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Brief Communication

Estimating Human Exposure to Titanium Dioxide from Personal Care Products Through a Social Survey Approach

Fan Wu†‡ and Andrea L Hicks†*
†Department of Civil and Environmental Engineering, University of Wisconsin-Madison, Madison, Wisconsin, USA
‡School of Environment and Guangdong Key Laboratory of Environmental Pollution and Health, Jinan University, Guangzhou, China

ABSTRACT

Titanium dioxide (TiO_2) has been widely applied in personal care products (PCPs), with up to 36% of TiO_2 in PCPs is present at the nanoscale. Due to the large quantity produced and the wide application of TiO_2, there is a great potential for human exposure through various routes and therefore a great potential to elicit adverse impacts. This work utilizes a social survey to generate information and estimate TiO_2 (bulk and nanoparticle [NP]) exposure to individuals through the daily use of PCPs. Households in the Madison, Wisconsin, USA metropolitan area were surveyed about their PCP usage. Survey results were then combined with usage patterns and TiO_2 content in each PCP category to estimate human exposures. Results indicate sunscreen and toothpaste are major contributors to TiO_2 dermal exposure. The estimated daily dermal route of exposure ranges from 2.8 to 21.4 mg TiO_2 per person per day. Toothpaste has the potential to be ingested though the oral route; 0.15 to 3.9 mg TiO_2 per day were estimated to be ingested when 10% toothpaste ingestion was assumed. The results generated in the present case study are generalizable in predicting individual TiO_2 exposure from PCPs when the usage pattern is available. In addition, this study can be further used for risk assessment and to refine the use of TiO_2 in PCPs. *Integr Environ Assess Manag* 2019;00:1–7. © 2019 SETAC

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INTRODUCTION

Titanium dioxide (TiO_2) is a naturally occurring metal oxide. The engineered TiO_2 nanoparticle (NP) is one of the most commonly used nanomaterials (with 1 or more dimensions within 1 to 100 nm) in consumer products (Shi et al. 2013). Global production of TiO_2 was approximately 6.1 million tonnes in 2016 and is projected to reach 7.8 million tonnes by 2022; furthermore, the global TiO_2 market is currently valued at US$13.3 billion and is expected to grow at 8.9% annually through 2025 (Research and Markets 2016). With the current and projected future large production volume and widespread usage, some specific applications may pose a greater potential risk of TiO_2 exposure to humans (Zhang et al. 2015). Particularly, those applications are ones that could lead to direct human exposure to TiO_2 via inhalation (e.g., cleaning aids, spray cosmetics, coatings), dermal exposure, such as personal care products (PCPs), or oral ingestion through food and drink, such as soda, cheese, and chewing gum (Lomer et al. 2001; Chen et al. 2013).

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* Address correspondence to Hicks5@wisc.edu
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Personal care products, including lotion, shampoo, deodorant, and toothpaste, are often laden with chemicals, some of which are considered emerging contaminants. However, limited information is available to estimate TiO_2 exposure through the use of PCPs, and specific usage of TiO_2 NPs is not transparently regulated in consumer products, especially in PCPs. According to the literature, nearly 35% of manufactured TiO_2 is used in PCPs (Keller et al. 2013), and up to 36% of TiO_2 is at the nanoscale in PCPs (Weir et al. 2012). The TiO_2 NPs are utilized in specific applications such as ultraviolet (UV) protection and preventing decoloration of products (Smijs and Pavel 2011). Consequentially, nanoscale TiO_2 in PCPs could result in human exposure and release of this material into the environment (Keller and Lazareva 2013). Mechanistically, TiO_2 NP can elicit toxicity due to the generation of reactive O species, affinity to attach to intracellular organelles and biological macromolecules, and cell membrane disruption (Shah et al. 2017). Although early studies suggest that TiO_2 NPs are toxic to some extent (Jovanović 2015; Heringa et al. 2016), the lack of sufficient in vivo chronic toxicity studies prevents conclusive results, and the potential chronic toxicity via various routes of exposure may still pose a concern to human health. Moreover, limited information exists on daily TiO_2 (including TiO_2 NP) exposure to humans through

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various routes, making it even more difficult to evaluate the relevant risks associated with TiO_2 usage.

In the present study, a social survey was utilized to generate personalized data and to estimate TiO_2 human exposure on a household basis through the use of 8 major PCPs. This approach allows for a quantitative estimate of the exposure to TiO_2 at an individual level. The Madison, Wisconsin, USA metropolitan area was selected as the study region. Results generated in the present study can be utilized to improve future regulations based on TiO_2 applications and pathways that are most likely to impact human health, refine the potential exposure concentrations for future TiO_2 risk characterization, and support decision making that is backed by data.

METHODS

Survey distribution and collection

The present study employed an Institutional Review Board (IRB)–approved social survey to collect information and estimate TiO_2 exposure at the household and individual levels in the Madison metropolitan area (IRB 2017-0883). The survey was distributed through various avenues, such as mailing lists, science outreach events, online postings, and fliers. The survey was collected from 3 April to 22 December 2018. The survey instrument was divided into a demographic section and multiple sections by PCP category, including toothpaste, shampoo, conditioner, lotion and skin cream, sunblock and sunscreen, deodorant and antiperspirant, shaving cream, other products. The survey respondents were asked to check whether the PCPs contained TiO_2 in the ingredient list, and then information was collected regarding the brand and number of products utilized. The demographics section asked for the respondent's gender, age, race, number of household members, and approximate household income. The full survey and details on its administration are provided in Supplemental Data. The products listed by the respondents were then cross-referenced with ingredient lists to confirm the presence or absence of TiO_2. Collected surveys needed to follow 3 criteria to be considered valid:

1) Citizens who resided outside the Dane County (Madison Metropolitan) area were excluded from the present study. The full list of the district's communities includes the cities of Madison, Fitchburg, Middleton, Monona, and Verona; the towns of Dunn–Kegonsa, Dunn, Pleasant Springs, Verona–Marty Farms, Verona, and Westport; and the villages of Cottage Grove, Dane, DeForest, Maple Bluff, McFarland, Shorewood Hills, Waunakee, and Windsor.
2) Incomplete surveys were not included in the final data analysis, and respondents had to be at least 18 years of age.
3) Participants had to ensure that they had read the informed consent in order to continue the survey; otherwise the survey was not able to be completed.

Data analysis

Survey results were then combined with the daily usage and quantity of TiO_2 previously identified in various PCPs to estimate the human exposure from the use of PCPs. Table 1 contains the summary of the average usage for each PCP type and the ranges of TiO_2 concentrations (both TiO_2 and TiO_2 NP) detected in various PCPs from a suite of research articles (Weir et al. 2012; Peters et al. 2014; Yang et al. 2014; Warheit et al. 2015; Rompelberg et al. 2016). Toothpaste and sunscreen are identified to have much higher concentrations than the other types of PCP. Because the TiO_2 concentrations detected previously in PCPs contain large range variations, lower and upper bound concentrations were taken or estimated from those cited studies. Additional research investigated the personal usage patterns of various types of PCP (Loretz et al. 2005, 2006, 2008; Bennett et al. 2010; Hall et al. 2011; Biesterbos et al. 2013). The average usage patterns were used to perform calculations in the present study.

RESULTS AND DISCUSSION

Estimated concentrations of TiO_2 exposure

Based on a total of 401 household survey responses, 213 PCPs were identified as containing TiO_2. Figure 1 summarizes the estimated TiO_2 exposure from the daily use of PCPs. Results suggest that TiO_2 exposures are emitted mainly through sunscreen and toothpaste. The majority of the PCP emissions clustered in the lower range, but higher TiO_2 were still observed when the higher bound concentrations were used (Figure 1B).

Table 1. Data used to calculate the concentration of TiO_2 used in each PCP category[a]

Product	PCP usage (mean) Grams/person/day	TiO_2 in PCP (mg Ti/g)	
		Low estimated concentration	High estimated concentration
Toothpaste	2.09	0.7	5.6
Sunscreen	0.4	14	90
Shampoo	11.76	0.01	0.1
Conditioner	13.1	0.01	0.1
Lotion	9.92	0.1	1
Deodorant	0.4	0.01	0.1
Shave cream	1 (grams/household/day)	0.01	0.1
Shower gel	10.1	0.1	1
Soap bar	2.5	0.1	1

PCP = personal care product.
[a]PCP usage data and TiO_2 in PCPs were gathered from the literature: Loretz et al. 2005, 2006, 2008; Bennett et al. 2010; Hall et al. 2011; Weir et al. 2012; Biesterbos et al. 2013; Peters et al. 2014; Yang et al. 2014; Warheit et al. 2015; Rompelberg et al. 2016.

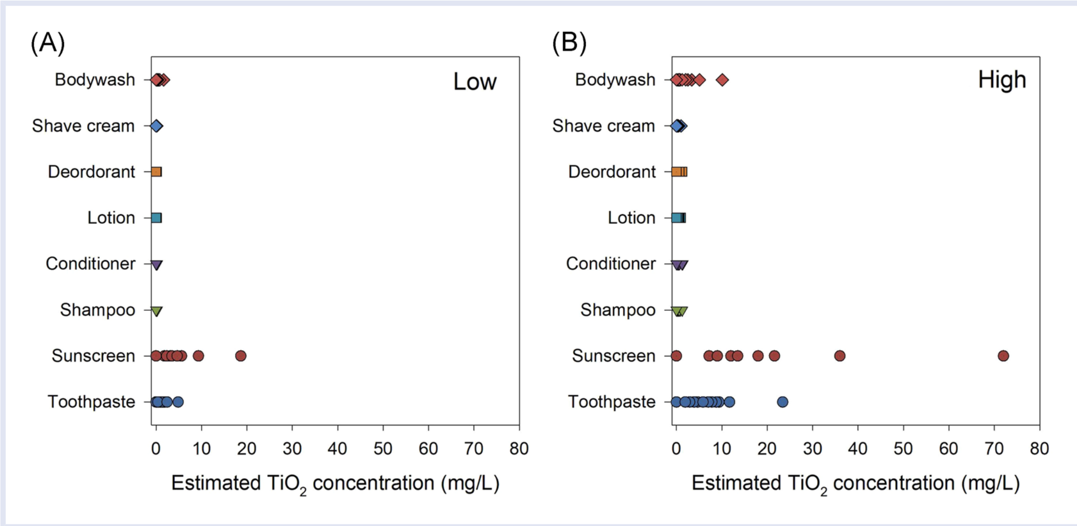

Figure 1. Summary of the estimated low (**A**) and high (**B**) TiO_2 concentrations exposed daily from the usage of each type of PCP. Each symbol in the figure represents an estimated TiO_2 exposure from the corresponding PCP. PCP = personal care product.

Figures 2A and 2B represent the low and high individual TiO_2 exposures, respectively, when the results were sorted by household income. When the exposure concentrations were compared among varying household incomes (1-way analysis of variance) using SigmaPlot (Systat Software; San Jose, California, USA), no significant difference was found in the individual TiO_2 exposures, suggesting that household income does not affect the average TiO_2 exposure. Figure 2C demonstrates the distribution and brackets of individual TiO_2 exposure in low and high exposure scenarios. More than 70% of individuals were exposed to TiO_2 in the range of 0 to 10 mg/d in low estimated concentrations (Figure 2A). When high estimated concentrations were used (Table 1), the distribution was spread more toward the higher concentrations. Taken together, results obtained from the surveyed population suggest that the majority of the population (more than 80%) are likely exposed to TiO_2 through the daily use of PCPs, mainly contributed from toothpaste, sunscreen, and bodywash. This finding is in line with the estimates from a survey study conducted by Keller et al. (2014) from a production perspective, where TiO_2 and other engineered nanomaterials (ENMs) were used in sunscreen, cosmetics, and toothpaste.

Individual exposure to TiO_2 and TiO_2 NP through various routes

The previous section estimated the overall exposure of humans to TiO_2 from PCPs because PCPs serve as a major source of TiO_2 through direct interaction with human bodies. However, TiO_2, especially TiO_2 NPs present in these PCPs, can reach various parts of the human body via exposure routes that include inhalation, injection, dermal deposition, and gastrointestinal tract absorption (Shi et al. 2013). Figure 3 estimates the source flow, quantity, and route of exposure from each surveyed PCP. The dermal route is considered the dominant route for TiO_2 exposure through PCP usage, due to the dermal application of most products. Three TiO_2 exposure scenarios, low estimate (Figure 3A), high estimate (Figure 3B), and the worst-case scenario (Figure 3C), were analyzed based on the different TiO_2 concentrations estimated in PCPs. The maximum TiO_2 exposure is the worst-case scenario, estimated on the basis of the sum of the highest exposure values calculated in each PCP category (Figure 3C). Results suggest the estimated average TiO_2 exposure through the dermal route ranges from 2.8 to 21.38 mg TiO_2 per person per day, with a maximum exposure of 181.8 mg TiO_2 per person per day. Sunscreen, toothpaste, and body wash are three of the biggest contributors to TiO_2 expose dermally. The average TiO_2 NP exposure concentrations from the use of PCPs is within the personal disposal concentrations predicted by Keller et al. (2013). They estimated nanoscale TiO_2 released per person ranges from 1.95 to 22.70 mg/d at various locations. Researchers found the nanoscale TiO_2 fraction in PCPs ranges from 10% to 36% (Weir et al. 2012; Peters et al. 2014; Yang et al. 2014; Warheit et al. 2015; Rompelberg et al. 2016). Based on their range, the estimated TiO_2 NP dermal exposures in our study likely range from 1 to 7.7 mg TiO_2 NP per person per day. Because PCPs are the only source considered in our study, it is expected the concentrations in the present study are lower than those predicted by Keller et al. (2013) since other consumer products were considered in their results, which can contribute to TiO_2 NP releases.

Although ingestion is not considered a major route for TiO_2 exposure through PCP usage, unintended exposure can still occur orally through ingestion of toothpaste, particularly for younger children (Shi et al. 2013). To estimate the oral route exposure, 10% toothpaste ingestion was assumed in the surveyed population average. Based on this assumption, 0.153 to 3.9 mg/d of TiO_2 (0.06–1.4 μg/d of TiO_2 NP) was estimated to be ingested. In comparison to a study conducted by Rompelberg et al. (2016), the estimated TiO_2 exposed solely from toothpaste usage for children age <6 years old can be up to 0.67 mg/kg body weight (bw) per

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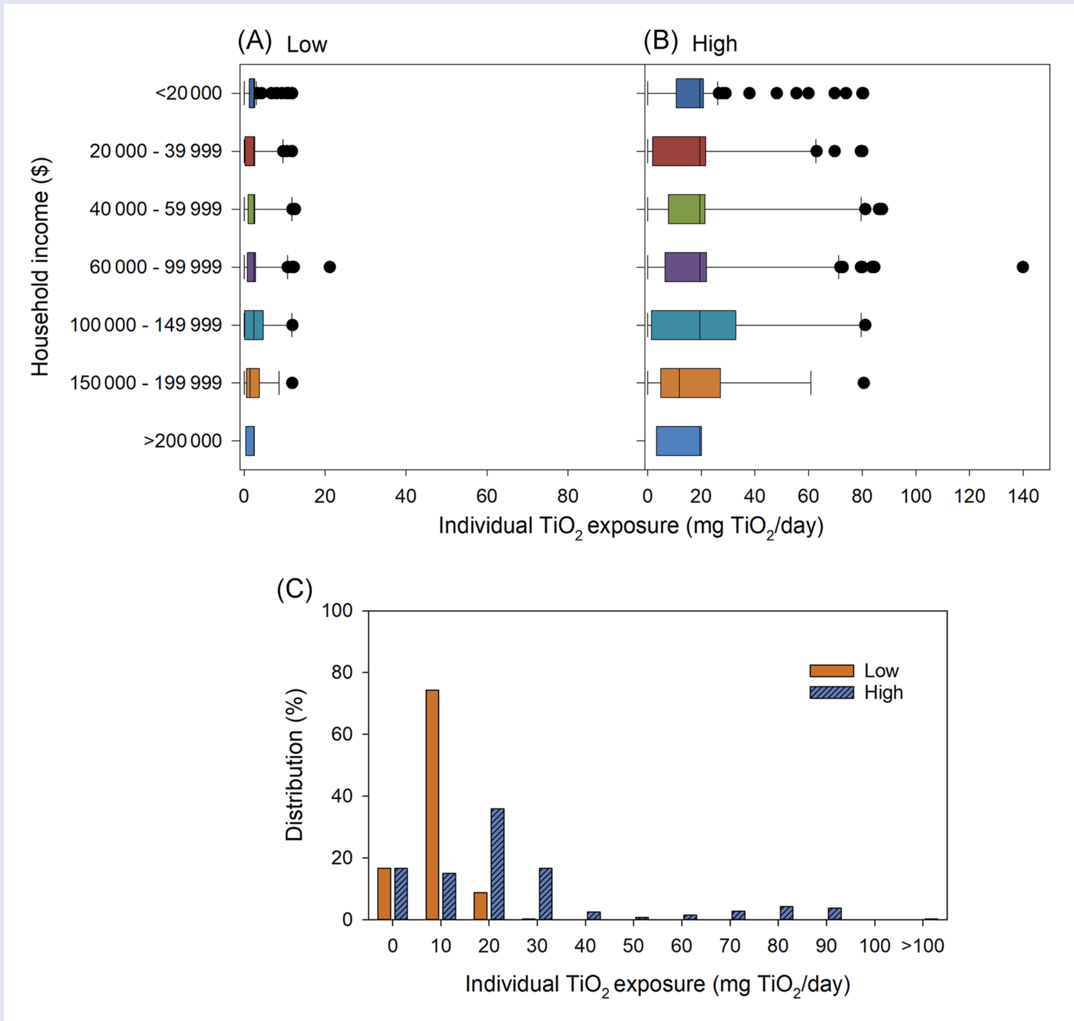

Figure 2. Estimated daily low (A) and high (B) individual TiO_2 exposure corresponding to the household income. Panel (C) shows the estimated distribution of individual TiO_2 exposure of the surveyed population.

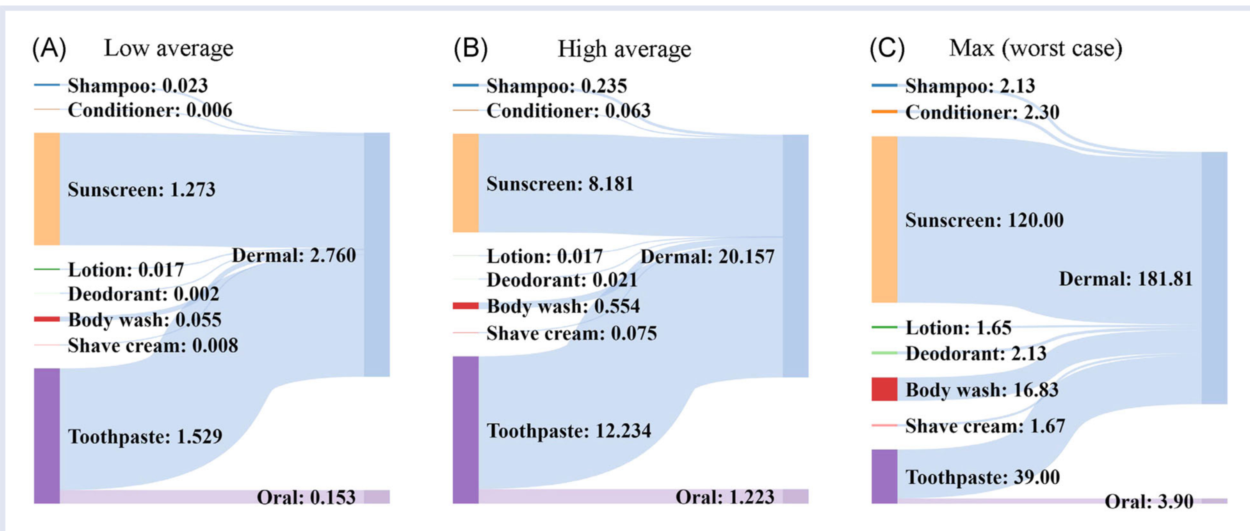

Figure 3. Estimated daily exposure of TiO_2 from the use of PCPs (mg TiO_2 per person per day): average low (2.91 mg TiO_2 per person per day) (A); average high (21.38 mg TiO_2 per person per day) (B); worst-case scenario derived from the maximum values of each product (185.71 mg TiO_2 per person per day) (C). Oral route exposure was estimated based on assuming 10% of toothpaste is ingested by the population at all ages.

day, whereas an older population's mean intake ranges from 0.19 to 0.55 μg/kg bw per day. Taking a person with 60 kg bw for instance, the TiO_2 exposure from toothpaste varies between 0.012 and 0.033 mg/d. These concentrations are similar to the low average exposure estimated in the present study (Figure 2B). In another study, the authors indicate that global per capita TiO_2 ingestion depended on the geographical locations of the population, with the United States and the United Kingdom having an estimated consumption of approximately 0.2 to 0.7 mg and approximately 1 mg TiO_2 per kilogram bw per day, respectively (Weir et al. 2012). The estimated concentrations in the present study were lower than the ingestion concentrations estimated by Weir et al. (2012), suggesting that other sources of TiO_2 ingested from food contributes to the oral route exposure.

TiO_2 NP impacts and discussion

In order to inform the design of environmental fate and toxicity studies on TiO_2, the present study adapted a social survey to collect information on upstream anthropogenic behavior, and estimated and identified the potential TiO_2 exposure concentrations related to the corresponding routes. To simplify the estimation, previously quantified ranges of TiO_2 concentrations in PCPs from the literature were used to estimate the potential daily TiO_2 exposure instead of quantifying Ti content in all the market-available products (Weir et al. 2012; Peters et al. 2014; Yang et al. 2014; Warheit et al. 2015; Rompelberg et al. 2016). In addition, limited extraction and quantification methods to determine TiO_2 NP fractions in these PCPs are still very challenging. The estimated daily exposure concentrations through a citizen science approach can provide personalized exposure data and could be used for future risk assessment with respect to each exposure route.

Our results suggest that dermal route exposure is the major concern for TiO_2 NP to interact with humans through PCP usage. From a toxicology perspective, several studies suggest that TiO_2 NPs have no effect because they cannot penetrate the intact human skin (Pflücker et al. 2001; Schulz et al. 2002; Crosera et al. 2015) and that they can even protect human skin against UV-induced adverse effects (Schilling et al. 2010; Park et al. 2011). However, others found that small TiO_2 NPs can penetrate skin and damage different organs in animals (Wu et al. 2009) and can pass through hairy skin when applied as an oil-in-water emulsion (Bennat and Müller-Goymann 2000). Although research shows conflicting findings and lack of evidence in significant dermal penetration of TiO_2 NPs from PCPs, research still found that TiO_2 NPs may pose a health risk to humans after dermal exposure over a relatively long period of time, which induces skin aging (Wu et al. 2009; Sadrieh et al. 2010). Although some studies indicate that TiO_2 NPs provoke toxicities only at high concentrations, there is a common agreement that TiO_2 NPs have greater potential to elicit adverse outcomes under specific environmental conditions, especially under UV inducement (Amiano et al. 2012). Other factors, such as the age of TiO_2 NPs, can impact the results due to the different morphology of the stratum corneum, and the oxidative activity and phototoxicity of TiO_2 NPs might create inflammation with UV induction, causing skin irritation and sensitization (Smulders et al. 2015). Because sunscreen typically has a long residence time on human skin, dermal exposure to TiO_2 NPs through using sunscreen is a major concern. It is particularly vital when interpreting the potential impact through dermal exposure such as when used as sunblock.

Although toothpaste ingestion is relatively low compared to ingestion from food sources, studies have found that health risks from the ingestion of TiO_2 NPs via food, supplements, and toothpaste are still possible (Heringa et al. 2016). A recent study observed a microbial composition shift from Proteobacteria to Firmicutes phyla in the presence of food and industrial grade TiO_2 ($36\ mg \cdot L^{-1} \cdot d^{-1}$) (partially nanoscale), indicating that TiO_2 may have adverse impacts when considering exposure and risk (Waller et al. 2017). Moreover, studies concluded that TiO_2 NPs can be absorbed by mammals after ingestion or injection and stored in various organs (Sang et al. 2013, 2014). TiO_2 NP also showed the potential to cause tissue damage, alter biochemical parameters, bioconcentrate, bioaccumulate, and biomagnify in animal bodies (Ramsden et al. 2009; Fouqueray et al. 2013). The estimated risk of ingested TiO_2 NP can be influenced by factors such as absorption, form of TiO_2, particle fraction, particle size, and physicochemical properties in relation to toxicity, among others. Although the risk is challenging to investigate, it should be tackled in order to refine future regulation of the application of TiO_2 NPs in food and supplements.

Exposure to TiO_2 through PCP usage is limited in the inhalation route; therefore, this route was not considered in the present study. However, spray-type PCPs (e.g., sunscreen and makeup) still enable respiratory route exposure. Several studies have concluded that there is no increase in toxicity, such as mortality (Fryzek et al. 2003), lung inflammatory response (Liao et al. 2009), or carcinogenic effect (Hext et al. 2005; Liao et al. 2008), associated with workplace TiO_2 exposure. However, conflicting results again suggest that when exposed to TiO_2 NPs, rats and mice experience significant lung inflammation (Ferin et al. 1992; Gurr et al. 2005; Grassian et al. 2006) and cell mutations (Trouiller et al. 2009). Previous studies assessed the health risk of TiO_2 NPs to workers from a chronic animal inhalation study with ultrafine TiO_2, in which a statistically significant increase in adenocarcinomas was observed (Heinrich et al. 1995; CDC 2011). Research also investigated the inhalation impacts of P25 TiO_2 NPs to wistar rats and 2 different strains of mice at an average concentration of $10\ mg/m^3$, where toxic effects were found on alveolar macrophages and alveolar lung particle clearance (Heinrich et al. 1995). In another study, Laurent et al. summarized no-observed-adverse-effect level (NOAEL) and lowest-observed-adverse-effect level (LOAEL) values of TiO_2 NPs in various in vivo studies and predicted the LOAEL (NOAEL) concentrations to be 0.0836 to 4.05 (0.0171–10.5) mg/kg bw per day for exposure through the inhalation route (Laurent et al. 2017). Tsang et al. (2017) used 2 studies

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(Heinrich et al. 1995; Bermudez et al. 2004) combining nano-TiO_2 and fine-TiO_2 to calculate carcinogenic ED50, and obtained a value of 1.58 μg/g wet lung (1.43 m^2/g dry lung). These values provide specific evidence for potential risks elicited by TiO_2 NP inhalation. Moreover, the International Agency for Research on Cancer (IARC) designates TiO_2 as a carcinogen, largely due to studies that have found increased lung cancers due to inhalation exposure in animals (WHO 2010). Therefore, the use of TiO_2 in PCPs should be carefully assessed, and direct inhalation should be minimized.

Although the present study was focused on the population residing in Madison, Wisconsin, there is a potential to project the results to a larger scale. The TiO_2 exposures estimated in the present study are dominated mainly by the PCP usage pattern and PCPs used in the household; data estimated in our study are generalizable whenever those 2 factors are available. Based on the present study, individuals can also estimate their daily TiO_2 exposure through the amount of household PCP usage. Therefore, an easily accessible inventory that includes the amount of TiO_2 used in each household PCP is urgently required. This cannot only project current results to a larger scale but can also refine the findings to be more beneficial for risk assessment, management, and regulation development.

CONCLUSION

The present study estimated the heterogenous TiO_2 exposure from PCPs via various routes. In addition, the present work provided a better idea of the range of TiO_2 exposure instead of just a single average exposure value. The information generated in the present study can be further used for risk assessment and to refine the use of TiO_2 in PCPs, specifically targeting the dermal and oral routes of exposure. Although this is a regional case study, generalization is achievable when the usage pattern and the TiO_2 concentrations in PCPs are more refined.

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Disclaimer—There are no conflicts of interest to declare.

Data Availabilty Statement—Please contact the authors Fan Wu (fwu64@wisc.edu) and Andrea L Hicks (Hicks5@wisc.edu) for any metadata or calculations not already provided.

SUPPLEMENTAL DATA

Supplemental Data contain the full survey and the validation criteria for the collected survey responses.

ORCID

Fan Wu http://orcid.org/0000-0001-8621-9449
Andrea L Hicks http://orcid.org/0000-0002-6426-9717

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