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Discovering Trends of Opioid-Borne Health Problems: Using a Combined Text Mining Technique

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Abstract

Objective: The use of opioids has progressively widened during the last two decades, and rapidly increasing consequent health problems from opioids prompted the current public health crisis. In spite of the crisis, no comprehensive research has been conducted to discover how opioid-born health problems have developed and how they led to the current epidemic. Because those problems are systematically reflected in academic publications, the first purpose of this research is to discover opioid-born health problems through the lens of scholarly publications using a text mining technique. The unigram has predominantly used in text mining regardless of fields, but this method has some inherent limitations to comprehensively discover knowledge. Therefore, the second purpose is to illustrate the advantages and disadvantages of unigram by introducing bigram and trigram and empirically demonstrate the benefits of employing a multigram method from the context of opioid-born health problems.

Methods: A combined NGram text mining technique (i.e., unigram, bigram, and trigram) was used as the analytical strategy, using 5815 abstracts retrieved from PubMed between 2000 and 2017.

Conclusions: Opioid was not a big threat to public health in the early 2000s and was mainly used for cancer pain. As the use of opioids is widened, consequential health problems progressively arise. Notable health problems include mental health, neonatal abstinence syndrome, veterans' health, emergency department visits, prescription opioid, opioid use disorder, injecting drugs, and opioid overdose deaths. This study is a small yet first attempt to comprehensively discover opioid-born health problems using a combined NGram method.

Keywords: *Data mining; Knowledge discovery, NGram; Opioids; PubMed; Text mining*

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Introduction

The mortality rate of opioid overdose has increased by 466.20% from 2000 to 2017 [1,2]. In 2016, 11.5 million Americans

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misused prescription opioids and 42,249 died from an opioid overdose, totaling to over 115 deaths a day [3,4]. It is mainly because opioid was prescribed for cancer pain in the early 2000s, but recently the prescriptions have widened to include non-medical use. As a consequence, opioid-born health problems such as neonatal abstinence syndrome (NAS), mental health, injecting drugs, opioid use disorder, and opioid overdose deaths among many other problems have recently sharply risen. These heightened opioid-born health problems prompted the Department of Health and Human Services to declare opioid overdose as a public health emergency [3]. Because academics respond to the current issues of the time, a systematic exploration of the trends can provide insights on a comprehensive view of both historic developments of opioid-born health issues and the current opioid epidemic. In spite of these benefits, little to no research has investigated how opioid-born health problems have developed and caused the current opioid epidemic. Massive textual data might have been a barrier for researchers to undertake the task. The recent development of text mining techniques, a branch of data mining, enables scholars to analyze enormous textual data and systematically discover knowledge buried in the text.

Text mining (TM) is a specialized data mining technique used to systematically extract major words or phrases from a collection of textual data [5,6]. While few studies have applied this method to healthcare research, the employed strategy is unigram [7-10] which is predominantly used in TM, regardless of the field. Unigram captures single word: if the terminology is composed of two or more words, compound words will be split into a single word, which makes it difficult to interpret the finding. For example, opioids can be used for cancer pain, chronic pain, and palliative pain among others. If unigram is applied, pain will emerge as a most frequent word, but the contextual meaning of pain is ambiguous. On the contrary, unigram can be superior to some compound terminologies. For example, methadone maintenance treatment can be used in different compound forms such as the treatment of methadone maintenance, methadone maintenance programs, or methadone therapy programs. Often some scholars use simply “methadone” or “methadone treatment.” Because the term, methadone, is clear enough to interpret the meaning without further information, unigram is a better choice. In this example, if researchers apply bigram or trigram to discover research trends, the validity of the finding will also be compromised. As such, applying a multigram method warrants the validity of finding.

Therefore, the first purpose of this research is to discover how opioid-born health problems have widely progressed over time using a combined text mining technique. The textual data is research abstract from PubMed. The retrieved abstracts were grouped into three periods: Period I (2000-2005), Period II (2006-2011), and Period III (2012-2017). This categorization has not only evenly spaced out the publication years, but it also coincides with changes in opioid-related deaths. The second purpose is to empirically illustrate the advantages and disadvantages of unigram, bigram, and trigram methods and demonstrate how the combined NGram method can comprehensively discover opioid-born health problems buried in huge textual data.

In order to enhance conclusion validity, this manuscript adopted the following steps: (1) the document normalization method was employed in order to put longer and shorter documents on the same scale, so different lengths of documents can be directly comparable; (2) if a specific word appears across entire documents (or corpus in the TM terminology), the word will be given a lower value, which enables the study to exact distinct themes. The multiplication of (1) and (2) will find distinct yet frequent themes from each period; (3) since unigram, bigram, and trigram will capture different research themes of each period, this study will employ three NGram methods (i.e., unigram, bigram, and trigram) in order to comprehensively discover research themes in each period and integrate these three methods to holistically discover the trends of opioid-born health problems.

Table 1 shows the number of age-adjusted opioid overdose deaths and the number of opioid-related academic publications between 2000 and 2017.1,3,11 The rate of opioid-related deaths increased by 466.20% from 2000 to 2017, and the rate of opioid-related publications increased by 836.78%% for the same period. By period, opioid-related deaths 67.89% increased from Period I to II, and 66.66% increased Periods II to III, and for publications 117.36% increased from Periods I and II and 123.40% increased from Periods II to III. Table 1 shows the number of deaths and publications in each year within the research period.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Death	8.4	9.5	11.9	12.9	13.8	14.9	17.6	18.5	19.6	20.0	21.1	22.8	23.2	25.1	28.7	33.1	42.2	47.6
Pub	59	73	79	89	104	128	152	185	211	217	282	293	327	454	480	592	691	769

Table 1: Statistics for age-adjusted opioid overdose deaths and publication between 2000 and 2017 [1,3,11].

Note: Deaths per 1,000

In order to demonstrate how well academic publication reflects opioid-born crisis, the opioid-related deaths and opioid-related publications are overlaid in Figure 1. As shown, publications follow a similar pattern of opioid-related deaths. The deaths and the publications are rapidly increased since 2012.

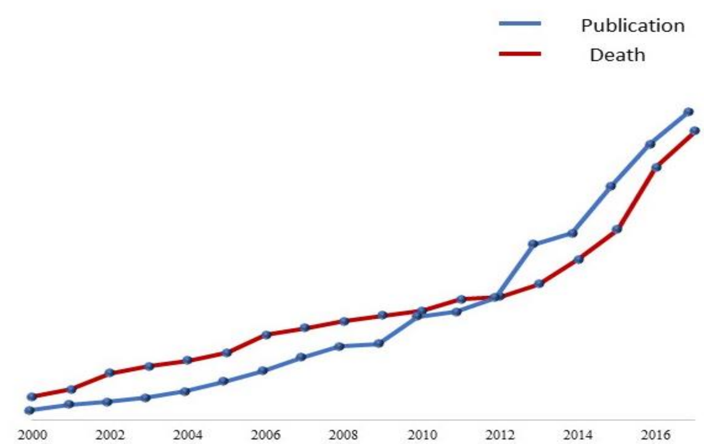

Figure 1: The overlay of the number of deaths and publications.

Materials and Methods

Data acquisition and methods

Opioid-related article abstracts were retrieved from PubMed [11]. Because the corpus of this research consists of opioid-related journal articles' abstracts, the search criteria were set to journal articles, abstract availability, human subject, English, and publication dates between 2000 and 2017. These criteria yielded the following results: 7,044 articles were retrieved, and 5,815 articles were retained after removal of duplicates. The search terms were the combinations opioid + health (3,230), opioid + medical (2,589), opium + health (83), opium + medical (87), opiate + health (606), and opiate + medical (449). All the data cleaning and text mining analysis were performed using the tm package, version 0.7-5, in R.

Preprocessing corpus

All documents were preprocessed together in order to keep consistency across the three groups of the documents. Three terms were unified under the term "opioid": opioid, opium and opiate because these terms were used to search for the same opioid-related research. TM algorithm treats the full name and the acronym differently, because of this, acronyms were converted to the full name while dropping the first appearing acronym in parenthesis in order to prevent them from counting twice. After completion of the preprocessing, the abstracts were categorized into three groups.

Data cleaning

Like any other text mining, this project went through the standardized data cleaning process: removal of punctuation, numbers, stop words, white space, and the conversion of capital letters to lower cases. Additionally, this project removed the words that commonly appear in research abstracts such as objective, purpose, aim, research methods, finding, background, and conclusion, however, the term "opioid" was not removed to capture its contextual meaning in the *corpus*. To elaborate, this research paper includes *bigram* and *trigrams*, and the term, "opioid," will be used in different contexts (e.g., opioid overdose death, opioid substitute program, non-medical prescription opioid, etc.). Furthermore, since the term, opioid, appears across the entire document, inverse documents frequency will assign the value of 0 (zero) to the term, opioid, meaning that it will not be captured as a frequently appearing word in unigram. Lastly, stemming was applied. Stemming in natural language process (NLP) is the process of reducing words to a common base form (i.e., stem). For example, "processing" becomes "process" after being stemmed, so the word "process" can then incorporate all the words stemming from process (e.g., processing, processes, processed).

N-grams

An N-gram is a consecutive word sequence of N terms from a given sentence. If it extracts a single word, it is referred to as *unigram*; if it retrieves a two-contiguous sequential word, it is *bigram*; and if it is a three-contiguous sequential word, it is called *trigram*. Below are examples of *unigram*, *bigram*, and *trigram* using the phrase, "*nonmedical prescription opioid use prompted mental health disorders and opioid overdose deaths*".

Unigram

[nonmedical] [prescription] [opioid] [use] [prompted] [mental] [health] [disorders] [and] [opioid] [overdose] [deaths]

Bigram

[nonmedical prescription] [opioid use] [prompted mental] [health disorders] [and opioid] [overdose deaths]

[prescription opioid] [use prompted] [mental health] [disorders and] [opioid overdose]

Trigram

[nonmedical prescription opioid] [use prompted mental] [health disorders and] [opioid overdose deaths]

[prescription opioid use] [prompted mental health] [disorders and opioid]

[opioid use prompted] [mental health disorders] [and opioid overdose]

In this example, the findings from unigram cannot provide accurate meaning of the opioid-born health issues; the findings from bigram can capture the contextual meaning of "nonmedical prescription," "mental health," and "overdose deaths"; and the findings from trigram can further clarify the contextual meanings from bigram.

Tokenization (document-term frequency matrix)

Tokenization is the process of converting textual data into a data frame. Using the cleaned data, all words are decomposed into a single word for unigram, consecutive two-word for bigram, and three-word for trigram. After tokenized, *people who inject drugs* becomes "people inject drug" after the application of cleaning and stemming, non-contextual words such as the word, "who," are dropped in the stop word process, and the stemming process removed "s" after "drugs", and "e" after "people." Table 2 shows a data frame. If a specific document has a specific phrase, it is marked as 1; it is 2 if the phrase occurs twice in the document. The examples of *bigrams* in Table 2 are after the cleaning and stemming processes.

	Emerg depart	Mental health	people inject	neonat abstin	…
Doc 1	2	2	1		
Doc 2		1		1	
Doc 3	1		1	3	
…					

Table 2: Data frame example of bigram.

Due to longer documents containing more terms, it is important to calculate the proportion of a specific word in a document, which is referred to as *Term Frequency* (TF) (i.e., number of times a term or phrase *t* appears in a document/total number of *terms* in the document). For example, "emerg depart" (i.e., *t*) appears three times *within* a document (i.e., *d*) with 150 *bigrams*. The proportion of the phrase is 3/150, and it is marked in the data frame as "0.02." It is *inverse document frequency* (IDF) that finds distinct terms from the *corpus*. For example, if "emerg depart" appears 600 times *across* 1,000 documents (or *corpus*), its log of 1000/600 = 0.221849, and thus the IDF value is "0.221849." TF-IDF is the multiplication of TF and IDF. In this example, the value of TF-IDF is "0.00443698" (0.02* 0.221849 =0.00443698). It is a value from one corpus. For example, if "emerg depart" appears 500 times in Period I, TF-IDF of the bigram for the period would be 2.21849 (0.00443698*500d). TF-IDF allows researchers to find distinct yet frequent phrases in the *corpus*. TF-IDF is the best-known weighting scheme in text retrieval [12].

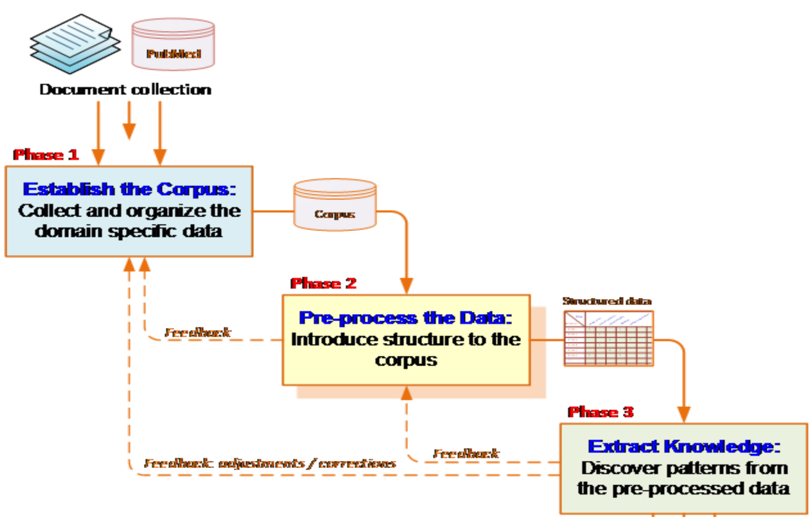

Figure 2: A Process for text mining and knowledge discovery [13].

TF-IDF is valid not only for *unigram* but also for *bigram*, *trigram*, and others [5], the mathematical calculations are as follows:

$$TF(t,d) = \frac{freq(t,d)}{\sum_i^n freq(t_i,d)} \quad IDF(t) = \log\left(\frac{N}{count(t)}\right) \quad TF\text{-}IDF(t,d) = TF(t,d) * IDF(t)$$

Figure 2 is a graphic presentation of the process from obtaining materials to discovering knowledge discussed in this section.

Results

All the analysis was performed using the *TM* package in *R-3.4.4*. As shown in the calculation of TF-IDF in the previous section, the value will go up as the number of publications increases, which means that the value of TF-IDF will be higher for Period III because 12.36%, 27.09%, and 60.55% are published in Period I, Period II, and Period III respectively. In order to directly compare on the same scale, this research used Period III as the baseline and assigned weights of 4.90 for Period I and 2.23 for Period II based on the rate of publications of each period.

Unigram

Figure 3 shows frequently appearing unigrams across the three periods. The most frequently appearing unigrams in Period I are pain, methadone, buprenorphine, heroin, analgesic, cocaine, alcohol, withdrawal, and detoxification. Based on these frequently appearing unigrams, one can speculate that opioid was mainly used for pain treatment, and methadone and buprenorphine treatments were popular.

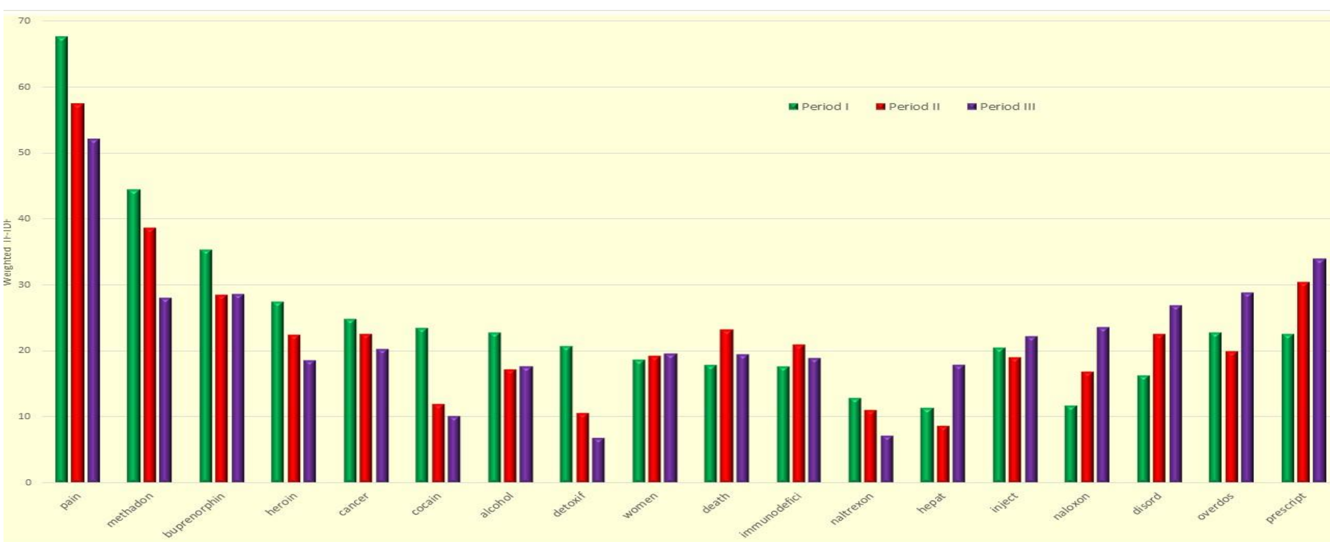

Figure 3: Weighted unigram TF-IDF across groups.

Other unigrams such as prescription, overdose, disorder, naloxone, and hepatitis are increasingly frequent in Period III. These frequently appearing words in Period III reflect some of the current opioid epidemic. While these findings from unigram can let one partially observe some health problems, some of the problems cannot be interpreted without further information.

More specifically, some of the unigrams such as methadone, buprenorphine, immunodeficiency, naltrexone, and naloxone can be interpreted with unigram. In fact, unigram is superior to bigram or trigram for these terms because researchers may use a different combination of words for the same research term. As such, if the researcher uses bigram or trigram for these research topics, the frequency of the research topic will not be accurate. Some other words such as pain, cancer, depend, addict, and women are difficult to interpret without further contextual information. For example, pain can be chronic, non-chronic, cancer, non-cancer, or non-malignant pain. Also, women can be used from the research subject of women group or pregnant women's NAS, which is a big emerging health problem. On the other hand, it is not clear that death, disorder, overdose, and prescription are related to opioid, cocaine, heroin, or something else. Therefore, those unigrams will be further investigated in bigram.

Bigram

The bigrams in Figure 4 offer a very different picture from the unigram in Figure 3, and some topics are newly emerged, which can only be discovered by employing bigram. The unigrams that require further contextual information are women, death, disorder, overdose, and prescription. The meaning of pain associated with opioid use becomes clear with bigram. Opioids were used for cancer, palliative, and chronic non-cancer. A notable finding on the use of opioids on pain over time is different: opioids were mainly used for cancer pain in Period I but were notably decreased over time for this purpose. Also, opioids for palliative pain care were popular in Periods I & II. On the contrary, the use of opioids for chronic non-cancer has gone up in Periods II & III. Next, the term, "women," did not emerge, but based on the term, "neonatal abstinence," women were most likely used in the context of pregnant women.

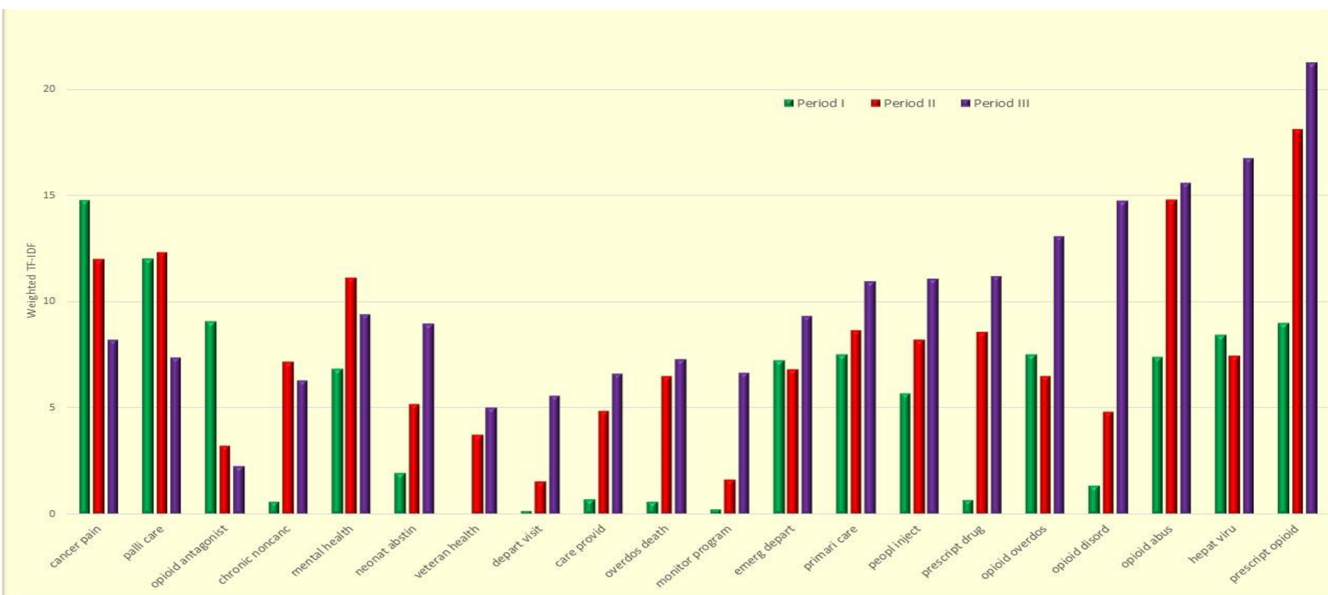

Figure 4: Weighted bigram TF-IDF across groups.

Newly surfaced bigrams can be categorized into two groups: clearly interpretable with bigram and require further contextual information. Clearly interpretable bigrams are opioid antagonist, mental health, neonatal abstinence, veteran's health, opioid disorder, and people inject. Opioid disorder might have used in the context of opioid [use] disorder. The term, "use," might have been dropped from the standard data processing.

Based on these findings from bigram, a research trend for opioid antagonist received heightened attention in Period I, but the research interests were sharply declined over time. On the contrary, neonatal abstinence, veteran's health, opioid [use] disorder, people inject prescription opioids are sharply increased over time. In fact, veteran's health was not a research interest in Period I but emerged as an important research subject and sparked scholarly interests in Period III. The mental health issue as a research subject was sparked in Period II. Those newly emerged bigrams reflect some of the current opioid epidemic.

The second group is composed of potentially differently interpretable findings. Those bigrams are emergency department & department visit, prescription drug & monitoring program, opioid overdose & overdose death, and primary care & care provider. Although they appear to be driven from the same stem, their TF-IDF values are very different, meaning that they might have used in different contexts. For example, emergency department can be used for emergency department visit or a research sample group (e.g., patients in the emergency department). Similarly, primary care can be used in conjunction with primary care provider or can be a research setting. Trigram can further clarify the contextual meaning of these terms.

Trigram

The trigram in Figure 5 is the result after the removal of the tokens discussed in unigram and bigram. Trigram clears some ambiguous meaning from bigram and at the same time, new research topics are surfaced. First, the discoveries that clarify ambiguous meaning from bigram are emergency department visits, prescription drug monitoring program, opioid overdose deaths, and primary care provider, which are sharply increased over time.

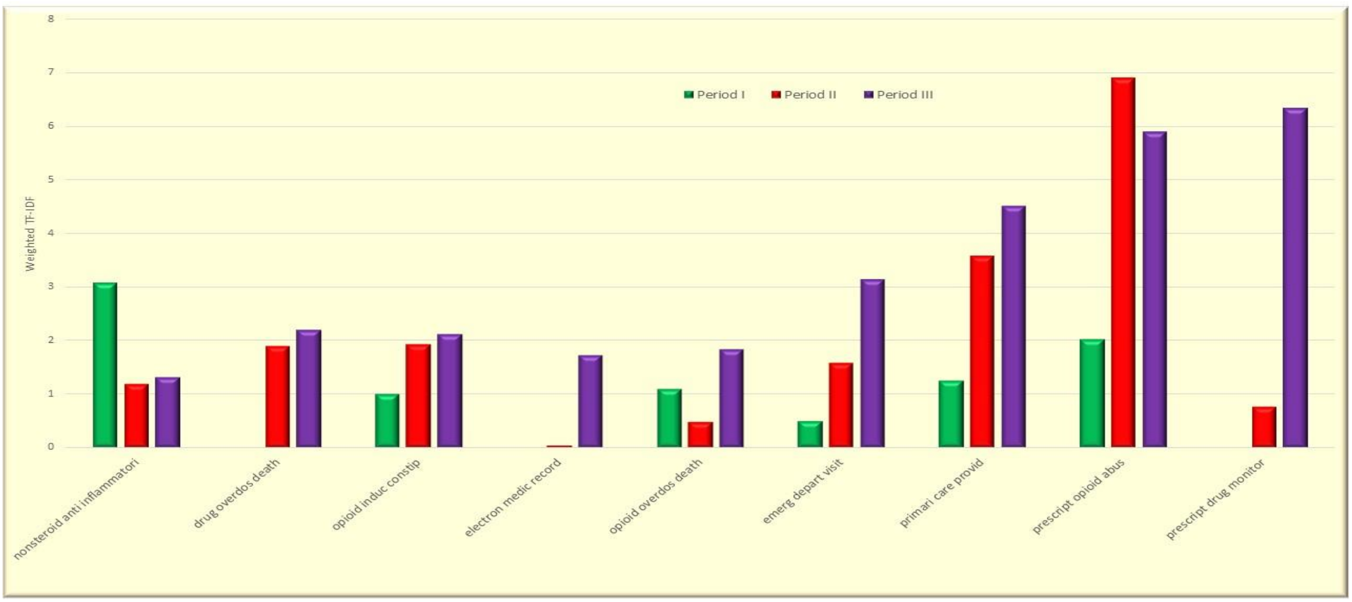

Figure 5: Weighted trigram TF-IDF across groups.

As the health problems have deepened from opioid misuse, prescription drug monitoring programs (PDMPs) was emerged as an important research topic to investigate the effectiveness of the programs. Since primary care providers (PCPs) treat non cancer-related pain, and they account for approximately 50% of the prescription opioids dispensed [14,15], the role of primary care provider might have emerged as an important research topic in Period III to combat the opioid epidemic.

Second, newly emerged research topics are nonsteroidal anti-inflammatory drugs (NSAIDs), opioid-induced constipation, and electronic medical records. One can interpret from the finding that NSAIDs were popularly used for pain treatments in Period I and significantly decreased over time, presumably replaced by opioids. Opioid-induced constipation problems increase over time as the opioid epidemic deepens. The development of health technology has prompted the scholarly discussion of electronic medical record in Period III. With the advancement of health technology, topics of electronic medical records frequently emerge.

Interpretation of research trends based on unigram, bigram, and trigram

The findings from unigram, bigram, and trigram are starkly different. If a researcher adopts unigram, which is common in the field, their findings will miss vital health issues such as neonatal abstinence syndrome, veteran's health, mental health, and people injecting drugs, opioid overdose deaths, and emergency department visits. All these opioid-born health problems are mainly responsible for the current opioid epidemic. Neonatal abstinence syndrome (NAS) occurs to a newborn that was exposed to addictive opioid drugs while in the mother's womb. NAS increased from 1.6 to 25.2 per live births during 2000 and 2010 [16]. The increases result in a surge in annual costs from $61 million in 2003 to $316 million in 2012 [17]. NAS increased infant deaths and thus has become major health issues in recent years [18]. Emergency department (ED) visits emerged as a health threat from July 2016 through September 2017 with 142,557 opioid-related ED visits [19]. This rate increased by 5.6% per quarter [19]. Veteran's health was not a big social issue until opioid prescription covers non-medical pain. In recent years veterans' health problem has been intensified because many veterans suffered from high rates of chronic pain and mental health issues because of post-traumatic stress disorder (PTSD) and injuries [20]. Injection abuse increased from 11.7% to 18.1% from 2004 to 2013 [21]. Injecting drugs are mainly responsible for increased risk for overdose, emergency department visits, and mortality because most of the injection is performed without doctor's supervision [22-24].

People with mental health disorders and substance abusers are more likely to be prescribed a higher opioid dose than individuals without those problems, and as such opioid overdose deaths are higher for those individuals [18,25,26]. As such, mental health disorders and substance abuse problems increase together because of their high correlations [25,27]. While bigram captured a lot of critical and yet unique research topics, some topics are solely captured in trigram. Those newly discovered opioid-born health problems are shown in Figure 5.

Discussion

As shown, unigram, bigram, and trigram portrayed very different research themes over time. While unigram is most predominantly used in the field, this research finding reveals that solely depending on one type of an NGram method (e.g., unigram, bigram, or trigram) to detect research trends can be misleading. More specifically, unigram will retrieve the most popularly used single word. As such, if a research terminology is comprised of two or three words, those subject terms may or may not be captured in unigram. On the other hand, if researchers use trigrams to detect research trends, it will yield the opposite problem. More specifically, unigram will not detect if a terminology is composed of two or more words or differently combined. As such, in order to discover research trends comprehensively, it is imperative to simultaneously employ unigram, bigram, and trigram as they together offer comprehensive pictures.

The contribution of this study is to holistically discover opioid-born health problems through the lens of scholarly publications while empirically demonstrating issues with adopting a single NGram method as a text mining strategy. Although opioid use has become a public health crisis and recently scholarly publications have soared, there has not been systematic research on how widespread use of opioids has causes health problems over time, which led to the current opioid epidemic. This study is a small and yet first attempt toward achieving that goal.

This study has some limitations. First, opioid-related articles are solely retrieved from PubMed. Therefore, if an opioid-related publication is not in the database, the article will not be included for the analysis. As such, the generalization of this study's findings requires caution. Second, this study used scholarly publications to investigate the evolution of opioid-related issues over time; however, popular press sources such as social media or news press can result in different themes.

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