Ten Years of Strong Opioid Analgesics Consumption in Malaysia and Other Southeast Asian Countries

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**Background:** It was reported that opioid consumption in developing countries was stagnated or decreased, but precise data on the consumption are unclear. This study examined the trends and patterns of opioid consumption in Malaysia and other four Southeast Asian countries.

**Materials and Methods:** Data of five strong opioids consumption (morphine, oxycodone, fentanyl, pethidine, and methadone) between 2005 and 2014 from Malaysia, Singapore, Indonesia, Thailand, and Vietnam were extracted from the Pain and Policy Studies Group. Defined daily doses per 1000 inhabitants per day (DDD/1000 inhabitants/day) was used for calculating the annual amount of opioid use.

**Results:** The total consumption of five strong opioids was increased in all five Southeast Asian countries during a 10-year study period. Malaysia was recorded with the largest increase of the opioid consumption (993.18%), followed by Indonesia (530.34%), Vietnam (170.17%), Singapore (116.16%), and Thailand (104.66%). Malaysia also had the highest total strong opioid consumption (11.2 DDD/1000 inhabitants/day), primarily for methadone. Among the opioids used for pain management, fentanyl was primarily used in Malaysia and Singapore but the greatest increase in these two countries was for oxycodone. Fentanyl was also primarily used in Indonesia while morphine was predominantly used in Thailand and Vietnam.

**Conclusion:** Growing trends of strong opioids consumption in all five Southeast Asian countries demonstrated in this study may indicate improved access to opioid analgesics in these countries. Given the increasing trends, it is important to ensure that the utilization of opioids is according to the guideline to prevent the negative consequences of opioids particularly when used in chronic non-cancer pain.

**Keywords:** Consumption, Malaysia, Southeast Asian countries, strong opioids, trends

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**INTRODUCTION**

Opioid analgesics such as fentanyl, oxycodone, and morphine have long been used for the treatment of pain. The World Health Organization considers the annual morphine consumption in each country as an indicator of access to opioids for pain management and the consumption of morphine has been regarded as a gold standard in the treatment of moderate to severe cancer pain. Morphine has also been included in the list of Essential Medicines to recognize the significance of morphine for improving patients’ health status and well-being.

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How to cite this article: Zin CS. Ten years of strong opioid analgesics consumption in Malaysia and other Southeast Asian countries. J Pharm Bioall Sci 2020;12:846-51.
There have been large inequalities between high-income countries and low- and middle-income countries (LMICs) in the global opioid consumption. It was reported that high-income countries which constituted 17% of the world’s population consumed almost all of the global opioid consumption (92%), whereas only 8% of the global consumption of opioids was attributed to the LMICs which constituted 83% of the world’s population. The imbalance of the global opioid consumption is likely to reflect inadequate pain management in the LMICs.

Although it was reported that the opioid consumption in the LMICs was stagnated or decreased, precise data on the consumption are unclear. Therefore, the current study was prompted to examine the trends of strong opioid consumption in Malaysia and other four Southeast Asian countries, which include Singapore, Indonesia, Thailand, and Vietnam. The inclusion of only these five countries and not all countries in the region is to provide in-depth data on strong opioid consumption from the individual country’s perspective rather than regional superficial data if all the countries were included. The in-depth data can serve as an indicator to assess the readiness for the treatment of moderate-to-severe pain.

**Materials and Methods**

**Study design and data source**

This study was a retrospective cross-sectional study that evaluated the consumption of strong opioids in five Southeast Asian countries (Malaysia, Singapore, Indonesia, Thailand, and Vietnam). Data of all available strong opioids (morphine, oxycodone, fentanyl, pethidine, and methadone) between 2005 and 2014 for the five countries were extracted from the Pain and Policy Studies Group (PPSG). The PPSG is the WHO Collaborating Centre for Pain Policy and Palliative Care that directly obtains data on opioid consumption from the International Narcotics Control Board (INCB) annually. The latest data was only available up to 2014 at the time of data extraction from the PPSG.

Defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. Given the present data, DDD per 1000 inhabitants per day (DDD/1000 inhabitants/day) is the most appropriate tool for comparing the consumption of opioid for each country. The reported amount of opioid from the PPSG in mg per capita were converted to DDD/1000 inhabitants/day by dividing the amount by its relevant DDD and then multiplied by 1000. This value was then divided by 365 to derive DDD/1000 inhabitants/day.

The DDDS used in the present study was according to a report published by the WHO Collaborating Centre for Drug Statistics Methodology, Anatomical Therapeutic Chemical Classification System (ATC classification index) 2018. The DDDS used in the current study were morphine (100 mg), fentanyl (transdermal) (1.2 mg), oxycodone (75 mg), and pethidine (400 mg). The DDD for methadone was 25 mg, an amount used in the methadone treatment for opioid dependence. The amount was used in the present study due to unavailability of DDD for analgesic use of methadone.

**Outcome measures**

The total consumption of all five strong opioids with methadone and without methadone was calculated annually to differentiate the use of opioids for opioid dependence and pain management. The total consumption of each of the strong opioid (fentanyl, morphine, methadone, oxycodone, and pethidine) in each country for each year was also characterized. However, data for oxycodone in Indonesia, Thailand, and Vietnam were not available.

Descriptive statistics were used to report the annual opioid consumption in each year. The percentage change in the annual consumption between 2005 and 2014 for each opioid in each country was also calculated. All analyses were performed using Stata/SE 15.1.

**Results**

**Total strong opioid consumption in five Southeast Asian countries with and without methadone**

Over a 10-year study period, the total strong opioid consumption with methadone was increased in all five Southeast Asian countries. Malaysia recorded the largest increase of strong opioid consumption (993.18% increase), followed by Indonesia (530.34% increase), Vietnam (170.17% increase), Singapore (116.16% increase), and Thailand (104.66% increase) [Table 1]. During the study period, the total overall opioid consumption with methadone in Malaysia was higher (11.204 DDD/1000 inhabitants/day) than that of Vietnam (0.244), Singapore (1.786), Thailand (0.971), and Indonesia (0.371).

From 2005 to 2014, the total consumption of four opioids without methadone (fentanyl, morphine, oxycodone, and pethidine) was increased in all five countries. Indonesia recorded the largest increase (591.67% increase), followed by Vietnam (198.23% increase), Singapore (121.06% increase), Thailand...
During the same period, the total consumption of the four opioids was the highest in Singapore (1.73 DDD/1000 inhabitants/day), followed by Malaysia (1.043), Thailand (0.545), Vietnam (0.208), and Indonesia (0.075).

Over the 10-year study period, the consumption of methadone increased the largest in Malaysia (1884.58% increase) compared with Indonesia (451.39% increase), Thailand (87.55% increase), Vietnam (68.98% increase), and Singapore (12.73% increase) [Table 1]. The consumption of methadone was the highest in Malaysia (10.161 DDD/1000 inhabitants/day), followed by Thailand (0.426), Indonesia (0.296), Singapore (0.056), and Vietnam (0.036). Ninety percent of the total opioid consumption in Malaysia was contributed by the consumption of methadone (10.161 DDD/1000 inhabitants/day), which was mainly used in opioid dependence programs.

### Table 1: Consumption of strong opioids between 2005 and 2014 in DDD per 1000 inhabitants per day in Southeast Asian countries

| Opioids     | 2005  | 2014  | Total 10 years consumption | Percent change from 2005 to 2014 |
|-------------|-------|-------|-----------------------------|---------------------------------|
| **Malaysia** |       |       |                             |                                 |
| Oxycodone   | 0.009 | 0.022 | 0.103                       | 143.29                          |
| Morphine    | 0.025 | 0.020 | 0.287                       | -19.91                          |
| Fentanyl    | 0.028 | 0.064 | 0.431                       | 128.61                          |
| Pethidine   | 0.024 | 0.020 | 0.222                       | -14.30                          |
| Methadone   | 0.091 | 1.808 | 10.161                      | 1884.58                         |
| Total with methadone | 0.177 | 1.934 | 11.204                      | 993.18                          |
| Total without methadone | 0.086 | 0.126 | 1.043                       | 47.23                           |

| Indonesia  |       |       |                             |                                 |
| Morphine   | 0.001 | 0.003 | 0.016                       | 340.78                          |
| Fentanyl   | 0.001 | 0.012 | 0.041                       | 1480.81                         |
| Pethidine  | 0.001 | 0.003 | 0.018                       | 167.19                          |
| Methadone  | 0.002 | 0.011 | 0.296                       | 451.39                          |
| Total with methadone | 0.005 | 0.030 | 0.371                       | 530.34                          |
| Total without methadone | 0.003 | 0.018 | 0.075                       | 591.67                          |

| Singapore  |       |       |                             |                                 |
| Oxycodone  | 0.001 | 0.030 | 0.186                       | 4116.24                         |
| Morphine   | 0.027 | 0.020 | 0.311                       | -27.02                          |
| Fentanyl   | 0.049 | 0.147 | 1.080                       | 196.31                          |
| Pethidine  | 0.015 | 0.009 | 0.153                       | -42.30                          |
| Methadone  | 0.004 | 0.005 | 0.056                       | 12.73                           |
| Total with methadone | 0.097 | 0.210 | 1.786                       | 116.17                          |
| Total without methadone | 0.093 | 0.205 | 1.730                       | 121.06                          |

| Thailand   |       |       |                             |                                 |
| Morphine   | 0.017 | 0.038 | 0.257                       | 121.63                          |
| Fentanyl   | 0.010 | 0.036 | 0.217                       | 254.81                          |
| Pethidine  | 0.009 | 0.006 | 0.071                       | -32.41                          |
| Methadone  | 0.033 | 0.061 | 0.426                       | 87.55                           |
| Total with methadone | 0.069 | 0.141 | 0.971                       | 104.66                          |
| Total without methadone | 0.036 | 0.080 | 0.545                       | 120.00                          |

| Vietnam    |       |       |                             |                                 |
| Morphine   | 0.004 | 0.011 | 0.093                       | 204.60                          |
| Fentanyl   | 0.003 | 0.011 | 0.083                       | 290.63                          |
| Pethidine  | 0.002 | 0.004 | 0.032                       | 68.98                           |
| Methadone  | 0.002 | 0.004 | 0.035                       | 68.98                           |
| Total with methadone | 0.011 | 0.031 | 0.244                       | 170.17                          |
| Total without methadone | 0.009 | 0.027 | 0.208                       | 198.23                          |

(120.0% increase), and Malaysia (47.23% increase). During the same period, the total consumption of the four opioids was the highest in Singapore (1.73 DDD/1000 inhabitants/day), followed by Malaysia (1.043), Thailand (0.545), Vietnam (0.208), and Indonesia (0.075).

Over the 10-year study period, the consumption of methadone increased the largest in Malaysia (1884.58% increase) compared with Indonesia (451.39% increase), Thailand (87.55% increase), Vietnam (68.98% increase), and Singapore (12.73% increase) [Table 1]. The consumption of methadone was the highest in Malaysia (10.161 DDD/1000 inhabitants/day), followed by Thailand (0.426), Indonesia (0.296), Singapore (0.056), and Vietnam (0.036). Ninety percent of the total opioid consumption in Malaysia was contributed by the consumption of methadone (10.161 DDD/1000 inhabitants/day), which was mainly used in opioid dependence programs.

### Consumption of fentanyl, oxycodone, morphine, and pethidine

#### Malaysia

Among the opioids used for pain management in Malaysia, fentanyl was predominantly used (0.431 DDD/1000 inhabitants/day) followed by morphine (0.287), pethidine (0.222) and oxycodone (0.103) during the 10-year study period. The consumption of oxycodone (143.29%) was increased at a higher rate...
than that of fentanyl (128.61%). In contrast, there was a decrease in the consumption of morphine (−19.91% decrease) and pethidine (−14.30% decrease) [Figure 1].

Indonesia
Fentanyl (0.041 DDD/1000 inhabitants/day) had the highest consumption in Indonesia followed by pethidine (0.018) and morphine (0.016). The increase in the consumption was the largest for fentanyl (1480.81% increase), followed by morphine (340.78% increase) and pethidine (167.19% increase).

Singapore
Fentanyl was also the most commonly used opioid (1.08 DDD/1000 inhabitants/day) in Singapore, followed by morphine (0.311), oxycodone (0.186), and pethidine (0.153) during the same study period. The consumption of oxycodone (4116.24% increase) and fentanyl (196.31% increase) was increased while a decrease was noted in the consumption of morphine (-27.02% decrease) and pethidine (−42.30% decrease).

Thailand
In Thailand, morphine was the most commonly used opioid during the study period (0.257 DDD/1000 inhabitants/day) followed by fentanyl (0.217) and pethidine (0.071). An increase was noted in the consumption of fentanyl (254.81% increase) and morphine (121.63% increase), whereas the utilization of pethidine decreased (−32.41% decrease).

Vietnam
Morphine (0.093 DDD/1000 inhabitants/day) appeared to be consumed the most in Vietnam compared with fentanyl (0.083) and pethidine (0.032). Fentanyl recorded the largest increase in utilization (290.63% increase), followed by morphine (204.60% increase) and pethidine (68.98% increase).

DISCUSSION
Over a 10-year study period, the total consumption of five strong opioids increased in all of the five Southeast Asian countries. Malaysia was noted with the largest increase in the consumption over time as well as the highest total consumption of the five strong opioids, primarily for methadone. As for the consumption of opioids that are mainly used for pain management (fentanyl, morphine, oxycodone, and pethidine), Singapore was recorded with the highest total consumption but the largest increase was noted for Indonesia.

The present study showed that the trends of opioids consumption in all of the five Southeast Asian countries increased over time despite the usage being lower than global average. This increasing trend is a positive direction that reflects the improvement in the availability of opioid analgesics in all the five countries. This direction is the first requirement for addressing further the issue of inadequacy of opioid analgesics in most of the countries.[11] To further improve the access to opioids, collaborative efforts from relevant departments such as by governments, non-governmental organizations, and health organizations are required.[12] Although the opioid consumption is very regional in nature and the drivers of changes are

Figure 1: Total consumption of oxycodone, morphine, fentanyl, and pethidine in each Southeast Asian country
different by countries, the focus in general should be directed on educational, cultural measures, regulatory enforcement, and health policy development.

Among the opioids for pain management, fentanyl was the most frequently used in Malaysia, although the greatest increase was marked for oxycodone. A similar trend of consumption was also seen in Singapore. Fentanyl and morphine in Malaysia are recommended for treating cancer pain and the availability of a new formulation of fentanyl transdermal patch may explain the preference to choose for fentanyl to morphine. The increasing use of oxycodone and the decreasing use of morphine as shown in the current study for Malaysia and Singapore were also seen in other countries such as Denmark, United Kingdom, and Nordic countries.[13-15] A previous study that evaluated the dose and duration of opioids at a tertiary hospital setting in Malaysia demonstrated a similar finding; the increasing use of oxycodone which was mainly used for non-cancer pain.[16] This finding reflects that the higher cost of oxycodone compared with morphine does not discourage the prescribers from prescribing oxycodone. Factors other than clinical and economic evidence could influence the choice of opioid, such as the convenience of dosing, availability of new formulations, anticipated adverse effects, and doctor or patient preferences.[14]

The current study also demonstrated that Indonesia used fentanyl the most while Thailand and Vietnam primarily used morphine. It is also noted that no data for oxycodone were available in these countries. The overall strong opioids consumption in these countries was low and their main utilization of fentanyl and morphine may reflect the usage was mainly for cancer pain[17,18] and limited for non-cancer pain. Moreover, lack of studies was found on the usage of opioids on non-cancer pain from the three countries. The consumption of pethidine was little in all countries and was decreased in Malaysia, Singapore, and Vietnam which may reflect the replacement of pethidine by other opioids due to the former’s accumulation of a toxic metabolite and inappropriateness for the treatment of chronic pain.[19]

The data on opioid consumption between the countries should be interpreted with caution due to the variability in methods of collecting and reporting the data.[20] For the data from INCB as used in the current study, the result might be incomplete or invalid for a particular year because some governments have issued inaccurate reports, have delayed the reporting or have not reported for a particular year or period.[9] The consumption data also do not distinguish among clinical uses of opioids and whether the opioids have been used by hospitals or other institutions. The information on dosage forms of an opioid or the availability of which products in a country are also not captured when using the opioid consumption data.

**Conclusion**

The overall increasing trends of strong opioids consumption in all five Southeast Asian countries may reflect the improvement in the access to opioid analgesics. Malaysia had the largest increase as well as the highest total of strong opioid consumption during the study period, primarily for methadone. Among the opioids for pain management, fentanyl was primarily used in Malaysia, Singapore, and Indonesia while the use of morphine predominates in Thailand and Vietnam. Given the positive trend of the consumption, it is important to ensure that the utilization of opioids is according to the guideline to prevent the negative consequences of opioids particularly when used in chronic non-cancer pain.

**Acknowledgement**

CSZ was supported by a fundamental research grant scheme from the Ministry of Higher Education Malaysia (FRGS 19-010-0618). CSZ initiated and developed the research questions and study design, conducted data management and analysis, drafted the manuscript and revised the final version submitted for publication.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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