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Epidemiologic and clinical features of cyanobacteria harmful algal bloom exposures reported to the National Poison Data System, United States, 2010–2022: a descriptive analysis

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Abstract

Background Harmful algal bloom occurrences have been increasingly reported globally and over time. Exposure to the variety of toxins and co-contaminants that may be present in harmful algal blooms can cause illness and even death. Poison control data is a valuable public health information source that has been used to characterize many types of toxin exposures, including harmful algal blooms. Prior studies have been limited by location and time, and knowledge gaps remain regarding cyanobacteria harmful algal bloom (cyanoHAB) exposure circumstances, and the breadth and severity of associated clinical effect.

Methods The objective of this study was to characterize epidemiologic and clinical features of cyanoHAB exposure cases reported to 55 US poison control centers and available in the National Poison Data System (NPDS). We identified 4260 NPDS cyanoHAB exposure cases reported from 2010 to 2022, including symptomatic exposure cases with and without clinical effects related to the exposure and asymptomatic exposure cases. We assessed demographics; exposure routes, locations, chronicity; clinical effects; and medical outcomes. We calculated case rates annually and 13-year case rates by US geographic division.

Results Over half of cyanoHAB exposure cases were children < 20 years old (***n*** = 2175). Most cyanoHABs exposures occurred in a "public area" (***n*** = 2902, 68.1%); most were acute (≤ 8 h) (***n*** = 3824, 89.8%). Dermal and ingestion routes and gastrointestinal effects predominated. 2% (***n*** = 102) of cases experienced a moderate or major medical outcome; no deaths were reported. National rates increased from 0.4 cases/1 million (1 M) person-years in 2010 to 1.4 cases/1 M person-years in 2022. The Mountain division had the highest 13-year rate (7.8 cases/1 M person-years).

Conclusions CyanoHAB exposure case rates increased 2010–2022, despite a decrease in all-cause exposure cases during the same period. NPDS data provide valuable public health information for characterization of cyanoHAB exposures, an emerging public health challenge.

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Keywords Cyanobacteria harmful algal bloom, cyanoHAB, Health outcomes, Exposure, Public health

Background

Uncontaminated water is a basic human need and the focus of many public health interventions [1, 2]. Like other types of microscopic algae (e.g., red tide), cyanobacteria, or blue-green algae, is a source of water contamination and a persistent problem in the US and around the world [3]. Cyanobacteria can proliferate in fresh, salt, or brackish water in large aggregations or blooms. Blooms are designated "harmful" to humans, animals, and the environment when they produce toxins, including microcystin, nodularin, anatoxin-a, and cylindrospermopsin; [2, 4] become too dense; deplete free oxygen in the water; or release harmful gases [4]. Exposure to cyanobacterial harmful algal bloom (cyanoHAB) toxins and/or co-contaminants can affect specific organs or multiple organ systems, including the liver, gastrointestinal system, upper respiratory tract, skin, and kidneys [5], leading to illness or, less commonly, death in humans [6] and animals [7].

Due to the potentially serious health effects associated with cyanoHAB exposures, some state and local jurisdictions conduct routine surveillance of cyanoHABs and investigate reports of potential exposures [8]. Responses to these reports and surveillance activities include public notification of cyanoHAB occurrences (e.g., press releases, brochures, signage, website and social media posts) so that these locations may be avoided [8]. Nationally, the National Oceanic and Atmospheric Administration National Centers for Coastal Ocean Science uses satellite imagery for near real-time environmental monitoring of harmful algal blooms, including cyanoHABs, in coastal regions and the Great Lakes [9]. The United States (US) Environmental Protection Agency routinely produces satellite imagery of cyanoHABs for over 2000 large inland lakes and reservoirs via the Cyanobacteria Assessment Network Application [10]. The Centers for Disease Control and Prevention's (CDC's) One Health Harmful Algal Bloom System (OHHABS) is a US-based surveillance system monitoring harmful algal blooms and the human and animal health effects related to harmful algal bloom exposures. CDC's OHHABS relies on voluntary submissions from state and territorial partners [11].

Toxins and potential co-contaminants (e.g., *Escherichia coli* [12], *Legionella* spp [13], waterborne adenoviruses or enteroviruses [14]) can exist simultaneously in cyanoHABs. Therefore, cyanoHAB exposures can lead to diverse clinical effects and illness, making creation of a single, well defined cyanoHAB clinical case definition elusive [5, 15]. CDC's OHHABS defines harmful algal bloom exposures for humans and animals using a combination of evidence to determine the likelihood of exposure. This evidence includes details related to physical contact with a harmful algal bloom or its products, signs and clinical effects, laboratory results, and medical professional diagnoses, as well as public health assessments [16].

America's Poison Centers is a non-profit organization that represents 55 member poison control centers (PCCs) which provide 24-hour access to poison exposure management and information about substances that are potential human toxins [17]. Individual PCCs serve all 50 US states, the District of Columbia, Puerto Rico, American Samoa, the Federated States of Micronesia, Guam, and the US Virgin Islands [17]. Over 75 million human "exposure cases" (i.e., confirmed or suspected contact with a substance that has been taken into the body regardless of toxicity or clinical manifestation [18]) have been processed by US PCCs since 2000, including > 2 million exposure cases in 2021 [17]. Following a call, each US PCC uploads de-identified case data to the National Poison Data System (NPDS), a data warehouse that collects near real-time poison exposure information [17]. Exposure cases in NPDS can be identified by specific toxins (i.e., product codes) or less specific groupings of toxins (i.e., generic codes) [17]. Since 2006, NPDS data have been utilized for public health surveillance and research purposes, with a focus on high consequence conditions (e.g., botulism, arsenic exposures) [19] and other diverse topics (e.g., snake envenomation [20], bupropion overdoses [21]).

NPDS data have previously been used to describe health effects of harmful algal blooms [22]. Specifically, Lavery et al. identified and re-contacted harmful algal bloom exposure cases processed by five PCCs during a 6-month period to further describe case exposure circumstances and health outcomes (e.g., clinical effects) [22]. Other studies, using different design approaches and data sources, have also documented health effects of cyanoHABs; [5, 23, 24] however, these studies were conducted over limited time periods and across smaller geographic areas. Importantly, knowledge gaps remain regarding cyanoHAB exposure circumstances, and the breadth and severity of associated clinical effects, across the US. Therefore, we examined 13-years of NPDS cyanoHAB exposure case data to characterize the circumstances of these exposures and their associated symptomology, and to further define affected populations, routes of exposure, clinical presentations, and severity of clinical effects.

Methods

Dataset creation

We identified all harmful algal bloom-related exposure cases in NPDS that occurred January 1, 2010 through December 31, 2022 with a NPDS product code for algal bloom (6779940) or with a NPDS generic code for cyanobacteria exposure (201107), "red tide" (310152), or unknown algae (310153). With this approach, we initially identified 7691 harmful algal bloom-related exposure cases among the >37 million exposure cases (any exposure) in NPDS that occurred 2010–2022. Of note, when an individual caller reports to a PCC that more than one person has been exposed at the same location, on the same day, and at the same time, each exposed person is designated as an exposure case and provided a unique identifier by the PCC. It is not possible to identify repeat exposures experienced by the same individual within these data.

From the 7691 harmful algal bloom-related exposure cases, we subsequently excluded exposure cases in which more than one product was involved ($n=948$); exposure reason was adverse drug reaction, intentional abuse, misuse (unintentional or intentional), intentional suicide, malicious, or therapeutic error ($n=190$); medical outcome was a "confirmed non-exposure" ($n=8$); substance was a tablet, capsule, or caplet ($n=571$); or exposure was not specified as harmful blue-green algae (e.g., "red tide") ($n=1200$) (Supplementary Fig. 1, Additional file 1). This resulted in the 4260 cyanoHAB exposure cases in our final dataset for analysis, including symptomatic exposure cases with and without clinical effects related to the exposure and asymptomatic exposure cases.

Available variables

For each exposure case, PCCs aim to collect case demographics and exposure and outcome information, including exposure route(s), exposure location(s), chronicity of exposure, clinical effects, and medical outcome, as described below [18].

- *Exposure route(s)* included "ingestion", "dermal", and "inhalation/nasal", among others [18]. More than one exposure route per exposure case was possible.
- *Exposure location(s)* consisted of the exposure site (e.g., "own residence", "public area") and the geographic location (i.e., state) of the caller reporting the exposure.
- *Chronicity of exposure* described the duration of exposure and was defined as "acute" if it occurred over ≤8 hours, "acute-on-chronic" if a single exposure was preceded by an exposure >8 hours, "chronic" if it occurred over >8 hours, or "unknown" if exposure duration was unknown [18].
- *Clinical effects* reflected the "signs, symptoms, and clinical findings associated with the exposure." The relationship of each clinical effect to the exposure was documented (e.g., "related to the exposure", "not related to the exposure"). Per protocol, PCCs coded a clinical effect as "unknown relation" when it was uncertain if the reported clinical effect was related to the cyanoHAB exposure. Similarly, PCCs coded a clinical effect as "not related" when the reported clinical effect was deemed to be unrelated to the cyanoHAB exposure.
- *Medical outcome* was indicated as "no effect", "minor effect", "moderate effect", or "major effect". Exposure cases with "no effect" developed no clinical effects from the exposure. Exposure cases with clinical effects from the exposure that were "minimally bothersome" and "resolved rapidly" were categorized as "minor effect" (e.g., self-limiting gastrointestinal (GI) clinical effects that did not involve dehydration). Exposure cases with prolonged clinical effects from the exposure that likely affected more than an isolated area of the body (e.g., hypotension) and responded to treatment (e.g., GI clinical effects that caused dehydration) were categorized as "moderate effect" medical outcomes. Exposure cases with clinical effects from the exposure that were life-threatening or caused significant "residual disability or disfigurement" (e.g., experienced repeat seizures; required mechanical ventilation) were considered "major effect" medical outcomes. An exposure case was considered to have a known medical outcome if follow-up was conducted by the PCC or the initial call occurred long enough after the exposure that the medical outcome was known with certainty. An exposure case was considered to have an unknown medical outcome if it was not followed because (1) the exposure was "judged as a nontoxic exposure" or determined to have "minimal clinical effects possible", or (2) the exposure case had a "potentially toxic exposure", but was unable to be followed to an outcome.

Analyses

We determined counts and percentages of cyanoHAB exposure cases, and their associated exposure route(s), exposure location(s), and chronicity of exposure by medical outcome category (Supplementary Tables 1 and 2, Additional file 1). Clinical effects "related to the exposure" were quantified and ordered to reflect the most common occurrences. Using US Census Bureau's American Community Survey (ACS) Demographic and Housing 5-year Estimates (2010–2022) for the 50 US States and Washington, D.C [25], we calculated national annual

cyanoHAB exposure case rates and national 13-year (i.e., 2010–2022) cyanoHAB exposure case rates by US Census Bureau defined geographic division [26]. Twelve exposure cases from unknown locations were excluded from the 13-year cyanoHAB exposure case rates; the remaining exposure cases (n=4248) were located within the US and were included in the 13-year rate calculation. Analyses were performed using SAS (SAS Version 9.4, 2016; SAS Institute Inc, Cary, NC, USA) and ArcGIS (ArcGIS [GIS software] Version 10.8.1, 2020; Environmental Systems Research Institute, Inc., Redlands, CA, USA).

Results

Exposures

Of the included cyanoHAB exposure cases (n=4260) identified in NPDS during 2010–2022, more than half (n=2175) were among children < 20 years of age; more cyanoHAB exposure cases were female than male (Table 1). The majority of exposure cases with known medical outcomes had "no effect" (n=1163, 27.3%). Just over 50% (n=2139) of exposure cases had "unrelated effect" or were not followed to a known medical outcome. Over half of the exposure cases not followed to a known medical outcome were either "judged as a non-toxic exposure" (n=137, 3.2%) or had a medical outcome of "minimal clinical effects possible" (n=1453, 34.1%). Most children with less serious medical outcomes (i.e., "no effect" or "minor effect") were 0–5 years old, while most children with more serious medical outcomes (i.e., "moderate effect") were 6–12 years old. Among exposure cases that experienced a medical outcome of "moderate effect," just over 54% were adults (n=53). Two children (13–19 years) and two adults had a medical outcome of "major effect" (n=4, 100%); there were no deaths.

Over 68% of all exposures, regardless of medical outcome, occurred in public areas (n=2902), while exposure cases' residences were the next most common location (n=1125, 26.4%) (Table 1). For exposures that occurred in a public area, proportions decreased as known effect severity increased ("no effect" n=968, 83.2%, "minor effect" n=584, 68.2%, "moderate effect" n=57, 58.2%). However, for exposures that occurred in the exposure case's own residence, proportions increased as known effect severity increased ("no effect" n=168, 14.5%, "minor effect" n=207, 24.2%, "moderate effect" n=31, 31.6%), with the exception of "major effect" ("public area" n=3, 75.0%, "own residence" n=0).

Each exposure case was exposed to cyanoHABs through 1 or more exposure routes. Exposures routes were predominantly dermal (n=3194, 75.0%) or ingestion (n=2283, 53.6%) (Table 1). For dermal exposures, proportions decreased with increasing effect severity ("no effect" n=1045, 89.9%, "minor effect" n=645, 75.4%, "moderate effect" n=56, 57.1%, "major effect" n=2, 50.0%). For ingestion exposures, proportions generally increased with increasing effect severity ("no effect" n=478, 41.1%, "minor effect" n=504, 58.9%, "moderate effect" n=58, 59.2%, "major effect" n=2, 50.0%).

Regarding chronicity of exposure, the majority of all exposures were reportedly acute (n=3824, 89.8%) in nature, regardless of medical outcome (Table 1). The proportion of both "chronic" and "acute-on-chronic" exposures were highest for those with "moderate effect" ("chronic": n=12, 12.2%; "acute-on-chronic": n=9, 9.2%). Chronic exposure cases, regardless of medical outcome, occurred at "own residence" (n=112, 10.0%) more often than "public areas" (n=124, 4.3%).

Outcomes

Across all 4260 cyanoHAB exposure cases, 1768 experienced clinical effects. Of these, 818 exposure cases experienced clinical effects that were "related" to the cyanoHAB exposure, while 1035 exposure cases had clinical effects with an unknown relationship to the cyanoHAB exposure. The "related" clinical effects most frequently reported were diarrhea, vomiting, nausea, rash, and abdominal pain; however, fever, throat irritation, and cough/choke were not uncommon (Table 2). Gastrointestinal signs (i.e., diarrhea, vomiting, abdominal pain, nausea) were reported most commonly for ingestion exposures (e.g., 671 reported GI clinical effects/355 exposure cases who reported clinical effects by ingestion route versus 490 reported GI clinical effects/272 exposure cases who reported clinical effects by dermal route). Rash was the clinical effect most commonly reported for a dermal exposure route (182 reported clinical effects/182 exposure cases who reported clinical effects by dermal route).

Rates

During the study period, the highest national rate of cyanoHAB exposure cases occurred in 2016 (2.5 cases per 1 million (1 M) person-years), followed by 2021 (1.5 cases per 1 M person-years) (Fig. 1). Although the rate of exposure cases over the study period varied across years, overall, we observed an increasing trend across the study period. Exposure case counts were highest during June – August each year, with some exceptions (e.g., peaks in September 2018 (n=105); a small peak in May 2021 (n=86)) (Fig. 2). During 2010–2022, the highest monthly peak of exposure cases occurred in July 2016 (n=597) followed by August 2019 (n=217) (Fig. 2).

By US Census Bureau division, Mountain had the highest exposure case 13-year rate (6.7 cases per 1 M person-years), followed by West North Central (1.5 cases per 1 M person-years), and Pacific (0.9 cases per 1 M person-years) with the second and third highest rates, respectively (Figs. 3).

Table 1 Cyanobacteria harmful algal exposure case characteristics by medical outcome, US, 2010–2022 ($n = 4260$)

	Known outcomes				Unknown outcomes				
Characteristics	**No effect (*N* = 1163, 27.3%)**	**Minor effect (*N* = 856, 20.1%)**	**Moderate effect (*N* = 98, 2.3%)**	**Major effect (*N* = 4, 0.1%)**	**Not followed, nontoxic exposure† (*N* = 137, 3.2%)**	**Not followed, minimal clinical effects possible (*N* = 1453, 34.1%)**	**Unable to follow, potentially toxic exposure (*N* = 128, 3.0%)**	**Effect probably unrelated to exposure (*N* = 421, 9.9%)**	**Total§ (*N* = 4260)**
Age group in years, *N*(%)									
0–5	191 (16.4)	184 (21.5)	13 (13.3)	0	33 (24.1)	313 (21.5)	22 (17.2)	87 (20.7)	843 (19.8)
6–12	187 (16.1)	155 (18.1)	21 (21.4)	0	16 (11.7)	279 (19.2)	22 (17.2)	86 (20.4)	766 (18.0)
13–19	127 (10.9)	103 (12.0)	11 (11.2)	2 (50.0)	4 (2.9)	139 (9.6)	10 (7.8)	40 (9.5)	436 (10.2)
20–49	270 (23.2)	281 (32.8)	30 (30.6)	0	24 (17.5)	374 (25.7)	43 (33.6)	122 (29.0)	1144 (26.9)
50 and over	47 (4.0)	60 (7.0)	18 (18.4)	2 (50.0)	6 (4.4)	132 (9.1)	8 (6.3)	51 (12.1)	324 (7.6)
Unknown adult (≥ 20 years)	137 (11.8)	52 (6.1)	5 (5.1)	0	18 (13.1)	125 (8.6)	16 (12.5)	32 (7.6)	385 (9.0)
Unknown child (≤ 19 years)	82 (7.1)	6 (0.7)	0	0	1 (0.7)	33 (2.3)	5 (3.9)	3 (0.7)	130 (3.1)
Unknown age	122 (10.5)	15 (1.8)	0	0	35 (25.5)	58 (4.0)	2 (1.6)	0	232 (5.4)
Gender, **N(%)**									
Male	440 (37.8)	403 (47.1)	51 (52.0)	2 (50.0)	47 (34.3)	689 (47.4)	52 (40.6)	204 (48.5)	1888 (44.3)
Female	478 (41.1)	428 (50.0)	47 (48.0)	2 (50.0)	56 (40.9)	669 (46.0)	68 (53.1)	215 (51.1)	1963 (46.1)
Unknown	245 (21.1)	25 (2.9)	0	0	34 (24.8)	95 (6.5)	8 (6.3)	2 (0.5)	409 (9.6)
Exposure site, **N(%)**									
Own residence	168 (14.4)	207 (24.2)	31 (31.6)	0	46 (33.6)	490 (33.7)	67 (52.3)	116 (27.6)	1125 (26.4)
Public area	968 (83.2)	584 (68.2)	57 (58.2)	3 (75.0)	88 (64.2)	878 (60.4)	50 (39.1)	274 (65.1)	2902 (68.1)
Other/Unknown	27 (2.3)	65 (7.6)	10 (10.2)	1 (25.0)	3 (2.2)	85 (5.8)	11 (8.6)	31 (7.4)	233 (5.5)
Route of exposure, **N(%)***									
Dermal	1045 (89.9)	645 (75.4)	56 (57.1)	2 (50.0)	99 (72.3)	989 (68.1)	76 (59.4)	282 (67.0)	3194 (75.0)
Ingestion	478 (41.1)	504 (58.9)	58 (59.2)	2 (50.0)	83 (60.6)	863 (59.4)	87 (68.0)	208 (49.4)	2283 (53.6)
Inhalation nasal	34 (2.9)	81 (9.5)	18 (18.4)	1 (25.0)	2 (1.5)	144 (9.9)	14 (10.9)	41 (9.7)	335 (7.9)
Other/Unknown	16 (1.4)	63 (7.4)	17 (17.3)	1 (25.0)	14 (10.2)	67 (4.6)	9 (7.0)	37 (8.8)	224 (5.3)
Chronicity, **N(%)‡**									
Acute	1085 (93.3)	770 (90.0)	76 (77.6)	4 (100.0)	130 (94.9)	1297 (89.3)	106 (82.8)	356 (84.6)	3824 (89.8)
Acute-on-chronic	25 (2.1)	27 (3.2)	9 (9.2)	0	2 (1.5)	50 (3.4)	6 (4.7)	19 (4.5)	138 (3.2)
Chronic	53 (4.6)	48 (5.6)	12 (12.2)	0	4 (2.9)	96 (6.6)	15 (11.7)	37 (8.8)	265 (6.2)
Unknown	0	11 (1.3)	1 (1.0)	0	1 (0.7)	10 (0.7)	1 (0.8)	9 (2.1)	33 (0.8)

* Individual exposure cases can have more than one route of exposure

† Clinical effects are not expected

‡ Chronicity refers to the duration of exposure and is defined as "acute" (i.e., an exposure occurring over ≤ 8 hours), "acute-on-chronic" (i.e., a single exposure that is preceded by an exposure that took place for > 8 hours), "chronic" (i.e., an exposure that took place for > 8 hours), or "unknown" (i.e., exposure duration is not known) [15] §Total Percentages by column may not add up to 100 due to rounding

Table 2 Clinical effects reported by cyanobacteria harmful algal bloom (cyanoHAB) exposure cases, US, 2010–2022 ($n = 818$)

Clinical effects	CyanoHAB exposure cases experiencing clinical effects*† ($n = 818$)
Diarrhea	269 (32.9)
Vomiting	226 (27.6)
Nausea	205 (25.1)
Rash	200 (24.4)
Abdominal pain	129 (15.8)
Other (miscellaneous)	112 (13.7)
Headache	100 (12.2)
Pruritis	94 (11.5)
Fever/hyperthermia	85 (10.4)
Throat irritation	83 (10.1)
Cough/choke	64 (7.8)
Dermal (irritation/pain)	50 (6.1)
Ocular irritation/pain	32 (3.9)
Dyspnea	27 (3.3)
Erythema/flushed	25 (3.1)
Other (respiratory)	22 (2.7)
All other effects‡	224 (27.4)

*Among cyanoHAB exposure cases that reported clinical effects "related to the (cyanoHAB) exposure"

†Exposure cases could experience more than one clinical effect

‡Clinical effects in this category each had < 20 exposure cases "related to the (cyanoHAB) exposure" associated with them

Discussion

Despite an overall decline in all-cause (i.e., for any reason) exposure cases reported to NPDS in recent years [17], cyanoHAB exposure case rates increased, from 0.4 cases per 1 M person-years in 2010 to 1.4 cases per 1 M person-years in 2022. The most notable peak occurred in 2016 (2.5 cases per 1 M person-years), the year that Utah Lake in Salt Lake County, Utah was closed for recreational purposes due to a sizable cyanoHAB bloom. The Utah Poison Control Center received over 400 calls associated with this cyanoHAB bloom event [27]. The event is also evident in the 13-year cyanoHAB exposure case rate which is higher for the Mountain division than for any other US geographic division. Awareness of cyanoHABs through state and territorial efforts or news reports of adverse health events can influence reporting of bloom events to state officials [8] and reporting of health effects to PCCs [28].

Clinical effects from cyanoHAB exposures often vary and depend on factors like exposure route and duration, and toxin amount and type. Consumption of cyanoHAB contaminated drinking water has been associated with muscle pain and clinical effects of the GI tract, skin, and ear [12]. Exposure to cyanoHAB contaminated water during recreational activities can result in a range of clinical effects including vomiting, diarrhea, cough, rash,

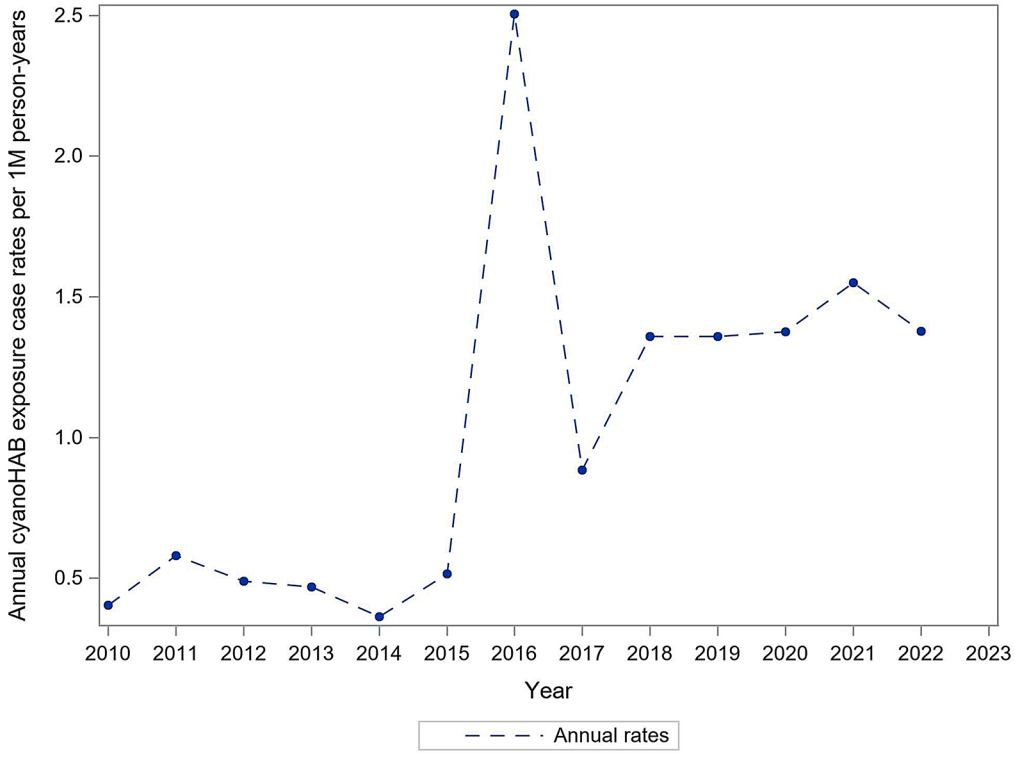

Fig. 1 Cyanobacteria harmful algal bloom (cyanoHAB) exposure case annual rates,*US, 2010–2022 ($n = 4260$). * Annual population estimates were obtained from the US Census Bureau's American Community Survey (ACS) Demographic and Housing Estimates 5-year Estimates (2010–2022) for the 50 US States and Washington, D.C [22]

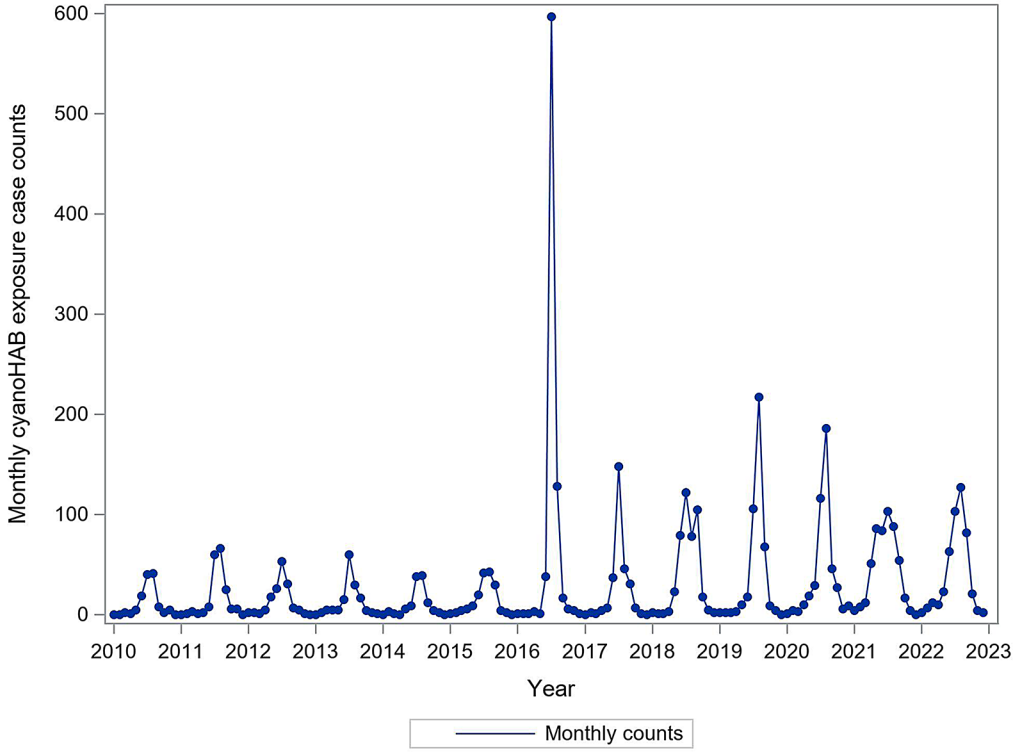

Fig. 2 Cyanobacteria harmful algal bloom (cyanoHAB) exposure case monthly counts, US, 2010–2022 ($n=4260$)

fever, pneumonia, and sore eyes and ears [5]. Some cyanoHAB exposure-related clinical effects might not be a direct result of the toxins themselves. For example, rash might be sequalae to allergic reactions or reactions to inflammatory cytokines [5] produced following cyanoHAB exposure.

In this study, the most common cyanoHAB exposure-related clinical effects involved the GI tract (i.e., diarrhea, vomiting, nausea, abdominal pain); though rash, headache, fever, and respiratory clinical effects were also reported. CyanoHAB exposure cases with GI clinical effects typically reported ingestion as the exposure route. CyanoHAB exposure cases with a dermal exposure route, but who experienced GI clinical effects, could have inadvertently ingested water [29] – a fact that might not have been recognized and documented in these data. CyanoHAB exposure cases with rash most frequently reported dermal exposure. The varying cyanotoxin types and mixtures that cases were exposed to, though unknown in this study, could have contributed to the observed variation in clinical effects.

As in other studies [24, 30, 31], we found that among cyanoHAB-related clinical effects experienced by cyanoHAB exposure cases, approximately a quarter (196 respiratory effects/818 exposure cases experiencing a related clinical effect) were respiratory system effects (i.e., throat irritation, cough/choke, dyspnea, other (respiratory)). Stewart et al. reported that individuals with recreational exposure to cyanoHABs in their study were twice as likely to have respiratory signs when cyanoHAB levels were high (cell surface area > 12.0 mm squared per milliliter (mm^2/ml)) compared to when cyanoHAB levels were low (< 2.4 mm^2/ml) [32]. In another study, individuals recreating in areas with documented aerosolized cyanoHABs did not have corresponding toxin in their blood plasma [14]. Pre-existing respiratory conditions might also increase an individual's risk for respiratory clinical effects following cyanoHAB exposure. In a case series of three children exposed to cyanoHAB-contaminated water while swimming, the only child who presented with respiratory clinical effects had a history of asthma [23].

Most cyanoHAB exposures in this study occurred in public places. This is consistent with the 2021 report from CDC's OHHABs which documents that 83% of all HAB events took place at lakes, reservoirs, and impoundments [11]. Among state health and environmental officials queried by Hardy et al. about where cyanoHAB exposures most likely take place, recreational exposure to cyanoHABs was generally recognized as an important to extremely important "public health concern" [8]. While recreational activities are an important means of exposure, recreational cyanoHAB exposures do not necessarily result in serious medical outcomes. Considering the cyanoHABs exposure cases with known effects in our study, twice as many "moderate" or "major"

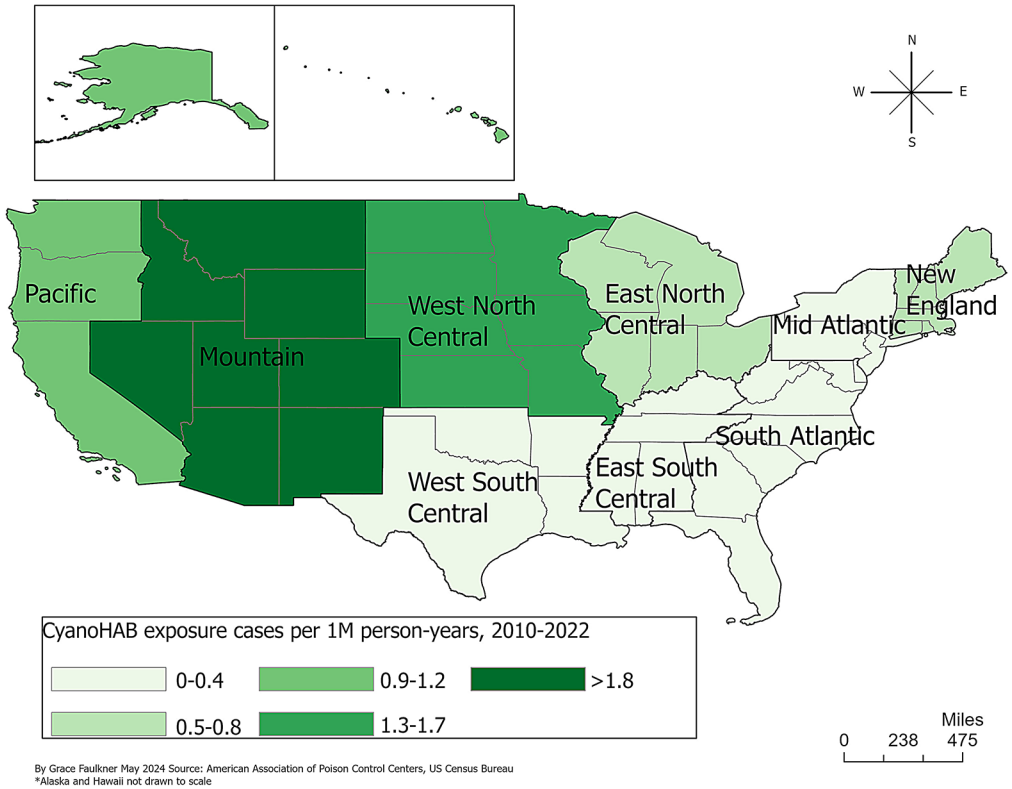

Fig. 3 Cyanobacteria harmful algal bloom (cyanoHAB) 13-year exposure case rates*/1M person-years by division, [23] US, 2010–2022 ($n=4248$†). *Annual population estimates were obtained from the US Census Bureau's American Community Survey (ACS) Demographic and Housing Estimates 5-year Estimates (2010–2022) for the 50 US States and Washington, D.C [22]. †Twelve exposure cases were from an unknown location and are not included in this figure

effects occurred at the exposure case's "own residence" compared to a "public area." This may be related to an increased opportunity for chronic exposure at a residence versus a public location. Chronic exposure to cyanoHABs can heighten clinical effects and increase risk for cancers of the digestive system and for non-alcoholic liver disease [33].

Children < 20 years of age represented over half of all cyanoHAB exposure cases in this study, a finding similar to that reported by Lavery et al. [22] Compared to adults, young children and adolescents might be apt to ignore cyanoHAB contamination warnings [34]. Children tend to engage in longer playtimes in water and have an increased likelihood of accidental water consumption during these activities [29]. With smaller bodies than adults, children can be at increased risk for more serious clinical outcomes than adults if exposed to the same amount of cyanoHAB contaminated water, especially depending on childhood developmental stage [34]. However, the more serious medical outcomes in this study were experienced by adults. Caregivers might have a lower threshold for calling a PCC regarding a child cyanoHAB exposure, regardless of illness severity, than for an adult cyanoHAB exposure.

CyanoHAB growth is facilitated by warm temperatures [3], as seen in the summer months. In this study, cyanoHAB exposure case counts peaked in July 2016, followed by the second highest peak in August 2019. The relative amounts and types of cyanoHAB genera [35] can vary greatly across a given geography and year to year, though increases tend to occur May to September [35]. Our results could be a reflection of this temporal variability in cyanoHAB growth.

There are several limitations to this study. CyanoHAB exposure cases captured in NPDS data are not necessarily a reflection of cyanoHAB exposures in the general population [17] and likely underestimate the true number of human cyanoHAB exposures in the US. CDC's OHHABS reported that, of the 117 human harmful algal bloom exposure cases in their database in 2021, 59% called a PCC [11]. For those exposure cases that do contact one of the 55 US PCCs, variability among centers could be seen as a limitation, however, requirements for demonstrated knowledge base standardization among PCC staff minimizes this variability. Another limitation is that not all cyanoHAB exposure cases in this study were followed for the entirety of their associated medical care; therefore, these cases do not have a known medical outcome.

We were unable to examine if the reported clinical effects or medical outcomes were associated with specific cyanotoxins or potential co-contaminants, including other pathogens (e.g., *Escherichia coli* [12], *Legionella* spp [13], waterborne adenoviruses or enteroviruses [14]), as this information was not available in NPDS. Attributing specific clinical effects to cyanoHAB exposures is generally difficult, even when prospectively monitoring water for cyanoHAB contamination and people for clinical effects [12]. Finally, there were a limited number of exposure cases experiencing "moderate effect" and "major effect" in this study. Future studies using additional years of data could help to characterize severe illness resulting from cyanoHAB exposures.

In conclusion, the rate of cyanoHAB exposure cases reported to NPDS increased overall from 2010 to 2022. CyanoHAB exposures more commonly occurred in public places or in the case's own residence. Serious medical outcomes were uncommon among cyanoHAB exposure cases. Over half of the exposure cases were children. Among the exposure cases with serious medical outcomes, more were adults and proportionally more reported exposure via ingestion.

NPDS data are a valuable public health information source [22] that can be used to characterize cyanoHAB exposures and provide insight into exposure circumstances, associated symptomology, affected populations, clinical presentations, and outcomes. Nationally, we observed a more than three-fold increase in annual cyanoHAB exposure case rates from 2010 to 2022, despite an overall reduction in all-cause exposure cases in NPDS during the same time period. As reporting of cyanoHABs exposure cases occurs more frequently, it becomes increasingly important to identify these exposure cases, especially given the potential for adverse effects. This study works to further characterize the constellation of clinical effects to allow for identification of cyanoHAB exposure cases in PCC or other medically relevant data with the potential to aid public health monitoring.

Disclaimers

America's Poison Centers (APC) maintains the NPDS, which houses de-identified case records of self-reported information collected from callers during exposure management and poison information calls managed by the country's PCC. NPDS data do not reflect the entire universe of exposures to a particular substance as additional exposures may go unreported to PCC; accordingly, NPDS data should not be construed to represent the complete incidence of US exposures to any substance(s). Exposures do not necessarily represent a poisoning and APC is not able to completely verify the accuracy of every report. Findings based on NPDS data do not necessarily reflect the opinions of APC.

The views expressed in this manuscript are those of the individual authors and do not necessarily reflect the views and policies of the US Environmental Protection Agency. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

Abbreviations

ACS	American Community Survey
CDC	Centers for Disease Control and Prevention
cyanoHAB	Cyanobacteria harmful algal bloom
GI	Gastrointestinal
NPDS	National Poison Data System
OHHABS	One Health Harmful Algal Bloom System
PCC	Poison Control Center
1M	One million

Supplementary Information

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Supplementary Material 1

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Author contributions

RAB, SR, MB, and EDH conceptualized the study. RAB created the manuscript, undertook the analysis, and created the tables and Fig. 1 and 2. MB procured the data and provided medical expertise. EDH provided algal bloom expertise. GF prepared Fig. 3. SR provided supervision and analysis expertise. All authors were involved in reviewing and editing the manuscript. All authors read and approved the final manuscript.

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Data availability

Data was procured from the National Poison Data System. In order to protect private medical records, these data are not publicly available. However, these data can be requested from America's Poison Centers via application at https://poisoncenters.org/national-poison-data-system.

Declarations

Ethics approval and consent to participate

This study was determined to be exempt by the North Carolina State University Institutional Review Board.

Consent to publish

Not applicable.

Competing interests

The authors declare no competing interests.

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