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## Healthcare Worker Exposures to the Antibacterial Agent Triclosan

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### Abstract

**Objective**—We sought to quantify absorption of triclosan, a potential endocrine disruptor, in healthcare workers with occupational exposure to soap containing this chemical.

**Methods**—A cross-sectional convenience sample of two groups of 38 healthcare workers at separate inpatient medical centers: Hospital One uses 0.3% triclosan soap in all patient care areas; Hospital Two does not use triclosan-containing products. Additional exposure to triclosan-containing personal care products was assessed through a structured questionnaire. Urine triclosan was quantified and the occupational contribution estimated through regression modeling.

**Results**—Occupational exposure accounted for an incremental triclosan burden of 206 ng/mL ( $p=0.02$ ), while triclosan-containing toothpaste use was associated with 146 ng/mL higher levels ( $p<0.001$ ).

**Conclusions**—Use of triclosan-containing antibacterial soaps in healthcare settings represents a substantial and potentially biologically relevant source occupational triclosan exposure.

### Introduction

Triclosan is a synthetic, chemical, antibacterial agent found in many commercially available products labeled “antibacterial,” including personal care products such as soaps, toothpaste, cosmetics, and acne creams; it is also present in other consumer products.<sup>1,2</sup> The majority of liquid soaps sold in the United States contain triclosan.<sup>3</sup> Occupational sources represent a potentially important exposure scenario because some, albeit not all, healthcare institutions commonly use triclosan-containing antibacterial soaps and because frequent handwashing

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among healthcare workers in such environments (range 0.7-30 times per hour)<sup>4</sup> is likely to facilitate triclosan exposure.

A growing body of scientific research calls into question the safety of triclosan. For example, *in vivo* and *in vitro* studies have shown endocrine effects such as thyroid hormone disruption<sup>5-7</sup> and perturbation of sex hormone homeostasis.<sup>8-14</sup> In addition, triclosan exposure may impair muscle function in animal models<sup>15</sup> and also has been associated with hay fever or allergies in humans.<sup>16-17</sup> Despite these potential effects, human toxicity from triclosan has not been established or excluded and, thus, this chemical has been tentatively categorized as having “insufficient evidence to classify as safe or effective” (Category IIISE) by the U.S. Food and Drug Administration (FDA).<sup>18</sup> Addressing this knowledge gap, the U.S. FDA recently proposed to include triclosan among a group of antibacterial products, requiring additional safety data and demonstration of clinical benefit over the use of plain soap.<sup>18</sup>

Triclosan is absorbed following trans-dermal or oral exposure. Quantification of triclosan in urine represents a key biomonitoring instrument for such absorption because triclosan (as free and conjugated metabolites) is excreted primarily in urine, with a half-life of about 11 hours in humans.<sup>19, 20</sup> In 2003-04, a U.S. population-based sample (n=2517) in the National Health and Nutrition Examination Survey (NHANES) showed that 75% had detectable urine triclosan levels.<sup>21</sup> Limited (n=91) but more recent biomonitoring data from California found that triclosan was detectable in 95% of the samples tested.<sup>22</sup>

Given the potential adverse human health effects of triclosan, better characterization of exposure risks is warranted. We hypothesized that biomonitoring would establish that the burden of triclosan in healthcare workers is indeed higher due to occupational exposure and that, among such persons, personal care product would superimpose even greater exposure. To test this, we compared urine triclosan levels among physicians and nurses at two hospitals in close geographic proximity: one that uses triclosan-containing hand washing soap and one that does not.

## Methods

### Design and Subjects

We carried out a cross-sectional study in a convenience sample of physicians and nurses at two hospitals. Hospital One uses a 0.3% triclosan-based soap in all patient care areas and restrooms (staff and public). Hospital Two uses plain soap and water, having previously phased-out triclosan-containing soaps. Both hospital sites also have a water-free alcohol based hand rub for hand hygiene (a product that does not contain triclosan). To be eligible for study inclusion, participants were required to be a physician (MD or DO) or nurse (RN) employed on a full-time basis at their hospital site (defined as regularly working 36 hours per week), and to have worked at least 8 of the 48 hours prior to study recruitment. Potential subjects also were required to complete a brief questionnaire (detailed below). Those otherwise eligible were excluded if they failed to provide a urine sample for triclosan analysis. Four otherwise eligible participants who did not provide a satisfactory urine sample were thus excluded.

Institutional Review Board approval was obtained from each of the two hospital study sites. Recruitment ran from March through August 2012. Questionnaire completion and spot urine sample collection occurred immediately following a brief presentation about the project at various staff meetings onsite (these included educational events as well as standard staff meetings). Following each presentation, healthcare workers were invited to participate. Altogether 15 separate recruitment presentations were made at times ranging from 6AM to 7PM.

### Exposure Questionnaire

We developed a brief survey questionnaire using an iterative process of review within the study team. Items on the timing of recent exposure took into account a triclosan half-life of approximately 11-hours; work exposure assessed the anticipated primary factor driving hand washing (patients directly cared for); and exposure to triclosan-containing personal product included toothpaste given the efficiency of buccal absorption<sup>23</sup> (specifically eliciting use of the only brand of triclosan-containing toothpaste on the US market, Colgate Total®). In addition, since four out of five liquid soaps contain triclosan<sup>3</sup>, home antibacterial soap use was also included, along with acne creams given their triclosan content.<sup>24</sup> The survey, although intentionally brief, did include items that also estimated potential exposure to phthalates to inform a future research project. The survey instrument exclusive of the phthalate items is available as an online supplement

### Laboratory Methods

The spot urine sample was collected in phthalate- and triclosan-free urine containers. Immediately following collection, urine samples (room temperature) were transported to the laboratory within one hour. Analysis of free and total triclosan in urine was carried out by liquid chromatography-tandem mass spectrometry. The limit of detection (LOD) for both analytes is 0.05 µg/L. Quantitation of each analyte was done by isotope dilution method using a 10-point calibration curve. Each analyte has a limit of quantitation (LOQ) of 0.1 µg/L. For details of the laboratory methods see the online supplement.

### Data Analysis

The mean and standard deviation for age and urinary creatinine were calculated for each hospital site stratum and for the entire cohort. We tested differences using the t-test for the age, the Wilcoxon test for the number of hours worked in the 48-hr period prior to participation, and the creatinine. Differences in categorical variables were tested using the chi-square test. Descriptive statistics for triclosan levels (free, conjugated and total) were calculated for each hospital site and for the entire study sample for all participants and for participants stratified by TCT use (since TCT was a major potential source of triclosan exposure, independent of hospital exposure). The overall differences in triclosan levels by hospital site and by TCT use analyzed together were tested by ANOVA; pairwise comparisons used the Wilcoxon rank sum for median values and the t-test for mean values. To facilitate comparison to national data (NHANES)<sup>21</sup>, the geometric mean urinary triclosan levels adjusted for creatinine were calculated for the exposed and unexposed groups.

We performed a multiple linear regression analysis among all study participants to analyze the combined effects of TCT use and hospital exposure, adjusting for the covariates of age and urinary creatinine. To further assess the role of other cofactors and to take into account the differing mix by site of profession and sex, we re-estimated the linear regression models stratified by site and further including in addition to the variables in the previous models profession, sex (male), number of workplace hand washings in past 24 hours, time worked over the past 48 hours, and personal use of antibacterial soaps.

## Results

We studied 76 participants, 38 from each hospital site (Table 1). The mean age was  $35\pm 9.6$  years, the majority was female, and the study population was divided fairly equally among physicians and nurses. There were, however, significant demographic differences between those studied at the two hospitals. Participants from Hospital One (which used triclosan-containing disinfectant soap) were 7.5 years older on average ( $p<0.001$ ) and included fewer physicians (13% vs. 84%,  $p<0.001$ ). Although the Hospital One group also had a higher proportion of females, this difference was not statistically significant. The nurses compared to physicians were less likely to be male 4 (10.3%) of 39 compared to 15 (40.5%) of 37 ( $p<0.01$ ).

Among the exposure cofactors of interest (Table 1), there were no statistically significant differences by hospital site, although the use of TCT was more prevalent among participants at Hospital Two. The median number of hours worked at Hospital One in the previous 48 hours (median=13) indicated sufficient time for occupational exposure at that site, as did the frequency of hand washing at work (median=8, range 0-40). Urinary creatinine, a marker of specimen concentration that might confound triclosan quantification, was similar in the two groups.

Table 2 shows observed values for urinary triclosan by hospital site for free, conjugated, and total triclosan, respectively. Because the use of TCT was a potent potential source of triclosan exposure independent of hospital site, the data were further stratified by that factor. Overall, values of free triclosan were more than an order of magnitude lower than conjugated triclosan among both TCT and non-TCT users. Because of the dominance of conjugated relative to free values, total triclosan levels were quite similar to the conjugated levels. Of the six highest observed total urinary triclosan values (range 416 to 505 ng/mL), three were from Hospital One (one of these had co-exposure to TCT) and three were from Hospital Two (all TCT users) (data not in Table).

Among non-TCT users, the urinary concentrations of total (non-conjugated and conjugated combined) triclosan were significantly higher at Hospital One compared to Hospital Two (median values 68.5 vs. 8.6 ng/mL;  $p=0.02$ ). In contrast, among TCT users the concentrations were higher but quite similar by hospital (255 vs. 258 ng/mL;  $p>0.8$ ). Among the two groups of TCT and non-TCT users combined, Hospital One manifested higher levels than Hospital Two, but this difference was not statistically significant. Free triclosan levels did not differ by hospital for either TCT stratum. All comparisons in Table 2 were tested non-parametrically; parametric testing, however, did not yield findings that were

substantively different (data not shown). The geometric mean total triclosan level was 92.92 ng/mL for Hospital One and 36.65 ng/mL for Hospital Two. The overall mean free triclosan/urinary creatinine ratio (microgram per mg) was  $0.04 \pm 0.08$  (median 0.011); the mean conjugated value was  $2.58 \pm 5.0$  (median 0.85).

In order to analyze the combined effects of TCT use and potential exposure to triclosan through hand soap in Hospital One, we tested models including both of these two risk factors, also including as covariates age and urinary creatinine. The parameter estimates for TCT use and site of hospital employment are shown in Table 3. Taking into account employment site, TCT use was associated with 142 and 146 ng/mL urine higher values for conjugated and total triclosan, respectively ( $p < 0.001$ ). Working in Hospital One was associated with a urine conjugated triclosan level of 205 ng/mL ( $p = 0.02$ ) and a very similar estimate for total triclosan (206;  $p = 0.02$ ). Use of TCT was associated with free triclosan ( $p = 0.051$ ); hospital employment site was not statistically associated with free triclosan in the multivariate analysis. Because of the inter-correlations among hospital site, profession (nurse vs. physician) and sex, we sought to examine further TCT use and occupational exposure as predictors of urinary triclosan stratified by hospital and taking into account other cofactors that might mediate exposure or modify the delivered dose (Table 4). There was no consistent pattern of association with the additional factors tested. The point estimate for the association of TCT with urinary free and conjugated triclosan was lower in Hospital One and higher in Hospital Two (and statistically significant for conjugated triclosan in the latter). Being a nurse in Hospital One was notable for an association with increased conjugated triclosan ( $p = 0.09$ ), while male sex in Hospital One was associated with a higher free triclosan ( $p = 0.052$ ) level. Inclusion of all of the additional covariates in these analyses only marginally increased the explanatory power of the model as compared to the restricted model limited to TCT use, hospital site, age and creatinine (as shown in Table 3): for free triclosan, model  $R^2 = 0.31$  (vs. 0.24) and conjugated triclosan  $R^2 = 0.62$  (vs. 0.60). Moreover, the estimated intercepts in these models did not differ statistically from zero, that is, we could not exclude as a chance observation a detectable level of triclosan that would be present without any of the modeled risk factors.

## Discussion

To our knowledge this is the first peer-reviewed biomonitoring study to measure triclosan levels among healthcare workers. The study underscores hospital exposure and use of TCT as important sources of exposure to triclosan. Among non-TCT users, there were significantly higher conjugated and total triclosan levels in those who worked in the hospital that used triclosan-containing soap in all patient care areas. In the hospital that did not use triclosan, TCT was the dominant contributor to the observed levels and, in the stratum of TCT users, obscured the differences between the two hospitals. Multivariate analysis, taking into account both TCT use and hospital, however, made it clear that both factors were independent predictors of the triclosan burden and that the occupational factor, overall, was associated with the largest estimated effect.

It is not surprising that TCT use correlated with higher urinary triclosan levels. Other studies have showed that buccal absorption of triclosan is high. For example, Allymr and

colleagues<sup>23</sup> reported that after brushing with 0.3% TCT for 14 days, subjects had triclosan blood levels that were increased by several orders of magnitude (from 0.009-0.81ng/g pre-exposure to 26-296ng/g after exposure; p=0.003). Lin et al measured blood levels of triclosan 4 hours after rinsing with 0.03% triclosan mouthwash and found that 7.5% of the total administered dose was absorbed.<sup>25</sup>

Of interest, the free triclosan levels did not differ by hospital for any stratum. This may be due to a conjugation that occurs locally by skin cells, consistent with findings in a rat model.<sup>26</sup> While conjugation also occurs in the liver, it is possible that dermal absorption does not contribute significantly to levels of free triclosan, thus explaining the pattern we observed.

As stated above, the geometric mean total urine triclosan was 92.92 ng/mL for the exposed and 36.65 ng/mL for the unexposed hospital. By comparison, a representative sample of the general U.S. population for adults (20 yrs. and older) in NHANES for the years 2009-10 observed a geometric mean total urine triclosan level of 15.5 ng/mL (95% CI 12.9-18.5).<sup>27</sup> Based on those data, Hospital One falls between the 75<sup>th</sup> and 90<sup>th</sup> percentile values of the NHANES data (61.8 and 262 ng/mL respectively), whereas Hospital Two falls between the 50<sup>th</sup> and 75<sup>th</sup> percentile (11.1 and 61.8 ng/mL respectively). Calafat et al (2008) found that in NHANES data, higher levels were seen during the third decade of life and among people with the highest household income, and that levels did not vary by ethnicity/race or sex.<sup>21</sup> Thus, the higher overall geometric mean levels we observed may be explained, at least partially, by higher socioeconomic status and older age.

Our study has several important limitations. A major limitation of our study design is its reliance on a cross-sectional, convenience sample of participants rather than employing an alternative design, such as a stratified random sample of the entire working populations of the two hospitals studied or, even more ideally, a cross-over intervention trial in which triclosan-containing soap was allowed, removed, and then re-added to the work environment. It is possible, for example, that those with the greatest triclosan exposure at work would be more concerned about their triclosan exposure levels and thus be more likely to participate, although this might also occur with randomly selected potential participants. Nonetheless, although this phenomenon might lead to an overestimate of exposure levels, it would not be likely to account for all of the hospital site-related effect that was observed. In addition, the sample size is small, especially in regard to the stratified analyses that might analyze possible interactions among risk factors. Because no pre-existing validated questionnaire assessing exposure to triclosan among hospital workers was available, we developed *de novo* the survey instrument used in this investigation. Moreover, the survey was constrained by brevity given the demanding work schedules of potential study participants. The relationship between the relevant exposure items and measured triclosan, however, supports the content validity of the survey. Our study relied on participant's recall of specific types of products used, which may have led to exposure misclassification. At the triclosan-exposed hospital, given two principal options for hand hygiene (water-free hand rub and the triclosan-containing soap), there were varying levels of exposure to triclosan. This was reflected in the wide range of reported hand washings with triclosan-containing soap while working in Hospital One. In addition, due to feasibility constraints we did not



measure serum triclosan levels, which would have required a phlebotomy protocol (and would also have been likely to hinder participation).

There are hundreds of triclosan-containing products the use of which, for the sake of brevity, were not included in the questionnaire and participants may have had sources of triclosan exposure that were not accounted for. This was not likely to have made a large contribution, however, given that the intercept of the model estimates was not statistically different than zero, although larger sample size would have provided greater study power in that regard. We were also limited by our inability to set a fixed recruitment schedule that might have reduced the variability in time from last exposure until urine sampling. For example, because the half-life of triclosan is less than 12 hours, those with work exposure on a previous shift but not yet exposed on the day of measurement would tend to have lower levels of triclosan detected than might have been measured sooner post-shift; similarly, exposure to TCT that occurred in the morning before work with sampling in the late afternoon might have had lower levels than had that person been sampled earlier. Nonetheless, although this effect to the extent present would have led to a lower estimate of effect, it should not have acted in a systematic way to account for the associations that we did observe.

Despite these limitations, our analysis has identified a role for occupational exposure in our participants' triclosan burden. Because biostatistical modeling based on a relatively small convenience sample is constrained by wide confidence intervals, however, further bio-monitoring studies with a larger sample size of randomly selected individuals would be necessary to confirm these results. This is all the more relevant because the effects of long-term, low level human triclosan exposure are unknown, but *in vivo* and *in vitro* experimental data have raised serious questions regarding potential adverse endocrine and other effects. Moreover, at least one such analysis focusing on skeletal and cardiac muscle impairment in mice studied triclosan concentrations in a range that has been reported in humans.<sup>15</sup> These endocrine disrupting and myotoxic effects seen have yet to be evaluated in human studies, and therefore health effects in humans at current exposure levels remain unknown. Large scale human studies at current exposure levels in vulnerable subpopulations such as the fetus or developing child have not been done, and are unlikely to be performed given feasibility constraints. Of note as well, beyond direct toxicity there are also human and wider environmental concerns associated with triclosan. For example, there is evidence to suggest that the use of triclosan may contribute to antibiotic resistance among selected pathogenic microbes.<sup>28</sup> Further, triclosan is biopersistent in the environment. The widespread, routine use of triclosan is called further into question in light of lack of proven antimicrobial efficacy for this chemical. A review of both microbial counts and infectious diseases prevention found that, that at typical concentrations, triclosan-containing soaps have no more efficacy than ordinary soap and water.<sup>29</sup>

Until the clinical benefit weighted against any potential human adverse health and wider negative environmental effects of triclosan have been delineated more fully, it may be best to take a precautionary approach as elucidated by Kriebel et al: “when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically”.<sup>30</sup>



## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Clinical Significance**

Triclosan is an antibacterial added to many products, including disinfectant soaps used in many health care facilities. Triclosan is a potential human endocrine disruptor with possible adverse health effects and wide population exposure. This study quantifies the contribution of occupational exposure among health care workers to the human triclosan burden.

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**Table 1**  
**Characteristics of Participants by Hospital of Employment among 76 Physicians and Nurses Studied**

Subject Characteristics	All (n=76)	Hospital One (n=38)	Hospital Two (n=38)	P value
Demographics				
Age in years, mean±SD	35.1±9.6	38.8 ± 11.4	31.3 ± 6.2	<0.001
Female Sex, n (%)	57 (75%)	31 (82%)	26 (68%)	0.15
Profession, n (%)				<0.001
Physician	37 (49%)	5 (13%)	32 (84%)	
Nurse	39 (51%)	33 (87%)	6 (16%)	
Exposure Co-factors				
Hours worked in last 48 hours, median (IQR)	16 (11)	13 (12)	19 (9.8)	0.19
Work hand washing in last 24 hours, median (IQR)	8 (8)	9 (14)	8 (7)	0.19
Use of TCT, n (%)	29 (39%)	11 (31%)	18 (47%)	0.15
Use of anti-bacterial soap outside of work, n (%)	51 (69%)	25 (68%)	26 (70%)	0.69
Urinary Cr, median (IQR)	74.0 (92.5)	61.8 (85.3)	85.0 (108.1)	0.23

Hospital One uses triclosan-containing soaps, Hospital Two does not (see Methods)

IQR= Interquartile Range; TCT= Triclosan-containing toothpaste

P value for comparison between hospital sites by chi square, t-test (age), or Wilcoxon (hours, creatinine)

**Table 2**  
**Urine Triclosan Concentration by Site of Hospital Employment Stratified by Triclosan-Containing Toothpaste Use**

Triclosan conjugation status by TCT use	All Participants		Hospital One		Hospital Two		P value
	Mean±SD ng/mL Urine	Median (IQR) ng/mL Urine	Mean±SD ng/mL Urine	Median (IQR) ng/mL Urine	Mean±SD ng/mL Urine	Median (IQR) ng/mL Urine	
TCT Users	N=29		N=11		N=18		
Free TRI	6.3±10.4	2.4 (6.7)	4.5±4.7	2.5 (4.4)	7.4±12.8	2.3 (9.1)	0.57
Con TRI	228.7±149.8	247.4 (237.7)	241.2±130.2	243.2 (203.4)	221.0±163.8	253.9 (292.4)	0.88
Total TRI	235.0±153.6	255.5 (265.5)	245.7±131.0	255.5 (199.4)	228.4±169.2	257.8 (329.9)	0.82
Non- Users	N=47		N=27		N=20		
Free TRI	2.1±6.1	0.5 (0.8)	3.2±7.9	0.6 (2.0)	0.7±1.5	0.1 (0.6)	0.21
Con TRI	93.6±126.4	45.4 (95.1)	137.0±146.1	68.4 (174.2)	39.3±66.7	7.7 (44.4)	0.02
Total TRI	95.7±130.3	45.6 (123.9)	140.3±151.1	68.5 (176.8)	40.0±67.9	8.6 (67.9)	0.02
All	N=76		N=38		N=38		
Free TRI	3.7±8.2	0.85 (3.7)	3.6±7.1	0.96 (3.1)	3.9±9.4	0.64 (5.7)	0.87
Con TRI	143.4±149.8	77.8 (221.1)	168.9±147.8	94.0 (266.5)	125.4±151.9	46.5 (246.5)	0.41
Total TRI	147.1±154.1	78.4 (269.8)	172.5±151.6	94.5 (276.1)	129.3±156.8	46.7 (252.7)	0.48

TCT=Triclosan Containing Toothpaste; TRI=Triclosan; Con=Conjugated; IQR=Interquartile range

Overall ANOVAs for Free Triclosan, Conjugated Triclosan, and Total Triclosan by hospital and TCT use all p<0.05.

P values are for the Wilcoxon test of between hospital differences for Triclosan urine concentrations.

**Table 3**  
**Hospital Worksite and Triclosan-containing Toothpaste as Predictors of Urinary**  
**Triclosan in Multiple Linear Regression Analysis**

Model tested	Model R <sup>2</sup>	Beta coefficient ± SE ng/mL Urine	P value
Free TRI	0.242		
TCT use		3.82 ± 1.93	0.051
Employed in Hospital 1		0.77 ± 4.93	0.88
Conjugated TRI	0.595		
TCT use		142.25 ± 32.61	<0.001
Employed in Hospital 1		204.90 ± 83.45	0.017
Total TRI	0.596		
TCT use		146.07 ± 33.51	<0.001
Employed in Hospital 1		205.66 ± 88.77	0.019

TRI =Triclosan; TCT=Triclosan Containing Toothpaste

All models also include age and urinary creatinine.

Age was not statistically significant in any model; urinary creatinine p =0.01 for free TRI only (parameter estimates not shown).

**Table 4**  
**Multivariate Linear Regression: Urinary Triclosan Stratified by Hospital**

Hospital One (Using Triclosan-Containing Soap)			
Triclosan Dependent Variable in Model Tested	Independent Predictors	Beta coefficient $\pm$ SE ng/mL Urine	P value
Free TRI	Nurses	6.0 $\pm$ 4.2	0.16
	TCT	0.8 $\pm$ 3.0	0.80
	Male Sex	6.4 $\pm$ 4.2	0.05
	Hand Washing Frequency	-0.02 $\pm$ 0.12	0.88
Conjugated TRI	Nurses	165.9 $\pm$ 93.6	0.09
	TCT	103.0 $\pm$ 66.3	0.13
	Male Sex	77.2 $\pm$ 70.6	0.28
	Hand Washing Frequency	0.5 $\pm$ 2.7	0.86
Hospital Two (Triclosan-Containing Soap Free)			
Free TRI	Nurses	-4.6 $\pm$ 5.8	0.43
	TCT	6.4 $\pm$ 3.4	0.08
	Male Sex	1.6 $\pm$ 3.8	0.68
	Hand Washing Frequency	-0.05 $\pm$ 0.28	0.85
Conjugated TRI	Nurses	30.0 $\pm$ 80.1	0.71
	TCT	177.1 $\pm$ 47.9	0.001
	Male Sex	-3.6 $\pm$ 52.9	0.95
	Hand Washing Frequency	0.40 $\pm$ 3.9	0.92

TRI = Triclosan; TCT= Triclosan Containing Toothpaste

Models also include the additional variables of age, urinary creatinine, hours worked in the previous 48, and the use of antibacterial soap (all  $p > 0.10$  in all models tested).