Exposures to Opioids Among Wisconsin Children and Adolescents, 2002–2016

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ABSTRACT

Background: Opioid overdoses and opioid-related fatalities have increased dramatically in Wisconsin over the past decade. The observed rise in morbidity and mortality parallels increased opioid prescribing and greater use of illicit drugs such as heroin. Increased availability of both prescription and illicit opioids may increase the risk of exposure and overdose among the pediatric population.

Methods: We examined demographics and temporal trends in opioid exposures among children aged 0–19 years using hospital encounter and Wisconsin Poison Control Center (WPC) data. Exposures were categorized by type of opioid.

Results: We identified 3,320 WPC calls and 2,725 hospital encounters involving opioids during 2002–2016. Within the hospital encounter data, the rate of opioid-involved exposures increased significantly in children aged 0–5 years and adolescents aged 13–19 years. The majority of opioid-related hospital encounters involved prescription opioids. However, the proportion of hospital encounters involving heroin increased significantly among 13–19 year olds from 2002–2016. Within WPC data, the proportion of calls involving tramadol increased among 0–5 year olds and 13–19 year olds. However, calls about opioid/acetaminophen combinations decreased significantly as a proportion of opioid exposures.

Discussion: These findings suggest the need for caregiver education regarding safe storage and disposal of prescription opioids to prevent unintentional or intentional exposure to these substances among young children and adolescents. Overdose rates among teens continue to rise and an increasing proportion are due to heroin; comprehensive treatment and prevention strategies targeting this demographic are needed.

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BACKGROUND

Opioid-related deaths and hospital encounters more than doubled in Wisconsin during 2006–2016.[1] The majority of these events are related to prescription opioids, which accounted for 69.0% of opioid-involved deaths and 59.0% of opioid-involved hospital encounters in 2016.[1] Nationally, trends in prescription opioid morbidity and mortality have paralleled substantial increases in opioid prescriptions.[2]

Increased prescribing of opioid analgesics in the United States has resulted in greater availability of these products to children and adolescents.[3] Nationally, Emergency Department (ED) visits and hospitalizations for opioid overdose have occurred with increasing frequency over the last decade,[4,5] and similar trends have been observed in calls to poison centers for opioid poisoning.[3] Studies indicate a bimodal distribution where young children (< 6 years) and adolescents (13+ years) are the most likely to experience an opioid exposure.[3,4] Younger children are more likely to be exposed unintentionally while teens are more likely to have an intentional exposure or a suicide attempt.[3] Despite sustained efforts to prevent and reduce opioid-related harm at the state level,[6] no analysis to date has sought to characterize opioid exposures for children and adolescents in Wisconsin.

The purpose of this investigation is to characterize opioid exposures for children and adolescents in Wisconsin using 2 data sources: hospital encounter data and Wisconsin Poison Center (WPC) data. Although hospital and emergency department data frequently are used for surveillance of nonfatal opi-

oid poisonings, diagnostic and external cause of injury codes provide limited information on specific substances or causative factors. Therefore, we included analysis of poison center calls to provide a more comprehensive picture of opioid exposures in the pediatric population.

METHODS

We obtained data from the National Poison Data System (NPDS)[7] to evaluate calls to WPC. WPC receives approximately 100 calls per day that are handled by nurses and pharmacists who are specialists in poison information. These specialists often home manage exposures and will refer patients to health care facilities for further evaluation and treatment, when applicable. Basic deidentified data from each call—including age and sex, exposure substance(s), route of exposure, and outcomes—are entered into the NPDS. The NPDS is a secure data system that provides poison center data to toxicologists and other health professionals. Cases included all children aged < 20 years for whom a call was placed during 2002–2016 regarding an exposure to any prescription opioid or heroin. (See Box.) Cases were excluded if the medical outcome was listed as "confirmed non-exposure" or "unrelated effect."

Data from the Office of Health Informatics (OHI) at the Wisconsin Department of Health Services (DHS) was obtained to evaluate hospital encounters (ie, hospitalizations and ED visits) in Wisconsin facilities related to opioid poisoning for children aged < 20 years. Data cover all reporting facilities within the state and are provided to OHI by the Wisconsin Hospital Association. Non-Wisconsin residents were excluded from these analyses. This secondary analysis of existing data sets was conducted as part of routine surveillance of state-level health outcomes by DHS. As such, this study was not subject to Institutional Review Board review.

To identify opioid poisonings that occurred during January 1, 2002 through September 30, 2015, we searched across all diagnoses and the first external cause of injury field for the following ICD-9-CM codes: 965.00 (poisoning by opium [alkaloids], unspecified, 965.01 (poisoning by heroin), 965.02 (poisoning by methadone), 965.09 (poisoning by other opiates and related narcotics), E850.0 (accidental poisoning by heroin), E850.1 (accidental poisoning by methadone), or E850.2 (accidental poisoning by other opiates and related narcotics). During October 1, 2015 through December 31, 2016, we searched across all diagnosis fields for the following ICD-10-CM codes with a 5th or 6th character of 1-4 and a 7th character of A or D indicating initial or subsequent encounters: T40.0X (poisoning by opium), T40.1X (poisoning by heroin), T40.2 (poisoning by other opioids), T40.3X (poisoning by methadone), T40.4X (poisoning by synthetic narcotics), T40.60 (poisoning by other and unspecified narcotics), and T40.69 (poisoning by other narcotics). This coding is consistent with schema utilized by the Centers for Disease Control and Prevention.[2]

Identified opioid-related exposure cases were analyzed for demographics, medical outcomes, and opioid type. Medical outcomes within WPC data were categorized using standard NPDS coding: (1) minor effects include those with transient and mild symptoms with no long-term sequelae, (2) moderate effects are more prolonged and/or of a systemic nature but non-life threatening and do not result in long-term harm, and (3) major effects include those which are life threatening or result in residual disability.[8] For hospital encounter data, we categorized opioid poisonings into 2 groups: prescription opioids and heroin. Because we searched across multiple fields to identify relevant ICD-9-CM and ICD-10-CM codes, these categories are not mutually exclusive. For WPC data, we limited our analyses to exposures to specific opioids for which there were at least 30 calls in the 15 years under study. The substances that met this threshold were buprenorphine, codeine, hydrocodone, methadone, morphine, oxycodone, tramadol, opioid/acetaminophen combinations, and heroin. All other or unknown opioids were grouped together and treated as a separate category.

For both datasets, we assessed trends in counts and rates over time. Rates were calculated using the Wisconsin's 2010 census data as the denominator. The statistical significance of both count and rate trends were assessed using the Kendall Tau-p. In both datasets we examined events in 3 age categories: 0–5 years, 6–12 years, and 13–19 years. These age categories were chosen to align with infancy/early childhood, middle childhood, and adolescence. All analyses were completed using SAS software, version 9.4 for Windows.

Box. Opioids Included in the Wisconsin Poison Control Data Set

- Alfentanil
- Acetaminophen with codeine
- Acetaminophen with hydrocodone
- Acetaminophen with other narcotics or narcotic analogs
- Acetaminophen with oxycodone
- Acetaminophen with propoxyphene
- Acetylsalicylic acid with codeine
- Acetylsalicylic acid with other narcotics or narcotic analogs
- Acetylsalicylic acid with oxycodone
- Acetylsalicylic acid with propoxyphene
- Buprenorphine
- Butorphanol
- Codeine
- Difenoxin
- Dihydrocodeine
- Fentanyl
- Heroin
- Hydrocodone
- Hydromorphone
- Ibuprofen with hydrocodone
- Levorphanol
- Meperidine
- Methadone
- Morphine
- Nalbuphine
- Other or unknown narcotics
- Oxycodone
- Oxymorphone
- Pentazocine
- Propoxyphene
- Remifentanil
- Sufentanil
- Synthetic opioids
- Analogs and precursors (excluding pharmaceutical preparations),
- Tapentadol
- Tramadol

RESULTS

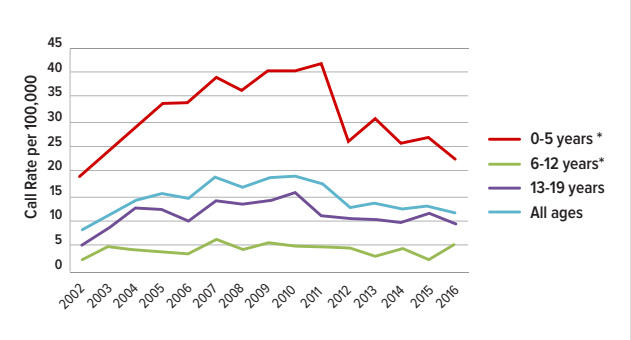
Exposure Calls to the WPC

There were 3,320 cases involving an opioid exposure in a child or adolescent called into the WPC during 2002–2016 that met our criteria (Table 1). For exposures reported to the WPC, most involved females (50.6%), but with age-dependent shifts in proportion (Table 1). Race data were not collected by the WPC. The largest proportion of calls were regarding exposures in children aged 0–5 years (60.8%; n = 2,019). Exposures among adolescents aged 13–19 years were about half as frequent (29.0%; n = 962),

Table 1. Characteristics of Opioid Exposures Reported to the Wisconsin Poison Center Among Children 0–19 Years, Wisconsin, 2002–2016 (N = 3,320)

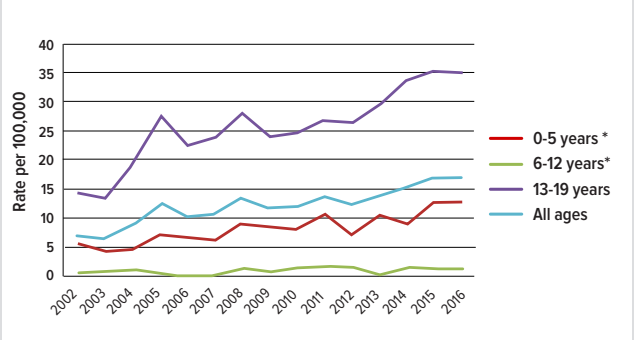
		Age							
		0-5	(%)	6-12	(%)	13-19	(%)	All	(%)
Sex	Female	962	47.6%	135	39.8%	584	60.7%	1681	50.6%
	Male	1055	52.3%	203	59.9%	376	39.1%	1634	49.2%
	Unknown	2	0.1%	1	0.3%	2	0.2%	5	0.2%
	Total	**2019**	**100.0%**	**339**	**100.0%**	**962**	**100.0%**	**3320**	**100.0%**
Exposure Reason	Adverse reaction	4	0.2%	5	1.5%	26	2.7%	35	1.1%
	Intentional	5	0.2%	17	5.0%	373	39.0%	395	11.9%
	Suicide attempt	1	0.0%	8	2.4%	344	36.0%	353	10.7%
	Therapeutic error	265	13.1%	213	62.8%	135	14.1%	613	18.5%
	Unintentional	1730	85.7%	90	26.5%	54	5.6%	1874	56.5%
	Other/unknown	14	0.7%	6	1.8%	24	2.5%	44	1.3%
	Total	**2019**	**100.0%**	**339**	**100.0%**	**956**	**100.0%**	**3314**	**100.0%**
Outcome	Minor effect	324	16.0%	76	22.4%	485	50.7%	885	26.7%
	Major effect	13	0.6%	0	0.0%	21	2.2%	34	1.0%
	Moderate effect	62	3.1%	9	2.7%	114	11.9%	185	5.6%
	Death	2	0.1%	0	0.0%	1	0.1%	3	0.1%
	No effect	816	40.4%	69	20.4%	129	13.5%	1014	30.6%
	Lost to follow-up	802	39.7%	185	54.6%	207	21.6%	1194	36.0%
	Total	**2019**	**100.0%**	**339**	**100.0%**	**957**	**100.0%**	**3315**	**100.0%**
Level of Care	Admitted to critical care unit	84	4.2%	6	1.8%	87	9.0%	177	5.3%
	Admitted to noncritical care unit	97	4.8%	6	1.8%	64	6.7%	167	5.0%
	Admitted to psychiatric facility	0	0.0%	0	0.0%	34	3.5%	34	1.0%
	Patient lost to follow-up/left against medical advice	87	4.3%	13	3.8%	104	10.8%	204	6.1%
	Patient refused referral/did not arrive at health care facility	35	1.7%	13	3.8%	73	7.6%	121	3.6%
	Treated/evaluated and released	504	25.0%	46	13.6%	324	33.7%	874	26.3%
	Data missing	1212	60.0%	255	75.2%	276	28.7%	1743	52.5%
	Total	**2019**	**100.0%**	**339**	**100.0%**	**962**	**100.0%**	**3320**	**100.0%**

Figure 1. Rate of Opioid-Related Exposure Calls to the Wisconsin Poison Control Center by Age Category



* Trend positive and significant at $P<0.05$.

Figure 2. Rate of Hospital Encounters for Opioid Poisoning in Wisconsin by Age Category



* Trend positive and significant at $P<0.05$.

and children aged 6 to 12 years accounted for the remaining 10.2% of calls (n = 339). Among those aged 0–5 years, 85.7% of exposures were categorized as unintentional. In contrast, among those aged 13–19 years, 75.0% were categorized as either intentional or a suicide attempt. Those in the 0–5 group were less likely to have exposures that resulted in major and moderate effects or death (3.8%) in comparison to those 13–19 years old among whom 14.2% had major and moderate effects or death. The rate of opioid exposure calls for all age groups combined increased from 8.1 per 100,000 in 2002 and reached a peak of 19.0 per 100,000 in 2010 (Figure 1 and Figure 2). This was followed by a decline to 11.6 per 100,000 in 2016. Overall, the rate increased slightly during 2002–2016, but this overall increase was not statistically significant ($P = 0.961$).

Hospital Encounters

We identified 2,725 hospitalizations or ED visits involving opioid poisoning among children and adolescents during 2002–2016. Children and adolescents who were hospitalized or treated in the ED for opioid poisonings were more likely to be female. This dis-

Table 2. Characteristics of Patients Hospitalized or Seen in the Emergency Department for Opioid Poisonings in Wisconsin Among Children 0–19 Years, Wisconsin, 2002–2016 (N = 2,725)

		Age							
		0-5	**(%)**	**6-12**	**(%)**	**13-19**	**(%)**	**All**	**(%)**
Sex	Female	256	49.2%	40	48.2%	1180	55.6%	1476	54.2%
	Male	264	50.8%	43	51.8%	942	44.4%	1249	45.8%
	Total	**520**	**100.0%**	**83**	**100.0%**	**2122**	**100.0%**	**2725**	**100.0%**
Race	Black	110	21.2%	14	16.9%	162	7.6%	286	10.5%
	White	285	54.8%	47	56.6%	1513	71.3%	1845	67.7%
	Other	40	7.7%	4	4.8%	94	4.4%	138	5.1%
	Unknown/Missing	85	16.3%	18	21.7%	353	16.6%	456	16.7%
	Total	**520**	**100.0%**	**83**	**100.0%**	**2122**	**100.0%**	**2725**	**100.0%**
Ethnicity	Hispanic	28	5.4%	6	7.2%	99	4.7%	133	4.9%
	Non-Hispanic	399	76.7%	61	73.5%	1666	78.5%	2126	78.0%
	Unknown/Missing	93	17.9%	16	19.3%	357	16.8%	466	17.1%
	Total	**520**	**100.0%**	**83**	**100.0%**	**2122**	**100.0%**	**2725**	**100.0%**

tribution changed depending on the age category of the patients (**Table 2**). Patients were primarily reported as being white (67.7%; n = 1,845). The majority of encounters (77.9%; n = 2,122) occurred among adolescents aged 13–19 years, while 19.1% (n = 520) occurred among children aged 0–5 years and 3.0% (n = 83) occurred among children aged 6–12 years. The rate of hospital encounters involving opioid poisoning among all children and adolescents increased from 7.1 per 100,000 to 16.9 per 100,000 during 2002–2016 (Figure 2, $P < 0.001$). For children aged 6–12 years, the rate increased over the time period from 0.7 per 100,000 to 1.6 per 100,000 ($P = 0.015$). The rate of hospital encounters involving opioid poisoning more than doubled during 2002–2016 for children aged 0–5 years (5.5 vs 12.8 per 100,000, $P < 0.001$) and for adolescents aged 13 to 19 years (14.2 vs 34.9 per 100,000, $P < 0.001$).

Trends in Opioid Type

The rates of calls to the WPC for exposures to tramadol showed a significant increase for both the 0–5 year age group (2.5% vs 16.3% of calls, $P = 0.007$) and the 13–19 year group (6.5% vs 24.0% of calls, $P < 0.001$) (Table 3). These increases were also significant when considered as counts rather than rates ($P = 0.029$, $P < 0.001$, respectively). Concurrently, calls for opioid/acetaminophen combinations decreased as a proportion of opioid exposures from 69.6% to 22.8% among children aged 0–5 years ($P < 0.001$), from 42.9% to 23.1% for those aged 6–12 ($P = 0.029$), and from 71.0% to 48.0% for those aged 13–19 years ($P < 0.001$). Although the numbers were small, the proportion of exposure calls related to buprenorphine among children 0–5 years old increased from 4.6% in 2010 to 9.8% in 2016 ($P < 0.001$). This trend also was significant using raw count data ($P = 0.002$). These calls first appeared in WPC data in 2010 and averaged about 12.6 instances per year through 2016. Several other substances made up larger proportions of exposure calls during this time period for certain age groups (Table 3). Although some trends were statistically significant, changing proportions did not always reflect meaningful changes in the raw numbers.

The majority of hospital and ED encounters for opioid poisoning involved prescription opioids (85.4%, n = 2,336). All hospital encounters involving heroin occurred in adolescents aged 13–19 years (14.6%, n = 398). Case counts involving heroin increased nearly 10-fold from 6 cases in 2002 to 59 cases in 2016 ($P < 0.001$) (Table 3), while the proportion of opioid poisoning hospital encounters that involved heroin more than quadrupled from 2002 to 2016 (7.3% vs. 32.0% of exposures, $P < 0.001$) (Table 3).

DISCUSSION

Our analysis reveals that opioids are an important cause of drug exposures and morbidity among the pediatric population in Wisconsin. Among children 0–5 years of age, unintentional exposures were the predominant reason for opioid-related calls to the WPC. Exploratory behaviors with increased hand and object-to-mouth contact are common in this age group,[9] and opioids are a leading cause of unsupervised medication exposures.[10] Encouragingly, WPC data indicate that exposure calls declined markedly for children in this age group since 2009, a trend that has been observed in a national analysis of poison center data.[3] However, the reason for the decline in Wisconsin is unknown and it occurred before declines in opioid prescribing were observed nationally in 2012.[11] Data from the Wisconsin Prescription Drug Monitoring Program (PDMP) shows a decline from a maximum of 5.2 million opioid prescriptions in 2014 to 4.8 million in 2016.[12] It is also possible that the WPC received fewer calls because of increased knowledge among medical professionals on treatment for exposed patients or because of the increased availability of online clinical reference tools. Additionally, as the proportion of acetaminophen-containing combination product exposures decreased, there was likely an associated decrease in the cases of concomitant acetaminophen toxicity. Treatment decisions regarding acetaminophen toxicity are often more complicated and difficult than those regarding opioid toxicity. Providers may be more likely to call the poison center seeking assistance

Table 3. Poison Center Calls and Medical Encounters for Opioid Exposures, by Age Group, Year of Exposure, and Opioid Type, Wisconsin 2002–2016

		Exposures Calls to Wisconsin Poison Center								Hospital and emergency department encounters for opioid poisonings in Wisconsin			
Substance:		**Oxycodone**		**Tramadol***		**Heroin**		**Opioid/Acetaminophen Combinations****		**Prescription Opioids**		**Heroin**	
		n (%)		**n (%)**		**n (%)**		**n (%)**		**n (%)**		**n (%)**	
Age: 0-5 years	2002	11	(13.9)	2	(2.5)	0	(0.0)	55	(69.6)	23	(100.0)	0	(0.0)
	2003	6	(6.1)	7	(7.1)	0	(0.0)	54	(54.5)	19	(100.0)	0	(0.0)
	2004	11	(9.2)	4	(3.3)	0	(0.0)	82	(68.3)	20	(100.0)	0	(0.0)
	2005	13	(9.2)	3	(2.1)	1	(0.7)	90	(63.8)	30	(100.0)	0	(0.0)
	2006	18	(12.5)	13	(9.0)	0	(0.0)	76	(52.8)	29	(100.0)	0	(0.0)
	2007	12	(7.2)	9	(5.4)	0	(0.0)	112	(67.1)	27	(100.0)	0	(0.0)
	2008	17	(10.9)	25	(16.0)	0	(0.0)	80	(51.3)	39	(100.0)	0	(0.0)
	2009	17	(9.8)	18	(10.3)	0	(0.0)	74	(42.5)	37	(100.0)	0	(0.0)
	2010	12	(6.9)	21	(12.1)	1	(0.6)	77	(44.5)	35	(100.0)	0	(0.0)
	2011	16	(9.0)	23	(12.9)	0	(0.0)	78	(43.8)	46	(100.0)	0	(0.0)
	2012	4	(3.6)	12	(10.8)	0	(0.0)	61	(55.0)	30	(100.0)	0	(0.0)
	2013	17	(13.4)	12	(9.4)	1	(0.8)	51	(40.2)	44	(100.0)	0	(0.0)
	2014	20	(18.9)	8	(7.5)	0	(0.0)	45	(42.5)	38	(100.0)	0	(0.0)
	2015	27	(24.8)	28	(25.7)	0	(0.0)	24	(22.0)	51	(100.0)	0	(0.0)
	2016	23	(25.0)	15	(16.3)	1	(1.1)	21	(22.8)	52	(100.0)	0	(0.0)
Age: 6-12 years	2002	2	(14.3)	1	(7.1)	0	(0.0)	6	(42.9)	4	(100.0)	0	(0.0)
	2003	1	(3.8)	1	(3.8)	0	(0.0)	12	(46.2)	5	(100.0)	0	(0.0)
	2004	1	(4.3)	0	(0.0)	0	(0.0)	13	(56.5)	6	(100.0)	0	(0.0)
	2005	2	(9.5)	0	(0.0)	0	(0.0)	17	(81.0)	2	(100.0)	0	(0.0)
	2006	2	(10.5)	1	(5.3)	0	(0.0)	8	(42.1)	1	(100.0)	0	(0.0)
	2007	2	(6.3)	6	(18.8)	0	(0.0)	19	(59.4)	3	(100.0)	0	(0.0)
	2008	1	(4.5)	1	(4.5)	0	(0.0)	16	(72.7)	7	(100.0)	0	(0.0)
	2009	5	(17.9)	2	(7.1)	0	(0.0)	12	(42.9)	5	(100.0)	0	(0.0)
	2010	2	(7.7)	5	(19.2)	0	(0.0)	7	(26.9)	8	(100.0)	0	(0.0)
	2011	6	(24.0)	1	(4.0)	0	(0.0)	6	(24.0)	9	(100.0)	0	(0.0)
	2012	3	(13.0)	3	(13.0)	0	(0.0)	9	(39.1)	8	(100.0)	0	(0.0)
	2013	1	(6.3)	1	(6.3)	1	(6.3)	8	(50.0)	3	(100.0)	0	(0.0)
	2014	3	(13.0)	4	(17.4)	0	(0.0)	7	(30.4)	7	(100.0)	0	(0.0)
	2015	4	(30.8)	0	(0.0)	0	(0.0)	5	(38.5)	7	(100.0)	0	(0.0)
	2016	7	(26.9)	3	(11.5)	0	(0.0)	6	(23.1)	8	(100.0)	0	(0.0)
Age: 13-19 years	2002	5	(16.1)	2	(6.5)	1	(3.2)	22	(71.0)	76	(92.7)	6	(7.3)
	2003	7	(14.3)	1	(2.0)	1	(2.0)	35	(71.4)	73	(92.4)	6	(7.6)
	2004	9	(12.2)	1	(1.4)	1	(1.4)	50	(67.6)	106	(93.8)	7	(6.2)
	2005	7	(9.9)	5	(7.0)	6	(8.5)	45	(63.4)	142	(88.8)	18	(11.3)
	2006	11	(19.0)	5	(8.6)	0	(0.0)	31	(53.4)	112	(85.5)	19	(14.5)
	2007	12	(15.0)	9	(11.3)	2	(2.5)	49	(61.3)	118	(86.8)	18	(13.2)
	2008	8	(10.4)	11	(14.3)	4	(5.2)	43	(55.8)	129	(81.6)	29	(18.4)
	2009	5	(6.3)	9	(11.4)	1	(1.3)	50	(63.3)	107	(79.3)	28	(20.7)
	2010	10	(11.6)	11	(12.8)	2	(2.3)	48	(55.8)	112	(83.0)	23	(17.0)
	2011	3	(5.0)	16	(26.7)	0	(0.0)	32	(53.3)	112	(76.2)	35	(23.8)
	2012	8	(14.3)	6	(10.7)	0	(0.0)	35	(62.5)	110	(76.9)	33	(23.1)
	2013	9	(16.4)	11	(20.0)	2	(3.6)	24	(43.6)	115	(73.2)	42	(26.8)
	2014	2	(3.8)	13	(25.0)	2	(3.8)	30	(57.7)	146	(80.7)	35	(19.3)
	2015	5	(8.2)	11	(18.0)	1	(1.6)	30	(49.2)	148	(78.7)	40	(21.3)
	2016	5	(10.0)	12	(24.0)	2	(4.0)	24	(48.0)	127	(68.0)	59	(32.0)

* Trend positive and significant at $P < 0.05$

** Trend negative and significant at p $P < 0.05$

Note 1: Trend tests are conducted on proportions (not counts).

Note 2: Exposures are not mutually exclusive. Counts of opioid type may not sum to case counts. Percentages may not sum to 100.

in those decisions. Thus, decreases in acetaminophen-containing combination product exposures leading to decreases in acetaminophen toxicity from these medications may account for a decrease in the number of calls to the WPC.

We observed declines in WPC calls regarding exposures to opioid/acetaminophen combinations. Changes in opioid prescribing practices among medical providers leading up to the designation of hydrocodone combination products as Schedule II drugs by the Drug Enforcement Agency (DEA) in 2014 may have promoted transition to alternatives.[13] Adherence to opioid prescribing guidelines also may be a contributing factor and may encourage providers to switch to tramadol.[14] Wisconsin PDMP data have shown an increase of 60.0% from 514,220 tramadol prescriptions in 2013 to 819,719 prescriptions in 2016.[12] This would be consistent with our observations that an increase in the number of calls to the WPC were due to tramadol over the study period. Although tramadol is considered to have an acceptable safety profile relative to morphine,[15] supra-therapeutic doses can result in serious side effects and death. Furthermore, tramadol has potential for abuse and dependence and can cause an atypical withdrawal syndrome due to its effects on serotonin and norepinephrine. The Food and Drug Administration (FDA) added a contraindication against the use of tramadol in patients < 12 years of age, and in 2015 tramadol was designated a schedule IV drug by the DEA. Any increased tramadol prescribing should be accompanied by appropriate adherence to FDA prescribing guidelines and education of patients on the safe storage of tramadol as for any other opioid.

Other studies have found increases in prescribing of buprenorphine.[3] We noted an increase in calls to the WPC regarding this substance for children 0–5 years old. Although the number of WPC calls remains relatively low, the upward trend is notable. National poison center data indicate that buprenorphine exposures have not declined in tandem with other opioids and are more likely to result in a hospital admission.[3] Changes in buprenorphine formulation and packaging have reduced ED visits for accidental ingestions in young children nationally,[16] but increased prescribing of buprenorphine for opioid use disorder and continued exposures among young children indicate a need for continued patient education.

Among adolescents, the rate of opioid-related hospital encounters increased significantly during 2002–2016. These rates were the highest among adolescents beginning in 2005. Similar trends have been observed in national hospitalization data.[4] Other studies of hospitalization, ED, and poison center data have shown misuse and self-harm to be the primary drivers behind opioid-related exposures in adolescents, as opposed to accidental overdose and therapeutic errors seen in young children.[4,17] The higher proportion of opioid-related encounters among adolescent females compared to males might be driven in part by self-inflicted injury; national ED data show that poisoning is the most common method of self-harm among females aged 10–24 years.[18] The upward trend in opioid-related hospital encounters is mirrored in national death data, with the poisoning death rate among adolescents aged 15–19 years nearly doubling during 2000–2009, in part due to an increase in prescription drug overdoses.[19]

The increasing proportion of hospital encounters related to heroin among adolescents is notable. Although heroin was responsible for fewer than 10.0% of encounters in 2002 in those aged 13–19 years, this increased more than 3-fold to 36.0% by 2016. This coincides with other statewide evidence suggesting increased heroin use in Wisconsin.[6,20] Nationally, hospitalizations due to heroin in adolescents increased 161% from 1997 to 2012,[4] a trend reflected in poisoning deaths of adolescents and young adults in national vital statistics. This presents a new challenge to health care providers and public health agencies as the opioid epidemic shifts toward increased use of heroin and other illicitly produced opioids.[21,22] Early identification of adolescents with substance use disorders and increased availability of medication-assisted treatment will be needed to address misuse of prescription opioids and reverse trends toward greater use of illicit opioids.[23,24]

Limitations

Some limitations in our data and analysis should be considered. In WPC data, more than half of the poison center calls regarding opioid exposures pertained to children in the youngest age category (0–5 years), while hospitalization data showed that the majority of hospital encounters (76.1%) involved adolescents (13–19 years). Although the reason for this discrepancy is not fully understood, it may be related to increased hand and object-to-mouth contact among young children.[9] It also might be related to the severity of the exposure (eg, parents might be more likely to call WPC for minor exposures in younger children). Additionally, a recent national study showed that adolescents were more likely to experience an intentional poisoning and experience a serious medical complication, which may be associated with greater likelihood of hospitalization.[3,4] As such, hospitalization data may reflect cases with higher severity while WPC data reflect less severe exposures. WPC data support this hypothesis as the majority of cases (n = 1,899; 57.2%) were indicated as having a "minor effect" or "no effect" from exposure. Other types of encounters with the health care system (eg, urgent care and primary care office visits) are not reflected in our data. Future research may consider these additional sources.

This study treats the WPC and hospitalization data as separate but parallel indicators of trends in opioid exposure and poisoning. However, it should be noted that WPC staff members often refer individual callers to medical facilities for treatment. As such, we are unable to identify duplicate cases that are likely to appear in both datasets. It is also important to note that WPC data are based on calls from the public and health care providers. As such, many factors can affect whether or not a case gets called into the WPC, including medical expertise of clinicians, awareness of the poison center, and perception of what constitutes a poisoning. Finally,

the current study includes data from hospitalizations during the transition from ICD-9 to ICD-10 codes during the 4th quarter of 2015. While the numbers appear to be consistent with the previous years and trends, it is possible that differences in the number of opioid-involved poisonings in 2015 and 2016 could be due to this change in coding and may misestimate the observed increase in the number of hospitalizations.

CONCLUSIONS

Our study provides important details regarding the substantial increases in opioid-related exposures in Wisconsin. Hospital encounters for opioid poisoning and calls to the WPC regarding opioid exposures at least doubled for young Wisconsinites in the 15-year period we considered. Moreover, specific substances were important to these trends. Among Wisconsin adolescents hospitalized for opioid poisoning, a growing proportion of cases were related to heroin. In WPC data, trends in exposure for both children and adolescents were driven by exposure to tramadol. As the US Food and Drug Administration (FDA) does not recommend prescribing tramadol to children under the age of 12,[25] it is likely that increase in exposures are related to children's access to others medications. It would be useful to repeat this analysis in several years to see if changes in prescribing practices have had an effect on the trends described here. Future research should also explore social determinants of health that are driving the high burden of overdoses among adolescents.

These findings suggest the need for parental education related to safe use, storage, and disposal of opioid medications and potential misuse of opioids among adolescents. Further, provider adoption of the Centers for Disease Control and Prevention or Wisconsin Medical Examining Board opioid prescribing guidelines is important in reducing the availability of prescription opioids.[26] These guidelines include recommendations for screening for conditions associated with higher risk for opioid misuse, including psychiatric conditions such as depression, which may be particularly important when adolescents receive opioid prescriptions.

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