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Exposure to glyphosate in the United States: Data from the 2013–2014 National Health and Nutrition Examination Survey

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Abstract

Background: Exposure to glyphosate, the most used herbicide in the United States, is not well characterized. We assessed glyphosate exposure in a representative sample of the U.S. population ≥ 6 years from the 2013–2014 National Health and Nutrition Examination Survey.

Methods: We quantified glyphosate in urine (N = 2,310) by ion chromatography isotope-dilution tandem mass spectrometry. We conducted univariate analysis using log-transformed creatinine-corrected glyphosate concentrations with demographic and lifestyle covariates we hypothesized could affect glyphosate exposure based on published data including race/ethnicity, sex, age group, family income to poverty ratio, fasting time, sample collection season, consumption of food categories (including cereal consumption) and having used weed killer products. We used multiple logistic regression to examine the likelihood of glyphosate concentrations being above the 95th percentile and age-stratified multiple linear regression to evaluate associations between glyphosate concentrations and statistically significant covariates from the univariate analysis: race/ethnicity, sex, age group, fasting time, cereal consumption, soft drink consumption, sample collection season, and urinary creatinine.

Results: Glyphosate weighted detection frequency was 81.2 % (median (interquartile range): 0.392 (0.263–0.656) μg/L; 0.450 (0.266–0.753) μg/g creatinine). Glyphosate concentration decreased from age 6–11 until age 20–59 and increased at 60+ years in univariate analyses. Children/adolescents and adults who fasted > 8 h had significantly lower model-adjusted geometric means (0.43 (0.37–0.51) μg/L and 0.37 (0.33–0.39) μg/L) than those fasting ≤ 8 h

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Declaration of Competing Interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material
Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2022.107620.

(0.51 (0.46–0.56) μg/L and 0.44 (0.41–0.48) μg/L), respectively. The likelihood (odds ratio (95 % CI)) of glyphosate concentrations being > 95th percentile was 1.94 (1.06–3.54) times higher in people who fasted ≤ 8 h than people fasting > 8 h (P = 0.0318).

Conclusions: These first nationally representative data suggest that over four-fifths of the U.S. general population ≥ 6 years experienced recent exposure to glyphosate. Variation in glyphosate concentration by food consumption habits may reflect diet or lifestyle differences.

1. Introduction

Glyphosate is a broad-spectrum, systemic herbicide and the active ingredient in glyphosate-based herbicides (GBHs), the most frequently used herbicides in the world (Benbrooke, 2016). Since their introduction in the late 1970s, the volume of GBHs applied in the United States has increased approximately 100-fold (Benbrooke, 2016) mainly because of patent expiration, increased promotion of non-till agriculture and introduction of glyphosate resistant crops (IARC, 2017; Coupe and Capel, 2016).

Glyphosate presence is widespread in the ecosystem (ATSDR, 2020a). Glyphosate is detected in particulate matter in the air emitted by rural roads, soils, including agricultural soils, sediments, water, and house dust (Ramirez Haberkon et al., 2021; Battaglin et al., 2014; Van Bruggen et al., 2018; Rendón-von Osten and Dzul-Caamal, 2017; Curwin et al., 2005). Glyphosate is also detected in a variety of foods, including fruits, cereals, and pulses (i.e., dried seeds of legumes) (USDA, 2011; Kolakowski et al., 2020; Zoller et al., 2018; EFSA, 2018; Rubio et al., 2014; Xu et al., 2019). Additionally, glyphosate has been detected in animal feed (Zhao et al., 2018), in the urine and organs of dairy cows, as well as in the urine of rabbits and hares (Krüger et al., 2014; Bai and Ogbourne, 2016). Increasing amounts of glyphosate available in the food chain may relate, in part, to excess application of GBHs to glyphosate resistant crops (Bohn and Millstone, 2019).

Scientific evidence suggests harmful effects of glyphosate and GHB on the brain, lungs, liver, intestines, and reproductive systems of several animal models (Roy et al., 2016; Cuhra et al., 2015; Mesnage et al., 2017; Altamirano et al., 2018; Guerrero Schimpf et al., 2017; Kumar et al., 2014; Tang et al., 2020). Additionally, glyphosate exposure has been associated with shifts in microbiome composition (Aitbali et al., 2018) and increased antibiotic resistance in mice. Antibiotic resistance can have severe impacts on plant, animal and human health (Hoffman et al., 2015; Van Bruggen et al., 2018).

On the other hand, evidence supporting glyphosate effects on human health, including its carcinogenicity is limited (Xu et al., 2019). In the last decade, several international agencies and organizations have assessed the carcinogenicity of glyphosate with mixed results (ATSDR, 2020a). In 2015, the International Agency for Research on Cancer (IARC) classified glyphosate as “probably carcinogenic in humans” (category 2A) and confirmed this classification in 2017 (IARC, 2015, 2017). By contrast, the European Food Safety Authority (EFSA) (EFSA, 2015) and the Joint FAO/WHO Meeting on Pesticide Residues, after separate assessments, concluded that glyphosate was unlikely to pose carcinogenic risk to humans (FAO/WHO, 2016). Similarly, the U.S. EPA, after reviewing the existing evidence, did not support any of the carcinogenic classifications (U.S. EPA, 2017). Recently, the European Union's Assessment Group on Glyphosate (EUAGG, 2021) concluded that glyphosate is safe for all proposed uses when used as directed and proposed to declassify it as carcinogenic. Lack of international standardization of risk assessment procedures has been cited to explain discrepancies among carcinogenicity assessments (Van Straalen and Legler, 2018).

Human exposure to glyphosate occurs through dermal contact, inhalation and diet (ATSDR, 2020a; Pierce et al., 2020; Bootsikeaw et al., 2021; Fagan et al., 2020). Upon exposure, most glyphosate is excreted unchanged (62–69 %) via feces (Williams et al., 2000). Human studies suggest that only 1–6 % of orally ingested glyphosate is rapidly eliminated as the unchanged compound in urine (Zoller et al., 2020; Faniband et al., 2021) with reported elimination half-life ranges of 5.5–10 h (Connolly et al., 2019; Zoller et al., 2020). Therefore, concentrations of glyphosate in urine have been used to assess human exposure to glyphosate in several occupational and population studies in the United States and abroad (Conrad et al., 2017; Curwin et al., 2007; Knudsen et al., 2017; Lemke et al., 2021; Mills et al., 2017; Parvez et al., 2018; Soukup et al., 2020; Trasande et al., 2020; Connolly et al., 2017; Curwin et al., 2005; Faniband et al., 2021; Rendón-von Osten and Dzul-Caamal, 2017; Zhang et al., 2020). However, the extent of glyphosate exposure in the U.S. general population is unknown. To fill in this data gap, we sought to establish, for the first time, the reference range of glyphosate urinary concentrations in a representative sample of the U.S. general population 6 years of age and older from the 2013–2014 National Health and Nutrition Examination Survey (NHANES).

2. Materials and methods

2.1. Study population

NHANES is a complex, multistage, probability sample of the civilian, non-institutionalized, U.S. population designed to provide statistical data on the prevalence, distribution, risk factors and effects of illness and disability in the United States (CDC, 2017). NHANES is conducted in two-year cycles by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). NHANES includes in person household interviews with demographic, socioeconomic, and health-related questionnaires, and dietary assessment, physical exams, and collection of biological samples (a portion of which are used to assess exposure to environmental chemicals) in mobile examination centers (MEC). NCHS Research Ethics Review Board reviewed and approved the NHANES protocol. All adult respondents gave informed written consent to participate in the survey; parents or guardians provided written permission for participants younger than 18 years. NHANES participants aged ≥ 18 years of age responded to NHANES questionnaires by themselves. For NHANES participants aged < 18 years, responses were provided by either the participant or a proxy (e.g. parent, guardian) depending on the specific questionnaire, as determined by NHANES documentation and procedures (CDC, 2018).

During the MEC examination, each NHANES participant provided one spot urine sample which was not necessarily a first morning void, and reported fasting status. For the dietary assessment, participants provided a 24-hour dietary recall of all foods and beverages consumed during the previous 24 h, which constituted the basis of the NHANES dietary intake database. This assessment included questions on time of food consumption, name of the eating occasion, detailed food descriptions and amounts of the reported foods (https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/1314/wweia_2013_2014_data.pdf, https://www.cdc.gov/nchs/data/nhanes/nhanes_13_14/Phone_Follow-up_Dietary_Interviewers_manual.pdf).

For this study, we analyzed 2,310 spot urine stored samples eligible for use in future research collected from a random one-third representative subsample of participants 6 years of age and older from the 2013–2014 NHANES cycle.

2.2. Quantification of urinary concentrations of glyphosate

Urine was collected at the MEC, and, within hours of collection, urine samples were aliquoted and frozen onsite. The frozen urine aliquots were shipped overnight on dry ice to the CDC's National Center for Environmental Health (NCEH) where they were stored at −70 °C until analysis.

At NCEH, we quantified glyphosate in 200 μL urine using an analytical method described in detail elsewhere (Schütze et al., 2021). Briefly, urine samples were diluted 1:1 with water, analytes were extracted and separated by ion chromatography and detected by isotope dilution-electrospray ionization tandem mass spectrometry. The limit of detection (LOD) was 0.20 μg/L. The LOD, calculated as $3S_0$, where S_0 is the standard deviation as the concentration approaches zero, was determined from repeated measurements of low-level standards spiked onto human urine (Taylor, 1987). The method precision was < 5 percent relative standard deviation (RSD) and accuracy (range of mean relative recovery) was 92–112 %. The NCEH laboratory successfully participated in international proficiency testing programs such as GEQUAS (https://app.g-equas.de/web/) and OSEQAS (https://www.inspq.qc.ca/sites/default/files/documents/ctq/ipaqe-participants-guide.pdf) to further confirm method accuracy.

An analytical run typically included 10 calibration standards, two reagent blanks, two low-concentration and two high-concentration urine-based quality control (QC) materials, and up to 36 NHANES samples as described before (Schütze et al., 2021). The analytical measurements followed strict quality control/quality assurance protocols to ensure data accuracy and reliability (Caudill et al., 2008). If the QC samples failed the statistical evaluation, all the study samples within the run were re-prepared and analyzed. The precision of the analytical measures (calculated as the %RSD of replicate determinations of the concentration of QC materials analyzed with the NHANES samples in a 10-month period) was 4.1 % and 2.9 % for the low- and high-concentration QC materials, respectively.

2.3. Statistical analysis

We analyzed the glyphosate public dataset using Statistical Analysis System (SAS) (version 9.4; SAS Institute Inc., Cary, NC) and SUDAAN (version 13, Research Triangle Institute, Research Triangle Park, NC). SAS and SUDAAN incorporate sample weights (i.e., WTSSCH2Y for this specific dataset) and design variables to account for unequal selection probabilities due to the complex, multistage, probability sample design of NHANES and to account for the oversampling of certain groups. Following NCHS's recommendation, we imputed a value equal to the LOD divided by the square root of 2 to concentrations below the LOD (Hornung and Reed, 1990).

Based on proxy or self-report, we stratified age in years at the last birthday in four groups (6–11, 12–19, 20–59, and 60+), and race/ethnicity in four groups (non-Hispanic Black persons, non-Hispanic White persons, all Hispanic persons, and Other persons, including all other non-Hispanic race/ethnicity persons). We calculated glyphosate geometric mean (GM) and select distribution percentile concentrations and their 95 % confidence interval (CI) by age group, sex, and race/ethnicity both in micrograms per liter (μg/L) and in micrograms per gram of creatinine (μg/g creatinine). We used the public 2013–2014 NHANES urinary creatinine concentrations, determined using a commercially available enzymatic assay, to account for urinary dilution (University of Minnesota, 2014).

We defined cereal consumption as "yes" or "no" based on the Food and Nutrient Database for Dietary Studies (https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/fndds/), a United States Department of Agriculture (USDA) database that provides the nutrient value of foods and beverages reported in "What We Eat in America," the self-reported dietary intake component of NHANES. We selected the codes of products associated with any cereal consumption in the USDA "What's In The Foods You Eat Search Tool" (https://reedir.arsnet.usda.gov/codesearchwebapp/(S(3klhccrwfticyogpyxbvfqab))/CodeSearch.aspx) (USDA, 2021), and assigned participants with any of the codes associated with cereal consumption as "yes" for consuming cereal. We defined consumption of other food and beverage categories (e.g., beer, vegetable, fruit, legume & nut & seed, drybeans, soft drinks) in a similar way. We considered that participants consumed soymilk based on the answer to question DBQ223E ("Do you drink soy milk?") from the diet and nutrition questionnaire of the NHANES dietary intake component.

We examined season of sample collection (i.e., winter (Nov 1–Apr 30), summer (May 1–Oct 31)), a variable available on the public NHANES datafiles. We determined whether participants reported the use of products to kill weeds in their lawn or garden in the prior week based on participants' response to the question "In the past 7 days, were any chemical products used in {your/his/her} lawn or garden to kill weeds?" within the pesticide module from the NHANES questionnaire (https://wwwn.cdc.gov/Nchs/Nhanes/2013–2014/PUQMEC_H.htm). We defined fasting time as ≤ 8 h (n = 1,281) or > 8 h (n = 1,007) based on self-report. For socioeconomic status, we classified NHANES participants' ratio of family income to poverty (PIR) as PIR > 1 (i.e., income higher than the poverty level) or PIR ≤ 1.

We conducted univariate analysis using the log-transformed creatinine-corrected concentrations of glyphosate and the following covariates: race/ethnicity, sex, age group, PIR, fasting time, season of sample collection, consumption of food categories (including cereal consumption) and having used products to kill weeds.

Because the concentration of glyphosate showed a U-shape curve with age group (decreased from age 6–11 until age 20–59 and increased at 60+ years) in univariate analyses (Table

S1), we conducted an age-stratified multiple regression analysis to evaluate associations between the log-transformed concentrations of glyphosate in people ≤ 19 years and people ≥ 20 years with selected covariates. The covariates, namely sex, race/ethnicity, age group, fasting time, cereal consumption, soft drink consumption, season of sample of collection, urinary creatinine and their two-way interaction terms, were selected for inclusion in the model because they demonstrated a P value < 0.05 in univariate analyses.

In addition, we conducted weighted multiple logistic regression to examine the likelihood of having glyphosate concentrations above the 95th percentile (arbitrary value selected to reflect higher than average exposures) with the same statistically significant covariates from the univariate analysis and their two interaction terms.

To reach both the final linear regression and logistic regression models, we used backward elimination with a threshold of P < 0.05 for retaining covariates and two-way interactions. We also evaluated potential confounding of the not significant predictor covariates by adding each covariate back to a model that included only significant predictors. If adding one of these excluded variables changed the β coefficient for any of the significant predictors ≥ 10 %, we re-added the variable to the model. We report Bonferroni adjusted P-values and 95 % CI for the odds ratios and adjusted geometric means for pairwise comparisons.

We used the public 2013–2014 NHANES data for another herbicide, 2,4-dichlorophenoxyacetic acid (2,4-D), which may be used in conjunction with glyphosate, to determine the weighted Pearson correlation between log10-transformed urinary concentrations of the two herbicides, glyphosate and 2,4-D.

3. Results

We quantified urinary concentrations of glyphosate in 2,310 samples from NHANES 2013–2014 participants. We present glyphosate GM and select percentiles concentrations stratified by age group, sex, and race/ethnicity as well as the corresponding weighted detection frequencies in Table 1. The weighted detection frequency of glyphosate was 81.2 %, and concentrations ranged from < LOD (0.20 μg/L) to 8.13 μg/L. The GM, median and 95th percentile glyphosate concentrations were 0.411 μg/L (0.443 μg/g creatinine), 0.392 μg/L (0.450 μg/g creatinine) and 1.58 μg/L (1.60 μg/g creatinine), respectively.

Results of the univariate analyses are shown in Table S1. Creatinine-corrected GM urinary concentrations were significantly higher for participants who reported having consumed cereal-containing products (P < 0.0001), who had not consumed soft drinks (P = 0.0018), who provided urine samples during the summer season (P = 0.0056) or who fasted eight hours or less (P < 0.0001). Race/ethnicity, age group, and sex were also significantly associated with glyphosate creatinine-corrected GM concentrations (Table S1). By contrast, creatinine-corrected GMs did not differ significantly by having used weed killers, by PIR, or after consuming other foods (e.g., beer, vegetables, fruit, legume & nut & seed, drybeans, soymilk). Of note, creatinine-corrected GM concentration of glyphosate was curvilinearly associated with age group (Table S1): GMs decreased from age 6–11 to age 20–59 and increased at 60+ years of age.

The age-stratified analysis (Tables 2 and S2) also showed a downward urinary glyphosate model-adjusted geometric mean (AGM) concentration trend at younger ages (≤19 years) (from 0.54 (0.46–0.64) to 0.41 (0.37–0.45) μg/L for age groups 6–11 to 12–19 years, respectively). In contrast, at older age groups (≥20 years), AGM concentrations showed a significant upward trend (from 0.36 (0.33–0.39) to 0.46 (0.4–0.53) μg/L for 20–59 years old and 60+ years, respectively). The final age-stratified linear regression analysis (Table 2) showed that fasting time ($P = 0.001$), an interaction term of cereal consumption and race/ethnicity ($P = 0.0194$), age ($P = 0.0004$), and urinary creatinine (β coefficient = 0.0018, $P < 0.0001$) were significant factors for adults (≥20 years), while fasting time ($P = 0.0103$), race/ethnicity ($P = 0.002$), age ($P = 0.0004$), and urinary creatinine (β coefficient = 0.0022, $P < 0.0001$) were significant factors for children and adolescents ≤ 19 years of age. Compared with All Hispanic persons who consumed cereal products, the AGM (Tables 2 and S2) of glyphosate was significantly higher for non-Hispanic White children and adolescents ($P = 0.0014$) and for non-Hispanic White adults ($P = 0.0424$). All other differences in AGM glyphosate concentrations by race/ethnicity were not statistically significant.

The age-stratified multivariate analysis showed that urinary AGM of glyphosate was significantly associated with an interaction with race/ethnicity and cereal consumption in adults ≥ 20 years of age, but not in children and adolescents ≤ 19 years of age (Table 2, Table S2). Glyphosate AGM concentrations in non-Hispanic White and Other race/ethnicity adults ≥ 20 years who consumed cereal-containing products were higher than in those who did not; by contrast, this pattern was reversed among All-Hispanic adults. However, none of the pairwise differences were statistically significant after Bonferroni adjustment. On the other hand, people who fasted >8 h had significantly lower AGM than those who fasted for 8 h or less (0.43 (0.37–0.51) vs 0.51 (0.46–0.56) μg/L for children and adolescents; 0.37 (0.33–0.39) vs 0.44 (0.4–0.48) μg/L for adults, respectively).

The final weighted multiple logistic regression model, to determine the odds of having urinary glyphosate concentrations above the 95th percentile (odds ratio (95 % CI)), had urinary creatinine ($P < 0.0001$), fasting time ($P = 0.0318$), race/ethnicity ($P = 0.0161$), and age group ($P = 0.0076$) as significant factors. People who fasted <8 h were 1.94 (1.06–3.54) times ($P = 0.03$) more likely than those who fasted >8 h to have concentrations of glyphosate above the 95th percentile (Table 3). Children 6–11 years old were 2.26 (0.98, 5.22) times more likely than 12–19 years old adolescents to have concentrations of glyphosate above the 95th percentile; however this difference was not statistically significant ($P = 0.0612$) after Bonferroni adjustment. All other differences by age group and race/ethnicity did not reach statistical significance.

The weighted log-transformed urinary concentrations of glyphosate and 2,4-D (Fig. S1) showed a statistically significant correlation (P-value < 0.001; weighted Pearson correlation coefficient ($r = 0.31$)).

4. Discussion

We present, for the first time, urinary concentrations of glyphosate in a representative sample of the United States general population 6 years of age and older. Approximately-four-fifths (81.2 %) of the population were estimated to have been recently exposed to glyphosate. Glyphosate reference ranges (i.e., geometric mean–95th percentile concentrations) in 2013–2014 NHANES are within the same order of magnitude as the ranges reported in non-occupational populations from several countries (Table S3) including young German adults (Conrad et al., 2017), Germans 18–80 years of age (Soukup et al., 2020), 3–17 year-old children and adolescents living in Germany (Lemke et al., 2021), Swedish young adults (Faniband et al., 2021), lactating mothers in Spain (Ruiz et al., 2021), adults in Ireland (Connolly et al., 2018), Danish mothers and their children (Knudsen et al., 2017) and general populations in France (Grau et al., 2022) and Australia (Campbell et al., 2022). The glyphosate concentration ranges observed in 2013–2014 NHANES participants were also comparable to those from other non-occupationally exposed populations in the United States (Table S3) (Mills et al., 2017; McGuire et al., 2016; Silver et al., 2021, Trasande et al., 2020, Lesseur et al., 2022). In contrast, the 2013–2014 NHANES glyphosate results differed from those of 71 pregnant women in Indiana with a reported mean urinary glyphosate concentration of 3.40 μg/L (minimum−maximum was 0.5–7.20 μg/L) (Parvez et al., 2018) and mean glyphosate concentrations of non-farming fathers, mothers and children (1.4, 1.2 and 2.7 μg/L, respectively) from the farm and non-farm family study (Curwin et al., 2007). Of note, geometric mean and/or median concentrations of glyphosate appear to be somewhat higher in NHANES and most of the U.S. studies compared to studies elsewhere. Different concentrations of glyphosate among studies can result, among other reasons, from differences in regulations and approved uses of glyphosate depending on the country or jurisdiction, as well as from differences in study design (e.g., first morning void vs spot sample vs 24-hour sample collection), analytical methods (e.g., differing sensitivities), diet, and populations evaluated.

Glyphosate and 2,4-D, another herbicide, are often applied together to optimize global farming production with a more efficient weed control (Carvalho et al., 2020). The glyphosate reference ranges are within the same order of magnitude of 2,4-D and other pesticides in the United States in 2013–2014 NHANES (CDC, 2022). The relatively modest correlation between urinary concentrations of glyphosate and 2,4-D in 2013–2014 NHANES participants suggests exposure to both herbicides and may also reflect differences in toxicokinetics of the two biomarkers because the elimination half-life in urine for glyphosate is 5.5–10 h (Connolly et al., 2019; Zoller et al., 2020) while for 2,4-D ranges from 10.2 to 28.5 h (Sauerhoff et al., 1977; ATSDR, 2020b).

The 2013–2014 NHANES participants who fasted >8 h had lower urinary glyphosate AGM concentrations than participants who fasted 8 h or less. Fasting time can help determine whether food intake may contribute to exposure to environmental chemicals, as observed before for some studies involving phthalates in which fasting times were also inversely associated with biomarkers concentrations (Aylward et al., 2011; Wittassek et al., 2011). Therefore, our results suggest that diet is a potential contributor to exposure to glyphosate. Similarly, results from another recent study (Fagan et al., 2020) suggest that diet is a primary source of glyphosate exposure and that shifting to an organic diet is an effective way to reduce body burden of glyphosate. Unfortunately, for the 2013–2014 NHANES participants examined, we did not have information on consumption of organic food.

Elementary-school aged children had the highest glyphosate AGM of all age groups considered in our NHANES analysis, suggesting that exposures can occur at young ages, in agreement with other studies (Trasande et al., 2020; Fagan et al., 2020; Nomura et al., 2022; Grau et al., 2022; Table S3). Although, the likelihood of having glyphosate concentrations above the 95th percentile was about three times higher for children 6–11 years of age than for adults, these results were not significantly different. Higher concentrations of pesticide exposure biomarkers in children than in adults are common in NHANES participants (CDC, 2022); however, the reasons for such age differences remain unclear. Compared to adults, children often eat and drink more relative to their body weight and spend more time playing on the ground, which can result in increased exposure to pesticides. Other studies have also reported higher glyphosate concentrations in children than in adults. For example, one study of 108 children suggested age differences in glyphosate concentrations may relate to elimination of the herbicide with age, dietary habits or even access to food free of contamination (Trasande et al., 2020). Some researchers suggested that the higher concentrations of glyphosate observed in children could result from nondietary sources of glyphosate exposure such as environmental exposure on school and park grounds (Fagan et al., 2020) and living close to agricultural areas (Ferreira et al., 2021). A study of 6,848 people from the French general population also reported higher glyphosate concentrations in the youngest participants with a continuous decrease with age (Grau et al., 2022). Similarly, two studies using samples from Northern and Western Europe reported glyphosate 95th percentiles in children 6–12 years old ranging from 0.18 to 1.03 μg/L (Buekers et al., 2022a), and somewhat lower 95th percentiles in adults that ranged between 0.24 and 0.37 μg/L (Buekers et al., 2022b). By contrast, a nationally-representative study in Germany (Lemke et al., 2021) reported similar glyphosate GM regardless of age for children 3–5, 6–10 and 10–13 years of age.

Fruits and fruit juices, vegetables, and cereals are potential sources of exposure to glyphosate. Based on analysis of dietary 2015–2018 NHANES data, the percentage of children and adolescents who consumed fruits or fruit juice on a given day decreased with age (Liu et al., 2020; Wambogo et al., 2020; Terry et al., 2020). However, trends in the percentage of children and adolescents who consumed any vegetables on a given day were unclear (Liu et al., 2020; Wambogo et al., 2020). Our findings from 2013 to 2014 NHANES suggest that consumption of other food categories, including vegetable and fruits, was not significantly associated with glyphosate concentrations. Additionally, in 2015–2018 NHANES, a higher percentage of children 6–11 years old reported consuming ready-to-eat cereal high in sugar content compared to adolescents 12–19 years of age (Terry et al., 2020) which may also explain our findings showing that children had higher glyphosate AGM concentrations and higher odds of having concentrations above the 95th percentile compared to adolescents.

A German study considered having access to a garden or green backyard in which glyphosate could have been applied and did not find significant associations with children's glyphosate exposure (Lemke et al., 2021). We did not have access to that type of information for the 2013–2014 NHANES participants examined though we observed no association between glyphosate creatinine-corrected concentrations and reported household use of products to kill weeds. Additional studies can help determine whether consumption of fruits, vegetables, and cereals, as well as use of glyphosate in children's outdoor play areas affects glyphosate exposure.

Non-Hispanic White persons had higher glyphosate AGMs than all Hispanic children and adolescents as well as adults who consumed cereal products. In a study conducted in Switzerland, cereals and pulses (e.g., beans, lentils, chickpeas) were considered the main contributors to dietary glyphosate intake (Zoller et al., 2018). Similarly, in a study performed in the United States, glyphosate was detected in 13 commercially available oat products tested to identify candidate reference materials to be used for glyphosate quantification (Cruz and Murray, 2021) which suggests common presence of glyphosate in cereals in the U.S. market. Noteworthy, cereal consumption was not associated with AGM concentrations in children 6–19 years in agreement with others' findings suggesting that consumption of cereals did not affect German children's and adolescents' exposure to glyphosate (Lemke et al., 2021).

5. Conclusions

In this first nationally representative assessment of exposure to glyphosate, we estimate that approximately 81 % of the U.S. general population 6 years of age and older had been recently exposed to glyphosate. The concentrations of glyphosate, which are within the same order of magnitude as those reported for another herbicide, 2,4-D, and other pesticides also in NHANES, define baseline concentrations of urinary glyphosate in a non-occupationally exposed population and provide a foundation for evaluating exposure changes over time. The observed differences in glyphosate concentrations by fasting status may reflect the relevance of diet as a potential exposure source. Further studies to assess dietary intake of glyphosate, to investigate the relationship between urinary glyphosate concentrations and health outcomes, and to identify other potential exposure determinants will be useful to better understand glyphosate exposure and its potential health effects.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Use of trade names is for identification only and does not imply endorsement by the CDC, the Public Health Service, or the US Department of Health and Human Services. The authors declare no competing financial interest.

Data availability

Data is publicly available on the NHANES website.

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Table 1

Geometric mean and select percentiles of glyphosate concentrations in urine concentrations (first row in μg/L, shaded row in μg/g creatinine) for the U.S. population ≥ 6 years of age. Data from the National Health and Nutrition Examination Survey 2013–2014.

	Geometric Mean (95 % CI)		Select percentiles (95 % CI) 50th		75th		90th		95th		Sample size	Weighted detection frequency
Total	0.411	(0.376–0.450)	0.392	(0.359–0.436)	0.656	(0.573–0.751)	1.11	(0.961–1.32)	1.58	(1.35–1.83)	2310	81.2
	0.443	(0.406–0.482)	0.450	(0.404–0.486)	0.753	(0.689–0.829)	1.17	(1.10–1.31)	1.60	(1.46–1.79)	2309	
Age group												
6–11 years	0.515	(0.437–0.606)	0.526	(0.441–0.602)	0.891	(0.620–1.18)	1.38	(1.15–1.78)	1.78	(1.39–2.30)	337	87.2
	0.653	(0.579–0.738)	0.643	(0.533–0.775)	1.00	(0.860–1.29)	1.70	(1.35–2.07)	2.26	(1.76–2.82)	337	
12–19 years	0.481	(0.422–0.547)	0.456	(0.387–0.506)	0.804	(0.670–0.963)	1.32	(1.02–1.65)	1.70	(1.32–2.06)	348	87.2
	0.414	(0.372–0.460)	0.421	(0.373–0.472)	0.676	(0.626–0.705)	0.946	(0.848–1.17)	1.34	(0.976–2.09)	348	
20–59 years	0.372	(0.340–0.406)	0.364	(0.337–0.393)	0.566	(0.496–0.671)	0.966	(0.826–1.09)	1.36	(1.03–1.84)	1114	77.4
	0.391	(0.354–0.431)	0.394	(0.343–0.445)	0.646	(0.583–0.700)	1.09	(0.941–1.24)	1.46	(1.18–1.63)	1113	
60 years and older	0.455	(0.397–0.521)	0.425	(0.365–0.502)	0.748	(0.604–0.911)	1.26	(0.959–1.70)	1.88	(1.46–2.08)	511	85.7
	0.552	(0.492–0.619)	0.603	(0.487–0.689)	0.961	(0.853–1.10)	1.38	(1.12–1.66)	2.00	(1.40–2.45)	511	
Gender												
Males	0.421	(0.380–0.466)	0.409	(0.363–0.468)	0.680	(0.595–0.788)	1.15	(0.974–1.36)	1.62	(1.27–1.97)	1153	80.9
	0.388	(0.357–0.421)	0.397	(0.353–0.435)	0.670	(0.604–0.738)	1.04	(0.956–1.11)	1.26	(1.12–1.52)	1152	
Females	0.402	(0.364–0.445)	0.379	(0.347–0.418)	0.622	(0.532–0.744)	1.07	(0.930–1.29)	1.56	(1.28–1.82)	1157	81.4
	0.502	(0.450–0.559)	0.504	(0.447–0.576)	0.858	(0.732–0.958)	1.40	(1.24–1.49)	1.81	(1.61–2.00)	1157	
Race/ethnicity												
All Hispanic persons	0.374	(0.333–0.419)	0.364	(0.320–0.434)	0.600	(0.499–0.703)	0.920	(0.787–1.08)	1.26	(1.07–1.39)	586	78.1
	0.391	(0.349–0.439)	0.385	(0.327–0.444)	0.668	(0.596–0.710)	1.01	(0.856–1.14)	1.29	(1.12–1.55)	585	
Non-Hispanic Black persons	0.461	(0.427–0.498)	0.446	(0.389–0.514)	0.706	(0.631–0.780)	1.21	(0.994–1.50)	1.64	(1.36–2.21)	464	86.8
	0.362	(0.309–0.423)	0.346	(0.283–0.469)	0.610	(0.508–0.707)	0.939	(0.791–1.07)	1.24	(1.01–1.60)	464	
Non-Hispanic White persons	0.417	(0.374–0.466)	0.392	(0.356–0.449)	0.662	(0.573–0.781)	1.17	(0.926–1.54)	1.70	(1.35–1.90)	930	81.9
	0.476	(0.431–0.526)	0.480	(0.435–0.533)	0.810	(0.722–0.910)	1.30	(1.13–1.48)	1.69	(1.49–2.04)	930	
Other persons	0.379	(0.322–0.445)	0.386	(0.304–0.442)	0.616	(0.485–0.917)	1.07	(0.969–1.24)	1.38	(1.08–2.12)	330	73.6
	0.431	(0.378–0.492)	0.433	(0.370–0.502)	0.788	(0.649–0.900)	1.12	(0.974–1.33)	1.50	(1.20–1.66)	330	

CI: Confidence Interval; Limit of detection: 0.20 μg/L; The weighted detection frequency represents the detection percentage of the population.

Table 2

Adjusted geometric mean (AGM)[a] and 95 % confidence interval concentrations of urinary glyphosate by the covariates included in the age-stratified multiple linear regression models for the U.S. population ≥ 6 years of age. Data from the National Health and Nutrition Examination Survey 2013–2014.

Effect	**Categories**	**Glyphosate AGM (95 % CI) (μg/L)**	
		Children and adolescents ≤19 years	**Adults ≥ 20 years**
Fasting time	>8 h	0.43 (0.37–0.51)	0.37 (0.33–0.39)
	≤8 h	0.51 (0.46–0.56)	0.44 (0.4–0.48)
Race/ethnicity[b]	AH	0.41 (0.37–0.45)	
	NHW	0.54 (0.46–0.64)	
	NHB	0.47 (0.4–0.56)	
	Others	0.47 (0.36–0.61)	
Age group (years)	6–11	0.54 (0.46–0.64)	NA
	12–19	0.41 (0.37–0.45)	NA
	20–59	NA[c]	0.36 (0.33–0.39)
	60+	NA	0.46 (0.4–0.53)
Race/Ethnicity*Cereal consumption	AH, Yes		0.34 (0.29–0.4)
	AH, No		0.4 (0.35–0.47)
	NHW, Yes		0.49 (0.43–0.56)
	NHW, No		0.42 (0.37–0.47)
	NHB, Yes		0.4 (0.34–0.48)
	NHB, No		0.4 (0.36–0.45)
	Others, Yes		0.42 (0.34–0.52)
	Others, No		0.38 (0.32–0.44)

[a]The AGM was estimated from the final model that included: a) race/ethnicity (P = 0.00264), cereal consumption (P = 0.3821), race/ethnicity*cereal consumption (P = 0.0194), fasting time (P = 0.001), age group (P = 0.0004), and urinaiy creatinine (P < 0.0001) (adult model); b) race/ethnicity (P = 0.002), age group (P = 0.0004), fasting time (P = 0.0103), and urinaiy creatinine (P < 0.0001) (children and adolescents' model). The β coefficient for creatinine was 0.0022 (children model) and 0.0018 (adult model). Confidence intervals and P-values were Bonferroni method adjusted for multiple comparisons.

[b]AH = All Hispanic persons; NHW = Non-Hispanic White persons; NHB = Non-Hispanic Black persons; Others = persons from all other non-Hispanic race/ethnicity groups.

[c]NA = Not applicable.

Table 3

Odds ratios and 95 % confidence intervals for having urinary glyphosate concentration above the 95th percentile from the multiple logistic regression analysis for the U.S. population ≥ 6 years of age. Data from the National Health and Nutrition Examination Survey 2013–2014.

Effect		OR (95 % CI)	P-Values
Fasting time (hours)	≤8 vs >8	1.94 (1.06–3.54)	**0.0318**
Race/Ethnicity[a]	NHW vs AH	2.00 (0.76–5.24)	0.3484
	Others vs AH	1.37 (0.5–3.74)	1
	NHB vs AH	1.06 (0.29–3.9)	1
	NHW vs NHB	1.89 (0.9–3.94)	0.1412
	Others vs NHB	1.29 (0.48–3.48)	1
	NHW vs Others	1.46 (0.68–3.15)	
Age group (years)	6–11 vs 20–59	2.9 (0.88–9.5)	0.1095
	12–19 vs 20–59	1.28 (0.5–3.27)	1
	60 + vs 20–59	1.91 (0.89–4.12)	0.1531
	6–11 vs 12–19	2.26 (0.98–5.22)	0.0612
	60 + vs 12–19	1.49 (0.62–3.61)	1
	6–11 vs 60+	1.51 (0.47–4.84)	1

P-values in bold font are statistically significant. The β coefficient for creatinine was 0.0105 ($P < 0.0001$). Confidence intervals and P-values were Bonferroni method adjusted for multiple comparisons.

[a] AH = All Hispanic persons; NHW = Non-Hispanic White persons; NHB = Non-Hispanic Black persons; Others = persons from all other non-Hispanic race/ethnicity groups.