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Association Between Triclocarban and Triclosan Exposures and the Risks of Type 2 Diabetes Mellitus and Impaired Glucose Tolerance in the National Health and Nutrition Examination Survey (NHANES 2013-2014)

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Abstract

Background: There has been increasing interest in the concept that exposure to environmental chemicals may be contributing factors to epidemics of diabetes mellitus (DM). Triclocarban and triclosan (TCs) are synthetic antibacterial chemicals that are widely used in personal care products. Studies have shown that TCs are endocrine disruptors that alter metabolic conditions. However, it remains unclear whether exposure to TCs is a risk factor for impaired glucose tolerance (IGT) and type 2 diabetes mellitus (T2DM).

Objective: We explored the hypothesis that TCs exposure is associated with an increased risk of IGT and T2DM.

Method: To test our hypothesis, we analyzed the U.S. National Health and Nutrition Examination Survey (NHANES) cross-sectional data from 2013-2014. IGT and T2DM were diagnosed based on an oral glucose tolerance test (OGTT) and the WHO standards. The levels of urinary TCs were measured using an HPLC-MS/MS method that NHANES investigators developed. The association between urinary TCs status and IGT and T2DM was examined separately in men and women using multivariable logistic regression models adjusted for age, race, BMI, education, ratio of family income to poverty, smoking, exercise and hypertension.

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Disclosure

The authors report no conflicts of interest.

Results: Nine hundred US participants (429 men and 471 women) were included in the analysis, of whom 242 (26.89%) were diagnosed with T2DM and 117 (13.00%) had IGT. Among women, there was a significant positive association between triclocarban, but not triclosan exposure and T2DM (OR: 1.79, 95% CI: 1.05, 2.05) after adjusting for potential confounding factors. Among men, no significant association between TCs exposure and IGT or T2DM was observed.

Conclusions: Triclocarban exposure may increase the risk of T2DM in the women, although additional studies are needed to confirm the results of this study and to investigate the underlying mechanisms.

Keywords

Triclocarban; Triclosan; T2DM; IGT

Introduction

Approximately 425 million adults (20–79 years old) are currently living with diabetes mellitus (DM) worldwide, which will rise to 629 million by 2045[1]. DM is the ninth leading cause of death and seriously affects public health[2]. Chronic hyperglycemia during DM is associated with long-term damage, dysfunction and different types of organ and tissue failure, especially the eyes, kidneys, nerves, heart and blood vessels[3]. There are two main types of diabetes: type 1 (T1DM) and type 2 (T2DM). By far, the most common form of diabetes is T2DM, accounting for 95% of diabetes cases in adults. T2DM is a chronic metabolic disorder characterized by hyperglycemia and insulin resistance (IR)[4], with impaired glucose tolerance (IGT) being an intermediate category between normal glucose tolerance and overt diabetes[5]. T2DM and IGT are considered to be stages in the progression of the same disease process. IGT is an early state of T2DM, and both IGT and T2DM are associated with impaired insulin secretion[6].

The etiology of T2DM appears to involve complex interactions between genetic and environmental factors[7]. Excess caloric consumption and a sedentary lifestyle are well-recognized risk factors for diabetes. However, there is growing interest in the contribution of “non-traditional” risk factors (e.g., environmental chemicals, stress, micronutrients, and the gut microbiome) to the etiology of this health condition. Research addressing the role of environmental chemicals in diabetes has rapidly expanded in the past decade. Studies have shown that the current increased risk of metabolic syndrome, insulin resistance and diabetes is associated with a large increase in the production and exposure of humans to environmental chemicals, such as dioxins, polychlorinated diphenyl ethers, and arsenic[8, 9]. Some endocrine-disrupting chemicals (EDCs) such as dioxins and bisphenol A (BPA) have been shown to reduce glucose uptake in the pancreas and impair insulin secretion, confirming the environmental etiology hypothesis of T2DM[10]. Moreover, as scientific evidence linking EDCs to the development of diabetes and other metabolic disorders continues to grow, a disproportionate exposure to diabetes-associated EDCs may be identified as a previously underappreciated contributor to disparities in metabolic risks[11].

Triclocarban (3,4,4’-trichlorocarbanilide; TCC) and triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol; TCS) are antimicrobial additives used in personal care

products[12, 13] that are present in >2,000 products, including soaps, toothpastes, detergents, clothing, toys, carpets, plastics, and paints[14–18]. Humans are exposed to TCS and TCC through direct contact with personal care products and from other sources including food, drinking water, and dust[19, 20]. Although the Food and Drug Administration (FDA) banned the use of TCC and TCS (TCs) in over-the-counter consumer antiseptic wash products since September 2016, most TCs chemicals are still in use and are present in high concentrations in other personal care products[21]. These two chemicals have been in widespread use for decades, and it is imperative to further understand the health effects of these chemical compounds that humans are consistently exposed to.

Both TCC and TCS are considered to be novel EDCs[18, 22] that are associated with adverse effects on metabolic disorders[23–27]. However, the association between TCs and gestational diabetes was shown to be inconsistent in previous studies[25, 28], and to the best of our knowledge, no studies have reported on the relationship between TCC and TCS exposure and T2DM.

Given their endocrine-disrupting properties and the association between TCC and TCS exposure and existing adverse health effects, especially metabolic disorders, we postulated that TCC and TCS exposure may be associated with an increased risk of T2DM. Thus, in this study, we investigated the cross-sectional relationship between TCC and TCS exposure and the risk of T2DM and IGT in the National Health and Nutrition Examination Survey (NHANES), a population of randomly selected civilian, noninstitutionalized residents across the United States.

Methods

Study Population

The National Health and Nutrition Examination Survey (NHANES) is a research program designed to assess the health and nutritional status of adults and children in the United States. The NHANES program began in the early 1960s and is a series of surveys targeting different populations or health topics[29]. The NHANES study protocol is described in detail elsewhere (National Center for Environmental Health, Centers for Disease Control and Prevention)[30]. The NHANES agreement has been reviewed and approved by the NCHS Research Ethics Committee. All participants provided written informed consent prior to participation. The survey is unique in that it combines interviews and medical examinations.

For the present study, we used publicly available NHANES data generated through surveys conducted in 2013-2014 in which demographic information was obtained from 10,175 participants. Using the unique survey participant identifiers, we can link the database of laboratory test results to other NHANES databases. After the databases were combined, we excluded participants who had missing data on their physical exam, DM questionnaire, OGTT, TCs, exercise, smoking and hypertension. After all exclusions, there remained an analytical sample of 900 participants, including 429 men and 471 women (Figure 1).

Urinary TCC and TCS measurements

Urine samples were collected from subjects in a standard urine collection cup and transferred to vials within 4 hours of collection. For each study participant, a single spot urine sample was collected for each participant during one of three daily examination session periods (i.e., morning, afternoon, and evening). The samples were processed and shipped on dry ice to the National Center for Environmental Health of the Centers for Disease Control and Prevention and stored at or below −20°C until analysis[31].

Urinary TCC and TCS concentrations were measured using restricted-entry materials (RAM) for on-line solid phase extraction (SPE) coupled with high-performance liquid chromatography-isotope dilution with peak focused tandem mass spectrometry (HPLC-MS/MS)[32]. The detection limit of TCC and TCS in 100 μL of urine is 0.1 and 1.7 μg/L, respectively[31, 33]. The National Center for Health Statistics develops and distributes quality control protocols for all contract laboratories, and all analytical reports meet the accuracy and precision of the Laboratory Science Department's quality control and quality assurance performance standards. In addition, the contract laboratories randomly performed repeat testing on 2.0% of all specimens[34].

Diabetes outcomes

In the current study population, people who were receiving diabetes treatment were directly classified as diabetics, while the rest of the individuals were grouped according to the OGTT results. The diagnostic criteria for diabetes described by the World Health Organization were used to identify cases of T2DM. These criteria include: a fasting blood glucose level of ≥7.0 mmol/l (126 mg/dl) or a 2-hours plasma glucose level of ≥11.1 mmol/l (200 mg/dl). Diagnostic criteria for IGT include a fasting plasma glucose level of <7.0 mmol/l (126 mg/dl) and 2-hour plasma glucose level of ≥7.8 and <11.1 mmol/l (140 and 200 mg/dl)[35].

Self-reported diabetes

Personal interview questionnaires were administered to NHANES participants to collect data on diabetes, pre-diabetes, insulin or oral hypoglycemic agents, and diabetic retinopathy.

Oral Glucose Tolerance Test

Fasting blood glucose tests were performed in the morning after 9 hours of fasting, and the results were recorded for all NHANES participants who were 12 years of age and older. After the initial venipuncture, participants were asked to drink a calibrated dose of TrutolTM (typically containing 75 grams of glucose) and had a second venipuncture for 2 hours (plus or minus 15 minutes) after drinking TrutolTM for the OGTT.

Hypertension

Personal interview questionnaires were administered to NHANES participants to collect data on their awareness, treatment and control of hypertension.

Smoking

The NHANES dataset contains detailed information on the use of cigarettes, pipes, cigars and other forms of tobacco and nicotine replacement therapy over the past five days before interview. Smoking variables are defined by whether or not smoking is occurs within 5 days[36].

Covariates

Additional information was ascertained at baseline using a questionnaire that included demographic variables, such as age, race, education level, the ratio of family income to poverty and lifestyle variables, such as height, weight, BMI and exercise.

Statistical Analysis

Continuous variables are presented as the means with SD or median with range P25 and P75, whereas categorical variables are presented as cases (n) and percentage (%). A multivariate logistic regression model was used to analyze the association between TCC and TCS exposure and IGT and T2DM. Odds ratio (OR) with 95% confidence interval (CI) was used to determine the degree of association. Model 1 was not adjusted; Model 2 was adjusted for age, race, BMI, education, the ratio of family income to poverty, and smoking; and Model 3 was additionally adjusted for hypertension and exercise. All data were analyzed using STATA (version 14 StataCorp LLC College Station, Texas, USA).

To examine associations between urinary TCs levels and IGT and T2DM status, we divided the study population into male and female sub-populations to consider the differences in prevalence of T2DM and the use of the personal care products containing TCs among men and women. The age-standardized prevalence of T2DM was somewhat higher in adult men than women[37], with women being more likely to use the personal care products containing TCs[38–40].

Results

Among 900 eligible participants, 541 participants without IGT or T2DM were assigned to healthy group in this study, 117 participants with IGT were assigned to the IGT group, and 242 participants with T2DM were assigned to the T2DM group. A significant difference in age distribution ($P < 0.001$) was observed among the three groups. The median age of the healthy, IGT, and T2DM groups was 40 years (range: 26, 57), 58 years (range: 43, 69), 56 years (range: 43, 70) respectively. The median age for the IGT and T2DM groups was higher than that of the healthy group. A significant difference in BMI ($P < 0.001$) was also observed, with subjects in T2DM group having a higher BMI than those in IGT and healthy groups. There were more individuals with hypertension among the IGT (52.14%) and T2DM (48.55%) subjects than the heathy subjects (26.25%) ($P < 0.001$). No statistical differences in gender, ethnicity, education, the ratio of family income to poverty, smoking or exercise. (Table 1).

Table 2 shows the association between the status of TCC exposure (detectable and non-detectable) and IGT or T2DM among 429 men and 471 women using multivariate logistic

regression analysis. In the healthy group, TCC was detectable in the urine of 39.16 and 35.74% of the male and female subjects, respectively. In the IGT group, TCC was detected in the urine of 41.51% of men and 46.88% of women, while in the T2DM group, TCC was detected in 48.60% of men and 51.18% of women. Referring to “healthy” as a reference group, the detectable rate of urinary TCC was significantly higher in T2DM group than in the reference group in women ($P < 0.05$). In model 1, a positive association was observed between TCC exposure and T2DM in women (OR=1.88, 95% CI: 1.23, 2.89, $P = 0.004$). In Model 2, after adjusting for age, ethnicity, BMI, education, ratio of family income to poverty, smoking, the association between TCC exposure and the risk of T2DM in women was also positive (OR=1.80, 95% CI: 1.06, 3.07, $P = 0.030$). In Model 3, after adjusting for age, ethnicity, BMI, education, ratio of family income to poverty, smoking, exercise and hypertension, the positive association remained between TCC exposure and the odds of T2DM in women (OR=1.79, 95% CI: 1.05, 2.05, $P = 0.032$). In summary, TCC exposure was a risk factor for T2DM in women.

TCS was detectable in the urine of 74.14 and 76.17% of male and female subjects in the healthy group, while TCS was detected in 81.13% of men and 68.75% of women in the IGT group and in 74.77% of men and 74.02% of women in the T2DM group. In all models, no significant associations between TCS exposure and IGT and T2DM were observed in either the male or female subjects ($P > 0.05$).

In addition, we compared the normal glucose tolerance group and abnormal glucose tolerance group (supplementary table 2). The results are consistent with our previous analysis.

Discussion

In this study, we identified a significant association between urinary TCC and the increased risk of T2DM in women after adjusting for known confounders using the National Health and Nutrition Examination Survey 2013-2014 data.

Studies on the association between TCs exposure and the risk of developing T2DM or gestational DM (GDM) are sparse and inconsistent. For TCS, a negative correlation between TCS exposure and GDM during pregnancy was observed in one study[25], while another study showed that TCS may be a risk factor for GDM[28]. In the present study, we demonstrated a null association between TCS and T2DM. For TCC, a previous study reported that TCC inhibited the aerobic glycolysis of glucose and increased anaerobic glycolysis and gluconeogenesis in male mice[41]. However, the results of our study supported the positive association between TCC exposure and T2DM in women but not men.

Previous studies have suggested a number of potential mechanisms underlying the association between TCs exposure and the development of T2DM. 1) TCs exposure may alter gut microbiome. Gastrointestinal microbial disorders have been confirmed in the etiology of DM[42]. Although data on the effects of TCs on human microbiota has been limited, it is possible that TCs may cause changes in the microbiome[43]. The exposure of

adolescent rats to TCC and TCS at doses comparable to those encountered by humans altered the gut microbiota in these animals[44]. TCC causes a significant imbalance in the neonatal gut microbiota through breast-feeding exposure[45]. However, a crossover control study has shown that the use of TCS for routine personal care does not have a major impact on the microflora in the gut and mouth, nor does it alter human endocrine function[15]. 2) TCs are thyroid hormone disruptors. Studies have shown that hypothyroidism is tied to T2DM[46]. In rats, TCS exposure reduced levels of thyroxine (T4) and triiodothyronine (T3) but did not affect thyroid stimulating hormone (TSH) levels[27]. TCS markedly lowered maternal T4 levels in rat dams during gestation and lactation[47]. TCC also has similar chemical properties to TCS[48]. 3) TCs exposure may be associated with the obesity/overweight status of individuals, which has been confirmed to be a risk factor for T2DM. A study of mice showed the placental maternal to fetal transfer of TCS, and exposed offspring were heavier than unexposed controls[49]. Using the NHANES database, one group observed that TCS exposure was associated with elevated BMI[50], while other groups observed that TCS exposure is negatively correlated with BMI and waist circumference[51] or had no significant correlation with obesity in children[52]. Overall, even though it is biologically plausible to consider TCs exposure a risk factor for T2DM, the results of the current study are largely inconsistent, and further studies are warranted to confirm our findings and examine the underlying mechanisms.

One of the interesting findings in this study is that there a gender difference was observed with respect to the relationship between TCC exposure and the risk of T2DM. We suspected that some covariances may be the cause of this gender discrepancy since this difference was only observed in adjusted models. There were indeed significant differences in BMI and hypertension between men and women in the cohort. The mean BMI was significantly higher in women than in men, and more women had hypertension than men in our study. However, the gender difference remained with or without adjusting for BMI or hypertension. Therefore, the observed gender discrepancy is unlikely to be due to the difference in BMI and hypertension in this study. Although there are no further definitive explanations for the gender difference, we believe it could be due to a number of possibilities. 1) TCs are widely used in a variety of consumer products, personal care products and cosmetics that are more commonly used by women. Therefore, TCs exposure is generally higher in women than in men[38–40]. 2) TCS and TCC are considered to be estrogen-like chemicals. Estrogen triggers transient and rapid cellular responses primarily through ERα in the cytoplasm to crosstalk with different signal transduction pathways. Studies have shown that TCs evoke weak responses mediated by aryl hydrocarbon, estrogen, and androgen receptors in vitro. At the molecular level, TCs also function as estrogen receptor (ER)-mediated ER agonists and downregulate endogenous ERα expression[53, 54]. The functions of ER are well known to be gender specific[55]. TCC also has a novel mechanism of action that destroys endocrine compounds[56]. The estrogen-interrupting activities and endocrine disrupting effects of TCC may explain the differences in the health effects on men and women.

Although TCC has similar chemical properties to TCS[48], we demonstrated an discrepancy between the relationship between TCC or TCS exposure and T2DM in this study. These results may be due to different exposure opportunities and much a higher detectable rate of TCS compared to TCC in this cohort. Human exposure to TCC may not be as prevalent as

TCS, probably because of the different levels of application or use of these two chemicals in antimicrobial consumer products[57]. The mechanism of action of TCC and TCS in vivo is different. TCS has been shown to potentially exert estrogenic activity at lower concentrations and exhibit antiestrogenic activity and/or cytotoxicity at high concentrations[53]. Both TCS and TCC are inhibitors of human CYP19A1, which is a human aromatase that produces estrogen from androgens. However, the inhibiting concentration (IC_{50}) values are different for these two compounds, and TCS binds to the steroid binding pocket of CYP19A1, whereas TCC does not bind to this target, indicating that they act through different mechanisms[48].

Our study has some limitations. First, the results of a cross-sectional study design are not as good as other studies such as cohort studies or longitudinal studies. Second, a major limitation of NHANES is that it is not geographically representative of the United States. The sample selected to be demographically representative, but because the two teams could only visit a total of 16 places a year, it is impossible to achieve a good geographic spread[58]. Third, some potential confounders/covariates are not available for this study population, such as family history. However, the lack of family history may not significantly affect the results, because the odds of T2DM was still significant after adjusting for other covariates. Finally, the study stratified the concentration of TCC and TCS according to whether it was higher than the detected value, possibly resulting in loss of data information. However, data stratification is more convenient for multi-factor analysis.

Conclusions

TCC, but not TCS exposure is associated with a significant risk of T2DM in adult women in NHANES data 2013–2014. There was a gender difference with respect to the relationship between TCC exposure and the risk of T2DM, a positive association that was only observed in women. The results of this study indicate that future studies are warranted to confirm these associations and to investigate the underlying mechanisms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Diabetes facts & figures. 2017; Available from: https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html.
2. Zheng Y, Ley SH, and Hu FB, Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol, 2018 14(2): p. 88–98. [PubMed: 29219149]
3. American Diabetes, A., Diagnosis and classification of diabetes mellitus. Diabetes Care, 2010 33 Suppl 1: p. S62–9. [PubMed: 20042775]

4. Wang X, et al. A cross-sectional study on the associations of insulin resistance with sex hormone, abnormal lipid metabolism in T2DM and IGT patients. Medicine (Baltimore), 2017 96(26): p. e7378. [PubMed: 28658166]
5. Harris MI, Impaired glucose tolerance in the U.S. population. Diabetes Care, 1989 12(7): p. 464–74. [PubMed: 2758951]
6. Pratley RE and Weyer C, Progression from IGT to type 2 diabetes mellitus: the central role of impaired early insulin secretion. Curr Diab Rep, 2002 2(3): p. 242–8. [PubMed: 12643180]
7. Chen L, Magliano DJ, and Zimmet PZ, The worldwide epidemiology of type 2 diabetes mellitus--present and future perspectives. Nat Rev Endocrinol, 2011 8(4): p. 228–36. [PubMed: 22064493]
8. Neel BA and Sargis RM, The paradox of progress: environmental disruption of metabolism and the diabetes epidemic. Diabetes, 2011 60(7): p. 1838–48. [PubMed: 21709279]
9. Bonini MG and Sargis RM, Environmental Toxicant Exposures and Type 2 Diabetes Mellitus: Two Interrelated Public Health Problems on the Rise. Curr Opin Toxicol, 2018 7: p. 52–59. [PubMed: 29392186]
10. Papalou O, et al. Endocrine Disrupting Chemicals: An Occult Mediator of Metabolic Disease. Front Endocrinol (Lausanne), 2019 10: p. 112. [PubMed: 30881345]
11. Ruiz D, et al. Disparities in Environmental Exposures to Endocrine-Disrupting Chemicals and Diabetes Risk in Vulnerable Populations. Diabetes Care, 2018 41(1): p. 193–205. [PubMed: 29142003]
12. Halden RU and Paull DH, Co-occurrence of triclocarban and triclosan in U.S. water resources. Environ Sci Technol, 2005 39(6): p. 1420–6. [PubMed: 15819193]
13. Dann AB and Hontela A, Triclosan: environmental exposure, toxicity and mechanisms of action. J Appl Toxicol, 2011 31(4): p. 285–311. [PubMed: 21462230]
14. Ribado JV, et al. Household triclosan and triclocarban effects on the infant and maternal microbiome. EMBO Mol Med, 2017 9(12): p. 1732–1741. [PubMed: 29030459]
15. Poole AC, et al. Crossover Control Study of the Effect of Personal Care Products Containing Triclosan on the Microbiome. mSphere, 2016 1(3).
16. Weatherly LM and Gosse JA, Triclosan exposure, transformation, and human health effects. J Toxicol Environ Health B Crit Rev, 2017 20(8): p. 447–469. [PubMed: 29182464]
17. Sapkota A, Heidler J, and Halden RU, Detection of triclocarban and two co-contaminating chlorocarbanilides in US aquatic environments using isotope dilution liquid chromatography tandem mass spectrometry. Environ Res, 2007 103(1): p. 21–9. [PubMed: 16678153]
18. Chen J, et al. Triclocarban enhances testosterone action: a new type of endocrine disruptor? Endocrinology, 2008 149(3): p. 1173–9. [PubMed: 18048496]
19. Kanama KM, et al. Assessment of Pharmaceuticals, Personal Care Products, and Hormones in Wastewater Treatment Plants Receiving Inflows from Health Facilities in North West Province, South Africa. J Toxicol, 2018 2018: p. 3751930. [PubMed: 30510574]
20. Chen J, et al. Nationwide reconnaissance of five parabens, triclosan, triclocarban and its transformation products in sewage sludge from China. J Hazard Mater, 2019 365: p. 502–510. [PubMed: 30466048]
21. Halden RU, et al. The Florence Statement on Triclosan and Triclocarban. Environ Health Perspect, 2017 125(6): p. 064501. [PubMed: 28632490]
22. Rochester JR, et al. Potential Developmental and Reproductive Impacts of Triclocarban: A Scoping Review. J Toxicol, 2017 2017: p. 9679738. [PubMed: 29333157]
23. Ley C, Pischel L, and Parsonnet J, Triclosan and triclocarban exposure and thyroid function during pregnancy-A randomized intervention. Reprod Toxicol, 2017 74: p. 143–149. [PubMed: 28939492]
24. Geens T, et al. Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals. Environ Int, 2015 76: p. 98–105. [PubMed: 25575039]
25. Ouyang F, et al. Maternal urinary triclosan level, gestational diabetes mellitus and birth weight in Chinese women. Sci Total Environ, 2018 626: p. 451–457. [PubMed: 29353787]

26. Yang S, et al. Low Thyroid Hormone in Early Pregnancy Is Associated With an Increased Risk of Gestational Diabetes Mellitus. J Clin Endocrinol Metab, 2016 101(11): p. 4237–4243. [PubMed: 27583471]
27. Hinther A, et al. Effects of triclocarban, triclosan, and methyl triclosan on thyroid hormone action and stress in frog and mammalian culture systems. Environ Sci Technol, 2011 45(12): p. 5395–402. [PubMed: 21574574]
28. Fisher BG, et al. Serum Phthalate and Triclosan Levels Have Opposing Associations With Risk Factors for Gestational Diabetes Mellitus. Front Endocrinol (Lausanne), 2018 9: p. 99. [PubMed: 29593656]
29. Introduction to NHANES. 2013-2014; Available from: https://www.cdc.gov/nchs/nhanes/about_nhanes.htm.
30. NHANES—About the National Health and Nutrition Examination Survey. [(accessed on 28 March 2018)]. Available from: https://www.cdc.gov/nchs/nhanes/about_nhanes.htm.
31. Calafat AM, et al. Urinary concentrations of triclosan in the U.S. population: 2003-2004. Environ Health Perspect, 2008 116(3): p. 303–7. [PubMed: 18335095]
32. Zhou X, Ye X, and Calafat AM, Automated on-line column-switching HPLC-MS/MS method for the quantification of triclocarban and its oxidative metabolites in human urine and serum. J Chromatogr B Analyt Technol Biomed Life Sci, 2012 881-882: p. 27–33.
33. Ye X, et al. Automated on-line column-switching HPLC-MS/MS method with peak focusing for the determination of nine environmental phenols in urine. Anal Chem, 2005 77(16): p. 5407–13. [PubMed: 16097788]
34. Mi SJ, et al. Associations of sleep patterns with metabolic syndrome indices, body composition, and energy intake in children and adolescents. Pediatr Obes, 2019: p. e12507. [PubMed: 30702801]
35. World Health Organization: Diabetes Programme. Available from: https://www.who.int/diabetes/action_online/basics/en/index2.html.
36. Smoking - Recent Tobacco Use. 2013-2014; Available from: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SMQRTU_H.htm.
37. Collaboration, N.C.D.R.F., Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. Lancet, 2016 387(10027): p. 1513–1530. [PubMed: 27061677]
38. Heffernan AL, et al. Use of pooled samples to assess human exposure to parabens, benzophenone-3 and triclosan in Queensland, Australia. Environ Int, 2015 85: p. 77–83. [PubMed: 26368661]
39. Liao C and Kannan K, A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. Arch Environ Contam Toxicol, 2014 67(1): p. 50–9. [PubMed: 24639116]
40. Iyer AP, et al. Urinary levels of triclosan and triclocarban in several Asian countries, Greece and the USA: Association with oxidative stress. Environ Res, 2018 160: p. 91–96. [PubMed: 28964967]
41. Li W, et al. Metabonomics reveals that triclocarban affects liver metabolism by affecting glucose metabolism, beta-oxidation of fatty acids, and the TCA cycle in male mice. Toxicol Lett, 2018 299: p. 76–85. [PubMed: 30261223]
42. Sohail MU, et al. Role of the Gastrointestinal Tract Microbiome in the Pathophysiology of Diabetes Mellitus. J Diabetes Res, 2017 2017: p. 9631435. [PubMed: 29082264]
43. Halden RU, Lessons Learned from Probing for Impacts of Triclosan and Triclocarban on Human Microbiomes. mSphere, 2016 1(3).
44. Hu J, et al. Effect of postnatal low-dose exposure to environmental chemicals on the gut microbiome in a rodent model. Microbiome, 2016 4(1): p. 26. [PubMed: 27301250]
45. Kennedy RC, et al. Temporal Development of Gut Microbiota in Triclocarban Exposed Pregnant and Neonatal Rats. Sci Rep, 2016 6: p. 33430. [PubMed: 27646684]
46. Uppal V, et al. Thyroid disorders in patients of type 2 diabetes mellitus. Indian J Clin Biochem, 2013 28(4): p. 336–41. [PubMed: 24426234]

47. Feng Y, et al. Endocrine Disrupting Effects of Triclosan on the Placenta in Pregnant Rats. PLoS One, 2016 11(5): p. e0154758. [PubMed: 27149376]

48. Li H, et al. Triclocarban and Triclosan Inhibit Human Aromatase via Different Mechanisms. Biomed Res Int, 2017 2017: p. 8284097. [PubMed: 29376079]

49. Enright HA, et al. Maternal exposure to an environmentally relevant dose of triclocarban results in perinatal exposure and potential alterations in offspring development in the mouse model. PLoS One, 2017 12(8): p. e0181996. [PubMed: 28792966]

50. Lankester J, et al. Urinary triclosan is associated with elevated body mass index in NHANES. PLoS One, 2013 8(11): p. e80057. [PubMed: 24278238]

51. Li S, et al. Urinary triclosan concentrations are inversely associated with body mass index and waist circumference in the US general population: Experience in NHANES 2003-2010. Int J Hyg Environ Health, 2015 218(4): p. 401–6. [PubMed: 25823951]

52. Trasande L, Attina TM, and Blustein J, Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. JAMA, 2012 308(11): p. 1113–21. [PubMed: 22990270]

53. Huang H, et al. The in vitro estrogenic activities of triclosan and triclocarban. J Appl Toxicol, 2014 34(9): p. 1060–7. [PubMed: 24740835]

54. Witorsch RJ and Thomas JA, Personal care products and endocrine disruption: A critical review of the literature. Crit Rev Toxicol, 2010 40 Suppl 3: p. 1–30.

55. Fernandez R, et al. Molecular basis of Gender Dysphoria: androgen and estrogen receptor interaction. Psychoneuroendocrinology, 2018 98: p. 161–167. [PubMed: 30165284]

56. Ahn KC, et al. In vitro biologic activities of the antimicrobials triclocarban, its analogs, and triclosan in bioassay screens: receptor-based bioassay screens. Environ Health Perspect, 2008 116(9): p. 1203–10. [PubMed: 18795164]

57. Ye X, et al. Urinary Concentrations of the Antibacterial Agent Triclocarban in United States Residents: 2013-2014 National Health and Nutrition Examination Survey. Environ Sci Technol, 2016 50(24): p. 13548–13554. [PubMed: 27993070]

58. The National Health and Nutritional Examination Survey (NHANES). Available from: http://russlopez.com/blog/2012/04/30/the-national-health-and-nutritional-examination-survey-nhanes/

Highlights:

- Women are more likely to be exposed to triclocarban and triclosan than men.
- Triclocarban exposure is positively associated with the risk of T2DM in women but not men in the USA.
- Triclosan exposure is not associated with the risk of T2DM in the USA.

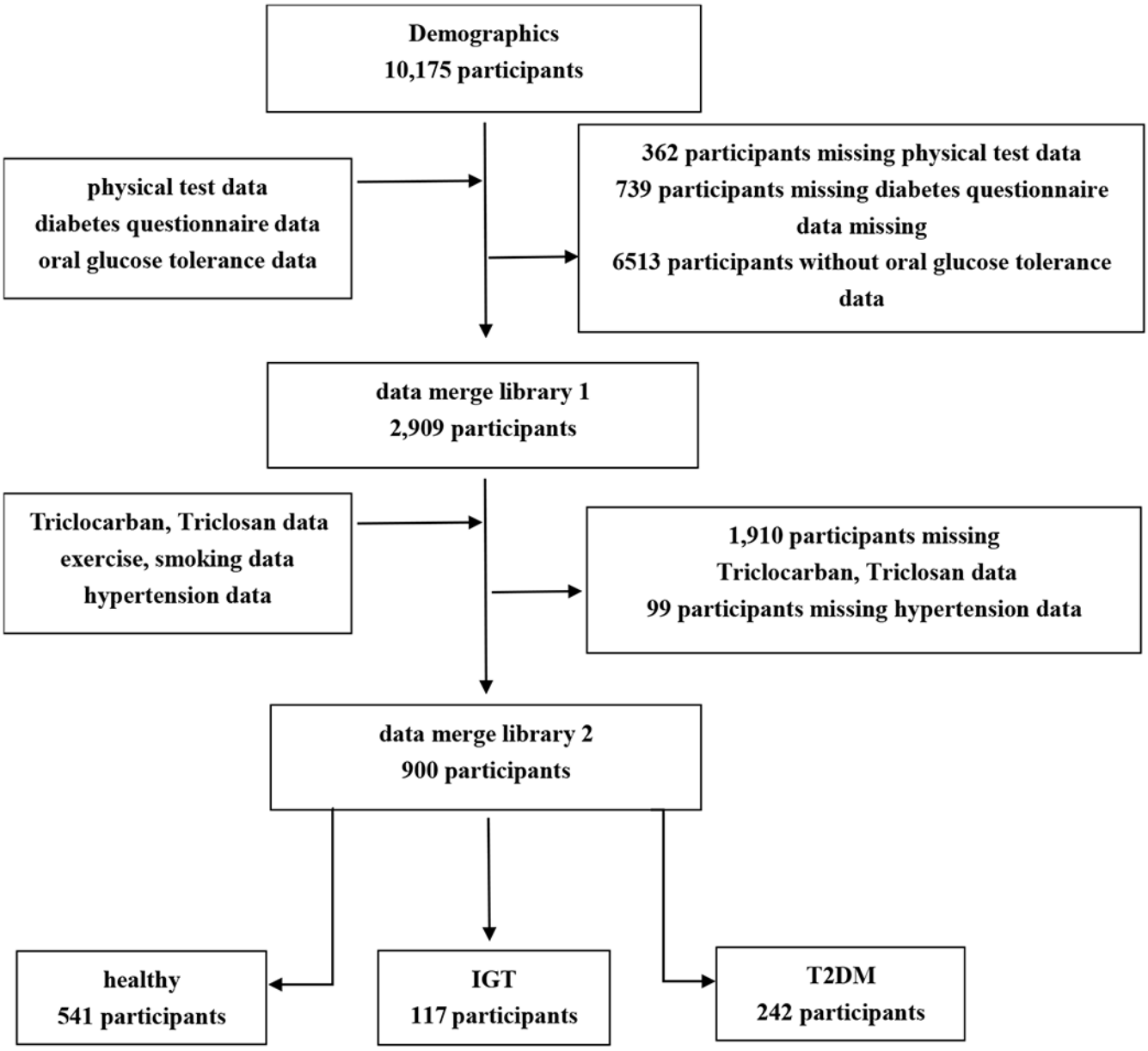

Figure 1.
Flowchart for inclusion of study participants.

Table 1.

Demographic and socio-behavioral characteristics and DM disease status of the study population (N=900)

Variables	Healthy (N=541)	IGT (N=117)	T2DM (N=242)	P-value
Age(years)	40 (26,57)	58 (43, 69)	56 (43, 70)	**<0.001** **
Age groups				
<45	323(59.70)	31(26.50)	66(27.27)	**<0.001** **
45-65	150(27.73)	45(38.46)	96(39.67)	
>65	68(12.57)	41(35.04)	80(33.06)	
Sex				
Men	264(48.80)	53(45.30)	112(46.28)	0.695
Women	277(51.20)	64(54.70)	130(53.72)	
Race				
Mexican American	65(12.01)	17(14.53)	30(12.40)	0.448
Other Hispanic	579(10.54)	11(9.40)	17(7.02)	
Non-Hispanic White	238(43.99)	47(40.17)	94(38.84)	
Non-Hispanic Black	98(18.11)	23(19.66)	60(24.79)	
Other Race	83(15.34)	19(16.24)	41(16.94)	
BMI (kg/m^2)	27.70±6.69	29.98±8.07	30.17±7.81	**<0.001** **
Education				
Less than 9th grade	41(7.96)	13(11.11)	20(8.62)	0.406
9-11th grade	93(18.06)	20(17.09)	51(21.98)	
High school graduate	102(19.81)	27(23.08)	54(23.28)	
Some college/AA degree	155(30.10)	30(25.64)	50(21.55)	
College graduate	124(24.08)	27(23.08)	57(24.57)	
Ratio of Family Income to Poverty				
Under standard level	412(76.16)	89(76.07)	180(74.38)	0.862
Above standard level	129(23.84)	28(23.93)	62(25.62)	
Smoking				
Yes	125(24.13)	17(14.91)	40(20.20)	0.078
No	393(75.87)	97(85.09)	158(79.80)	
Hypertension				
Yes	142(26.25)	61(52.14)	117(48.55)	**<0.001** **
No	399(73.75)	56(47.86)	124(51.45)	
Exercise				
<150min	124(22.92)	22(18.80)	39(16.12)	0.082
>=150min	417(77.08)	95(81.20)	203(83.88)	

Note:

*, P< 0.05;

**, P <0.01.

Table 2.

Association between TCs exposure and the risk of IGT and T2DM among 429 men and 471 women in NHANES (2013-2014)

Model	HEALTHY		IGT					T2DM				
	N	Prev. (%)	N	Prev. (%)	OR	P-value	95%CI	N	Prev. (%)	OR	P-value	95%CI
Men												
model 1												
Triclocarban	103	39.16	22	41.51	1.10	0.750	0.61-2.01	52	48.60	1.47	0.096	0.93-2.31
Triclosan	195	74.14	43	81.13	1.50	0.284	0.71-3.15	80	74.77	1.03	0.901	0.62-1.73
model 2												
Triclocarban	103	39.16	22	41.51	0.94	0.847	0.49-1.80	52	48.60	1.26	0.419	0.72-2.21
Triclosan	195	74.14	43	81.13	2.12	0.067	0.95-4.72	80	74.77	1.38	0.310	0.74-2.59
model 3												
Triclocarban	103	39.16	22	41.51	0.94	0.862	0.49-1.81	52	48.60	1.29	0.375	0.73-2.27
Triclosan	195	74.14	43	81.13	2.12	0.066	0.95-4.76	80	74.77	1.36	0.339	0.72-2.57
Women												
model 1												
Triclocarban	99	35.74	30	46.88	1.59	0.099	0.92-2.75	65	51.18	**1.88**	**0.004***	**1.23-2.89**
Triclosan	211	76.17	44	68.75	0.69	0.219	0.38-1.25	94	74.02	0.89	0.640	0.55-1.44
model 2												
Triclocarban	99	35.74	30	46.88	1.47	0.214	0.80-2.70	65	51.18	**1.80**	**0.030***	**1.06-3.07**
Triclosan	211	76.17	44	68.75	0.87	0.671	0.48-1.68	94	74.02	1.11	0.721	0.62-2.01
model 3												
Triclocarban	99	35.74	30	46.88	1.45	0.234	0.79-2.67	65	51.18	**1.79**	**0.032***	**1.05-2.05**
Triclosan	211	76.17	44	68.75	0.86	0.650	0.44-1.67	94	74.02	1.09	0.780	0.60-1.97

Note:

*, P <0.05;

**, P< 0.01.

Model 1: unadjusted model;

Model 2: adjusted for age, race, BMI, education, ratio of family income to poverty, smoking;

Model 3: adjusted for age, race, BMI, education, ratio of family income to poverty, smoking, exercise and hypertension.