Reporting Rates of Liquid Laundry Detergent Packet Exposures Reported to the National Poison Data System (NPDS): Transition Period Data Surveillance

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SIGNATURE PAGE

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EXECUTIVE SUMMARY

Key Findings:

During the transition period (01 July 2013 to 31 December 2016) of implementation of the American Society for Testing and Materials (ASTM) standards to reduce unintentional exposures to liquid laundry detergent packets in children, 43,507 unintentional-general exposures in children <6 years of age involving liquid laundry detergent packets were reported to the National Poison Data System (NPDS).

- Most (90.0%) exposures involved children <4 years of age (42.6% in children <2 years of age; 47.4% in children 2 to <4 years of age).
- Stratifications were done by level of severity to explore factors associated with clinically significant outcomes:
  - 38.7% of exposures involved healthcare facility (HCF) treatment, 3.7% involved HCF admission, and 0.3% involved a severe medical outcome (major effect or death).
- The vast majority (88.6%) of exposures involved oral route of ingestion, but exposures resulting in severe medical outcomes more commonly reported aspiration (14.6% in severe medical outcomes; 0.3% in all exposures) of the liquid laundry detergent packet.
- Contributing factors (scenarios) associated with exposures most commonly referred to improper storage of the liquid laundry detergent packet.
- Cumulative rates and trends over time were explored using both population and sales data adjusted rates and are summarized in the following table.
  - During the transition period, sales-adjusted rates of exposures appeared to be decreasing over time.

Type of Exposure Rate	Cumulative Population-Adjusted Rate[a]	Population-Adjusted Seasonal Rate[a] Range (First and Last Quarterly Peak)	Cumulative Sales-Adjusted Rate[b]	Sales-Adjusted Seasonal Rate[b] Range (First and Last Four Week Interval Peak)
All Exposures	**181.705** (CI 180.006, 183.420)	**14.312** (CI 13.836, 14.796) *2014Q3* to **15.035** (CI 14.548, 15.530) *2016Q2*	**3.511** (CI 3.478, 3.544)	**4.582** (CI 4.311, 4.861) *21 June 2014* to **3.695** (CI 3.487, 3.910) *21 May 2016*
Healthcare Facility Treatment	**70.290** (CI 69.236, 71.360)	**6.082** (CI 5.774, 6.399) *2014Q3* to **5.379** (CI 5.089, 5.676) *2016Q2*	**1.359** (CI 1.339, 1.380)	**1.990** (CI 1.813, 2.176) *21 June 2014* to **1.345** (CI 1.221, 1.475) *21 May 2016*
Healthcare Facility Admission	**6.770** (CI 6.448, 7.108)	**0.699** (CI 0.597, 0.809) *2014Q2* to **0.413** (CI 0.336, 0.498) *2016Q3*	**0.131** (CI 0.125, 0.138)	*No seasonal trend apparent*
Severe Medical Outcome	**0.543** (CI 0.457, 0.645)	*No seasonal trend apparent*	**0.010** (CI 0.009, 0.012)	*No seasonal trend apparent*

[a] *Rate per 100,000 US children <6 years of age and 95% Confidence Interval (CI).*
[b] *Rate per 1,000,000 packets sold and 95% Confidence Interval (CI).*

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BACKGROUND

In late 2015, voluntary standards were created by the American Society for Testing and Materials (ASTM) to help reduce unintentional exposures to liquid laundry detergent packets in children. These changes included requirements for an aversive agent, opaque packaging, packaging that is difficult to open by children, warning statements about the dangers of putting liquid laundry detergent packets in the mouth, and that liquid laundry detergent packets should be kept away from children[1]. As with all safety interventions, it is important to measure the impact of effectiveness of such changes. An evaluation model has been proposed by comparing characteristics and rates of National Poison Data System (NPDS) exposures to liquid laundry detergent packets in the period prior to the implementation of ASTM standards (baseline) to the period after full implementation of the standards (post). This report describes characteristics and rates of NPDS exposures reported in the transition period, which represents the period between the baseline and post periods and includes adoption of some of the ASTM safety standards.

OBJECTIVE

The objective of this report is to describe exposures to liquid laundry detergent packets reported to the National Poison Data System (NPDS) between 01 July 2013 and 31 December 2016 to establish a safety profile of the transition period towards implementation of the voluntary ASTM standards:

1) Describe demographics, exposure characteristics, and associated outcomes of NPDS exposures to liquid laundry detergent packets.
2) Describe cumulative rates of all liquid laundry detergent packet exposures and liquid laundry detergent packet exposures associated with clinically significant outcomes.
3) Describe trends over time in rates of all liquid laundry detergent packet exposures and liquid laundry detergent packet exposures associated with clinically significant outcomes.

METHODS

Through work with the ASTM Laundry Packets Data team, the baseline period was defined as 01 July 2012 to 30 June 2013, the transition period was defined as 01 July 2013 to 31 December 2016, and the post period was defined as 01 January 2017 to 31 December 2017. These periods were determined based on the availability of data and in relation to the period of implementation of the ASTM standards. This report will focus on the transition period. The baseline report was completed on 06 October 2017 and the post period evaluation report will be completed after all data have been received.

Data Sources

National Poison Data System (NPDS)
The National Poison Data System (NPDS) is the data repository for the regional poison centers of the American Association of Poison Control Centers (AAPCC). AAPCC member centers offer coverage for the entire United States, providing free medical management services to both healthcare professionals and the general public. Exposure information is collected using a standardized coding system and database. These patient data are auto-uploaded in real time from the member poison centers to the NPDS. An exposure is defined as an actual or suspected contact with any substance which has been ingested, inhaled, absorbed, applied to, or injected into the body, regardless of toxicity or clinical manifestation. For the purposes of this report an exposure represents one unique case.

The NPDS database consists of categorical variables, which capture patient demographics, exposure details (including exposure reason, chronicity, and products involved), medical outcome, clinical effects, therapies, and scenario information. The NPDS definitions associated with these variables are outlined in Appendix A.

The NPDS was searched to identify human exposures from 01 July 2013 through 31 December 2016 to liquid laundry detergent packets. Cases that were confirmed later to be non-exposures were excluded. Exposures involving children <6 years of age with the NPDS exposure reason of unintentional-general were included. The exposure reason of unintentional-general is the reason code reserved for unintended exposures to substances not for a specific reason[2].

US Census Data
Quarterly population counts for children <6 years of age were obtained to generate population-adjusted rates of exposures[3] for the quarter corresponding to the start of the transition period.

The 2017 model of the US Census Bureau's monthly postcensal resident population estimates were averaged for each quarter to generate estimates. For the cumulative population, the monthly estimates were averaged over the entire time period to generate an overall population estimate.

Nielsen Sales Data
Sales data reported by Nielsen through its Strategic Planner Service for the Liquid Laundry Packs category were obtained in four week intervals and used to generate sales-adjusted exposure rates. Because sales data are received in four week increments, the intervals do not align perfectly with the transition period calendar dates (01 July 2013 to 31 December 2016). In order to capture the entire transition period, sales-adjusted rates of exposure were calculated using exposures and sales starting with the four week interval beginning 23 June 2013 and ending with the four week interval ending 31 December 2016. Furthermore, selection of the transition period start date of 23 June 2013 provides continuous sales-adjusted rate analysis without overlap as sales-adjusted rates were provided through the four week interval ending 22 June 2013 for the baseline report. The 23 June 2013 start date was applied only to the evaluation of sales-adjusted rates of exposure.

Data Analysis

National Poison Data System Summary
Descriptive statistics were used to describe the variables of interest for all unintentional-general exposures in children <6 years of age. Variables described included demographics, exposure characteristics, level of healthcare facility (HCF) treatment, medical outcome, clinical effects, therapies, and scenarios (Appendix A). For this summary, related clinical effects and performed therapies were described.

Additional subanalyses were performed for exposures involving clinically significant outcomes: exposures involving HCF treatment (level of HCF treatment: treated/evaluated and released, admitted to non-critical care unit, admitted to critical care unit, admitted to psychiatric care facility), exposures involving HCF admission (level of HCF treatment: admitted to non-critical care unit, admitted to critical care unit, admitted to psychiatric care facility), and exposures with severe medical outcomes (medical outcome: major effect and death). Importantly, these stratifications are not mutually exclusive as they are composite groupings of progressing levels of severity of treatment and/or medical outcome, and a single case may exist in all or just one of the stratifications.

National Poison Data System Fatality Summary
Fatality information for direct deaths is summarized in aggregate and on a case level. Each direct death fatality abstract was evaluated and summarized on a case-level for year, age, gender, reason for exposure, route, substances involved, relative contribution of the liquid laundry detergent packet to the fatality (Appendix B), cause rank of each substance (if applicable), autopsy results, and other relative details reported in the case record narratives.[2]

Cumulative and Trends Over Time Rates Summary
US Census data were used to calculate population-adjusted rates of exposures per 100,000 children <6 years of age. Nielsen sales data were used to calculate reported exposure rates per 1 million units (i.e., packets) sold. Exposure rates and corresponding 95% confidence intervals were calculated utilizing a log-linear Poisson regression model.

Rates were calculated both cumulatively for the entire transition period and for each time point. For all rate calculations, the average of the monthly population estimates was used and the total of sales was used. For population-adjusted rates, cumulative and quarterly rates were generated corresponding to the calendar dates of the transition period (01 July 2013 to 31 December 2016) in accordance with the availability of US Census data. Sales-adjusted rates were calculated cumulatively for the period of 23 June 2013 to 31 December 2016 and by four week intervals in accordance with the availability of the Nielsen sales data. All calculations and analyses were done in SAS, version 9.4 (SAS Institute,
Cary, NC, USA).

RESULTS

National Poison Data System (NPDS) Summary

A total of 43,507 unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age were reported to the National Poison Data System (NPDS) from 01 July 2013 to 31 December 2016. The median age of patients was 2.0 years, with 90.0% involving a child <4 years of age. The slight majority (51.9%) of patients was male (Table 1).

Stratifications were also done by the level of treatment and medical outcome involved, with 38.7% (n=16,830) of exposures involving healthcare facility (HCF) treatment, 3.7% (n=1,621) involving HCF admission, and 0.3% (n=130) involving a severe medical outcome (major effect or death). The median age of patients differed slightly by level of treatment and medical outcome (all exposures (2.0 years); exposures involving HCF treatment (2.0 years); exposures involving HCF admission (1.4 years); exposures with severe medical outcomes (1.5 years)), and the percentage of exposures involving children <2 years of age increased with increasing severity of exposures (all exposures (42.6%); exposures involving HCF treatment (49.5%); exposures involving HCF admission (67.2%); exposures with severe medical outcomes (69.2%)). Exposures with severe medical outcomes were also more likely to involve male children (62.3%) compared to the other levels of treatment and medical outcome stratifications (all exposures (51.9%); exposures involving HCF treatment (52.1%); exposures involving HCF admission (53.1%); Table 1).

Table 1. Demographics of All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Characteristics	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Age				
Mean (SD), years	2.1 (0.99)	1.9 (0.98)	1.6 (0.86)	1.7 (0.92)
Median, years	2.0	2.0	1.4	1.5
Age (categorical)				
<2 years	18,541 (42.6%)	8,337 (49.5%)	1,089 (67.2%)	90 (69.2%)
2 to <4 years	20,633 (47.4%)	7,029 (41.8%)	462 (28.5%)	34 (26.2%)
4 to <6 years	4,231 (9.7%)	1,432 (8.5%)	67 (4.1%)	6 (4.6%)
≤5 years	102 (0.2%)	32 (0.2%)	3 (0.2%)	0 (0.0%)
Gender				
Female	20,839 (47.9%)	8,048 (47.8%)	758 (46.8%)	49 (37.7%)
Male	22,600 (51.9%)	8,767 (52.1%)	860 (53.1%)	81 (62.3%)
Unknown	68 (0.2%)	15 (0.1%)	3 (0.2%)	0 (0.0%)

[a]*All exposures includes unintentional-general exposures in children <6 years of age.*

The majority (96.0%) of all unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age occurred at the patient's own residence, which did not differ by level of treatment or medical outcome stratification (Table 2).

Ingestion was the most common (88.6%) route of exposure followed by ocular (15.2%) and dermal (11.9%) exposures. Exposures with severe medical outcomes were more likely to involve aspiration (14.6%) than the other stratifications (all exposures (0.3%); exposures involving HCF treatment (0.8%); exposures involving HCF admission (4.1%); Table 2). A greater percentage (20.9%) of exposures involving HCF treatment involved an ocular route than all exposures (15.2%), exposures with severe medical outcomes (18.5%), and exposures involving HCF admission (5.7%). An acute exposure of one substance was most commonly (99.8%) reported, which did not vary by level of treatment or medical outcome stratification (Table 2).

Table 2. Exposure Characteristics of All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Characteristics	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Exposure Site				
Own Residence	41,786 (96.0%)	16,230 (96.4%)	1,555 (95.9%)	123 (94.6%)
Other Residence	1,249 (2.9%)	398 (2.4%)	35 (2.2%)	3 (2.3%)
Workplace	14 (<0.1%)	6 (<0.1%)	1 (0.1%)	0 (0.0%)
Health Care Facility	19 (<0.1%)	15 (0.1%)	4 (0.2%)	0 (0.0%)
School	23 (0.1%)	11 (0.1%)	0 (0.0%)	0 (0.0%)
Other	354 (0.8%)	144 (0.9%)	22 (1.4%)	4 (3.1%)
Unknown	62 (0.1%)	26 (0.2%)	4 (0.2%)	0 (0.0%)
Route of Exposure[b]				
Ingestion	38,560 (88.6%)	14,312 (85.0%)	1,582 (97.6%)	113 (86.9%)
Aspiration (with ingestion)	146 (0.3%)	128 (0.8%)	67 (4.1%)	19 (14.6%)
Inhalation/Nasal	154 (0.4%)	69 (0.4%)	6 (0.4%)	1 (0.8%)
Ocular	6,626 (15.2%)	3,515 (20.9%)	92 (5.7%)	24 (18.5%)
Dermal	5,191 (11.9%)	1,651 (9.8%)	90 (5.6%)	14 (10.8%)
Parenteral	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	14 (<0.1%)	4 (<0.1%)	0 (0.0%)	0 (0.0%)
Unknown	16 (<0.1%)	6 (<0.1%)	1 (0.1%)	0 (0.0%)
Chronicity				
Acute	43,419 (99.8%)	16,782 (99.7%)	1,615 (99.6%)	129 (99.2%)
Acute-on-chronic	69 (0.2%)	38 (0.2%)	5 (0.3%)	1 (0.8%)
Chronic	10 (<0.1%)	5 (<0.1%)	0 (0.0%)	0 (0.0%)
Unknown	9 (<0.1%)	5 (<0.1%)	1 (0.1%)	0 (0.0%)
Number of Substances				

Characteristics	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Mean (SD)	1.0 (0.16)	1.0 (0.15)	1.0 (0.19)	1.1 (0.27)
Median	1.0	1.0	1.0	1.0

[a]*All exposures includes unintentional-general exposures in children <6 years of age.*
[b]*A single exposure may involve more than one route.*

Slightly less than half (44.2%) of all unintentional-general exposures involving laundry detergent packets in children <6 years of age were recommended to or received HCF treatment. Of those that received HCF treatment (n=16,830), 90.4% were treated without being admitted, while 9.6% were admitted to a non-critical or critical care unit and <0.1% were admitted to a psychiatric care facility. Of those exposures that resulted in a severe medical outcome (n=130), 99.2% were recommended to or received HCF treatment and 73.6% (n=95/129) were admitted to a HCF (Table 3).

Table 3. Level of Healthcare Facility (HCF) Treatment of All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Characteristics	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Recommended to or Received HCF Treatment				
Yes	19,226 (44.2%)	16,830 (100.0%)	1,621 (100.0%)	129 (99.2%)
No	23,817 (54.7%)	---	---	1 (0.8%)
Unknown	464 (1.1%)	---	---	0 (0.0%)
Level of Treatment[b]				
Treated/evaluated and released	15,209 (79.1%)	15,209 (90.4%)	---	30 (23.3%)
Admitted to non-critical care unit	1,005 (5.2%)	1,005 (6.0%)	1,005 (62.0%)	13 (10.1%)
Admitted to critical care unit	612 (3.2%)	612 (3.6%)	612 (37.8%)	81 (62.8%)
Admitted to psychiatric care facility	4 (<0.1%)	4 (<0.1%)	4 (0.2%)	1 (0.8%)
Patient refused referral/did not arrive at HCF	685 (3.6%)	---	---	0 (0.0%)
Patient lost to follow-up/left AMA	1,711 (8.9%)	---	---	4 (3.1%)

[a] *All exposures includes unintentional-general exposures in children <6 years of age.*
[b] *Demoninator is the number of exposures that were recommended to or received healthcare facility treatment.*

The majority (73.9%) of all unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of ages were followed to a known outcome. Approximately half (48.1%) of exposures involved a minor effect, followed by no or unrelated effect (19.5%), moderate effect (6.0%), and major effect (0.3%; Table 4). Two deaths (<0.1%) were reported and are summarized in a subsequent section (Table 4).

Table 4. Medical Outcome of All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Medical Outcome	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Followed to a Known Outcome	**32,169 (73.9%)**	**15,635 (92.9%)**	**1,571 (96.9%)**	**130 (100.0%)**
Death	2 (<0.1%)	2 (<0.1%)	2 (0.1%)	2 (1.5%)
Major Effect	128 (0.3%)	123 (0.7%)	93 (5.7%)	128 (98.5%)
Moderate Effect	2,611 (6.0%)	2,288 (13.6%)	611 (37.7%)	---
Minor Effect	20,945 (48.1%)	11,247 (66.8%)	785 (48.4%)	---
No Effect or Unrelated Effect	8,483 (19.5%)	1,975 (11.7%)	80 (4.9%)	---
Not Followed to Known Outcome	**11,338 (26.1%)**	**1,195 (7.1%)**	**50 (3.1%)**	**---**
Unable to follow, potentially toxic	2,121 (4.9%)	188 (1.1%)	28 (1.7%)	---
Not followed, non-toxic	652 (1.5%)	24 (0.1%)	1 (0.1%)	---
Not followed, minimal clinical effects expected	8,565 (19.7%)	983 (5.8%)	21 (1.3%)	---

[a]*All exposures includes unintentional-general exposures in children <6 years of age.*

A total of 85 unique clinical effects were reported, with the 30 most common related clinical effects presented in Table 5 (full listing of related clinical effects presented in Appendix C). Vomiting was the most commonly (42.7%) reported clinical effect among all unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age. Vomiting was also the most common clinical effect among exposures involving HCF treatment (58.1%), HCF admission (78.9%), and severe medical outcomes (66.2%). Drowsiness/lethargy, dyspnea, tachycardia, and respiratory depression were each reported in <5% of all exposures, but increased in frequency with increasing severity of exposures and were each reported in more than 20% of exposures involving severe medical outcomes (Table 5).

Table 5. Top 30 Related Clinical Effects[a] Among all Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Related Clinical Effects	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Vomiting	18,568 (42.7%)	9,777 (58.1%)	1,279 (78.9%)	86 (66.2%)
Ocular - Irritation/pain	5,437 (12.5%)	3,015 (17.9%)	74 (4.6%)	21 (16.2%)
Cough/choke	4,781 (11.0%)	2,562 (15.2%)	517 (31.9%)	46 (35.4%)
Red eye/conjunctivitis	3,335 (7.7%)	2,020 (12.0%)	52 (3.2%)	15 (11.5%)
Drowsiness/lethargy	1,550 (3.6%)	1,274 (7.6%)	328 (20.2%)	40 (30.8%)
Other	1,435 (3.3%)	970 (5.8%)	314 (19.4%)	37 (28.5%)
Nausea	1,405 (3.2%)	782 (4.6%)	122 (7.5%)	9 (6.9%)
Oral irritation	1,086 (2.5%)	440 (2.6%)	101 (6.2%)	4 (3.1%)
Edema	711 (1.6%)	503 (3.0%)	29 (1.8%)	2 (1.5%)
Erythema/flushed	707 (1.6%)	369 (2.2%)	28 (1.7%)	4 (3.1%)
Throat irritation	686 (1.6%)	421 (2.5%)	131 (8.1%)	8 (6.2%)
Lacrimation	663 (1.5%)	455 (2.7%)	9 (0.6%)	5 (3.8%)
Corneal abrasion	626 (1.4%)	604 (3.6%)	23 (1.4%)	4 (3.1%)
Excess secretions	505 (1.2%)	402 (2.4%)	154 (9.5%)	21 (16.2%)
Diarrhea	488 (1.1%)	297 (1.8%)	58 (3.6%)	5 (3.8%)
Dermal - Irritation/pain	437 (1.0%)	217 (1.3%)	5 (0.3%)	2 (1.5%)
Rash	414 (1.0%)	214 (1.3%)	20 (1.2%)	0 (0.0%)
Dyspnea	334 (0.8%)	303 (1.8%)	162 (10.0%)	33 (25.4%)
Abdominal pain	256 (0.6%)	125 (0.7%)	16 (1.0%)	1 (0.8%)
Agitated/irritable	245 (0.6%)	174 (1.0%)	57 (3.5%)	12 (9.2%)
Tachycardia	162 (0.4%)	157 (0.9%)	83 (5.1%)	28 (21.5%)
Bronchospasm	153 (0.4%)	145 (0.9%)	95 (5.9%)	12 (9.2%)

Related Clinical Effects	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Burns	141 (0.3%)	137 (0.8%)	10 (0.6%)	6 (4.6%)
Burns (superficial)	129 (0.3%)	93 (0.6%)	11 (0.7%)	3 (2.3%)
X-ray findings(+)	129 (0.3%)	127 (0.8%)	104 (6.4%)	25 (19.2%)
Hyperventilation/tachypnea	121 (0.3%)	119 (0.7%)	80 (4.9%)	18 (13.8%)
Photophobia	92 (0.2%)	72 (0.4%)	2 (0.1%)	1 (0.8%)
Respiratory depression	72 (0.2%)	72 (0.4%)	62 (3.8%)	29 (22.3%)
Dysphagia	61 (0.1%)	53 (0.3%)	31 (1.9%)	4 (3.1%)
Pallor	51 (0.1%)	37 (0.2%)	15 (0.9%)	4 (3.1%)

[a]*More than one related clinical effect can be reported per exposure.*
[b]*All exposures included unintentional-general exposures in children <6 years of age.*

Dilute/irrigate/wash (74.3%) and food/snack (10.3%) were the most common therapies performed among all unintentional-general exposures involving liquid laundry detergent packets in children <6 years of age. Dilute/irrigate/wash was also the most common therapy performed in exposures involving HCF treatment (69.3%), HCF admission (53.1%), and severe medical outcomes (53.8%). Fluids, IV (30.4%) and oxygen (12.5%) were also commonly performed among exposures involving HCF admission. Among exposures resulting in severe medical outcomes, the most commonly performed therapies following dilute/irrigate/wash were oxygen (50.0%), intubation (43.8%), fluids, IV (40.0%), and ventilator (40.0%; Table 6).

Table 6. Therapies Performed[a] Among All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Performed Therapies	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Dilute/irrigate/wash	32,304 (74.3%)	11,667 (69.3%)	861 (53.1%)	70 (53.8%)
Food/snack	4,477 (10.3%)	1,326 (7.9%)	132 (8.1%)	9 (6.9%)
Other	2,191 (5.0%)	1,218 (7.2%)	306 (18.9%)	37 (28.5%)
Antibiotics	919 (2.1%)	879 (5.2%)	69 (4.3%)	20 (15.4%)
Fluids, IV	731 (1.7%)	722 (4.3%)	493 (30.4%)	52 (40.0%)
Other emetic	728 (1.7%)	310 (1.8%)	37 (2.3%)	2 (1.5%)
Antiemetics	624 (1.4%)	621 (3.7%)	114 (7.0%)	6 (4.6%)
Steroids	244 (0.6%)	229 (1.4%)	108 (6.7%)	19 (14.6%)
Oxygen	240 (0.6%)	239 (1.4%)	202 (12.5%)	65 (50.0%)
Bronchodilators	222 (0.5%)	219 (1.3%)	137 (8.5%)	25 (19.2%)
Antihistamines	151 (0.3%)	111 (0.7%)	17 (1.0%)	0 (0.0%)
Calcium	117 (0.3%)	21 (0.1%)	2 (0.1%)	0 (0.0%)
Intubation	109 (0.3%)	109 (0.6%)	105 (6.5%)	57 (43.8%)
Sedation (other)	101 (0.2%)	101 (0.6%)	68 (4.2%)	33 (25.4%)
Ventilator	98 (0.2%)	98 (0.6%)	95 (5.9%)	52 (40.0%)
Benzodiazepines	51 (0.1%)	51 (0.3%)	31 (1.9%)	18 (13.8%)
Fresh air	22 (0.1%)	6 (<0.1%)	1 (0.1%)	0 (0.0%)
Alkalinization	11 (<0.1%)	11 (0.1%)	11 (0.7%)	8 (6.2%)
Charcoal, single dose	11 (<0.1%)	10 (0.1%)	0 (0.0%)	0 (0.0%)
Neuromuscular blocker	11 (<0.1%)	11 (0.1%)	10 (0.6%)	5 (3.8%)
Vasopressors	9 (<0.1%)	9 (0.1%)	8 (0.5%)	3 (2.3%)
Naloxone	6 (<0.1%)	6 (<0.1%)	4 (0.2%)	1 (0.8%)
Atropine	4 (<0.1%)	4 (<0.1%)	3 (0.2%)	1 (0.8%)

Performed Therapies	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
CPR	3 (<0.1%)	2 (<0.1%)	2 (0.1%)	2 (1.5%)
Cathartic	3 (<0.1%)	2 (<0.1%)	0 (0.0%)	0 (0.0%)
Lavage	3 (<0.1%)	3 (<0.1%)	2 (0.1%)	0 (0.0%)
Glucose, > 5%	2 (<0.1%)	2 (<0.1%)	2 (0.1%)	1 (0.8%)
Anticonvulsants	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Antihypertensives	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Cardioversion	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Fomepizole	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
NAC, IV	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	0 (0.0%)
Octreotide	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	0 (0.0%)

[a]*More than one performed therapy can be reported per exposure.*
[b]*All exposures included unintentional-general exposures in children <6 years of age.*

Table 7 describes the scenarios, or factors that contributed to the event, among unintentional-general exposures involving liquid laundry detergent packets in children <6 years of age. Six percent (5.8%) of all exposures reported one or more scenarios, with the majority involving storage within sight of the child (43.6%), followed by other (unspecified; 22.8%), product temporarily open because it was in use (10.0%), and product stored in unlocked, low cabinet in kitchen or bathroom (7.7%). A slightly higher percentage (7.1%) of exposures involving HCF admission reported one or more scenarios than the other level of treatment and medical outcome stratifications (all exposures (5.8%); exposures involving HCF treatment (6.3%); exposures with severe medical outcomes (3.8%); Table 7). Among all levels of treatment and medical outcome stratifications, stored within sight of child, product temporarily open because it was in use, and stored in unlocked, low cabinet in kitchen or bathroom were the most common scenarios reported.

Table 7. National Poison Data System (NPDS) Scenario of All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Scenario	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Was a Scenario Reported?				
No	40,964 (94.2%)	15,763 (93.7%)	1,506 (92.9%)	125 (96.2%)
Yes	2,543 (5.8%)	1,067 (6.3%)	115 (7.1%)	5 (3.8%)
Scenario[b]				
Stored within sight of child	1,110 (43.6%)	435 (40.8%)	24 (20.9%)	3 (60.0%)
Other	579 (22.8%)	318 (29.8%)	29 (25.2%)	0 (0.0%)
Product temporarily open because product was in use	254 (10.0%)	82 (7.7%)	14 (12.2%)	1 (20.0%)
Stored in unlocked, low cabinet in kitchen or bathroom	196 (7.7%)	70 (6.6%)	23 (20.0%)	0 (0.0%)
Product stored inappropriately (other than above)	152 (6.0%)	61 (5.7%)	9 (7.8%)	1 (20.0%)
Product always left out	119 (4.7%)	52 (4.9%)	4 (3.5%)	1 (20.0%)
Child caused exposure (gave to sibling or pet, etc)	84 (3.3%)	33 (3.1%)	9 (7.8%)	0 (0.0%)
Patient thought product or pill was a food	51 (2.0%)	14 (1.3%)	0 (0.0%)	0 (0.0%)
Scenario unknown (not allowed with other options)	41 (1.6%)	15 (1.4%)	3 (2.6%)	0 (0.0%)
Child or pet accessed medication/product from purse	10 (0.4%)	3 (0.3%)	1 (0.9%)	0 (0.0%)
Patient confused or mentally incompetent	10 (0.4%)	4 (0.4%)	0 (0.0%)	0 (0.0%)
Inadequate decontamination after product use	8 (0.3%)	4 (0.4%)	0 (0.0%)	0 (0.0%)
Container transfer involved	7 (0.3%)	1 (0.1%)	1 (0.9%)	1 (20.0%)
CRC present, opened by patient	4 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Child or pet accessed medication/product from suitcase	4 (0.2%)	1 (0.1%)	0 (0.0%)	0 (0.0%)
Exposure occurred during routine product use	4 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other gas/fume/vapor exposure	3 (0.1%)	1 (0.1%)	0 (0.0%)	0 (0.0%)
No CRC, by purchasers request or choice	2 (0.1%)	2 (0.2%)	0 (0.0%)	0 (0.0%)

Scenario	All Exposures[a] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Unknown CRC Status	2 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CRC present, not secured or closed	1 (<0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other pesticide exposure	1 (<0.1%)	1 (0.1%)	1 (0.9%)	0 (0.0%)

[a]*All exposures includes unintentional-general exposures in children <6 years of age.*
[b]*A single exposure may involve more than one scenario.*

National Poison Data System (NPDS) Fatality Summary

Two fatalities involving an unintentional-general exposure to a liquid laundry detergent packet in a child <6 years of age were reported during the study period (01 July 2013 and 31 December 2016). Both fatalities occurred in 2013. Both fatalities involved ingestion of the liquid laundry detergent packet, one in a 7 month old male and the other in a 16 month old male. The exposure was determined to be undoubtedly responsible for the 7 month old's fatality and unknown for the 16 month old's fatality. For the 16 month old, the detergent bag showed chewing marks. The 7 month old's ingestion was witnessed (Table 8).

Table 8. Case Characteristics of Fatalities Involving Liquid Laundry Detergent Packets

Year	Age, Gender	Exposure Reason; Route	Chronicity	Products or Substances Involved (Cause Rank, if applicable)	Relative Contribution of Exposure to Fatality	Autopsy Findings (if applicable) and Other Details Reported	Additional Information Reported in Case Notes
2013[4]	7 Month, Male	Unintentional – General; Ingestion	Acute	Laundry Detergents: Liquid (unit dose)	Undoubtedly Responsible	• Mild hyperemia of the oropharynx and trachea without evident burns or ulcerations • Significant asymmetric pulmonary congestion on right and some cerebral edema • UDS negative • Central post-mortem blood: propylene glycol of 33 mg/dl • Gastric contents: propylene glycol of 370 mg/dL	• Bit into laundry detergent packet and contents entered his mouth • Immediately experienced cough with increased somnolence then vomiting and seizure in route to the emergency department • Experienced cardiac arrest 3 hours after exposure and could not be resuscitated

Year	Age, Gender	Exposure Reason; Route	Chronicity	Products or Substances Involved (Cause Rank, if applicable)	Relative Contribution of Exposure to Fatality	Autopsy Findings (if applicable) and Other Details Reported	Additional Information Reported in Case Notes
2013	16 Month, Male	Unintentional – General; Ingestion	Acute	Laundry Detergents: Liquids (unit dose)	Unknown	• Initial skull x-ray showed occipital fracture that was later determined to be suture line • Severe cerebral edema and hemorrhage around suture line • Epidural hemorrhage most likely due to edema	• Ingestion not witnessed; thought to have "popped the plastic" of the laundry detergent packet and "ingested the fluid within" • Immediately vomited then another round of vomiting 30 minutes later with progressive lethargy • Developed cardiac arrest upon paramedic arrival and remained unresponsive • Brain flow study 3 days after exposure showed brain death and was pronounced dead • Active Division of Child Protection and Permanency case

Population-Adjusted Rates Summary

Cumulative Population-Adjusted Rates of All Exposures and Exposures with Clinically Significant Outcomes

The population-adjusted rate of reported unintentional-general exposures involving a liquid laundry detergent packet from 01 July 2013 to 31 December 2016 was 181.705 exposures per 100,000 US children <6 years of age (CI 180.006, 183.420; Table 9). This equates to one exposure per every 550 US children <6 years of age.

Table 9. Cumulative Population-Adjusted Rates of All Exposures

Numerator/Denominator	Count	Cumulative Rate of All Exposures per 100,000 Children <6 Years of Age (95% CI)
All Exposures	43,507	**181.705 (180.006, 183.420)**
Total Population	23,943,755	

The population-adjusted rate of reported exposures to a liquid laundry detergent packet that involved HCF treatment during the transition period was 70.290 per 100,000 US children <6 years of age (CI 69.236, 71.360; Table 10). This equates to one HCF treatment per every 1,423 US children <6 years of age. The population-adjusted rate of reported exposures to a liquid laundry detergent packet that involved HCF admission during the transition period was 6.770 per 100,000 US children <6 years of age (CI 6.448, 7.108; Table 11). This equates to one HCF admission per every 14,771 US children <6 years of age. The population-adjusted rate of reported exposures to a liquid laundry detergent packet involving severe medical outcomes during the transition period was 0.543 per 100,000 US children <6 years of age (CI 0.457, 0.645; Table 12). This equates to one severe medical outcome per every 184,162 US children <6 years of age.

Table 10. Cumulative Population-Adjusted Rates of Exposures Involving HCF Treatment

Numerator/Denominator	Count	Cumulative Rate of Exposures Involving HCF Treatment per 100,000 Children <6 Years of Age (95% CI)
Exposures Involving HCF Treatment	16,830	**70.290 (69.236, 71.360)**
Total Population	23,943,755	

Table 11. Cumulative Population-Adjusted Rates of Exposures Involving HCF Admission

Numerator/Denominator	Count	Cumulative Rate of Exposures Involving HCF Admission per 100,000 Children <6 Years of Age (95% CI)
Exposures Involving HCF Admission	1,621	**6.770 (6.448, 7.108)**
Total Population	23,943,755	

Table 12. Cumulative Population-Adjusted Rates of Exposures Involving Severe Medical Outcomes

Numerator/Denominator	Count	Cumulative Rate of Exposures with Severe Medical Outcomes per 100,000 Children <6 Years of Age (95% CI)
Exposures with Severe Medical Outcomes	130	**0.543 (0.457, 0.645)**
Total Population	23,943,755	

Population-Adjusted Rates of All Exposures Over Time

Over time, counts of unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age fluctuated seasonally with decreases in the fall and winter months (4th and 1st quarters). During the transition period, counts of exposures seemed to be following an upward trend, while the total population of US children <6 years of age remained consistent (Table 13; Figure 1).

In alignment with the seasonality in reported exposures, peak rates were reported during the 2nd or 3rd quarter of each year. Comparing the first seasonal peak in 3rd quarter 2014 with the last seasonal peak of 2nd quarter 2016, the rates were 14.312 exposures per 100,000 US children <6 years of age (CI 13.836, 14.796) and 15.035 exposures per 100,000 US children <6 years of age (CI 14.548, 15.530), respectively. Comparing the first seasonal low point in 4th quarter 2013 with the last seasonal low point of 4th quarter 2016, the rates were 10.169 exposures per 100,000 US children <6 years of age (CI 9.769, 10.577) and 11.621 exposures per 100,000 US children <6 years of age (CI 11.194, 12.057), respectively (Table 13; Figure 2).

Table 13. Population-Adjusted Rates of All Exposures by Quarter (01 July 2013 to 31 December 2016)

Quarter	Exposure Count	Total Population Count	Rates of All Exposures per 100,000 Children <6 Years of Age (95% CI)
2013Q3 (01 July 2013 to 30 September 2013)	2,906	23,968,981	12.124 (11.687, 12.569)
2013Q4 (01 October 2013 to 31 December 2013)	2,436	23,955,652	10.169 (9.769, 10.577)
2014Q1 (01 January 2014 to 31 March 2014)	2,633	23,939,357	10.999 (10.582, 11.423)
2014Q2 (01 April 2014 to 30 June 2014)	3,199	23,894,773	13.388 (12.928, 13.856)
2014Q3 (01 July 2014 to 30 September 2014)	3,419	23,888,650	14.312 (13.836, 14.796)
2014Q4 (01 October 2014 to 31 December 2014)	2,914	23,909,828	12.187 (11.749, 12.634)
2015Q1 (01 January 2015 to 31 March 2015)	2,828	23,930,320	11.818 (11.386, 12.257)
2015Q2 (01 April 2015 to 30 June 2015)	3,451	23,929,371	14.422 (13.944, 14.907)
2015Q3 (01 July 2015 to 30 September 2015)	3,507	23,939,980	14.649 (14.168, 15.138)
2015Q4 (01 October 2015 to 31 December 2015)	3,266	23,971,382	13.625 (13.161, 14.096)
2016Q1 (01 January 2016 to 31 March 2016)	3,019	23,982,978	12.588 (12.143, 13.041)
2016Q2 (01 April 2016 to 30 June 2016)	3,603	23,963,893	15.035 (14.548, 15.530)
2016Q3 (01 July 2016 to 30 September 2016)	3,540	23,964,050	14.772 (14.289, 15.263)
2016Q4 (01 October 2016 to 31 December 2016)	2,786	23,973,356	11.621 (11.194, 12.057)

Figure 1. All Exposures and Population Counts by Quarter (01 July 2013 to 31 December 2016)

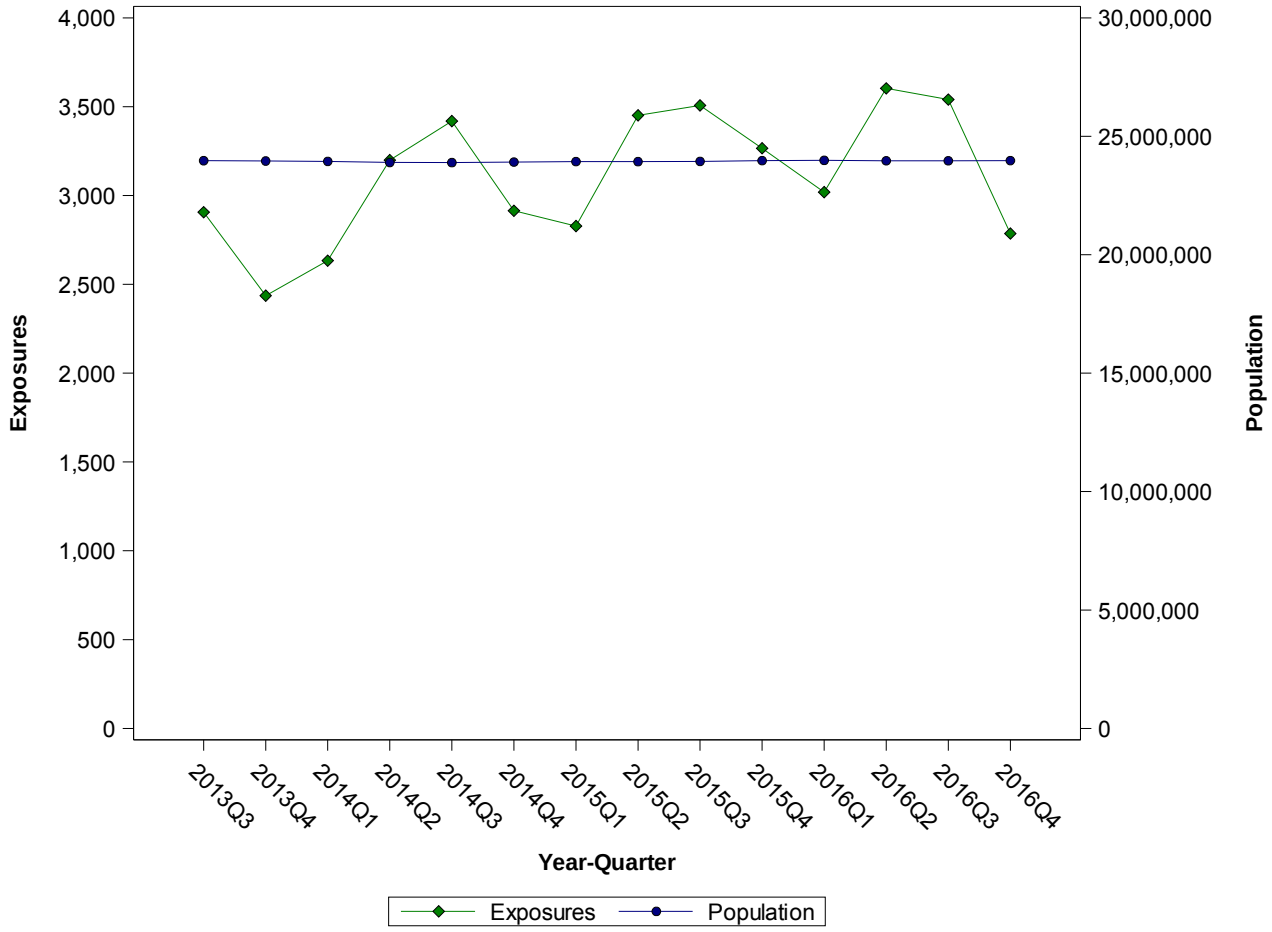
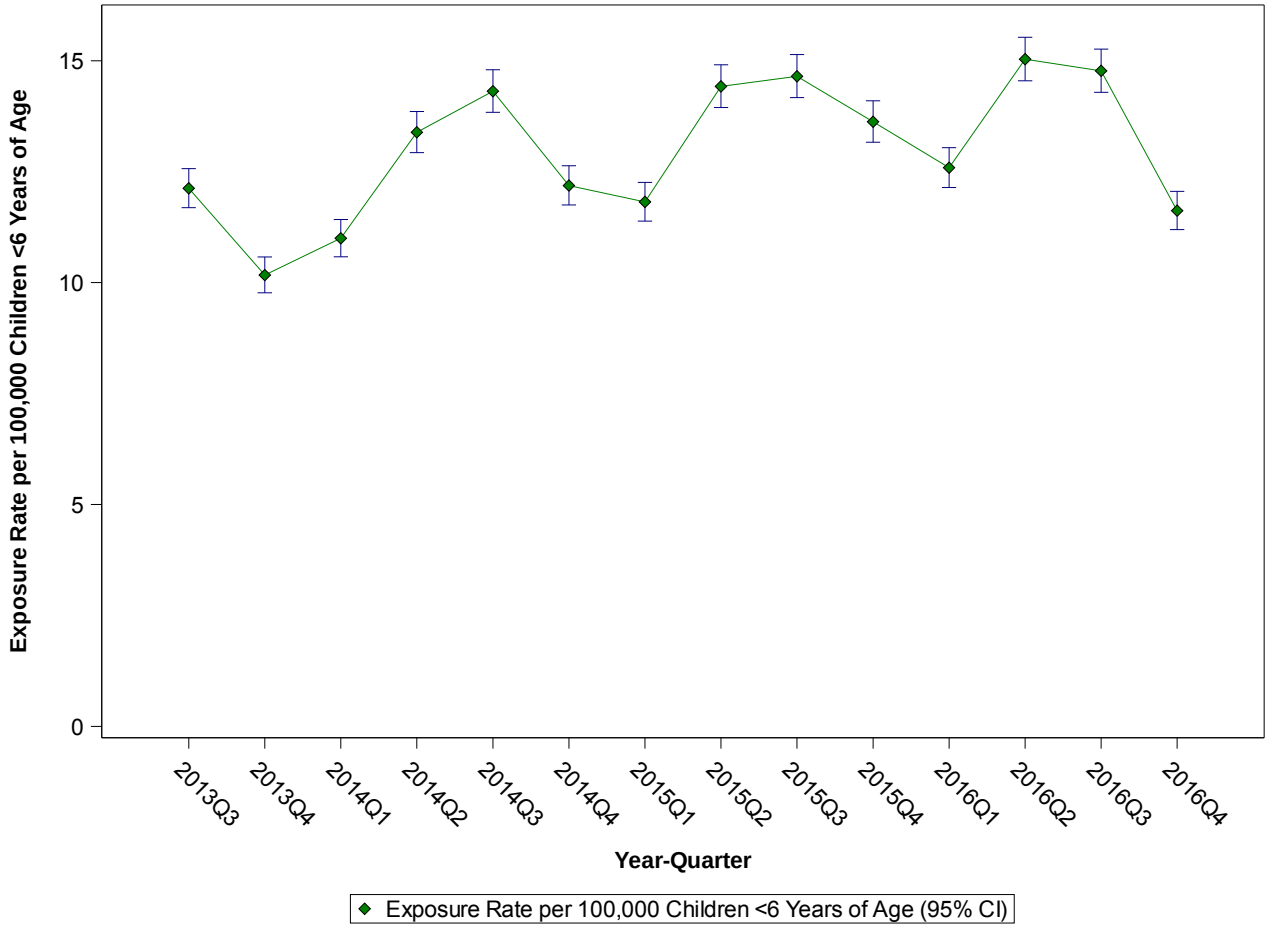


Figure 2. Population-Adjusted Rates of All Exposures by Quarter (01 July 2013 to 31 December 2016)



Population-Adjusted Rates of Exposures with Clinically Significant Outcomes Over Time
Over time, counts of exposures involving HCF treatment fluctuated seasonally in the same pattern as all exposures with decreases in the fall and winter months (4th and 1st quarters), with no apparent increase or decrease in reported exposures over time. During the same time period the total population of US children <6 years of age remained consistent (Table 14; Figure 3).

In alignment with the seasonality in reported exposures involving HCF treatment, peak rates of exposures were reported during the 2nd or 3rd quarter of each year. Comparing the first seasonal peak in 3rd quarter 2014 with the last seasonal peak of 2nd quarter 2016, the rates were 6.082 exposures per 100,000 US children <6 years of age (CI 5.774, 6.399) and 5.379 exposures per 100,000 US children <6 years of age (CI 5.089, 5.676), respectively. Comparing the first seasonal low point in 4th quarter 2013 with the last seasonal low point of 4th quarter 2016, the rates were 4.070 exposures per 100,000 US children <6 years of age (CI 3.819, 4.329) and 4.025 exposures per 100,000 US children <6 years of age (CI 3.775, 4.283), respectively (Table 14; Figure 4).

Table 14. Population-Adjusted Rates of Exposures Involving Healthcare Facility Treatment by Quarter (01 July 2013 to 31 December 2016)

Quarter	Exposure Count	Total Population Count	Rates of Exposures Involving HCF Treatment per 100,000 Children <6 Years of Age (95% CI)
2013Q3 (01 July 2013 to 30 September 2013)	1,119	23,968,981	4.669 (4.399, 4.946)
2013Q4 (01 October 2013 to 31 December 2013)	975	23,955,652	4.070 (3.819, 4.329)
2014Q1 (01 January 2014 to 31 March 2014)	1,068	23,939,357	4.461 (4.198, 4.733)
2014Q2 (01 April 2014 to 30 June 2014)	1,361	23,894,773	5.696 (5.397, 6.002)
2014Q3 (01 July 2014 to 30 September 2014)	1,453	23,888,650	6.082 (5.774, 6.399)
2014Q4 (01 October 2014 to 31 December 2014)	1,146	23,909,828	4.793 (4.519, 5.074)
2015Q1 (01 January 2015 to 31 March 2015)	1,075	23,930,320	4.492 (4.228, 4.765)
2015Q2 (01 April 2015 to 30 June 2015)	1,348	23,929,371	5.633 (5.337, 5.938)
2015Q3 (01 July 2015 to 30 September 2015)	1,396	23,939,980	5.831 (5.529, 6.141)
2015Q4 (01 October 2015 to 31 December 2015)	1,275	23,971,382	5.319 (5.031, 5.615)
2016Q1 (01 January 2016 to 31 March 2016)	1,093	23,982,978	4.557 (4.291, 4.832)
2016Q2 (01 April 2016 to 30 June 2016)	1,289	23,963,893	5.379 (5.089, 5.676)
2016Q3 (01 July 2016 to 30 September 2016)	1,267	23,964,050	5.287 (5.000, 5.582)
2016Q4 (01 October 2016 to 31 December 2016)	965	23,973,356	4.025 (3.775, 4.283)

Figure 3. Exposures Involving Healthcare Facility Treatment and Population Counts by Quarter (01 July 2013 to 31 December 2016)

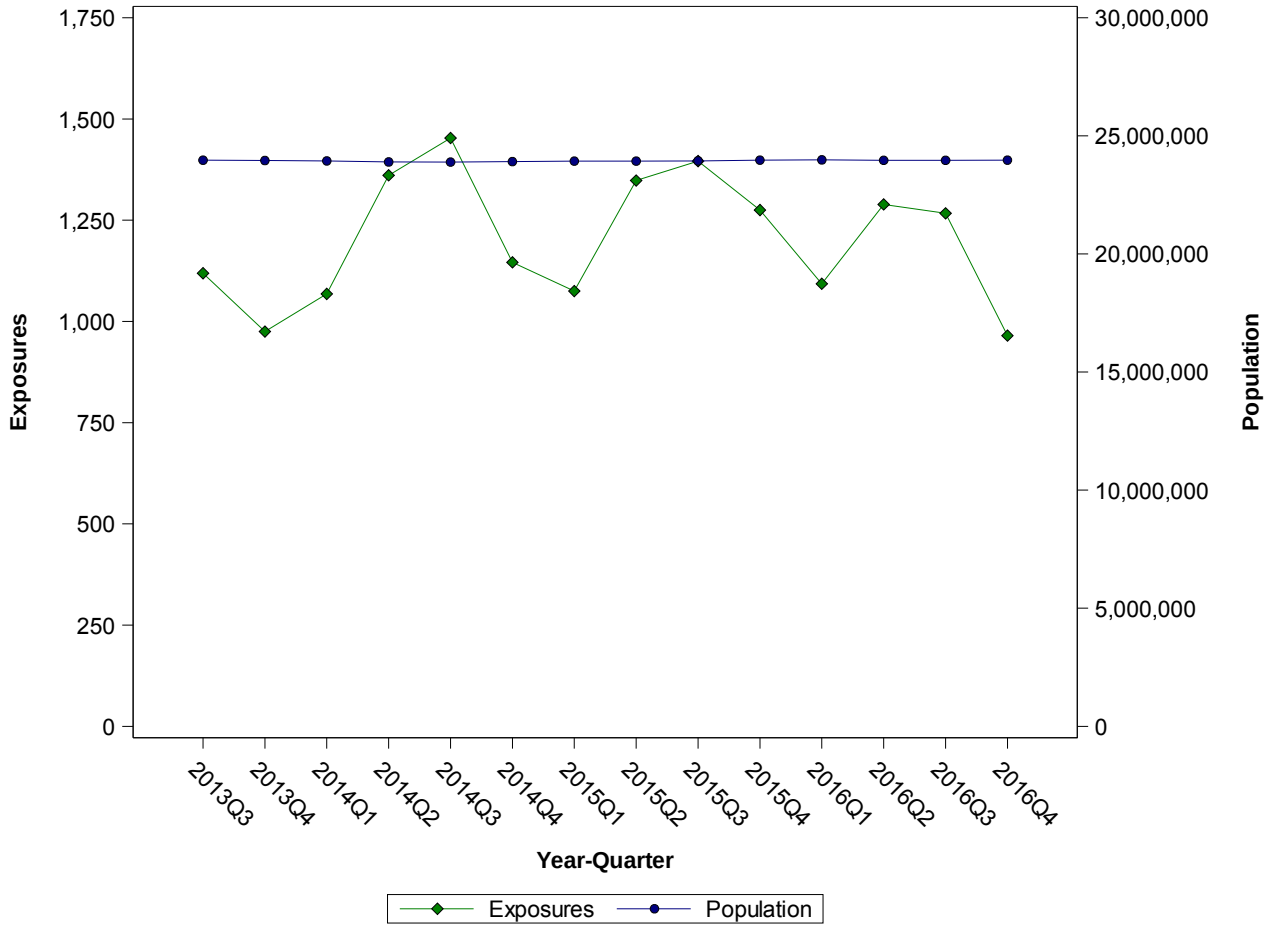
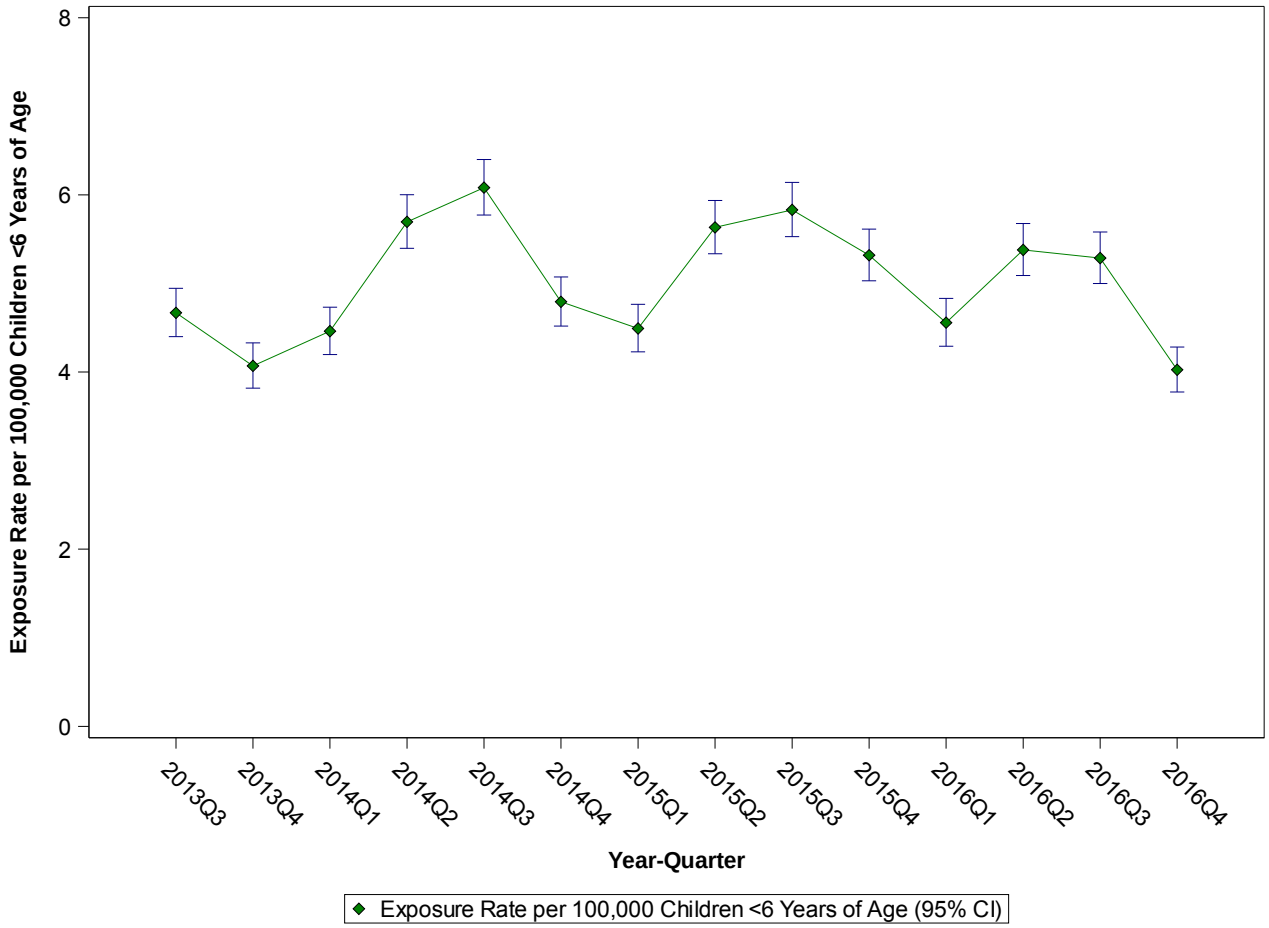


Figure 4. Population-Adjusted Rates of Exposures Involving Healthcare Facility Treatment by Quarter (01 July 2013 to 31 December 2016)



Over time, counts of exposures involving HCF admission fluctuated seasonally in the same pattern as all exposures with decreases in the 4th and 1st quarters but demonstrated a downward trend in reporting frequency over time. During the transition period, the total population of US children <6 years of age remained consistent (Table 15; Figure 5).

In alignment with the seasonality in reported exposures involving HCF admission, peak rates were reported during the 2nd or 3rd quarters of each year. Comparing the first seasonal peak in 2nd quarter 2014, with the last season peak of 3rd quarter 2016 during the transition period, the rates were 0.699 exposures per 100,000 US children <6 years of age (CI 0.597, 0.809) and 0.413 exposures per 100,000 US children <6 years of age (CI 0.336, 0.498), respectively. Comparing the first seasonal low point in in 1st quarter 2015 with the last seasonal low point of 4th quarter 2016, the rates were 0.422 exposures per 100,000 US children <6 years of age (CI 0.344, 0.508) and 0.284 exposures per 100,000 US children <6 years of age (CI 0.220, 0.355), respectively (Table 15; Figure 6).

Table 15. Population-Adjusted Rates of Exposures Involving Healthcare Facility Admission by Quarter (01 July 2013 to 31 December 2016)

Quarter	Exposure Count	Total Population Count	Rates of Exposures Involving HCF Admission per 100,000 Children <6 Years of Age (95% CI)
2013Q3 (01 July 2013 to 30 September 2013)	117	23,968,981	0.488 (0.404, 0.580)
2013Q4 (01 October 2013 to 31 December 2013)	125	23,955,652	0.522 (0.434, 0.617)
2014Q1 (01 January 2014 to 31 March 2014)	139	23,939,357	0.581 (0.488, 0.681)
2014Q2 (01 April 2014 to 30 June 2014)	167	23,894,773	0.699 (0.597, 0.809)
2014Q3 (01 July 2014 to 30 September 2014)	154	23,888,650	0.645 (0.547, 0.750)
2014Q4 (01 October 2014 to 31 December 2014)	125	23,909,828	0.523 (0.435, 0.618)
2015Q1 (01 January 2015 to 31 March 2015)	101	23,930,320	0.422 (0.344, 0.508)
2015Q2 (01 April 2015 to 30 June 2015)	142	23,929,371	0.593 (0.500, 0.695)
2015Q3 (01 July 2015 to 30 September 2015)	120	23,939,980	0.501 (0.416, 0.595)
2015Q4 (01 October 2015 to 31 December 2015)	105	23,971,382	0.438 (0.358, 0.526)
2016Q1 (01 January 2016 to 31 March 2016)	84	23,982,978	0.350 (0.279, 0.429)
2016Q2 (01 April 2016 to 30 June 2016)	75	23,963,893	0.313 (0.246, 0.388)
2016Q3 (01 July 2016 to 30 September 2016)	99	23,964,050	0.413 (0.336, 0.498)
2016Q4 (01 October 2016 to 31 December 2016)	68	23,973,356	0.284 (0.220, 0.355)

Figure 5. Exposures Involving Healthcare Facility Admission and Population Counts by Quarter (01 July 2013 to 31 December 2016)

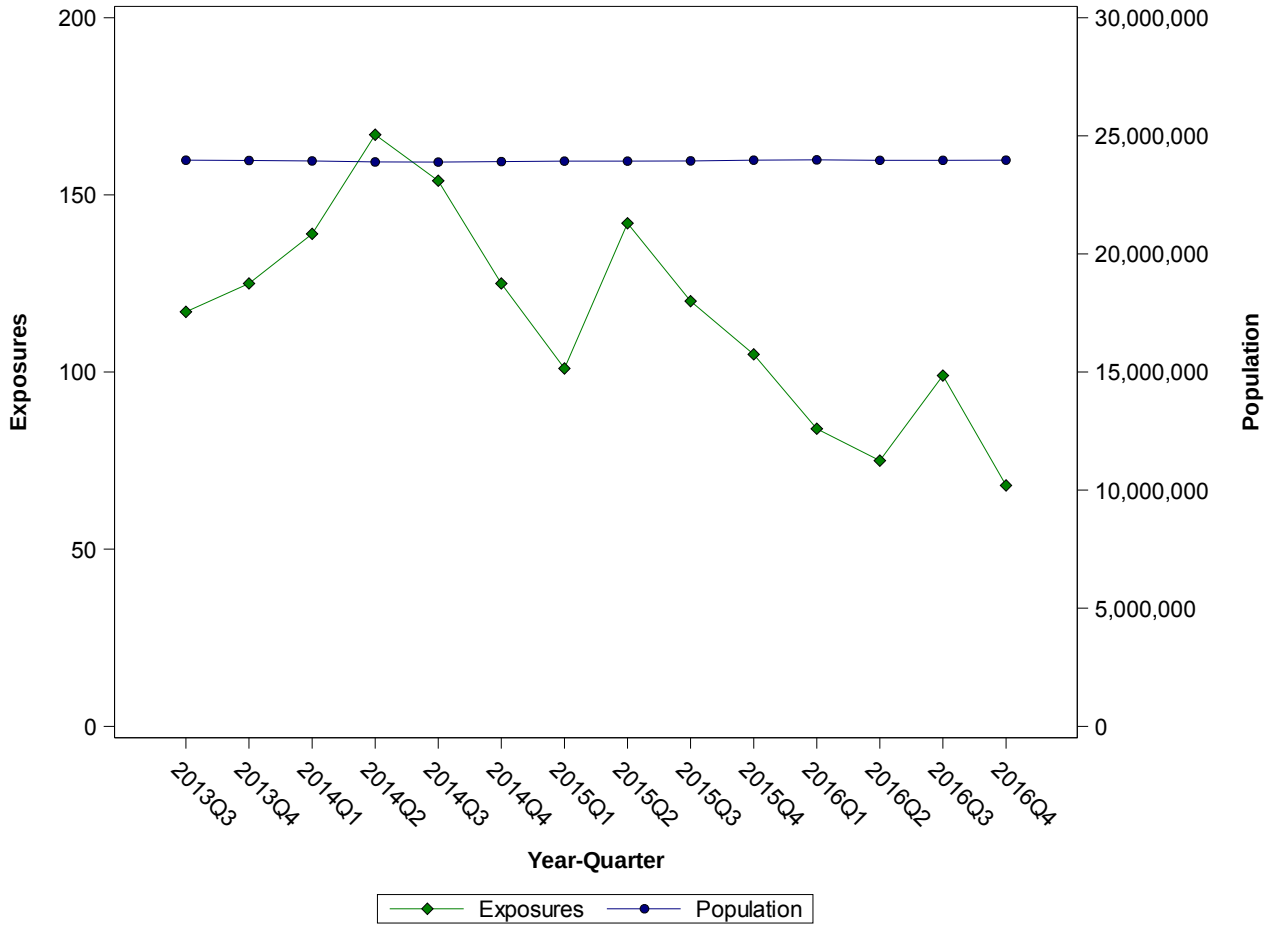
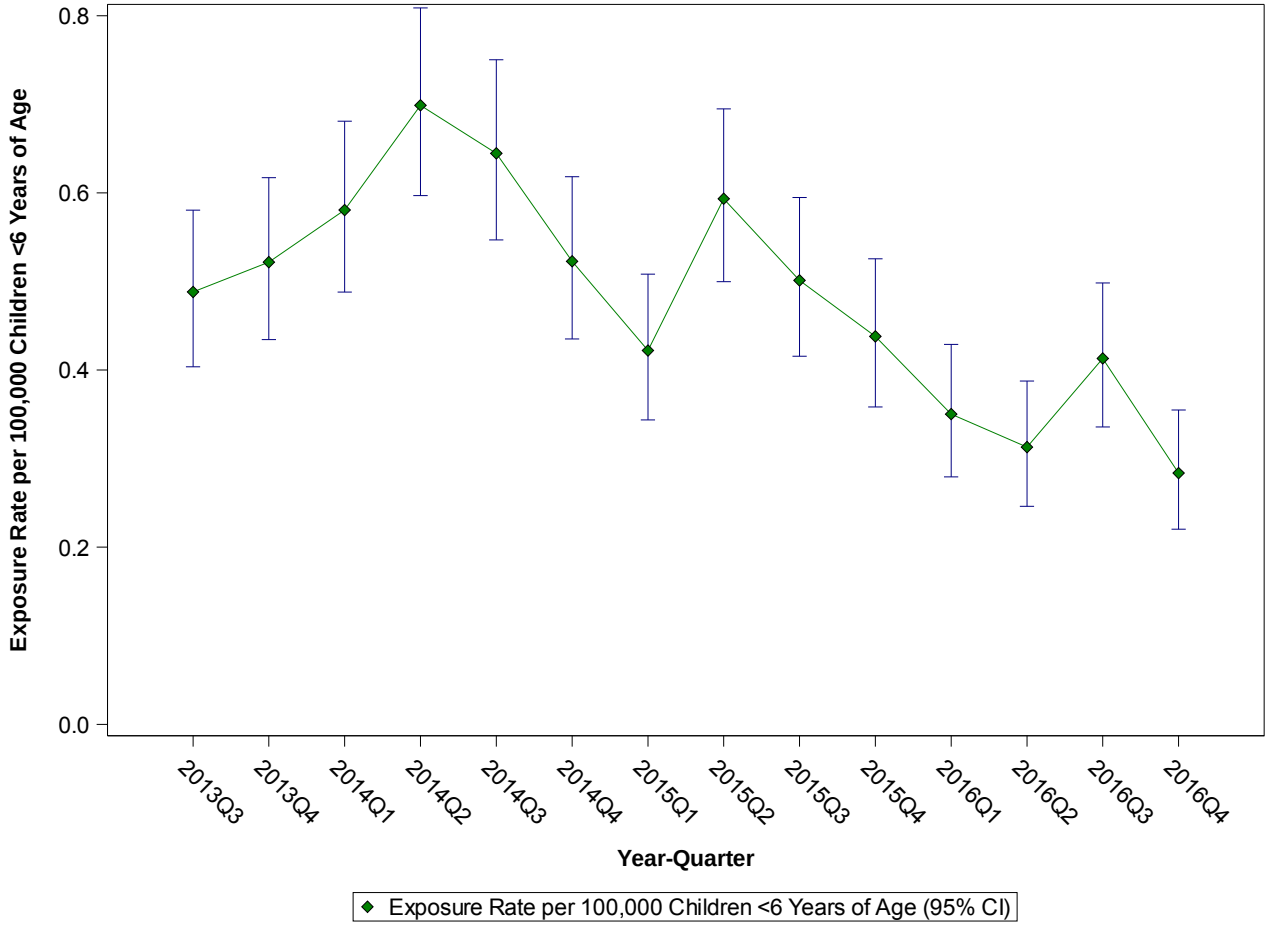


Figure 6. Population-Adjusted Rates of Exposures Involving Healthcare Facility Admission by Quarter (01 July 2013 to 31 December 2016)



Over time, counts of exposures involving severe medical outcomes fluctuated with no apparent seasonal trend but with an overall decrease in reporting frequency. During the same time period the total population of US children <6 years of age remained consistent (Table 16; Figure 7).

The population-adjusted rate of reported exposures involving severe medical outcomes fluctuated from a rate of 0.071 per 100,000 US children <6 years of age (CI 0.041, 0.108) in 3rd quarter 2013 to a rate of 0.013 per 100,000 US children <6 years of age (CI 0.003, 0.030) in 3rd 2016 (Table 16; Figure 8). An apparent downward trend in population-based rates was observed, but due to the low exposure volume and wide confidence intervals, a comparison of peak and low rates during the study period is not appropriate.

Table 16. Population-Adjusted Exposure Rates Resulting in Severe Medical Outcomes by Quarter (01 July 2013 to 31 December 2016)

Quarter	Exposure Count	Total Population Count	Rates of Exposures Resulting in Severe Medical Outcomes per 100,000 Children <6 Years of Age (95% CI)
2013Q3 (01 July 2013 to 30 September 2013)	17	23,968,981	0.071 (0.041, 0.108)
2013Q4 (01 October 2013 to 31 December 2013)	10	23,955,652	0.042 (0.020, 0.071)
2014Q1 (01 January 2014 to 31 March 2014)	11	23,939,357	0.046 (0.023, 0.077)
2014Q2 (01 April 2014 to 30 June 2014)	16	23,894,773	0.067 (0.038, 0.104)
2014Q3 (01 July 2014 to 30 September 2014)	18	23,888,650	0.075 (0.045, 0.114)
2014Q4 (01 October 2014 to 31 December 2014)	11	23,909,828	0.046 (0.023, 0.077)
2015Q1 (01 January 2015 to 31 March 2015)	10	23,930,320	0.042 (0.020, 0.071)
2015Q2 (01 April 2015 to 30 June 2015)	8	23,929,371	0.033 (0.014, 0.060)
2015Q3 (01 July 2015 to 30 September 2015)	9	23,939,980	0.038 (0.017, 0.066)
2015Q4 (01 October 2015 to 31 December 2015)	4	23,971,382	0.017 (0.005, 0.037)
2016Q1 (01 January 2016 to 31 March 2016)	4	23,982,978	0.017 (0.005, 0.037)
2016Q2 (01 April 2016 to 30 June 2016)	4	23,963,893	0.017 (0.005, 0.037)
2016Q3 (01 July 2016 to 30 September 2016)	3	23,964,050	0.013 (0.003, 0.030)
2016Q4 (01 October 2016 to 31 December 2016)	5	23,973,356	0.021 (0.007, 0.043)

Figure 7. Exposures Resulting in Severe Medical Outcomes and Population Counts by Quarter (01 July 2013 to 31 December 2016)

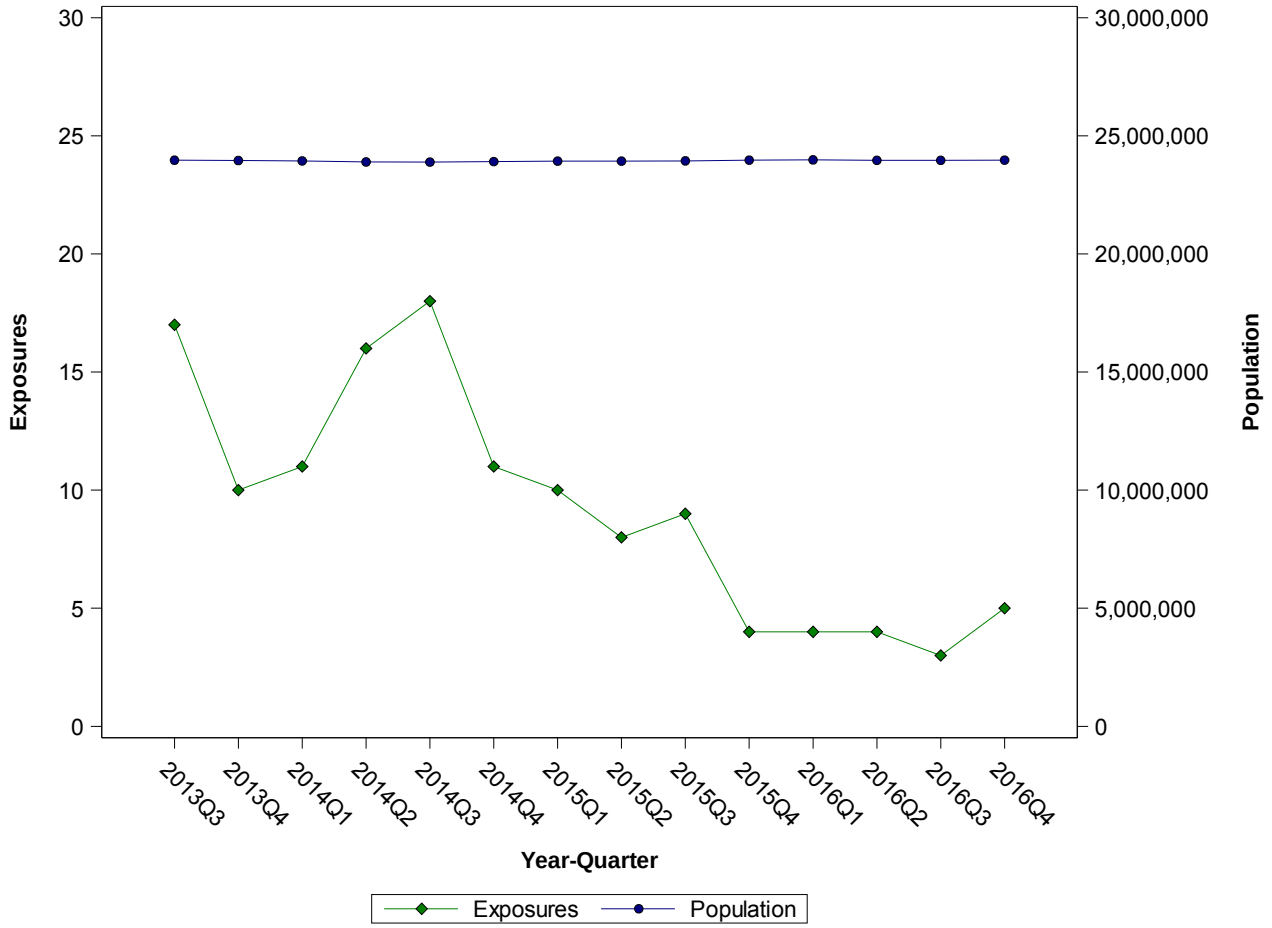
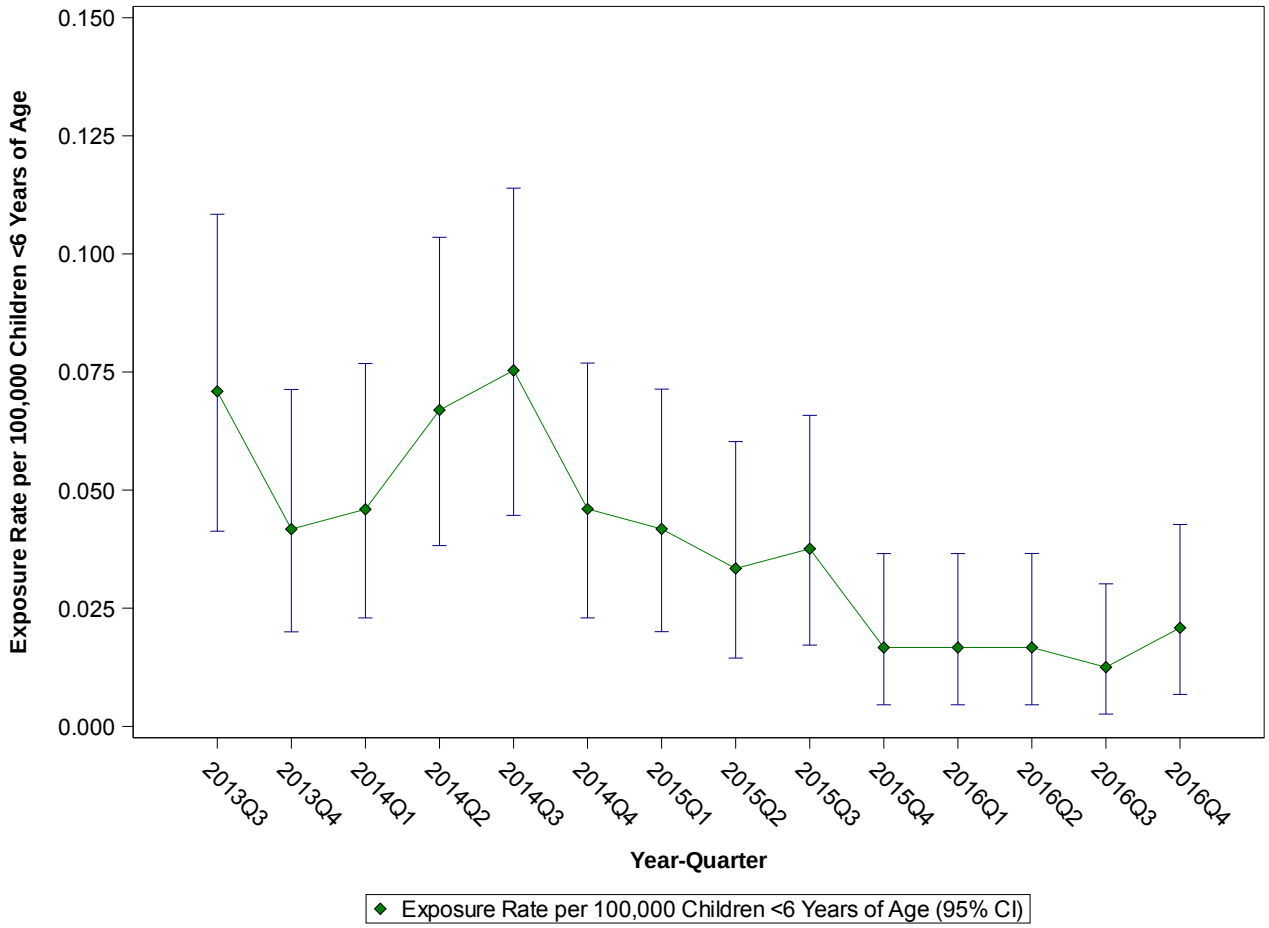


Figure 8. Population-Adjusted Rates of Exposures Resulting in Severe Medical Outcomes by Quarter (01 July 2013 to 31 December 2016)



Sales-Adjusted Rates Summary

Cumulative Sales-Adjusted Rates of All Exposures and Exposures with Clinically Significant Outcomes

Sales-adjusted rates were calculated using the four week intervals beginning 23 June 2013 to the four week interval ending 31 December 2016 based on sales data availability. The sales-adjusted rate of reported exposures to a liquid laundry detergent packet for this period was 3.511 exposures per 1 million packets sold (CI 3.478, 3.544; Table 17). This equates to one exposure per 0.285 million packets sold.

Table 17. Cumulative Sales-Adjusted Rates of All Exposures

Numerator/Denominator	Count	Cumulative Rate of All Exposures per 1,000,000 Packets Sold (95% CI)
All Exposures	43,752	**3.511 (3.478, 3.544)**
Total Sales	12,461,764,708	

The sales-adjusted rate of reported exposures to a liquid laundry detergent packet involving HCF treatment during the transition period was 1.359 per 1 million packets sold (CI 1.339, 1.380; Table 18). This equates to one HCF treatment per 0.736 million packets sold. The sales-adjusted rate of reported exposures to a liquid laundry detergent packet involving HCF admission during the transition period was 0.131 per 1 million packets sold (CI 0.125, 0.138; Table 19). This equates to one HCF admission per 7.63 million packets sold. The sales-adjusted rate of reported exposures to a liquid laundry detergent packet involving severe medical outcomes during the transition period was 0.010 per 1 million packets sold (CI 0.009, 0.012; Table 20). This equates to one severe medical outcome per 100 million packets sold.

Table 18. Cumulative Sales-Adjusted Rates of Exposures Involving Healthcare Facility Treatment

Numerator/Denominator	Count	Cumulative Rate of Exposures Involving HCF Treatment per 1,000,000 Packets Sold (95% CI)
Exposures Involving HCF Treatment	16,936	**1.359 (1.339, 1.380)**
Total Sales	12,461,764,708	

Table 19. Cumulative Sales-Adjusted Rates of Exposures Involving Healthcare Facility Admission

Numerator/Denominator	Count	Cumulative Rate of Exposures Involving HCF Admission per 1,000,000 Packets Sold (95% CI)
Exposures Involving HCF Admission	1,633	**0.131 (0.125, 0.138)**
Total Sales	12,461,764,708	

Table 20. Cumulative Sales-Adjusted Rates of Exposures with Severe Medical Outcomes

Numerator/Denominator	Count	Cumulative Rate of Exposures with Severe Medical Outcomes per 1,000,000 Packets Sold (95% CI)
Exposures with Severe Medical Outcomes	130	**0.010 (0.009, 0.012)**
Total Sales	12,461,764,708	

Sales-Adjusted Rates of All Exposures Over Time

When examined by four week intervals corresponding to sales periods, counts of unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age fluctuated seasonally with an increase through the first five to eight months of the year followed by a decrease through the end of the year. During the same time period the total sales fluctuated slightly with a steady increase over time (Table 21; Figure 9).

The sales-adjusted rate of reported unintentional-general exposures involving liquid laundry detergent packets in children <6 years of age fluctuated throughout the transition period, with a peak in the sales-adjusted rate of exposure in the four week interval ending 20 July 2013 (4.982 per million packets sold (CI 4.658, 5.317)) and a low in the sales-adjusted rate of exposure in the four week interval ending 31 December 2016 (2.165 per million packets sold (CI 2.010, 2.325)). Comparing the seasonal peak in 2014 to the seasonal peak in 2016, the rates were 4.582 per million packets sold (CI 4.311, 4.861) in the four week interval ending 21 June 2014 and 3.695 per million packets sold (CI 3.487, 3.910) in the four week interval ending 21 May 2016. Comparing the first seasonal low point in 2014 with the last seasonal low point in 2016, the rates were 3.370 exposures per million packets sold (CI 3.128. 3.620) in the four week interval ending 01 February 2014 and 2.165 exposures per million packets sold (CI 2.010, 2.325) in the four week interval ending 31 December 2016 (Table 21; Figure 10).

Table 21. Sales-Adjusted Rates of All Exposures by Four Week Interval (23 June 2013 to 31 December 2016)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of All Exposures per 1,000,000 Packets Sold (95% CI)
23 June 2013 to 20 July 2013	878	176,228,963	4.982 (4.658, 5.317)
21 July 2013 to 17 August 2013	935	195,923,666	4.772 (4.471, 5.083)
18 August 2013 to 14 September 2013	825	198,831,756	4.149 (3.871, 4.437)
15 September 2013 to 12 October 2013	884	189,728,555	4.659 (4.357, 4.971)
13 October 2013 to 09 November 2013	759	189,855,974	3.998 (3.718, 4.287)
10 November 2013 to 07 December 2013	747	192,893,990	3.873 (3.600, 4.155)
08 December 2013 to 04 January 2014	665	185,611,612	3.583 (3.316, 3.860)
05 January 2014 to 01 February 2014	721	213,956,221	3.370 (3.128, 3.620)
02 February 2014 to 01 March 2014	844	232,885,277	3.624 (3.384, 3.873)
02 March 2014 to 29 March 2014	887	243,496,603	3.643 (3.407, 3.886)
30 March 2014 to 26 April 2014	918	230,264,949	3.987 (3.733, 4.249)
27 April 2014 to 24 May 2014	924	227,820,254	4.056 (3.798, 4.321)
25 May 2014 to 21 June 2014	1,066	232,636,163	4.582 (4.311, 4.861)
22 June 2014 to 19 July 2014	1,029	243,531,931	4.225 (3.971, 4.487)
20 July 2014 to 16 August 2014	1,076	254,650,805	4.225 (3.977, 4.482)
17 August 2014 to 13 September 2014	1,038	260,544,201	3.984 (3.745, 4.230)
14 September 2014 to 11 October 2014	1,041	249,220,913	4.177 (3.927, 4.435)
12 October 2014 to 08 November 2014	933	259,506,292	3.595 (3.368, 3.830)
09 November 2014 to 06 December 2014	873	261,748,236	3.335 (3.118, 3.560)
07 December 2014 to 03 January 2015	806	259,951,250	3.101 (2.890, 3.318)
04 January 2015 to 31 January 2015	849	283,829,321	2.991 (2.793, 3.196)
01 February 2015 to 28 February 2015	857	264,812,881	3.236 (3.023, 3.456)
01 March 2015 to 28 March 2015	926	278,942,632	3.320 (3.109, 3.537)
29 March 2015 to 25 April 2015	980	266,267,713	3.681 (3.454, 3.914)
26 April 2015 to 23 May 2015	1,008	268,069,072	3.760 (3.532, 3.996)
24 May 2015 to 20 June 2015	1,160	275,907,638	4.204 (3.966, 4.450)
21 June 2015 to 18 July 2015	1,058	268,363,850	3.942 (3.708, 4.183)
19 July 2015 to 15 August 2015	1,103	281,773,843	3.914 (3.687, 4.149)
16 August 2015 to 12 September 2015	1,066	293,314,307	3.634 (3.419, 3.856)
13 September 2015 to 10 October 2015	1,064	266,552,970	3.992 (3.755, 4.235)
11 October 2015 to 07 November 2015	986	282,026,373	3.496 (3.281, 3.718)
08 November 2015 to 05 December 2015	1,011	297,973,693	3.393 (3.187, 3.605)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of All Exposures per 1,000,000 Packets Sold (95% CI)
06 December 2015 to 02 January 2016	940	290,601,182	3.235 (3.031, 3.445)
03 January 2016 to 30 January 2016	948	316,167,331	2.998 (2.811, 3.192)
31 January 2016 to 27 February 2016	915	334,235,847	2.738 (2.563, 2.918)
28 February 2016 to 26 March 2016	941	315,910,549	2.979 (2.791, 3.172)
27 March 2016 to 23 April 2016	1,022	316,651,931	3.228 (3.033, 3.428)
24 April 2016 to 21 May 2016	1,176	318,236,039	3.695 (3.487, 3.910)
22 May 2016 to 18 June 2016	1,089	316,567,950	3.440 (3.239, 3.647)
19 June 2016 to 16 July 2016	1,109	356,018,984	3.115 (2.934, 3.301)
17 July 2016 to 13 August 2016	1,125	351,674,468	3.199 (3.015, 3.389)
14 August 2016 to 10 September 2016	1,118	356,942,908	3.132 (2.951, 3.318)
11 September 2016 to 08 October 2016	933	335,661,035	2.780 (2.604, 2.961)
09 October 2016 to 05 November 2016	939	344,522,260	2.726 (2.554, 2.903)
06 November 2016 to 03 December 2016	854	346,044,054	2.468 (2.305, 2.636)
04 December 2016 to 31 December 2016	726	335,408,265	2.165 (2.010, 2.325)

Figure 9. All Exposures and Sales Count by Four Week Interval (23 June 2013 to 31 December 2016)

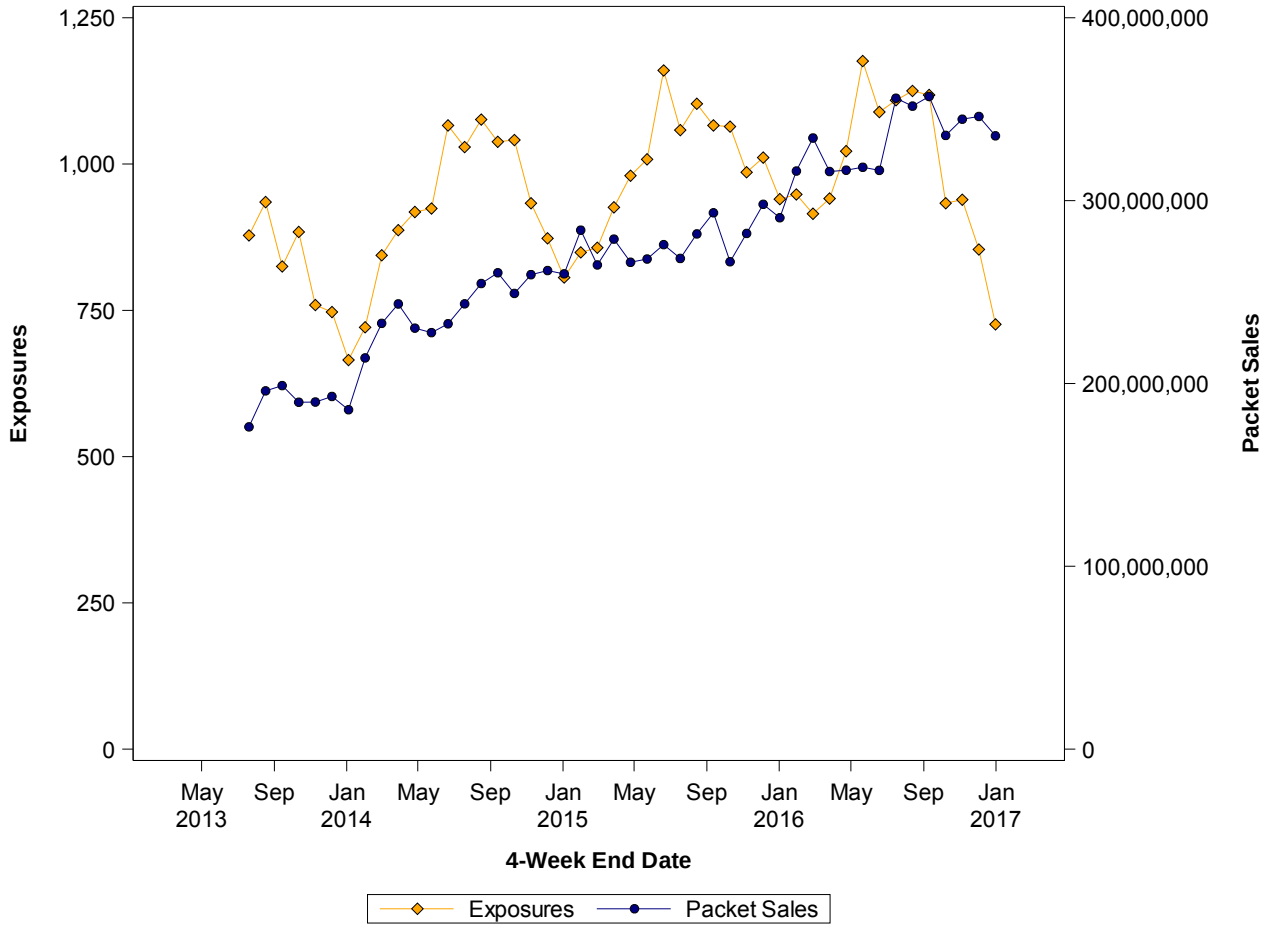
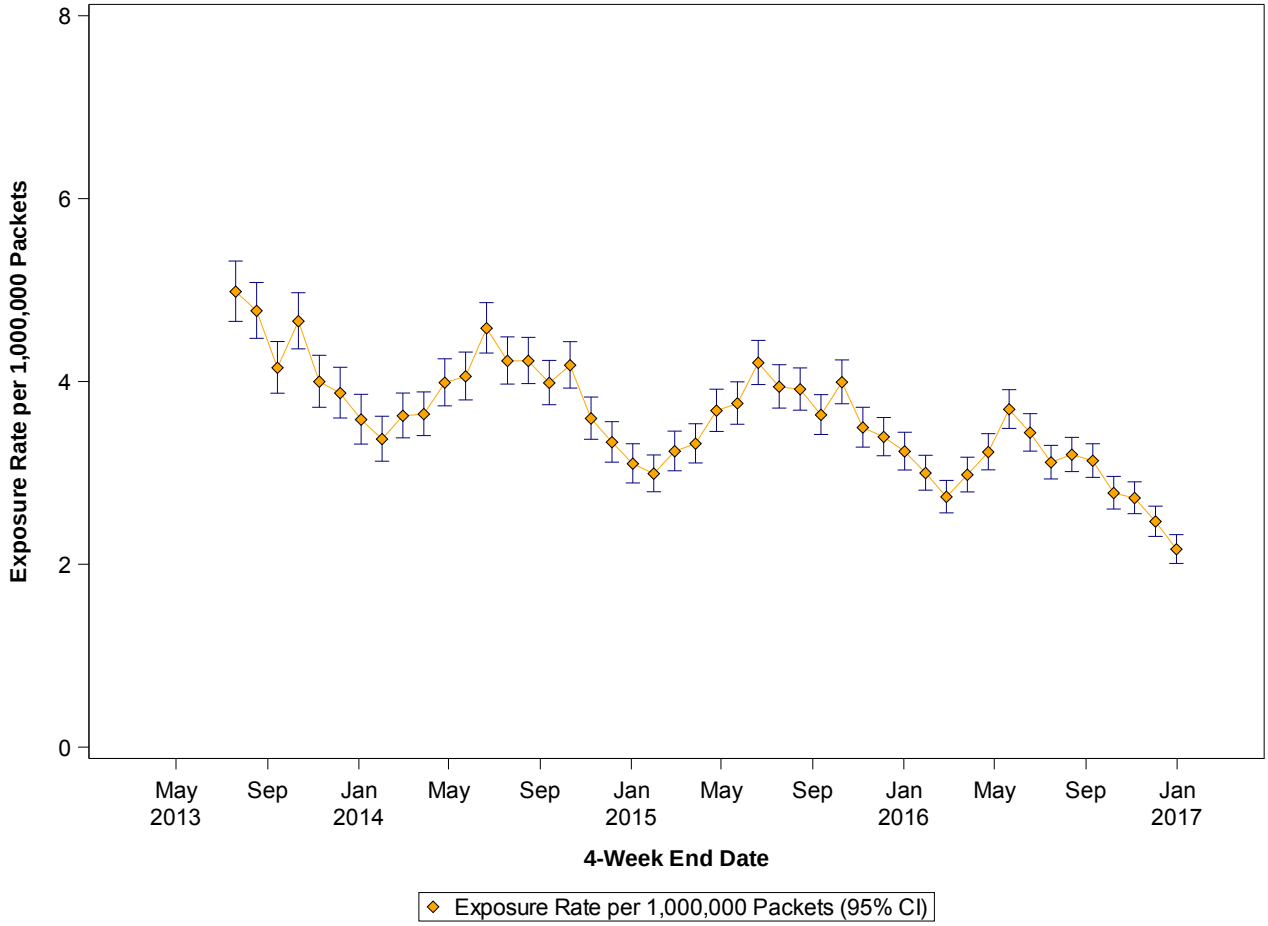


Figure 10. Sales-Adjusted Rates of All Exposures by Four Week Interval (23 June 2013 to 31 December 2016)



Sales-Adjusted Rates of Exposures with Clinically Significant Outcomes Over Time
When examined by four week intervals corresponding to sales periods, counts of exposures involving HCF treatment fluctuated seasonally in the same pattern as all exposures with increases over the initial part of the year followed by decreases through the end of the year. During the same time period the total sales fluctuated slightly with a steady increase over time (Table 22; Figure 11).

The sales-adjusted rate of reported exposures involving treatment in a HCF fluctuated throughout the transition period, with a peak in the sales-adjusted rate of exposure in the four week interval ending 21 June 2014 (1.990 per million packets sold (CI 1.813, 2.176)) and a low in the sales adjusted rate of exposure in the four week interval ending 31 December 2016 (0.730 per million packets sold (CI 0.642, 0.825)). Comparing the seasonal peak in 2014 to the seasonal peak in 2016, the rates were 1.990 per million packets sold (CI 1.813, 2.176) in the four week interval ending 21 June 2014 and 1.345 per million packets sold (CI 1.221, 1.475) in the four week interval ending 21 May 2016. Comparing the first seasonal low point in 2014 with the last seasonal low point in 2016, the rates were 1.337 exposures per 1,000,000 packets sold (CI 1.186, 1.496) in the four week interval ending 01 February 2014 and 0.730 per 1,000,000

packets sold (CI 0.642, 0.825) in the four week interval ending 31 December 2016 (Table 22; Figure 12).

Table 22. Sales-Adjusted Rates of Exposures Involving Healthcare Facility Treatment by Four Week Interval (23 June 2013 to 21 December 2016)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Involving HCF Treatment per 1,000,000 Packets Sold (95% CI)
23 June 2013 to 20 July 2013	349	176,228,963	1.980 (1.778, 2.193)
21 July 2013 to 17 August 2013	355	195,923,666	1.812 (1.628, 2.005)
18 August 2013 to 14 September 2013	334	198,831,756	1.680 (1.504, 1.865)
15 September 2013 to 12 October 2013	340	189,728,555	1.792 (1.607, 1.987)
13 October 2013 to 09 November 2013	328	189,855,974	1.728 (1.546, 1.920)
10 November 2013 to 07 December 2013	282	192,893,990	1.462 (1.296, 1.637)
08 December 2013 to 04 January 2014	261	185,611,612	1.406 (1.241, 1.582)
05 January 2014 01 February 2014	286	213,956,221	1.337 (1.186, 1.496)
02 February 2014 to 01 March 2014	333	232,885,277	1.430 (1.280, 1.587)
02 March 2014 to 29 March 2014	369	243,496,603	1.515 (1.365, 1.674)
30 March 2014 to 26 April 2014	376	230,264,949	1.633 (1.472, 1.802)
27 April 2014 to 24 May 2014	384	227,820,254	1.686 (1.521, 1.858)
25 May 2014 to 21 June 2014	463	232,636,163	1.990 (1.813, 2.176)
22 June 2014 to 19 July 2014	446	243,531,931	1.831 (1.665, 2.005)
20 July 2014 to 16 August 2014	447	254,650,805	1.755 (1.596, 1.922)
17 August 2014 to 13 September 2014	463	260,544,201	1.777 (1.619, 1.943)
14 September 2014 to 11 October 2014	421	249,220,913	1.689 (1.532, 1.854)
12 October 2014 to 08 November 2014	369	259,506,292	1.422 (1.281, 1.571)
09 November 2014 to 06 December 2014	347	261,748,236	1.326 (1.190, 1.469)
07 December 2014 to 03 January 2015	308	259,951,250	1.185 (1.056, 1.321)
04 January 2015 to 31 January 2015	325	283,829,321	1.145 (1.024, 1.273)
01 February 2015 to 28 February 2015	311	264,812,881	1.174 (1.048, 1.308)
01 March 2015 to 28 March 2015	371	278,942,632	1.330 (1.198, 1.469)
29 March 2015 to 25 April 2015	381	266,267,713	1.431 (1.291, 1.578)
26 April 2015 to 23 May 2015	411	268,069,072	1.533 (1.389, 1.685)
24 May 2015 to 20 June 2015	440	275,907,638	1.595 (1.449, 1.747)
21 June 2015 to 18 July 2015	421	268,363,850	1.569 (1.422, 1.722)
19 July 2015 to 15 August 2015	425	281,773,843	1.508 (1.368, 1.655)
16 August 2015 to 12 September 2015	437	293,314,307	1.490 (1.353, 1.633)
13 September 2015 to 10 October 2015	421	266,552,970	1.579 (1.432, 1.734)
11 October 2015 to 07 November 2015	377	282,026,373	1.337 (1.205, 1.475)
08 November 2015 to 05 December 2015	394	297,973,693	1.322 (1.195, 1.456)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Involving HCF Treatment per 1,000,000 Packets Sold (95% CI)
06 December 2015 to 02 January 2016	369	290,601,182	1.270 (1.144, 1.403)
03 January 2016 to 30 January 2016	350	316,167,331	1.107 (0.994, 1.226)
31 January 2016 to 27 February 2016	323	334,235,847	0.966 (0.864, 1.075)
28 February 2016 to 26 March 2016	328	315,910,549	1.038 (0.929, 1.154)
27 March 2016 to 23 April 2016	374	316,651,931	1.181 (1.064, 1.304)
24 April 2016 to 21 May 2016	428	318,236,039	1.345 (1.221, 1.475)
22 May 2016 to 18 June 2016	384	316,567,950	1.213 (1.095, 1.337)
19 June 2016 to 16 July 2016	390	356,018,984	1.095 (0.989, 1.207)
17 July 2016 to 13 August 2016	403	351,674,468	1.146 (1.037, 1.260)
14 August 2016 to 10 September 2016	400	356,942,908	1.121 (1.013, 1.233)
11 September 2016 to 08 October 2016	338	335,661,035	1.007 (0.902, 1.117)
09 October 2016 to 05 November 2016	342	344,522,260	0.993 (0.890, 1.101)
06 November 2016 to 03 December 2016	287	346,044,054	0.829 (0.736, 0.928)
04 December 2016 to 31 December 2016	245	335,408,265	0.730 (0.642, 0.825)

Figure 11. Exposures Involving Healthcare Facility Treatment and Sales Counts by Four Week Interval (23 June 2013 to 31 December 2016)

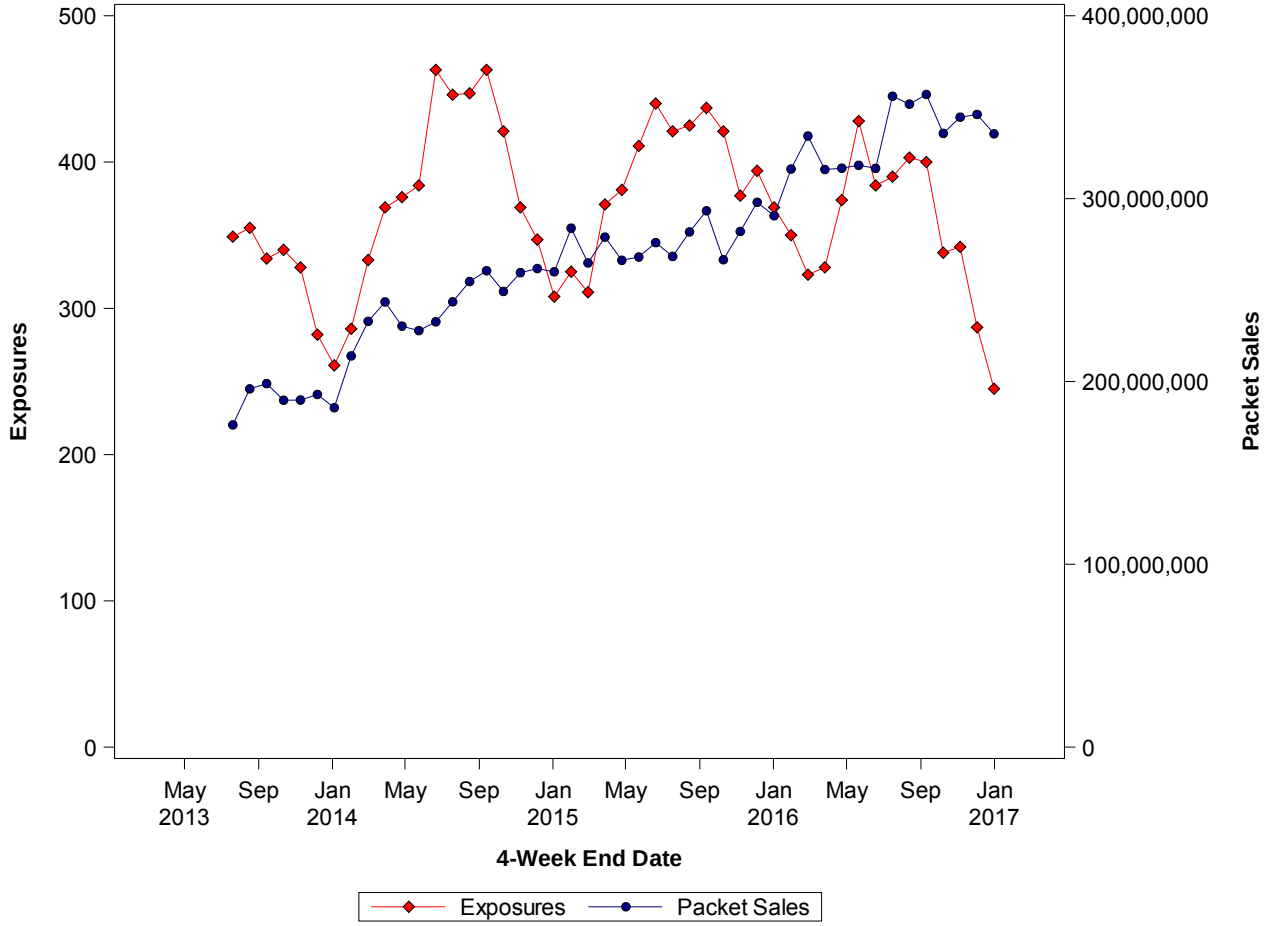
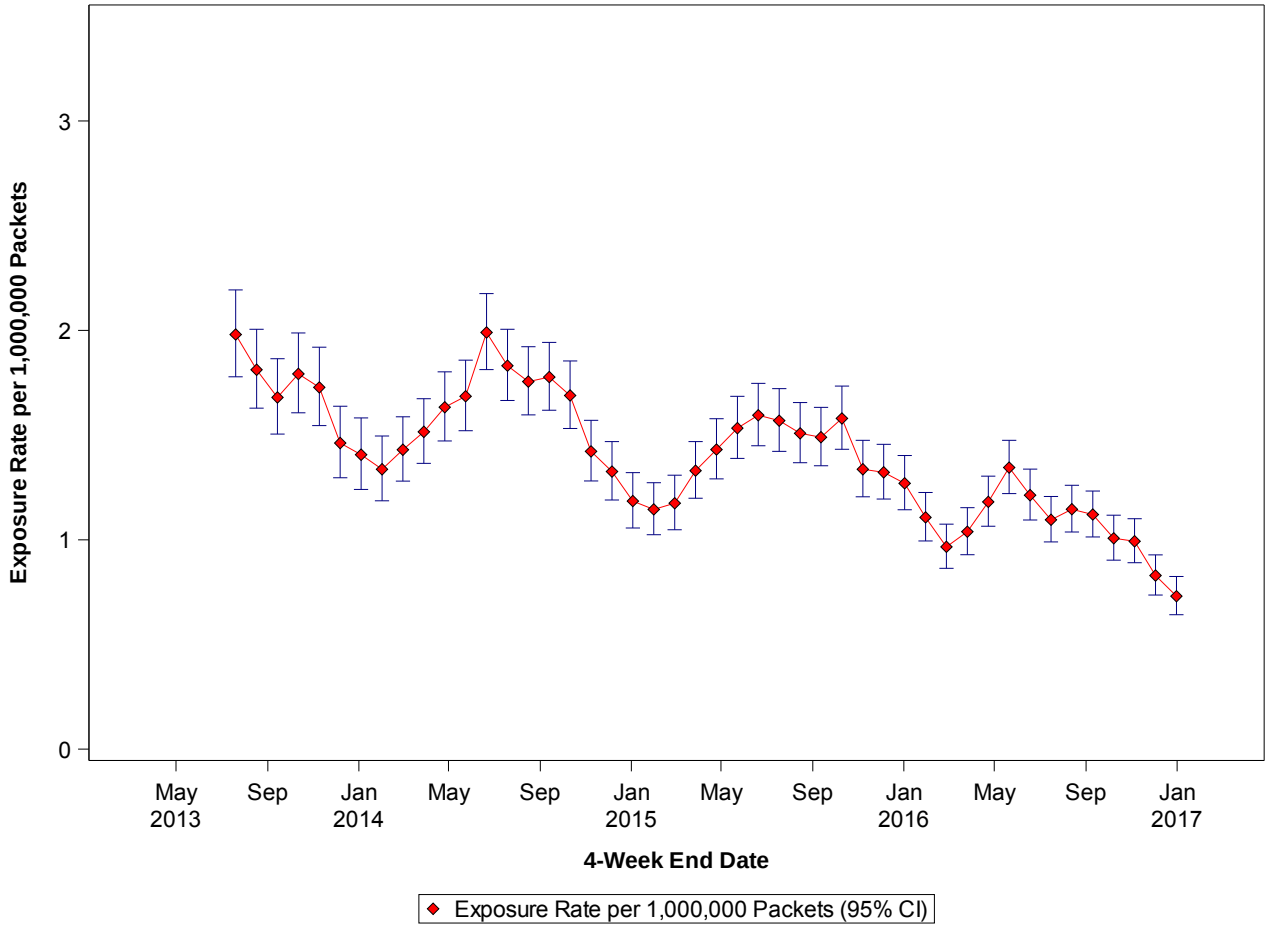


Figure 12. Sales-Adjusted Rates of Exposure Involving Healthcare Facility Treatment by Four Week Interval (23 June 2013 to 31 December 2016)



When examined by four week intervals corresponding to sales periods, counts of exposures involving HCF admission fluctuated without an apparent seasonal pattern throughout the study period. A decrease in reported exposures was observed in the second half of the study period. During the same time period the total sales fluctuated slightly with a steady increase over time (Table 23; Figure 13).

The sales-adjusted rate of reported exposures involving an admission to a HCF fluctuated throughout the transition period without an apparent pattern. A peak in the sales-adjusted rate of exposure was observed in the four week interval ending 21 June 2014(0.254 per million packets sold (CI 0.193, 0.322)) and a low in the sales-adjusted rate of exposure was observed in the four week interval ending 31 December 2016 (0.051 per million packets sold (CI 0.030, 0.077)). Without a clear seasonal pattern in reported sales-adjusted rates of exposure, seasonal peak and low rates could not be compared (Table 23; Figure 14).

Table 23. Sales-Adjusted Rates of Exposures Involving Healthcare Facility Admission by Four Week Interval (23 June 2013 to 31 December 2016)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Involving HCF Admission per 1,000,000 Packets Sold (95% CI)
23 June 2013 to 20 July 2013	39	176,228,963	0.221 (0.157, 0.296)
21 July 2013 to 17 August 2013	37	195,923,666	0.189 (0.133, 0.254)
18 August 2013 to 14 September 2013	28	198,831,756	0.141 (0.094, 0.198)
15 September 2013 to 12 October 2013	44	189,728,555	0.232 (0.169, 0.305)
13 October 2013 to 09 November 2013	44	189,855,974	0.232 (0.168, 0.305)
10 November 2013 to 07 December 2013	37	192,893,990	0.192 (0.135, 0.258)
08 December 2013 to 04 January 2014	28	185,611,612	0.151 (0.100, 0.212)
05 January 2014 to 01 February 2014	29	213,956,221	0.136 (0.091, 0.189)
02 February 2014 to 01 March 2014	43	232,885,277	0.185 (0.134, 0.244)
02 March 2014 to 29 March 2014	58	243,496,603	0.238 (0.181, 0.303)
30 March 2014 to 26 April 2014	42	230,264,949	0.182 (0.131, 0.242)
27 April 2014 to 24 May 2014	45	227,820,254	0.198 (0.144, 0.259)
25 May 2014 to 21 June 2014	59	232,636,163	0.254 (0.193, 0.322)
22 June 2014 to 19 July 2014	55	243,531,931	0.226 (0.170, 0.289)
20 July 2014 to 16 August 2014	45	254,650,805	0.177 (0.129, 0.232)
17 August 2014 to 13 September 2014	52	260,544,201	0.200 (0.149, 0.257)
14 September 2014 to 11 October 2014	41	249,220,913	0.165 (0.118, 0.219)
12 October 2014 to 08 November 2014	37	259,506,292	0.143 (0.100, 0.192)
09 November 2014 to 06 December 2014	44	261,748,236	0.168 (0.122, 0.221)
07 December 2014 to 03 January 2015	34	259,951,250	0.131 (0.091, 0.178)
04 January 2015 to 31 January 2015	26	283,829,321	0.092 (0.060, 0.130)
01 February 2015 to 28 February 2015	27	264,812,881	0.102 (0.067, 0.144)
01 March 2015 to 28 March 2015	42	278,942,632	0.151 (0.109, 0.199)
29 March 2015 to 25 April 2015	40	266,267,713	0.150 (0.107, 0.200)
26 April 2015 to 23 May 2015	42	268,069,072	0.157 (0.113, 0.207)
24 May 2015 to 20 June 2015	50	275,907,638	0.181 (0.135, 0.235)
21 June 2015 to 18 July 2015	40	268,363,850	0.149 (0.106, 0.199)
19 July 2015 to 15 August 2015	43	281,773,843	0.153 (0.110, 0.201)
16 August 2015 to 12 September 2015	33	293,314,307	0.113 (0.077, 0.154)
13 September 2015 to 10 October 2015	29	266,552,970	0.109 (0.073, 0.152)
11 October 2015 to 07 November 2015	32	282,026,373	0.113 (0.078, 0.156)
08 November 2015 to 05 December 2015	35	297,973,693	0.117 (0.082, 0.159)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Involving HCF Admission per 1,000,000 Packets Sold (95% CI)
06 December 2015 to 02 January 2016	28	290,601,182	0.096 (0.064, 0.135)
03 January 2016 to 30 January 2016	24	316,167,331	0.076 (0.049, 0.109)
31 January 2016 to 27 February 2016	26	334,235,847	0.078 (0.051, 0.110)
28 February 2016 to 26 March 2016	26	315,910,549	0.082 (0.054, 0.117)
27 March 2016 to 23 April 2016	18	316,651,931	0.057 (0.034, 0.086)
24 April 2016 to 21 May 2016	26	318,236,039	0.082 (0.053, 0.116)
22 May 2016 to 18 June 2016	22	316,567,950	0.069 (0.044, 0.101)
19 June 2016 to 16 July 2016	29	356,018,984	0.081 (0.055, 0.114)
17 July 2016 to 13 August 2016	26	351,674,468	0.074 (0.048, 0.105)
14 August 2016 to 10 September 2016	38	356,942,908	0.106 (0.075, 0.143)
11 September 2016 to 08 October 2016	30	335,661,035	0.089 (0.060, 0.124)
09 October 2016 to 05 November 2016	19	344,522,260	0.055 (0.033, 0.083)
06 November 2016 to 03 December 2016	24	346,044,054	0.069 (0.044, 0.100)
04 December 2016 to 31 December 2016	17	335,408,265	0.051 (0.030, 0.077)

Figure 13. Exposures Involving Healthcare Facility Admission and Sales Count by Four Week Interval HCF (23 June 2013 to 31 December 2016)

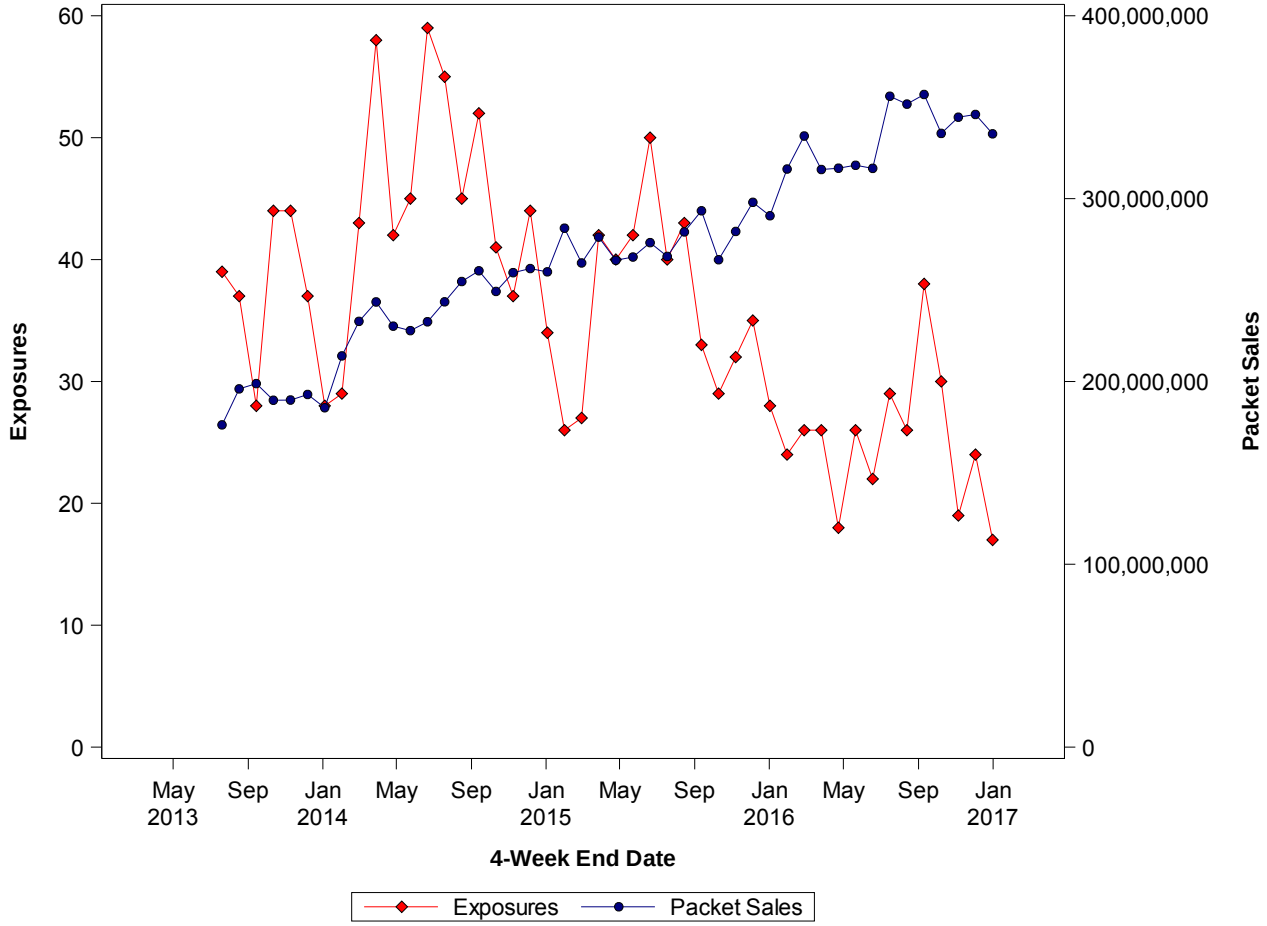
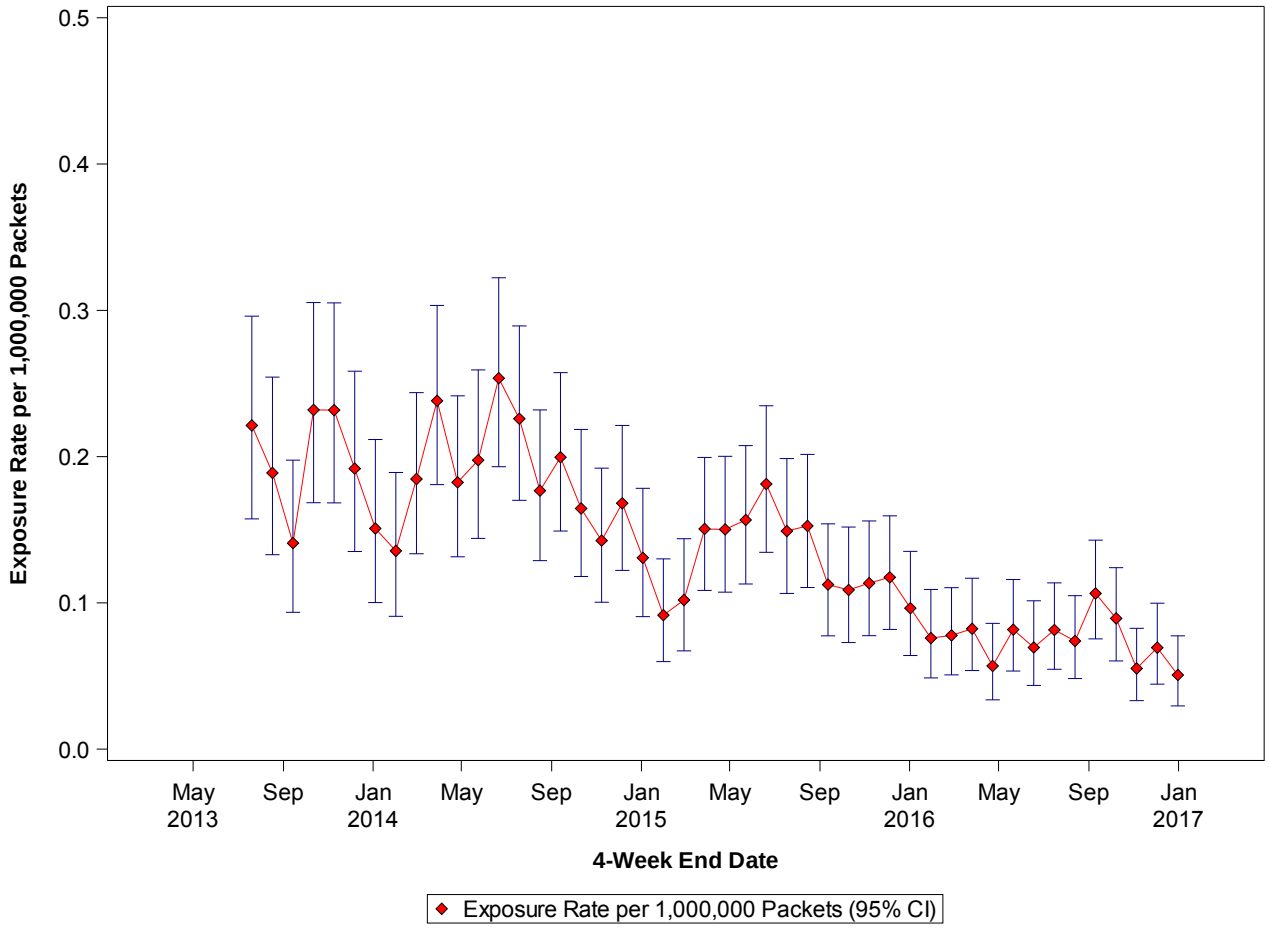


Figure 14. Sales-Adjusted Rates of Exposures Involving Healthcare Facility Admission by Four Week Interval (23 June 2013 to 31 December 2016)



When examined by four week intervals corresponding to sales, counts of exposures involving severe medical outcomes fluctuated without an apparent seasonal pattern throughout the study period. An overall decrease in reporting frequency was observed over time. During the same time period the total sales fluctuated slightly with a steady increase over time (Table 24; Figure 15).

The sales-adjusted rate of reported exposures involving a severe medical outcome fluctuated from 23 June 2013 to 31 December 2016 with a rate of 0.000 due to no severe medical outcomes reported in four week intervals ending 01 February 2014, 18 July 2015, 21 May 2016, and 13 August 2016. The peak rate of 0.041 per 1 million packets sold (CI 0.018, 0.074) was observed in the four week interval ending 17 August 2013. As the number of severe medical outcomes reported during each four week interval remained low (range 0 to 8), the rate calculations generated wide confidence intervals and were less precise. Thus, a comparison of rates during the study period is not appropriate (Table 24; Figure 16).

Table 24. Sales-Adjusted Rates of Exposures Resulting in Severe Medical Outcomes by Four Week Intervals (23 June 2013 to 31 December 2016)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Resulting in Severe Medical Outcomes per 1,000,000 Packets Sold (95% CI)
23 June 2013 to 20 July 2013	1	176,228,963	0.006 (0.000, 0.021)
21 July 2013 to 17 August 2013	8	195,923,666	0.041 (0.018, 0.074)
18 August 2013 to 14 September 2013	4	198,831,756	0.020 (0.005, 0.044)
15 September 2013 to 12 October 2013	7	189,728,555	0.037 (0.015, 0.069)
13 October 2013 to 09 November 2013	3	189,855,974	0.016 (0.003, 0.038)
10 November 2013 to 07 December 2013	3	192,893,990	0.016 (0.003, 0.037)
08 December 2013 to 04 January 2014	1	185,611,612	0.005 (0.000, 0.020)
05 January 2014 to 01 February 2014	0	213,956,221	0.000 (0.000, 0.017)
02 February 2014 to 01 March 2014	6	232,885,277	0.026 (0.009, 0.050)
02 March 2014 to 29 March 2014	4	243,496,603	0.016 (0.004, 0.036)
30 March 2014 to 26 April 2014	7	230,264,949	0.030 (0.012, 0.057)
27 April 2014 to 24 May 2014	4	227,820,254	0.018 (0.005, 0.038)
25 May 2014 to 21 June 2014	3	232,636,163	0.013 (0.003, 0.031)
22 June 2014 to 19 July 2014	6	243,531,931	0.025 (0.009, 0.048)
20 July 2014 to 16 August 2014	6	254,650,805	0.024 (0.009, 0.046)
17 August 2014 to 13 September 2014	8	260,544,201	0.031 (0.013, 0.055)
14 September 2014 to 11 October 2014	2	249,220,913	0.008 (0.001, 0.022)
12 October 2014 to 08 November 2014	3	259,506,292	0.012 (0.002, 0.028)
09 November 2014 to 06 December 2014	4	261,748,236	0.015 (0.004, 0.033)
07 December 2014 to 03 January 2015	3	259,951,250	0.012 (0.002, 0.028)
04 January 2015 to 31 January 2015	1	283,829,321	0.004 (0.000, 0.013)
01 February 2015 to 28 February 2015	3	264,812,881	0.011 (0.002, 0.027)
01 March 2015 to 28 March 2015	5	278,942,632	0.018 (0.006, 0.037)
29 March 2015 to 25 April 2015	3	266,267,713	0.011 (0.002, 0.027)
26 April 2015 to 23 May 2015	3	268,069,072	0.011 (0.002, 0.027)
24 May 2015 to 20 June 2015	3	275,907,638	0.011 (0.002, 0.026)
21 June 2015 to 18 July 2015	0	268,363,850	0.000 (0.000, 0.014)
19 July 2015 to 15 August 2015	2	281,773,843	0.007 (0.001, 0.020)
16 August 2015 to 12 September 2015	2	293,314,307	0.007 (0.001, 0.019)
13 September 2015 to 10 October 2015	5	266,552,970	0.019 (0.006, 0.038)
11 October 2015 to 07 November 2015	2	282,026,373	0.007 (0.001, 0.020)
08 November 2015 to 05 December 2015	1	297,973,693	0.003 (0.000, 0.012)

Four Week Interval Date	Exposure Count	Total Packets Sales Count	Rates of Exposures Resulting in Severe Medical Outcomes per 1,000,000 Packets Sold (95% CI)
06 December 2015 to 02 January 2016	1	290,601,182	0.003 (0.000, 0.013)
03 January 2016 to 30 January 2016	2	316,167,331	0.006 (0.001, 0.018)
31 January 2016 to 27 February 2016	1	334,235,847	0.003 (0.000, 0.011)
28 February 2016 to 26 March 2016	1	315,910,549	0.003 (0.000, 0.012)
27 March 2016 to 23 April 2016	1	316,651,931	0.003 (0.000, 0.012)
24 April 2016 to 21 May 2016	0	318,236,039	0.000 (0.000, 0.012)
22 May 2016 to 18 June 2016	1	316,567,950	0.003 (0.000, 0.012)
19 June 2016 to 16 July 2016	2	356,018,984	0.006 (0.001, 0.016)
17 July 2016 to 13 August 2016	0	351,674,468	0.000 (0.000, 0.010)
14 August 2016 to 10 September 2016	2	356,942,908	0.006 (0.001, 0.016)
11 September 2016 to 08 October 2016	1	335,661,035	0.003 (0.000, 0.011)
09 October 2016 to 05 November 2016	3	344,522,260	0.009 (0.002, 0.021)
06 November 2016 to 03 December 2016	1	346,044,054	0.003 (0.000, 0.011)
04 December 2016 to 31 December 2016	1	335,408,265	0.003 (0.000, 0.011)

Figure 15. Exposures Resulting in Severe Medical Outcomes and Sales Count by Four Week Interval (23 June 2013 to 31 December 2016)

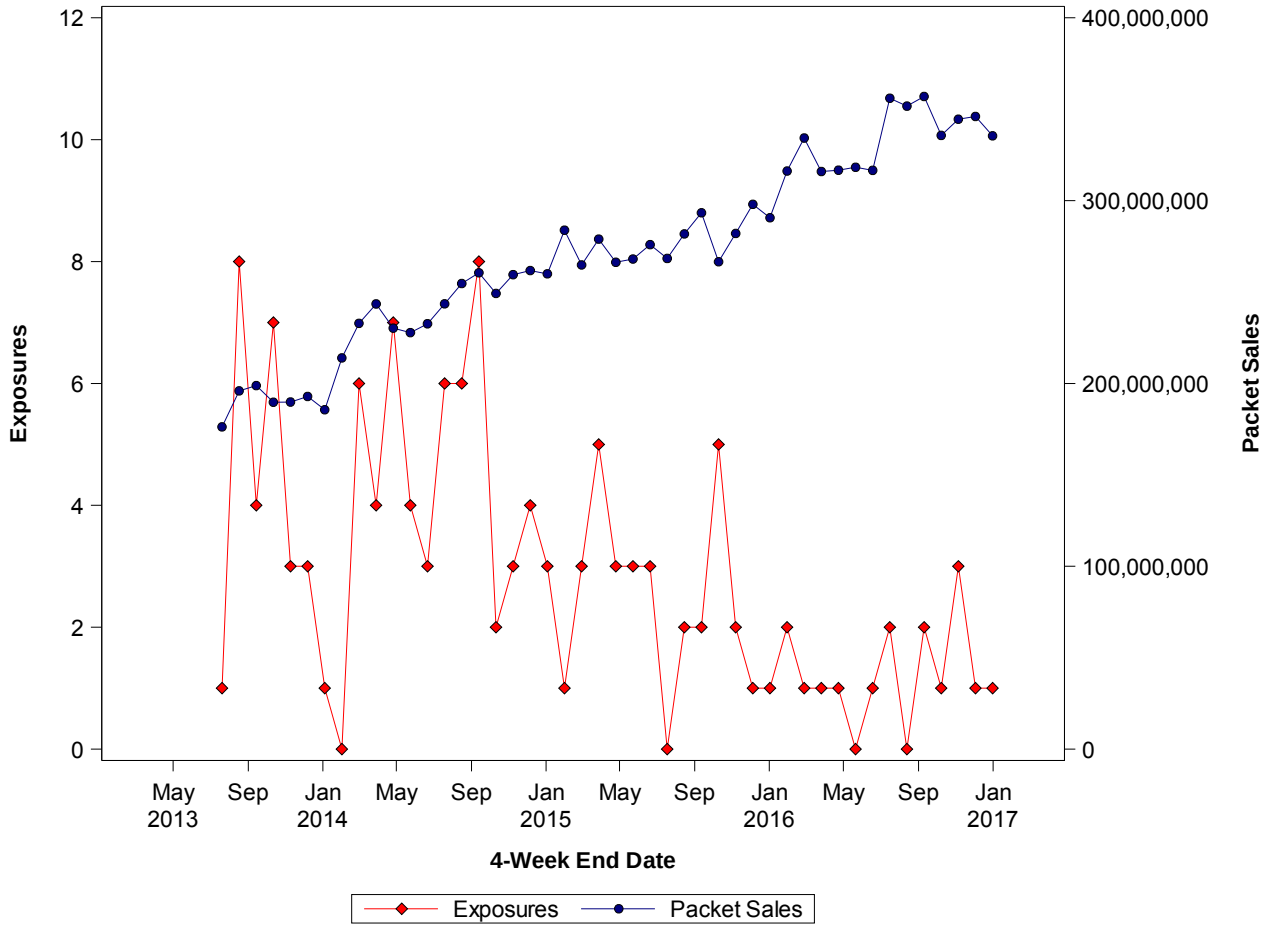
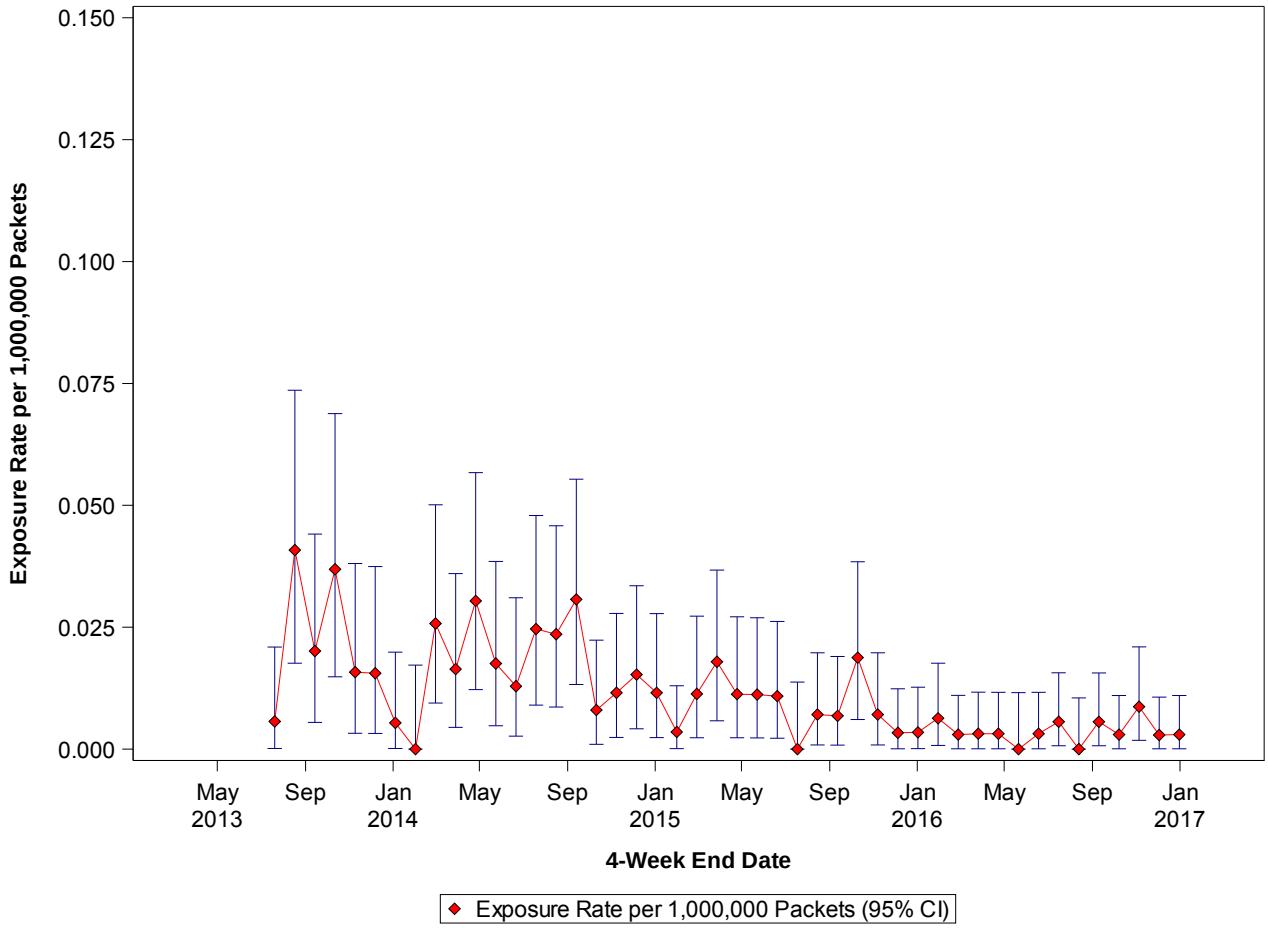


Figure 16. Sales-Adjusted Rates of Exposures Resulting in Severe Medical Outcomes by Four Week Interval (23 June 2013 to 31 December 2016)



SUMMARY

Through work with the ASTM Laundry Packets Data team, three distinct surveillance periods were determined in relation to implementation of the voluntary standards to reduce unintentional pediatric exposures to liquid laundry detergent packets: the baseline period was defined as 01 July 2012 to 30 June 2013, the transition period was defined as 01 July 2013 to 31 December 2016, and the post period was defined as 01 January 2017 to 31 December 2017. These periods were determined based on the availability of data and in relation to the period of implementation of the ASTM standards. Focusing on the transition period, this surveillance report describes the 43,507 unintentional-general exposures involving a liquid laundry detergent packet in children <6 years of age reported to the National Poison Data System (NPDS) between 01 July 2013 to 31 December 2016.

Most of the exposures reported in the transition period involved children <4 years of age. Over a third of all liquid laundry detergent packet exposures involved healthcare facility (HCF) treatment, with over 90.0% of exposures that received HCF treatment being released without admission. In total, less than 4.0% of exposures resulted in HCF admission. Most exposures were followed to a known outcome, with minor effects being reported in a little under half of all exposures. Severe medical outcomes (major effect n=128, death n=2) were reported in <0.4% of all exposures.

Exposures involving children <2 years of age were associated with higher percentages of HCF admission and severe medical outcomes. While the most common route of exposure to a liquid laundry detergent packet was ingestion, aspiration was associated with more severe medical outcomes. Regardless of severity of the outcome, product storage was most commonly cited as a contributing factor to the exposure. The relationship between exposure to a liquid laundry detergent packet and death was determined to be undoubtedly responsible in one fatality and was unknown in the other fatality reported during the transition period. Both children were ≤16 months old further suggesting that young children may be at greatest risk for severe outcomes after unintentional ingestion of liquid laundry detergent packets. More thorough examination of these fatalities, including any available autopsy results may provide additional insights about the risk of severe outcomes after ingestion of a liquid laundry detergent packet.

Rates were evaluated cumulatively and over time using the US population <6 years of age and sales data for all exposures, exposures involving HCF treatment, HCF admission, and severe medical outcomes. These rates are summarized in Table 25. Rates of exposures calculated by adjusting for the US population indicate that approximately 182 exposures to a liquid laundry detergent packet per 100,000 US children <6 years of age were reported during the transition period. When the rate of exposure was adjusted for product sales, approximately 4 exposures occurred for every 1,000,000 packets sold were reported. Rates of exposures resulting in severe medical outcomes (major effect or death) adjusted for the population and for product sales were approximately 54 exposures per 10 million US children <6 years of age and 1 per 100 million packets sold. Over time, exposure counts fluctuated seasonally with decreases in the fall and winter months (4^{th} and 1^{st} quarters). As sales increased over the study period, rates corresponded to trends in exposures with peak rates occurring in the middle part of the year and decreases thereafter, with a trend towards an overall decrease over time.

Table 25. Summary of Population-Adjusted and Sales-Adjusted

Type of Exposure Rate	Cumulative Population-Adjusted Rate[a]	Population-Adjusted Seasonal Rate[a] Range (First and Last Quarterly Peak)	Cumulative Sales-Adjusted Rate[b]	Sales-Adjusted Seasonal Rate[b] Range (First and Last Four Week Interval Peak)
All Exposures	**181.705** (CI 180.006, 183.420)	**14.312** (CI 13.836, 14.796) *2014Q3* to **15.035** (CI 14.548, 15.530) *2016Q2*	**3.511** (CI 3.478, 3.544)	**4.582** (CI 4.311, 4.861) *21 June 2014* to **3.695** (CI 3.487, 3.910) *21 May 2016*
Healthcare Facility Treatment	**70.290** (CI 69.236, 71.360)	**6.082** (CI 5.774, 6.399) *2014Q3* to **5.379** (CI 5.089, 5.676) *2016Q2*	**1.359** (CI 1.339, 1.380)	**1.990** (CI 1.813, 2.176) *21 June 2014* to **1.345** (CI 1.221, 1.475) *21 May 2016*
Healthcare Facility Admission	**6.770** (CI 6.448, 7.108)	**0.699** (CI 0.597, 0.809) *2014Q2* to **0.413** (CI 0.336, 0.498) *2016Q3*	**0.131** (CI 0.125, 0.138)	*No seasonal trend apparent*
Severe Medical Outcome	**0.543** (CI 0.457, 0.645)	*No seasonal trend apparent*	**0.010** (CI 0.009, 0.012)	*No seasonal trend apparent*

[a]*Rate per 100,000 US children <6 years of age and 95% Confidence Interval (CI).*
[b]*Rate per 1,000,000 packets sold and 95% Confidence Interval (CI).*

Interpretation of NPDS data are limited in that exposures are reported by caregivers who self-select to contact a poison center. Furthermore, as the primary purpose of poison centers is to manage exposures, exposures may be both underreported and have some variation in quality and completeness. Though sales data are not a perfect measure of product availability, analysis of sales-adjusted rates of exposure can normalize reporting rates in the context of product availability. Population-adjusted rates provide additional context for changes in trends over time.

These analyses show that rates of exposure decreased over the transition period, but more severe medical outcomes remained infrequent. Certain characteristics appeared to contribute to the exposure and were associated with severe medical outcomes, including exposures in children <2 years of age and aspiration of the product. As with many accidental exposures, improper product storage was identified as the primary contributor to exposure. Comparison of these characteristics along with rates of exposure and trends in outcome during the baseline and post-ASTM standard implementation periods should be encouraged to evaluate the impact of the safety standards.

DISCLAIMERS

American Association of Poison Control Centers

The American Association of Poison Control Centers (AAPCC; http://www.aapcc.org) maintains the national database of information logged by the country's regional poison centers (PCs) serving all 50 United States, Puerto Rico, and the District of Columbia. Case records in this database are from self-reported calls: they reflect only information provided when the public or health care professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure), or request information/educational materials. Exposures do not necessarily represent a poisoning or overdose. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to PCs and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

Nielsen

The analyses performed in this report are based in part on data reported by Nielsen through its Strategic Planner Service for the Liquid Laundry Packs category for four week intervals from 23 June 2013 through 31 December 2016, for the Total US market for Nielsen's Expanded All Outlets Combined channel which includes Food, Drug, Mass Merchandise, Club, Dollar, and Military/Deca. Conclusions drawn from the use of Nielsen data do not reflect the views of Nielsen.

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APPENDICES

Appendix A: National Poison Data System (NPDS) Definitions

EXPOSURE
Actual or suspected contact with any substance which has been ingested, inhaled, absorbed, applied to, or injected into the body, regardless of toxicity or clinical manifestation.

REASON FOR EXPOSURE

Unintentional Exposure
An unintentional exposure results from an unforeseen or unplanned event. Includes all subtypes: unintentional general, environmental, occupational, therapeutic error, misuse, bite/sting, food poisoning and unintentional unknown.

1) **Unintentional-General:** All unintended exposures that are not specifically defined by another unintentional subtype. Most unintentional exposures in children should be coded here. Never use this code if there is another code that fits the case.
2) **Unintentional-Environmental:** Any passive, non-occupational exposure that results from contamination of air, water, or soil. Environmental exposures are usually, but not always, caused by man-made contaminants.
3) **Unintentional-Occupational:** Any exposure that occurs as a *direct* result of the person being on the job or in the workplace.
4) **Unintentional-Therapeutic error:** An unintentional deviation from a proper therapeutic regimen that results in the wrong dose, incorrect route of administration, administration to the wrong person, or administration of the wrong substance. Includes instances in which any type of substance (medications, herbals, non-pharmaceuticals or other products) is substituted for a medication. Drug interactions (or drug/food interactions) resulting from unintentional administration of drugs/foods which are known to interact should also be included.
5) **Unintentional-Misuse:** Unintentional improper or incorrect use of a non-pharmaceutical substance. Unintentional misuse differs from intentional misuse in that the exposure was unplanned or not foreseen by the patient.
6) **Unintentional-Bite/sting:** All animal bites and stings, with or without envenomation.
7) **Unintentional-Food poisoning:** All suspected or confirmed food poisoning regardless of clinical manifestation. This would include ingestion of any food contaminated with microorganisms. Select this reason even if the patient develops no symptoms from the contaminated food.

CHRONICITY
Chronicity of the exposure.

Acute: A single, repeated or continuous exposure occurring over a period of eight hours or less.

Acute-on-Chronic: A single exposure that was preceded by a continuous, repeated, or intermittent exposure occurring over a period exceeding eight hours.

Chronic: A continuous, repeated, or intermittent exposure to the same substance lasting longer than eight hours.

Unknown: It is not possible to determine whether the exposure is acute, acute-on-chronic, or chronic.

MEDICAL OUTCOME
Case followed to known outcome:

A response is appropriate in this area only if follow-up continues until medical outcome can be documented with reasonable certainty.

Unrelated effect: Based upon all the information available, the exposure was probably not responsible for the effect(s).

No effect: The patient developed no symptoms as a result of the exposure. Follow-up is required to make this determination unless the initial poison center call occurs sufficiently long enough after the exposure that the poison center is reasonably certain no effects will occur.

Minor effect: The patient exhibited some symptoms as a result of the exposure, but they were minimally bothersome to the patient. The symptoms usually resolve rapidly and often involve skin or mucous membrane manifestations. The patient has returned to a pre-exposure state of wellbeing and has no residual disability or disfigurement.

Moderate effect: The patient exhibited symptoms as a result of the exposure which are more pronounced, more prolonged or more of a systemic nature than minor symptoms. Usually some form of treatment is or would have been indicated. Symptoms were not life-threatening and the patient has returned to a pre-exposure state of well-being with no residual disability or disfigurement.

Major effect: The patient has exhibited symptoms as a result of the exposure which were life-threatening or resulted in significant residual disability or disfigurement.

Death: The patient died as a result of the exposure or as a direct complication of the exposure where the complication was unlikely to have occurred had the toxic exposure not preceded the complication. Only includes deaths which are probably or undoubtedly related to the exposure.

Case <u>not</u> followed to a known outcome:
In some circumstances it is not appropriate or possible to follow a patient to a reasonably certain medical outcome.

Not followed, judged as nontoxic exposure. The patient was not followed, per clinical judgement the exposure was likely to be nontoxic because:

- the agent involved was nontoxic
- the amount implicated in the exposure was insignificant (nontoxic), and/or
- the route of exposure was unlikely to result in a clinical effect

Not followed, minimal clinical effects possible. The patient was not followed because, in the clinical judgment of the specialist in poison information, the exposure was likely to result in only minimal toxicity of a trivial nature. This outcome is selected only when reasonably certain, in a worst case scenario, that the patient will experience no more than a minor effect. This also includes cases that refused follow-up if the exposure would possibly result in minimal clinical effects and would cause no more than a minor effect.

Unable to follow, judged as a potentially toxic exposure. The patient was lost to follow-up (or the poison center neglected to provide follow-up) and in the judgment of the specialist in poison information the exposure was significant and may have resulted in toxic manifestations with a moderate, major or fatal outcome.

Death, indirect report: A reported fatality is coded as “indirect” if no inquiry was placed to the poison center. For example, if the case was obtained from a medical examiner who sends post mortem reports to the poison center or from a newspaper article. An inquiry to the poison center after the patient died is not necessarily indirect. For example, a medical examiner calling with a question about the cause of death or a family member calling with a question about a toxicology laboratory result is not an indirect report.

CLINICAL EFFECT
Reported signs, symptoms and clinical findings associated with an exposure, recorded by relationship to the exposure.

THERAPIES
Therapies that were recommended and/or performed in relation to the exposure reported.

SCENARIO
A description of the events that led to the reported exposure.

Appendix B: National Poison Data System (NPDS) Relative Contributions to Fatality (RCF)

Undoubtedly responsible
In the opinion of the Case Review Team (CRT) the Clinical Case Evidence establishes beyond reasonable doubt that the SUBSTANCES actually caused the death.

Probably responsible
In the opinion of the CRT the Clinical Case Evidence suggests that the SUBSTANCES caused the death, but some reasonable doubt remained.

Contributory
In the opinion of the CRT the Clinical Case Evidence establishes that the SUBSTANCES contributed to the death, but did not solely cause the death. That is, the SUBSTANCES alone would not have caused the death, but combined with other factors, were partially responsible for the death.

Probably not responsible
In the opinion of the CRT the Clinical Case Evidence establishes to a reasonable probability, but not conclusively, that the SUBSTANCES associated with the death did not cause the death.

Clearly not responsible
In the opinion of the CRT the Clinical Case Evidence established beyond a reasonable doubt that the SUBSTANCES did not cause this death.

Unknown
In the opinion of the CRT the Clinical Case Evidence is insufficient to impute or refute a causative relationship for the SUBSTANCES in this death.

Appendix C: All Related Clinical Effects Among All Unintentional-General Exposures to Liquid Laundry Detergent Packets by Level of Treatment and Severe Medical Outcome

Related Clinical Effects	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Vomiting	18,568 (42.7%)	9,777 (58.1%)	1,279 (78.9%)	86 (66.2%)
Ocular - Irritation/pain	5,437 (12.5%)	3,015 (17.9%)	74 (4.6%)	21 (16.2%)
Cough/choke	4,781 (11.0%)	2,562 (15.2%)	517 (31.9%)	46 (35.4%)
Red eye/conjunctivitis	3,335 (7.7%)	2,020 (12.0%)	52 (3.2%)	15 (11.5%)
Drowsiness/lethargy	1,550 (3.6%)	1,274 (7.6%)	328 (20.2%)	40 (30.8%)
Other	1,435 (3.3%)	970 (5.8%)	314 (19.4%)	37 (28.5%)
Nausea	1,405 (3.2%)	782 (4.6%)	122 (7.5%)	9 (6.9%)
Oral irritation	1,086 (2.5%)	440 (2.6%)	101 (6.2%)	4 (3.1%)
Edema	711 (1.6%)	503 (3.0%)	29 (1.8%)	2 (1.5%)
Erythema/flushed	707 (1.6%)	369 (2.2%)	28 (1.7%)	4 (3.1%)
Throat irritation	686 (1.6%)	421 (2.5%)	131 (8.1%)	8 (6.2%)
Lacrimation	663 (1.5%)	455 (2.7%)	9 (0.6%)	5 (3.8%)
Corneal abrasion	626 (1.4%)	604 (3.6%)	23 (1.4%)	4 (3.1%)
Excess secretions	505 (1.2%)	402 (2.4%)	154 (9.5%)	21 (16.2%)
Diarrhea	488 (1.1%)	297 (1.8%)	58 (3.6%)	5 (3.8%)
Dermal - Irritation/pain	437 (1.0%)	217 (1.3%)	5 (0.3%)	2 (1.5%)
Rash	414 (1.0%)	214 (1.3%)	20 (1.2%)	0 (0.0%)
Dyspnea	334 (0.8%)	303 (1.8%)	162 (10.0%)	33 (25.4%)
Abdominal pain	256 (0.6%)	125 (0.7%)	16 (1.0%)	1 (0.8%)
Agitated/irritable	245 (0.6%)	174 (1.0%)	57 (3.5%)	12 (9.2%)
Tachycardia	162 (0.4%)	157 (0.9%)	83 (5.1%)	28 (21.5%)
Bronchospasm	153 (0.4%)	145 (0.9%)	95 (5.9%)	12 (9.2%)
Burns	141 (0.3%)	137 (0.8%)	10 (0.6%)	6 (4.6%)
Burns (superficial)	129 (0.3%)	93 (0.6%)	11 (0.7%)	3 (2.3%)
X-ray findings(+)	129 (0.3%)	127 (0.8%)	104 (6.4%)	25 (19.2%)
Hyperventilation/tachypnea	121 (0.3%)	119 (0.7%)	80 (4.9%)	18 (13.8%)
Photophobia	92 (0.2%)	72 (0.4%)	2 (0.1%)	1 (0.8%)

Related Clinical Effects	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Respiratory depression	72 (0.2%)	72 (0.4%)	62 (3.8%)	29 (22.3%)
Dysphagia	61 (0.1%)	53 (0.3%)	31 (1.9%)	4 (3.1%)
Pallor	51 (0.1%)	37 (0.2%)	15 (0.9%)	4 (3.1%)
Fever/hyperthermia	50 (0.1%)	44 (0.3%)	35 (2.2%)	8 (6.2%)
Esophageal injury	49 (0.1%)	48 (0.3%)	43 (2.7%)	14 (10.8%)
Oral burns (including lips)	48 (0.1%)	38 (0.2%)	18 (1.1%)	6 (4.6%)
Oropharyngeal edema	47 (0.1%)	47 (0.3%)	28 (1.7%)	4 (3.1%)
Acidosis	45 (0.1%)	45 (0.3%)	39 (2.4%)	16 (12.3%)
Hives/welts	37 (0.1%)	23 (0.1%)	1 (0.1%)	0 (0.0%)
ADR to treatment	36 (0.1%)	19 (0.1%)	4 (0.2%)	0 (0.0%)
Blurred vision	35 (0.1%)	14 (0.1%)	0 (0.0%)	0 (0.0%)
Pneumonitis	31 (0.1%)	31 (0.2%)	27 (1.7%)	9 (6.9%)
Anorexia	30 (0.1%)	24 (0.1%)	5 (0.3%)	2 (1.5%)
Burns 2 - 3 degree	23 (0.1%)	20 (0.1%)	4 (0.2%)	2 (1.5%)
Pain (not dermal, GI, ocular)	23 (0.1%)	8 (<0.1%)	3 (0.2%)	0 (0.0%)
Pruritus	19 (<0.1%)	11 (0.1%)	1 (0.1%)	0 (0.0%)
Hematemesis	17 (<0.1%)	16 (0.1%)	8 (0.5%)	2 (1.5%)
Papilledema	15 (<0.1%)	9 (0.1%)	2 (0.1%)	7 (5.4%)
Coma	13 (<0.1%)	12 (0.1%)	11 (0.7%)	8 (6.2%)
Hypotension	13 (<0.1%)	13 (0.1%)	12 (0.7%)	4 (3.1%)
Ataxia	12 (<0.1%)	12 (0.1%)	5 (0.3%)	0 (0.0%)
Electrolyte abnormality	11 (<0.1%)	11 (0.1%)	7 (0.4%)	3 (2.3%)
Visual defect	11 (<0.1%)	8 (<0.1%)	0 (0.0%)	0 (0.0%)
Anion gap increased	10 (<0.1%)	10 (0.1%)	9 (0.6%)	3 (2.3%)
Cyanosis	10 (<0.1%)	10 (0.1%)	8 (0.5%)	3 (2.3%)
Gastric burns	10 (<0.1%)	10 (0.1%)	9 (0.6%)	2 (1.5%)
Dizziness/vertigo	8 (<0.1%)	7 (<0.1%)	0 (0.0%)	0 (0.0%)
Confusion	7 (<0.1%)	6 (<0.1%)	4 (0.2%)	1 (0.8%)
Bullae	6 (<0.1%)	3 (<0.1%)	1 (0.1%)	0 (0.0%)
Bleeding (other)	5 (<0.1%)	4 (<0.1%)	0 (0.0%)	0 (0.0%)
Hypertension	5 (<0.1%)	5 (<0.1%)	5 (0.3%)	0 (0.0%)
Respiratory arrest	5 (<0.1%)	4 (<0.1%)	4 (0.2%)	4 (3.1%)
Dehydration	4 (<0.1%)	4 (<0.1%)	2 (0.1%)	0 (0.0%)

Related Clinical Effects	All Exposures[b] (N=43,507)	Exposures Involving HCF Treatment (N=16,830)	Exposures Involving HCF Admission (N=1,621)	Exposures with Severe Medical Outcomes (N=130)
Ecchymosis	4 (<0.1%)	4 (<0.1%)	0 (0.0%)	0 (0.0%)
Pulmonary edema	4 (<0.1%)	4 (<0.1%)	4 (0.2%)	3 (2.3%)
Pupil(s) nonreactive	4 (<0.1%)	4 (<0.1%)	0 (0.0%)	0 (0.0%)
Seizure (single)	4 (<0.1%)	4 (<0.1%)	4 (0.2%)	2 (1.5%)
Diaphoresis	3 (<0.1%)	2 (<0.1%)	2 (0.1%)	0 (0.0%)
Other LFT abnormality	3 (<0.1%)	3 (<0.1%)	2 (0.1%)	1 (0.8%)
Chest pain (including noncardiac)	2 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Headache	2 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Hyperglycemia	2 (<0.1%)	2 (<0.1%)	2 (0.1%)	0 (0.0%)
Mydriasis	2 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Other coagulopathy	2 (<0.1%)	2 (<0.1%)	2 (0.1%)	1 (0.8%)
Tremor	2 (<0.1%)	2 (<0.1%)	1 (0.1%)	2 (1.5%)
AST, ALT>1,000	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Bradycardia	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Cardiac arrest	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Esophageal stricture	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Fetal death	1 (<0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypothermia	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Muscle weakness	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Numbness	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
PT prolonged	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)
Puncture wound/sting	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Slurred speech	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Syncope	1 (<0.1%)	1 (<0.1%)	0 (0.0%)	0 (0.0%)
Urinary retention	1 (<0.1%)	1 (<0.1%)	1 (0.1%)	1 (0.8%)