

highly active against staphylococci, enterococci, pneumococci and streptococci. However, the appearance of some staphylococci and enterococci with decreased susceptibility to tigecycline must be an alarm for a future emergence of tigecycline-resistant Gram-positive bacteria in our country.<sup>6</sup>

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## Transparency declarations

None to declare.

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## Use of antibacterial consumer products containing quaternary ammonium compounds and drug resistance in the community

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Sir,

Quaternary ammonium compounds (QACs), such as benzalkonium chloride (BAC), are broad-spectrum antimicrobials widely used for decades to disinfect environmental surfaces in clinical and industrial settings. Reports examining the relationships between biocide use and bacterial resistance among isolates from the community setting are limited.<sup>1</sup> We assessed the effect of antibacterial product usage in the home environment on susceptibility to BAC to determine whether there is a correlation between BAC and triclosan MICs and antibiotic resistance.

Data were collected as part of a longitudinal double-blind, randomized clinical trial conducted in a Northern Manhattan neighbourhood.<sup>2</sup> Participant enrolment began in October 2000, with a 12 month follow-up period. At baseline, 238 households were enrolled, and 224 (94.1%) households completed the study. Households were randomly assigned to receive either antibacterial or non-antibacterial personal hygiene and household cleaning products. Households randomized to the antibacterial group received a liquid kitchen spray containing QACs (0.08% alkyl dimethyl benzyl ammonium chlorides and 0.02% alkyl benzyl ammonium chlorides), an ‘all-purpose’ surface cleaner containing QACs (2.7% alkyl benzyl ammonium chlorides) and an antimicrobial handwashing soap containing 0.2% triclosan. The non-antibacterial group received similar products lacking antimicrobial ingredients. Informed consent was obtained from each household, and The Institutional Review Board of Columbia University Medical Center approved the study.

At the beginning (baseline) and at the end of the follow-up period, a culture was obtained from a randomly selected hand of the primary caregiver in the household. The hand culture was taken before and after washing with the assigned liquid hand-washing product.

The sample collection and bacterial culture methods have been described in detail previously.<sup>3</sup> Antibiotic susceptibility was determined using MicroScan WalkAway 96 SI (Dade Behring, Deerfield, IL, USA) and classified using the recommendations from the CLSI. All Gram-negative bacteria were tested against gentamicin, imipenem and ciprofloxacin. Additional tested antibiotics that were only applicable to certain species included: amikacin and ticarcillin/clavulanate for *Acinetobacter baumannii* and *Acinetobacter lwoffii*, trimethoprim/sulfamethoxazole for *Enterobacter agglomerans* and *Enterobacter cloacae*, trimethoprim/sulfamethoxazole, piperacillin/tazobactam and ceftriaxone for *Klebsiella pneumoniae*, and piperacillin/tazobactam and ceftazidime for *Pseudomonas fluorescens/putida*. Antibiotic resistance was defined as resistance or intermediate resistance to at least one antimicrobial agent among all agents tested. Staphylococcal species were tested against oxacillin to ascertain methicillin resistance. The MICs for each isolate of BAC and triclosan were determined using a modified agar

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dilution method from 0.5 to 256 mg/L and 0.012 to 32 mg/L, respectively.<sup>2</sup> As there are no uniform definitions for ‘resistance’ to BAC and triclosan, the median MIC for the isolates of each species at the baseline data collection period was used as a breakpoint to dichotomize susceptibility as high or low for both biocides. ‘High’ susceptibility was defined as an MIC greater than the median value and ‘low’ susceptibility was defined as an MIC less than or equal to the median value for each species at baseline. Regression models with generalized estimating equations (GEEs) were used to assess whether high BAC MICs were associated with high triclosan MICs. Finally, GEEs were used to assess whether high BAC MICs were associated with antibiotic susceptibility of bacterial species. Statistical analyses were conducted using SAS Version 8.02 (Cary, NC, USA).

A total of 645 hand isolates were examined for their BAC and triclosan MICs: 264 at baseline and 381 at the end of the year. At baseline, there was no significant association for any species between high BAC and triclosan MICs (all  $P > 0.05$ ). However, after 1 year of assigned product use, there was a significant association between high BAC and triclosan MICs for *A. lwoffii* (OR = 6.57, 95% CI = 1.30–33.33) and for all species combined (OR = 2.18, 95% CI = 1.44–3.29) (Table 1). At the end of 1 year of assigned product usage, there was also a significant association between high BAC MICs and antibiotic resistance for all species combined (Table 1), but not for each species individually (all  $P > 0.05$ ). Among the Gram-negative

**Table 1.** Associations between susceptibility to BAC and triclosan and antibiotic resistance

	Odds of high triclosan MICs <sup>a</sup> among species with high BAC MICs <sup>b</sup>	
	OR (95% CI)	<i>P</i>
All species combined <sup>c</sup>		
baseline ( <i>n</i> = 264)	1.06 (0.61–1.85)	0.83
end of year ( <i>n</i> = 381)	2.18 (1.44–3.29)	<0.001
	Odds of antibiotic resistance among species with high BAC MICs <sup>b</sup>	
	OR (95% CI)	<i>P</i>
All species combined <sup>c</sup>		
baseline ( <i>n</i> = 227)	0.94 (0.46–1.92)	0.87
end of year ( <i>n</i> = 317)	2.45 (1.38–4.36)	<0.01
GNB species <sup>c</sup>		
baseline ( <i>n</i> = 145)	0.38 (0.13–1.09)	0.07
end of year ( <i>n</i> = 117)	3.71 (1.32–10.46)	0.01
Staphylococcal species <sup>c</sup>		
baseline ( <i>n</i> = 82)	3.41 (1.16–10.06)	0.03
end of year ( <i>n</i> = 200)	1.56 (0.74–3.30)	0.25

<sup>a</sup>High triclosan MICs refer to organisms with an MIC greater than the median of the triclosan MIC distribution.

<sup>b</sup>High BAC MICs refer to organisms with an MIC greater than the median of the BAC MIC distribution.

<sup>c</sup>Bacterial species included Gram-negative bacteria (GNB) (*A. baumannii*, *A. lwoffii*, *K. pneumoniae*, *E. agglomerans*, *E. cloacae* and *P. fluorescens/putida*) and staphylococcal species (*Staphylococcus warneri*, *Staphylococcus epidermidis*, *Staphylococcus capitis* and *S. aureus*).

bacterial isolates, the association was significant after 1 year (OR = 3.71, 95% CI = 1.32–10.46). There was a significant association between high BAC MICs and antibiotic resistance at baseline, but not at the end of the year among staphylococcal isolates (Table 1).

This is the first randomized intervention study to assess the relationships between antibacterial product usage, BAC MICs, triclosan MICs and antibiotic susceptibility among isolates obtained from the household setting. We found that after 1 year of assigned product usage, bacterial isolates with high BAC MICs were more likely to have high MICs of triclosan and be resistant to one or more antibiotics.

The current body of literature is inconclusive regarding the potential for decreased susceptibility to biocides among antibiotic-resistant bacteria or increased antibiotic resistance among bacterial isolates with increased tolerance to QACs and other biocides. In one study, hospital isolates adapted to BAC were found to be less susceptible to other QACs, but not resistant to other biocides or antibiotics.<sup>4</sup> However, other instances of isolates displaying decreased susceptibility to both QACs and antibiotics have been reported.<sup>5,6</sup> Although we observed a significant relationship between high BAC MICs and antibiotic resistance among staphylococcal species at baseline, the relationship was not apparent at the end of the year. Of note, there was a large decrease in the number of methicillin-resistant *Staphylococcus aureus*-positive isolates over the year, limiting statistical power to detect a significant association. Our findings raise concern that the exposure of bacteria to antibacterial-containing products, such as QACs, may exert a selective pressure resulting in the co-selection of genes encoding reduced susceptibility for both biocides and antibiotics. As the potential role of disinfectants and biocides in minimizing the spread of infectious diseases in homes has not been established, concern over potential decreased susceptibility to biocides and resistance to antibiotics is warranted.

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## Transparency declarations

None of the contributing authors has a commercial or other association that might pose a conflict of interest.

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### Failure of particulate bioglass to prevent experimental staphylococcal infection of open tibial fractures

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Sir,

Bioactive glasses are special glass systems that are generally composed of SiO<sub>2</sub>, CaO, P<sub>2</sub>O<sub>5</sub> and Na<sub>2</sub>O.<sup>1</sup> Since their introduction, bioactive glasses have been used to treat a variety of medical conditions including conductive deafness, alveolar ridge resorption and bone loss resulting from periodontal disease, and to fill cystic and surgically created defects.<sup>2</sup> Some of the conditions are eminently prone to microbial infections, such as infected frontal sinuses.<sup>3</sup> Based on these circumstances, Stoor *et al.*,<sup>4</sup> through *in vitro* experiments, first proved that the bioactive glass powder S53P4 had a broad antibacterial effect on microorganisms. Then, Allan *et al.*<sup>5</sup> found that particulate 45S5 Bioglass<sup>®</sup> exerted a considerable antibacterial effect against certain oral bacteria *in vitro*. Thereafter, many other experiments have shown that particulate bioactive glass has a broad and certain antibacterial effect *in vitro*. But whether particulate bioactive glasses have the same antibacterial effect *in vivo* as *in vitro* is still unknown up to now. This study initially investigated the antibacterial effect of particulate Bioglass<sup>®</sup> (grain size

**Table 1.** Infection of the two groups

Group	Negative	Positive	P <sup>a</sup>
Control (n = 10)	4	6	0.35
Bioglass <sup>®</sup> (n = 9)	3	6	

<sup>a</sup>P, probability value; Fisher's exact method.

range from 355 to 500 µm, consisting of 45 wt% SiO<sub>2</sub>/24.5 wt% Na<sub>2</sub>O/24.5 wt% CaO/6 wt% P<sub>2</sub>O<sub>5</sub>) *in vivo* by examining its efficacy in reducing the rate of infection by *Staphylococcus aureus* after the fixation of open tibial fractures in rabbits. An *in vivo* test was carried out with male rabbits split into two groups infected with *S. aureus* ATCC 25923 at the right tibial fracture sites fixed with plates and screws, with 300 mg of particulate Bioglass<sup>®</sup> implanted in the fracture and surrounding area for the Bioglass<sup>®</sup> group, in accordance with the guidelines of the Local Animal Welfare Committee. Six weeks after the operation, the anteroposterior and lateral radiographs of the right tibia were taken and scored, the specimens from the plate and the bone were collected for microbiological evaluation, and the tibias were cut off for histopathological examination and scoring. There was no significant difference between the rates of infection in the control group (60%) and the Bioglass<sup>®</sup> group (66.7%) ( $P = 0.35$ ; Table 1). Similarly, there were no significant differences between the radiographic and histological scores of the control group (4.5 and 2.5, respectively) and the Bioglass<sup>®</sup> group (4 and 3, respectively) ( $P = 0.96$  and  $0.32$ , respectively; Wilcoxon test). It has been suggested that bioglass exerts antibacterial activity by increasing pH, osmotic effects and calcium ion concentrations.<sup>4,5</sup> The failure of Bioglass<sup>®</sup> to prevent infection in this model may reflect the difference between *in vitro* and *in vivo* environments. For example, when bioglass particles are released into local body fluids *in vivo*, the local pH may not change due to the buffering capacity of the fluids.

One possible limitation of the current study is that only a single strain of *S. aureus* was used, and a single body site was investigated. Although the initial results presented here showed no evidence for efficacy of bioglass *in vivo*, scope remains for studies with other strains or species of bacteria and other body sites.

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### Transparency declarations

None to declare.