and 30 November 2020, found similar evidence.[20] Based on a month as the median follow-up period, 15,112 (3.45%) of 438,128 patients had persistent opioid use. The use of prescription opioids after discharge also increased 30-day all-cause mortality, with an OR of 1.68 (1.53–1.86).

The fatal risk directly induced by opioids is not a significant issue in Hong Kong, with a very small number of deaths when compared to other leading causes of mortality, such as malignant neoplasms and pneumonia. In total, there were roughly 113.3 deaths (range: 96–130, SD: 15.2) directly from other opioids (codeine or morphine) in Hong Kong every year between 2001 and 2004, 33.2 deaths (range: 17–59, SD: 15.5) between 2005 and 2010, and 32.0 deaths (range: 19–48, SD: 9.6) between 2011 and 2016.[7] Middle-aged, young-old (aged between 55 and 70), and divorced people were more likely to die from other opioids (codeine or morphine). Since 2011, a significant demographic shift in mortality patterns has occurred, with a 6.5-fold increase in deaths from other opioids (codeine or morphine) in people aged 60 compared to the 2001-2010 period (OR: 6.50 [3.97, 10.65]). Opioid-related deaths have also shifted to regions with less neighbourhood deprivation, more highly educated citizens, and a mix of private and public housing residents.[8]

Although opioid use may not directly increase the risk of death, it may indirectly cause deaths due to factors such as self-harm and suicide. In 2022, a population-cohort study used the Hong Kong Hospital Authority's Clinical Data Analysis and Reporting System (CDARS) to examine connections between specific drug-related disorders and the risk of self-harm or suicide in Hong Kong.[13] This study identified 8270 relevant CDARS cases between 2004 and 2016, who were aged 10 or older and had visited the accident and emergency department of a representative hospital for one of the following drug-related disorders: 1) opioid, 2) ketamine, 3) methamphetamine, 4) sedative, hypnotic, or anxiolytic, 5) amphetamine or related stimulant, 6) cocaine, 7) cannabis, 8) hallucinogen, and 10) polydrug.

The most prevalent group, opioid use disorder, was represented by 2523 cases (30.51%). When compared to the other drug-related disorders, opioid use disorder had the highest risk of self-harm or suicide, with an

adjusted hazard ratio (aHR) of 27.323 [95% CI: 19.71–38.32; p-value < 0.0001] controlled for gender and age. The aHR was 15.97 [95% CI: 10.73–23.23; p-value < 0.0001] for the best model defined by this study, which adjusted for gender, age, self-harm diagnosis, concurrent self-harm diagnosis, drug use disorder diagnosis, and any psychiatric disorder (comprising depression, bipolar disorder, alcohol and tobacco abuse disorder, personality disorder, anxiety disorder, and schizophrenia) and any physical illness (comprising asthma, diabetes, epilepsy, HIV, cancer, and dermatitis or eczema) diagnosis before or on the index date. The above findings consistently show that opioid consumption in Hong Kong is associated with a high fatal risk due to indirect and underlying causes of death, even though the level of consumption itself is not high.

NON-FATAL HEALTH CONSEQUENCES FROM OPIOID USE IN HONG KONG

Non-fatal health consequences in Hong Kong as a result of opioid use should also be noted. There are several significant consequences of opioid use: 1) substance abuse, 2) mental distress, and 3) side effects on physical health and healthy behaviours. According to a population-cohort study conducted in 2022, people with opioid use disorder had a high prevalence of comorbidity with psychiatric disorders.[13] About 424 of the 2523 opioid use disorder cases (16.81%) had some type of psychiatric disorder, 125 cases (4.95%) had depression, 110 cases (4.36%) had schizophrenia, and 84 cases (3.33%) had personality disorders. Approximately 134 cases (5.31%) had an alcohol and tobacco use disorder. Additionally, other than people with cancer (85 cases, 3.37%), comorbidities related to physical illness and conditions among opioid use disorder cases included 72 cases (2.8%) of asthma, 57 cases (2.26%) of epilepsy, 42 cases (1.66%) of diabetes, and 34 cases (1.35%) of dermatitis or eczema.

Comorbidities may also exacerbate issues of substance abuse or mental distress, as well as the side effects on physical conditions or healthy behaviours. In another population-based cohort based on CDARS data, Wei et al. (2021) compared people with and without substance use disorders.[14] After matching, individuals with substance use disorders had a much higher percentage of decedents from non-heroin opioid poisoning than those without disorders (4.2% vs 0.5%). According to related studies, opioids were the most abused substance in the accident and emergency (A&E) department of Hong Kong's public hospitals (27.1%) between 2004 and 2016.[15,16] Opioids in particular were one of the major substances causing patients with substance abuse to return to the hospital. According to a recent population-based study, prescribing opioids on discharge was linked to an increased risk of developing persistent opioid use (OR: 2.30 [2.19-2.40]), 30-day emergency department visits (OR: 1.28 [1.23-1.33]), and 30-day readmission (OR: 1.17 [1.13-1.20]).[20] For the first three and a half months of 2023, the Hong Kong Department of Health had received 28 reports of adverse drug reactions as follows: four from codeine, three from fentanyl, ten from morphine, four from oxycodone, and seven from tramadol. The prevalence of opioid-related side effects in Hong Kong, such as nausea, drowsiness, itching, and dizziness, has yet to be determined.

Thus, a better public health surveillance system is essential, partially due to changes in social behaviours/health awareness among the Hong Kong population. A population-based study found that fewer people were taking medications for chronic pain in 2013 compared with data from 1999 (34.9% in 2013 vs 47.6% in 1999, p-value = 0.019).[17] The proportion of people taking analgesics (opioids) as oral pain medication dropped from 0.9% to 0.09%, although the result was statistically insignificant. Fewer people used pharmaceutical analgesics by injection in 2013 (1.6% in 2013 vs 10.3% in 1999, p-value < 0.0001). Furthermore, improved public health concern is critical, owing in part to changes in social behaviours and health awareness among the Hong Kong population. A population-based study discovered that fewer people were taking chronic pain medications in 2013 than in 1999 (34.9% in 2013 vs 47.6% in 1999, p-value = 0.019).[17] The number of people using addictive analgesics (opioids) for oral pain relief decreased from 0.9% to 0.09%, though the difference was statistically insignificant. Pharmaceutical analgesics by injection were used by fewer people in 2013 (1.6% in 2013 vs 10.3% in 1999, p-value = 0.0001). Furthermore, another population-based study found the following:

1. Chronic pain patients with neuropathic characteristics were less likely to receive prescribed oral medication, including both additive and non-additive analgesics (e.g. NSAIDs) (p-value = 0.0226).
2. Oral analgesics were less useful (p-value = 0.0215).[18] This could be due to apprehension about using opioids.

Notably, the above differences were not statistically significant. In addition, the above study indicated a higher percentage of individuals using additive analgesics (opioids) among chronic pain patients with neuropathic characteristics compared to those without neuropathic characteristics (3.8% vs 1%), but a lower percentage of chronic pain patients with neuropathic characteristics using NSAIDs (1.3% vs 2.4%).[18] According to another Hong Kong study, individuals with cancer pain may have fatalistic beliefs, posing a barrier to optimising pain control.[19] Because 79% of respondents believed that medications could not relieve cancer pain, they identified pain as an unavoidable component of hospitalisation. About 52% of respondents expressed concern about becoming addicted to opioid analgesics. Approximately half of those polled thought opioid analgesics should only be used as a last resort.

HEALTH POLICY IMPLICATIONS

Overall, our empirical case of Hong Kong indicates a low risk of opioid-related mortality. However, the risk of side effects and morbidity cannot be overlooked. Concerns about social behaviours and health awareness, as well as a lack of policies and protocols addressing local opioid use, can be issues. This evidence may be useful for global comparison, as "relatively low-risk" does not always imply "always" good. It is critical to understand how to create a "no one left behind" framework to support local citizens, especially in high-risk areas due to high levels of dependence and addiction to opioids.

However, whether there are relevant policies to target opioid risk is always a question. Using Hong Kong as an empirical case, the local government established the "Steering Committee on Primary Healthcare Development" in November 2017 to improve primary healthcare services. In December 2022, the Hong Kong government's official policy framework, known as the "Primary Healthcare Blueprint" was released. This policy framework established four domains of healthcare strategy to improve the overall health of the Hong Kong population: 1) prevention-oriented healthcare services, 2) community-based healthcare systems, 3) family-centric healthcare support, and 4) early detection with timely intervention. In addition, the Hong Kong government released a policy-oriented action plan in 2018, titled "Towards 2025: Strategy and Action Plan to Prevent and Control NCD in Hong Kong," with nine targets for health actions to: 1) reduce premature mortality from noncommunicable diseases, 2) reduce harmful alcohol use, 3) reduce physical inactivity, 4) reduce salt intake, 5) reduce tobacco use, 6) contain the prevalence of raised blood pressure, 7) halt the rise in diabetes and obesity, 8) apply drug therapy and counselling to prevent heart attacks and strokes, and 9) increase the availability of affordable basic technologies and essential medicines to treat major noncommunicable diseases. All of these targets, however, were not directly related to the risk of opioid use.

This situation is similar to that in most cities in East Asia. Particularly, the most significant social and health concern among East Asian cities is population ageing. Therefore, most healthcare protocols (similar to Hong Kong's blueprint noted previously) target chronic illnesses, which are more relevant to the direct causes affecting the ageing population. For opioid risk, it progressively becomes a serious issue because it more notably affects the indirect health effects of ageing individuals, such as side effects in pain patients after treatments. There are many social and health issues due to a lack of "knowledge, attitude, and practice" (KAP) secondary to a low health awareness among these patients in East Asian cities. A recent example of non-prescription drug use is seen in Japan. As in China, there are Japanese individuals who adopt the use of traditional (or herbal) medicine. This has led to a "bloom" of traditional medicine used for pain relief in Japan, which is not only being sold to locals but also to visitors. However, it has recently been found that such traditional medicine-based pain relievers contain an excessive amount of codeine. As a result, Japan may benefit from setting emergency policies that restrict visitors from buying these pain relievers in order to reduce the overuse of these drugs due to the lack of transparency and awareness surrounding the potential presence and side effects of opioids.

Thus, patients need to be informed about the benefits and drawbacks of using opioid analgesics to reduce misconceptions and concerns. Furthermore, it is critical to develop guidelines and protocols for the use of opioids in various treatments, as this can reduce adverse health risks (e.g. mortality risk, substance abuse) among the local population. Finally, more population-based studies should be conducted in different cities to clarify the associations between opioid use and side effects on both mental and physical conditions.

CONCLUSION

Understanding opioid usage/challenges and health-related implications is vital for risk reduction because disparities due to opioid consumption/access are documented globally. Medical treatment strategies and cultural practices in Asian areas with high population density differ greatly from those in Westernised countries, and opioid risk usage/challenges in these Asian populations has been underreported. Hong Kong was chosen as our study location for a worldwide comparison, as it is representative of the East Asian community. In general, opioid consumption in Hong Kong is modest in comparison to European/

American countries and neighbouring regions. However, patterns of opioid utilisation in Hong Kong differ from those found elsewhere. Although the risk of death from opioid consumption is relatively low, death counts have steadily climbed since 2011, shortly after the registration of prescription opioids for medical applications (e.g. oxycodone). Furthermore, the demographic pattern for deaths from other opioids (codeine or morphine) has migrated toward the middle-aged, young-old, and divorced, and decedents lived in areas with low neighbourhood deprivation, which could be influenced by social behaviours, cultural practices, and health awareness. In Hong Kong, opioid usage is also linked to additional comorbidities with tragic outcomes (e.g. self-harm, suicide) and adverse health consequences (e.g. substance abuse, mental distress, side effects on physical conditions/health behaviours). These are risk factors that can further induce high levels of dependence and addiction to opioids. Furthermore, the Hong Kong government has established several health policy frameworks, such as the "Primary Healthcare Blueprint" and “Towards 2025: Strategy and Action Plan to Prevent and Control NCD in Hong Kong”; however, none of these frameworks explicitly address opioid usage hazards. Thus, the central question is how to improve location-specific solutions to reduce opioid hazards. Our findings suggested that “relatively low-risk” may not always be “good.” Creating a “no one left behind” framework to support local communities is thus critical, particularly in areas with high opioid risk.

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