Pilot-scale expanded assessment of inorganic and organic tapwater exposures and predicted effects in Puerto Rico, USA

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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 data
Data are summarized in Supporting Information (Figs. S1–S3, Tables S1–S17) and publicly available in Romanok et al. (2021) and U.S. Geological Survey (2021). Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.147721.
A pilot-scale expanded target assessment of mixtures of inorganic and organic contaminants in point-of-consumption drinking water (tapwater, TW) was conducted in Puerto Rico (PR) to continue to inform TW exposures and corresponding estimations of cumulative human-health risks across the US. In August 2018, a spatial synoptic pilot assessment of than 524 organic and 37 inorganic chemicals was conducted in 14 locations (7 home; 7 commercial) across PR. A follow-up 3-day temporal assessment of TW variability was conducted in December 2018 at two of the synoptic locations (1 home, 1 commercial) and included daily pre- and post-flush samples. Concentrations of regulated and unregulated TW contaminants were used to calculate cumulative in vitro bioactivity ratios and Hazard Indices (HI) based on existing human-health benchmarks. Synoptic results confirmed that human exposures to inorganic and organic contaminant mixtures, which are rarely monitored together in drinking water at the point of consumption, occurred across PR and consisted of elevated concentrations of inorganic contaminants (e.g., lead, copper), disinfection byproducts (DBP), and to a lesser extent per/polyfluoroalkyl substances (PFAS) and phthalates. Exceedances of human-health benchmarks in every synoptic TW sample support further investigation of the potential cumulative risk to vulnerable populations in PR and emphasize the importance of continued broad characterization of drinking-water exposures at the tap with analytical capabilities that better represent the complexity of both inorganic and organic contaminant mixtures known to occur in ambient source waters. Such health-based monitoring data are essential to support public engagement in source water sustainability and treatment and to inform consumer point-of-use treatment decision making in PR and throughout the US.
1. Introduction

The magnitudes, routes, aggregated dose-response relations, and potential adverse health outcomes of human exposures to complex mixtures of environmental contaminants of historical and emerging concern are global research priorities (e.g., Carlin et al., 2013; Cui et al., 2016; Landrigan et al., 2018). The role of drinking-water contaminant exposures is a focus of long-term and ongoing research into human-health outcomes in Puerto Rico (PR). United States (US) (e.g., Haddock et al., 1985; Hannon et al., 1987; Watkins et al., 2019).

PR occurrence rates are higher than in the US mainland and among the highest globally (Watkins et al., 2019) for preterm birth (gestation <37 weeks), infant mortality (March of Dimes, 2019; Martin et al., 2019), early-onset puberty (Haddock et al., 1985; Hannon et al., 1987), childhood asthma (Centers for Disease Control and Prevention (CDC), 2019), obesity (e.g., Garza et al., 2011; Otero-Gonzalez and Garcia-Fragoso, 2008), and metabolic syndrome (Pérez et al., 2008). Based on widely documented environmental contamination (e.g., Guzman-Rios et al., 1987; Hunter and Arbona, 1995; Skanavis, 1999) and growing evidence for developmental effects of environmental contaminants in wildlife and humans (e.g., Colborn et al., 1993; Eroschenko, 1981; McLachlan, 1980; Tyler et al., 1998), dietary and environmental contaminant exposures were hypothesized in the early 1980s as potentially important contributors to PR’s elevated rates of adverse birth, reproductive development, obesity, and metabolic disease outcomes (e.g., Haddock et al., 1985; Hannon et al., 1987; Sáenz de Rodriguez et al., 1985).

The National Institutes of Health (NIH)/National Institute of Environmental Health Science (NIEHS) Superfund Research Program’s Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) birth cohort (PROTECT Center Northeastern University, 2020) was formed in PR’s hydrologically vulnerable northern karst region (Padilla et al., 2011; Padilla and Vesper, 2018; Torres et al., 2018b) in 2010, specifically to explore potential links between environmental contaminant exposure and preterm delivery or other adverse pregnancy outcomes. The northern karst region, which covers approximately 19% of the land surface, contains two of the island’s most spatially extensive and productive drinking-water aquifers (Lugo et al., 2001; Molina, 2015). The region is notable for one of the highest densities of Resource Conservation and Recovery Act (RCRA) and Comprehensive Environmental Response, Compensation, and Liability Act (Superfund) sites in the nation (U.S. Environmental Protection Agency, 2020f; Yu et al., 2015) and a record of groundwater contamination and drinking-water supply-well closures (Guzman-Rios et al., 1987; Torres et al., 2018a; Zack et al., 1987) due, in part, to historical waste disposal in wells, sinkholes, and other preferential recharge features (Hunter and Arbona, 1995; Padilla et al., 2011).

Compared to female participants in the National Health and Nutrition Examination Survey (NHANES), pregnant women in the PROTECT cohort exhibited lower exposure biomarkers for select classes of persistent organic pollutants, including per/polyfluoroalkyl substance(s) (PFAS), polybrominated diphenyl ether(s) (PBDE), polychlorinated biphenyls (PCB), and
several persistent pesticides (Watkins et al., 2019) but elevated exposure biomarkers for several phthalates (Cantonwine et al., 2014; Ferguson et al., 2019), phenols (Meeker et al., 2013), polycyclic aromatic hydrocarbons (Cathey et al., 2018), metals (Ashrap et al., 2020), and triclosan/triclocarban (Ashrap et al., 2018). The highest reported US rate of violation of Safe Drinking Water Act (SDWA) rules for regulated constituents (e.g., Natural Resources Defense Council, 2017; U.S. Environmental Protection Agency, 2021c), the presence of organic chemicals, including phthalates, in groundwater and tapwater (TW) (Lin et al., 2020; Torres et al., 2018a; Yu et al., 2015), adverse reproductive effects of in utero phthalate-mixture exposures in male and female mammalian models (Hannas et al., 2013; Howdeshell et al., 2015; Repouskou et al., 2019), and elevated phthalate urinary biomarkers in the PROTECT cohort (Cantonwine et al., 2014; Ferguson et al., 2019) support drinking water as a potentially important vector of human exposure to and effects of environmental contaminants in PR. A recent PROTECT assessment of 18 trace elements and 200 mostly unregulated organics (Lin et al., 2020) indicated increased TW exposures and risks in PR after Hurricane Maria in 2017 and highlighted the need for broader characterization of potential TW inorganic and organic contaminants to further inform health risks.

TW contaminant mixtures and potential drivers/controls (e.g., source-water quality, treatment, premise plumbing) in a range of source-water vulnerability settings are acknowledged public-health data gaps globally (Doria, 2010; Doria et al., 2009; Villanueva et al., 2014), in the US mainland (Allaire et al., 2018; Pierce and Gonzalez, 2017; Sedlak, 2020) and in PR (e.g., Natural Resources Defense Council, 2017; U.S. Environmental Protection Agency, 2021c) and are the foci of ongoing TW exposure research by U.S. Geological Survey (USGS), U.S. Environmental Protection Agency (EPA), NIEHS, Colorado School of Mines (Mines) and others (e.g., Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021). In August 2018, the USGS, EPA, NIEHS, Mines, and University of Puerto Rico Mayaguez (UPR-M) conducted a spatial pilot assessment of expanded TW exposures (524 organic and 37 inorganic analytes) in 14 homes and commercial locations distributed across PR, including in the northern karst region to: 1) complement and expand on previous and ongoing efforts to identify potential additional TW contaminants that may contribute to adverse health outcomes and 2) continue to inform TW exposures and cumulative risk (exposure, toxicity/hazard: e.g., Moretto et al., 2017; National Research Council, 1983; U.S. Environmental Protection Agency, 2003) to human health across the US. A follow-up assessment of TW exposure temporal variability, conducted in December 2018 at two of the synoptic locations (1 home, 1 commercial), included daily pre- and post-flush samples collected over 3 consecutive days. For both synoptic and temporal assessments, the potential human-health risks of individual and cumulative TW exposures were explored based on multiple lines of evidence, comprising: 1) cumulative detections and concentrations of chemicals (e.g., pesticides, pharmaceuticals) with designed, molecular bioactivities (Bradley et al., 2020; Bradley et al., 2018), 2) individual (RQ) and cumulative ($\Sigma_{RQ}$) contaminant risk quotients (Goumenou and Tsatsakis, 2019; U.S. Environmental Protection Agency, 2003; U.S. Environmental Protection Agency, 2011) based on human-health benchmarks, including Safe Drinking Water Act (SDWA) National Primary Drinking Water Regulations (NPDWR) public-health advisories (U.S. Environmental Protection Agency, 2017; U.S. Environmental Protection Agency, 2021a), and 3) cumulative Exposure-
Activity Ratio(s) ($\Sigma_{EAR}$) (Blackwell et al., 2017). The same general sampling protocol and analytical toolbox employed previously (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) were preserved herein to inform TW chemical and biological exposures in PR, while supporting inter-study comparisons.

2. Methods

2.1. Site selection and sample collection

Based on 2010 USGS water-use statistics (Molina-Rivera, 2014), approximately 99% of PR’s freshwater domestic use (population served: 96%) was from Puerto Rico Aqueducts and Sewers Authority (PRASA) water supplies, with the remaining 1% of domestic use comprising small, non-PRASA community water supply (NPCWS; domestic use: 0.75%; population: 3%) or self-supply (SS; domestic use: 0.25%; population served: 1%; primarily private wells) (Molina, 2015; Molina-Rivera, 2014). EPA is not authorized to regulate or monitor self-supply, defined as fewer than 15 connections and 25 people (U.S. Environmental Protection Agency, 2021b).

For the one-time, pilot-scale, spatial assessment (synoptic), a single TW sample was collected in August 2018 from 14 locations (7 commercial locations all PRASA; 7 residential locations including 3 PRASA, 3 NPCWS, and 1 private well) spatially distributed across PR (Fig. 1). Sample sites were selected to 1) emphasize the more populated northern half of the island, 2) substantially overlap with previous study locations (e.g., Lin et al., 2020), 3) provide equal coverage of residential and commercial settings, and 4) consistent with PR water-use statistics (Molina-Rivera, 2014), focus on public-supply, predominantly PRASA with some coverage of the smaller NPCWS commonly found at elevation along the central cordillera. Cold-water taps were sampled at varying times throughout the day without pre-cleaning, screen removal, or flushing (Romanok et al., 2018). EPA Lead and Copper Rule (LCR) monitoring protocols (first-draw, 6 h-stagnant sampling, U.S. Environmental Protection Agency, 2008; U.S. Environmental Protection Agency, 2020c) were not employed. For the December 2018 temporal sampling, two of the spatial-synoptic locations (1 commercial, 1 domestic; both PRASA) were sampled every 24 h over 3 consecutive days to assess daily temporal variability and flushing effects, as follows: no-flush (first-draw, 6 h-stagnant sampling) samples were collected followed approximately 30 min later by collection of a second (flushed) sample. Complete sampling details are provided elsewhere (Romanok et al., 2021; Romanok et al., 2018).

2.2. Analytical methods

TW samples were analyzed using 10 target-organic (524 unique analytes) and 9 inorganic/field (37 analytes) methods and 11 microbial (13 analytes; temporal assessment only) methods (Table S2), as discussed (Bradley et al., 2020; Bradley et al., 2018; Romanok et al., 2018) and presented in detail previously (American Public Health Association et al., 2017; Ball and McCleskey, 2003; Fishman and Friedman, 1989; Furlong et al., 2014; Graham et al., 2010; Hergenreder, 2011; Hladik et al., 2008; Hoffman et al., 1996; Loftin et al., 2016; Pfaff, 1993; Rose et al., 2016; U.S. Environmental Protection Agency, 2014), with the following exceptions. Per/polyfluoroalkyl substances (PFAS) were analyzed (Murray
et al., 2019) at Mines, as described (Bradley et al., 2020; Murray et al., 2019; Romanok et al., 2018). Phthalates were analyzed at UPR-M by liquid-liquid extraction (LLE) (U.S. Environmental Protection Agency, 1996) gas chromatography/mass spectrometry (GC/MS) (U.S. Environmental Protection Agency, 1998), as described (Torres et al., 2018b). Artificial sweeteners (acesulfame K, aspartame, neotame, saccharin, sucralose) were analyzed by solid-phase extraction (SPE) ultra-performance liquid chromatography/tandem mass spectrometry (UPLC/MS/MS) with electrospray ionization (ESI) and multiple reaction monitoring (MRM), as described (Ferrer and Thurman, 2010). Lastly, unusually high concentrations of chlorination byproducts in collected TW samples raised analytical interference concerns for the pesticide method, for which the TW sampling protocol does not include pretreatment of the sample vial with reductant (anti-oxidant) (Romanok et al., 2018). Consequently, nominal pharmaceutical and pesticide samples, which differed only in ascorbic acid (reductant) preservation in the former, were analyzed by both methods to assess the effect of TW residual oxidant on pesticide-analyte recovery efficiencies. Analytical results are in Tables S3–S9b and Romanok et al. (2021).

In vitro estrogen (ER) (Wilson et al., 2004; Wilson et al., 2002), androgen (AR) (Hartig et al., 2002; Hartig et al., 2007), and glucocorticoid (GR) (Conley et al., 2017a) bioactivities were assessed by EPA, as described previously (Conley et al., 2017a; Conley et al., 2017b; Medlock Kakaley et al., 2020). Bioassay standards, controls, and samples were run in quadruplicate, and endocrine activities were identified by tiered screening or comparison to field blanks (ER only), as detailed in Medlock Kakaley et al. (2020). Biological equivalencies (BioEq) were calculated with an enrichment factor of 10,000 (Escher and Leusch, 2011) and values greater than assay method detection limits were considered endocrine active (Medlock Kakaley et al., 2020).

### 2.3. Data handling, quality assurance, statistics, and screening-level risk assessments

Quantitative (≥limit of quantitation, ≥LOQ) and semi-quantitative (between LOQ and long-term method detection limit, MDL (Childress et al., 1999; U.S. Environmental Protection Agency, 2020a)) results were treated as detections (Childress et al., 1999; Mueller et al., 2015). Quality-assurance/quality-control included analyses of three field blanks, multiple laboratory blanks, and stable-isotope surrogates in most organic methods. Only calcium (Ca), silica (Si), sodium (Na) and zinc (Zn) were detected in inorganic field blanks (Table S8) and only below environmental concentrations; their reporting limits were adjusted to the maximum value detected in the blank. Among those organic compounds detected at least once in TW samples, t-butyl alcohol (maximum 0.330 μg L⁻¹), 1,1-difluoroethane (maximum 0.018 μg L⁻¹), and 8 PFAS (maximum 0.0033 μg L⁻¹) were detected in organic-field blanks (Table S8); their reporting limits were adjusted to twice the highest blank concentration. The median stable-isotope surrogate recovery (Table S9a) for all samples and relevant methods (DBP, pesticides, pharmaceuticals) was 99.7% (interquartile range: 90–107%).

A screening-level assessment (Goumenou and Tsatsakis, 2019; U.S. Environmental Protection Agency, 2003; U.S. Environmental Protection Agency, 2011) of potential cumulative biological activity of mixed-organic contaminants in each TW sample was
conducted as described (Blackwell et al., 2017; Bradley et al., 2021) using the toxEval version 1.1.0 package (De Cicco et al., 2018) of the open source statistical software R (R Development Core Team, 2019). Individual EAR (ratio of measured environmental concentration (MEC) to the activity concentration at cutoff (ACC) (Filer et al., 2017) from the May 2019 invitroDBv3.2 release of the ToxCast™ database (U.S. Environmental Protection Agency, 2020d)) were summed (presumptive concentration addition model (e.g., Altenburger et al., 2018; Cedergreen et al., 2008; Ermler et al., 2011; Thrupp et al., 2018)) across all active endpoints to estimate sample-specific cumulative EAR ($\sum_{EAR}$). Non-specific-endpoint, baseline, and unreliable response-curve assays were excluded (Blackwell et al., 2017; Bradley et al., 2021). $\sum_{EAR}$ results and exclusions are summarized in Tables S10–S12 and S15–S16. A benchmark-based HI assessment of aggregate inorganic and organic contaminant risk of each TW sample also was conducted using toxEval v1.1.0 to sum the RQ (ratio of MEC to the corresponding health-based benchmark) of individual detections to estimate sample-specific cumulative RQ($\sum_{RQ}$) (Corsi et al., 2019). For each detected analyte, the lowest available human health-based benchmark concentration among EPA maximum contaminant level (MCL) goal (MCLG) (U.S. Environmental Protection Agency, 2021a), WHO guideline value (World Health Organization (WHO), 2011), USGS Health-Based Screening Level (HBSL, (Norman et al., 2018)), or among state drinking-water MCL, health advisory (DWHA), or notification level (NL) was employed. MCLG of zero were set to the method reporting limit, except for lead (Pb), which was set to 1 μg L$^{-1}$ as suggested (Lanphear et al., 2016). $\sum_{RQ}$ results and respective health-based benchmarks are summarized in Tables S13–S14 and S17. Corsi et al. (2019) reported approximate contaminant-specific equivalency of the widely employed RQ screening-level threshold of concern of 0.1 and EAR = 0.001.

3. Results and discussion

3.1. TW spatial synoptic chemical exposures and in vitro activities

Detections of regulated and unregulated inorganic and organic analytes were common in the August 2018 synoptic sampling of PR TW (Tables 1, S3–S4; Figs. 1–2, S1–S2). In this study, 87% of the target organic analytes were not detected in any TW sample. However, 67 (13%) of the 524 unique organic target analytes and 27 (79%) of the 34 inorganic target analytes assessed in this study were detected at least once. Notable among the inorganics (Table S3), copper (Cu) was detected in every sample, with a maximum of 2290 μg L$^{-1}$ (median: 223 μg L$^{-1}$; interquartile range (IQR): 130–381 μg L$^{-1}$). Lead (Pb) was detected in 64% (9 of 14) of synoptic TW samples, with a maximum of 10.5 μg L$^{-1}$ (median: 0.8 μg L$^{-1}$; IQR: nd-2.0 μg L$^{-1}$). Detections of Cu and, especially, Pb in drinking water are generally attributed to distribution-system and premise-plumbing materials (Triantafyllidou and Edwards, 2012). In contrast, to the Lin et al. (2020) findings, arsenic (As) was not detected (reporting limit: 2 μg L$^{-1}$) in any TW sample in this study.

Cumulative detections and concentrations of organic analytes ranged 7–31 (median: 18; IQR: 13–27) and 6.2–153 μg L$^{-1}$ (median: 59.5 μg L$^{-1}$; IQR: 46.2–101 μg L$^{-1}$), respectively (Table S4). Consistent with common chlorine-based disinfection of public-supply drinking water (Richardson and Plewa, 2020) and the fact that 13 of the 14 TW samples were
from regulated public supplies, disinfection byproducts (DBP) were detected in all TW samples in this study and comprised 83% or more of the mass concentration of detected organics in 10 of 14 TW sample locations. Engineered, biologically active pesticides and pharmaceuticals were detected in 10 of 14 TW samples. The number of pesticides detected in the single unregulated, private-well TW sample (14) was more than twice that observed in any other location (6). Note, the comparison of surrogate recoveries for pharmaceutical and pesticide samples with and without ascorbic acid preservation, confirmed the importance of ascorbic acid preservation for pharmaceutical analysis of chlorine-disinfected drinking water but found no systematic improvement for pesticide analysis (Fig. S3; Table S9b). In agreement with previous reports of phthalates in tapwater and groundwater (Padilla et al., 2011; Torres et al., 2018b) and of phthalate biomarkers in urine (Cantonwine et al., 2014; Ferguson et al., 2019) in the PROTECT study area, these endocrine-active contaminants (Lyche, 2011; Pak et al., 2011) were detected in 9 of 13 TW locations (no C4 phthalate sample) in this study. Volatile organic chemicals (VOC), including regulated chemicals like tetrachloroethene (PCE) and trichloroethene (TCE), were detected in 11 of 14 TW samples, and PFAS compounds, which currently have no SDWA NPDWR enforceable public-supply drinking water standard, were detected in half (7/14) of the synoptic samples. Likewise, NPDWR-unregulated artificial sweeteners, which along with pharmaceuticals are most readily attributed to human wastewater sources, were detected in 9 of 14 TW samples, suggesting that de facto wastewater reuse was widespread. No significant in vitro endocrine bioactivity (ER, AR, GR) was detected in any synoptic or temporal sample in this study.

These spatial synoptic results corroborated and substantially expanded (2–3 fold increase in analytical coverage including important classes, like DBP) on recent findings (Lin et al., 2020) that human exposures to chemicals via TW are widespread in PR and comprised mixtures of inorganic and organic contaminants, which are rarely monitored together at the point of consumption. Common detections of contaminants, which often derive from (e.g., Cu, Pb) or are known to change substantially within (e.g., DBP) distribution systems and premise plumbing, reinforce the previously stated (e.g., Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) importance of assessing drinking-water exposures at the point-of-consumption employing an analytical toolbox that more defensibly represents the breadth and complexity of inorganic and organic contaminant mixtures documented to occur in ambient drinking-water sources (e.g., Bradley et al., 2017; Moschet et al., 2014). The results are consistent with previous TW exposure studies in PR (Lin et al., 2020; Padilla and Vesper, 2018; Yu et al., 2015), the US (Bradley et al., 2018; Evans et al., 2019; Stoiber et al., 2019) and elsewhere (de Jesus Gaffney et al., 2015; Gonzalez et al., 2013; Leusch et al., 2018; Stalter et al., 2020; Tröger et al., 2018). In line with Safe Drinking Water Information System (SDWIS) violation reporting (accessible online at U.S. Environmental Protection Agency, 2021d), however, several measured concentrations of DBP with well-documented public-health concerns, including bromodichloromethane and, more broadly, trihalomethanes (THM), were markedly higher than observed in the previous TW studies by this group (e.g., Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) in the mainland US. Consequently, multiple lines of evidence were employed in the following sections to characterize the potential individual and cumulative human-health risks (Moretto et al., 2017; National Research Council, 1983; U.S. Environmental Protection Agency, 2003).
of the observed TW contaminant exposures. The synoptic results also indicated substantial spatial variability in TW exposures, including greater than 4-fold and 20-fold differences in numbers and corresponding cumulative concentrations of detected organic analytes, respectively, across all study locations. The potential contribution of temporal variability to the observed spatial variability was explored at two of the synoptic locations and is discussed in a separate section below.

3.2. TW spatial synoptic individual contaminant RQ screening

EPA NPDWR MCL are enforceable, public-supply drinking-water standards established as close to the MCLG as possible to address documented human-health concerns but set in consideration of contemporaneous technical and economic feasibility (U.S. Environmental Protection Agency, 2020e). MCL are promulgated (U.S. Environmental Protection Agency, 2017; U.S. Environmental Protection Agency, 2021a) for 5 of the 30 individual inorganic and 9 of the 67 individual organic analytes detected in this study and for the DBP class of THM. Only one detected inorganic (Cu) exceeded its MCL (1300 μg L\(^{-1}\)) and only in one sample (Table S3); WHO (World Health Organization (WHO), 2011) guidelines for Cu (2000 μg L\(^{-1}\)) and Pb (10 μg L\(^{-1}\)) were exceeded in one sample each. In December 2020, EPA revised the Lead and Copper Rule (LCR) to include a new Trigger Level for Pb of 10 μg L\(^{-1}\) (U.S. Environmental Protection Agency, 2020b). Among the organics, only di(2-ethylhexyl) phthalate (DEHP) exceeded its MCL (6 μg L\(^{-1}\)) and comparable WHO drinking-water guidance value (8 μg L\(^{-1}\)) in synoptic samples; both were exceeded in the same four locations.

More important from a public health standpoint, EPA also promulgates non-enforceable, public-supply MCLG, which are based only on risk to the health of presumptive “most vulnerable” sub-populations (e.g., infants, children, pregnant women, elderly, immune-compromised) and do not consider technical or economic constraints (U.S. Environmental Protection Agency, 2020e; U.S. Environmental Protection Agency, 2021a). NPDWR MCLG exist for 6 of the 30 individual inorganic and 14 of the 67 individual organic analytes detected in the synoptic assessment. Exceedances of MCLG for 2 inorganics and 9 organics indicate potential risk of adverse health effects of TW exposures in PR (Tables S3–S4).

The MCLG for Cu is based on gastrointestinal upset from short-term exposure and liver and kidney damage from long-term exposure in vulnerable groups (U.S. Environmental Protection Agency, 2021a), including infant, genetically susceptible (Wilson disease), and disease-compromised (hemodialysis, chronic liver disease) subpopulations (Georgopoulos et al., 2001; Stern, 2010). Drinking-water Pb is a human-health concern (Levallois et al., 2018; Navas-Acien et al., 2007; Triantafyllidou and Edwards, 2012), largely due to associations between elevated exposures and neurocognitive impairment in infants and children (Lanphear et al., 2016; Levallois et al., 2018; Triantafyllidou and Edwards, 2012). The American Academy of Pediatrics’ (Lanphear et al., 2016) recommends that drinking-water Pb not exceed 1 μg L\(^{-1}\), the typical method detection limit for public-supply LCR compliance monitoring (U.S. Environmental Protection Agency, 2008; U.S. Environmental Protection Agency, 2020c). Accordingly, the EPA MCLG for Pb is zero. Detection of Pb in 64% of the synoptic TW samples is, thus, a concern for adverse developmental outcomes.
in PR. Critically, these synoptic results do not necessarily capture worst-case TW Cu or Pb exposures in these locations. Flushing of premise plumbing effectively decreases the concentration of plumbing-derived TW contaminants, such as Cu and Pb (e.g., temporal study herein, Triantafyllidou and Edwards, 2012; U.S. Environmental Protection Agency, 2016b), and prior TW use on the day of sampling was common.

At least two organic MCLG exceedances were observed in every synoptic sample and samples from three sites had 7 exceedances each. MCLG exceedances for individual organics included 4 VOC, 1 phthalate, and 4 DBP (Table S4). The 4 VOC (tetrachloromethane, PCE, TCE, 1,2-dichloropropane) have well-established carcinogenic concerns and concomitant MCLG of zero (U.S. Environmental Protection Agency, 2018; U.S. Environmental Protection Agency, 2021a) and, with the exception of the latter compound, were detected in multiple synoptic TW samples. Notably, tetrachloromethane (carbon tetrachloride) was detected in 50% of the synoptic TW locations in this study. Likewise, the phthalate, diethylhexyl phthalate (DEHP), has no known safe exposure level and a corresponding MCLG of zero; DEHP was detected (exceedance) in approximately 64% (9/14) of the synoptic sample locations. Likewise, the three DBP – bromodichloromethane, tribromomethane, and dichloromethane – have no known safe levels of exposure and MCLG of zero, which was exceeded in 100%, 86%, and 21% of synoptic TW sample locations, respectively. The remaining exceedance was trichloromethane (MCLG = 70 µg L⁻¹) in one TW synoptic location.

With respect to DBP exceedances, the disease prevention benefits of chemical disinfection prior to distribution and of residual disinfectant at the tap are well-documented (Reynolds et al., 2008; Schoenen, 2002) and a noted concern in hurricane-impacted locations like PR (e.g., Keenum et al., 2021). However, the carcinogenic/genotoxic potentials of regulated (U.S. Environmental Protection Agency, 2017; U.S. Environmental Protection Agency, 2021a) and unregulated DBP (Jeong et al., 2015; Krasner et al., 2016; Muellner et al., 2007; Pressman et al., 2010; Richardson et al., 2007; Villanueva et al., 2018; Wang et al., 2015), evidence linking TW DBP exposure to DBP biomarkers in blood (Rivera-Núñez et al., 2012) and to bladder cancer (Hrudey et al., 2015; Hrudey and Fawell, 2015), and the remaining majority of largely unidentified DBP in drinking water (Krasner et al., 2006; Weinberg et al., 2002) are a clear public-health tradeoff (Hrudey, 2009) and growing public-health concerns (Hrudey and Fawell, 2015; Richardson and Plewa, 2020). Multiple exceedances of THM MCL and ubiquitous exceedance of DBP MCLG raise concerns for potential adverse health impacts of TW exposures and reemphasize the need for improved understanding of the exposure-effects relations and cumulative risks of regulated, unregulated, and unidentified DBP (Krasner et al., 2006; Richardson and Plewa, 2020; Weinberg et al., 2002).

No synoptic TW samples exceeded the current EPA advisory of 0.070 µg L⁻¹ for perfluorooctane sulfonate/perfluorooctanoic acid (PFOS/PFOA) combined (U.S. Environmental Protection Agency, 2016a). However, PFAS are targets of a rapidly expanding list of more protective health-based advisories and drinking-water regulations (Post, 2020) at the US state and federal levels (for example see living list at, Interstate Technology Regulatory Council, 2021), due to global occurrence in humans, other biota, and various environmental matrices (Suja et al., 2009), clear environmental and human
persistence (Post et al., 2012; Post et al., 2017), documented human-health concerns (Grandjean et al., 2012; Grandjean and Budtz-Jørgensen, 2013; Macon et al., 2011; Post, 2020; Tucker et al., 2015), and widespread drinking-water exposures (e.g., Association of State Drinking Water Administrators, 2018; Boone et al., 2019; Bradley et al., 2020; Bradley et al., 2018; Hu et al., 2016; Sunderland et al., 2019). At least one PFAS compound was detected in 50% (7/14) of the synoptic TW samples in this study, with 8 PFAS detected at least once at individual concentrations up to 0.014 μg L\(^{-1}\) for PFOS, which equals the US Department of Health and Human Services’ Agency for Toxic Substances and Disease Registry (Agency for Toxic Substances and Disease Registry, 2018) minimum risk level (MRL) and exceeds the newly established New York State drinking-water MCL of 0.01 μg L\(^{-1}\) for PFOS (New York State, 2020). Three TW samples from commercial sites exceeded California’s 0.0065 μg L\(^{-1}\) notification level for PFOS (California State Water Resources Control Board, 2020). The 0.001 μg L\(^{-1}\) drinking-water safe-exposure threshold suggested for PFAS (as PFOA) (Grandjean and Budtz-Jørgensen, 2013; Grandjean and Clapp, 2015), based on immunotoxicity in children (Grandjean et al., 2012; Grandjean and Budtz-Jørgensen, 2013) and mice mammary-gland development (Macon et al., 2011; Tucker et al., 2015), was exceeded in 6 of the 7 homes where PFAS were detected. Multiple PFAS detections are consistent with recent results in PR (Lin et al., 2020) and with previous TW findings throughout the US (Boone et al., 2019; Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021; Hu et al., 2016). Thus, pointedly keeping in mind that the 45 target PFAS assessed herein are fractional indicators of the 3000+ globally produced PFAS compounds (Wang et al., 2017); with variable structures, undefined environmental persistence, and poorly understood health consequences (Blake and Fenton, 2020; Conley et al., 2019; Gomis et al., 2018; Piekarski et al., 2020; Wang et al., 2017); these results emphasize the need for further assessment of cumulative adverse health risks; including adverse gestational, peri-natal, post-natal, and latent adult effects (Blake and Fenton, 2020); of environmentally relevant PFAS exposure levels in point-of-use drinking water in PR and throughout the US mainland and for potential management as a chemical class (Kwiatkowski et al., 2020).

3.3. TW spatial synoptic aggregated contaminant HI risk screening: \(\sum_{EAR} \) and \(\sum_{RQ} \)

We conducted a bioactivity-based \(\sum_{EAR} \) screening-level assessment (Goumenou and Tsatsakis, 2019; U.S. Environmental Protection Agency, 2003; U.S. Environmental Protection Agency, 2011) of potential cumulative molecular bioactivity across all endpoints for TW contaminants detected in PR synoptic samples, as described (Blackwell et al., 2017; Bradley et al., 2021), using high-throughput exposure-effects data for the 10,000+ organics and approximately 1000 vertebrate-cell-line molecular endpoints (Filer et al., 2017; Richard et al., 2016) available in the invitroDBv3.2 release (publicly available at U.S. Environmental Protection Agency, 2020d) of the ToxCast database (Fig. 3; Tables S11–12). The approach estimates potential cumulative activity at sensitive and possibly more protective sublethal molecular endpoints, but also has notable limitations (Schroeder et al., 2016). These include 1) limited to no coverage of inorganic contaminant effects, 2) incomplete analytical coverage (potential orders-of-magnitude underestimation) of actual environmental organic-contaminant exposures, 3) incomplete ToxCast coverage of detected
organics, and 4) uncertain transferability of molecular-scale results to higher levels of biological organization, including organ and organism scales. Importantly, the approach employed herein, which aggregates individual and cumulative contaminant bioactivity ratios across all endpoints without restriction to recognized modes of action, provides a useful precautionary screening-tool for further investigation of potential effects but may not accurately reflect biological relevance.

Less than half (32/68) of the organics detected in synoptic TW samples in this study had exact Chemical Abstract Services (CAS) number matches in the ToxCast invitroDBv3.2 database (Tables S11–12). Individual chemical EAR or whole sample $\sum_{\text{EAR}}$ of 1 (solid red line, Fig. 3) or higher indicate exposure concentrations expected to modulate molecular endpoints in vitro. Site-specific $\sum_{\text{EAR}}$ equaled or exceeded 1 in 80% (8/10) of the PRASA TW samples, ranging 0.38–2.05 (median: 1.38; IQR: 1.06–1.58). $\sum_{\text{EAR}}$ values in the NPCWS TW samples were lower (median: 0.49; range: 0.26–0.67). In all cases, $\sum_{\text{EAR}}$ was dominated by the DBP, chlorodibromomethane and, to a lesser extent, 1,1,1-trichloropropanone, with the EAR for chlorodibromomethane alone exceeding 1 in 60% (6/10) of synoptic TW samples from PRASA locations. Notably, no ToxCast exposure-activity data were available for bromodichloromethane, which has no known safe level of exposure and an MCLG of zero; this DBP was detected in every synoptic TW sample and typically at substantially higher concentrations than chlorodibromomethane. Other notable contributors to $\sum_{\text{EAR}}$ in these synoptic TW samples included phthalates. The lowest $\sum_{\text{EAR}}$ value (0.14) was observed in the single self-supply TW sample and attributable primarily to the herbicide, bromacil, and multiple other agricultural pesticides.

Acknowledging the incomplete (47%) ToxCast coverage of detected organics and especially DBP, the previously described (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) 2–3 orders-of-magnitude potential analytical underestimation of the presumptive TW exposure space (640 analytes versus 100,000+ commercial organic compounds (Monteiro and Boxall, 2010; Wang et al., 2020) and un-quantifiable numbers of environmental degradates and metabolites ( Dobson, 2004; Vasquez et al., 2014), and the increased TW vulnerability of specific populations (e.g., Blake and Fenton, 2020; Rosen et al., 2017; Triantafyllidou and Edwards, 2012), a precautionary $\sum_{\text{EAR}} = 0.001$ (Fig. 3; dotted red line) screening-level for further investigation of potential effects was deemed appropriate, as described (Bradley et al., 2018). Exceedance of $\sum_{\text{EAR}} = 0.001$ in every synoptic TW sample in this study argues for further investigation of the cumulative risk to vulnerable populations from PR TW exposures, even when considering only those organic contaminant mixtures detected herein.

With respect to higher levels of biological organization, the zebrafish (Danio rerio) embryo assay is a well-established model system for vertebrate developmental toxicology (Dasgupta et al., 2020; Sipes et al., 2011; Truong et al., 2020; Truong et al., 2013) and human genetics (Howe et al., 2013), disease (Dooley and Zon, 2000; Zang et al., 2018), and drug development (Cassar et al., 2020; Gibert et al., 2013); The zebrafish embryo high-content-screening metrics in ToxCast are, thus, important exceptions to ToxCast’s predominantly
molecular endpoints (Filer et al., 2017; Richard et al., 2016), for which aggregate exposure or adverse outcome pathways (AOP) to individual and population scales are currently limited (Ankley and Edwards, 2018; Vinken et al., 2017). Thus, cumulative zebrafish EAR values $Σ_{EAR - ZF} ≥ 0.001$ for TW samples from four synoptic locations also indicate possible organism-level effects to humans and support further assessment of the cumulative risks of TW exposures to vulnerable populations in PR.

A benchmark-based $Σ_{RQ}$ HI approach was employed to assess potential cumulative risks from TW exposures to mixtures of inorganic and organic contaminants (Fig. 3). A precautionary approach using the lowest available federal or state health-based benchmark for each detected TW chemical, typically a drinking-water advisory based solely on human health, was employed. A benchmark value equal to the analytical detection limit was employed for those chemicals with NPDWR MCLG of zero (Table S13). For every synoptic TW sample, $Σ_{RQ}$ exceeded 1 and multiple compound-specific RQ exceeded the 0.1 screening-level of concern (Fig. 3). Primary drivers of $Σ_{RQ} ≥ 1$ were DBP and phthalates, among the organics, and frequently Pb and Cu among the inorganics. Exceedance of $Σ_{RQ} = 1$ in every synoptic TW sample in this study, without adjusting for analytical underestimation of the presumptive TW exposure space reinforces the need for further assessment of TW contaminant cumulative risk to vulnerable populations in PR.

3.4. TW temporal assessment of chemical exposures

Site-specific temporal variability and its potential contribution to the observed synoptic spatial variability were explored at two synoptic locations (1 commercial, 1 home; Tables 2 and S5–S6). Consistent with the predominance of PRASA public drinking-water supply in PR, both locations were in PRASA service areas. Little variability was observed day-to-day or within days between stagnant and flushed samples for field parameters (pH, specific conductance, temperature), major ions, or alkalinity (Table S5) or microbial indicators (Table S7). However, day-to-day variability was apparent for some trace elements (e.g., iron (Fe) at C4; Zn at D2) and marked concentration decreases between stagnant and flushed samples were observed for several metals, including, notably, Cu, Pb, nickel (Ni), and Zn and, to a lesser extent, aluminum (Al) and manganese (Mn). Among these, Pb was detected daily in stagnant, unflushed samples at C4 in excess of the 10 μg L$^{-1}$ WHO drinking-water guideline (one sample exceeding the EPA AL of 15 μg L$^{-1}$), but concentrations were decreased by at least an order of magnitude in flushed samples collected 30 min later (Table 2). A similar pattern was apparent for Ni at D2 (Table S5). This repeating pattern in flushed samples indicated proximal premise plumbing as the probable primary source for both inorganics. Similar albeit incomplete reductions in concentrations of Al, Cu, Mn, and Zn are consistent with contributions from proximal premise plumbing against background contributions from more distal sources potentially including the public supply source water.

Substantial variability in cumulative concentrations of detected organic analytes was observed at both temporal TW-sample locations, ranging 40.8–75.7 μg L$^{-1}$ at the commercial location in Mayaguez and 61.6–121 μg L$^{-1}$ at the domestic location in Dorado over 3 days and 6 samples (Tables 2 and S6). The primary driver of the observed temporal variability in TW mass concentrations in both sample locations was the DBP, acetonitrile,
which varied more than an order of magnitude over the 3-day sampling period. Kimura et al. (2015) recently demonstrated the formation of acetonitrile from acetaldehyde, itself a long-reported DBP (Krasner et al., 1989) formed during ozonation or chlorination.

3.5. TW temporal aggregated contaminant HI risk screening: $\sum_{EAR}$ and $\sum_{RQ}$

As observed during the synoptic assessment, less than half (20/41) of the organics detected in temporal TW samples had exact CAS matches in the ToxCast invitroDBv3.2 database (Table S15). Site-specific $\sum_{EAR}$ exceeded 1 in every TW sample collected at D2 during the synoptic and temporal assessments. $\sum_{EAR}$ exceeded 0.1 in every TW sample collected at C4, ranging from 0.381 for the synoptic assessment sample up to a maximum of 0.933 during the temporal assessment. As in the corresponding synoptic samples at these sites, the DBP, chlorodibromomethane, remained a primary contributor to $\sum_{EAR}$, alone exceeding 0.65 in all samples. However, 1,1,1-trichloropropanone was the primary contributor to $\sum_{EAR}$ at D2, exceeding 1 in all samples. $\sum_{EAR} - ZF$ was less than the 0.001 screening level in all temporal TW samples from both locations. Importantly, no acceptable activity concentration at cutoff (ACC) was available in the ToxCast invitroDBv3.2 database for acetonitrile, the primary driver of observed temporal variability in cumulative organic concentrations at both locations; consequently, little temporal variability in $\sum_{EAR}$ was observed (Fig. 4).

The benchmark-based $\sum_{RQ}$ exceeded 1 in every temporal TW sample collected in this study, with multiple compound-specific RQ exceedances of 1 at both locations (Table S17). Primary drivers of $\sum_{RQ} \geq 1$ were DBP and Pb. Exceedance of $\sum_{RQ} = 1$ in every temporal TW sample in this study emphasizes the need for further assessment of TW contaminant cumulative risk to vulnerable populations in PR and indicates that this risk may persist for at least days.

4. Conclusions

The current study employed a standardized, broad characterization of inorganics and organics applied previously by this group in the US mainland (Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) to 1) complement and expand on prior characterizations of TW mixed contaminant exposures and corresponding risk implications in PR TW (e.g., Lin et al., 2020; Padilla et al., 2011; Padilla and Vesper, 2018; Torres et al., 2018a; Yu et al., 2015); 2) contribute to ongoing public-health research into the potential role of drinking water contaminant exposures in PR adverse health outcomes (e.g., PROTECT Center Northeastern University, 2020); 3) inform source-water sustainability and drinking-water treatment decision making from utility to end-user; and 4) support interstudy comparison and a cohesive national perspective on cumulative contaminant risk at the drinking-water point of exposure. Approximately 99% of PR’s population (96% PRASA; 3% NPCWS) relies on public-supply drinking water (Molina, 2015; Molina-Rivera, 2014), which is regulated, monitored, and treated for NPDWR drinking-water contaminants under the SDWA (U.S. Environmental Protection Agency, 2021a). Based on SDWIS data, PR has the highest rate of violation of SDWA rules in the US (Natural Resources Defense Council, 2017; U.S. Environmental Protection Agency, 2021d). Most of the TW analytes assessed
here and in the earlier Lin et al. (2020) study, however, are currently unregulated organic contaminants. The spatial synoptic results presented here confirmed and expanded on earlier findings (e.g., Lin et al., 2020) that human exposures to TW contaminants occurred across PR and comprised broad mixtures of inorganic and organic contaminants, which are rarely monitored together in drinking water and even less so at the point of consumption. The TW synoptic results herein support concerns that drinking water in PR is an important vector of human exposures to chemical mixtures, which may contribute to increased risk of the adverse health effects described in PR. Exceedance of the $\Sigma_{EAR} = 0.001$ screening level in every synoptic TW sample and of $\Sigma_{EAR} = 1$ in most, argues for further investigation of the cumulative risk to vulnerable populations from PR TW organic exposures to elevated DBP concentrations and to a lesser extent phthalates, PFAS, and a range of other anthropogenic contaminants. Exceedance of $\Sigma_{RQ} = 1$ in every synoptic TW sample in this study, without adjusting for analytical underestimation of the presumptive TW exposure space (Dobson, 2004; Monteiro and Boxall, 2010; Vasquez et al., 2014; Wang et al., 2020) indicates substantially elevated cumulative risk when considering organic and inorganic contaminant (e.g., Pb, Cu) exposures simultaneously. Measured concentrations of DBP with well-documented public-health concerns and, more broadly, THM, were markedly higher than those observed in previous TW studies by this group (e.g., Bradley et al., 2020; Bradley et al., 2018; Bradley et al., 2021) in the mainland US, illustrating the intrinsic public-health tradeoff of chlorine disinfection (Hrudey, 2009; Hrudey and Fawell, 2015), the importance of better understanding of exposure-effects relations and cumulative adverse health risks of regulated, unregulated, and unidentified drinking-water DBP (Cortés and Marcos, 2018; Hrudey and Fawell, 2015; Richardson and Plewa, 2020), and the need for improved source-water pre-treatment technologies to reduce and remove DBP precursors, like natural organic matter, prior to disinfection (Bond et al., 2014; Bond et al., 2012; Chu et al., 2011). Importantly, the results support consideration of consumer point-of-entry (e.g., home, kitchen) and point-of-use (tap) treatment as an integral additional line of protection for public-supply TW during normal operation and outbreak conditions (e.g., Bradley et al., 2020; Sedlak, 2020). The results emphasize the importance of continued characterization of drinking-water exposures at the point-of-consumption (tap) with analytical coverage that more defensibly represents the breadth and complexity of inorganic and organic contaminant mixtures known to occur in ambient source waters (e.g., Bradley et al., 2017; Moschet et al., 2014). Equally important, increased availability of health-based monitoring data, including results below current, technically- and economically-constrained enforceable standards (e.g., MCL), is essential to support public engagement in source water sustainability and drinking-water treatment and to inform consumer point-of-use treatment decision making in PR and throughout the US.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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HIGHLIGHTS

• Tapwater (TW) assessed in 13 public and 1 private-supply sites across Puerto Rico
• 524 organics/34 inorganics/11 microbial indicators/3 bioactivities analyzed
• Enforceable standards exceeded for Cu, Pb, and disinfection byproducts (DBP).
• Human-health only benchmark(s) (e.g., MCLG) exceeded in every TW location.
• Substantial stagnant/flush (Cu, Pb) and day-to-day (DBP) TW variability observed
Fig. 1.
Relative (percentage of maximum observed across all sites by contaminant class) cumulative (sum of all detected) concentrations (%) for classes of organic contaminants in tapwater samples collected from commercial (C1–7) and domestic (D1–7) locations in Puerto Rico during 2018. Numbers above bars indicate number of analytes detected in the sample for that contaminant class. Sample locations are anonymized.
Fig. 2. Detected concentrations (circles, μg L\(^{-1}\)) and number of sites (right axes) for 68 organic analytes (left axis, in order of decreasing total detections across all samples) detected in samples of treated public water supply (left plot, 10 total samples), treated community water supply (center plot, 3 total samples), and untreated self-supply (SS, right plot, 1 sample) commercial and domestic tapwater collected in Puerto Rico during August 2018. Circles (●) are data for individual samples. Boxes, centerlines, and whiskers indicate interquartile range, median, and 5th and 95th percentiles, respectively.
Fig. 3.
Top. Individual EAR values (circles) and cumulative EAR ($\sum_{\text{EAR}}$; sum of all detected; red triangles, ▲) across all assays for 32 organic analytes listed in ToxCast and detected in synoptic samples of treated public water supply (D1–7; C1–3), treated community water supply (C4–6), and untreated self-supply (C7) commercial (C1–7) and domestic (D1–7) tapwater collected in Puerto Rico during August 2018. Solid and dotted red lines indicate concentrations shown to modulate effects in vitro and effects-screening-level thresholds (EAR = 0.001), respectively. Bottom. Human health benchmark-based individual RQ values (circles) and cumulative RQ ($\sum_{\text{RQ}}$; sum of all detected; red triangles, ▲) for inorganic and organic analytes listed in Table S14 and detected in tapwater samples. Solid and dotted red lines indicate benchmark equivalent concentrations and effects-screening-level threshold of concern (RQ = 0.1), respectively. Boxes, centerlines, and whiskers indicate interquartile range, median, and 5th and 95th percentiles, respectively, for both plots. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Fig. 4.
Top. Individual EAR values (circles) and cumulative EAR ($\sum_{\text{EAR}}$, sum of all detected; red triangles, ▲) across all assays for 20 organic analytes listed in ToxCast and detected in overnight stagnant (S) and flushed (F) temporal samples of treated public-supply commercial (C4) and domestic (D2) tapwater collected in Puerto Rico over three consecutive days in December 2018. Solid and dotted red lines indicate concentrations shown to modulate effects in vitro and effects-screening-level thresholds (EAR = 0.001), respectively. Bottom. Human health benchmark-based individual RQ values (circles) and cumulative RQ ($\sum_{\text{RQ}}$, sum of all detected; red triangles, ▲) for inorganic and organic analytes listed in Table S14 and detected in tapwater samples. Solid and dotted red lines indicate benchmark equivalent concentrations and effects-screening-level threshold of concern (RQ = 0.1), respectively. Boxes, centerlines, and whiskers indicate interquartile range, median, and 5th and 95th percentiles, respectively, for both plots. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Concentrations (µg L\(^{-1}\)) of copper (Cu) and lead (Pb) and cumulative detections (\(\#\)) and concentrations (µg L\(^{-1}\)) of organic contaminant classes detected in synoptic TW samples collected from 14 sites during August 2018. See Tables S3–S4 for individual organic results.

| ID\(^a\) | Source\(^b\) | Inorganic | Organic Class (sum detections and concentrations) |
|--------|-------------|-----------|--------------------------------------------------|
|        |             | Cu | Pb | DBP | THM | Pest | PFAS | Pharm | Phthalates | Sweeteners | VOC | TOTAL |
|        |             | µg/L | µg/L | # | µg/L | # | µg/L | # | µg/L | # | µg/L | # | µg/L | # | µg/L |
| C1     | PRASA       | 292  | –   | 6 | 106.08 | 3 | 0.1074 | 7 | 0.0221 | 3 | 0.0396 | 0 | –   | 2 | 2.49 | 2 | 0.3 | 29 | 114.56 |
| C2     | PRASA       | 714  | 4.4 | 10 | 73.69 | 3 | 0.0936 | 9 | 0.0265 | 2 | 0.0084 | 1 | 76.0 | 3 | 2.65 | 3 | 0.3 | 31 | 152.78 |
| C3     | PRASA       | 2290 | 2.0 | 12 | 107.32 | 7 | 0.1554 | 2 | 0.0008 | 1 | 0.0199 | 2 | 4.5 | 2 | 0.33 | 2 | 2.0 | 27 | 114.53 |
| C4     | PRASA       | 17.7 | –   | 10 | 65.74 | 5 | 63.59 | 0 | –   | 0 | –   | 0 | –   | 0 | –   | 1 | –   | 11 | 65.76 |
| C5     | PRASA       | 400  | 2.7 | 5 | 10.93 | 4 | 10.25 | 1 | 0.0026 | 6 | 0.0354 | 0 | –   | 0 | –   | 2 | 0.49 | 4 | 0.2 | 18 | 11.70 |
| C6     | PRASA       | 324  | –   | 12 | 52.11 | 6 | 41.27 | 0 | –   | 0 | –   | 0 | –   | 0 | –   | 1 | 1.2 | 13 | 53.31 |
| C7     | PRASA       | 830  | 10.5| 11 | 40.96 | 7 | 38.56 | 6 | 0.1312 | 4 | 0.0080 | 0 | –   | 2 | 1.2 | 2 | 0.05 | 7 | 3.2 | 32 | 45.52 |
| D1     | PRASA       | 154  | –   | 9 | 78.34 | 6 | 77.39 | 0 | –   | 0 | –   | 0 | –   | 3 | 15.8 | 1 | 0.16 | 2 | 0.2 | 15 | 94.48 |
| D2     | PRASA       | 21.6 | –   | 14 | 62.82 | 8 | 51.23 | 0 | –   | 0 | –   | 0 | –   | 1 | 0.016 | 2 | 3.4 | 0 | –   | 0 | 17 | 66.24 |
| D3     | PRASA       | 134  | 1.9 | 10 | 92.54 | 6 | 91.38 | 2 | 0.0880 | 5 | 0.0083 | 0 | –   | 2 | 10.0 | 2 | 0.23 | 1 | 0.1 | 22 | 102.92 |
| D4     | NPCWS       | 3.9  | –   | 9 | 32.04 | 5 | 31.44 | 1 | 0.0300 | 0 | –   | 0 | –   | 2 | 17.8 | 0 | –   | 0 | –   | 12 | 49.87 |
| D5     | NPCWS       | 314  | –   | 14 | 44.65 | 8 | 34.90 | 1 | 0.0114 | 0 | –   | 0 | –   | 2 | 3.9 | 0 | –   | 0 | 0.1 | 18 | 48.62 |
| D6     | NPCWS       | 144  | –   | 4 | 2.87 | 4 | 2.87 | 0 | –   | 0 | –   | 0 | –   | 2 | 3.3 | 0 | –   | 1 | –   | 0 | 7.61 |
| D7     | SS          | 128  | –   | 4 | 2.84 | 2 | 2.57 | 14 | 5.6738 | 2 | 0.0010 | 0 | –   | 0 | –   | 3 | 0.48 | 2 | 0.7 | 25 | 9.72 |

\(^a\) ID in Fig. 1. “C” and “D” prefixes indicate commercial and domestic samples, respectively.

\(^b\) “PRASA”, “NPCWS”, and “SS” indicate Puerto Rico Aqueducts and Sewers Authority and non-PRASA community-water-supply and private well self-supply TW samples, respectively.

\(^c\) “–” indicates not detected. See Tables S2 and S8 for reporting level and blank limit details.

\(^d\) Bold Red and Black font indicate EPA MCL or AL (U.S. Environmental Protection Agency, 2021a) and WHO guideline (World Health Organization (WHO), 2011) exceedances, respectively.
Table 2

Concentrations (μg L\(^{-1}\)) of copper (Cu) and lead (Pb) and cumulative detections (#) and concentrations (μg L\(^{-1}\)) of organic contaminant classes and of all organics detected in TW samples collected from two sites during the August synoptic and follow-up December 2018 temporal sampling. Temporal data are stagnant-overnight and 30 min follow-up TW samples collected at the same times over 3 consecutive days. See Tables S5–S6 for individual organic results.

| ID  | Date/time | Inorganic | Organic class (sum detections and concentrations) |
|-----|-----------|-----------|--------------------------------------------------|
|     |           | Cu μg/L   | Pb μg/L  | DBP # μg/L | THM # μg/L | Pest # μg/L | PFAS # μg/L | Pharm # μg/L | Sweeteners # μg/L | VOC # μg/L | TOTAL μg/L |
| C4  | August    | 18        | 10      | 65.74      | 5          | 63.59      | --          | --          | 0 --                    | 0 --       | 1 0.02     | 11 65.78  |
|     | December  | 19.9      | 12      | 60.58      | 7          | 40.59      | 6 0.0563    | 1 0.0011    | 0 --                    | 2 0.10     | 15 49.51  |
|     | day1 0900 | 13.0      | 11      | 44.38      | 6          | 42.73      | 1 0.0042    | 0 --        | 2 0.12                  | 1 0.07     | 15 44.57  |
|     | December  | 19.9      | 12      | 60.58      | 7          | 40.59      | 6 0.0563    | 1 0.0011    | 0 --                    | 2 0.10     | 15 49.51  |
|     | day1 0930 | 13.1      | 12      | 48.67      | 7          | 44.23      | 0 --        | 0 --        | 1 0.23                  | 2 0.61     | 18 40.84  |
|     | day2 0900 | 9         | 11      | 44.07      | 6          | 42.41      | 0 --        | 0 --        | 1 0.09                  | 2 1.16     | 18 40.84  |
|     | December  | 19.9      | 12      | 60.58      | 7          | 40.59      | 6 0.0563    | 1 0.0011    | 0 --                    | 2 0.10     | 15 49.51  |
|     | day2 0930 | 13.1      | 12      | 48.67      | 7          | 44.23      | 0 --        | 0 --        | 1 0.23                  | 2 0.61     | 18 40.84  |
|     | day3 0900 | 10        | 13      | 75.03      | 7          | 42.67      | 0 --        | 4 0.0063    | 0 --                    | 1 0.07     | 21 75.74  |
|     | December  | 19.9      | 12      | 60.58      | 7          | 40.59      | 6 0.0563    | 1 0.0011    | 0 --                    | 2 0.10     | 15 49.51  |
|     | day3 0930 | 10        | 13      | 75.03      | 7          | 42.67      | 0 --        | 4 0.0063    | 0 --                    | 1 0.07     | 21 75.74  |
| D2  | August    | 22        | 14      | 62.82      | 8          | 51.23      | 0 --        | 0 --        | 1 0.0151                | 0 --       | 15 62.84  |
|     | December  | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day1 0900 | 13.0      | 11      | 44.38      | 6          | 42.73      | 1 0.0042    | 0 --        | 2 0.12                  | 1 0.07     | 15 44.57  |
|     | December  | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day1 0930 | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day2 0900 | 9         | 11      | 44.07      | 6          | 42.41      | 0 --        | 0 --        | 1 0.09                  | 2 1.16     | 18 40.84  |
|     | December  | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day2 0930 | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day3 0900 | 10        | 13      | 75.03      | 7          | 42.67      | 0 --        | 4 0.0063    | 0 --                    | 1 0.07     | 21 75.74  |
|     | December  | 13.1      | 12      | 62.27      | 6          | 34.55      | 0 --        | 5 0.0077    | 1 0.0463                | 2 0.04     | 22 62.44  |
|     | day3 0930 | 10        | 13      | 75.03      | 7          | 42.67      | 0 --        | 4 0.0063    | 0 --                    | 1 0.07     | 21 75.74  |

\(a\) ID in Fig. 1. “C” and “D” prefixes indicate commercial and domestic samples, respectively.

\(b\) “-“ indicates not detected. See Table S2 for reporting limit details.

\(c\) Bold Black and Red font indicate WHO guideline (World Health Organization (WHO), 2011) and EPA AL (U.S. Environmental Protection Agency, 2021a) exceedances, respectively.

\(d\) “na” indicates “not analyzed.”