

computed), in the case of biomedical research involving human beings, it is crucial to satisfy the ethical requirements of ensuring that the *s*-size is strictly related to the aims of the study and therefore appropriately calculated in the most parsimonious way. Finally, absolutely justified approximated procedures generally requiring a smaller *s*-size may be preferred, given the well-known conservative nature of the binomial test and the unsatisfactory coverage of Clopper-Pearson's CI.

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Conflict of interest is not associated with positive conclusions in toothpaste trials: a systematic survey



Letter to the Editor

Conflict of interest (COI) is defined as divergence between individual's private interests and professional obligations—whether professional actions or decisions are motivated by personal gain, such as direct financial relationships, academic advancement, clinical revenue streams, or community standing [1,2]. In a recent review, 70% of randomized controlled trial (RCT) protocols reported a contract on publication rights between industry and academic investigators; and in 86% of these, industry had the authority to disapprove or review articles before journal publication [3]. Many television commercials abound related to dentin hypersensitivity (DH) toothpastes, prompting our interest.

As part of an ongoing systematic review and network meta-analysis of desensitizing toothpaste trials to treat DH (Prospero #CRD42018086815), we considered this potential relationship by examining study characteristics, directionality of conclusions, and industry funding associated with COI. We developed search strategies and conducted electronic searches up to February 2018 in Medline, Embase, Cochrane Reviews, CENTRAL, ProQuest, Clinical Trials, and the WHO International Clinical Trials Registry Platform. Pairs of independent reviewers screened titles/abstracts, selected full texts, and extracted data. We constructed multivariable logistic regression models for COI and positive conclusions. We included the following variables for the COI model: sample size, percentage of females enrolled in the study, year of publication, loss to follow-up, number or intervention arms, time of follow, region, and conclusion. In the model of positive conclusion, we included the same variables, additionally including reported funding.

We included 121 RCTs; the majority (70, 58%) was judged as having COI and reported a positive conclusion (82, 68%). Although the large majority of trials were funded through dental industries (70, 58%) and government (8, 7%), many (43, 36%) were unfunded or did not report funding.

In our multivariable model, studies with COI had larger sample sizes and more females enrolled (Table 1). In addition, similar to other reviews, RCTs with larger samples were less

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Table 1

Multivariable logistic regression models comparing conflict of interest and positive conclusion related to independent variables

Conflict of interest ^a and independent variables	OR _{adj} (95% CI) [†]	P-value
Sample size		
Smaller (≤ 100 participants)		
Larger (> 100 participants)	5.36 (2.03–14.12)	0.001
Percentage of females enrolled in the study		
$\leq 70\%$ were women		
$> 70\%$ were women	3.41 (1.34–8.70)	0.010
Region		
Other ^c		
Asia	1.19 (0.22–6.51)	0.841
Europe	1.28 (0.20–7.90)	0.791
North America	2.36 (0.41–13.52)	0.336
Positive conclusion^b and independent variables		
Funding		
No funding/no reported		
Government	0.38 (0.07–2.22)	0.268
Dental industry	0.51 (0.21–1.23)	0.134
Region		
Other ^c		
Asia	0.89 (0.14–5.75)	0.910
Europe	0.32 (0.05–2.21)	0.247
North America	0.66 (0.09–4.41)	0.665

Hosmer-Lemeshow goodness-of-fit test for the multivariable model for conflict of interest (COI) ($P = 0.598$)[†] and for positive conclusion ($P = 0.995$)^{††}.

^a We judged a study having COI “yes”: when there was a disclosure that the study was sponsored by dental industry, a dental industry provided the toothpastes, or if any author worked for a dental industry; and we judged “no” COI: there was a disclosure reporting that the study did not receive funding, or there was a disclosure reporting funding from either government or university grant.

^b We considered a “positive conclusion”: when the report made a statement favoring treatment over placebo or positive control (fluoride was a positive control) or when it was a noninferiority trial that favored one treatment or “nonpositive conclusion”: when the conclusion stated that treatment and placebo or positive control were similar or when in a noninferiority trial, the treatments were similar or when the conclusion favored the positive control rather than the treatment.

^c Middle East Countries ($n = 4$), Australia ($n = 1$), Chile ($n = 1$), and multicountries ($n = 2$) involved in the study.

likely to be discontinued [4]. We postulate that in studies with COI, there may be more effort to include higher sample sizes to try to reduce the proportion of dropouts. Women have been shown to be more willing to cooperate with dental hygiene protocols and less likely to miss dental appointments compared to men [5,6]. Therefore, including more women could reduce missing data and could reduce dropouts. In our second model, positive conclusion was not affected by any

variable as shown in our multivariable model, which is similar to the results found in other dental subspecialty fields, where the conclusion was not associated to COI or funding [7,8].

The association of sample size and percentage of women with COI would not be considered a methodological problem of the trials; rather, such characteristics may improve the likelihood of sufficient statistical power and the compliance of the intervention. No variable was associated with a positive conclusion in the DH toothpaste trials in our models, suggesting a high level of transparency to their findings. Consumers of DH trial information should feel somewhat confident that study conclusions reflect the current science in this area.

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Improving representation in telephone-based health care access surveys requires purposeful efforts to include prepaid cell phone users



To the Editor

Access to health care and its impact on health status had been at the forefront of American health policy well before the passage of the Affordable Care Act (ACA). Four years after ACA implementation, the American public still rates

health care as a top priority [1]. To better understand the impact ACA has upon access to health care (e.g., insurance, primary care, preventive care, unmet medical needs) and health status, states such as California, Colorado, and Ohio, all of which expanded Medicaid to include persons up to 138% of the federal poverty level (FPL) (\$28,767 in 2018), conduct surveys of residents to estimate uninsured rates, health status, and access and utilization of care [2–4].

To reach populations of interest, most of these surveys implement telephone surveys, for which respondents are selected through the random selection of their telephone number. Research indicates that in the first half of 2017, 52% of all adults, including 75% of young adults (25–34 years) and 70% of adults who rent their home, were cell phone only users [5]. Although adjusting sample frames to increased cell phone use results in an improved demographic distribution of completed interviews, difficulties remain for capturing oversamples of low socioeconomic (SES) and minority populations.

One new aspect for surveying low SES persons and minorities is the large growth in prepaid cell phone plans—estimated at 33% of cell phone users [6]. Prepaid plans fix the number of minutes a cell phone owner can use in a month, resulting in a respondent burden in terms of cell phone minutes used for the survey and cell phone costs—interviewees are often reluctant to use 20 to 30 of their limited plan minutes to take a health survey. Persons on prepaid plans are significantly more likely to be a minority, less than 138% FPL, and to experience household budget stress (Fig. 1)—the type of persons who experience difficulties obtaining health care coverage and who are typically under-represented in telephone surveys. This indicates that contact difficulties with prepaid cell phone users increases the chances of biased survey estimates.

To address the increase of overall cell phone and prepaid phone use, in particular, the 2015 Ohio Medicaid Assessment Survey, a general population survey of Ohio residents, conducted an experiment to test whether using a \$10 respondent incentive would increase the number of prepaid cell phone users in the respondent sample [4]. The study had two critical findings worth noting for future health survey designs. First, persons on prepaid plans are significantly associated with lower access to health care, lower health care utilization, health statuses, and higher rates of health risk behaviors, unmet health care needs, and chronic conditions—this held for working-aged adults and children with or without Medicaid (Fig. 1). Second, the \$10 incentive, because it covers part of the prepaid cell phone user's costs, does increase the proportion of completed interviews for those with a prepaid plan. Therefore, based on our experiment, we determined that increasing the proportion of prepaid cell phone users in the respondent sample will decrease bias in key survey outcomes by increasing the representation of difficult to include populations.

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