THE BURDEN OF THE OPIOID CRISIS ON THE STATE OF MARYLAND WITH A FOCUS ON THE IMPACT OF FENTANYL

TESTIMONY OF
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PROVIDED TO
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FOR A HEARING ENTITLED
“DEFEATING FENTANYL: ADDRESSING THE DEADLIEST DRUGS FUELING THE OPIOID CRISIS”

PRESENTED
APRIL 11th, 2018

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EXECUTIVE SUMMARY

The opioid crisis has its roots in the beliefs and medical practices of the last century. Now more Americans die from overdoses annually than car crashes, a trend that appears to be exacerbated by the appearance of illicit fentanyl. The emergency departments (EDs) of the University of Maryland Medical System (UMMS) provides a window into the problem. We continue to see rising numbers of non-fatal opioid overdoses, costly ED visits related to substance abuse, and deaths caused by opioids. In response to the opioid crisis, emergency physicians have decreased the amount of opioids they prescribe, increased the amount of naloxone (the opioid-reversal drug) available, and added peer counselors, who identify and connect high-risk patients to substance abuse treatment. Congress can help alleviate the burden of the opioid crisis on our EDs by creating more permanent funding for naloxone distribution programs, substance abuse treatment programs, and research.

Major Findings

- Visits to the major UMMS emergency departments for non-fatal overdoses increased 13.6% in the past 2 years (from 2,129 in 2016 to 2,420 in 2017).
- The charges for these ED visits increased 17.2% ($5,713,638 in 2016; $6,701,851 in 2017).
- Fatal overdoses due to opioids in Maryland increased 11.7% in the past 2 years (from 1,344 in 2016 to 1,501 in 2017) and 328.4% over the past decade (457 in 2007).[1]
- Deaths associated with fentanyl in Maryland increased 56.2% over the past 2 years (751 in 2016; 1,173 in 2017) and 69-fold over the past decade (17 in 2007).[1]
- Evidence of recent fentanyl use was found in 75% of patients presenting to UMMS ED as non-fatal opioid overdoses (50 of 66 patients tested, January 2018-March 2018).[2]
- Physicians in UMMS EDs have responded by writing fewer prescriptions for opioids (19.5% of all ED visits in 2016; 13.3% of all visits in 2017) and those prescriptions are more in compliance with safe prescribing practices (63.1% in 2016, 72.2% in 2017).
- UMMS emergency physicians have increased the availability of naloxone (writing 18 prescriptions in the first quarter of 2016 and 184 in the final quarter of 2017).
- Increased funding for research, case managers, and substance abuse programs will help physicians respond to changing patterns of drug use and enable them to refer and admit patients to treatment at any time of day or night.

Testimony of

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Chairman and Professor

Department of Emergency Medicine

University of Maryland School of Medicine

Provided to

Judiciary Committee of the United States Senate

For a Hearing Entitled

"Defeating Fentanyl: Addressing the Deadliest Drugs Fueling the Opioid Crisis"

April 11th, 2018

INTRODUCTION AND OBJECTIVES

Members of the United States Senate,

On behalf of the University of Maryland School of Medicine, the State of Maryland, the University of Maryland Medical System (UMMS), and my fellow emergency physicians across the United States, I thank you for the opportunity to present our unique perspective on one of the major crises of our time: the dramatic increase in opioid abuse and opioid-related deaths.

I am speaking to you as Professor and the founding Chairman of the Department of Emergency Medicine within the University of Maryland School of Medicine. I am the EM Physician-in-Chief of the UM Emergency Medicine Statewide Network which staffs and operates 17 Emergency Departments across the State and cares for over 700,000 patients per year – or approximately 20% of all ED visits in Maryland. I have been in practice for 36 years and have spent my entire career at our flagship hospital, the University of Maryland Medical Center (UMMC), located in downtown Baltimore. The citizens of Baltimore have struggled with opioid abuse and its ramifications for decades, but the depth and severity of the current opioid crisis has shocked me and my fellow physicians.

My intention in this report is to describe how the opioid crisis has affected our patients and our practice of medicine. The report is organized in four sections. The first presents definitions of terms and a brief history of the opioid problem. The second provides evidence regarding the current burden of opioid addiction in terms of emergency department visits,

hospitals costs, and fatal and non-fatal overdoses. It also describes how the arrival of fentanyl has exacerbated the opioid problem. The third section describes what emergency physicians, in partnership with addictions specialists and public health officials, have done to address the opioid crisis. Lastly, I will propose resources that Congress could provide to help us help our patients combat this crisis, which claimed more lives last year than motor vehicle crashes.

SECTION 1: DEFINITIONS AND A BRIEF HISTORY OF THE CURRENT CRISIS

Definitions

Opioid: As defined by the National Institute on Drug Abuse[3], opioids are a class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and pain relievers available legally by prescription, such as oxycodone, hydrocodone, codeine, and morphine. These drugs are chemically related and interact with opioid receptors on nerve cells in the body and brain. Opioid pain relievers are generally safe when taken for a short time and as prescribed by a doctor, but because they produce euphoria in addition to pain relief, they are attractive for misuse (taken in a different way or in larger quantity than prescribed or without a doctor's prescription). The level of euphoria varies widely across this class of drugs. Opioids come in many forms (pills, powders, and tars) and they can be taken by mouth, insufflated (i.e., sniffed), and injected under the skin or into the bloodstream.

The first opioid, opium, was derived from the sap of the opium poppy in many cultures before the common era. The concentrated form of the active ingredient of opium is morphine, which is commonly used today to treat pain in hospitalized patients. Chemically modified versions of opium and morphine have also been produced: hydromorphone and oxycodone are semi-synthetic compounds, and methadone and fentanyl are entirely synthetic drugs. These modified substances show up only on specialized drug screens.

Opioid overdose: An overdose occurs when a person takes more drug (in terms of number of pills or total dose) than their body can tolerate. Overdose manifests as a broad spectrum of signs and symptoms. A mild opioid overdose can cause sleepiness, constricted pupils, slow breathing, and a sense of euphoria. A severe overdose can slow a person's breathing into apnea and cause sleepiness that can deepen into complete unresponsiveness. A prolonged episode of extremely shallow breathing or apnea can lead to permanent brain injury, seizures, and death. Over time and with increasing use, the body becomes habituated to opioids; therefore, someone who is opioid naive could overdose on a small amount or a low concentration of drug, whereas a daily user might experience only overdose after taking multiple

large doses over a short time. It is possible for someone to survive an opioid overdose without receiving treatment.

Naloxone (tradename Narcan®): Naloxone is a drug that attaches to the opioid receptor in humans without passing on a signal, blocking the physiological action of opioids in the body. A patient's response to naloxone depends on when it is given, how much is given, and what opioids were taken. A small amount of naloxone might have no effect in someone who has taken a very large dose of opioids or a high-potency opioid such as fentanyl. A larger amount might allow that person to breathe at a more normal rate but they will still be somnolent and hard to rouse. An even larger amount could allow the person to become fully awake and alert until the naloxone wears off, at which point they could relapse into an overdose state. In persons who are habituated and need to take opioids throughout the day to complete activities of daily living, naloxone administration could precipitate withdrawal. If a person who has overdosed has had a very low breathing rate or has not been breathing at all for a prolonged period, late administration of naloxone will not reverse any brain damage they may have suffered. In summary, naloxone is a critical tool in counteracting opioid overdose, but the impact of the drug is highly dependent on patient factors (how much they have taken, the potency of what they took) and the timing of its administration (how long they have been in overdose).

Opioid withdrawal: Withdrawal covers a spectrum of signs and symptoms that emerge when a person goes without opioids after their body has become habituated to the drug. It begins 6 to 24 hours after their last dose. People in opioid withdrawal commonly present with cravings, transitioning to dilated pupils, sweating, hairs standing on end, retching, and vomiting and diarrhea. The experience partially depends on the person's use pattern and their preferred drug, but the opioid withdrawal syndrome generally lasts 3 to 5 days and, although it is clearly uncomfortable, it is not fatal.

Substance use disorder: According to the National Institute on Drug Abuse, "[a]ddiction is defined as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain—they change its structure and how it works. These brain changes can be long-lasting and can lead to the harmful behaviors seen in people who abuse drugs."[4]

History of the Current Opioid Crisis

In the 1990s, there was a belief that physicians in the United States were under-treating acute pain (i.e., pain that is expected to be short-lived and associated with a new injury or a

surgical procedure) and chronic pain (lasting at least 3 months, often in the context of a medical condition such as diabetes).[5,6] Most physicians, both then and now, feel strongly that the seriously injured and those suffering from severe pain at the end of life (e.g., pain caused by cancer) should be treated aggressively.[7-9] Some small clinical studies and position papers at the time suggested that opioid pain medications might not be as addictive as perceived[10,11] and that chronic, non-cancer pain might be more prevalent than initially thought.[12,13] National professional medical societies and the Joint Commission (then called the Joint Commission on Accreditation of Healthcare Organizations [JCAHO]) began advocating aggressive pain control,[14-16] often with opioids. The Veterans Health Administration (VA) launched the "Pain as the Fifth Vital Sign" campaign in 1998.[17,18] Since that time, the United States has seen a three-fold increase in the use of pain medications[19] and is now the world's largest consumer of prescription opioid pain medications. In 2012, almost one-third of emergency department (ED) visits resulted in an opioid prescription—260 million opioid prescriptions were written during that year.[20,21]

Hydrocodone provides an example of how prescription opioids are marketed and increased in use. Hydrocodone is a semisynthetic opioid medication derived from codeine that was first approved for use by the Food and Drug Administration (FDA) in 1943.[22] Hydrocodone-containing products marketed under a variety of names such as Vicodin, Lortab, Norco, Norcet, Allay, Anexsia, Cogesic, Hy-Phen, Tycolet, Zydone, and Zyfrel, and they are the most frequently prescribed opioids in the United States. The United States accounts for 99% of all hydrocodone prescriptions worldwide.[23]

The Impact of a Flood of Prescription Opioids

In 2010, researchers at the Centers for Disease Control and Prevention (CDC) and elsewhere linked the increase in prescription opioid use to an increase in opioid abuse and drug overdoses.[24-27] For accounting purposes, the CDC reports fatal opioid overdoses as a "Poisoning" death within the "Unintentional Injury" cause of death category. The CDC reported that poisoning became the most common cause of unintentional death in 2011 (Figure 1). Between 2011 and 2016, unintentional deaths went from the 5th, to the 3rd most common cause of death in the United States, more so than lung disease and stroke. People began to switch from prescription opioids to heroin, largely because of the high cost of prescription opioids and the difficulty in obtaining them; heroin is cheaper and more accessible.[28,29] In 2013, drug overdose became the most common cause of death overall in the homeless.[30] In 2018, the CDC reported that there were more than 64,000 fatal overdoses in the United States. The National

Center for Vital Statistics also reported that life expectancy in the United States had dropped for the second year in a row, partly due to an increase in the number of fatal opioid overdoses.[31,32]

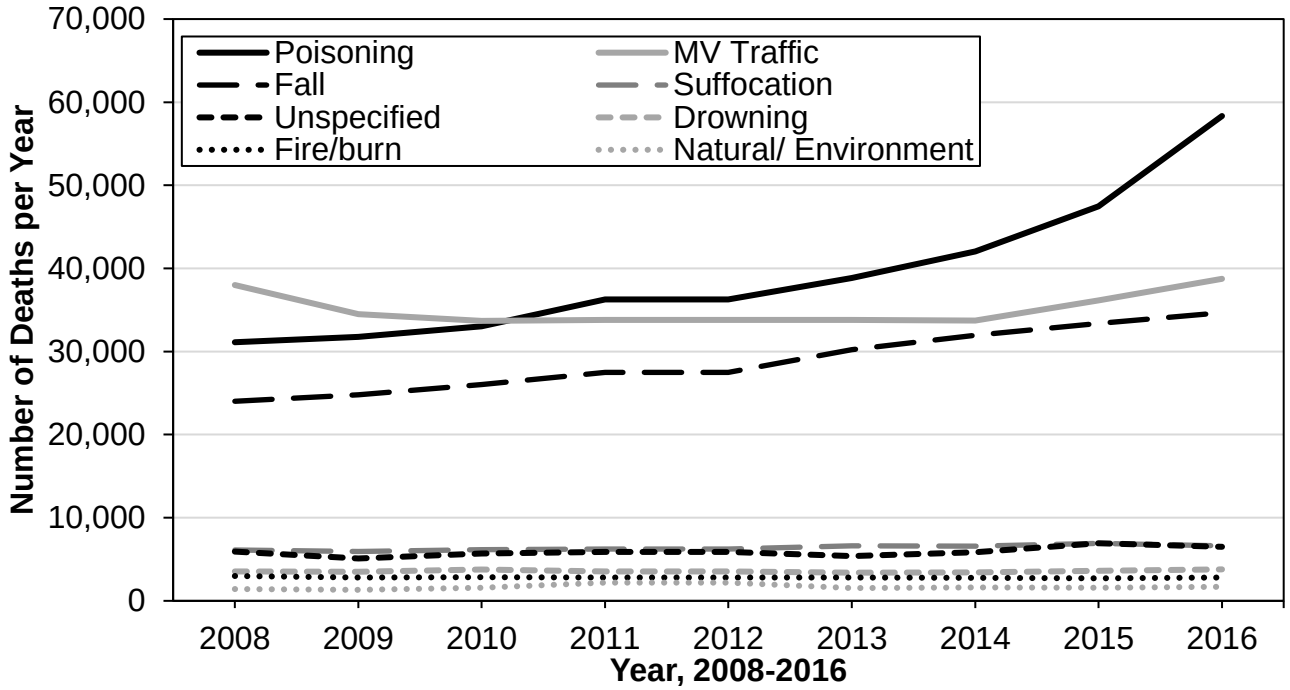

Figure 1. Unintentional Injury Deaths in the United States, by cause and year, 2008-2016[33]

Data Sources Used in this Report

No one source of information accurately captures how much the opioid crisis has impacted the UMMS, Baltimore City, or the State of Maryland. To provide you with the most up-to-date information, we have relied on several sources, including ED visits from our electronic medical record, reports from government agencies, and published and unpublished research data. Although we administer a statewide network of emergency departments, the hospitals that house those emergency departments do not all run on the same record system and many record systems are incompatible with each other. This report provides quantitative information from four of the largest emergency departments in UMMS: University of Maryland Medical Center (UMMC), Baltimore Washington Medical Center (BWMC), University of Maryland: University of Maryland Saint Joseph's Medical Center (SJMC), and University of Maryland Medical Center: Midtown Campus (MTC). These four emergency departments treat a combined total of approximately 220,000 patients annually, or nearly half of all of the patients treated in UMMS emergency departments. This report highlights some of the efforts by physicians, public health officials, and government agencies, to address the opioid crisis, but it is not intended to be a comprehensive listing. All patient data used in this report was approved by the University of

Maryland Institutional Review Board (Appendix A) and provided by the University of Maryland, Baltimore Helping Advance Research By Organizing Resources (HARBOR).

SECTION 2: THE BURDEN OF THE OPIOID CRISIS

Emergency departments serve as the safety net in the American health care system. They receive and treat patients who have no other access to medical care. Accordingly, the emergency physicians at UMMS of hospitals treat patients from every racial and ethnic background, regardless of their ability to pay, 24 hours a day, 7 days a week, 356 days a year (Table 1). Our patient population is representative of the residents in the communities where our facilities are located. Their medical conditions are representative of the problems these communities face. The opioid crisis has affected our communities and therefore our medical system in profound ways. Figures 2 and 3 show the home ZIP code of patients presenting to one of the main UMMS ED with complaints of an overdose. One can see that this problem affects patients from all over the state of Maryland. There are also some areas that are affected more than others.

ZIP code 21217 includes Sandtown-Winchester, a neighborhood in West Baltimore and the home of Freddie Gray. Between 2016 and 2017, this ZIP code was the origin of 206 people who presented to one of the main UMMS EDs as a non-fatal overdose (Figure 3). This is an incredibly high number for a such a small community, equivalent to 555 non-fatal overdoses per 100,000 residents.[34] The true number of non-fatal overdoses is likely higher than what is presented in this report, as some patients will have been transported to ED in other neighboring hospital systems or may not have sought medical care at all. There were 694 fatal opioid overdoses in the City of Baltimore in 2016, or 112 per 100,000 residents. It is expected that there will have been more than 700 fatal overdoses in Baltimore in 2017. In comparison, consider a different rate: Baltimore is thought to be one of the most violent cities in the Western Hemisphere. The murder rate in Baltimore is 55.2 per 100,000, or half of the fatal overdose rate and one-tenth of the non-fatal overdose rate.

The number of non-fatal overdoses in our West Baltimore neighborhood of Sandtown-Winchester is but a fraction (4.5%) of the 4,549 overdoses treated in UMMS hospitals over the same time (Table 2). Maryland has seen a steep increase in the number of ED visits related to the use of heroin and prescription opioids. In 2008, the age-adjusted rate for being treated at an ED in Maryland for heroin use was 5.3 persons of every 100,000 individuals. In 2014, that rate had quintupled to 26.4 per 100,000.[35] Similarly, in 2008, 9.0 persons per 100,000 were treated in a Maryland ED

Table 1. Demographics of Patients Treated in Major UMMS EDs, 2016-2017. UMMC, University of Maryland Medical Center; BWMC, Baltimore Washington Medical Center; SJMC, University of Maryland Saint Joseph's Medical Center; MTC, University of Maryland: Midtown Campus

	UMMC		BWMC		SJMC		MTC		Total	
Mean age, SD	44.6	16.4	44.0	23.2	49.6	24.35	45.1	17.85	45.4	21.4
Male, N (%)	56,426	50.5	84,380	44.6	37,818	42.1	29,261	51.25	207,885	46.5
Race, N (%)										
White	22,776	20.6	117,267	63.0	54,831	62.1	5,901	10.6	200,775	45.6
Black	83,449	75.4	52,205	28.0	26,790	30.3	48,078	86.7	210,522	47.8
Asian	758	0.7	3,241	1.7	1,327	1.5	255	0.5	5,581	1.3
Hispanic	11	0.01	56	0.03	24	0.03	7	0.01	98	0.02
Native American	151	0.1	476	0.3	192	0.2	63	0.1	882	0.2
Pacific Islander	31	0.03	163	0.1	51	0.1	10	0.02	255	0.1
Other race	3,514	3.2	12,731	6.8	5,127	5.8	1,145	2.1	22,517	5.1
Payor, N (%)										
Maryland MCO	52,471	47.4	14,592	26.1	15,607	17.7	30,185	54.4	112,855	36.4
Medicare	22,421	20.2	13,843	24.8	27,688	31.3	12,020	21.7	75,972	24.5
Medicaid	7,790	7	1,906	3.4	1,986	2.2	3,691	6.7	15,373	5
Commercial	8,727	7.9	8,005	14.3	17,946	20.3	2,297	4.1	36,975	11.9
Self-pay	9,912	9	5,357	9.6	7,235	8.2	4,873	8.8	27,377	8.8
Military	699	0.6	2,904	5.2	611	0.7	99	0.2	4,313	1.4
Blue Shield	7,847	7.1	8,708	15.6	16,485	18.7	2,083	3.8	35,123	11.3
Other insurance	861	0.8	526	0.9	801	0.9	217	0.4	2,405	0.8
Not Reported*	-	-	130,371	-	-	-	2	-	130,373	-
Disposition, N (%)										
Discharge	87,778	79.3	141,681	76.1	63,336	71.7	45,948	82.8	338,743	76.9
Admit	19,979	18.0	40,161	21.6	23,303	26.4	8,930	16.1	92,373	21.0
Transfer	2,845	2.6	4,050	2.2	1,601	1.8	525	0.9	9,021	2.0
Deceased	126	0.1	311	0.2	119	0.1	64	0.1	620	0.1
Time of arrival to Emergency Department, N (%)										
12AM-6AM	16,921	15.3	20,912	11.2	8,970	10.2	7,972	14.4	54,775	12.4
6AM-12PM	28,605	25.8	48,228	25.9	22,682	25.7	13,943	25.1	113,458	25.7
12PM-6PM	36,928	33.4	63,470	34.1	31,641	35.8	18,891	34.1	150,930	34.2
6PM-12AM	28,274	25.5	53,602	28.8	25,066	28.4	14,661	26.4	121,603	27.6
Total Visits, N	110,728		186,212		88,359		55,467		440,766	

*Because of the large number of patients treated at BWMC who did not have a reported payor, proportions are calculated without that number.

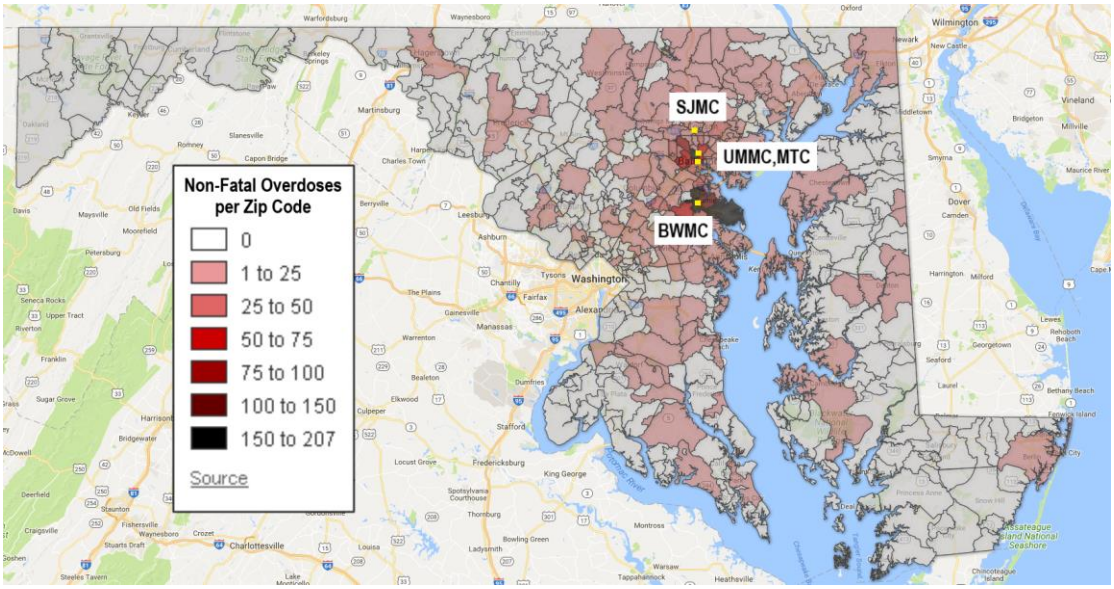

Figure 2. Map of Maryland showing the home ZIP codes of patients presenting with non-fatal opioid overdoses treated in major UMMS EDs. UMMC, University of Maryland Medical Center; BWMC, Baltimore Washington Medical Center; SJMC, University of Maryland Saint Joseph's Medical Center; MTC, University of Maryland: Midtown Campus.

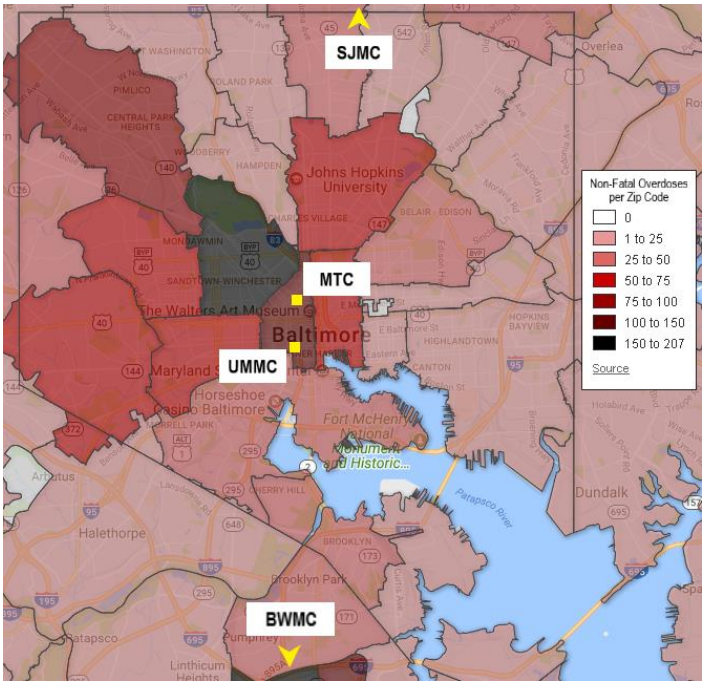

Figure 3. Map of Baltimore City showing the home ZIP codes of patients presenting with non-fatal overdoses treated in major UMMS EDs. UMMC, University of Maryland Medical Center; BWMC, Baltimore Washington Medical Center; SJMC, University of Maryland Saint Joseph's Medical Center; MTC, University of Maryland: Midtown Campus.

because of prescription opioid use; that rate had more than doubled by 2014 (18.2 per 100,000). Within UMMS, the number of ED visits for overdose was 2,129 visits in 2016 and 2,420 visits in 2017, a 13.6% increase. These visits strain the medical system (Table 3), costing $5.7 million in 2016 and $6.7 million in 2017, an increase of 17.2%.

Table 2. Number of Overdose-Related Visits to UMMS Hospitals, per quarter, in 2016 and 2017

	2016				2017			
	UMMC	**BWMC**	**SJMC**	**MTC**	**UMMC**	**BWMC**	**SJMC**	**MTC**
Q1	81	175	52	88	109	247	75	137
Q2	100	231	54	171	197	235	49	261
Q3	135	265	63	153	105	218	52	204
Q4	105	247	71	138	104	217	60	150
Total (N)	2,129				2,420			

UMMC, University of Maryland Medical Center; BWMC, Baltimore Washington Medical Center; SJMC, University of Maryland Saint Joseph's Medical Center; MTC, University of Maryland: Midtown Campus.

Table 3. Charges Associated with ED Visits for Overdoses at UMMS Hospitals, 2016 and 2017

	2016				2017			
	UMMC	**BWMC**	**SJMC**	**MTC**	**UMMC**	**BWMC**	**SJMC**	**MTC**
Visits (N)	421	918	240	550	515	917	236	753
Mean Charge ($)	3,296	-	3,784	3,459	3,433	2,906	4,186	3,150
Total ($)	1,384,268	1,525,837*	908,246	1,895,287	1,768,069	1,592,659	987,977	2,353,146
System Cost ($)	5,713,638				6,701,851			

UMMC, University of Maryland Medical Center; BWMC, Baltimore Washington Medical Center; SJMC, University of Maryland Saint Joseph's Medical Center; MTC, University of Maryland: Midtown Campus

*Estimated total charges for BWMC in 2016 have been adjusted for number of visits and time.

As the opioid crisis has worsened in Baltimore, clinicians have seen an increase in overdose spikes. During the summer of 2017, on two separate occasions, more than 25 people with apparent opioid overdoses were rushed to area hospitals over the course of an afternoon.[36]

When we interview patients in this situation, they state that spikes are typical when a batch of stronger-than-usual product is being sold on the street. Dealers will give away the first few doses of a new batch in order to determine how potent it is and to what degree it needs to be diluted. This phenomenon continues today: On two occasions just this past month, over a dozen patients were transported to area hospitals and multiple people died because dealers had provided free test doses.

We have also seen a rise in atypical opioid overdoses, where patients develop agitated delirium (distinct from acute withdrawal) after receiving naloxone. This response to naloxone is atypical and suggests that adulterants have been combined with the opioid. Many of these patients become violent and, paradoxically, require sedation immediately after being revived with naloxone. This atypical response is new and is a clear threat not only to the patients but also to the health care workers caring for them.

The Impact of Illicit Fentanyl

Fentanyl is a synthetic opioid that has many of the same physiological effects as heroin and morphine. Fentanyl was discovered in 1960 and approved by the Food and Drug Administration in 1968 for the management of acute pain in hospitalized patients (e.g., postoperative and cancer break-through pain), chronic pain in opioid-tolerant patients, and sedation of ventilated patients.[37] The arrival of illicit fentanyl and fentanyl analogues in Baltimore has been associated with a drastic increase in both fatal and nonfatal opioid overdoses.

Because fentanyl's chemical structure is completely different from that of heroin, morphine, and other opioids of abuse, it does not show up on standard hospital drug screens. Some UMMS hospitals are changing their testing panels to capture fentanyl but, in the meantime, the lack of test results makes it difficult to ascertain accurate numbers of current users and of fatal and non-fatal overdoses. One of the few institutions that regularly tests for fentanyl is the Office of the Chief Medical Examiner of Maryland (OCME). They count any death where an opioid was detected (e.g., heroin, fentanyl, or prescription opioid) as an opioid-related death. According to the OCME, fentanyl-associated deaths more than tripled from 2015 to 2016, from 192 to 751 (Table 4).[1] Heroin-associated deaths have a similar, but less-pronounced increase from 534 to 903 over the same period (69.1%). The counts for 2017 are preliminary, but the number of heroin-associated deaths decreased 6.2% (847), whereas fentanyl-associated deaths continued to rise (56.2%, 1,173). Overall, the number of fentanyl-associated deaths has increased 69-fold since 2007. An ongoing study of patients presenting to the University of Maryland: Midtown Campus with general drug-related complaints (overdose,

withdrawal, or seeking drug abuse treatment) found that 75% (50 of 66) showed evidence of recent fentanyl use.[2] Many of the patients who presented as an opioid overdose and tested positive for fentanyl did not show any evidence of drug use on routine hospital urine drug testing (screen includes heroin and morphine). In separate study examining the patients who presented during a spike of atypical opioid overdoses, half (4 of 8) tested positive for fentanyl and fentanyl analogues.[38] These findings support reports from the Drug Enforcement Agency, advising that heroin is being mixed with fentanyl and sold to unwitting users.[39] The decreasing number of heroin-associated deaths in the face of rising fentanyl deaths, along with the appearance of non-fatal opioid overdoses only testing positive for fentanyl, suggests that fentanyl may be replacing heroin.

Table 4. Opioid-related deaths* in Maryland by substance and year, 2007-2017.[1]

	2007	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**
Prescription	214	208	170	225	255	237	235	252	270	323	312
Heroin	298	215	251	170	187	298	324	424	534	903	847
Fentanyl	17	17	23	31	22	23	22	141	192	751	1,173
Carfentanyl**	-	-	-	-	-	-	-	-	-	0	57
Total†	457	390	391	364	398	492	518	654	777	1,344	1,501

*2017 counts are preliminary. **Carfentanyl testing began in 2016, first detected in 2017.
†Columns sum to more than presented total because multiple substances were detected.

Illicit fentanyl is dangerous because it is potent: it is thought to be 80 times more potent than morphine and hundreds of times more potent than heroin.[40,41] This potency has direct benefits for drug distributors. It is cheaper to produce, it can be smuggled in more compact containers and therefore is easier to distribute, it can be diluted ("cut") further to increase profits, and it can be added to heroin to increase its strength. The factors that increase the drug's profitability also increase its danger to the end user. Illicit fentanyl is created through a series of chemical reactions, and depending on the expertise of the chemist, the concentration of the fentanyl end-product may vary widely and may contain many dangerous by-products. Powdered fentanyl is then diluted unreliably with baking soda and other additives by non-professionals. These powders vary in size and consistency and tend to clump, yielding a poorly mixed product with a wide range of physiological activity. Because of these inconsistencies, one user may get virtually no active drug while the next gets enough for a lethal overdose. Dealers have

attempted to compensate for an erratically potent product by giving away test doses to users when a new batch of product arrives. Dealers then determine how much they need to dilute the current batch by watching how many people overdose or die. These patients then present in waves or spikes.

As a result, it is often the end user who pays the greatest price. Many end users have a specific stable dose or dollar amount that they have bought for years. If they buy their usual amount, not knowing that fentanyl has been added, they risk accidental overdose. This effect extends to users who have relapsed—they buy their usual dose of heroin but unexpectedly get fentanyl and then overdose. Also, for those in the market for stronger drugs that deliver a stronger experience, fentanyl accelerates the path toward fatal overdose.

These trends are likely to worsen because a new opioid called carfentanyl recently arrived in Baltimore. Carfentanyl is a fentanyl analog: it has much of the same structure and physiological properties as fentanyl, but some small chemical changes drastically increase its potency. It is reported to be 125 times more potent than fentanyl and 10,000 times more potent than heroin.[40] As with fentanyl, few institutions regularly test for carfentanyl. However, Maryland's OCME began testing for if in 2016, and in 2017 it was found to be the cause of 57 deaths.[1] Increased research funding would help clinicians and public health officials track and respond to these changes in drug use trends.

Naloxone is effective against fentanyl, carfentanyl, and other opioids of abuse.[43] But because of the strength of these new analogs, naloxone must be administered in much larger doses to reverse an overdose, especially compared with heroin. Naloxone generally lasts in the body longer than heroin, so one or two doses of naloxone is usually sufficient to reverse most heroin overdoses. But naloxone has a shorter duration of action than fentanyl, so multiple doses or a continuous infusion of naloxone is usually required to ensure a patient does not relapse after the first dose wears off. Paramedics have reported they have found increasing numbers of users who have died with a needle still in their arm, suggesting the onset of action is so fast the patients did not have the time to remove the needle prior to succumbing to the effects of the drug. Clinicians have reported an increasing number of overdose patients who need to be put onto a ventilator (a breathing machine).

SECTION 3: HOW EMERGENCY PHSYCIANS ARE ADDRESSING THE OPIOID CRISIS

Emergency physicians and public health officials have responded to the opioid crisis in a variety of ways. In its 2017 session, the Maryland General Assembly passed the HOPE (Heroin

and Opioid Prevention Effort) Act, which emphasizes the importance of naloxone prescribing, enhances access to outpatient substance abuse treatment, establishes statewide 24-hour crisis hotlines, and creates protocols for the discharge of high-risk patients.[44] Maryland state has also released statues for opioid-prescribers that are modeled off those produced by the Centers for Disease Control and Prevention (CDC).[45,46] As emergency physicians, our efforts have been focused on three main targets: 1) changing opioid prescribing practices, 2) increasing access to naloxone, especially for at-risk patients, and 3) enhancing access to substance abuse treatment resources.

Changes in Prescribing Practices

In 2016, the CDC issued guidelines for managing chronic pain with opioids.[46] They suggest that physicians recommend non-opioid medications such as acetaminophen (sold as Tylenol© and ibuprofen (Motrin©) first. If pain control is not achieved, then opioid medications can be considered, but physicians should prescribe the lowest effective dose to be used for the shortest amount of time. The CDC also advised physicians to avoid combinations of drugs, such as opioids and benzodiazepines, because both drug classes sedate and impair breathing, putting the patient at risk for overdose. These guidelines do not apply to people who are admitted to a hospital or who have a serious cause of pain (e.g., cancer). In the same year, the Veterans Administration issued guidelines for the management of pain with opioids, which recognized the increasing evidence of prescription opioid abuse.[47] In 2016, New York City issued a policy that limited emergency physicians to prescribing three days of pain medication to their patients.[48]

Our research demonstrated that emergency physicians in the nationwide system of VA hospitals have decreased the number of opioids they prescribe. We examined a study group of 1,708,545 individuals who visited VA EDs 6,721,134 times between 2009 and 2015.[49,50] The proportion of visits to VA EDs during which a prescription for an opioid was written was 13.3%in 2009, peaked at 14.5 % in 2011, and then fell to 12.3% in 2015 (Figure 4). The average number of pills prescribed fell from 43 in 2009 to 33 in 2015 (Figure 4). The proportion of prescriptions that complied with guidelines increased from 25.0% to 32.4% (Figure 5). The proportion of prescriptions for 30 pills or more decreased from 35.2% to 21.4% (Figure 5). The most commonly prescribed medication was hydrocodone-acetaminophen (51.6% of all prescriptions). During the same period, emergency physicians in the VA system increased the number of non-steroidal anti-inflammatory drug they prescribed (NSAID): in 2009, NSAIDs were prescribed during 12.1% of all VA ED visits, and the percentage increased to 14.1% in 2015.

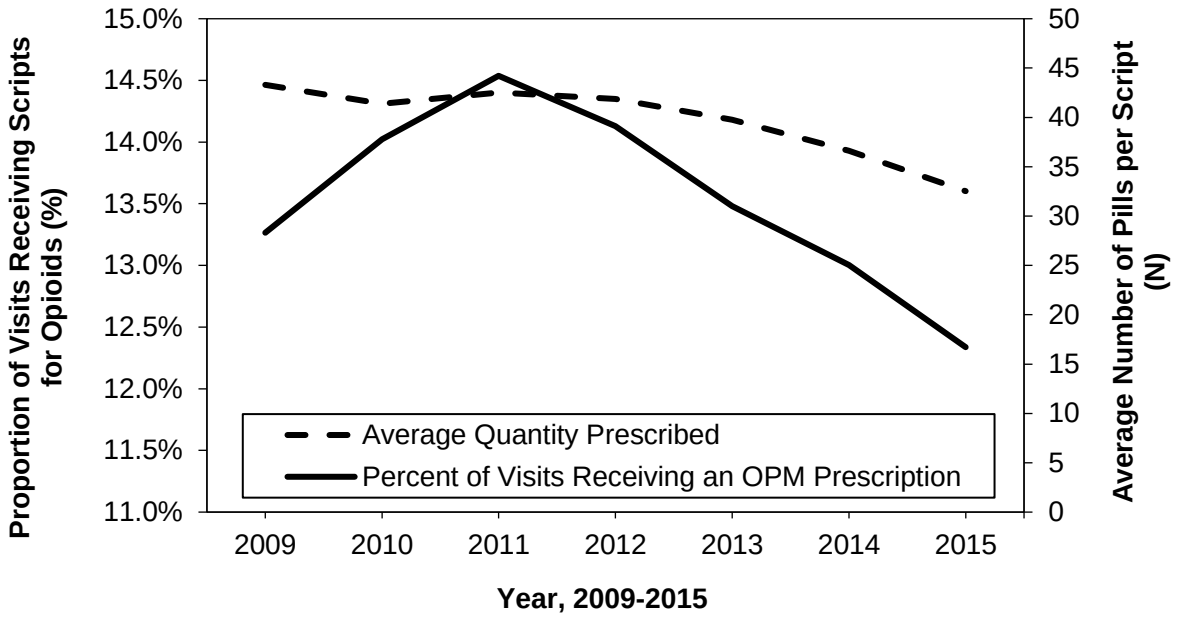

Figure 4. Proportion of Veterans Administration Emergency Department Visits Resulting in a Prescription for Opioids and the Average Number of Pills Prescribed per Script, 2009–2015[49,50]

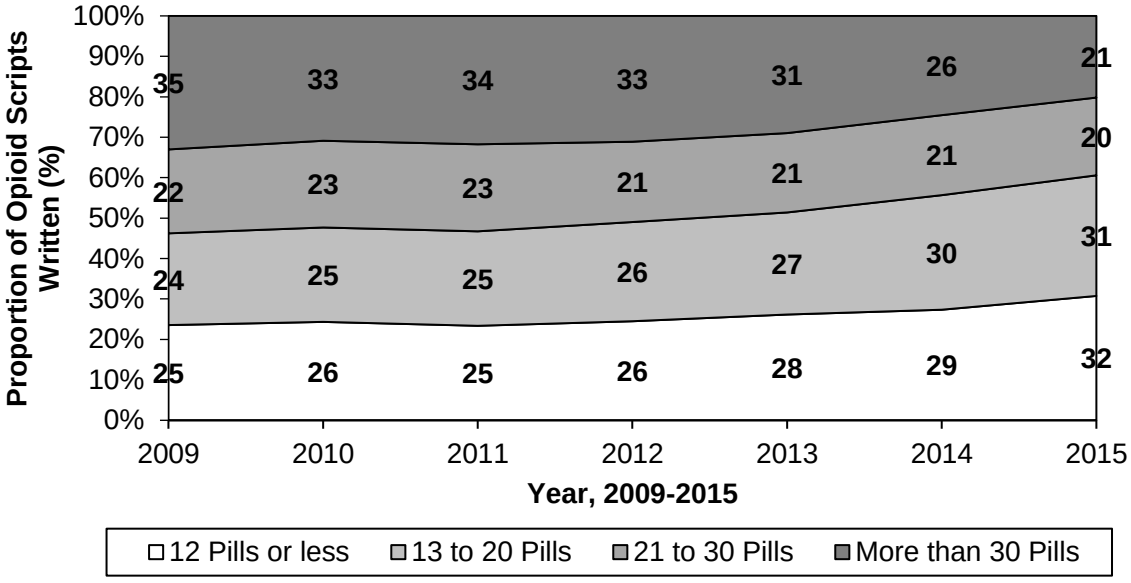

Figure 5. Proportion of Opioid Prescriptions Written Within Prescribing Guidelines, Veterans Administration Emergency Departments, 2009–2015[49,50]

We have seen similar trends in Maryland. From January 2016 to December 2017, 229,084 patients visited the main UMMS EDs (UMMC, BWMC, SJMC, and MTC) a total of 440,766 times. The number of opioid prescriptions decreased in that timeframe. In the first quarter of 2016, an opioid prescription was written during 19.5% of visits; the percentage declined to 13.3% of visits by the end of 2017 (Figure 6). The average number of pills per prescription was 15.4 at the beginning of 2017, falling to 13.9 in 2017. The proportion of prescriptions written in compliance with guidelines increased from 63.1% to 72.2%, while the proportion written for more than 30 pills decreased from 1.7% to 1.0% (Figure 7).

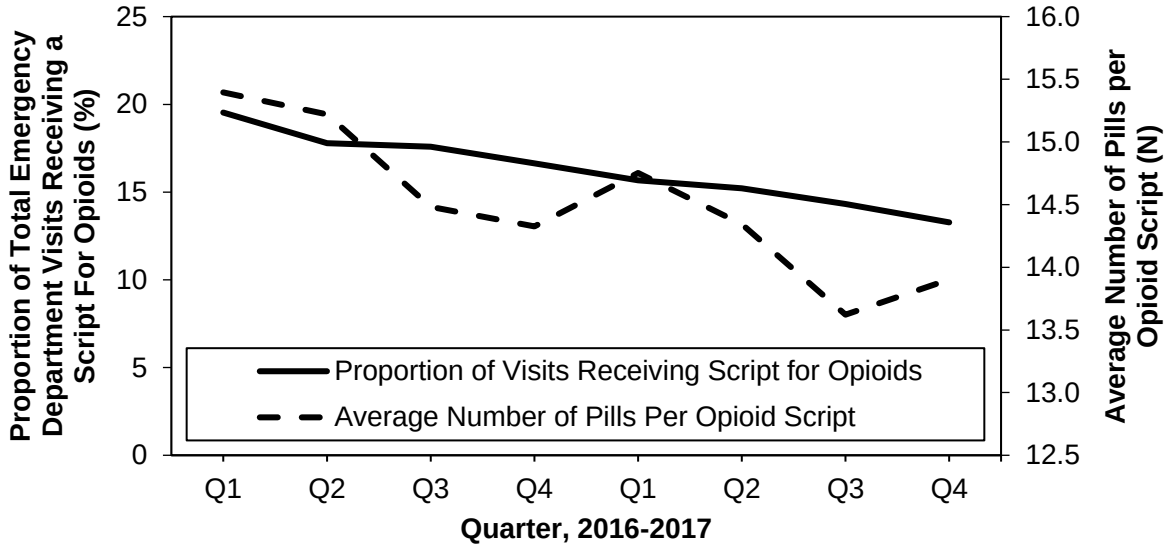

Figure 6. Proportion of UMMS ED Visits Receiving Prescriptions for Opioids and the Average Number of Pills per Opioid Prescription, 2016–2017

This trend toward safer prescribing persisted even in subgroups that traditionally always received opioids. One such group is those patients who present with non-traumatic dental pain (i.e., pain caused by cavities, not a jaw fracture). This group accounts for only 1 in 250 patients seen in VA EDs (0.4%) yet it receives more than 1 in 18 opioid prescriptions (5.4%).[49,50] To explore this subgroup that received a disproportionately large number of opioid scripts, we examined the records of patients presenting to the ED at BWMC with complaints of non-traumatic dental pain. We found that 4,960 unique patients who presented 7,545 times between 2012 and 2017. Just as in the VA, many of these patients with dental pain were given a

prescription for opioids (81.2%). This percentage was highest in 2012 (91.2%) and fell to 70.4% in 2017 (Figure 9).

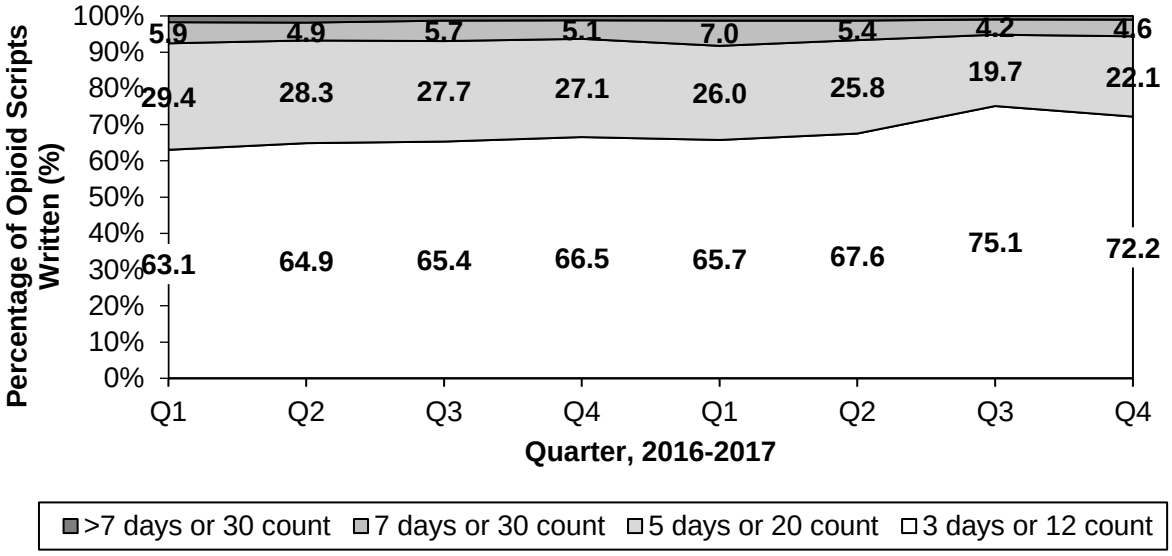

Figure 7. Proportion of UMMS Emergency Department Visits Receiving Prescriptions for Opioids Written Within Guidelines, 2016–2017

The proportion of patients receiving prescriptions written in compliance with guidelines was high in 2012. (71.0%) and increased further, to 78.8%, in 2017 (Figure 9). Very few prescriptions were written for more than 30 pills in 2012 (6.7% of visits for dental pain), and they had become even less common by the end of the study period (0.5% of visits). The proportion of patients receiving an non-steroidal anti-inflammatory drug (NSAID) like ibuprofen for dental pain tripled from 5.7% to 17.2%. Similarly, those receiving no prescription increased from 3.1% to 19.3%.

These data suggest that, since the opioid crisis became known, emergency physicians across the United States, and in Maryland in particular, have responded by decreasing the number of prescriptions they write for opioids and the number of pills in those prescriptions. As a result, the proportion of prescriptions written in accordance with prescribing guidelines has increased, even for complaints that frequently were treated with opioids.

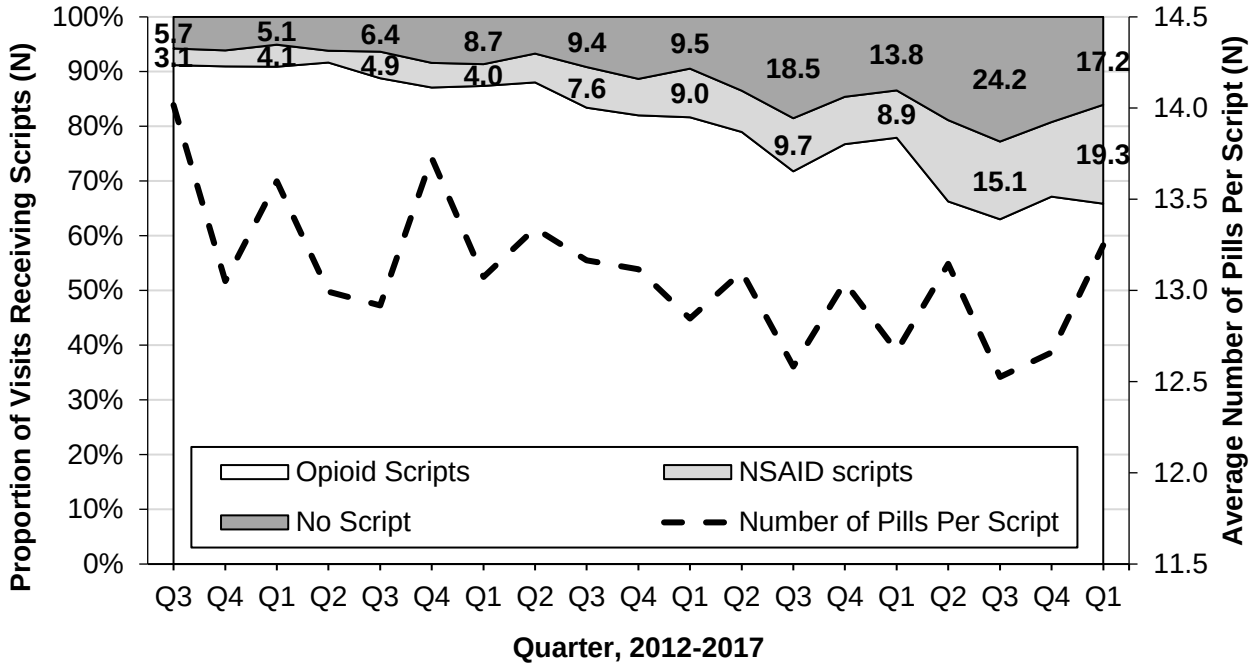

Figure 8. Proportions of Patients Presenting to BWMC and Receiving Medications for Dental Pain, 2012–2017. NSAID, Non-steroidal anti-inflammatory drug

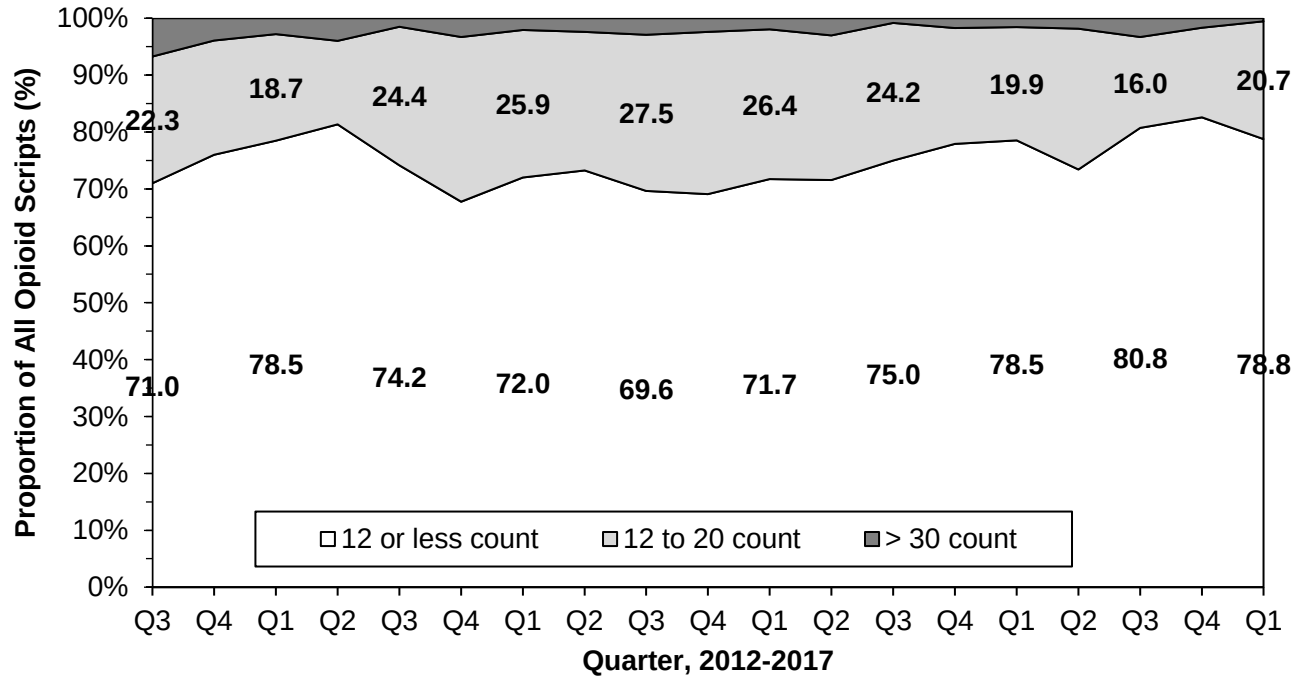

Figure 9. Proportion of Opioid Prescriptions Written Within Prescribing Guidelines for Patients Presenting with Dental Pain, BWMC, 2012–2017. *No scripts were written for between 20 and 30 pills

Increased Naloxone Availability

In response to the increasing numbers of opioid overdose deaths in Baltimore City, Dr. Leana Wen, the city's Health Commissioner and emergency physician, organized the "Don't Die" campaign in 2015.[51] Focused on recognition of opioid overdose, increasing the availability of naloxone, and educating laypersons on how to administer naloxone, the Campaign has helped to save more than 800 lives since 2015. Dr. Wen issued a standing order for naloxone, which can be printed from the Baltimore City Health Department's website and is redeemable at any pharmacy (Appendix B).[52] Dr Howard Haft, Maryland Deputy Secretary for Public Health Services, issued a similar standing order that allows pharmacists to dispense naloxone to anyone, including those who may be in a position to emergently assist someone experiencing an overdose (Appendix B).[53] Dr Wen published online naloxone training videos, allowed pharmacists to teach patients how to administer naloxone, and offered administration classes to the public.[52] Later that same year, the Maryland General Assembly approved a Good Samaritan Law that provides enhanced legal protection (specifically immunity from arrest and prosecution) for persons who administer naloxone to someone who has overdosed or who notify the authorities of someone who has overdosed.[54]

The HOPE Act made it mandatory that all hospitals create and execute discharge plans for patients deemed to be at high-risk for opioid overdose. This group includes patients who were brought to the ED as the result of an overdose as well as those who have a major injury and need large doses of pain medications in recovery.[44] In response to these initiatives in Baltimore City and in the State of Maryland, emergency physicians in the UMMS have increased their naloxone prescribing (Figure 10).

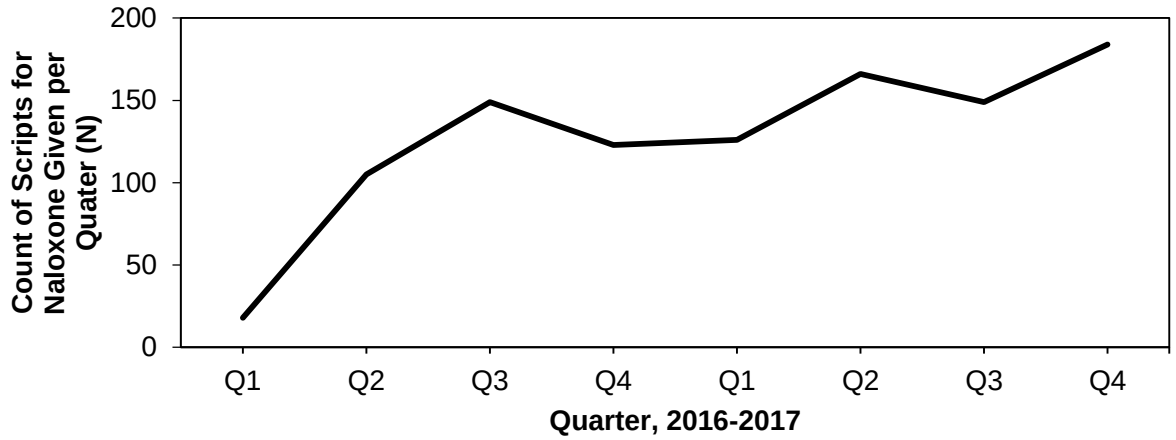

Figure 10. Number of Prescriptions for Naloxone Given by Emergency Physicians in UMMS per Quarter, 2016–2017

Screening, Brief Intervention, and Referral to Treatment (SBIRT)

As a part of the legislative and public health efforts mentioned in this report, emergency departments in the UMMS network have begun to employ more peer counselors and social workers to address the needs of the growing numbers of patients with substance abuse problems. Patients presenting to the ED as the result of an overdose obviously would benefit from referral to treatment. But many patients who have a history of recent drug use come to the ED for other reasons. In October 2016, the UMMC created a peer counselor program designed to identify ED patients who might benefit from an intervention. Counselors have screened 59,497 patients, or 91.7% of all patients seen at UMMC during 2017. One in six (N=9,884, 16.6%) admitted to drug use in the past 12 months. Of those, 10.0% (986) were homeless and 10.9% (1,080) were unemployed. 10.4% (1,029) of admitted drug users had a known psychiatric diagnosis, but only 2.4% (238) were in treatment for their psychiatric disease.

The most common drugs patients used were marijuana (N=5,237 [53.0%]), heroin (3,660 [37.0%]), cocaine (2,894 [29.3%]), and prescription drugs (205 [2.1%]). On average, patients used more than one substance (average=1.21). Interventions by our counselors led to 392 patients going into substance abuse treatment, with 140 of them being started on buprenorphine for opioid maintenance in the ED. Currently the SBIRT counselors are funded through a patchwork of hospital funds and federal and state grants. They are identifying patients at risk of dying from an overdose and getting them into treatment, but the service is not funded in a sustainable way.

Overdose Survivor Outreach Program

For patients who come to an ED in overdose but are unwilling to enter treatment, the Overdose Survivor Outreach Program makes peers (persons with a history of substance abuse but now in recovery) available to them for follow up. Peers are located in Baltimore City hospitals and emergency departments in order to link patients to treatment services, to provide naloxone training, and to serve as a point of contact if someone decides to enter care.

SECTION 4: HOW CONGRESS CAN HELP

Despite interventions by public health officials and emergency physicians, the opioid crisis continues to worsen. The number of deaths due to opioids continues to climb. The US Congress can join us and support in our response to the opioid crisis by taking the following actions:

- Enact federal legislation modeled on the Maryland HOPE Act:
    - Keep naloxone's cost low and keep naloxone training available and affordable.
    - Create robust Good Samaritan protection for people who administer naloxone to someone in overdose.
    - Ensure that naloxone is cheap and available to hospitals so that physicians can continue to treat people in overdose when they arrive.
- Provide funding for social workers and peer counselors to identify at-risk patients and link them to substance abuse treatment programs.
- Ensure that treatment resources are available at any time of day for the people who want to use them and for the physicians who want to refer patients to them.
- Provide funding to clinicians and researchers to support their efforts to track current and emerging patterns of drug use.

CONCLUSIONS

Throughout this report, we have highlighted a number of ways that the opioid crisis has affected our nation's medical system: the number of ED visits related to substance abuse is increasing, the number of fatal and non-fatal overdoses is increasing, and the costs associated with assessing and treating drug-abusing patients are increasing. Emergency physicians, in concert with addictions specialists and public health experts, have begun to address the crisis by making naloxone more available, by decreasing the amount of opioids that they prescribe, and by making substance abuse specialists available in EDs to identify high-risk patients and get them into treatment.

Postscript: What Is Not Covered in This Report

In this report on the effect of the opioid crisis on emergency departments in the State of Maryland, we have not covered several related aspects of the problem. For example, the human immunosuppression virus (HIV) and acquired immune deficiency syndrome (AIDS) have increased in prevalence due to the epidemic, and this association deserves its own report. Also, it is difficult to attribute general conditions associated with substance abuse, such as hepatitis, necrotizing fasciitis, and endocarditis, to one specific substance, so they are not covered in this report. Similarly, socioeconomic factors that go hand-in-hand with substance abuse, such as homelessness and poverty, are beyond the scope of this report.

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APPENDIX A

University of Maryland Institutional Review Board Approval

University of Maryland, Baltimore
Institutional Review Board
Phone: (410) 706-5037
Fax: (410) 706-4189
Email: hrpo@umaryland.edu

NOT HUMAN RESEARCH DETERMINATION

Date: March 23, 2018

To: Zachary Dezman
RE: HP-00079790
Name: Report to United States Senate on the Burden of the Opioid Crisis on Maryland Emergency Departments and Maryland State

This letter is to acknowledge that the UMB IRB reviewed the information provided and has determined that the submission does not require IRB review. This determination has been made with the understanding that the proposed project does not involve a systematic investigation designed to develop or contribute to generalizable knowledge **OR** a human participant (see definitions below).

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities are human subject research in which the organization is engaged, please submit a new request to the IRB for a determination.

Definitions –

Human Research: Any activity that either:

- Is "Research" as defined by DHHS and involves "Human Subjects" as defined by DHHS ("DHHS Human Research"); or
- Is "Research" as defined by FDA and involves "Human Subjects" as defined by FDA ("FDA Human Research").

Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Research as Defined by FDA: Any experiment that involves a test article and one or more human subjects, and that meets any one of the following:

- Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
- Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the

individual, or (2) information that is both Private Information and Identifiable Information. For the purpose of this definition:

- Intervention means physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- Interaction means communication or interpersonal contact between investigator and subject.
- Private Information means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- Identifiable Information means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

Human Subject as Defined by FDA: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen (identified or unidentified) a medical device is used.

Please keep a copy of this letter for future reference. If you have any questions, please do not hesitate to contact the Human Research Protections Office (HRPO) at (410) 706-5037 or HRPO@umaryland.edu.

APPENDIX B

Example Naloxone Standing Orders

STANDING ORDER FOR BALTIMORE CITY PHARMACISTS

Pharmacists may dispense any of the following naloxone formulations.

Check formulation dispensed: **Refill=PRN**

☐**Narcan:** Nasal Spray (4mg of naloxone hydrochloride in 0.1mL). 2 pack kit (up to 2 kits).
Directions: Spray into one nostril. May repeat x1, if no response after 3 minutes.

☐**Evzio:** Auto-injector (Naloxone 2 mg). 2 pack kit (up to 2 kits).
Directions: Use as instructed by device. May repeat x1, if no response after 3 minutes.

☐**Intranasal:** Naloxone (2mg/2mL) single dose Luer-Lock prefilled syringe. Qty= 2 or 4 syringes. Dispense with intranasal mucosal atomizer device.
Directions: Spray one-half of syringe (1 mL) into each nostril upon signs of opioid overdose. May repeat x1, if no response after 3 minutes.

For more information about naloxone visit www.dontdie.org.

For substance use treatment call the 24/7 Crisis, Information, and Referral Line: 410-433-5175.

Leana S. Wen, M.D., M.Sc., FAAEM
Commissioner of Health, City of Baltimore

NR# 122527943

This prescription does not require completion of a specialized training in overdose recognition and response or possession of a training certificate.

Updated June 1, 2017

Maryland Overdose Response Program
Statewide Naloxone Standing Order

Background

Naloxone is a prescription medication indicated for the reversal of respiratory depression or unresponsiveness due to opioid overdose. Under Maryland law,[1] a physician employed by the Maryland Department of Health and Mental Hygiene (DHMH) may prescribe naloxone by issuing a standing order which authorizes dispensing to any individual who may be at risk of opioid overdose or in a position to assist someone experiencing an opioid overdose. A person-specific paper or electronic prescription is not required to dispense under this standing order, and an individual is not required to have previously received training or education on opioid overdose response to be dispensed naloxone. An individual prescribed and dispensed naloxone under this standing order may possess naloxone and the necessary supplies for its administration and administer it to anyone they believe may be experiencing an opioid overdose. More information about opioid overdose response, naloxone and guidance to pharmacists regarding this standing order is available from the Maryland Overdose Response Program and online at www.naloxonemd.org.

Statewide Standing Order

This standing order is issued by **Howard Haft, M.D. (NPI # 1639132152), Deputy Secretary for Public Health Services, DHMH**. The standing order authorizes any Maryland-licensed pharmacist to dispense naloxone to any individual in accordance with the conditions of this order, enumerated below.

Dispense **two (2) doses** of naloxone hydrochloride and necessary paraphernalia for administration. The specific naloxone formulation shall be selected from the list below in accordance with the individual's preference or training to administer a particular formulation.

1. **For intranasal administration**
   - NARCAN® 4mg/0.1mL nasal spray. Include face shield for rescue breathing if available.
     Directions for use: Administer a single spray of NARCAN® in one nostril. Repeat after 3 minutes if no or minimal response.
     Or
   - 2mg/2mL single-dose Luer-Jet prefilled syringe. Include one luer-lock mucosal atomization device (MAD 300) per dose dispensed. Include face shield for rescue breathing if available.
     Directions for use: Spray 1 mL in each nostril. Repeat after 3 minutes if no or minimal response.
2. **For intramuscular injection**
   - 0.4mg/mL in 1mL single dose vials. Include one 3cc, 23g, 1" syringe per dose dispensed. Include face shield for rescue breathing and alcohol swabs if available.
     Directions for use: Inject 1 mL IM in shoulder or thigh. Repeat after 3 minutes if no or minimal response.
3. **For intramuscular or subcutaneous injection**
   - EVZIO® 2mg/0.4mL auto-injector, #1 Two-pack
     Directions for use: Follow audio instructions from device. Place on thigh and inject 0.4 mL. Repeat after 3 minutes if no or minimal response.

I declare this standing order as a statewide prescription for the dispensing of naloxone.

Howard Haft, M.D., Deputy Secretary for Public Health Services, DHMH

Effective Date: June 1, 2017 Expiration Date: June 1, 2019