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Editorial

Let's Not Waste the Crisis!

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It has been nearly three years since the advent of COVID-19 to the human history in 2020 and it seems that today is not the end of the story. COVID-19 may stay with us at least in a few more years. The pandemic severely hit individual lives and business in many countries. In Thailand, the country GDP plummeted by about 6.2% in 2020.[1] In response to the pandemic, Thailand established the Centre for COVID-19 Situation Administration (CCSA) under the Emergency Decree in March 2020. The CCSA is responsible for steering all disease control measures and managing the information of COVID-19 in timely and integrating manner. The function of CCSA is in line with one of the recommendations of the World Health Organization's Joint Intra-Action Review of the Public Health Response to COVID-19, which suggests a setting up of advanced national digital database for public health response. Under the leadership of the CCSA, many health information system initiatives were introduced, such as, Co-Lab system (national recording of laboratory tests on COVID-19) and Co-Ward system (national monitoring on health facility consumption related to COVID-19).

However, the system is yet to be perfect. Despite the introduction of several health information initiatives above, there are still rooms for improvement. One of the concrete examples is the discrepancy in death report between government agencies. During January 2020–December 2021, the CCSA reported 61 COVID-19 deaths in 2020, and 21,637 in 2021, while the death registry of the Strategy and Planning Division, the Office of Permanent Secretary, Ministry of Public Health, revealed the death toll with written cause of death as COVID-19 of 54 in 2020 and 29,175 in 2021.

This discrepancy faces explanation difficulty. There may be some possible reasons behind. First is the difference in the timing and protocol of data collection. Every COVID-19 death reported to the Department of Disease Control will be informed to the CCSA for public announcement on a day-by-day basis.[2] Some deaths are roughly verified by the local health personnel by clinical judgement with epidemiological linkage. While the death registry of the Strategy and Planning Division conglomerated the death toll from various sources at the end of the year. In addition, the death registry depends on ICD-10 codes as suggested by the World Health Organization, that is., U07.1 or U07.2. U07.1 is applied where virus can be identified by laboratory testing, whereas U07.2 is for clinical or epidemiological diagnosis without laboratory confirmation. The bottom line is such codes must be clearly indicated in order to count this as COVID-19 death in the death registry. Second, though not directly explaining the discrepancy of the numbers in 2021, is the change in the policy direction towards COVID-19 by considering it as endemic disease under the concept of "living with COVID-19". In mid-2022, the focus of the CCSA had changed from all deaths with evidence of SARS-CoV-2 positive (die with) to deaths directly attributed to COVID-19 (die from). The change in the reporting criteria may cause further discrepancy of the numbers unless correction of the reporting system between agencies is exercised.

It might be pitiful if many efforts on health digital technology and data integration platform developed during the pandemic remained stagnant after the crisis. We all know that there are many public health threats that may arise in the future. A sound data management system is not just only a correct count of the number. A better data information system is an essential weapon for effective public response to any coming health threats. To achieve effective data informed decision making, it is vital to establish a clear data integration process both within and across organizations. Also, there are many other functions that need deliberate consideration, such as how to manage public perception on the data, how to address the issue of data confidentiality and privacy, and how to define clear ownership of the data while remaining openness to the wider public. Learning from the past is the only key. Let's not waste the crisis.

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First-generation Cluster of Coronavirus Disease 2019 (COVID-19) Related to Boxing Stadiums in Bangkok and the Bangkok Metropolitan Region, March 2020

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Abstract

In March 2020, clusters of COVID-19 cases were reported among attendees of a boxing stadium in Bangkok. This study aimed to investigate and describe the outbreak and identify its source. We conducted a descriptive analysis of cases and transmission patterns, performed a walk-through survey and interviewed stadium staffs for possible factors related to disease spreading. COVID-19 cases were those who had a history of visiting Bangkok or the Bangkok Metropolitan boxing stadiums, or contacting confirmed cases visiting boxing stadiums within 14 days of developing symptoms with laboratory confirmation using the RT-PCR method. An active case finding was accomplished through social media and the national disease surveillance system. High-risk contacts were self-quarantined and nasopharyngeal specimens were collected. Attack rate among boxing event attendees on 6 Mar 2020 was 11.0% (268/2,431). Attack rate among contacts of the first generation was 5.4% (110/2,024), and the second-generation contacts was 2.6% (6/229). Behavioral risks during the event included cheering and gambling among attendees. Some did not wear face masks. We recommend postponing all sporting matches as the most reasonable practice during an epidemic. To prevent and control future outbreaks, gambling should be restricted or limited to online payment and strict control measures should be considered.

Keywords: COVID-19, boxing stadiums, Thailand

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global threat, with over 800,000 confirmed cases and over 40,000 deaths worldwide up to early April 2020.[1] On 3 Jan 2020, Thailand established an Emergency Operation Center (EOC) and implemented the COVID-19 surveillance system at airports and hospitals. Anyone who met the criteria for a patient under investigation (PUI) would be tested for COVID-19 and reported through the system.[2] In Thailand, there were 1,875 cases with 15 deaths at the beginning of April 2020. Ten percent of all cases were related to boxing stadiums.[3]

Traditional Thai boxing is a popular sport in Thailand with many tourists attending boxing camps and stadiums each year.[4] On the sixth of March, 2020 a large boxing event was held at Lumpinee Stadium, one of well-known boxing stadiums in Thailand.[5] On 13 Mar 2020, the master of ceremonies (MC) at this event announced that he was infected with COVID-19.[6]

On 15 Mar 2020, a positive SARS-CoV-2 cluster was notified among persons who visited boxing stadiums. We aimed to confirm the diagnoses, identify the source of the outbreak, and describe its epidemiological characteristics.

Methods

A PUI was anyone with a body temperature ≥37.5 °C or a history of fever with one of the following symptoms during 23 Feb–7 Apr 2020: cough, rhinorrhea, sore throat, difficult breathing or dyspnea; or anyone with a confirmed diagnosis of pneumonia. Those who had a history of visiting a boxing stadium in Bangkok or the Bangkok Metropolitan or contacting a confirmed case who visited a boxing stadium within 14 days before developing symptoms, were also investigated. A confirmed case was a PUI with laboratory confirmation of SARS-CoV-2 by reverse transcription-polymerase chain reaction (RT-PCR) method. Asymptomatic infections were defined as anyone without symptoms but had laboratory confirmation of SARS-CoV-2 by the RT-PCR method. A high-risk contact was defined as a person who had close activities, i.e., sharing food and drinks, talking, or working with a case within a 1-meter distance for more than 5 minutes or being coughed or sneezed at directly without wearing appropriate personal protective equipment (PPE); or persons who came into contact with a case within a 1-meter distance for more than 15 minutes without wearing appropriate PPE. These criteria were adapted from the national COVID-19 investigation guideline.[7]

An active case finding was performed utilizing media announcements by the government to attendees of the boxing match on 6 Mar 2020 at Lumpinee Stadium. Some attendees were tested for COVID-19 by government services while others were tested at a private hospital. Since all COVID-19 cases must be reported to the EOC system, we searched for cases in the EOC database. We also used Facebook to identify cases using a snowball technique in case they were not reported to the EOC system. We investigated individuals by telephone or field investigation if the number of high-risk contacts was excessive. During our investigations, we determined the individual's relationship with the boxing stadium (visitor, competitor, staff), symptoms (if any), their 14-day travel history before symptoms onset, exact location (zone) in the stadium during the event, COVID-19 test history and result, and history of patient contact. Only high-risk contacts were traced, tested, and monitored during their 14-day self-quarantine period.

An environmental survey searched for potential sources of disease spread in the stadium, especially during the event. We observed the building structure and ventilation system, capacity and seating/zoning arrangements, number of restrooms, and availability of sanitizers. We interviewed boxing stadium officers about COVID-19 measures on the event day, the cleaning of boxing materials, and the participants' activities. At the boxing stadium we observed the surroundings, and the airflow.

After entering the data into a spreadsheet, we double-checked its completeness and cleaned it before analysis. We imported the cleaned data into Stata and performed descriptive statistics showing percentages to measure the magnitude and describe epidemiological characteristics of the outbreak.[8] Mean with minimum and maximum was used to describe age. We categorized cases into three generations but detailed only the first generation. We classified the cases by participant type, location of hospital, and presence of symptoms. We performed a retrospective cohort study of high-risk contacts to explore risk factors of being a COVID-19 case. We included all high-risk contacts of the first- and second-generation cases related to this event who had complete data on gender, age, and relationship with a case (household member or not). We followed these contacts and if they had a positive SARS-CoV-2 result, then they were defined as a case; otherwise, a non-case. We performed logistic regression to identify factors associated with being a case, presenting crude and adjusted odds ratios with 95% confidence interval (CI). *P*-values <0.05 were considered statistically significant.

Results

Attack rate among boxing event attendees on 6 Mar 2020 was 11.0% (268/2,431). This was the first-generation case who were linked to boxing stadiums and classified into six groups: 1) boxing fan, 94 cases; 2) MC or reporter, 5 cases; 3) staff or merchant, 43 cases; 4) attendant, 123 cases; 5) boxer, 2 cases; 6) unidentified, 1 case. We monitored 2,024 high-risk contacts and identified 110 confirmed cases (second generation), attack rate was 5.4%. The second-generation cases were household contacts (44.6%), colleagues (24.6%), close contacts from activities (22.7%), health care workers (1.8%), passengers traveling on the same flight with a case (0.9%), and unidentified (5.4%). Consequently, there were 229 high-risk contacts of second-generation cases of which we identified six confirmed third-generation cases, attack rate was 2.6%. We discovered that 83.3% of the cases were household contacts and 16.7% had a history of close contact activities (Figure1).

Since attendees came from several provinces of Thailand, some were hospitalized outside of Bangkok. We were able to obtain their isolation place at 82% (220/268), and we discovered three cases isolated in their home. As shown in Figure 2, the majority of cases, however, were contained in Bangkok and the Bangkok Metropolitan hospitals.

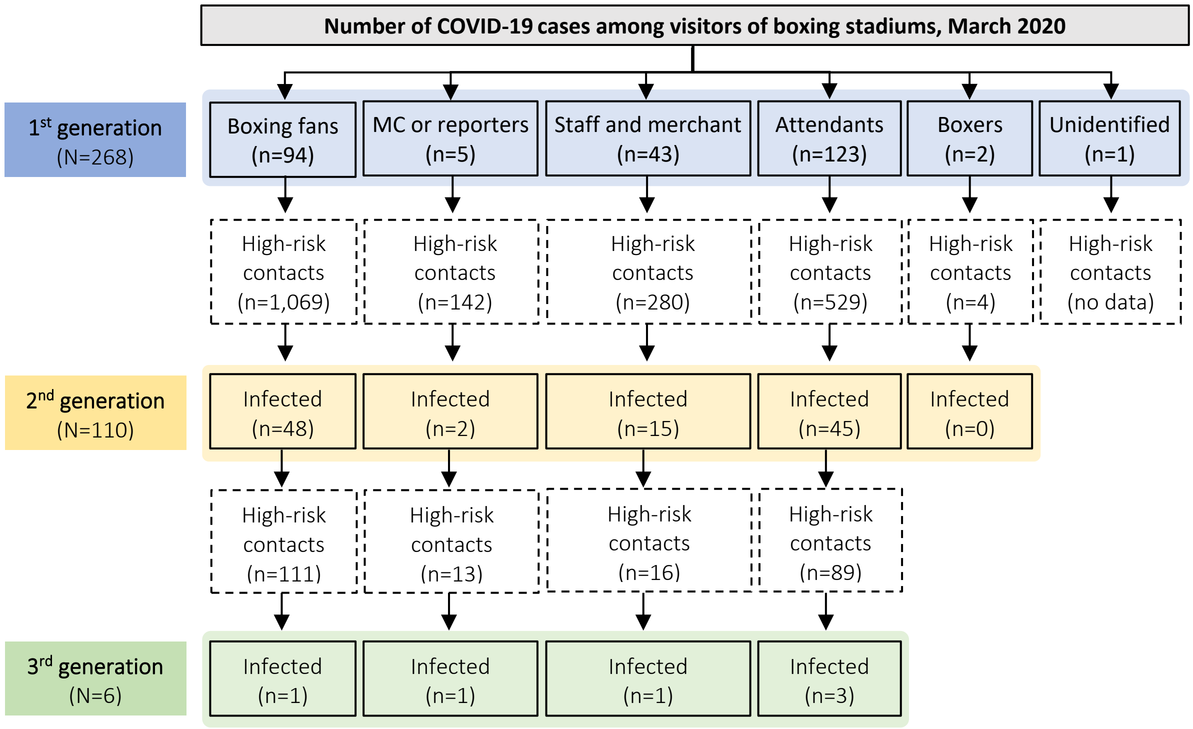
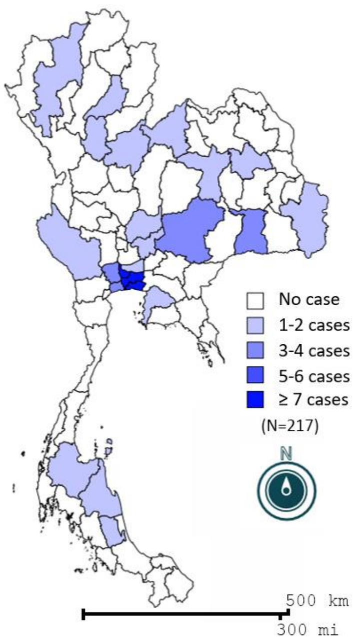


Figure 1. Number of confirmed COVID-19 cases liked to boxing stadiums in Bangkok and the Bangkok Metropolitan, March 2020

Province	Number of cases	Population[a]	Incidence rate per 100,000 population
Nonthaburi	54	1,276,745	4.2
Bangkok	107	5,588,222	1.9
Samut Prakan	14	1,351,479	1.0
Samut Sakhon	5	586,199	0.9
Phatthalung	2	523,077	0.4
Nakhon Pathom	3	920,729	0.3
Chonburi	4	1,566,885	0.3
Pathum Thani	3	1,176,412	0.3
Phrae	1	437,350	0.2
Surin	3	1,378,221	0.2
Surat Thani	2	1,067,726	0.2
Sukhothai	1	587,883	0.2
Loei	1	638,736	0.2
Saraburi	1	643,828	0.2
Nakhon Ratchasima	4	2,633,207	0.2
Songkhla	2	1,428,609	0.1
Chachoengsao	1	720,718	0.1
Lopburi	1	742,928	0.1
Phitsanulok	1	849,481	0.1
Kanchanaburi	1	891,976	0.1
Chiang Mai	2	1,784,370	0.1
Kalasin	1	977,175	0.1
Nakhon Si Thammarat	1	1,550,721	0.1
Khon Kaen	1	1,794,531	0.1
Ubon Ratchathani	1	1,866,697	0.1



Note: [a]Population in 2020 was obtained from the Department of Provincial Administration Registration.[9]

Figure 2. Distribution of admission of the cases linked to boxing stadiums in Bangkok and the Bangkok Metropolitan in Thailand, March 2020 (n=217)

Of the first-generation cases, the male-to-female ratio was 11 to 1. The mean (min–max) age was 49 (14–84) years. The most common symptoms included fever (59%), cough (48%), myalgia (34%), and sore throat (24%). Other symptoms included diarrhea (20%), fatigue (20%), anorexia (20%), headache (19%), runny nose (18%), sputum production (15%), and difficult breathing (12%) and there were 35 asymptomatic infections. Nine (3%) developed respiratory failure and needed a respirator. Five cases died; resulted in the case fatality ratio 1.9% (5/268).

Figure 3 shows the epidemic curve of the first-generation cases with the 35 asymptomatic patients excluded. The first cluster of cases occurred on 7 Mar 2020 after they visited multiple boxing stadiums. After the closing of Lumpinee and Rajadamnern stadiums and the investigation began, the number of cases declined.

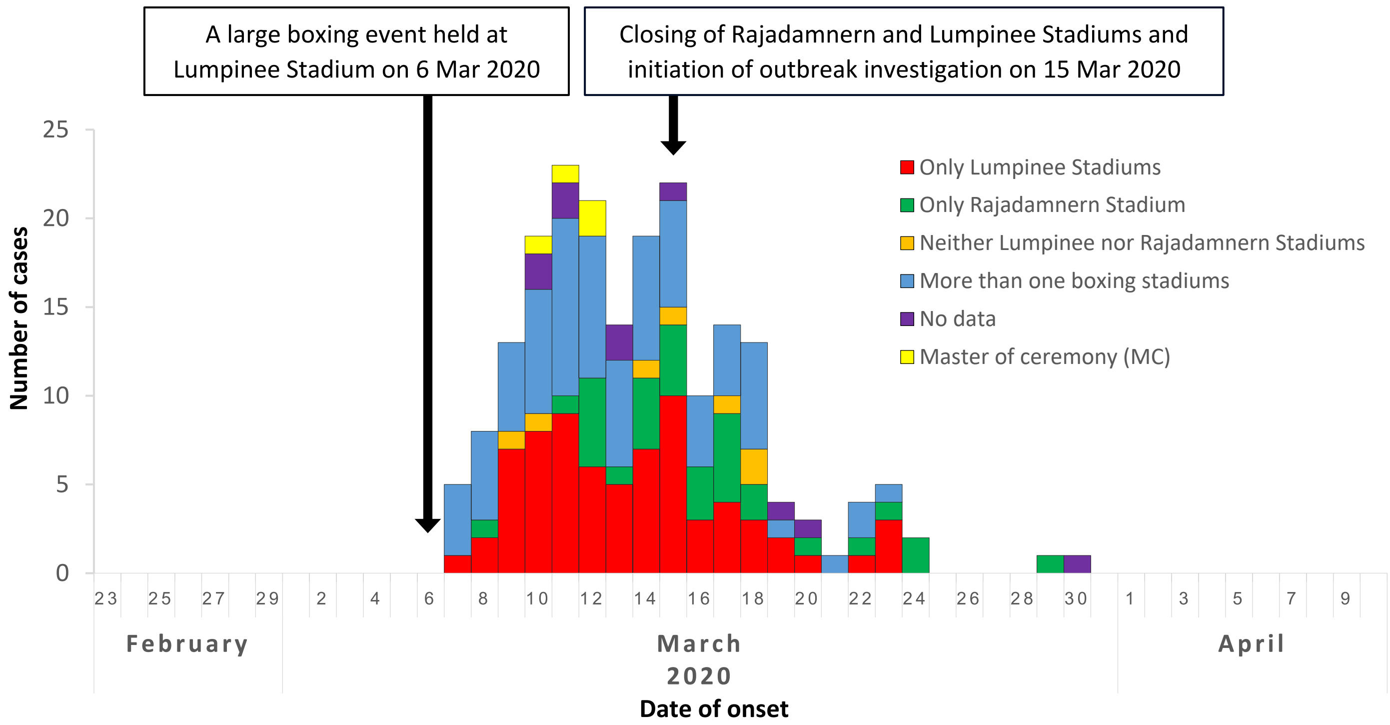


Figure 3. Number of confirmed COVID-19 cases linked to boxing stadiums in Bangkok and the Bangkok Metropolitan Region during March 2020 by date of onset (n=202)

Lumpinee Boxing Stadium staff mentioned that the event was held from 6 PM to midnight. The stadium capacity was 5,000 persons. Food courts and souvenir shops were located outside the stadium. Boxing matches are normally held on Tuesdays, Fridays, and Sundays with approximately 200 attendees per round. At the event on 6 Mar 2020, there were 2,431 attendees distributed in four distinct zones: a very important person zone (20 persons), the ringside (272 persons), zone 2 (500 persons), and zone 3 (1,639 persons). The highest attack rate occurred in zone 2 (6%, 30/500) where most of the boxing fans were packed. Their behaviors included cheering and gambling. Some did not wear face masks. The attack rate of the very important person zone was 5% (1/20). Some of the attendees of the event went to the stage to receive awards and were interviewed by the MC. The ticketing system of the stadium is paper-based. Fever screening was performed using environmental handheld thermometers. Boxing equipment was cleaned once a week, and shared microphones were used by the MC. During the walk-through survey, we noticed the stadium lacked an airflow ventilation system. There were also no sanitizers, tissue paper, nor hand-washing facilities in the restrooms.

We identified 411 high-risk contacts of first- and second-generation cases who had complete important information and found 42 additional cases. As shown in Table 1, after adjusting for age and gender, the only significant risk factor for COVID-19 infection among high-risk contacts was being a household member (adjusted odds ratio=2.04, 95% CI: 1.01–4.15).

Table 1. Risk factors of developing COVID-19 among high-risk contacts of cases related to boxing stadiums in Bangkok and the Bangkok Metropolitan, Thailand, March 2020

Factors	Cases, n (%) n=42	Non-case, n (%) n=369	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Gender (n=410)				
Female	26 (61.9)	170 (46.2)	Reference	
Male	16 (38.1)	198 (53.8)	0.56 (0.31, 1.02)	0.77 (0.40, 1.49)
Age group (years) (n=411)				
≤14	3 (7.1)	34 (9.2)	Reference	
>14–30	8 (19.1)	88 (23.6)	1.03 (0.29, 3.67)	1.21 (0.34, 4.28)
>30–45	14 (33.3)	82 (22.2)	1.80 (0.55, 5.90)	2.04 (0.62, 6.68)
>45–60	15 (35.7)	121 (32.8)	1.36 (0.42, 4.45)	1.80 (0.55, 5.93)
>60	2 (4.8)	44 (11.9)	0.54 (0.09, 3.04)	0.67 (0.12, 3.78)
Household member of a case (n=411)				
No	13 (31.0)	190 (51.5)	Reference	
Yes	39 (69.1)	179 (48.5)	2.18 (1.17, 4.08)	2.04 (1.01, 4.15)

Discussion

This COVID-19 outbreak, which may have originated in a boxing stadium in Bangkok, was widespread as attendees were from many provinces of Thailand. Droplets, direct contact, aerosols, and fomite transmission are possible ways to spread respiratory infection in sports settings.[10,11] Additionally, in an overcrowded stadium, there were no effective social distancing measures established.[12] Similarly, a COVID-19 outbreak in San Siro Stadium in Italy was reported to be due to an insufficient safe distance between attendees and a prolonged exposure time among potentially infected cases.[13]

In our study, the second-generation cases were mostly household members of confirmed cases. This implies limited spread across the community. We found that being a household member of a case was a significant risk factor for developing COVID-19. Many outbreaks reported secondary attack rates ranging from 0.5–6.6% and estimated household secondary attack rates ranging from 19–50%.[14–16] However, since household specimens are routinely collected due to Thailand's national guidelines and are easily traceable from patients. The results might show a higher positivity rate among households, compared with the other groups, which could inflate the association of being a case among household away from the null.

The case fatality rate of this outbreak (1.9%) was higher than the national rate (1.3%) as of 10 Apr 2020.[17] This might be due to the age of the attendees of this boxing event being higher than the national average. COVID-19 fatality is also known to be associated with increasing age.[18]

Cheering, gambling, and lack of fixed seating arrangements allowed participants to walk around the stadium freely, all of which could be risk behaviors for disease transmission. Cheering or having loud conversations releases micrometer particles into the air, which carry viruses that can cause infection.[19] Additionally, shared microphones and contaminated boxing equipment support fomite transmission which may also play a role in disease transmission; however, the relative importance of this route of transmission versus direct exposure to respiratory droplets remains unknown.[20,21]

The first cluster of cases had visited multiple boxing stadiums and developed symptoms one day after the event. The incubation period of COVID-19 ranged from 1–18 days, therefore, one day after the event is at the low end of the scale if they were infected during the event.[22] COVID-19 can be transmitted by asymptomatic carriers during the incubation period.[23] Asymptomatic patients in their incubation period or those with mild symptoms who previously went to many boxing stadiums before attending the boxing event on the sixth of March could transmit the disease during a long exposure time if attendees already had SARS-COV-2 infection.[24]

This study had limitations which should be mentioned. First, some patients sought treatment at private hospitals, which may not report to the national surveillance system. However, we identified some cases via social media to reduce this shortfall. Second, low-risk contacts were not traced which could bias the results. However, national guidelines state that low-risk contacts should observe their symptoms for 14 days and seek treatment if any symptoms appear. Third, the source of infection was not clearly identified because attendees had traveled from many provinces in Thailand. Finally, we conducted most interviews over the phone resulting in somewhat limited data collection.

Recommendations

Postponing all sports matches during a pandemic is recommended. The Tokyo 2020 Summer Olympic and Paralympic Games in Japan were postponed due to COVID-19.[25,26] Use of an electronic ticketing system would be a feasible strategy for tracing attendees.[24] In the stadiums, a standard ventilation system and fixed seats should also be installed. Additionally, gambling should be limited to an online system to improve social distancing. An appropriate handheld thermometer is recommended. We recommend installing sanitizers, soap dispensers, tissue paper, and hand-washing facilities at all boxing stadiums. Boxing equipment should be cleaned frequently, especially during outbreaks. This evidence could lead to Thailand's decision to contain the outbreak, and strict control measures, i.e., compulsory wearing of face masks, limiting the number of participants at sporting events to practice social distancing should be considered, particularly during an epidemic.

Conclusions

A large outbreak investigation in March 2020 involving 2,431 attendees of a boxing stadium in Bangkok was conducted. We reviewed and traced cases through the national surveillance system and social media. We identified 268 COVID-19 cases linked to a boxing event. Most high-risk contacts were household members of the cases. Some attendees cheered and gambled during the event, increasing the risk of disease transmission. During an epidemic, we recommend that all sports events be postponed. Gambling should be limited to an online payment system. Screening participants' temperatures may not be as effective for disease prevention as mask-wearing and limiting the number of participants.[27,28]

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Disclaimer

The findings, figures, and opinions expressed in this paper are those of the authors and do not necessarily reflect the position of the Ministry of Public Health, Thailand.

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Situation and Spatial Analysis of the COVID-19 Epidemic in Business Establishments: Comparison between the Delta and Omicron Variants in Thailand, July 2021–May 2022

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Abstract

COVID-19 outbreaks in business establishments cause a stagnant economy. In Thailand, the COVID-19 situation in business establishments has never been investigated. This study aims to (1) describe the situation and (2) compare characteristics, including spatial patterns, of COVID-19 cases in business establishments between the Delta (July–December 2021) and Omicron (January–May 2022) predominant periods. A cross-sectional study was conducted using secondary data extracted from the Department of Disease Control's database, which was linked to listed company and factory databases. The study population included all reported COVID-19 cases. The proportions of case characteristics between the delta and omicron dominant periods were compared using Pearson's Chi-square test. Spatial autocorrelation was tested using Moran's I statistics. During July 2021–May 2022, 443,448 COVID-19 cases were reported in business establishments. The proportions of cases in factories and construction camps decreased from 41.3% and 6.7% in the Delta dominant period to 14.4% and 1.7% in the Omicron dominant period, respectively. A high number of cases occurred in businesses operating food production, wholesale/retail, transportation, and accommodation. Clustering patterns were evident in the central and eastern regions of Thailand where many business establishments are located. Public health agencies should promote organizational COVID-19 prevention measures and increase worker's awareness in high-risk industries.

Keywords: COVID-19, spatial autocorrelation, business establishments, Thailand

Introduction

Over the past few years, many countries around the world have been confronted with outbreaks of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, and announced by the World Health Organization as a pandemic on 11 Mar 2020.[1] From the first reported case to July 2022, there were approximately 574 million cases and more than 6.4 million deaths.[2] Thailand reported its first case on 13 Mar 2020.[3] Since then, there have been several outbreaks due to constant virus mutations. One of the biggest waves in Thailand began in mid-2021 when the Delta variant was introduced. This variant was very contagious, causing numerous outbreaks in various settings, such as schools, prisons, and business enterprises.[4] After cases subsided, Thailand faced another wave, caused by the Omicron variant in early-2022. This variant was found to be more contagious, but less severe, than Delta.[5]

Widespread COVID-19 outbreaks in communities can introduce the COVID-19 infection into business establishments via workers who live in the community. Uncontrolled infections in these establishments cause businesses to temporarily close. If the outbreak occurs in many establishments, the country's economy will suffer. The Ministry of Public Health realized the importance of COVID-19 outbreaks in such establishments. Consequently, in August 2021 the Thai government introduced the so-called "Bubble and Seal" measure for prevention and control of COVID-19 in specific areas, especially factory settings.[6]

The COVID-19 situation in business establishments has never been investigated, Therefore, this study aims to (1) examine the COVID-19 situation in business establishments, and (2) compare epidemiological characteristics and spatial patterns of the COVID-19 epidemic in business establishments between the time periods when the Delta and Omicron variants were predominant.

Methods

A cross-sectional study was conducted using secondary data retrieved from three databases, namely (1) confirmed COVID-19 cases and deaths associated with COVID-19 reported to the Department of Disease Control (DDC), Ministry of Public Health, (2) a list of factories that were registered with the Ministry of Industry, and (3) companies that were registered with the Ministry of Commerce. These databases were linked together to acquire the data on COVID-19 cases/deaths in the business establishments.

The study population included all laboratory-confirmed COVID-19 cases diagnosed by real-time reverse transcription polymerase chain reaction (RT-PCR) that were reported to the DDC between July 2021–May 2022. We divided cases into two study periods: July–December 2021 (the period that the Delta variant was dominant) and January–May 2022 (the period that the Omicron variant was dominant). We limited the study to May 2022 because the DDC changed the guidelines for COVID-19 case reporting, which affected the number of cases recorded.

Selected variables included gender, age, nationality, date of case report, province where the COVID-19 cases were isolated, type of establishment, and type of industry. Businesses were divided into three types—companies, factories and construction camps. The type of industry was classified based on the Ministry of Labor's guideline—"Thailand Standard Industrial Classification (TSIC) 2009".[7] Examples of Thailand Standard Industrial Classification 2009 industrial types included wholesale and retail trade, transport and storage, food and beverages manufacturing, accommodation and food service activities, and construction.

Microsoft Excel 2019 and STATA version 14.2 were used for data analysis. Descriptive statistics included frequencies, percentages, and means with standard deviation (SD). A comparison of epidemiological characteristics of the COVID-19 epidemic in the establishments between the two study periods were performed using Pearson's Chi-square test while Student's t-test was used to compare differences in age. The significance level was set at 0.05.

The spatial distribution of COVID-19 cases in the establishments by province were analyzed using GeoDa version 1.20. Percentile maps of cases in the establishments were created. To determine the spatial pattern, the global spatial autocorrelation was computed using Moran's I statistic with the formula shown below:[8,9]

$$I = \frac{\sum_{i=1}^{N}\sum_{j=1}^{N} w_{ij}(y_i - \bar{y})(y_j - \bar{y})}{\frac{1}{N}\sum_{i=1}^{N}(y_i - \bar{y})^2 \sum_{i=1}^{N}\sum_{j=1}^{N} w_{ij}}$$

where I is Moran's I statistic indicating global spatial autocorrelation.

w_{ij} is a matrix of spatial weights. If two provinces are neighbors, a weight of 1 will be given. If not, 0 will be given instead.

y_i, y_j are the numbers of COVID-19 patients in the establishments reported from province i and j.

$\bar{y}$ is the mean number of COVID-19 patients in the establishments reported from each province.

N is the number of provinces.

Values of Moran's I statistic generally range from −1 to +1. A value of +1 indicates "perfect clustering" of similar values. Conversely, a value of −1 suggests "perfect dispersion" while a value of 0 refers to "perfect randomness" or no autocorrelation. A pseudo *p*-value was calculated based on the permutation technique to determine the statistical significance with a level of 0.05.[8]

Results

Comparison of Epidemiological Characteristics of COVID-19 in Business Establishments between the Two Study Periods

During July 2021–May 2022, 4,191,156 COVID-19 cases were reported in Thailand. We characterized this epidemic by two periods or waves; wave 1: July–December 2021, and wave 2: January–May 2022. The total number of cases reported from business establishments during the study period was 443,448 (10.6%) and, as shown in Figure 1, this distribution had a similar epidemic pattern with the whole country. Of 1,964,134 cases reported to DDC in the first wave, there were 21,507 deaths (case-fatality rate (CFR)=1.09%). Compared to the second wave, the CFR was substantially lower at 0.38% (8,390 deaths/2,227,022 cases). As shown in Table 1, the CFR in business establishments was lower than the national rate for both waves. Furthermore, the CFR from COVID-19 in the establishments during wave 1 was significantly higher than that during wave 2 (0.61% versus (vs.) 0.14%).

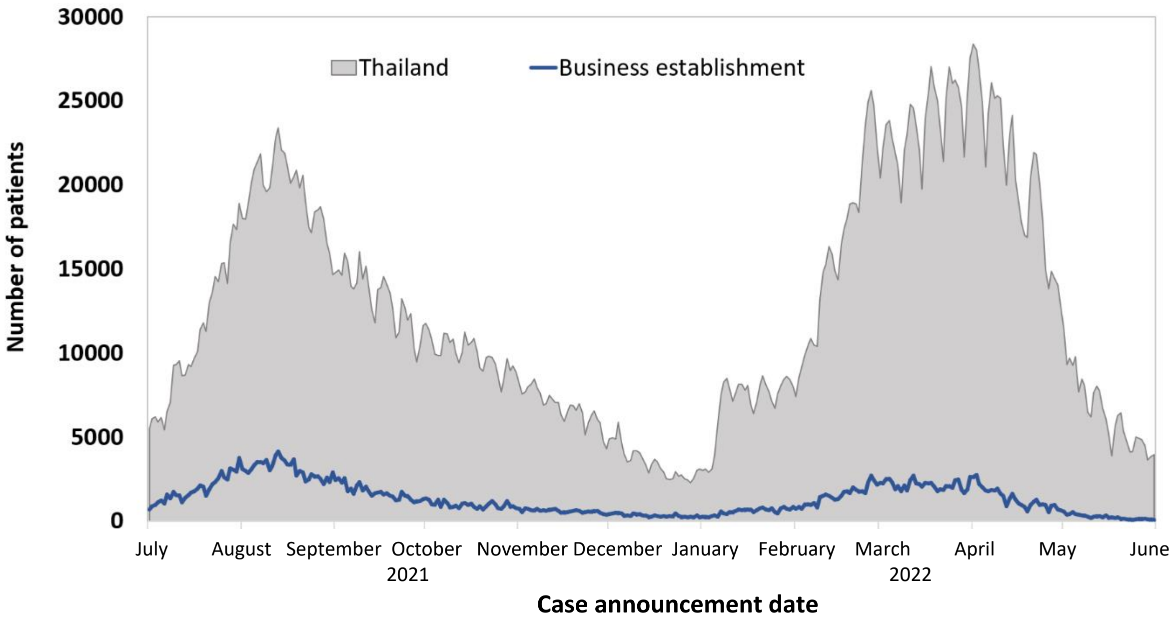

Figure 1. Epidemic curve of COVID-19 cases in business establishments, compared to the situation nationwide in Thailand, July 2021–May 2022

Among cases reported from business establishments, the proportion of males (range: 46.6–49.3%) was slightly lower than that for females (49.7–53.2%). The mean (SD) age of cases in period 1 was significantly lower than in period 2 (35.2±10.5 vs. 35.4±10.2). In period 1, most (75.1%) cases were Thai, followed by Myanmar (15.0%), and Cambodian (3.3%) whereas in period 2, Thais accounted for 94.3%. In period 1, about half (52.0%) of all cases worked in a company while 41.3% and 6.7% worked in factories and construction camps, respectively. However, in period 2, the majority of cases worked in companies (83.9%) while the proportions in factories (14.4%) and construction camps (1.7%) were significantly less compared to period 1 (Table 1).

Table 1. Epidemiological characteristics of COVID-19 cases in Thai business establishments: a comparison between two study periods

Characteristics	July 2021–May 2022	Period 1: July–December 2021	Period 2: January–May 2022	*P*-value[a]
Cases	443,448	266,393	177,055	
Deaths	1,876	1,630	246	
Case fatality rate (%)	0.42	0.61	0.14	<0.001
Gender				<0.001
Male	213,739 (48.2%)	131,209 (49.3%)	82,530 (46.6%)	
Female	226,706 (51.1%)	132,495 (49.7%)	94,211 (53.2%)	
Not identified	3,003 (0.7%)	2,689 (1.0%)	314 (0.2%)	
Age				<0.001[b]
Mean (SD)	35.3 (10.5)	35.2 (10.5)	35.4 (10.2)	
Nationality				<0.001
Thai	366,978 (82.8%)	200,015 (75.1%)	166,963 (94.3%)	
Myanmar	44,836 (10.1%)	39,851 (15.0%)	4,985 (2.8%)	
Cambodian	9,579 (2.2%)	8,698 (3.3%)	881 (0.5%)	
Laotian	1,359 (0.3%)	1,033 (0.4%)	326 (0.2%)	
Others	1,510 (0.3%)	769 (0.2%)	741 (0.4%)	
Not identified	19,186 (4.3%)	16,027 (6.0%)	3,159 (1.8%)	
Type of business establishment				<0.001
Company	287,157 (64.8%)	138,555 (52.0%)	148,602 (83.9%)	
Factory	135,495 (30.5%)	110,071 (41.3%)	25,424 (14.4%)	
Construction camp	20,796 (4.7%)	17,767 (6.7%)	3,029 (1.7%)	

Note: Numbers in table are frequency with percentages in brackets unless stated otherwise.
[a]P-value is based on Pearson's chi-square test unless stated otherwise. [b]P-value is based on Student's t-test.

A comparison of the top 10 ranked companies and factories with COVID-19 cases classified by type of industry is shown in Table 2. In period 1, the industries with the highest proportion of cases were wholesale and retail trade (9.2%), followed by transport and storage (2.5%) and food and beverages manufacturing (1.0%). In period 2, wholesale and retail trade (4.8%) still ranked first while the second and third ranked industries were accommodation and food service activities (2.3%), and transport and storage (1.0%). For factories, in period 1, food and beverages manufacturing (27.1%) had the highest proportion of cases, followed by computer, electronic and electric products manufacturing (14.2%) and rubber and plastics products manufacturing (9.5%). However, in period 2, computer, electronic and electric products manufacturing (15.5%) ranked first, followed by food and beverages manufacturing (13.4%) and machinery, motor vehicles and other transport equipment manufacturing (11.5%).

Table 2. The top 10 ranked companies and factories with COVID-19 cases and, classified by type of industry: a comparison between the two study periods

Period 1: July–December 2021			Period 2: January–May 2022		
Companies classified by industrial types	**No. of cases**	**%**	**Companies classified by industrial types**	**No. of cases**	**%**
1. Wholesale and retail trade	12,731	9.2	1. Wholesale and retail trade	7,152	4.8
2. Transport and storage	3,505	2.5	2. Accommodation and food service activities	3,474	2.3
3. Food and beverage manufacturing	1,422	1.0	3. Transport and storage	1,533	1.0
4. Accommodation and food service activities	1,213	0.9	4. Financial and insurance activities	1,371	0.9
5. Construction	1,198	0.9	5. Food and beverage manufacturing	7,83	0.5
6. Agriculture, forestry and fishing	1,104	0.8	6. Real estate activities	622	0.4
7. Financial and insurance activities	1,095	0.8	7. Construction	561	0.4
8. Textiles and garments manufacturing	1,066	0.8	8. Information and communication	456	0.3
9. Others	7,689	5.5	9. Others	2,745	1.8
10. Unspecified	107,532	77.6	10. Unspecified	129,905	87.4
Factories classified by industrial types	**No. of cases**	**%**	**Factories classified by industrial types**	**No. of cases**	**%**
1. Food and beverage manufacturing	29,812	27.1	1. Computer, electronic and electric products manufacturing	3,951	15.5
2. Computer, electronic and electric products manufacturing	15,663	14.2	2. Food and beverages manufacturing	3,395	13.4
3. Rubber and plastics products manufacturing	10,450	9.5	3. Machinery, motor vehicles and other transport equipment manufacturing	2,925	11.5
4. Machinery, motor vehicles and other transport equipment manufacturing	9,179	8.3	4. Rubber and plastics products manufacturing	1,445	5.7
5. Textile and garment manufacturing	5,693	5.2	5. Metals manufacturing	1,057	4.2
6. Metals manufacturing	5,417	4.9	6. Other non-metallic minerals products manufacturing	975	3.8
7. Transport and storage	2,630	2.4	7. Textiles and garments manufacturing	945	3.7
8. Medical goods and related items	2,617	2.4	8. Chemical and pharmaceutical products manufacturing	349	1.4
9. Others	9,911	9.0	9. Others	2,121	8.3
10. Unspecified	18,699	17.0	10. Unspecified	8,261	32.5

Comparison of Spatial Patterns of COVID-19 in Business Establishments between the Two Study Periods

The spatial distribution of COVID-19 cases in business establishments is displayed on the percentile maps shown in Figure 2 (upper panel). A higher number of cases in business establishments were located in the central and eastern regions of Thailand. Most of the provinces that reported a high number of cases in the first period also reported a relatively high number of cases in the second period. By comparing the number of cases in each province between the two periods, a high correlation coefficient (r) of 0.8958 (*p*-value <0.001) and the scatterplot shown in Figure 2 (lower panel) indicate a positive linear relationship, suggesting similarity of spatial patterns between both study periods.

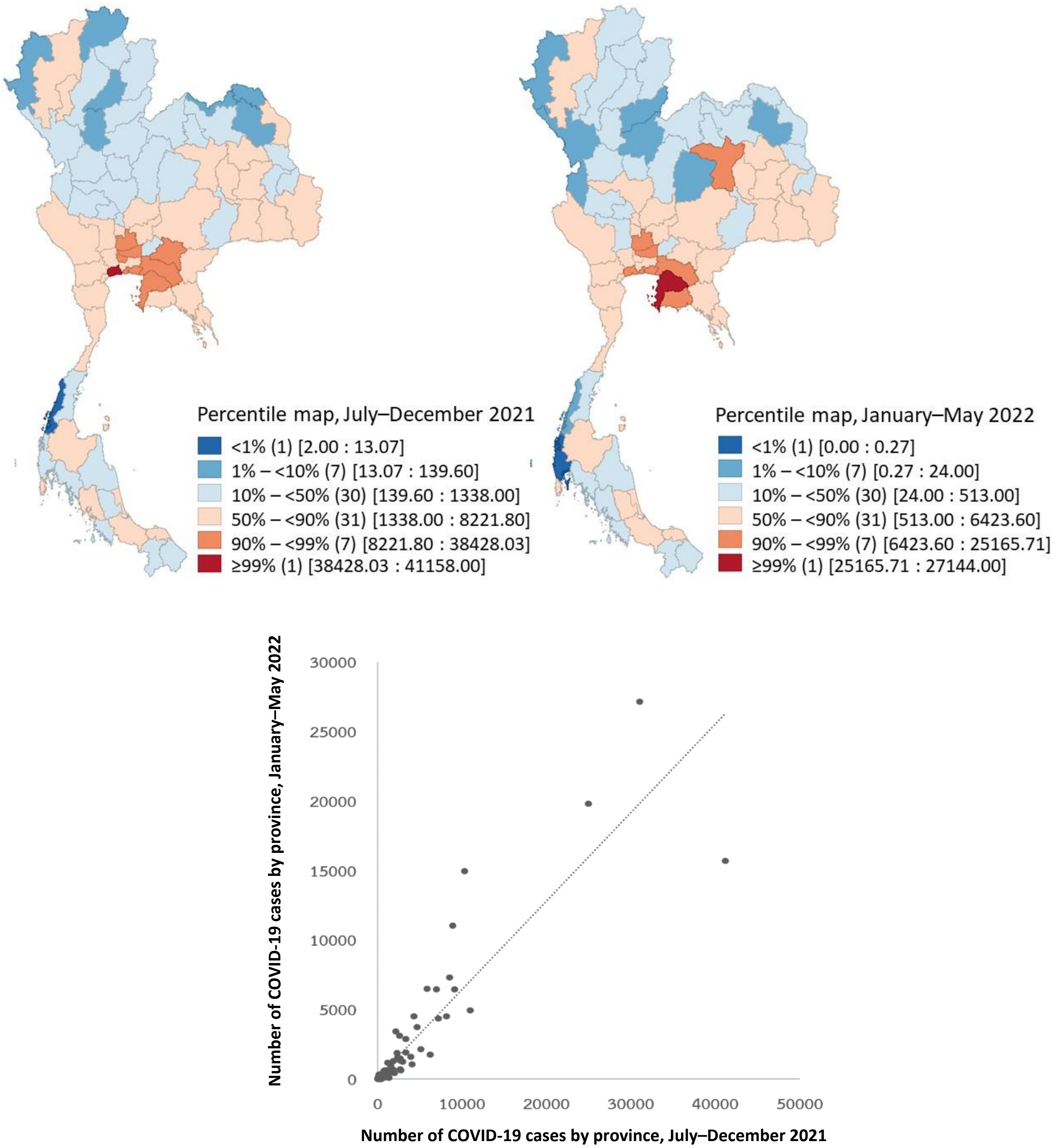

Figure 2. Comparison of spatial patterns of COVID-19 cases in business establishments between two selected time periods (July–December 2021 vs. January–May 2022) using percentile maps (upper panel) for period 1 (left) and period 2 (right) and a scatter plot (lower panel) of the number of COVID-19 cases in each province for the two periods

Concerning the spatial pattern of cases, Moran's I statistic was 0.131 (pseudo *p*-value=0.039) in the first period and 0.210 (pseudo *p*-value=0.009) in the second period (Figure 3), suggesting a clustering pattern for both periods. As can be seen from the percentile maps that correspond to the low positive Moran's I value, besides the large cluster of provinces located in the central and eastern regions, there were also clusters of provinces with high number of cases in other areas in the northern region (Chiang Mai Province), the lower part of northeastern region and the southern region (Songkhla Province) of Thailand.

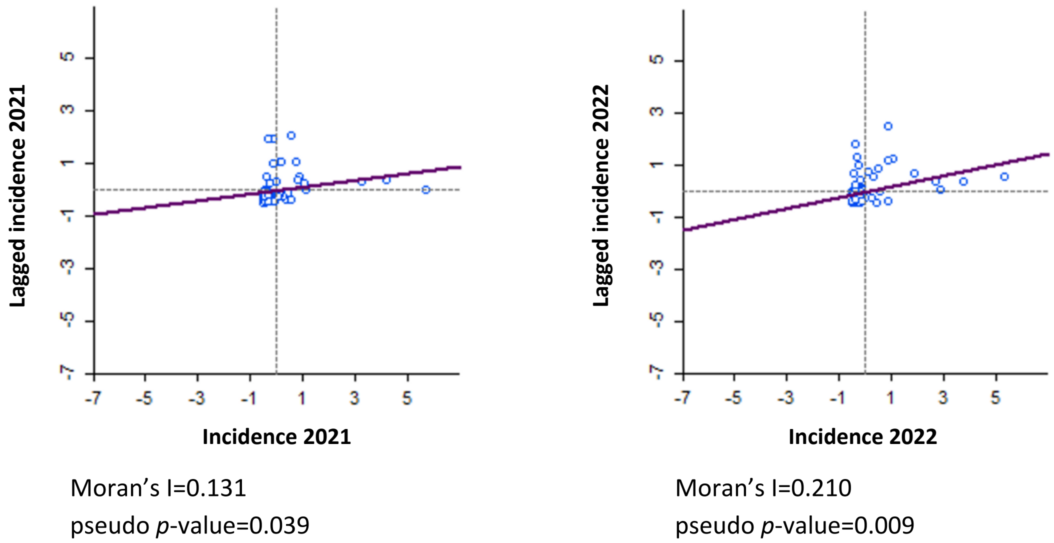

Figure 3. Analysis of spatial pattern on the COVID-19 cases in business establishments in Thailand using Moran's I statistics: a comparison between two study periods (July-December 2021 (left) vs. January–May 2022 (right))

Discussion

This situational and spatial epidemiological comparative study of COVID-19 among workers in business establishments in two study periods found that the case fatality rate was significantly lower than that among the general population. This suggests a stronger health status among people in the working age compared to the general population. Furthermore, the CFR among workers in the first period was greater than that in the second period. This is not surprising because the first period contained predominately cases with the Delta variant, while the second period saw Omicron emerge as the predominant variant. Several studies have demonstrated that Omicron is more transmissible but less severe than Delta.[10–12]

We found that the proportions of COVID-19 cases in factories and construction camps substantially decreased from 41.3% and 6.7% to 14.4% and 1.7%, respectively. This result can be explained by the COVID-19 prevention and control protocols being implemented in specific areas, the so-called "Bubble and Seal" measure.[6] This measure includes self-assessment, social distancing, hand washing, mask wearing, temperature testing, segregation practices in the establishment, antigen test kit testing, quarantine, case isolation, and vaccination. The "Bubble and Seal" measure was launched by the Ministry of Public Health in August 2021, aiming at controlling the spread to COVID-19 in factories and construction camps. Until June 2022, approximately 2,860 factories had reportedly adopted this measure; however, other establishments might have adopted similar measures.[13] Additionally, Thailand's Ministry of Labor also introduced another COVID-19 control measure called the "factory sandbox", aiming at major industries, such as motor vehicles manufacturers, electronics products, food, and medical equipment, in some provinces where several factories are located.[14] Despite the occurrence of the high infectivity of the Omicron variant, the implementation of these two measures could possibly be a factor limiting the COVID-19 spread in the factories and construction camps. However, the effectiveness of the two measures has not been studied. Another possible explanation for the decrease in the proportion of cases in the second period could be the higher vaccine coverage among workers.

Regarding the industrial types, we found that companies involved in wholesale and retail, transport and storage, and accommodation and food services industries had the highest number of COVID-19 cases among their workers compared to other industries. This is possibly because these industries have more workers than the other industries. Furthermore, workers in these industries tend to have close contact with many people, resulting in an increased chance to contract COVID-19. For factory settings, the highest number of COVID-19 cases were found in factories involved in the manufacture of food, electronics products, and rubber and plastics products. This finding is consistent with a study in Ontario, Canada where most of the COVID-19 outbreaks (44.7%) in the establishments occurred in the manufacturing industry.[15] Moreover, other studies on COVID-19 outbreaks in food factories in Ireland and Germany were in accordance with the situation in Thailand where manufacturing of food and beverages is a high-risk business.[16–17] However, to prevent and control COVID-19 in food factories, besides promoting personal hygiene and administrative or organizational controls, many studies also recommended that working environment, such as common contact areas, and ventilation, especially in workplaces that are crowded, should be disinfected more often.[16–18] The measures mentioned previously can be applied to other types of industries where appropriate, and should be considered based on the context and size of the enterprises.[19]

We found that spatial patterns of COVID-19 in business establishments was similar in the two study periods, consistent with the high correlation coefficient of 0.8958. The percentile maps suggested that the high-risk areas are located in the central and eastern regions, and some provinces that are considered as economic hubs of the regions, such as Chiang Mai (north), and Songkhla (south). A possible explanation could be that despite these provinces having a relatively high COVID-19 vaccine coverage with 78–100% (as of 5 Mar 2022), many people of working age tend to migrate to work in these areas.[20] Subsequently, they have a higher chance of contracting COVID-19. Additionally, the central and eastern regions are relatively highly populated, which is a key factor for the spread of infectious disease such as COVID-19.[21]

This study has some limitations. First, data on the number of workers in each business establishment were not available at the time of analysis since the databases provide by the ministries of Industry and Commerce contained the number of workers when the factory of company was first registered and the numbers may have changed over time. Secondly, some business establishments reported an infection rate more than 100%. Thus, numerator-based statistics using the number of patients instead of rate were used for data analysis. Moreover, one of the main objectives of this study was to compare the spatial patterns between two time periods when the Delta and Omicron variants were predominant, therefore, the lack of appropriate population size or denominator for calculating rate is not a serious issue. Thirdly, due to the short study period of 11 months, we could not explore the complete time trend of the COVID-19 infections in business establishments in Thailand. Finally, data on COVID-19 cases in companies by industry type were >75% incomplete thus, our results may not reflect the actual situation in Thailand.

Public Health Action and Recommendations

A spatial epidemiological analysis is a useful tool that can assist in identifying and understanding the geographical patterns of infectious diseases and anticipating high-risk areas. Subsequently, we can strengthen surveillance, including prevention and control measures, in the high-risk areas of COVID-19. We found that the central and eastern regions of Thailand, and some provinces that are considered as economic hubs, were at a higher risk than other areas. Our recommendations for control and prevention measures are as follows. Health officials should work in collaboration with network partners, such as the Ministry of Industry and the Ministry of Labor, to provide health literacy and raise awareness of COVID-19 among workers in the industries that are prone to infection, such as food and beverages manufacturing and services. All business establishments should closely monitor the COVID-19 situation in their areas and impose organizational measures to prevent and control the spread of COVID-19 in their establishment. Finally, lessons learned from the enterprises or construction camps that have successfully controlled the COVID-19 should be reviewed in order to find best practices as a model for prevention and control of COVID-19 in other establishments.

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Identification and Priority Setting for Occupational Carcinogens (OCs) in Industries in Thailand

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Abstract

Several chemicals, including occupational carcinogens (OCs), have been used in Thailand. Apart from asbestos and silica, other OCs need to be identified for further monitoring and management. The study aimed to identify and conduct priority setting of these carcinogens in Thailand. The methods of the study were applied from Hanlon's method for priority setting. The first step was to identify OCs from the lists of the National Hazardous Substance Registry by using the criteria as follows: 1) being classified as OCs by Loomis et al., and 2) having high amount of import/export in the country during 2018–2020. After that, the identified agents were ranked according to three criteria: 1) size of the problem, 2) severity of the problem, and 3) feasibility of interventions. The results found that 18 occupational carcinogens were identified and 12 of them were still allowed to be used in the country. According to available information, seven agents were matched for priority setting, and the top three scored OCs included 1) arsenic and inorganic arsenic compounds, 2) trichloroethylene, and 3) formaldehyde. Further action plan includes health risk assessment, setting up of health surveillance, and implementation of preventive and control measures in the target workplaces.

Keywords: occupational carcinogen, priority setting, arsenic, industry, Thailand

Introduction

Occupational cancer is one of the serious occupational health problems worldwide. The International Labour Organization (ILO) estimated that each year, at least 666,000 persons died from occupational cancer.[1] From recent estimation, occupational cancer accounted for 26% of the 2.4 million deaths due to work-related diseases globally every year.[2] The Global Burden of Disease 2016 estimated that 349,000 deaths and 7.2 million disability-adjusted life years (DALYs) in 2016 were due to exposure to occupational carcinogens (OC).[3] Out of the 349,000 deaths, lung cancer accounted for 86% of the deaths, mesothelioma for 7.9% and laryngeal cancer for 2.1%. Of more than 1,000 substances classified by the International Agency Research on Cancer (IARC) to date, 122 agents are classified as group 1 (carcinogenic to humans).[4] According to Loomis et al., at least 47 agents listed in group 1 were identified as OCs.[5] Moreover, other studies have been conducted to identify the priority of OCs. For example, the Global Burden of Disease 2016 showed that asbestos caused the highest number of deaths; the others included secondhand smoke (14%), silica (14%) and diesel engine exhaust (5%).[3]

In Thailand, cancer is the first leading cause of death with 19% of total deaths.[6] The data from the Global Cancer Observatory showed 190,636 newly diagnosed cancers with 124,866 deaths in the country in 2020.[7] However, the number of reported cases with occupational cancer has been very few. According to the report from the Thai Workmen's Compensation Fund, only six cases of occupational cancer were claimed during 2016–2020.[8] The problems of under-reported cases may be due to several reasons, such as lack of awareness among workers, employers, and medical doctors, long latency period of exposure, and no information of carcinogens' exposure in workplaces.

Nowadays, several types of chemicals are used and produced with high amounts in industries in Thailand. According to the report under the Department of Industrial Work (DIW), Ministry of Industry showed that nearly 4 million tons of toxic chemicals were imported for industrial use and approximately 2.5 million tons were exported to other countries annually during 2018–2020.[9] Some of these chemicals are carcinogens. Relevant international agencies, such as World Health Organization, ILO, and the International Commission on Occupational Health urged every country to set up policy and measures to protect workers from occupational cancer by focusing on primary prevention, e.g., eliminating or reducing exposure to known and probable carcinogens.[10–12] Until now, asbestos and silica are the only two OCs which have been selected for the national occupational disease prevention and control program.[13] Moreover, all forms of asbestos have already been selected to be the first priority for banning by the Thai Government since 2011 following the third National Health Assembly.[14] Therefore, identifying other important OCs is necessary for further health surveillance and management. This study aimed to identify OCs in industries and to conduct priority setting of these carcinogens.

Methods

The design of the study was adapted from Hanlon's methods for priority setting.[15] The methods of this study included two steps, consisting of identification of OCs and ranking of the identified OCs (Figure 1). The first step was to review literature and information regarding OCs from IARC monographs and relevant publications. Data and information of hazardous substances used in Thailand were collected from the hazardous substances database under the DIW.[9] According to the Thailand Hazardous Substances Act B.E. 2535 (1992), hazardous substances are classified into four categories, 1–4.[16] All hazardous substances in category 4 are prohibited for production, import, export, or possession in the country. All controlled chemical substances with clear identifiers are listed in annex 5 (5.1). Information regarding each substance in annex 5.1 includes name of chemical (or mixtures), CAS number, coding number, and amount of import and export annually.

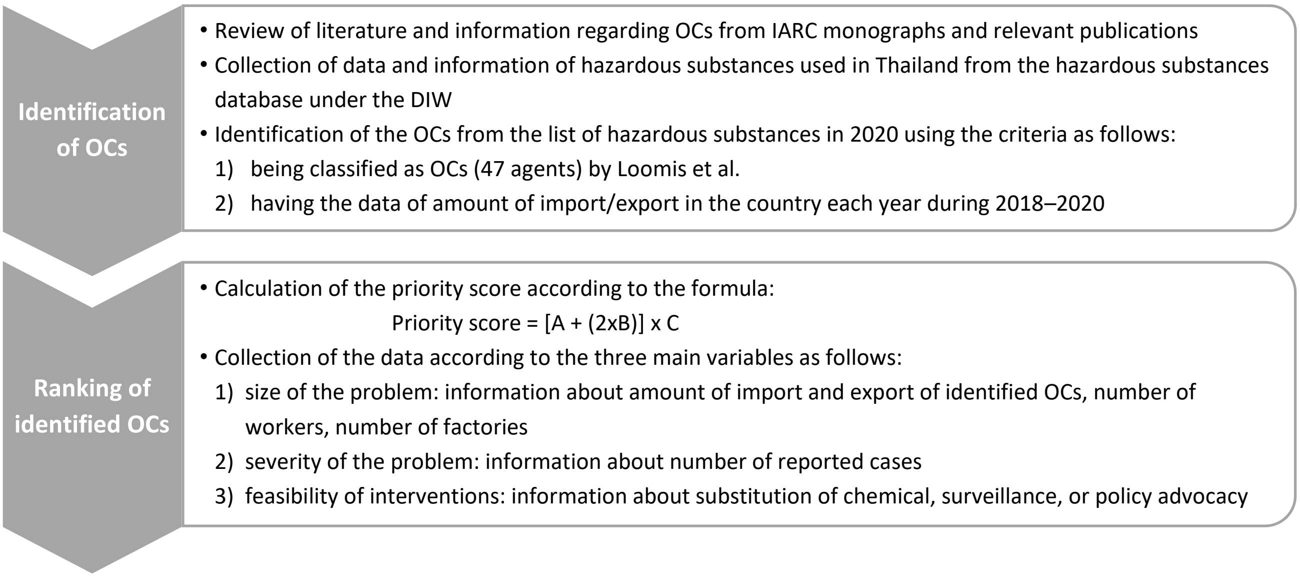

Figure 1. Two main steps of the Hanlon's method for priority setting

The next step was to identify OCs from the list of hazardous substances in 2020 using the criteria as follows: 1) being classified as OCs (47 agents) by Loomis et al., and 2) quantifying data concerning the amount of import/export in the country each year during 2018–2020.[5] However, all forms of asbestos (including chrysotile) and all acids were excluded from the study. The ranking of identified OCs was performed by calculating priority score using the formula below:

$$\text{Priority score} = [A + (2xB)] \times C$$

where A was size of the problem: [(RIEx3) + (RWx2) + (RFx1)] / 6.

RIE (ranking score for sum of amount of import and export of identified OCs) was quartile of sum of amount of import and export.

RW (ranking score of number of workers) was quartile of number of workers.

RF (ranking score of number of factories) was quartile of number of factories.

B was severity of the problem (4=having some reported cases of CA, 3=having some reported cases of severe poisoning, 2=public concern, and 1=none).

C was feasibility of interventions (4=substitution of chemical + surveillance + policy advocacy (e.g., international/national policy agenda recommended by World Health Organization/ILO), 3=surveillance + policy advocacy, 2=policy advocacy only, and 1=none).

In the study, number of factories and number of workers were collected from the lists of industries registered with DIW.[17] The information under the industry registry includes registration number, name of enterprise, address, type of industry, and number of workers, et cetera. However, this database has no information about chemicals used or produced (types and amount of chemicals) in each enterprise. Therefore, types of enterprises possibly using each target carcinogen were identified by seeking information from literature review for each chemical. For example, benzene may be produced from petrochemical manufacturing. Then petrochemical companies were sorted out and data about number of enterprises and number of workers were collected and summarized. After finishing collection of information for all selected carcinogens, the data of three factors were distributed from minimum number to the highest number. Then we divided into four quartiles and gave score 1 for the lowest quartile, score 2 for higher one, until score 4 for the highest numbers. To calculate the final step for the size of the problem (A), we weighed the ranking scores of three factors according to the formula.

The severity of the problem was scored by using information about availability of reported cases of cancer or other severe systemic poisoning caused by each carcinogen (see formula). The data were mainly reviewed and collected from annual reports under the Division of Occupational and Environmental Diseases, Department of Disease Control, during 2015–2020. The annual reports carried out regularly by the division summarize the disease situation based on three data sources—1) outbreak investigation, 2) ICD-10 related to environmental and occupational diseases, and 3) other related reports from stakeholders such as office of disease prevention and control or hospitals. Besides health data, the contents on the annual reports also include environmental monitoring data and control and prevention measures. The other sources of data to identify reported cancer cases were from published paper of case reports or research studies. Moreover, the feasibility of interventions was scored by reviewing whether each carcinogen has other chemical substitution available or available technique for health surveillance (see formula). After complete collection of information, the process of selected carcinogens' prioritization was arranged in a consensus meeting among experts and stakeholders.

Results

Totally 864 chemicals were listed as hazardous substances according to Thailand Hazardous Substances Act B.E. 2535 (1992) annex 5 (5.1) in 2020. According to the lists of 47 OCs by Loomis et al., 18 OCs (total 41 items of agents, e.g., asbestos has 5 items of agents) were identified in the report of hazardous substances lists (Table 1). Of these 18 OCs, 9 OCs were classified as category 4; 11 OCs were classified as category 3; and 1 OC was classified as category 2. Therefore, only 12 OCs were allowed to be used in the country, i.e., all OCs in category 4 were not allowed. However, three OCs (arsenic and inorganic arsenic compounds, asbestos, and chromium (VI) compounds) were classified as both categories 3 and 4. All acid chemicals which were classified as an OC (acid mist) by Loomis et al., were excluded in the study. Chrysotile was the only single type of asbestos, classified as category 3, which was still allowed to be used in the country.

Table 1. Occupational carcinogens classified within each category

Category	Name of chemicals	Number
1	-	-
2	formaldehyde	1
3	1,3-butadiene, 2-naphthylamine, 4-aminobiphenyl, arsenic and inorganic arsenic compounds, asbestos (chrysotile), benzene, benzidine, cadmium and cadmium compounds, chromium (VI) compounds, trichloroethylene, vinyl chloride	11
4	arsenic and inorganic arsenic compounds (copper arsenate hydroxide, lead arsenate, calcium arsenate), asbestos (except chrysotile), beryllium and beryllium compounds, bis (chloromethyl) ether, chromium (VI) compounds (sodium chromate), nickel compounds, pentachlorophenol, polychlorinated biphenyls, sulfur mustard (also mustard gas)	9
Total		**18†**

Notes: All acids were excluded. †Three agents (arsenic and inorganic arsenic compounds, asbestos, and chromium (VI)) are classified in both categories 3 and 4.

After identifying amount of chemicals, seven chemicals from categories 2 and 3 were selected for further priority ranking. The rest of the OCs from category 3 in Table 1 had no information about amount of import/export during 2018–2020. Only 2-naphthylamine had data about very few amounts of import in 2018 and 2019, but no data of import in 2020 and no data of export at all. The seven OCs include benzene, vinyl chloride, 1,3-butadiene, formaldehyde, trichloroethylene, chromium (VI) compounds, and arsenic and inorganic arsenic compounds. Amount of import and export of these agents are shown in Table 2. Approximately 20,000 tons of all seven OCs were imported to be used in the country each year. Nevertheless, nearly one million tons of the seven OCs were exported to other countries. The highest amount of import and export of listed carcinogens was benzene, probably due to very high manufacturing of petrochemicals in eastern industrial estates in the country. Similarly, the production of vinyl chloride and 1,3-butadiene was also high because of the same reason. However, arsenic and inorganic arsenic compounds were imported to be used in the country only, but not enough production for export.

Regarding number of factories and exposed workers, over 200,000 workers from 1,411 enterprises may be exposed to these seven OCs (Table 2). Trichloroethylene was the top of the agents with the highest number of factories and exposed workers. More than 70% of all workers (157,187) were exposed to trichloroethylene in their working environment; while, nearly half of all target factories (657) used this chemical in the process of their manufacturing. Formaldehyde was the second highest number of both factories and exposed workers. Although benzene was the agent with the highest production, only 2.8% of all target workers were exposed to this chemical.

Table 2. Average amount of import and export of seven chemicals during 2018–2020, and distribution of seven carcinogens by number of factories and number of exposed workers

Name of carcinogens	Number of import (tons/year)	Number of export (tons/year)	Number of factories (%)	Number of exposed workers (%)
Benzene	2,914.67	755,245.00	78 (5.5%)	6,068 (2.8%)
Vinyl chloride	0.05	106,397.67	9 (0.7%)	1,000 (0.5%)
1,3-Butadiene	10,943.56	62,176.67	23 (1.6%)	1,355 (0.6%)
Formaldehyde	2,801.41	505.66	367 (26.0%)	34,897 (15.9%)
Trichloroethylene	1,939.83	7.96	657 (46.6%)	157,187 (71.9%)
Chromium (VI) compounds	1,399.11	54.80	230 (16.3%)	8,349 (3.8%)
Arsenic and inorganic arsenic compounds	318.10	-	47 (3.3%)	9,894 (4.5%)
Total	**20,316.73**	**924,387.76**	**1,411 (100%)**	**218,750 (100%)**

Notes: 1) Chrysotile, acids, and 2-naphthylamine were excluded.
2) RIE scores: 1=318.1–1,700, 2=1,701–3,307, 3=3,308–89,758, and 4=89,759–758,159.67
3) RF scores: 1=9–35, 2=36–78, 3=79–298, and 4=299–657
4) RW scores: 1=1,000–3,711, 2=3,712–8,349, 3=8,350–22,395, and 4=22,396–157,187

After reviewing reported cases caused by these seven carcinogens from the Health Data Center (HDC) and other published reports, only skin cancer cases caused by arsenic were identified.[18,19] An outbreak of 1,500 cases with arsenic poisoning and 1,231 cases with skin cancer caused by arsenic have been found since 1987. Most cases were exposed to drinking water with arsenic contamination from old tin-mines in the south of the country. Furthermore, some cases of acute trichloroethylene poisoning were diagnosed from an institute of occupational medicine hospital (unpublished information). Other carcinogens, e.g., benzene, 1,3-butadiene, and vinyl chloride, raise health concerns among workers and the public in the area of large petrochemical industries.[20–22] These studies also showed that levels of exposure from these carcinogens were very high. However, there have been no report of confirmed cancer cases caused by those chemicals until now.

Regarding the feasibility of intervention, arsenic, trichloroethylene, formaldehyde, and chromium (VI) compounds may have other alternatives for substitution in manufacturing. The laboratory analysis of biomarkers for all these chemicals are also available. Health surveillance and control of arsenic poisoning is one of the major public health issues in terms of occupational and environmental health in the country. Based on the ranking using the formula, (Table 3), arsenic and inorganic arsenic compounds were the top priority with the highest scores, followed by trichloroethylene and formaldehyde, respectively; while, chromium (VI) compounds were the last with the lowest scores.

Table 3. Ranking of scores for selected occupational carcinogens

Name of carcinogens	Size of problems	Severity (scorex2)	Feasibility	Total score
1. Arsenic and inorganic arsenic compounds	1.83	8	4	39.32
2. Trichloroethylene	3	6	4	36
3. Formaldehyde	3	4	4	28
4. Benzene	3	4	3	21
5. Vinyl chloride	2.5	4	3	19.5
6. 1,3-Butadiene	2	4	3	18
7. Chromium (VI) compounds	1.67	2	4	14.68

Discussion

From this study, at least 18 OCs were identified using the existing data from national registration for hazardous substances. However, all acids were excluded from the study because there are several kinds of acid and all acids are generally used in most types of factories. It is so difficult for policy makers, especially relevant government agencies, such as public health sectors, to set up a policy for their management. Agents, which were produced or by-produced during the process of manufacturing, were not listed in the study, including diesel engine exhaust, leather dust, silica dust, welding fumes, and wood dust. Other carcinogens, such as, outdoor air pollution including particulate matter, solar radiation, and secondhand tobacco smoke, were also excluded because they are not classified as registered chemicals to be used for manufacturing. All radionuclides are registered to another national authority, the Office of Atoms for Peace.[23] Therefore, the group of those carcinogens were not included in the results.

Until now, several countries, especially the developed countries, have made efforts to study about OCs in terms of identification of new agents/risk factors, the burden of disease from occupational exposure, priority setting of these agents and development of effective control measures.[24–28] A good example of a project on the estimation of the burden of occupational cancer was conducted by an international group of experts, called the carcinogen exposure (CAREX) network.[29] An interesting finding showed that 32 million workers in the European Union were exposed to agents covered by CAREX. The most common exposures were solar radiation, environmental tobacco smoke, crystalline silica, diesel exhaust, and wood dust. Another example was a project of occupational cancer burden in Great Britain, demonstrating that asbestos, mineral oils, solar radiation, silica, and diesel engine exhaust were the top five of priority carcinogens.[30]

The study of priority setting for occupational cancer was performed by CAREX Canada in 2015 using four criteria, including 1) the likelihood of presence and /or use in Canadian workplaces; 2) toxicity of the substances; 3) feasibility of producing a carcinogen profile; and 4) special interest from the public and scientific communities.[31] The results showed that 103 agents were prioritized as high (n=11), medium (n=33) and low (n=59). The industrial chemicals classified as high priority exposure included 1-bromopropane, 1,2-dichloropropanem acrolein, dimethylformamide, and furan. Another study in Australia, called “the Australian Work Exposures Study” was conducted which aimed to investigate the current prevalence of occupational exposure to carcinogens.[32] The study showed similar finding as the most common carcinogens of exposure were solar radiation, diesel engine exhaust, environmental tobacco smoke, benzene, and silica. Up to now, all studies have been conducted in developed countries. The findings might not be able to compare with the situation in Thailand.

For this study, the method for priority setting of OCs was used by applying the Hanlon technique. Currently, there are several methods for prioritization in public health.[15] The Hanlon’s method was developed by J.J. Hanlon. Researchers, public health professionals, and health policy makers use or apply this method in their works.[33,34] The method is simple and inexpensive. The method in this study should be recommended to use for priority setting of OCs in other countries, especially in developing countries. The data of the study were collected and analyzed by the existing information and registry from relevant governmental agencies. Additionally, representatives from those relevant agencies and stakeholders were invited to give some feedback and suggestions in the workshop at the end of the study. This process could support to give consensus of the results and may lead to further policy development.

Although the results of the study are very useful as a starting point for policy development and implementation of preventive and control measures, some limitations of the study have to be concerned. For example, the exact amount of target chemical used in each factory was not available. Furthermore, numbers of workers working in the small-scale enterprises or in the informal sectors may not be included in the study. The reason was that the regulations under the DIW require enterprises with some particular size and machines to report to the department. In addition, number of workers were not the same as number of exposed workers. The exact number of exposed workers were not compulsory to be reported according to the Thailand Hazardous Substances Act B.E. 2535 (1992). If we need to tackle these problems in the future, we need to use other different methods by conducting walk-through surveys in enterprises. Another major limitation was that data of exposure levels were not available. Moreover, there was considerable debate on feasibility's score among participants during the workshop.

Conclusions

Eighteen OCs were identified from this study. Among these, 12 agents were still allowed to be used or produced in industries in the country. Apart from asbestos, at least seven other OCs have to be considered for further policy development. Arsenic and inorganic arsenic compounds was the top priority. Meanwhile, improvement of chemical information database is very important. Further action plans should include health risk assessment, setting up of health surveillance, and implementation of preventive and control measures in target workplaces.

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Conflicts of Interest

There are no conflicts of interest.

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SARS-CoV-2 Clearance from *Andrographis paniculata*, *Boesenbergia rotunda*, and Favipiravir among Mild COVID-19 Cases in Klong Prem Central Prison during Mid-2021: a Retrospective Study

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Abstract

This study aims to assess the effectiveness of two herbal medicines, *Andrographis paniculata* (Burm.f.) Nees capsule (AP) and *Boesenbergia rotunda* (Linn.) Mansf. extract capsule (BR), on the rate of SARS-CoV-2 virus clearance among inmates of Klong Prem Central Prison, Bangkok. Cases with mild COVID-19 were allocated into four groups: four capsules of AP thrice daily (n=30), one capsule of BR once daily (n=30), a combination of AP and BR (AP-BR) (n=30), or favipiravir (n=30) for five days. The primary outcome was time until undetected SARS-CoV-2 infection after starting treatment. The median period of SARS-CoV-2 clearance was shorter in the AP and AP-BR groups (9 days) compared to the BR (11 days) and favipiravir (13 days) groups. No one developed pneumonia; however, one participant in the AP group developed hyperkalemia. Our results suggest that *A. paniculata* with or without *B. rotunda* may be used as an alternative treatment for mild COVID-19 when access to favipiravir is limited. Further clinical trials are needed to determine their efficacy and safety.

Keywords: *Andrographis paniculata*, *Boesenbergia rotunda*, favipiravir, mild COVID-19

Background

In June 2021, more than 15,000 prisoners in Bangkok and surrounding provinces were infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). An alpha variant was identified from the specimens of prisoners. At that time, there was no vaccine for prevention of COVID-19, and available treatment was limited. Only favipiravir, imported from Japan and China, was recommended for COVID-19 cases with pneumonia.[1]

Nearly 5,000 inmates in the Klong Prem Central Prison had mild COVID-19 infections. Due to their mild illness, they did not qualify to receive favipiravir as treatment. Consequently, the Department of Corrections, Ministry of Justice, in collaboration with the Ministry of Public Health, initiated a project to curb COVID-19 outbreaks in prisons by treating the cases with herbal medicines. Two herbs were identified as having potential effects against SARS-Cov-2; *Andrographis paniculata* (Burm. f.) Nees capsule (AP) and *Boesenbergia rotunda* (Linn.) Mansf. extract capsule (BR).

Andrographolide is the major active component in *A. paniculata*. In an *in vitro* study, *A. paniculata* extract and andrographolide significantly inhibited the production of infectious virions of SARS-CoV-2.[2] The result from a randomized controlled trial showed promising efficacy and safety of *A. paniculata* in cases with mild COVID-19 due to its anti-inflammatory effect.[3] In contrast, real-world data revealed that treatment with *A. paniculata* might increase the risk of pneumonia, but confounding factors that may affect clinical outcomes were not excluded due to the study's observational design.[4] Currently, the Department of Medical Services (DMS), Ministry of Public Health recommends using *A. paniculata* for cases with symptomatic COVID-19 without pneumonia.[5]

B. rotunda has been used in Thai cuisine as a cooking spice. An *in vitro* study showed that *B. rotunda* extract and panduratin A, a major active compound in *B. rotunda*, potentially inhibited protease enzyme of SARS-CoV-2.[6] However, the effect of *B. rotunda* extract as treatment for COVID-19 has yet to be studied in humans.

The primary objective of this study was to compare the period between treatment initiation and undetected SARS-CoV-2 in cases with mild COVID-19. A secondary objective was to assess the safety of these regimens, in particular, development of adverse events and pneumonia.

Methods

Study Design

In May 2021, a project to explore alternative treatments for controlling the spread of SAR-CoV-2 was initiated. All inmates of Klong Prem Central Prison with mild COVID-19 were informed about the project and invited to participate in the study, of which 120 agreed.[7] Those who refused to participate received *A. paniculata* four capsules three times a day for five days. Participants were randomly assigned into one of four treatment groups: *A. paniculata* (AP), *B. rotunda* (BR), a combination of AP and BR (AP-BR), or favipiravir. The strength and dosage of each treatment regimen is shown in Table 1. The medical records of participants were retrieved after approval from the Director General of the Department of Corrections. The study flowchart is displayed in Figure 1.

Table 1. Dosage regimens of each treatment group (of standardized AP capsules, BR extract capsules, a combination of AP capsules and BR extract capsules, and favipiravir)

Treatment	Strength	Dosage regimen
AP capsules	400 mg (andrographolide 12 mg)	4 capsules thrice daily for 5 days
BR extract capsules	500 mg	1 capsule once daily for 5 days
AP capsules and BR extract capsules	AP 400 mg, BR 500 mg	4 AP capsules thrice daily for 5 days, 1 BR capsule daily for 5 days
Favipiravir tablets	200 mg	9 tablets twice on day 1, followed by 4 tablets twice a day for 5 days

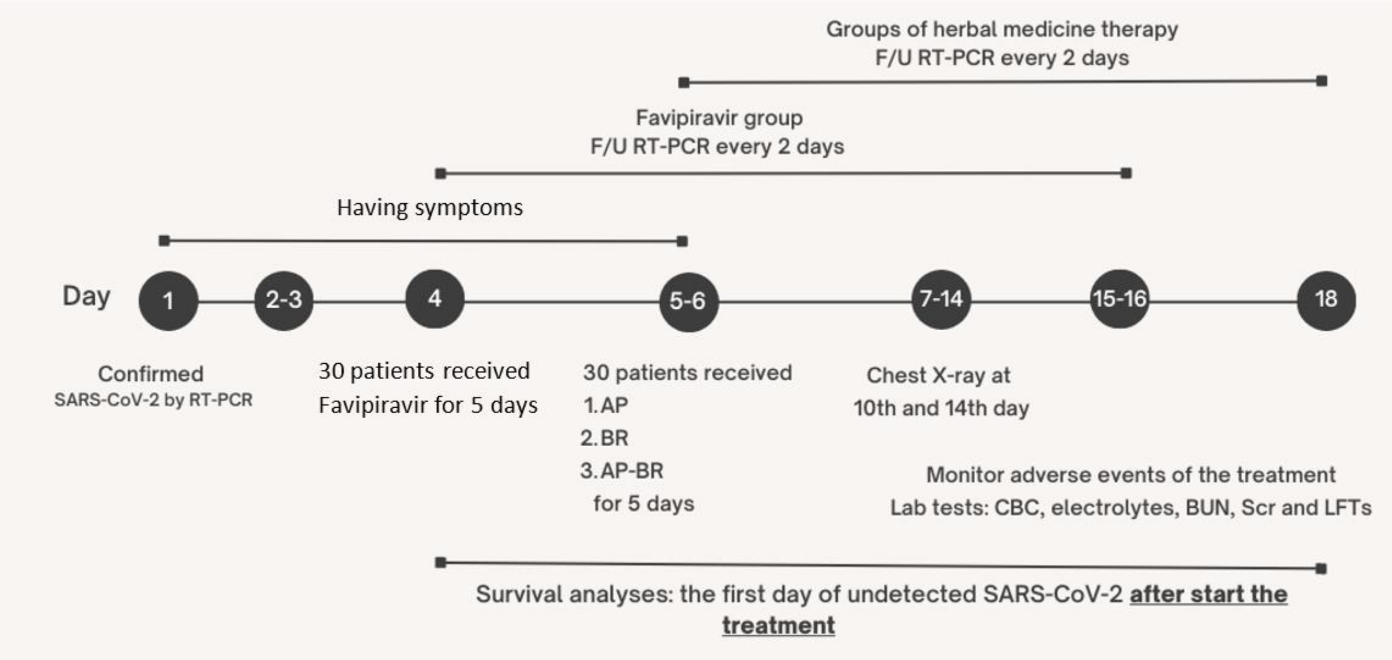
Note: AP: Andrographis paniculate, BR: Boesenbergia rotunda

Outcome Assessment

SARS-CoV-2 viral loads in all cases were measured using cycle threshold (Ct) values of ORF1a/b gene and N gene at baseline. Reverse transcription polymerase chain reaction (RT-PCR) assays of nasopharyngeal swab specimens were conducted every two days after treatment initiation. The primary outcome was the interval between the day of starting treatment (day 1) and the day when the participant returned a negative SAR-CoV-2 test. The secondary outcomes were the development of pneumonia and adverse events on day 14. Data collected from medical records included age, body mass index (BMI), underlying diseases, Ct values of ORF1a/b gene and N gene, date and results of RT-PCR tests, and results of chest X-rays on days 10 and 14. Complete blood counts (CBC), electrolytes, blood urea nitrogen (BUN), serum creatinine, and liver function tests were performed on day 14 to monitor the safety of the interventions.

Study Products

A. paniculata (Burm. f.) Nees capsule (AP) is manufactured by the Chaophya Abhaibhubejhr Hospital Foundation, Thailand. Each capsule contains 3% andrographolide in 400 milligrams (mg) of dried AP powder (andrographolide 12 mg per capsule). *B rotunda* (Linn.) Mansf. extract capsule (BR) is manufactured by the Pharma Herbal Company, Thailand. Each capsule contains 8% panduratin A and 18% pinostrobin in 500 mg powder (28 mg of panduratin A and 63 mg of pinostrobin).



Note: AP: Andrographis paniculate, BR: Boesenbergia rotunda, AP-BR: a combination of AP and BR, CBC: complete blood counts, BUN: blood urea nitrogen, Scr: serum creatinine, LFTs: liver function tests, F/U: follow-up

Figure 1. Study diagram of collected and analyzed health information on COVID-19 therapy

Data Analysis

Baseline characteristics of participants such as age, Ct values and duration of COVID-19 illness before receiving treatment were summarized using mean and standard deviation (SD) whereas BMI and underlying diseases were summarized using frequencies and percentages. Comparison of baseline characteristics among the four groups were tested using analysis of variance for continuous variables and Pearson's chi-square test for categorical variables. The median interval from treatment initiation to the first day of undetected SARS-CoV-2 with 95% confidence interval in each group was calculated. Analysis of time-to-event outcome was performed using survival analysis. Kaplan-Meier survival curves were created to compare the distribution of the outcome between groups. Multiple comparisons will be conducted if the log-rank test shows statistical significance to find out which groups were different. Cox-regression analysis was performed to determine associated risk factors for undetected SARS-CoV-2 within 14 days. The level of statistical significance was set at 0.05.

Ethical Approval

Ethical approval to conduct the study was not required due to the public health emergency. In addition, both products used in the study were approved by the Thai Food and Drug Administration as herbal medicine (for *A. Paniculata*) and dietary supplement (for *B. rotunda*). However, verbal informed consent was requested and obtained from participants before interview and sample collection.

Results

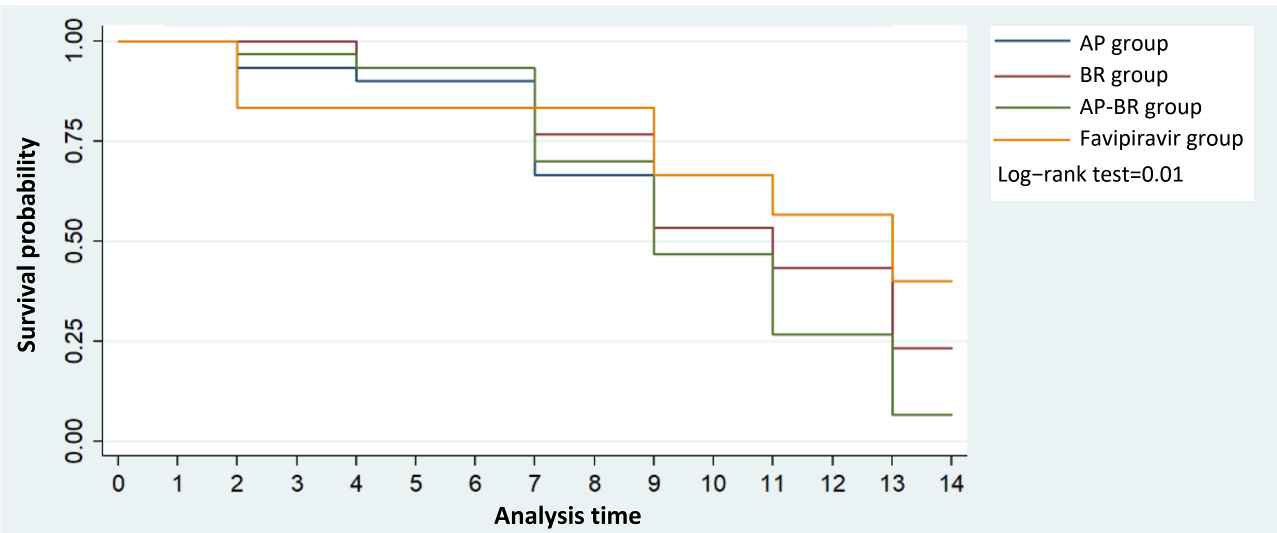
All participants in this study reported muscle pain. The mean (SD) age of participants was 37.4 (8.7) years and all were male. Table 2 shows a comparison of the baseline characteristics between the four groups. The mean age and mean BMI of the four groups were not significantly different. Most (85.8%) did not have any underlying chronic diseases; however, the AP group had a higher percentage of participants with underlying diseases (three hypertension and four asthma) than the other groups (*p*-value 0.005). Regarding mean Ct values of ORF1a/b gene and N gene, the AP-BR group had the highest amount of viral load compared to other groups, followed by the AP, BR, and favipiravir groups (*p*-value <0.05). There was a significant difference in the mean duration of illness prior to initiation of treatment among the four groups (*p*-value <0.001). The mean duration of illness prior to treatment among participants who received favipiravir (3.9 days) was shorter than that for the other groups (AP 6.0 days, BR 5.5 days, and AP-BR 6.0 days).

Table 2. Comparison of baseline characteristics between the four groups

Characteristic	N (%)					*P*-value
	Total (N=120)	AP (n=30)	BR (n=30)	AP and BR (n=30)	Favipiravir (n=30)	
Age (years) (Mean±SD)	37.4±8.7	39.9±9.5	37.3±8.4	34.7±7.8	37.6±8.6	0.140[a]
BMI (kg/m²)						0.757[b]
<18.5	4 (3.3)	0 (0.0)	2 (6.7)	0 (0.0)	2 (6.7)	
18.5–22.9	67 (56.7)	18 (60.0)	18 (60.0)	16 (53.3)	16 (53.3)	
23.0–24.9	25 (20.8)	6 (20.0)	4 (13.3)	8 (26.7)	7 (23.3)	
25.0–29.9	17 (14.2)	6 (20.0)	4 (13.3)	4 (13.3)	3 (10.0)	
≥30	6 (5.0)	0 (0.0)	2 (6.7)	2 (6.7)	2 (6.7)	
Underlying chronic diseases						0.005[b]
No	103 (85.8)	21 (70.0)	30 (100.0)	27 (90.0)	25 (83.3)	
Yes	17 (14.2)	9 (30.0)	0 (0.0)	3 (10.0)	5 (16.7)	
Ct value (mean ± SD)						
ORF1a/b gene	24.9±6.7	24.5±5.7	26.0±7.7	21.8±4.5	27.3±7.2	0.008[a]
N gene	26.2±6.5	25.4±5.6	27.1±7.5	23.7±5.0	28.4±7.0	0.028[a]
Period of illness[c] (days) (Mean±SD)	5.4±1.1	6.0±0.0	5.5±1.1	6.0±0.0	3.9±1.0	<0.001[a]

Note: [a]Analysis of variance, [b]Fisher's exact test, [c]Prior to treatment initiation

Participants in the AP and AP-BR groups had a median period of 9 days from treatment initiation to the first day of undetected SARS-CoV-2, this was shorter than that among participants in the favipiravir (13 days) and BR (11 days) groups (Table 3). Although the favipiravir group had lower amounts of detected SARS-CoV-2 on treatment initiation, AP, BR, and AP-BR groups had shorter duration of detected SARS-CoV-2 compared to the favipiravir group (log-rank test 0.01) (Figure 2). Multiple comparisons revealed that participants in the AP and AP-BR groups had a significantly higher rate of SARS-CoV-2 virus clearance than the favipiravir group, with log-rank tests of 0.005 and 0.006, respectively. The percentage of participants with undetected SARS-CoV-2 within 14 days since diagnosis of COVID-19 was higher in the AP (57%), AP-BR (54%) and BR (50%) groups compared to the favipiravir group (45%, *p*-value >0.05).



Number at risk	Day														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
AP	30	30	28	28	27	27	27	20	20	14	14	8	8	6	2
BR	30	30	30	30	28	28	28	23	23	16	16	13	13	7	7
AP-BR	30	30	29	29	28	28	28	21	21	14	14	8	8	2	2
Favipiravir	30	30	25	25	25	25	25	25	25	20	20	17	17	12	12

Figure 2. The Kaplan–Meier survival curve for comparing the first day of undetected SARS-CoV-2 PCR test after treatment by AP (Blue), BR (Purple), AP and BR (Green) and Favipiravir (Orange)

Table 3. A median period from treatment start to the first day of undetected SARS-CoV-2

Treatment (n)	Median period (days)	95% CI
AP (30)	9	7.25–11.00
BR (30)	11	9.00–13.00
AP-BR (30)	9	9.00–11.00
Favipiravir (30)	13	9.26–14.00

Cox-regression analysis showed that neither age, BMI, nor underlying diseases were associated with undetected SARS-CoV-2 within 14 days after receiving treatment (Table 4). During treatment, none of the participants developed pneumonia. Regarding adverse events of treatment, there was no difference in alanine aminotransferase (ALT) levels among the four groups and all participants had ALT $\geq$2 times of upper limit of normal (*p*-value 0.65, Table 5). One participant in the AP group developed hyperkalemia (serum potassium 7.0 milliEquivalents per liter). Hematologic and kidney adverse events were not seen

Table 4. Hazard ratio and 95% confidence intervals from cox-regression analysis between risk factors and event of undetected SARS-CoV-2 within 14 days (n=120)

Variables	Hazard ratio	95% CI
Age	0.99	0.96–1.01
BMI	1.00	0.95–1.06
Underlying diseases	1.27	0.70–2.32

Table 5. Monitoring of hepatotoxicity from the treatment

Treatment group	Number of participants who had ALT $\geq$2 x ULN (%)
AP	5 (16.7)
BR	3 (10.0)
AP-BR	2 (6.7)
Favipiravir	4 (13.3)

Note: ALT: alanine aminotransferase, ULN: upper limit of normal, Chi-square test: p-value=0.65

Discussion

This is the first study to assess the effectiveness of *A. paniculata* and *B. rotunda* on increasing the rate of viral clearance of SARS-CoV-2. Other studies assessing the effectiveness of AP treatment primarily aimed to investigate clinical recovery.[3,5] We found that mild COVID-19 cases treated with *A. paniculata* (with or without *B. rotunda*) had a shorter period of viral clearance compared to favipiravir, which corroborates with a clinical trial by Zhang et al who administered the sulfonate form of *A. paniculata* to their participants with mild to moderate COVID-19 infection.[8]

The latest DMS guidelines for COVID-19 management recommends starting treatment with *A. paniculata* and favipiravir within 5 days of symptoms onset.[6] In this study, participants in the favipiravir group received their treatment before the other groups because the conventional medicine arrived before the herbal medicines. Since the treatment groups were initiated on different days, findings of survival analyses, therefore, should be interpreted with caution. In this study, participants treated with herbal medicine showed a faster viral clearance period compared to those given favipiravir. The AP and AP-BR groups showed a shorter median period (9 days) between the start of the treatment and the first day of undetected SARS-COV-2 compared to the BR (11 days) and favipiravir (13 days) groups. This result contrasts with previous studies that reported early treatment with favipiravir (approximately 4 days after symptom onset) enhanced viral clearance to 6–10 days.[9,10] SARS-CoV-2 viral clearance varied among our participants, and our small sample size did not allow a more precise estimate of this outcome.

The percentage of participants with undetected SARS-CoV-2 within 14 days post-infection was higher in the AP group than the BR group, which may be attributed to the dosage of *B. rotunda* extract. The effective dosage of *B. rotunda* extract for the treatment of COVID-19 is not yet known; therefore, further clinical trials to determine the optimum dosage and regimen are needed.

Categorized at 14 days, more than half of the participants in this study that were treated with herbal medicine had a shorter period of viral clearance compared to the natural viral clearance duration of 16 days reported among mild COVID-19 cases infected with the alpha variant.[11] Given the severity of COVID-19 as a life-threatening disease, the findings from this study are, potentially, of clinical significance.

In summary, both *A. paniculata* and *B. rotunda* were primarily demonstrated to be safe for the treatment of mild COVID-19. None of the participants in this study developed pneumonia. Furthermore, our results showed no difference in hepatic adverse events among all groups. One participant who received *A. paniculata* developed hyperkalemia. Therefore, potential adverse events should be further investigated in larger studies. Currently, there is an ongoing clinical trial assessing the efficacy and safety of *A. paniculata* and *B. rotunda* compared to standard supportive treatment among asymptomatic COVID-19 cases in Thailand.[12]

The findings of this study should be interpreted with caution due to certain limitations. Firstly, generalization of the results is limited due to the small sample sizes in each group. Secondly, only young male participants were included in this study. Thirdly, several factors may influence the Ct values of ORF1 a/b gene and N gene, such as specimen type, the timing of sample collection, collection technique, transportation method, and storage conditions, none of which were collected in this study.

Recommendations

The DMS guidelines recommend that physicians consider *A. paniculata* and favipiravir for symptomatic COVID-19 cases without pneumonia. Although *A. paniculata* is more accessible than favipiravir, the quality of the product should be emphasized to the public. Only standardized products with andrographolide should be used. The dosage of andrographolide given to our study participants was 144 mg per day while DMS recommends 180 mg. We used 144 mg for two reasons. Firstly, the majority of Thai residents have already received the COVID-19 vaccine, which can help mitigate disease *severity* when infected. Additionally, in our study, we found that mild COVID-19 cases responded well to *A. paniculata*, even though they did not get vaccinated. Secondly, *A. paniculata* has been shown to have dose-dependent side-effects such that lower dose utilization would minimize side effects.[13]

Although *B. rotunda* was shown to have a slower viral load clearance than *A. paniculata*, possibly due to its unknown effective dose, patients may use it for health promotion, not treatment for COVID-19, as this product is already available in the market as a dietary supplement.

Conclusion

A. paniculata and *B. rotunda* use is associated with a quicker viral clearance in mild COVID-19 infections compared to favipiravir and may be used as an alternative when access to favipiravir is limited. Further clinical trials are needed to assess the efficacy and safety of these two herbal medicines for the treatment of mild COVID-19. Healthcare providers should be aware of possible adverse effects such as hyperkalemia.

Declarations

Consent for Publication

Not applicable

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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Authors' Contributions

PP guided and revised the manuscript. AM and PK revised the manuscript. MT analyzed study data and wrote the first draft of the manuscript. TP analyzed study data. KC, CC, DM, and TK carried out the research. All authors approved the final manuscript.

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The Grammar of Science: "Dummy" That Is Not So Dummy!

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"Dummy" means many things. In the Merriam-Webster dictionary, "Dummy" is a person who is incapable of speaking, habitually silent, or a stupid person.[1] It could also mean an imitation, copy, or likeness of something used as a substitute. "Dummy" may have the appearance of being real, apparently acting for oneself while really acting for or at the direction of another. So how the smart "Dummy" that is not a stupid dummy gets into analyzing the data in research?

Types of Measurement in Research

Let's start at the very beginning. The measurement is the core of science which have evolved profoundly during the past century. Different methods of scaling and estimation were introduced by behavioral psychologists and statisticians.[2] In 1946, Stanley Smith Stevens wrote an article titled "On the Theory of Scales of Measurement" providing definition of measurement as the assignment of numerals to objects or events according to rules.[3] Stevens classified four types of measurement scales: (1) nominal, (2) ordinal, (3) interval, and (4) ratio scales. The scales are defined in terms of their mathematical transformations that can be conducted without changing their properties and the statistical operations that are considered permissible for each.[2,3] The scales form a specific hierarchy from the statistical point of view.

The simplest and lowest measurement is a nominal scale. As the word implies, "nominal" scale is the "name" given to two or more exhaustive categories. Numeric numbers could be assigned to each of the categories to represent different characteristics; for example, "Gender" could be categorized as 1=Male or 2=Female; "Race" as 1=White, 2=Black, 3=Asian. As the number is simply the name of the assigned category; thus, it does not mean that #1 < #2 or #2 < #3. The statistical methods which can be used with nominal scales are mostly the non-parametric statistics.

An ordinal scale is next level of measurement scaling. As the word implies, "ordinal" scale is the numeric numbers assigned to the categories based on their "order", the simplest form of "ranking". For ordinal scale, the categories are ordered along a continuum, for example, "Severity of disease" are categorized as 1=Mild, 2=Moderate, 3=Severe. The numbers assigned to the ordered categories represent degree of the differences, but not equal distances between the numbers. In the meaning of severity, #1 < #2 and #2 < #3 but the distance between #1 & #2 may not be the same as #2 & #3. Ordinal data are typically analyzed using non-parametric statistics.

Interval scale is the measurement scale representing "continuous" numbers with the "same distance/interval" between the two numbers; the distances are the same between #1 & #2 and #2 & #3, and so on. Interval scale has no "absolute zero". For example, "Temperature" can be measured in Centigrade, Fahrenheit, or Kelvin scales; each scale has its own zero point. The arbitrary zero of degree in Celsius scale is at the -32 degree in Fahrenheit scale. Interval scale data could be analyzed using either parametric or non-parametric statistical techniques:

Ratio scale has the same properties as interval scale but it has a "true zero point". When number 0 is assigned to the characteristic measured, it means the measured entity is presumed to be absent. For example, in measuring "Weight" in either Kilogram or Pound scales, 0 means no weight in both scaling units. Ratio scale and interval scale are generally used inter-changeably and analyzed with the same statistical methods.

Use of Interval/ratio Scaled Predictors in Regression Analysis

The purpose of regression analysis is to quantify the relationship between an outcome variable with one or more predictors that are measured in different types of measurement scales. As an example, in linear regression model the outcome is measured as continuous variable (interval/ratio scale) and the predictor variables could be measured in any type of the measurement scales. When a predictor is interval or ratio scale in the regression model, it denotes how much difference might be for the outcome variable when comparing the predictor with a one-unit difference.

The following examples, used a dataset from a textbook, show a linear regression model quantifying several risk factors of mothers on their baby birth weight.[4] As shown in the model, when comparing mothers with "Age" difference for one year (21 vs. 20 years old), their "Baby weight" are different for about 12.36 grams and not statistically significant difference (p-value=0.219) (Figure 1).

bwt	Coef.	Std. Err.	t	P>|t|
age	12.36433	10.02055	1.23	0.219
_cons	2657.333	238.804	11.13	0.000

$$Linear\ Model: \quad Estimated\ Mean(bwt) = \beta_0 + \beta_1 age$$
$$= 2657.333 + 12.36433\ age$$
$$when\ \ age = 20 \quad Estimated\ Mean(bwt_{age=20}) = \beta_0 + \beta_1\ (20)$$
$$= 2657.333 + 12.36433(20) = 2904.620$$
$$when\ \ age = 21 \quad Estimated\ Mean(bwt_{age=21}) = \beta_0 + \beta_1\ (21)$$
$$= 2657.333 + 12.36433(21) = 2916.984$$

$$thus\ \ Mean\ difference:$$
$$Estimated\ Mean(bwt_{age=21}) - Estimated\ Mean\ (bwt_{age=20}) = (\beta_0 + 21\beta_1) - (\beta_0 + 20\beta_1) = \boldsymbol{\beta_1}$$
$$= 2916.984 - 2904.620 = 12.364$$

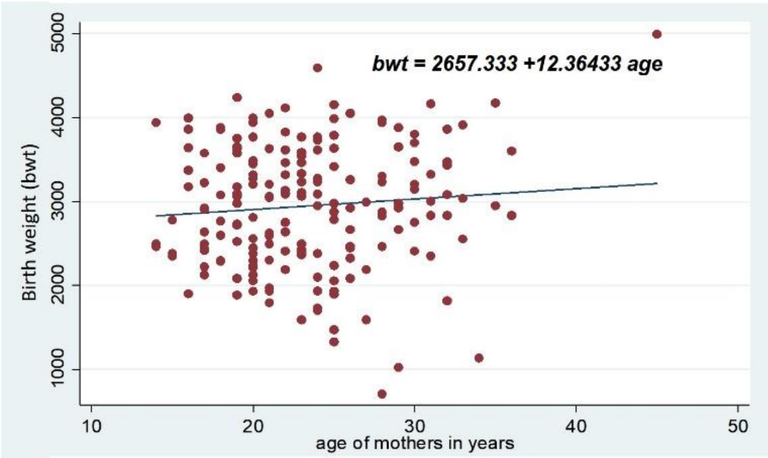

Figure 1. A linear regression model quantifying the effect of maternal age on baby birth weight

Use of Nominal/ordinal Scaled Predictors in Regression Analysis

When the predictor is measured in nominal or ordinal scale, it constitutes as a fixed scale and not equal distances between numbers. In such case, the nominal/ordinal predictor should be transcribed as the so-called "Dummy" variable.

Dummy variable is sometimes called "indicator" variable, "design" variable, "Boolean" indicator, or "proxy" variable.[5,6] As implied by the name, "Dummy" can be considered as a stand-in for a real person, an artificial attribute of the characteristics. A dummy variable in regression analysis is a numeric stand-in for a qualitative fact or a logical proposition.[6] Dummy variable is generally coded as 0 and 1; code 1 stands for "this unit belongs to category X" and 0 stands for "this unit does not belong to category X".[7] Thus, the dummy variable acts like "switch" that turn the category on and off.[8] For example, "Smoking" may be coded as a dummy variable as: 1=smoking vs. 0=non-smoking.

In a regression model, a dummy variable with a value of 0 will cause its coefficient to disappear from the equation. As shown in the model, when comparing "Smoking status" of the mothers (Yes-1 vs. No-0), their "Baby weight" are different about 281.71 grams and statistically significant difference (Figure 2).

bwt	Coef.	Std. Err.	t	P>|t|
smoke_0_1	-281.7133	106.9687	-2.63	0.009
_cons	3054.957	66.93324	45.64	0.000

$$Linear\ Model: \quad Estimated\ Mean(bwt) = \beta_0 + \beta_1 smoke\_0\_1$$
$$= 3054.957 - 281.7133\ smoke\_0\_1$$
$$when\ \ smoke = 0\ (no) \quad Estimated\ Mean(bwt_{smoke=0}) = \beta_0 + \beta_1\ (0)$$
$$= 3054.957 - 281.7133\ (0) = 3054.597$$
$$when\ \ smoke = 1\ (yes) \quad Estimated\ Mean(bwt_{smoke=1}) = \beta_0 + \beta_1\ (1)$$
$$= 3054.957 - 281.7133\ (1) = 2773.243$$
$$thus\ \ Mean\ difference: \quad Estimated\ Mean(bwt_{smoke=1}) - Estimated\ Mean\ (bwt_{smoke=0})$$
$$= (\beta_0 + 1\beta_1) - (\beta_0 + 0\beta_1) = \boldsymbol{\beta_1}$$
$$= 2773.243 - 3054.957 \ = \ -281.714$$

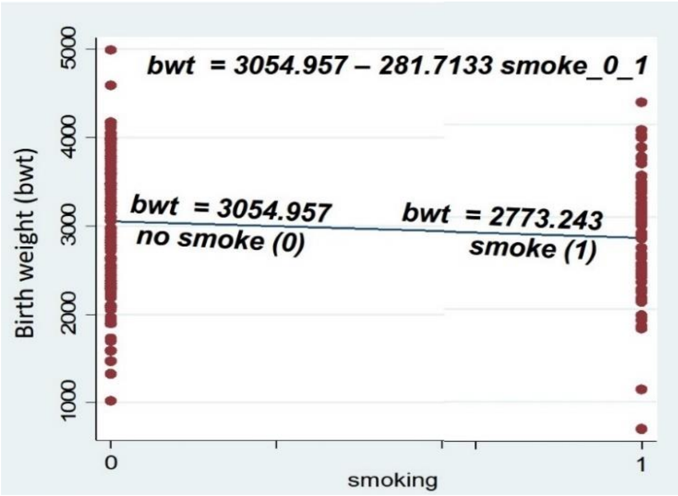

Figure 2. A linear regression model of the effect of smoking status (0,1) on baby birth weight

When the predictor is a nominal scale with two categories and the coding of the category is one-unit apart, the model will result in the same outcome estimate, but the intercept of the model will be different. When smoking status is coded as No-1 and Yes-2, the mean difference between the two groups is still -281.71 but the intercept is 3336.67 instead of 3054.95 grams (Figure 3). If the coding of the predictor is not one-unit apart, the mean difference and the intercept will be different in compensation for the values assigned to the two categories. It is more practical to use dummy variable coded as (0,1) rather than other coding scheme.

bwt	Coef.	Std. Err.	t	P>|t|
smoke_1_2	-281.7133	106.9687	-2.63	0.009
_cons	3336.67	157.7418	21.15	0.000

$$Linear\ \ Model: \quad Estimated\ Mean(bwt) = \beta_0 + \beta_1 smoke\_1\_2$$
$$= 3336.67 - 281.7133\ smoke\_1\_2$$
$$when\ \ smoke = 1\ (no) \quad Estimated\ Mean(bwt_{smoke=0}) = \beta_0 + \beta_1\ (1)$$
$$= 3336.67 - 281.7133\ (1) = 3054.597$$
$$when\ \ smoke = 2\ (yes) \quad Estimated\ Mean(bwt_{smoke=2}) = \beta_0 + \beta_1 (2)$$
$$= 3336.67 - 281.7133\ (2) = 2773.243$$

Figure 3. A linear regression model of the effect of smoking status (1,2) on baby birth weight

When a predictor variable composes of more than two categories, more than one dummy variable must be generated to represent all characteristics. For example, "Race" variable is originally categorized as:1=White, 2=Black and 3=Asian. When creating dummy variable for Race, one can create a dummy variable called "White" and assign the coding 1= "is White" and 0= "is not White" and create other dummy variables as "Black" and "Asian" in the same fashion (Figure 4).

ID	bwt (g)	Age	Original Var
			Race
1	2523	19	1 (white)
2	2551	38	1 (white)
3	2662	28	3 (asian)
4	2600	21	3 (asian)
5	2498	17	2 (black)
6	2567	41	2 (black)

→

ID	bwt (g)	Age	Dummy Var (New)		
			White	Black	Asian
1	2523	19	1	0	0
2	2551	38	1	0	0
3	2662	28	0	0	1
4	2600	21	0	0	1
5	2498	17	0	1	0
6	2567	41	0	1	0

Figure 4. An example of dummy variable creation with three values

However, there is a redundancy in the above coding scheme; if we know that someone is not "White" and not "Black", then they are "Asian". Using all created dummy variables in a regression model would lead to a "dummy variable trap" with multicollinearity, i.e., one dummy variable can be predicted with the help of other dummy variables.[9,10] So, in this case, the regression model should be designed to include only two of the three dummy-coded variables as predictors. That is, generally, the number of dummy-coded variables needed in the model is k-1 dummy variables, where k stands for the total number of categories. The category that is left out is called the "reference" category. Choosing which category of the dummy variable to be a reference group is arbitrary, depending on the researcher's logic. As shown in the model, when "Race" variable with three categories is transformed into two dummy variables as "Black" and "Asian", with "White" as a reference groups, the estimated means of the three groups can be calculated (Figure 5). The mean difference refers to the difference of the outcome estimates between the other two groups against the reference group

ID	bwt (g)	Age	Original Var
			Race
1	2523	19	1 (white)
2	2551	38	1 (white)
3	2662	28	3 (asian)
4	2600	21	3 (asian)
5	2498	17	2 (black)
6	2567	41	2 (black)

→

ID	bwt (g)	Age	Dummy Var (Reference: White)		Dummy Var (Reference: Age ≤25)	
			Black	Asian	Age 26–35	Age >35
1	2523	19	1	1	0	0
2	2551	38	1	1	0	0
3	2662	28	0	0	1	0
4	2600	21	0	0	1	0
5	2498	17	0	0	0	1
6	2567	41	0	0	0	1

bwt	Coef.	Std. Err.	t	P>|t|
race_w1_b2~3				
black	-384.0473	157.8744	-2.43	0.016
asian	-299.7247	113.6776	-2.64	0.009
_cons	3103.74	72.88169	42.59	0.000

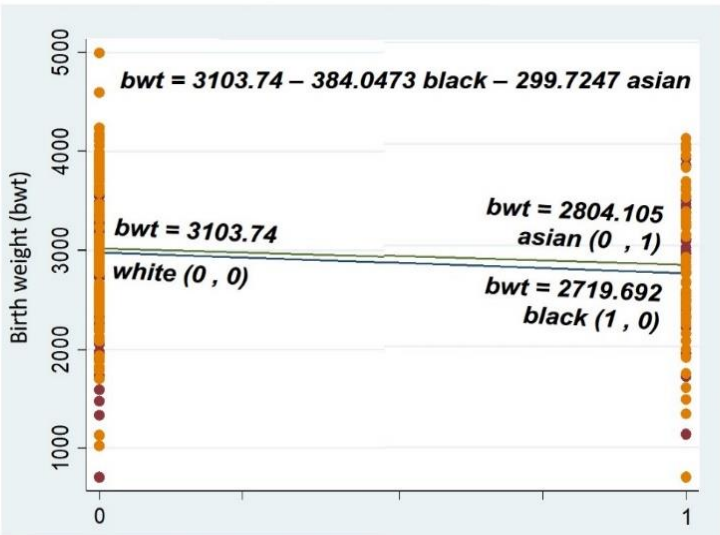

Figure 5. A linear regression model of the effect of race on baby birth weight using dummy variable creation

$$Linear\ Model: \quad Estimated\ Mean(bwt) = \beta_0 + \beta_1 black + \beta_2\, asian$$
$$= 3103.74 - 384.0473\ black - 299.7247\ asian$$

$$when\ race = white \quad Estimated\ Mean(bwt_{race=white}) = \beta_0 + \beta_1\,(0) + \beta_2\,(0)$$
$$(black = 0\ ;\ asian = 0) \quad = 3103.74 - 384.0473\,(0) - 299.7247\,(0) = 3103.740$$

$$when\ race = black \quad Estimated\ Mean(bwt_{race=black}) = \beta_0 + \beta_1\,(1) + \beta_2\,(0)$$
$$(black = 1\ ;\ asian = 0) \quad = 3103.74 - 384.0473\,(1) - 299.7247\,(0) = 2719.692$$

$$when\ race = asian \quad Estimated\ Mean(bwt_{race=asian}) = \beta_0 + \beta_1\,(0) + \beta_2\,(1)$$
$$(black = 0\ ;\ asian = 1) \quad = 3103.74 - 384.0473\,(0) - 299.7247\,(1) = 2804.015$$

$$thus\ Mean\ difference: Estimated\ Mean(bwt_{race=black}) - Estimated\ Mean\ (bwt_{race=white})$$
$$(black - white) \quad = (\beta_0 + 1\beta_1 + 0\beta_2) - (\beta_0 + 0\beta_1 + 0\beta_2) = \boldsymbol{\beta_1}$$
$$= 2719.692 - 3103.740 = -384.048$$

$$Mean\ difference: Estimated\ Mean(bwt_{race=asian}) - Estimated\ Mean\ (bwt_{race=white})$$
$$(asian - white) \quad = (\beta_0 + 0\beta_1 + 1\beta_2) - (\beta_0 + 0\beta_1 + 0\beta_2) = \boldsymbol{\beta_2}$$
$$= 2804.015 - 3103.740 = -299.725$$

Figure 5. A linear regression model of the effect of race on baby birth weight using dummy variable creation (cont.)

Tips for Using Dummy Variables in Statistical Analysis

It is not good to have a dummy variable for every (k-1) category when there are too few observations in certain category because a dummy variable for such category would be too rare to be meaningful and statistically significant. Thus, a created dummy variable may represent mixed or combined categories. For example, "Race" could be coded as: 1=White, 2=Black, 3=Others (combined all other races besides White and Black).

With the ordinal scale data, the "ranks" of the category, sometimes called "bins", could be formulated into dummy variables. Bins or ranks can act as sets of different characteristics, representing categorical, non-probabilistic set membership.[6] For example, a variable of "Severity of disease" (measures as ordinal scale) could be assumed as three types/sets of membership (nominal scale) of patients in either one of the categories of: 1=Mild, 2=Moderate and 3=Severe. By transforming an ordinal variable to dummy variables, although ordinality of the variable will not be directly considered in the regression equation, researchers can still observe the effect of ordinal nature of the variable on the outcome variable by looking at the pattern of regression coefficient values. The regression coefficients of the transformed dummy categories may reflect levels of strength of association, say dose-response pattern, between the outcome and the inherent exposure levels.

For the predictor that is continuous variable, a one-unit difference of the predictor values might have small and not significant effect on the outcome estimates, thus another way to develop a more meaningful regression model is to use independent dummy variable that represent the continuous values in a set of levels. For example, "Age" of-mother in the above example could be transformed as a set of age risk factors that might affect "Baby-weight"; two dummy variables of age group could be generated as "Age 26–35", "Age >35" with "Age ≤25" as a reference group. The cut-off points for grouping depends on the researcher's logic; it could be based on biological, clinical, social or other point-of-views.

Not only in regression model, dummy variables can be used in any statistical analysis when the researchers want to assess the effect of such variable in the models. A dummy variable is used as an independent variable in t-test, ANOVA; or as a predictor in a linear regression model. On the other hand, a dummy variable is used as a dependent or outcome variable in Binary logistic regression, Poisson regression; or as the endpoint variable in Cox's proportional hazard regression.

After all, dummy variable is not just a fake dummy of the real person. It is important and even crucial to apply dummy variables intelligently in the statistical procedures in order to have the meaningful study results.

Suggested Citation

Kaewkungwal J. The grammar of science: "dummy" that is not so dummy! OSIR. 2022 Dec;15(4):138–43.

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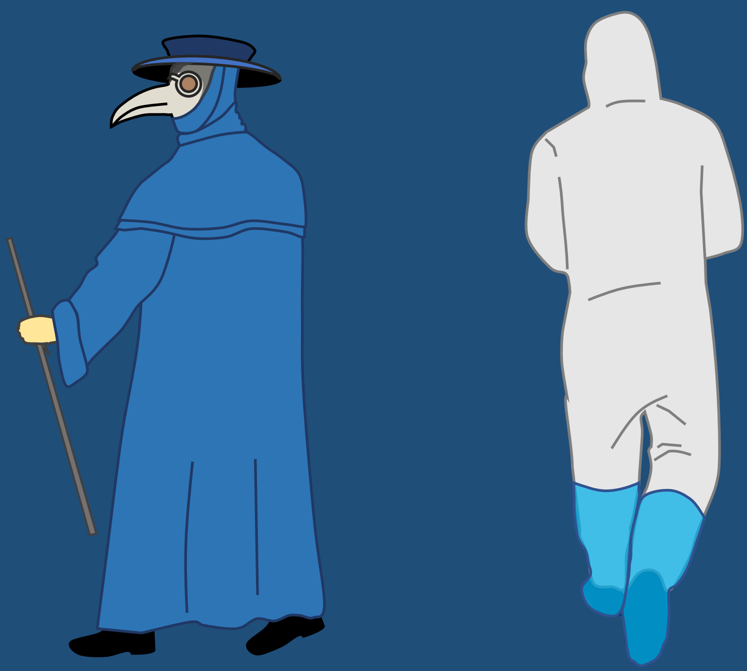

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