E-Cigarette and Liquid Nicotine Exposures Among Young Children

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abstract

OBJECTIVES: To investigate exposures to liquid nicotine (including electronic cigarette devices and liquids) among children <6 years old in the United States and evaluate the impact of legislation requiring child-resistant packaging for liquid nicotine containers.

METHODS: Liquid nicotine exposure data from the National Poison Data System for January 2012 through April 2017 were analyzed.

RESULTS: There were 8269 liquid nicotine exposures among children <6 years old reported to US poison control centers during the study period. Most (92.5%) children were exposed through ingestion and 83.9% were children <3 years old. Among children exposed to liquid nicotine, 35.1% were treated and released from a health care facility, and 1.4% were admitted. The annual exposure rate per 100 000 children increased by 1398.2% from 0.7 in 2012 to 10.4 in 2015, and subsequently decreased by 19.8% from 2015 to 8.3 in 2016. Among states without a preexisting law requiring child-resistant packaging for liquid nicotine containers, there was a significant decrease in the mean number of exposures during the 9 months before compared with the 9 months after the federal child-resistant packaging law went into effect, averaging 4.4 (95% confidence interval: −7.1 to −1.7) fewer exposures per state after implementation of the law.

CONCLUSIONS: Pediatric exposures to liquid nicotine have decreased since January 2015, which may, in part, be attributable to legislation requiring child-resistant packaging and greater public awareness of risks associated with electronic cigarette products. Liquid nicotine continues to pose a serious risk for young children. Additional regulation of these products is warranted.

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WHAT'S KNOWN ON THIS SUBJECT: Since their introduction to the US market in 2007, use of electronic cigarettes has been increasing. There has been a concurrent increase in liquid nicotine exposures reported to US poison control centers among children <6 years old.

WHAT THIS STUDY ADDS: From January 2012 through April 2017, there were 8269 liquid nicotine exposures reported among young children, peaking in January 2015. The annual exposure rate increased by ∼1400% from 2012 to 2015 and then decreased by ∼20% from 2015 to 2016.

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Electronic cigarettes (e-cigarettes) are handheld devices that produce an aerosol (commonly known as a vapor) for inhalation from a solution that often contains nicotine, flavoring, and solvents.[1] Since their introduction, there has been an increase in the use of e-cigarettes in the United States.[2,3] There also has been an increase in liquid nicotine exposures from e-cigarette devices and liquids reported to US poison control centers (PCCs), frequently among children younger than 6 years of age.[4,5] These exposures are concerning because a small volume of concentrated nicotine solution could easily deliver the estimated lethal dose of 6.5 to 13.0 mg/kg body weight to a young child,[6] and at least 2 young children have already died of liquid nicotine.[7–10] Children exposed to e-cigarette liquid nicotine have 5.2 times higher odds of a health care facility admission and 2.6 times higher odds of having a serious medical outcome than children exposed to cigarettes.[8]

Authors of case reports have described liquid nicotine exposures in both adults and children in several countries.[7,10–16] In state-specific studies, an increase in e-cigarette exposures reported to PCCs has been noted.[17,18] Authors of other studies using the National Poison Data System (NPDS) have described trends in exposures to cigarettes and e-cigarettes in all age groups[9] and specifically among children <6 years old.[8] Increased awareness of the risks of liquid nicotine exposures led to state and federal legislation requiring child-resistant packaging for liquid nicotine containers.[19] Although there have been previous studies of liquid nicotine exposure among young children, there has not been a study on exposure rates after the passage of laws requiring child-resistant packaging for liquid nicotine containers.

In this study, we analyze data from the NPDS to investigate the characteristics and trends of liquid nicotine exposures and is the first to compare liquid nicotine exposures among young children before and after adoption of legislation requiring child-resistant liquid nicotine packaging.

TABLE 1 States With and Without a State Law Requiring Child-Resistant Packaging for Liquid Nicotine Containers Before the Federal Law

Legislation Type	State	Effective Date
States with a state law		
	New York	December 29, 2014
	Illinois, Minnesota, and Vermont	January 1, 2015
	New Mexico	June 19, 2015
	Indiana and Wyoming	July 1, 2015
	Arkansas	July 22, 2015
	North Dakota	August 1, 2015
	Missouri	August 28, 2015
	Texas	October 1, 2015
	Virginia	October 1, 2015[a]
	North Carolina	December 1, 2015
	Maine and Tennessee	January 1, 2016
	Massachusetts	March 15, 2016
	Washington	June 28, 2016
	Oregon	July 1, 2016
States without a state law		
	Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Iowa, Kansas, Kentucky, Louisiana, Maryland, Michigan, Mississippi, Montana, Nebraska, Nevada, New Hampshire, New Jersey, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Carolina, South Dakota, Utah, West Virginia, and Wisconsin	July 26, 2016

[a] Retailers could sell previous inventory until January 1, 2016.

METHODS

Study Design and Data Sources

Data from the NPDS were analyzed to investigate liquid nicotine exposures (including e-cigarette devices and liquids) among children <6 years old. The NPDS is maintained by the American Association of Poison Control Centers (AAPCC) and includes reported exposure data from the regional PCCs serving the 50 US states, District of Columbia, and several US territories. Exposure data from the PCCs are uploaded to the NPDS on a near–real time basis.[20]

Federal and state legislation requiring child-resistant packaging for liquid nicotine containers was identified by using the Thomson Reuters Westlaw database.[21] Official legislative databases for individual states were accessed for additional details as needed. A list was compiled of the effective dates for state legislation, defined as the date when it was illegal for liquid nicotine to be sold without child-resistant packaging in that state (Table 1).

Case Selection Criteria

Liquid nicotine exposures among children <6 years old from January 1, 2012, through April 30, 2017, were extracted from the NPDS by using the AAPCC generic codes for e-cigarette devices and liquids. In this study, we only included single-substance human exposures occurring within the 50 US states or District of Columbia with the reason "Unintentional – General." Cases with a medical outcome of "confirmed nonexposure" or "unrelated effect" were excluded.

Study Variables

Liquid nicotine exposures were characterized by age and sex of the child, date of exposure, route of exposure, level of health care received, medical outcome, and "related" clinical effects. The AAPCC defines "minor effect," "moderate effect," and "major effect" for medical outcome as follows. "Minor effect" indicates that the individual developed some minimally bothersome signs and symptoms, typically limited to the skin or mucous membranes, which resolved quickly with no resulting disability or disfigurement. In a "moderate effect," the individual exhibited signs or symptoms that were not life-threatening but were more pronounced, prolonged, or systemic than minor symptoms. Treatment was indicated, and the individual had no residual disability or disfigurement. In a "major effect," the individual displayed life-threatening signs or symptoms, or symptoms that caused significant residual disability or disfigurement.[20]

For this study, the 50 states and District of Columbia were dichotomized into states with and without a child-resistant packaging law for liquid nicotine containers (Table 1). States were considered to have such a law if that law went into effect before July 26, 2016, the date when the federal Child Nicotine Poisoning Prevention Act of 2015 (Public Law No. 114-116) went into effect.[22]

Statistical Analysis and Ethical Considerations

SPSS 24.0 (IBM Corp, Armonk, NY) and SAS Enterprise Guide 7.11 HF3 (SAS Institute, Inc, Cary, NC) were used to analyze data. Overall and state-specific exposure rates were calculated by using the July 1 US Census Bureau population estimates for children <6 years old for 2012–2016.[23] Exposure rates were only calculated for the years with 12 months of complete data (2012–2016). Trends for the monthly number of exposures were analyzed by using piecewise linear regression with breakpoints at November 2012 and January 2015. To assess the effect of the federal law for liquid nicotine child-resistant containers, only states without a similar preexisting law were included. The difference in number of exposures before and after the law was calculated for each state by using data from 9-month periods before (October 2015–June 2016) and after (August 2016–April 2017) the federal law went into effect. A paired *t* test was used to assess the equality of the mean number of exposures during the 9 months before and after the federal law went into effect. Statistical significance was determined by using $\alpha = .05$. The institutional review board of the authors' institution judged this study as exempt.

RESULTS

General Characteristics

From January 1, 2012, to April 30, 2017, there were 8269 liquid nicotine exposures among children <6 years old reported to US PCCs. The median age of exposed children was 2.0 years (interquartile range = 1.3–2.0). The number of exposures ($n = 3146$) peaked at 1 year of age, and children <3 years old accounted for 83.9% ($n = 6940$) of exposures. Most (92.5%, $n = 7649$) children were exposed through ingestion and 55.3% ($n = 4572$) of exposures were among boys. More than one-third (35.1%, $n = 2902$) of exposed children were treated and/or evaluated and released, and 1.4% ($n = 115$) were admitted to the hospital. One-fifth of exposed children (20.3%, $n = 1677$) experienced a minor effect, followed by moderate effect (1.6%, $n = 132$) and major effect (0.1%, $n = 8$). One death occurred to a 1-year-old boy. One-fourth (24.6%, $n = 2032$) of children exposed to liquid nicotine experienced 1 or more related clinical effects. Severe clinical effects were rare, and included coma ($n = 4$), seizure ($n = 4$), respiratory arrest ($n = 3$), and cardiac arrest ($n = 1$).

Exposure Rates and Trends

For years with 12 months of complete data (2012–2016), the rate of liquid nicotine exposure was 6.4 exposures per 100 000 US children <6 years old. State-specific rates ranged from 1.6 (Washington, DC) to 22.2 (OK) (Fig 1). The overall exposure rate per 100 000 children increased by 1398.2% from 0.7 in 2012 to 10.4 in 2015, and subsequently decreased by 19.8% from 10.4 in 2015 to 8.3 in 2016 (Fig 2).

The monthly number of liquid nicotine exposures was lowest in February and July 2012 (8 exposures each month) and peaked in January 2015 (274 exposures; Fig 3). There was no significant change in the monthly number of exposures from January through November of 2012 ($m = -0.3$, $P = .816$), followed by a significant increase of 2390.1% ($m = 8.6$, $P < .001$) from November 2012 through January 2015, and then a significant decrease of 48.2% ($m = -3.9$, $P < .001$) from January 2015 through April 2017. From August 2016 (175 exposures), the first month after the federal Child Nicotine Poisoning Prevention Act went into effect, to April 2017 (142 exposures), there was an 18.9% decrease in the number of monthly liquid nicotine exposures.

Among states without a preexisting law, there was a significant difference ($P = .002$) in the mean number of exposures during the 9 months before compared with the 9 months after the Child Nicotine Poisoning Prevention Act of 2015 went into effect, averaging 4.4 (95% confidence interval: −7.1 to −1.7) fewer exposures per state during the

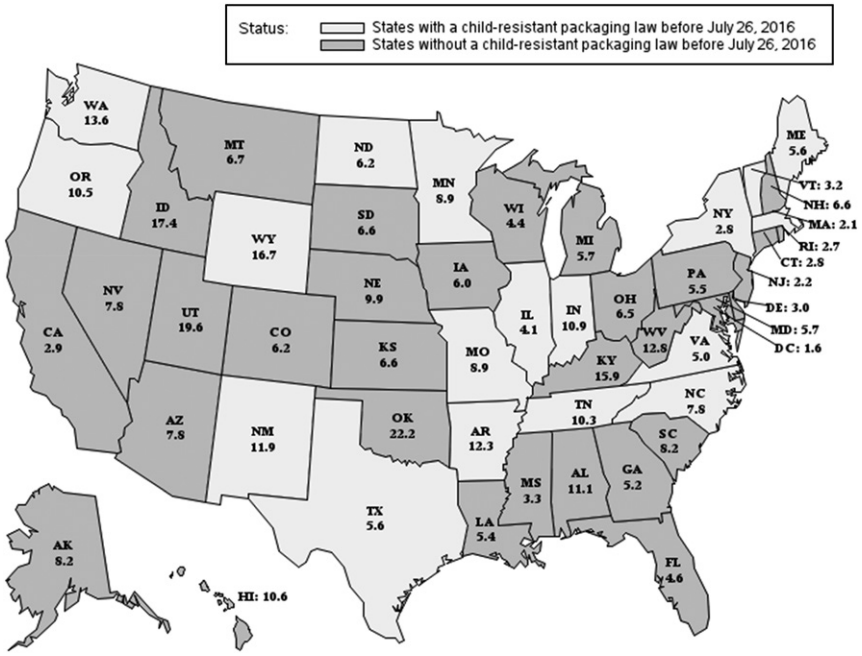

FIGURE 1

State-specific rates of liquid nicotine exposure per 100 000 children <6 years old, NPDS 2012–2016. AK, Alaska; AL, Alabama; AR, Arkansas; AZ, Arizona; CA, California; CO, Colorado; CT, Connecticut; DE, Delaware; FL, Florida; GA, Georgia; HI, Hawaii; IA, Iowa; ID, Idaho; IL, Illinois; IN, Indiana; KS, Kansas; KY, Kentucky; LA, Louisiana; MA, Massachusetts; MD, Maryland; ME, Maine; MI, Michigan; MN, Minnesota; MO, Missouri; MS, Mississippi; MT, Montana; NC, North Carolina; ND, North Dakota; NE, Nebraska; NH, New Hampshire; NJ, New Jersey; NM, New Mexico; NV, Nevada; NY, New York; OH, Ohio; OK, Oklahoma; OR, Oregon; PA, Pennsylvania; RI, Rhode Island; SC, South Carolina; SD, South Dakota; TN, Tennessee; TX, Texas; UT, Utah; VA, Virginia; VT, Vermont; WA, Washington; WI, Wisconsin; WV, West Virginia; WY, Wyoming.

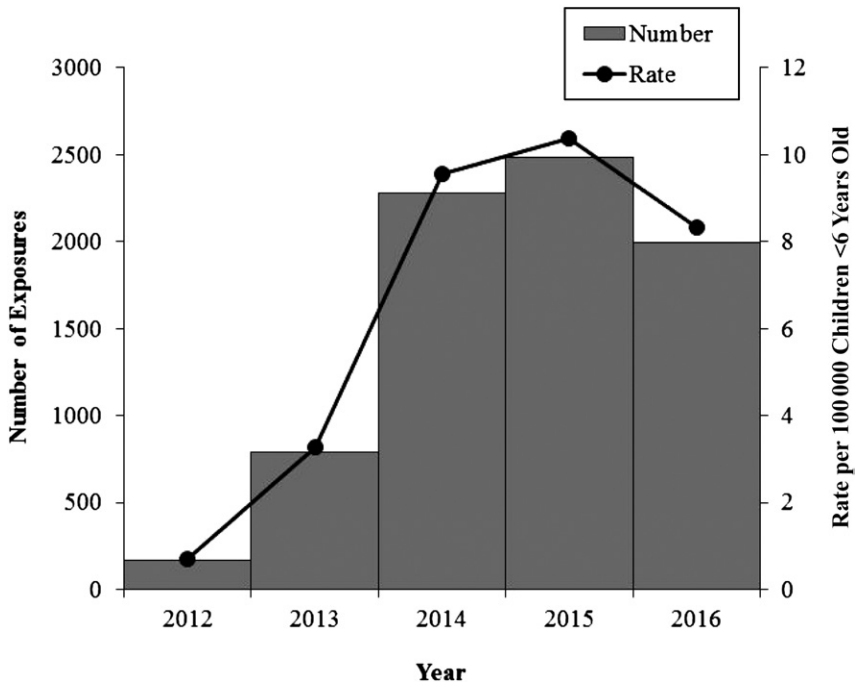

FIGURE 2

Annual number and rate of liquid nicotine exposures among children <6 years old, NPDS 2012–2016.

9 months after implementation of the law.

DISCUSSION

During the study period, there were >8200 exposures to liquid nicotine among children <6 years old reported to US PCCs. Although serious medical outcomes were not common, authors of previous studies have found that e-cigarette and liquid nicotine exposures more often are serious and result in health care facility admission than exposures to traditional cigarettes.[8,9] Previous reports have described the severe consequences that can occur from liquid nicotine exposure, including death.[7–16]

The use of e-cigarettes has increased rapidly since their introduction in the United States in 2007. In 2009, 0.6% of US adults reported ever using an e-cigarette, with studies reporting increasing use.[2,24] The authors of a 2014 report indicated that 12.6% of adults had ever used an e-cigarette.[25] Younger adults (18–24 years old) have reported a high prevalence of e-cigarette use.[26] Among middle and high school students, e-cigarettes were the most commonly used tobacco product in 2016, with 4.3% and 11.3% reporting use, respectively.[3] E-cigarette sales at convenience stores and other outlets grew from 2011 to 2015.[27] Furthermore, from 2014 to 2015, there was a 303.7% increase in e-cigarette liquid sales specifically.[27] Although nicotine-free products are available, 99.0% of e-cigarette products sold in the United States in 2015 contained nicotine.[28]

As the use of e-cigarettes increased, so did the number of liquid nicotine exposures reported to US PCCs. The authors of 1 study reported that exposures among children <6 years old increased by 0.55 additional exposures per month between June 2010 and December 2012 and then accelerated to 6.03

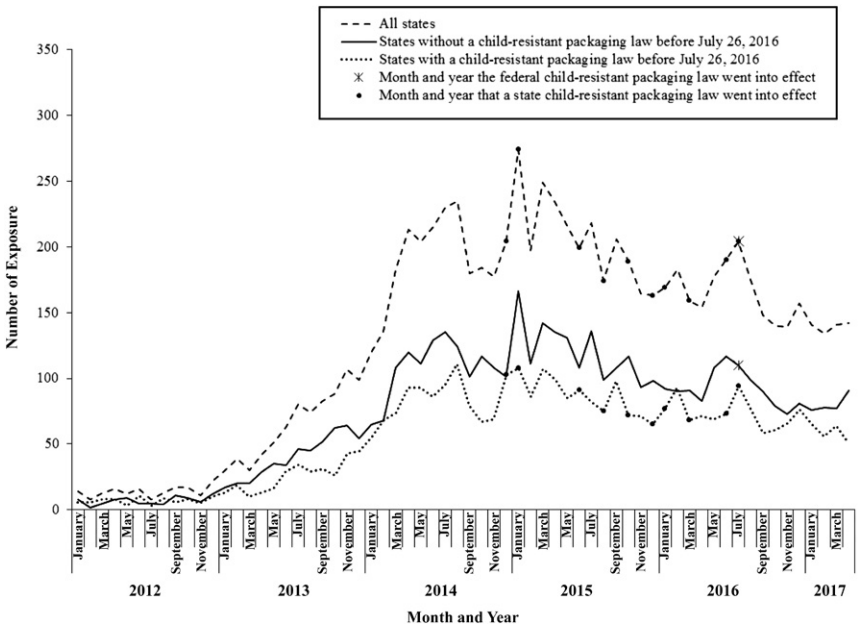

FIGURE 3

Monthly number of liquid nicotine exposures among children <6 years old by state child-resistant packaging law status, NPDS January 2012–April 2017.

additional exposures per month between January 2013 and September 2013.[4] The authors of another study observed an ~1500% increase in monthly e-cigarette and liquid nicotine exposures among children <6 years old from January 2012 to April 2015.[8] Our study is the first to report a more recent reversal in this trend. In this study, the monthly number of reported liquid nicotine exposures climbed until January 2015, followed by an overall downward trend through April 2017.

In July 2014, the Child Nicotine Poisoning Prevention Act was initially introduced in the US Congress.[29] By mid-January 2015, at the peak of the children's exposures, state legislation in New York, Minnesota, Vermont, and Illinois requiring child-resistant packaging for liquid nicotine containers had gone into effect. Fourteen additional states (Table 1) soon followed before the federal law's effective date.[22]

During the 9 months after the effective date (July 26, 2016) of the federal law, there was an overall decrease of 18.9% in the monthly number of liquid nicotine exposures. Among states that had not previously enacted a similar state law, there was a significant decrease in the mean number of liquid nicotine exposures among children <6 years old when comparing the 9 months before and after the federal law. Although the federal law may have contributed to this decline, its impact is uncertain because of a number of potentially confounding factors and the lack of a comparison group. The frequency of exposures had been decreasing before its enactment. Various factors likely contributed to the observed decrease, including state legislation requiring child-resistant packaging; efforts by public health professionals, clinicians, and child safety advocates to inform child caregivers of the risk of liquid nicotine exposures; and widespread media attention. State legislation may have influenced child exposures even in states without liquid nicotine packaging laws because manufacturers may have begun to distribute child-resistant containers throughout the United States rather than produce different products for states with and without these requirements.

We were unable to detect differences in monthly liquid nicotine exposures before and after enactment of individual state legislation requiring child-resistant packaging for liquid nicotine containers because of the small number of exposures in individual states. Other factors also may have washed out the effects of these laws, such as continued presence of previously-purchased non–child-resistant containers in children's homes. In addition, manufacturers and retailers were aware of the impending implementation dates of these state laws and may have begun to distribute child-resistant liquid nicotine containers before these dates.

Prevention

Although child-resistant packaging requirements for liquid nicotine containers have been established, more comprehensive requirements could further reduce the likelihood of serious poisonings. Flow restrictors effectively limit young children's ability to empty the contents of liquid medicine bottles.[30] Applying this technology to liquid nicotine bottles could limit the dose ingested by children who gain access to these bottles. Additionally, the Child Nicotine Poisoning Prevention Act only applies to liquid nicotine bottles and does not address the packaging or design of e-cigarette devices themselves. Chambers in refillable e-cigarette devices in which the liquid nicotine is held are another source of exposure. Child-resistant chambers in e-cigarette devices could

help prevent liquid nicotine exposure among young children.

Liquid nicotine comes in a variety of candy, fruit, dessert, and other flavors that may be attractive to young children. By 2014, there were 7764 unique flavors found across all e-cigarette brands.[31] The majority of exposures in this study occurred through ingestion, which is associated with the exploratory behavior common among young children, but also may be influenced by the attractiveness of liquid nicotine flavors, scents, and packaging to a young child. For instance, a bestselling e-liquid sold at an online site is named "Fruit Hoops" and has packaging that features images of colorful cereal.[32] The American Academy of Pediatrics and other health organizations have called on the US Food and Drug Administration (FDA) to ban the use of flavors and attractive labeling for liquid nicotine.[33]

E-cigarette liquid can be purchased at different nicotine concentrations, typically varying from 0 to 36 mg/mL.[34] Concentrated nicotine solutions, such as 60 mg/mL, are also available to consumers, who can then dilute and mix their own e-cigarette liquids.[16,34] A young child can easily ingest a lethal dose in 1 swallow.[6] In 1 case report, a 15 month-old child died after ingesting a dose of 4.1 mg/kg of liquid nicotine.[10] The 1 death in our study was previously reported.[7] Fatalities from liquid nicotine poisonings could be prevented by limiting the volume and concentration of liquid nicotine packaged in containers to a sublethal dose for an average young child. This approach has been used for >50 years for such products as children's aspirin.[35]

Future research should be conducted to assess the effect of flow restrictors, flavoring, labeling, concentration, and other product-related factors on liquid nicotine exposure and outcome rates among young children.

The FDA passed a final rule on May 10, 2016, deeming all tobacco products, including e-cigarettes and liquid nicotine refill containers, under its authority. This required all e-cigarette products that went into market after February 15, 2007, to apply for FDA approval and also established several requirements that had to be implemented by varying deadlines.[36] However, in May 2017, the FDA announced delays in enforcement of future compliance deadlines for several of these requirements. Additionally, in July 2017, the FDA revealed a new regulatory plan that includes extending premarket review for e-cigarettes to August 2022 and seeking public comment on regulation of "kid-appealing flavors in e-cigarettes."[37] In addition, the US Department of Justice has requested extensions in lawsuits that have challenged the FDA's authority to enforce its deeming rule.[38] The final outcome of these actions will determine the FDA's future role in regulating e-cigarettes and liquid nicotine.

Study Limitations

This study has several limitations. Exposure calls to PCCs are voluntary; therefore, the NPDS underestimates the true incidence of exposures to liquid nicotine nationwide. NPDS data may not be representative of the entire spectrum of liquid nicotine exposures because of potential reporting bias. Exposures reported to PCCs do not necessarily represent ingestion, poisonings, or overdoses because exposures are not generally confirmed with definitive laboratory testing. Information provided to PCCs is by self-report, which cannot be completely verified by the PCCs or AAPCC. Differentiation of liquid nicotine exposures due to e-cigarette devices versus e-cigarette liquids was uncertain, thus limiting the ability to assess the impact of child-resistant packaging laws that only apply to e-cigarette liquid containers. Although calls to PCCs regarding liquid nicotine exposures have decreased since January 2015, the relationship of this decline with child-resistant packaging legislation is only an association; there are many other factors that may have influenced exposures and call rates. Despite these limitations, the NPDS is a comprehensive data source useful for investigating liquid nicotine exposures in the United States.

CONCLUSIONS

Liquid nicotine can pose a serious poisoning risk for young children. The frequency of liquid nicotine exposures among children <6 years old has decreased since January 2015, which may, in part, be attributable to adoption of child-resistant packaging laws for liquid nicotine containers and greater public awareness of the risks associated with these products. Additional measures, including child-resistant e-cigarette devices, use of flow restrictors on liquid nicotine containers, and regulations on e-cigarette liquid flavoring, labeling, and concentrations, could further reduce the incidence of these exposures and the likelihood of serious medical outcomes when exposures do occur.

ABBREVIATIONS

AAPCC: American Association of Poison Control Centers
e-cigarette: electronic cigarette
FDA: Food and Drug Administration
NPDS: National Poison Data System
PCC: poison control center

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