A Bibliometric Analysis of Opioid in Malaysia

Che Suraya Zin, Nor Asma Diyana Abdullah, Noorul Atiqah Ramli, Noorsyahiruh Khadir, Nor Shahfiza Zain, Nor Fatin Rosley, Siti Halimah Bux

Kulliyyah of Pharmacy, International Islamic University Malaysia, Kuantan, Pahang, Malaysia

Opioid analgesics have been widely used for the treatment of pain. In USA, it was reported an increase in opioid prescribing is parallel with the increase of opioid use disorders such as misuse, abuse, and opioids overdose-related death. Little is known about the opioid situation and its related research in Malaysia. Therefore, this bibliometric study provided an overview on the productivity of opioid research in Malaysia. All published articles on opioid research in Malaysia from 2006 to 2018 were included, where they were retrieved from online databases. Then, the data were analysed, presented and discussed using standard bibliometric indicators, such as growth of publications, number of citation journals, geographical distribution, and issues addressed in the publications. Total of 78 research articles on opioids published between 2006 and 2018 were identified. The relative growth rate (RGR) of publications during the study period was 12.24%. The most common issue studied was the methadone maintenance therapy. Most articles were published in the indexed journals (98.72%) and the predominant journal was the Drug and Alcohol Dependence (11.54%). The article on buprenorphine and naltrexone reported the highest citations of 85. It can be concluded that research evaluating opioids in pain management particularly in patients with non-cancer pain in Malaysia is limited and requires further exploration.

**KEYWORDS:** Bibliometric, Malaysia, methadone, morphine, opioid research

**INTRODUCTION**

Opioids are strong analgesics that have established indication for the treatment of acute pain, postsurgical pain, and cancer pain.[1] Examples of opioids are fentanyl, morphine, buprenorphine, methadone, oxycodone, and tramadol.[2] Although opioids can provide pain relief, it is also associated with undesirable side effects such as constipation, cognitive impairment, and opioid dependence.[3]

Despite the established indication for the aforementioned pain conditions, opioid use in chronic non-cancer pain (CNCP) is controversial due to the lack of evidence supporting the effectiveness for this condition. Opioid overdose-related death is commonly associated with long-term opioid therapy in CNCP caused by “opioids overdose triad,” which consist of pinpoint pupils, unconsciousness, and respiratory depression.[4] Careful monitoring is required when opioids are being used for long-term to ensure adequate pain control while preventing the harmful effects of opioids.[5]

There is limited research on opioids in Malaysia and little is known about the progress of opioid research in this country. Therefore, this bibliographic study, which is a quantitative method used to classify, analyze, and investigate the knowledge structure and development of opioid research based on analysis of related publications was carried out.[5]
This bibliometric study examined, among others, the growth of publications, number of citations, types of journal, and issues addressed by the articles. The outcomes of this study can guide researchers to fill the gap of opioid research in Malaysia.

MATERIALS AND METHODS
This bibliometric study did not require the ethical approval as there was no patient involvement in the study.

Search databases
In this study, information about opioid research in Malaysia was retrieved from several databases including Google Scholar, PubMed, ScienceDirect, and Scopus. Among these databases, only Scopus and ScienceDirect had the analytical function of “source type,” which allowed us to analyze whether the retrieved articles are journal publications, books or conference proceedings. This study included published research articles that had been published from 2006 to 2018, excluding review articles, books or conference proceedings.

Search terms
Search terms that had been used in this study started with the broad term “opioids” and “Malaysia.” However, since only some of the publications could be retrieved, a second approach was used by searching specific opioid drugs such as methadone, buprenorphine, morphine, fentanyl, tramadol, naloxone, oxycodone, remifentanil, mitragynine, and heroin.

Outcome measures
The retrieved articles were analyzed according to several categories such as annual growth, types of journal, citation analysis, geographical distribution, and issues addressed by the articles.

Annual growth rate
Growth analysis presented as annual growth rate (AGR) was defined as the percentage change in the number of publications over a period of 1 year which was calculated based on the following equation:

\[ AGR = \left( \frac{\text{Ending Value} - \text{Beginning Value}}{\text{Beginning Value}} \right) \times 100 \]

The growth analysis was also presented as relative growth rate (RGR) which was defined as the increase in number of publications per unit of time which was from 2006 to 2018. The RGR was calculated based on the following equation:

\[ \text{RGR} = \log_e W_2 - \log_e W_1 \times \left( T_2 - T_1 \right) \]

where \( \log_e W_i \) is log of initial number of articles, \( \log_e W_f \) is log of final number of articles after a specific period of interval, and \( T_2 - T_1 \) is the unit difference between the initial time and the final time.

Type of journals
The types of journal which published the research were identified in terms of their index and the impact factor. They were then categorized based on indexed (Scopus or ISI) and non-indexed. This information was obtained from Journal Guide, Master Journal list (MJL Clarivate) and Scopus Preview.

Number of citations
The citation analysis was also recorded and presented as frequency, percentage, and total number of citations. The average number of citations per research article was calculated. The articles with the highest number of citations were identified.

Geographical distribution
Geographical distribution of the author affiliation was examined to characterize which institutions and states have actively participated in opioid study in Malaysia. The affiliation is based on the first author. However, if the author affiliation is outside Malaysia, then the author in Malaysia was used.

Issue addressed by the research
Issues addressed by the research were analyzed and were recorded accordingly.

Statistical analysis
Descriptive statistics for categorical variables such as frequencies and percentages were presented. For continuous data, mean, median, and standard deviation were represented. All analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). The geographical data was analyzed and visualized using online software, Visme.com (Easy Webcontent, Frederick, MD, USA).

RESULTS
Total research articles retrieved
The total research articles retrieved during the study period from 2006 to 2018 were 78 articles with a fluctuating growth of the research during the study duration.

Annual growth rate and relative growth rate of articles
The mean number of publications from 2006 to 2018 was 4.33 research articles per year. The highest productivity with a total of 12 articles (15.38%) was observed in 2013. Meanwhile, the lowest productivity was observed in 2006 and 2009 in which two articles
(2.56%) were published respectively. The AGR ranged approximately −75.00% to 200.00% due to fluctuating pattern throughout the study period and RGR for the 13 years’ study duration was 12.24%.

**Type of journals (indexed or non-indexed)**
There were 98.72% (n = 78) indexed journals (61.54% ISI and 37.18% Scopus) and 1.28% (n = 1) non-indexed journals. The most common ISI indexed journal was the *Journal of Drug and Alcohol Dependence* (11.54%, n = 9). *The Lancet* was the ISI indexed journal that has the highest impact factor of 59.102. The most common Scopus journal was the *Medical Journal of Malaysia* with a total of five articles.

**Citation analysis**
The total citations for all research articles included during the study period were 1255 citations with the mean of 16.09 citations per article. The article with the highest number of citations was published in *The Lancet* with a total number of 85 citations and the title of research was “Heroin Dependence Treatment in Malaysia: A Randomized, Double-Blind, Placebo-Controlled Comparison of Buprenorphine and Naltrexone Maintenance Treatment.” The top five journals with the highest citations included *The Lancet*, *Molecular Diagnosis & Control*, *International Journal of Drug Policy*, and *The American Journal of Drug and Alcohol Abuse*.

**Geographical distribution of the opioid research**
The overall distribution of opioid research showed that Wilayah Persekutuan was the highest, with 32 researches (41.02%). This was proportional to Universiti Malaya (UM), which is located in this state and represented as most productive institution [Figure 1]. This was followed by Penang (15.38%; n = 12) and Kelantan (11.54%; n = 9). Pahang and Selangor have 8 (10.26%) and 7 (8.97%) opioid research conducted, respectively. Other states that conducted opioid research included Johor with 4 (5.13%) research and Terengganu with 3 (3.84%) research, whereas Melaka, Negeri Sembilan, and Perak conducted only one research each.

**Issue investigated by the research**
The two main issues examined were the methadone maintenance therapy (MMT) (28.20%; n = 22) and the efficacy of opioids for relieving pain (25.64%; n = 20). The types of opioid studied in the research were methadone (n = 21), buprenorphine (n = 9), fentanyl (n = 4), heroin (n = 5), mitragynine (n = 3), and remifentanil (n = 1), whereas tramadol and morphine resulted seven research articles accordingly. For tramadol, the first research in Malaysia emerged in 2007 with the average citation of 12.86 (median = 1).

**DISCUSSION**
This study showed that there were 78 published research articles during the 13-year duration from 2006 to 2018 in Malaysia. The growth rate of opioid research in Malaysia was fluctuating which may reflect the inconsistent focus on opioid research in this country. The primary research was on MMT, which was mainly used for opioid addiction.[6] This MMT was introduced by the government in 2005 as a harm reduction therapy in treating opioid addiction[6] and most of research involving MMT showed in this study was focusing on the effectiveness and appropriateness of the MMT therapy. Most of the MMT issues were published in *Journal Drug and Alcohol Dependence*, which was the top journal in the study. This is not surprising as most of the issues investigated involved dependence and addiction which was one of the main scopes of the journal.

This study is unable to compare the overall growth of opioid research in Malaysia with other countries due to unavailability of such study in the latter. However, a bibliometric study on a specific opioid, tramadol, has been published thus providing some data that can be compared.[7] A previous research on tramadol was conducted in Palestine investigating the overview of

![Figure 1: Geographical distribution of the opioids research conducted in Malaysia based on the first author affiliation](image-url)
research productivity on tramadol. The analysis was based on 2059 articles published from 1978 to 2013. From this bibliometric study, tramadol has shown to be an opioid of interest worldwide. The first tramadol research was published in 1978 in German followed by rapid development after 1995. The average citation was 17.62 (median = 6) citations per article. Compared to this bibliometric study, the research on tramadol in Malaysia has actively progressed after 2007. The citation analysis on tramadol research in Malaysia showed an average of 12.86 (median = 8.0) citations per article. This may mean that issues investigated in tramadol research have received a close review or attention among researchers both from Malaysia and abroad.

In Malaysia, the state with the most number of authors and coauthors of opioid research was Wilayah Persekutuan. This is parallel with the number of higher learning institutions that were involved in research in this state. The most active institution conducting research on opioids in Wilayah Persekutuan was UM. This bibliometric analysis of opioids is the first of its kind in Malaysia; hence, it is able to provide some insight on the progress of opioids research in this country. Among the limitations to this study it can be acknowledged that some articles could have been left out if the specific search terms used were not included in their titles, abstract, or keyword. However, such articles may not be relevant to this study as all databases have been scrutinized including articles that have met the inclusion criteria of this study.

**CONCLUSION**

This study depicted that the pattern of opioid research in Malaysia is fluctuating, in which there is no definite increasing or decreasing trend. The most common issue investigated in opioid research in Malaysia is on the methadone harm reduction program and the lack of research involving opioid use in patients. Therefore, it is encouraged for future research to focus on opioid use in the controversial management of pain in patients with CNCP.

**Financial support and sponsorship**

CSZ was supported by a research grant from the Ministry of Education Malaysia (Fundamental Research Grant Scheme, FRGS 19-010-0618).

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. Exp Clin Psychopharmacol 2008;16:405-16.
2. Opioids list [homepage on the Internet]. Ottawa, Canada: Government of Canada; [updated 2018 October 1; cited 2019 July 16]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/list-opioids.html.
3. Ramsin B, Andrea MT, Sukdeb D, Ricardo MB, Rajive A, Nalini S, et al. Opioid complications and side effects. Pain Physician J 2008;11.
4. Information sheet on opioids overdose [homepage on the Internet]. Geneva, Switzerland: World Health Organization; [updated 2018 Aug; cited 2019 July 16]. Available from: http://www.who.int/substance_abuse/information-sheet/en/.
5. What is Bibliometric Analysis [homepage on the Internet]. Pennsylvania, PA, USA: IGI Global; [updated 2013 April 10; cited 2019 July 17]. Available from: https://www.igi-global.com/dictionary/bibliometric-analysis/2406.
6. norsiah A, Salina A, Salmah N, Norliza CM, Norni A, Maimunah, et al. Malaysian methadone treatment outcome study (MyTOS). Kuala Lumpur, Malaysia: Ministry of Health; 2016.
7. Sweileh WM, Shraim NY, Zyoud SH, Al-Jabi SW. Worldwide research productivity on tramadol: a bibliometric analysis. Springerplus 2016;5:1108.
8. List of Universities in Each State [homepage on the Internet]. Kuala Lumpur, Malaysia: Malaysia University Portal; [updated 2018 December 23; cited 2019 Aug 24]. Available from: https://www.malaysiauniversity.net/states-university/.
9. Top Universities in Malaysia [homepage on the Internet]. Singapore; [updated 2019; cited 2019 September 15]. Available from: https://www.topuniversities.com/universities/universiti-malaya-um.